ISSN 1029 - 385 X (Print) ISSN 2519 - 7134 (Online)

MEDICAL FORUM MONTHLY

APNS Member | CPNE Member | ABC Certified

RECOGNISED BY PMC & HEC

Journal of all Specialities

"Medical Forum" Monthly Recognised and Index by

- PMDC with Index Pakistan No.48 since 1998
- HEC since 2009
- Pakmedinet Since 2011
- Medlip (CPSP) Since 2000
- PASTIC & PSA Since 2000
- NLP Since 2000
- WHO, Index Medicus (IMEMR) Since 1997
- EXCERPTA MEDICA, Netherlands Since 2000
- EMBASE SCOPUS Database Since 2008
- Registered with International Standard Serial Number of France bearing ISSN 1029-385X (Print), ISSN 2519-7134 (Online) Since 1992
- Registered with Press Registrar Govt. of Pak bearing No.1221-B Copr. Since 2009
- ABC Certification Since 1992
- On Central Media List Since 1995
- Med. Forum Published under Medical Academic Foundation (MAF) from Lahore Since 1989
- Open Access, Peer Review & Online Journal
- Email: med_forum@hotmail.com, medicalforum@gmail.com
- website: www.medforum.pk

Med. Forum, Vol. 32, No.10 October, 2021 ISSN 1029-385-X (Print) ISSN 2519-7134 (Online)

CONTENTS

Editorial

Original Articles

Editorial

Child Abuse Cases in Pakistan – A Serious Concern

Mohsin Masud Jan

Editor

Child abuse is unfortunately a common occurrence in Pakistan. According to a study of NGO, eight children were abused every day in Pakistan while 51% in these girls and 49% boys. Out of reported cases 985 were of sodomy, 787 rape, 89 pronography and 80 murder cases after sexual abuse.

Child abuse cases increases day by day. WHO has identified violence against children as a growing public health issue. Violence against children as a challenge in developing world including Pakistan.

A majority of the child abuse cases in Pakistan go unreported, said child protection experts of Aga Khan University's (AKU) Institute for Educational Development.

Even though Pakistan had a range of laws to protect children, poor implementation of regulations alongside a low conviction rate was causing child abuse to be a persistent problem in society.

Experts also highlighting ways to report child abuse, including dialling 15 to contact police and 1121 to contact the child protection authority.

Globally, seven out of ten cases of child abuse take place at homes, such as residences of victims or offenders.

This figure was likely to be same in Pakistan but cautioned that the underreporting of crimes meant that the statistics from NGOs and the government were likely to underestimate the scale of the problem.

There are many reasons why cases go unreported. These include fear of the perpetrator, concerns about being stigmatised by society, economic dependence, inability to recognise child abuse as being improper, poor awareness of ways to complain and lack of trust in the system.

How neighbourhoods, schools and parents could take steps to reduce the risk of abuse which could happen to children of any race, socioeconomic group, religion or culture.

Lubna Khan from United Kingdom highlighted importance of having a coordinated, multi-agency model that prioritised the children's well-being.

She noted that each school in the UK had designated child protection officers and all the teachers had to take clearance through the government's Disclosure and Barring Service, which screened them for criminal conduct.

She informed that teachers in the UK were regularly trained and the education sector regulator, Ofsted, also assessed the schools' ability to keep the children safe.

Azra Naseem, Director of AKU's Blended and Digital Learning Network, described how a child could be exposed to disturbing content online, be contacted by a stranger on gaming or social network sites, or be a perpetrator themselves if they shared problematic images or content.

She noted that parents, teachers and other stakeholders should have knowledge about the risks of their children accessing the internet and should discuss these issues with their kids.

She also highlighted the importance of dialogue and digital literacy initiatives in protecting children online.

Professor Farid Panjwani, said that the long-term impact of child abuse on society and how Pakistan's response to the challenge could be improved.

Dr. Enam noted the importance of acknowledging the feelings of the victims of abuse and providing them with support. "Make sure to listen to and support your children. Tell them that they did the right thing by telling you and never silence them or tell them to ignore or forget about the problem. With proper support and timely care, good outcomes are possible helping child and adolescent survivors recover."

All the experts noted that in the long term, Pakistan needed to invest in awareness programmes to change social norms that perpetuate a culture of silence.

The focus should be on supporting children and parents, working directly with children to build their knowledge on how and where to seek help and protection, and educating parents, teachers and adults to identity signs of abuse and make sure that children receive care and protection.

Original Article

Knowledge About Dry Socket

The Internship Dentists Knowledge About Dry Socket

Farah Farhan, Faiza Hassan, Muhammad Wajahat Ghafoor, Ayesha Azam, Esha Yousaf and Rameen Mazhar

ABSTRACT

Objective: To assess the knowledge of dry socket among internship dentists, and to reduce the incidence in future.
Study Design: Cross-sectional study
Place and Duration of Study: This study was conducted at the Oral Pathology department, Foundation University college of Dentistry and Hospital, Foundation University Islamabad from March 2021 to June 2021.
Materials and Methods: A quantitative cross-sectional study was conducted on dental internee residents of Rawalpindi & Islamabad. A questionnaire-based Performa was distributed among 200 dental internees. An informed consent was obtained from the participants. Inclusion & exclusion criteria were chalked out and followed. Results were recorded in Microsoft excel sheet and analyzed by SPSS version 20 software.
Results: 74.5% of internees considered traumatic extraction whereas 25.5% considered bacterial infection as a cause of dry socket. 86% of internees agreed that dry socket occurs more frequently in mandible than maxilla.14.5% of participants considered analgesics not to be effective in management whereas 19.5 % of participants lacked in their knowledge regarding analgesics.
Conclusion: Within the confines of our study, the knowledge of our dental internees about alveolar osteitis is acceptable. But we need a proper integration of different subjects to enhance student's knowledge, concepts and their implementation in patient management under the umbrella of a separate Dental education department.
Key Words: Alveolar Osteitis, Oral Contraceptives, Patient management

Citation of article: Farhan F, Hassan F, Ghafoor MW, Azam A, Yousaf F, Mazhar R. The Internship Dentists Knowledge About Dry Socket. Med Forum 2021;32(10):2-6.

INTRODUCTION

Dry socket also known as "Alveolar Osteitis" occurs when the blood clot in the extraction socket fails to develop, dissolves or dislodges before wound healing has occurred[1]. Dry socket is a common complication of tooth extraction[2]. Pain is one of the most important symptom of dry socket[2].

Blum (2002) has described dry socket as "post-op pain in and around the extraction site which increases in severity at any time between 1 and 3 days after the extraction". Dry socket was first described by Crawford in 1896[3]. Occurrence of dry socket is approximately 1% - 5% of all extractions and up to 38% of impacted mandibular 3rd molar extractions[4]. Dry socket more commonly occurs in mandibular molar region because of high bone density and less vascularity of the mandible.

Department of Oral Pathology, Foundation University college of Dentistry and Hospital, Foundation University Islamabad.

Correspondence: Dr. Muhammad Wajahat Ghafoor, Senior Lecturer of Oral Pathology, Foundation University college of Dentistry and Hospital, Foundation University Islamabad.
Contact No: 03215296982
Email: wajahatghafoor@ymail.com

Received: July, 2021
Accepted: August, 2021
Printed: October, 2021

The pathogenesis of dry socket is associated with the increased fibrinolytic activity that results in disintegration of the blood clot[5]. Many factors are associated with the breakdown of blood clot. One of these is the presence of higher pre- and post-operative microbial counts particularly anaerobic bacteria seen in patients with poor oral hygiene and presence of pre-extraction periapical infection, pericoronitis or periodontitis[6].

Traumatic extractions are also a major causative factor. Birn (1973) proposed that there is an increased localized inflammation due to trauma during extraction. This leads to release of tissue activators which increase the levels of plasmin leading to increase in fibrinolytic activity[7].

Tobacco smoking is also a predisposing factor to dry socket due to increased vasoconstrictive activity of nicotine[5]. Alveolar osteitis is more commonly seen in females than males due to the possible hormonal cause. Females using oral contraceptives are more commonly affected due to the increased fibrinolytic activity of estrogen present in oral contraceptives. Other factors that increase the risk of dry socket are inadequate irrigation following extraction that does not effectively decontaminate the extraction socket by bacteria and local anesthesia with vasoconstrictors that causes temporary local ischemia[8,9].

Following extraction of a tooth patient does not immediately develop signs and symptoms of dry socket. Patient usually reports after 24 hours with severe,

throbbing pain which becomes more severe over time and can radiate to ear. Accumulation of food particles or mechanical stimulation of the exposed bone by the tongue results in acute pain[4]. The pain increases in intensity till 3-4 post op days. It is usually associated with foul taste and halitosis. Clinically, whitish bone is visible in the socket instead of the dark blood clot. Socket is filled with saliva and debris. The mucosa around the socket is red and tender. There are no visible signs of infection i.e. suppuration, fever or swelling[9].

Pre-operatively, patient should be asked about any previous history of dry socket as some patients are more susceptible to develop this post-extraction complication. The most common predisposing factors for developing dry socket are patient's age, history of previous infection & difficult or traumatic extraction[10]. It is reported that 0.12% chlorhexidine rinse prior to extraction and one week post-extraction prevents the occurrence of dry socket[3]. Extractions should be carried out with minimal trauma to prevent damage to bone. Following extraction, socket edges should be squeezed together for a few minutes to assist clot formation[9]. Topical placement of anti-fibrinolytic agents in the extraction site may also contribute in reduced incidence of dry socket[11].

Post-operatively the use of straws that produces suction movement of cheek muscles should be avoided as this may dislodge the blood clot. Patient should avoid spitting forcefully till 2-3 post op days. Avoid smoking and tobacco for at least 48 hours following extraction and when resumed, inhale very gently. Maintenance of adequate oral hygiene to prevent breaking down of the blood clot from germs and infection also prevents the occurrence of dry socket.

Management of dry socket can range from simple irrigation to surgical intervention and dressing placement[12]. Food particles and bacteria in the socket are irrigated with normal saline. After irrigation a medicated dressing that contains eugenol and a topical anesthetic is placed in the socket that provides immediate relief from pain, usually within 5 minutes. Depending on the severity of pain, dressing is changed every alternate day for the next 3-5 days. Post-operatively analgesics are prescribed such as NSAIDs, e.g. Ibuprofen or a mixture of narcotic with acetaminophen in case of severe pain[13]. Patient is advised warm saline rinses and maintenance of oral hygiene to promote healing of the socket[14].

To prevent the occurrence of dry socket in susceptible patients, primary closure of the socket is advised to enhance healing by primary intention[12].

The basic treatment of dry socket is to irrigate bacterial material, debris & food particles out of the socket and subsequently filling the socket with a medicament having obtundent properties[4].

The objective in treating a dry socket is to optimize the lesion in such a way that the socket is capable of forming a layer of epithelium that covers the exposed bone and contributes in healing of the socket[4].

MATERIALS AND METHODS

The current study was conducted on dental internees residents of Twin cities Rawalpindi & Islamabad from March 2021 – June 2021. Ethical approval was obtained from Ethical Approval Committee FUMC, FUI Islamabad. A questionnaire-based Performa was distributed among 200 dental internees targeting dental institutes of Rawalpindi & Islamabad. An informed consent was obtained from the participants & confidentiality of information collected was taken care of. Internees in FUCD, MIHS, IMDC, IIDC and AFID were included in this study.

Inclusion & exclusion criteria is as follows:

- Dental internees, living in Rawalpindi and Islamabad were eligible for this study.
- Post Graduate trainees were not included.

Results were recorded in Microsoft excel sheet and analyzed by SPSS version 20 software.

RESULTS

This was a descriptive type of study which included dental internees from various colleges of Rawalpindi & Islamabad. Data was collected from 200 dental internees. 81.5% of the participants were females and 18.5% were males. All of the participants were aware of alveolar osteitis. 92% of the internees agreed with the fact that pain in dry socket increases in severity usually at 3rd post-operative day. 98% of the internees were in favor of the opinion that dry socket is caused by disintegration of the blood clot within the extraction socket. 95.5% of the participants considered whitish bone whereas 4.5% considered blood clot as content of dry socket. Halitosis was considered as a common finding of dry socket by 90% of the participants. Lack of compliance in following post-operative instructions and smoking tobacco was also considered as a contributing factor for dry socket by 96% of internees.

74.5% of internees considered traumatic extraction whereas 25.5% considered bacterial infection as a cause of dry socket. 86% of internees agreed that dry socket occur more frequently in mandible than maxilla whereas 10% of the participants were unsure about their answer. 73.5% agreed that females are more susceptible in developing a dry socket but 22% of the participants were unclear in their answer. 80% of participants considered that vasoconstrictors increase the risk of developing a dry socket, 8% disagreed and 12% were not sure about the effect of vasoconstrictors on dry socket. 70% of the participants agreed that chlorhexidine if used as a pre-operative irrigant reduces the risk of dry socket, 13.5% considered it as a risk factor in developing dry socket and 16.5% of the

participants didn't have significant knowledge regarding use of chlorhexidine.

Effect of use of oral contraceptives and antibiotics on the incidence of dry socket is presented in Figure 1 & Table 1 respectively.

Regarding management 91.5% considered zinc oxide and eugenol dressing an effective remedy for dry socket & 66% of participants considered the use of analgesics that can range from NSAIDs to narcotics to be effective.14.5% of participants considered analgesics not to be effective in management whereas 19.5 % of participants lacked in their knowledge regarding analgesics.

Table No.1: Erythromycin and metronidazole are effective in prevention of dry socket

	Frequency	Percentage
Agree	55	27.5
Disagree	62	31
Unclear	83	41.5

Dry socket occurred three times less frequently in females on oral contraceptives than in those who are not taking them

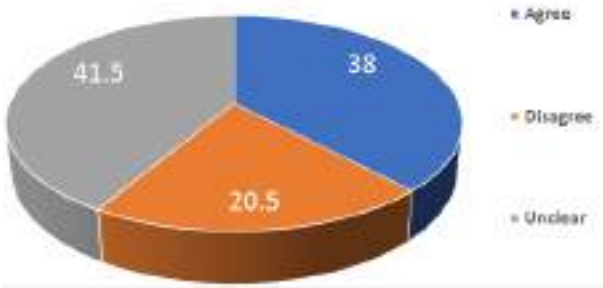


Figure No.1: Effect of use of oral contraceptives and antibiotics on the incidence of dry socket is presented in.

DISCUSSION

Dry socket also known as 'Alveolar osteitis' is the most common sequelae of extraction of teeth leading to discomfort and pain for the patients and also a constant source of annoyance for the dentists.

In our study most of the internees agreed to the fact that dry socket is caused by disintegration of the blood clot within the extraction socket due to the fibrinolysis activity leading to clot dissolution, this is also depicted in[15,16].

Another finding in our study that relates to other studies is that dry socket is complemented with a whitish bony socket[3], halitosis is an important finding of dry socket agreed on by most of our participants which narrates to studies[10].

Another important fact that is addressed by various authors in literature is the role of atraumatic extraction technique as it may hinder wound and socket healing later on. In our study most of the participants emphasized on this fact and it is also stressed upon in literature[17].

In relation to anatomical socket the prevalence of dry socket is more in lower jaw as compared to upper jaw reason being dense bone, reduced blood supply and decreased granulation tissue formation in mandible and was agreeable to most of our participants which falls in accordance to literature[15,16].

Yogesh Losch et al. proposed in their literature that dry socket is more common in females than males[18]. In another study of AlHindi M, the results showed that out of 7 patients having dry socket, female to male ratio was 6:1[19]. Our study also shows similar results.

As stated by John Mamoun and other researchers that smoking and use of oral contraceptives contribute in the occurrence of dry socket as they both reduce blood circulation in the extraction socket[4,6,20].

In a study conducted on dental internees in Al Farabi dental college KSA, 94.8 % of the participants agreed with the statement that risk of dry socket is significantly higher in smokers as compared to non-smokers[3]. Similarly, in the current study 96% of internees consider smoking as a major risk factor of dry socket lesions.

Rahul Sharma et al. in their research article stated that estrogen levels are raised due to oral contraceptives[21]. Increased fibrinolytic activity of estrogen as described by AlHindi M[19] contributes in occurrence of dry socket[21]. In the present study only 20.5% of the internees agree with this correct information that dry socket occurs more frequently in females on oral contraceptives[6,18,20,22]. Another study done by Mazen Doumani et al shows similar results[3]. Hence, dental internees are lacking in their knowledge regarding use of oral contraceptives and their effect on healing of extraction socket.

In the current study the use of vasoconstrictors is considered to significantly increase the risk of dry socket. Similar results are found in the study of Rahul Sharma et al[21]. However the study of Mazen Doumani et al. shows that the internees are not well aware of vasoconstrictor use[3].

Another finding in our study that correlates with other studies is that Chlorhexidine when used pre-operatively reduces the risk of dry socket[3,23,24].

In our study very few internees agreed with the statement that antibiotics e.g. erythromycin, metronidazole etc. are effective in prevention of dry socket, this result is also consistent with another local study[24,25]. However in a study conducted by Mazen Doumani et al. many internship dentists considered role of antibiotics crucial in prevention of dry socket[3]. Another international study shows same results[22].

In our study, almost all the participants considered zinc oxide eugenol dressing effective in management of dry socket lesions due to its anti-bacterial and obtundent properties, this result is also established in literature[3.22.24].

As dry socket is a painful condition, analgesics play a very important role in its management. Results of our study agreed with the significance of use of analgesics and this result is also consistent with other studies[3].

CONCLUSION

Within the confines of our study, the knowledge of our dental internees about alveolar osteitis is acceptable, except for a few points. The reason being lack of integration of different subjects during under graduate education in dental institutes, resulting in poor translation of knowledge and execution in clinical practice. So, we need a proper integration of different subjects to enhance students' knowledge, concepts and their implementation in patient management under the umbrella of a separate Dental education department.

Author's Contribution:

Concept & Design of Study:	Farah Farhan
Drafting:	Faiza Hassan, Muhammad Wajahat Ghafoor
Data Analysis:	Ayesha Azam, Esha Yousaf, Rameen Mazhar
Revisiting Critically:	Farah Farhan, Faiza Hassan
Final Approval of version:	Farah Farhan

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Cawson RA, Odell EW. Cawson's Essentials of Oral Pathology and Oral Medicine E-Book: Arabic Bilingual Edition: Elsevier Health Sciences; 2014.
2. Khalifah M. Curettage versus Zinc Oxide Eugenol as a Treatment Modality in Patients with Dry Socket. Egyptian Dent J 2021;67(1-January (Oral Surgery)):235-9.
3. Doumani M, Habib A, Doumani A, Alhameed A, Alshami B, Alhababi A, et al. The intership dentist's knowledge about dry socket. Int J Recent Scientific Res 2017;8:19941-3.
4. Mamoun J. Dry socket etiology, diagnosis, and clinical treatment techniques. J Korean Assoc Oral Maxillofacial Surgeons 2018;44(2):52-8.
5. Mudali V, Mahomed O. Incidence and predisposing factors for dry socket following extraction of permanent teeth at a regional hospital in Kwa-Zulu Natal. South African Dental J 2016;71(4):166-9.
6. Sharma S. Assessment of risk factors associated with dry socket-A clinical study. J Advanced Medical and Dental Sciences Res 2021;9(3):85-8.
7. Nejat A, Eshghpour M, Danaeifar N, Abrishami M, Vahdatinia F, Fekrazad R. Effect of Photobiomodulation on the Incidence of Alveolar Osteitis and Postoperative Pain following Mandibular Third Molar Surgery: A Double-Blind Randomized Clinical Trial. Photochemistry and photobiol 2021.
8. Bowe DDC. The management of dry socket alveolar Osteitis 2011.
9. Odell EW. Cawson's essentials of oral pathology and oral medicine e-book: Elsevier Health Sciences; 2017.
10. Taberner-Vallverdú M, Sánchez-Garcés MÁ, Gay-Escoda C. Efficacy of different methods used for dry socket prevention and risk factor analysis: A systematic review. Medicina oral, patologia Oraly Cirugia Bucal 2017;22(6):e750.
11. Younis MHA, Ra'ed O. Dry socket: frequency, clinical picture, and risk factors in a palestinian dental teaching center. Open Dentistry J 2011;5:7.
12. Sheikh MA, Kiyani A. Pathogenesis and management of dry socket (alveolar osteitis). Pak Oral Dental J 2010;30(2).
13. Chemaly D. How do I manage a patient with dry socket? J (Canadian Dental Association) 2013; 79:d54-d.
14. Pavel F, Machado L. Contemporary oral and maxillofacial surgery. Journal of the California Dental Association. 1994;22(4):35-8, 40, 2.
15. Khan AH. Prevalence and association of dry socket in oral health and dental management. OHDM 2017;16(4):1-6.
16. Mudali V, Mahomed O. Incidence and predisposing factors for dry socket following extraction of permanent teeth at a regional hospital in Kwa-Zulu Natal. South African Dental J 2016;71:166-9.
17. Alwraikat AA. Alveolar osteitis: incidence and risk factors following third molar surgery in Jordan. Pak Oral Dent J 2009;29(1):19-22.
18. Chakravarthi S. Platelet rich fibrin in the management of established dry socket. J Korean Assoc Oral Maxillofacial Surgeons 2017;43(3): 160-5.
19. AlHindi M. Dry socket following teeth extraction: effect of excessive socket saline irrigation. J Oral Health Dent Sci 2017;1(1):2-5.

20. Suri N, Dutta A, Siddiqui N, Kaur K, Jangra D. A literature review on dry socket. IP Int J Maxillofacial Imaging 2021;6(4):97-100.
21. Sharma R, Joshi S, Arora S, Kapadia J, Latif AAA, Khilji I. Assessment of risk factors of dry socket after tooth extraction. J Advanced Med Dental Sciences Res 2021;9(1).
22. Kumar N. Dry Socket Etiopathogenesis, Management and Prevention: A Brief Systematic Review of Literature. Eur J Molecular Clin Med 2020;7(9):24-9.
23. Halabi D, Escobar J, Alvarado C, Martinez N, Muñoz C. Chlorhexidine for prevention of alveolar osteitis: a randomised clinical trial. J Applied Oral Sci 2018;26.
24. Muravev NV, Diachkova EY, Larionova EV, Tarasenko SV. Medicinal Methods for Prevention And Treatment of Alveolar Osteitis. Annals of Dental Specialty 2021;9(1):16.
25. Khooharo TS, Hassan SU, Shaikh AH. Prevention of dry socket in mandibular 3rd molars with single preoperative oral dose of metronidazole and amoxicillin compared to conventional therapy. JPMA J Pak Med Assoc 2021;71(2 (B)):585-9.

Original Article

Eclampsia in Pregnant Women

Impact of Seasonal Variation on the Frequency of Eclampsia in Pregnant Women Having Gestational Amenorrhea More Than Twenty Weeks

Romana Ramzan[1], Afshan Sultana[3], Sajida Yousfani[1], Najma Bano Shaikh[1], Nisa Mohsin[3] and Muhammad Nadeem Chohan[2]

ABSTRACT

Objective: To assess the impact of seasonal variation on the frequency of eclampsia in pregnant women having gestational amenorrhea more than 20 weeks.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Obstetrics and Gynecology Department LUMHS Jamshoro from 28th October 2016 to 28th October 2017.

Materials and Methods: A total of 130 primigravida pregnant women, >20 weeks of gestational age were included in this study. Diagnosis of eclampsia was made by consultant obstetrician and the patient was managed by her under her direct supervision. Frequencies of eclampsia in pregnant women were noted in various seasons like summer, autumn, winter and spring.

Results:-Women average age was 24.98±2.56 years. Frequency of eclampsia in the pregnant women having gestational amenorrhea was observed in 2.23% (130/5831) women. Incidence of eclampsia was 26.15% (34/5831) in spring season, 23.08% (38/5831) in summer season and 16.92% (22/5831) in autumn season, 33.8% (44/5831) in winter season but statistically there was no significant difference among different seasons (p=0.499). Similarly incidence of eclampsia was also not significant between monsoon and dry season (4% vs. 3.8%, p= 0.96).

Conclusion: The results of current study revealed no significant impact of seasonal changes on eclampsia. As eclampsia is very common in pregnant women, efforts should be taken to understand its aetiologies as possible prevention may reduce the patient burden and feto maternal morbidity/mortality.

Key Words: Eclampsia, gestational amenorrhea, seasonal variation, winter, summer

Citation of article: Ramzan R, Sultana A, Yousfani S, Shaikh NB, Mohsin N, Chohan MN. Impact of Seasonal Variation on the Frequency of Eclampsia in Pregnant Women Having Gestational Amenorrhea More Than Twenty Weeks. Med Forum 2021;32(10):7-10.

INTRODUCTION

Eclampsia is a complication of severe preeclampsia, it is defined as new onset seizures/coma and clinical features of preeclampsia during pregnancy or postpartum period. It occurs after the 20th week of gestation or in the postpartum period[1]. About 80% of eclamptic seizures occur during intrapartum period or within the first 48 hours of delivery. Rarely it may occur before 20 weeks' of gestation. Some times eclampsia may occur without hypertension[2]. The incidence of hypertension in pregnancy is about 10% and half of the cases are due to Eclampsia and preeclampsia[3].

Eclampcia can increase the maternal morbidity/ mortality and it is associated with neonatal problems like prematurity, perinatal death, placental abruption and intrauterine growth restriction.[4] Worldwide the incidence of preeclampsia/eclampsia is 2-8%.[5] In Pakistan 34% of maternal death occur due to eclampcia[6].

Previous studies from tropical areas shows increased incidence of eclampcia in winter and monsoon season comparing the summer and dry season.[7] According to various literature evidence, there is protective effect of dehydration on seizures that's why in summer season seizures are less evident while overhydration and hyponatraemia are associate with seizures. In winter season vasospasm and release of vasoactive substances can be a proposed mechanism for hypertension[8]. Plasma volume change in various seasons can be a risk factor for preeclampsia[9].

[1.] Department of Obstet and Gynea / Pediatrics[2], Liaquat University of Medical and Health Sciences Jamshoro.
[3.] Department of Obstet and Gynea, Isra Medical University Hyderabad.

Correspondence: Muhammad Nadeem Chohan, Assistant Professor Pediatrics, LUMHS Jamshoro.
Contact No: 03340397861
Email: nadeem.chohan@lumhs.edu.pk

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

A local study from Peshawar showed that the Frequency of eclampsia in pregnant women was more common during winter season (34.25%) and least common during autumn (17.59%)[17]. This study was conducted at a region of Sindh Province, which has total different climate and contains all 5 seasons like winter, summer, autumn, spring and Moon Soon Season. This region have specific seasons that is in winter season there is no severe coldness and in summer season temperature is between 40 and 42 degree Celsius, that is totally different from the rest of other regions in Pakistan. . This study will make a base to compare the effects of various seasons in Pakistan on eclampsia in pregnant women. Our hospital is a tertiary care teaching hospital, we deal lot of eclamptic women throughout the year, so we planned this study to assess the impact of season on eclampcia in pregnant women having gestational amenorrhea more than 20 weeks.

MATERIALS AND METHODS

Eclampsia is defined as Systolic Blood pressure >140 or Diastolic Blood Pressure >90 mmHg on two separate occasions with 24 hours urinary proteinuria >300 mg along with seizures in Pregnant women. Sindh is in the temperate zone (between tropics and Polar Regions) having dry climate. Winter: Cool and dry season (December to February). Spring: Hot and dry season (March to May). Summer: Hot season (June to September), humidity season (July/August) Autumn: Cooler humid season (October to November).

This cross sectional study was done Obstetrics and Gynecology Department, with Non Probability consecutive sampling from 28th October 2016 to 28th October 2017 (total 1 year duration). Sample size is calculated by taking prevalence (p) of eclampsia 19% (1), margin of error 5%, confidence interval 95%. The sample size comes out to be at least n=130 patients of eclampsia. It included all pregnant women having gestational age more than 20 weeks. All Booked or un-booked patients of age 18 to 30 years and primigravida after 20 weeks of gestation was included in this study. Patients having history of eclampsia in previous pregnancies, eclampsia in other family members, fits, diabetes, hypertension, renal disorders, drug addiction, Multi-fetal pregnancy or smoking during pregnancy were excluded from the study.

Permission of ethical review committee was taken. Informed consent was taken from the attendant of the patient who fulfilled the selection criteria. A predesigned Performa was used for documenting, socio-demographics, personal history, medical history, obstetrical history, environmental temperature, humidity level and season of presentation. Physical examination and other routine investigations were performed according to standard protocol. Diagnosis of eclampsia was made by consultant obstetrician and the patient was managed by her or under her direct supervision.

Statistical analysis was performed by using statistical packages for social science version 22). Means with standard deviations were calculated for quantitative variables like maternal age, weight, Body Mass Index (BMI), gestational age, parity, Systolic and diastolic blood Pressure and Hemoglobin, environmental temperature, humidity level. Frequencies with proportions were calculated for qualitative variables like number of eclamtics (Seasonal variation), anemia, education, economic status. Chi square test was applied to obtain P-value. Level of significance was up to 0.05. Stratification was done for age, education, economic and BMI to determine their effect on outcome eclampsia and seasonal variation (spring, autumn, summer, winter). Post stratification chi-square test was applied.

RESULTS

Table No.1: Various characteristics of women (N=130)

Characteristics	n	%
Age Distribution Of The Women		
<= 20 years	7	5.38
21 – 25 years	75	57.69
26 – 30 years	48	36.92
Education Status Of The Women		
Illiterate	10	7.69
Below Matric	34	26.15
Matric	45	34.62
Intermediate	30	23.08
Graduate / Post graduate	11	8.46
Economic Status Of The Women		
> 25,000	36	27.69
10,000 – 25,000	94	72.31
Frequency of Eclampsia with Seasonal Variation in the Pregnant Women Having Gestational Amenorrhea		
Autumn	22	16.69
Spring	34	26.15
Summer	30	23.08
Winter	44	33.85

Table No.2: Descriptive Statistics of Characteristics of Study Patients

Variables	Mean	SD
Age (Years)	24.98	2.56
Weight (kg)	72.68	10.43
Height (cm)	157.26	5.89
BMI (kg/m^2)	29.42	4.15
Gestational Age (weeks)	29.86	4.66
SBP (mmHg)	127.00	8.41
DBP (mmHg)	78.13	5.20
SBP 2nd time (mmHg)	125.9	7.10

DBP 2nd time (mmHg)	82.92	7.14
Heart Beat (beat/min)	12.28	1.30
Environment Temperature	24.09	8.43
Humidity	79.49	12.19

A total of 5831 deliveries were recorded during the study period, of which 130 patients developed eclampsia (2.23%). Most of the pregnant women were between 21 to 25 years of age as shown in table 1. The average age of the women was 24.98±2.56 years. Other characteristics of the women and average environmental temperature and humidity are also presented in table 1. Education status of the patients was also observed and shown in bar table 1. Family income status of 94(72.31%) women were 10, 000 to 25,000 in rupees and 36(27.69%) were above Rs. 25,000 as shown in table 1.

Frequency of eclampsia with seasonal variation in the pregnant women having gestational amenorrhea is shown in table 1. Eclampsia was 23.08% in summer season, 26.15% in spring, 16.92% autumn and 33.85% in winter season. Stratification analyses were also performed and observe that rate of eclampsia with seasonal variation was not significant with respect to different age groups (p=0.18) as shown in tale 1. It was also not significant with respect to education status of the patients, economic status and BMI of the patients as shown in table 2 and 3.

Table No.3: Frequency of eclampsia with seasonal variation in the pregnant women having gestational amenorrhea

Eclampsia with seasonal variation	Winter	Spring	Summer	Autumn	P-Value	Chi-Square	df
AGE DISTRIBUTION OF THE WOMEN							
<= 20 years	2 (71.4%)	0(0%)	0(0%)	2(28.6%)	0.18	8.806	6
21 – 25 years	22(29.3%)	2(26.7%)	21(16%)	12(16%)			
26 – 30 years	17(35.4%)	14(29.2%)	9(18.8%)	8(16.7%)			
EDUCATION STATUS OF THE WOMEN							
Illiterate	5(50%)	2(20%)	1(10%)	2(20%)	0.28	0.28	8
Below Matric	11(32.4%)	7(20.6%)	10(29.4%)	5(17.6%)			
Matric	20(44.4%)	11(24.4%)	9(20%)	5(11.1%)			
Intermediate	8(26.7%)	11(36.7%)	6(20%)	5(16.7%)			
Graduate and Above	0(0%)	3(27.3%)	4(36.4%)	4(36.4%)			
ECONOMIC STATUS							
≤ 25,000 Rs.	31(33%)	25(26.6%)	22(23.4%)	16(17%)	0.99		
> 25,000 Rs	13(36.1%)	9(25%)	8(22.2%)	6(16.7%)			
BMI							
≤ 25	10(43.5%)	3(13%)	3(13%)	7(30.4%)	0.125	9.98	
25.1 to 30	17(28.8%)	21(35.6%)	13(22%)	8(13.6%)			
>30	17(35.4%)	10(20.8%)	14(29.2%)	7(14.6%)			

DISCUSSION

In our study frequency of eclampsia with seasonal variation in the pregnant women having gestational amenorrhea was 33.85% in summer season, 26.15% in spring, 23.85% autumn and 16.15% in winter season. The difference between various seasons is not statistically significant. However, it should be considered that this study was performed in a region where temperate meteorological condition were present and various climatic conditions were lacking. It may be due to lack of significant difference in respect of temperature or humidity among seasons in this area. For example, spring and summer are slightly similar, and autumn and winter are slightly similar. In a study by Janani F, et al results were different from our study showing preeclampsia was highest among women with deliveries in summer while it was lowest among women with deliveries in winter ($P < 0.001$).[10] Bibi H, et al conducted a study at Abottabad, they found 132 (1.04%) incidence of eclampsia. The results were different from our study, in winter and spring season (November to April) there were 80 (1.33%) cases and in summer and autumn season (May to September) 52(0.79%) cases (p value 0.0474)[11]. The difference in result may be due to extreme of cold in Abottabad as compared to our study area (Hyderabad). Soroori ZZ, at al from Iran found similar results like us, they revealed in their study that incidence of eclampsia was 3.3%). It was more in spring (3.6%), and lower in summer season (3%), but the results were not statistically significant[12]. In a local study Halimi S, at al found 108 (0.46%) cases of eclampsia during study period. There were more cases in winter (34.25%), 17.59% in autumn, 21.29% in summers and 26.85% in spring[13]. Nanbakhsh F, at al found in their study that month and season of conception had no significant corelation with preeclampsia. Although it increased from April to August and then it decreased until March but the results were not statically significant (p=0.243). In another study, conception in the summer had more eclampsia as compared to conception in autumn and winter season

with statically significant results (p<0.04). Conceptions in warm seasons (spring and summer) had more eclampsia comparing the conception in cold seasons (autumn and winter) (p=0.038) [14].

In a study by Shahgheibi S, at al mean age of eclamptic women was 30.5 ± 6.60 years. In winter season preeclampsia was present in 30% women. Relation between the season of conception and the month of preeclampsia was not significant (P = 0.67)[15]. In a study from Rwanda overall prevalence of eclampsia was 0.3%. Two thirds of patients presenting with PEC/EC were admitted during the rainy season (OR 1.36, p=0.002). Season at conception did not affect the prevalence of PEC/EC at admission. There was no difference in the severity of the disease based on seasonality[16].

Our results were not similar to a local study from Peshawar that showed that most common season for eclampsia in pregnant women was winter (34.25%), this difference may be due to more poor socioeconomic status and multigravida women in their study[17].

CONCLUSION

The results of current study revealed no significant impact of seasonal changes on eclampsia. As eclampsia is very common in pregnant women, efforts should be taken to understand its aetiologies as possible prevention may reduce the patient burden and feto maternal morbidity/mortality.

Author's Contribution:

Concept & Design of Study:	Romana Ramzan
Drafting:	Afshan Sultana, Sajida Yousfani
Data Analysis:	Najma Bano Shaikh, Nisa Mohsin, Muhammad Nadeem Chohan
Revisiting Critically:	Romana Ramzan, Afshan Sultana
Final Approval of version:	Romana Ramzan

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Warrington JP. Placental ischemia increases seizure susceptibility and cerebrospinal fluid cytokines. Physiol Rep 2015;3(11):
2. Douglas KA, Redman CW. Eclampsia in the United Kingdom. BMJ 1994;309 (6966):1395-400.
3. Craici I, Wagner S, Garovic VD. Preeclampsia and future cardiovascular risk: formal risk factor or failed stress test? Ther Adv Cardiovasc Dis 2008; 2(4):249-59.
4. Zeisler H, Llurba E, Chantraine F, Vatish M, Staff AC, Sennström M, et al. Predictive value of the Flt-1: PlGF ratio in women with suspected preeclampsia. New EJ Med 2016; 374 (1):13-22.
5. Salam RA, Das JK, Ali A, Bhaumik S, Lassi ZS. Diagnosis and management of preeclampsia in community settings in low and middle-income countries. J Family Med Prim Care 2015;4(4):501.
6. Khowaja AR, Qureshi RN, Sheikh S, Zaidi S, Salam R, Sawchuck D, et al. Community's perceptions of pre-eclampsia and eclampsia in Sindh Pakistan: a qualitative study. Reprod Health 2016;13(1):36.
7. Ishrat S. Seasonal variation in eclampsia: is it temperature or humidity? Intel J of Multidis-ciplinary Res Rev 2015;1(1):25-29.
8. Ghosh U, Deb D, Mondal SK, Das AK. Seasonal variation in the occurrence of eclampsia: a three year retrospective cohort study in a tertiary centre in eastern India. J Evol Med Dent Sci 2013;2(44): 8629-8637.
9. Shahgheibi S, Rezaie M, Kamangar TM, Zarea S, Yousefi SR. The Effect of Season on the Prevalence of Preeclampsia. J Clin Gynecol Obstet 2016;5(3):81-4.
10. Janani F, Changaee F. Seasonal variation in the prevalence of preeclampsia. J Family Med Prim Care 2017;6:766-9.
11. Bibi H, Noor S, Hammad M. seasonal variation in the incidence of preeclamcia and eclampcia among the patients presenting in the catchment area of Ayub Medical Teaching Hospital Abbottabad KJMS 2018;11(3):353-56.
12. Soroori ZZ, Sharami SH, Faraji R. Seasonal variation of the onset of preeclampsia and eclampsia. JRMS 2007; 12(4): 198-202
13. Halimi S, Halimi SMA. Eclampsia and its association with external factors. J Ayub Med Coll Abbottabad 2010;22(3):110-12
14. Nanbakhsh F, Broomand F, Mohaddesi H, Nefoozi S, Mazloomi P. Seasonal variation in the incidence of preeclampsia based on the time of conception. Life Sci J 2012;9(4):1310-1314] (ISSN: 1097-8135). http://www.lifesciencesite.com.
15. Shahgheibia S, Rezaiea M, Kamangarb TM, Zareaa S, Yousefia SR. The Effect of Season on the Prevalence of Preeclampsia. J Clin Gynecol Obstet 2016; 5(3):81-84.
16. Leon M, Lisa BM, Jacqueline SM, Diomede N Rulisa, Stephen, et al. Seasonal Variation in the Incidence of Preeclampsia and Eclampsia in Kigali, Rwanda. Obstet Gynecol 2019; 133: 178S.
17. Halimi S, Halimi SM. Eclampsia and its association with external factors. J Ayub Med Coll Abbottabad 2010; 22(3):110-2.

Original Article

Assessment of Drug Compliance Among Diabetic Patients

Drug Compliance Among Diabetic

Muhammad Abas Khan

ABSTRACT

Objective: Assessment of compliance in diabetic patients to anti-diabetic medications.
Study Design: Descriptive study
Place and Duration of Study: This study was conducted at the Medical Department, Lady Reading Hospital, Peshawar from March 2021 to August 2021.
Materials and Methods: The study was done on 196 diabetic patients of both genders with age above 18 years. All patients with diabetes taking antidiabetic medications were involved. Clinical and demographic details were noted about diabetes duration, name, number and dose of medicine taken and existence of comorbid condition noticed. For data entry and statistical analysis SPSS version 21.0 was used. Chi-square test at p value ≤0.05 at 95% confidence level was considered significant statistically.
Results: Amongst 196 patients, 50 (25.5%) were male and 146 (74.49%) were female. Age of the patients age was ranging from 18 to 93(55.99 ±10.31) years; 120 (61.2%) were in 40-60 age group and 60 (30.6%) were over 60 years. Compliance was not good in 110 (56.12%) patients and compliance was good in 86 (43.88%) patients; 68 (34.7%) had taken DPP4 inhibitors while 70(35.7%) were on drug combination; compliance was Good in those on beguindes and combinations (p=0.001).
Conclusion: Most of the patients in our study had poor compliance to anti-diabetic medicine.

Key Words: Drug Compliance, diabetes, Anti-diabetic medications, Comorbidities.

Citation of article: Khan MA. Assessment of Drug Compliance Among Diabetic Patients. Med Forum 2021;32(10):11-15.

INTRODUCTION

Diabetes mellitus is the rapidly growing health issue globally. International Diabetes Federation (IDF) has declared that there were 415 million people with diabetes in 2015, with a estimated 642 million by 2040[1].Diabetes is not only a disease of the elderly as about 50% of the patients are aged between 40 and 59 years[2].The Low income countries are faced with growing burden of diabetes and nutritional diseases [3].In a recent study frequency of diabetes in Cameroon is 5.8% [4], and studies from the Global Burden of Disease (GBD) 2016 study showed that diabetes mellitus is reason for about 132,000 disability adjusted life years (DALY) and about 4000 deaths in Cameroon [5].so this shows that the load of diabetes on is huge in terms of morbidity as well as mortality[6]. Diabetes management includes change in lifestyle and antidiabetic drugs[7].

Department of Medicine, Muhammad Teaching Hospital, Peshawar KPK.

Correspondence: Dr. Muhammad Abas Khan, Senior Registrar, Department of Medicine, Muhammad Teaching Hospital, Peshawar KPK.
Contact No: 0307-0096727
Email: drabbaskhan83@gmail.com

Received: September, 2021
Accepted: September, 2021
Printed: October, 2021

Noncompliance to treatment is a chief hurdle in treatment of diabetes. The struggle done to enhance patients compliance of to treatment are not useful usually[8]. Vrijens et al defined compliance as the limit to which patient follows the recommendations for treatment prescribed[9]. Non compliance includes not beginning the treatment, pharmacy prescription is not filled, taking the dose wrongly, or stopping the treatment early[8,9]. The technique of compliance assessment to medication includes electronic monitoring method, counting the pills, caregiver and patients reports[10]. A study in the UAE hospital revealed a frequency of compliance to antidiabetic drugs as 84%[11], whilest studies in Uganda and Ethiopia disclosed frequency of 83.3% and 85.1 respectively[12,13]. On other hand studies in Botswana and Switzerland showed lower frequency of 52%and 40 respectively[14,15]. Factors related to non compliance to antidiabetic medication include poverty, young age, forgetting the drugs, education level, diabetic complications and difficulty in taking medication alone[11,14,16,17]. Non-compliance for antidiabetic drugs results in high healthcare cost for country, higher morbidity and death[18–20]. Despite of high number of studies on non-adherence to antidiabetic medications, there is scarce information in diabetic patients in pakistan.so the aim of our study is to firm the frequency and recognise factors related with non-compliance to antidiabetic drugs in type 2 diabetes mellitus patients in our local area. It will help in the management of such patients to

adhere to the medications and decrease the complications of uncontrolled diabetes.

MATERIALS AND METHODS

This was a descriptive study done in the Out Patient Department of Lady Reading Hospital Peshawar; from 1st March 2021 to 31st Aug 2021. A total of 196 diabetic patients were involved in the study. Size of the sample was calculated using the WHO Sample Size Calculator, with 95% confidence level, 5% margin of error and 15% prevalence population proportion. Consecutive sampling technique was utilised. All adult diabetic patients, of either gender; 18 years of age or above, visiting OPD; taking anti-diabetic drugs for 6 months at least and voluntarily consenting, were included in the study. Patients of age less than 18 unconscious, confused and psychiatric patients were excluded from the study. Diabetes was defined as Fasting blood sugar level > 7.0 mmol/L (or 2 hour postprandial blood sugar level > 11.1 mmol/L). Blood sugar > 11.1 mmol/L.

Drug Compliance was defined as the limit to which a patient follows in accordance with does prescribed and interval of anti-diabetic drug(s).Compliance was calculated in accordance with the proportion of days covered (PDC) by the patient as detailed by David Nau11.The patient taking medications in the last 30 days was found, divided by the total number of days (30) and calculated in percentage. The cutoff value was 80%; score of 80% and above was labelled as 'Good' Compliance and less than 80% was expressed as 'Poor' Compliance. The study was done after Institutional Research Ethical Review Board approval. Written informed consent was taken from all the participating patients. Bio data of all patients were determined. A detailed history was taken from the patient including diagnosis and diabetes duration, drugs history, dose, name, drug frequency, its side effects, cost and compliance to medication. Patient's socioeconomic and education status was determined comorbidites were recorded. A detailed clinical examination was done by a consultant physician and findings noted. Relevant laboratory investigations like fasting and random blood sugar, glycated hemoglobin, serum urea, creatinine, electrolytes, triglycerides, cholesterol and urine analysis. All information was noted in the predesigned proforma. Patients data were entered and analyses was done using SPSS (IBM Corporation) version 21 software. Mean ± standard deviations calculation was done for the continuous (numerical) variables. Percentages and frequencies were calculated for all the categorical variables. The statistical significance was set at p value equal to or less than 0.05.Results were presented in the shape of graphs and tables which were compared with local and international studies.

RESULTS

Out of 196 patients considered in the study, 50 (25.5%) were male and 146 (74.49%) were female; Overall compliance for medication in the study patients was 'good' in 86 (43.88%) patients and 'poor' in 110 (56.12%). There was no statistical significant difference between men and women in the two groups, (p =0.8); 43.15% male and 46% female had good compliance. In the same way 56.16% men and 58% women had 'poor' compliance, as shown in Table 1.Age of the patients was ranging between 18 to 93 years; mean age was 55.99 ±10.31 years.

Among 196 patients, 120 (61.2%) were in 40-60 age group. Compliance in various age groups showed that in the below 40 years group, 6% had good compliance; in 40-60 age group 58% had good compliance; similarly in the over 60 years, 34.88% had good compliance. Nevertheless regarding compliance in various age groups no statistical variation between the groups (p =0.45) was noted as shown in the Table 2. Diabetes mellitus type 2 duration ranged from 1 to 20 years with mean of 6.63 ±3.992 years. Duration significantly correlated with compliance to medication (p <0.001).

Table No.1: Gender and compliance to medication

Compliance to medication		Gender		Total
		Male	Female	
Poor complaince	Within compliance	82/110(74.55%)	28/110(25.45%)	110(100%)
	Within gender	82/146(56.16%)	28/50(58%)	110/196(56.6%)
Good complaince	Within compliance	63/86(73.26%)	23/86(26.74%)	86(100%)
	Within gender	63/146(43.15%)	23/50(46%)	86/196(43.4%)
Total	Within compliance	146/196(74.48%)	50/196(25.5%)	196(100%)
	Within gender	100%	100%	100%

Table No.2: Age groups and compliance to medications

Age groups	Compliance to medication		Total
	Poor compliance	Good compliance	
Less than 40 years	10(9.09%)	6(5.88%)	16(8.2%)
40 to 60 years	70(63.63%)	50(58.14%)	120(61.2%)
Above 60 years	30(27.27%)	30(34.88%)	60(30.6%)
Total	110(56.12%)	86(43.88%)	196(100%)

Table No.3: Drug groups and compliance to medications

Drug groups	Compliance to medication		Total
	Poor compliance	Good compliance	
Biguanides	9(8.18%)	14(16.27%)	23(11.7%)
Sulphonylureas	2(1.82%)	1(1.16%)	3(1.5%)
DPP4 inhibitors	55(50%)	13(15.11%)	68(34.7%)
GLP 1 receptor agonists	20(18.18%)	12(13.95%)	32(16.3%)
Combination of drugs	24(21.8%)	46(53.48%)	70(35.7%)
Total	110(100%)	86(100%)	196(100%)

The number of antidiabetic drugs utilised was ranging between 1 to 5 with mean 3.98 ±1.705. Among 196 patients, 68 (34.7%) were on DPP4 inhibitors whilst 70 (35.7%) were on drug combination. Compliance related to drug groups is displayed in Table 3. Patients taking biguanides and combinations were having good compliance whilst those on DPP4 inhibitors were having poor compliance. The correlativity of compliance with drugs was significant ($p < 0.001$).

Among 196 diabetic patients 73 (37.2%) patients were having no comorbidites. 123 (62.8%) patients were having various comorbidites. Amongst these 123 patients commonest comorbidity was dyslipidemia in 47 (24%), perused by Hypertension in 27 (13.8%) patients. CKD was the least common comorbidity and noted in 1 patient. The correlativity of comorbidites with compliance was having no significance ($p = 0.877$).

DISCUSSION

Medication compliance is a global problem as reported from various regions; some studies are in agreement with our study while others are in contrast to ours, as explained below. Compliance to medication in our study was 'good' in 43.4% patients and 'poor' in 56.6%. Gender wise no statistical significant difference between the two groups ($p = 0.8$) was noted. Compliance in 43.15% male and 46% female had good compliance. Mean age of our patients was 55.99 ±10.31; 61% were between 40-60 years and 30% were above 60; however, there was no substantial variation among various age groups ($p = 0.45$). Poor antidiabetic medications compliance was mostly due to younger age, alcohol abuse, placement on insulin therapy, Forgetfulness, financial problem, symptoms disappearance and being too busy.54.4% of our study patients were having poor compliance to their antidiabetic medications. A same result was noted in Malaysia by Ahmad et al.[21] they determined that 53 percent of their participants were noncomplaint to drugs. Other study done by Abebe et al. in Ethiopia expressed a frequency of 54.1 percent [26].nevertheless low rate of non-compliance was noted in Uganda [13], Palestine[28] and Nigeria[27] showing rates of 16.7, 42% and 27.5% respectively. This variation in levels of adherence can be due to differences in socio-economic conditions. In multiple studies, patients over 60 years were having a 52% lower odds of non-adherence to their drugs in contrast to those less than 60 years. This is in accordance with studies elsewhere [29] that non-compliance to drugs is commonly found in younger patients[30],less knowledge of disease, side effect fears and complicated regimen [31]. Old patients having long disease period are more aware from diabetes and the significance of blood sugar control for prevention of complications[12].Patients on insulin alone has two times more non-adherence in contrast to patients on oral hypoglycaemic agents. Insulin is injected via subcutaneous route [32]. Affordability is another issue as insulin price is also higher [33].A twice increase in non-compliance occur with abuse of alcohol. Use of Alcohol decreases frequency of patient's visit to hospitals [34].Our result is same to those of Ahmed et al who noted that abuse of alcohol was related with poor compliance to diabetic medications[35]. Forgetfulness and low economy for buying medications is noted as very common reason for poor complaince[36]. Jingi et al. Identified the medicine Affordability for Diabetes as great issue in the West region of Cameroon[37]. Forgetting the dose is also a serious issue. To treat forgetfulness of patients, regularly arranged follow up visiting is needed, counselling with members of family are needed[38]. Mobile technology for sending motivating message reminders have shown improvement in compliance to drugs in HIV patients[39]. Diabetes care providering institutions can gain from such studies to for improving drug compliance in diabetic patients with diabetes. Jimmy et al suggested recognition of patient issues to drug compliance and adaptation for appropriate methods can improve drug compliance[40]. Our study has some limitations as it was conducted in the OPD and Private Consultation Clinic where the patient's reported compliance might not be true representation of community; a community based study will be more suitable to determine the true compliance to medications.on the other hand our study has slot of merits, as a valid 21 medicine compliance tool was utilised. This is amongst the fewer struggles in Pakistan to provide evidence on antidiabetic medication in type 2 diabetes mellitus patients. These results will be important for policy makers and government when they plan strategy to improve control of diabetes in Pakistan.

CONCLUSION

Most of patients in our study had non-adherence to anti-diabetic drugs. There was no statistical variance between various age groups and gender in relating to compliance. Beguindes and combination of drugs had good compliance. More studies are needed to determine various factors responsible for poor compliance to anti-diabetic medications.

Author's Contribution:

Concept & Design of Study:	Muhammad Abas Khan
Drafting:	Muhammad Abas Khan
Data Analysis:	Muhammad Abas Khan
Revisiting Critically:	Muhammad Abas Khan
Final Approval of version:	Muhammad Abas Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. International Diabetes Federation.Diabetes Atlas: International Diabetes Federation 2015.
2. Hu FB, Satija A, Manson JE. Curbing the diabetes pandemic: the need for global policy solutions. JAMA 2015;313(23):2319–20.
3. Malik VS, Willett WC, Hu FB. Global obesity: trends, risk factors and policy implications. Nat Rev Endocrinol 2013;9(1):13–27.
4. Bigna JJ, Nansseu JR, Katte JC, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract 2018;137:109–18.
5. GBD 2016 DALYs and HALE Collaborators. Global, regional, and national disability-adjusted life-years (DALYs), a systematic analysis for the global burden of disease study 2016. Lancet (London, England) 2017;390(10100):1260–344.
6. Mbanya JC, Motala AA, Sobngwi E, et al. Diabetes in sub-Saharan Africa. Lancet (London, England) 2010;375(9733):2254–66.
7. Cramer JA. A systematic review of adherence with medications for diabetes. Diabetes Care 2004; 27(5):1218–24.
8. Hugtenburg JG, Timmers L, Elders PJ, et al. Definitions, variants, and causes of non-adherence with medication: a challenge for tailored interventions. Patient Preference Adherence 2013;7:675–82.
9. Vrijens B, De Geest S, Hughes DA, et al. A new taxonomy for describing and defining adherence to medications. Br J Clin Pharmacol 2012;73(5): 691–705.
10. Garber MC, Nau DP, Erickson SR, et al. The concordance of self-report with other measures of medication adherence: a summary of the literature. Med Care 2004;42(7):649–52.
11. Arifulla M, John LJ, Sreedharan J et Al.. Patients' adherence to anti-diabetic medications in a Hospital at Ajman, UAE. Malaysian J Med Sci: MJMS 2014;21(1):44–9.
12. Abebaw M, Messele A, Hailu M, Zewdu F. Adherence and associated factors towards antidiabetic medication among type II diabetics University of Gondar Hospital, Northwest Ethiopia 2016;8579157:2016.
13. Bagonza J, Rutebemberwa E, Bazeyo W. Adherence to anti diabetic medication among patients with diabetes in eastern Uganda; a cross sectional study. BMC Health Serv Res 2015; 15:168.
14. Huber CA, Reich O. Medication adherence in patients with diabetes mellitus: does physician drug dispensing enhance quality of care? Evidence from a large health claims database in Switzerland. Patient Preference Adherence 2016;10:1803–9.
15. Rwegerera GM, Moshomo T, Gaenamong M, et al. Antidiabetic medication adherence and associated factors among patients in Botswana; implications for the future. Alex J Med 2018;54(2):103–9.
16. Tiv M, Viel JF, Mauny F, et al. Medication adherence in type 2 diabetes: the ENTRED study 2007, a French population based study. PLoS One 2012;7(3):e32412.
17. Rwegerera GM. Adherence to anti-diabetic drugs among patients with type 2 diabetes mellitus at Muhimbili National Hospital, Tanzania. The Pan African Med J 2014;17:252.
18. Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. Med Care 2005;43(6):521–30.
19. Hutchins V, Zhang B, Fleurence RL et al. A systematic review of adherence, treatment satisfaction and costs, in fixed-dose combination regimens in type 2 diabetes. Curr Med Res Opin 2011;27(6):1157–68.
20. Chisholm-Burns MA, Spivey CA. The 'cost' of medication non-adherence: consequences we cannot afford to accept. J Am Pharmacists Association: JAPhA 2012;52(6):823–6.
21. Ahmad NS, Ramli A, Islahudin F, Paraidathathu T. Medication adherence in patients with type 2 diabetes mellitus treated at primary health clinics in Malaysia. Patient Preference Adherence 2013; 7:525–30.
22. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Med Care 1986; 24(1):67–74.
23. Krousel-Wood M, Muntner P, Jannu A, Desalvo K, Re RN. Reliability of a medication adherence measure in an outpatient setting. Am J Med Sci 2005;330(3):128–33.

24. Sodergard B, Halvarsson M, Tully MP, et al. Adherence to treatment in Swedish HIV-infected patients. J Clin Pharm Ther 2006;31(6):605–16.
25. World Medical Association. World medical association declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA 2013;310(20):2191–4.
26. Abebe SM, Berhane Y, Worku A. Barriers to diabetes medication adherence in north West Ethiopia. Springer Plus 2014;3:195.
27. Pascal IG, Ofoedu JN, Uchenna NP, et al. Blood glucose control and medication adherence among adult type 2 diabetics in Nigeria. N Am J Med Sci 2012;4(7):310–5.
28. Elsous A, Radwan M, Al-Sharif H, Abu Mustafa A. Medications adherence and associated factors among patients with type 2 diabetes mellitus in the Gaza strip, Palestine. Front Endocrinol 2017;8:100.
29. Krueger K, Botermann L, Schorr SG. Age-related medication adherence in patients with chronic heart failure: a systematic literature review. Int J Cardiol 2015;184:728–35.
30. Rodgers PT, Ruffin DM. Medication non-adherence: part II--A pilot study in patients with congestive heart failure. Manag Care Interface 1998;11(9):67–9 75.
31. van der Wal MH, Jaarsma T, Moser DK, et al. Compliance in heart failure patients: the importance of knowledge and beliefs. Eur Heart J 2006; 27(4):434–40.
32. American Diabetes Association. Insulin administration. Diabetes Care 2003;26(suppl 1): s121–s4.
33. Gill G. Diabetes in Africa-puzzles and challenges. Ind J Endocrinol Metabolism 2014;18(3):249–51.
34. Armstrong MA, Midanik LT, Klatsky AL. Alcohol consumption and utilization of health services in a health maintenance organization. Med Care 1998;36(11):1599–605.
35. Ahmed AT, Karter AJ, Liu J. Alcohol consumption is inversely associated with adherence to diabetes self-care behaviours. Diabet Med 2006;23(7): 795–802.
36. Kalyango JN, Owino E, Nambuya AP. Non-adherence to diabetes treatment at Mulago Hospital in Uganda: prevalence and associated factors. Afr Health Sci 2008;8(2):67–73.
37. Jingi AM, Noubiap JJ, Ewane Onana A, Nansseu JR, et al. Access to diagnostic tests and essential medicines for cardiovascular diseases and diabetes care: cost, availability and affordability in the west region of Cameroon. PLoS One 2014;9(11): e111812.
38. Shams N, Amjad S, Kumar N, Ahmed W, Saleem F. Drug non-adherence in type 2 diabetes mellitus; predictors and associations. J Ayub Med College, Abbottabad: JAMC.2016;28(2):302–7.
39. Pop-Eleches C, Thirumurthy H, Habyarimana JP, et al. Mobile phone technologies improve adherence to antiretroviral treatment in a resource-limited setting: a randomized controlled trial of text message reminders. AIDS (London, England) 2011;25(6):825–34.
40. Jimmy B, Jose J. Patient medication adherence: measures in daily practice. Oman Med J 2011; 26(3):155–9.

Original Article

Effect of Intra-Canal Cryotherapy on Post-Endodontic Pain Within 24hrs in Single Rooted Teeth

Madiha Zaighum[1], Sheba Ramzan[2], Mehak Imtiaz[1], Mehwish Memon[2], Talha Asad Khan[1] and Hina Hassan[1]

ABSTRACT

Objective: To evaluate the effect of 2.5°C cold saline irrigation as final irrigant on postoperative pain after single-visit root canal treatment in 24 hours in teeth with symptomatic apical periododntitis.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Operative Dentistry at Isra Dental College Hyderabad from July 2019 to December 2019.

Materials and Methods: 60 patients were after fulfilling the inclusion criteria were eligible and included to the study. The teeth were randomly divided into two groups (n = 30) (i.e. the control group and the cryotherapy group). In the cryotherapy group, final irrigation with 2.5°C saline solution for 5 min was performed following completion of root canal therapy, whereas in control group same solution stored at the root temperature was used. Treatments were performed in a single visit. Participants were asked to rate the intensity of their postoperative pain using visual analogue scale at 24 h.

Results: Data was analysed by Student's t test and Fissure Exact Test. In the cryotherapy group level of reported postoperative pain was significantly lower than the control group ($P < 0.05$, t-test).

Conclusion: The outcome of this investigation indicates that cryotheraphy is one of benefacial strategy in reduction of postoperative pain in single visit endodontic treatment in teeth with symptomatic apical periodontitis.

Key Words: cryotherapy, endodontic pain, postoperative pain

Citation of article: Zaighum M, Ramzan S, Imtiaz M, Memon M, Khan TA, Hassan H. Effect of Intra-Canal Cryotherapy on Post-Endodontic Pain Within 24hrs in Single Rooted Teeth. Med Forum 2021;32(10):16-19.

INTRODUCTION

Elimination of Post-operative pain is related to the success of endodontic therapy, many clinical studies have reported its occurance in 3 and 58% of patients.[1,2] Post-operative endodontic pain is more common scenario in teeth with necrosed pulp, but still the relationship between post-operative pain and pulpal status is controversial.

Multiple factors have been associated in eliciting pain in cases of irreversible pulpitis, pulp necrosis with symptomatic periapical periodontitis such as biological factors,inflammatory mediators, inflammatory exduates and psychological status.[3,4]

[1.] Department of Operative Dentistry, Isra Dental College Hyderabad.
[2.] Department of Operative Dentistry, Liaquat University of Medical Health Sciences Jamshoro.

Correspondence: Dr. Madiha Zaighum, Assistant Professor of Operative Dentistry at Isra Dental College Hyderabad.
Contact No: 0331-8878544
Email: madihaz_pk@hotmail.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

The regime mostly used to control post operative endodontic pain is usullay through medications .commonly prescribed drugs are nonsteroidal anti-inflammatory drugs, paracetamol, or corticosteroids. These drugs are associate with side effects so different strategies have been tried to reduced post operative pain.[5]

Use of proper irrigant solution and elimination of microbes and their remanents has a profound effect on the reduction of post operative pain. the most commonly used root canal irrigation solution is Sodium hypochlorite (NaOCl) which have both tissue-dissolving and antimicrobial properties.[6] NaOCl have high surface tensiondue to which its penetration into irregularities of the root canal system is somewhat limited in canals with fins, isthmi and dentinal tubules.[7] In addition NaOCl also do not have any residual antimicrobial activity[8], infected or contaminated dentin may turn a potential source of persistent apical periodontitis.

In 2004 Nadler et al.,[9] stated that "Cryotherapy is the application of cold material to lower the temperature of the surrounding tissues to control pain". by using cold saline (2.5 °C) for 5 min whch can reduce temperature of the outer surface of the root more than 10 °C which can reduce the effects of inflammation on the peri-radicular tissue.[10] In an in-vitro study, a higher reduction in the Enterococcus faecalis count was

obtained by sodium hypochlorite (NaOCl) followed by cryotherapy when compared to NaOCl alone.[11]

MATERIALS AND METHODS

The study was approved by the local clinical research ethics committee of the ISRA Dental College Hyderabad, before starting treatment patients an informed consent was obtained and preoperative pain was recorded using visual analogue scale (VAS). 60 adult patients with either gender, age range between 18 to 60 years. Single rooted carious teeth. With pain associated with affected teeth confirmed by vertical percussion were included in the study Patients with Previously root canal treated teeth. Immature teeth with incomplete root formation. Teeth with internal or external resorption. Multi rooted teeth. Teeth with periodontal disease and mobility were excluded.

Data Collection Procedure: The 60 patients were randomly divided by envelop method into two equal groups (60 in each) group A and B respectively. The preoperative apical diagnosis was determined according to the radiograph and percussion test. Then anaesthesia (lidocaine 2% with adrenaline 1:80000) was given to the patient, and rubber dame was placed. For each tooth, proper access cavity preparation was done, followed by pulp extirpation and working length determination then canals were enlarged with the hand files to size 25. The canals were irrigated with NaOCl then final irrigation was done with either 2.5 C saline˚ or saline at room temperature for 2 min using side vented needle, then root canal treatment was completed. and patients were instructed to record their postoperative pain after 24 hours using the (VAS) scale. A refrigerator was used to obtain 2.5 C saline. And thermometer was used to measure the temperature.

RESULTS

There were total 60 patients who took part in this study. The age of the patients was between 18 to 60 years which were divided into different age groups (fig 1) with the mean age of 37.2 years. (table 1) The sample was divided equally into two groups namely Group A and Group B representing control group and cryotherapy group respectively. (Table 2), shows the gender distribution of both groups. There were 43.3% and 50% males in group A and B respectively. Also, 56.7% and 50% females were in control and cryotherapy groups correspondingly. The results in (Table 3) depicts The frequency of Postoperative pain was found to be higher in Control group in 24 hours then the cryotherapy Group and it was statistically significant ($p < 0.05$) with mean pain score0.60 SD±.498 for group A and 0.30 SD ±.466 for group B. Moreover, to test if there exist a relationship between postoperative pain and periapical radiolucency in both Groups, we have applied the Fisher's Exact Test, shows that the incidence of postoperative pain was higher in patients with periapical radiolucency.

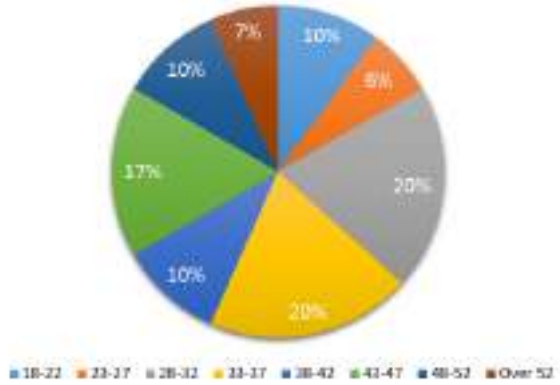


Figure No.1: Frequency of Different Age Groups

Table No.1: Age of Patients

Mean	37.2
Std. Deviation	10.2
Minimum	18 Years
Maximum	56 Years

Table No.2: Gender distribution of patients

Gender Distribution		
Group A	Males 13(43.3%)	Females 17(56.7%)
Group B	Males 15(50%)	Females 15(50%)

Table No.3: Number and Percentage of Post-Operative Pain After 24 Hours

	Group	pain		P-Value
		Yes	No	
Post-Operative pain	A	18 (60%)	12 (40%)	0.019
	B	09 (30%)	21 (70%)	

Table No.4: Mean and Standard Deviation of Post-Operative Pain

	Group A		Group B	
	Mean	SD	Mean	SD
Post-operative Pain	.60	±.498	.30	±.466

DISCUSSION

In this prospective cross sectional study cryotherapy was compared with the classic final irrigation protocol in teeth with symptomatic periapical periodontitis to reduce the post operative pain within 24 hours.

The maximum postoperative pain was reported in single visit root canal treatment for symptomatic periapical periodontitis in 24 hours, which reduces significantly afterwards.[12] In this study the pulpal status

was no considered because the pulp status effect on post-endodontic pain is controversial.[13]

in this study Intracanal cryotherapy was used s a final irrigant with cold saline at a temperature of 2.5℃ which reduces more than 10˚C external root surface temperature.[14] That is effective in reversing the effects of inflammation in short term application.

Cryotherapy is one of the innovative strategy to reduce post operative pain in single visit root canal treatment, in this study it was compared with room temperature normal saline irrigation as a final flush. We found statsitcal siginificant difference between two groups in reduction of post operative pain in first 24 hours which is in accordance with the studies of Al-Nahlawi et al., 2016;[15] Keskin et al., 2016[16] who also reported in reduction of post-operative pain in teeth with symptomatic apical periodontitis.in present study the teeth were selected irrespective of their pulpal status which is in contrast to the previous mentioned studies.

Alharthi and colleagues in 2019[17] found through their research on the" Effect of intra-canal cryotherapy on post-endodontic pain in single-visit RCT: A randomized controlled trial" that there is no effect of temperature of normal saline in reduction of post endodontic pain in 24 hours as a final flush which is in contrast to our study which shows significant difference between control and cryotherapy in reduction of post operative pain.

In this study postoperative pain association with periapical radioluceny has been analysesed through fissure test,that showed postoperative pain incidence is more in teeth with periapical radiolucency irresepective of the irrigation regimn which is in accordance with the studies conducted to evalute the post operative pain and periapical radiolucency in single visit root canal treatment.[18-22]

CONCLUSION

Post-operative endodontic pain reduction is most important aim of root canal treatment, mostly analgesic is prescribed for pain reduction, cryotherapy is one of beneficial strategy in reduction of postoperative pain in single visit endodontic treatment.

Author's Contribution:

Concept & Design of Study:	Madiha Zaighum
Drafting:	Sheba Ramzan, Mehak Imtiaz
Data Analysis:	Mehwish Memon, Talha Asad Khan, Hina Hassan
Revisiting Critically:	Madiha Zaighum, Sheba Ramzan
Final Approval of version:	Madiha Zaighum

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Rosenberg PA. Clinical strategies for managing endodontic pain. Endod Topics 2002;3:78–92.
2. Sathorn C, Parashos P, Messer H. The prevalence of postoperative pain and flare-up in single-and multiple-visit endodontic treatment: a systematic review. Int Endod J 2008;41:91–9.
3. Ince B, Ercan E, Dalli, M, Dulgergil C T, Zorba Y O, Colak H. Incidence of postoperative pain after single-and multi-visit endodontic treatment in teeth with vital and non-vital pulp. Eur J Dent 2009;3: 273-279.
4. Ng YL, Glennon J, Setchell D, Gulabivala K. Prevalence of and factors affecting post-obturation pain in patients undergoing root canal treatment. Int Endod J 2004;37:381–91.
5. Attar S, Bowles WR, Baisden MK, Hodges JS, McClanahan SB. Evaluation of pretreatment analgesia and endodontic treatment for post-operative endodontic pain. J Endod 2008;34:652–5.
6. Siqueira JF. Microbial causes of endodontic flare-ups. Int Endod J 2003;36:453–63.
7. Luddin N, Ahmed HMA. The antibacterial activity of sodium hypochlorite and chlorhexidine against Enterococcus faecalis: A review on agar diffusion and direct contact methods. J Conserv Dent 2013; 16: 9–16.
8. Haapasalo M, Shen Y, Qian W, Gao Y. Irrigation in endodontics. Dent Clin North Am 2010;54: 291–312.
9. Nadler S, Weingand K, Kruse R. The physiologic basis and clinical applications of cryotherapy and thermotherapy for the pain practitioner. Pain Physician 2004; 7:395–399.
10. Vera J, Ochoa J, Vazquez-Carcaño M, Romero M, Arias A, Sleiman P. Effect of intracanal cryotherapy on reducing root surface temperature. J Endod 2015;41:1884–1887.
11. Mandras N, Allizond V, Banche G, Roana J, Piazza L, Viale P, et al. Antimicrobial efficacy of cryotreatment against enterococcus faecalis in root canals. Lett Appl Microbiol 2013;56:95–98.
12. Law A, Nixdorf D, Aguirre A, Reams G, Tortomasi A, Manne B. Dental PBRN collaborative group; predicting severe pain after root canal therapy in the national dental PBRN. J Dent Res 2015;94:37S–43S.
13. Sipavičiūtė E, Manelienė R. Pain and flare-up after endodontic treatment procedures. Baltic Dental Maxillofacial J 2014;16:25–30.
14. Vera J, Ochoa J, Vazquez-Carcaño M, Romero M, Arias A, Sleiman P. Intracanal Cryotherapy Reduces Postoperative Pain in Teeth with Symptomatic Apical Periodontitis: A Randomized Multicenter Clinical Trial. J Endod 2018;44(1):4-8.

15. Al-Nahlawi T, Abo Hatab T, AbdAlrazak M, Al-Abdullah A. Effect of Intracanal Cryotherapy and Negative Irrigation Technique on Postendodontic Pain. J Contemp Dent Pract 2016;17(12):990-996.
16. Keskin C, Özdemir O, Uzun I, Güler B. Effect of Intracanal Cryotherapy On Pain After Single-Visit Root Canal Treatment: Aus Endod J 2016;43(2): 83-88.
17. Alharthi AA, Aljoudi MH, Almaliki MN, Almalki MA, Sunbulb MA. Effect of intra-canal cryotherapy on post-endodontic pain in single-visit RCT: A randomized controlled trial. Saudi Dent J 2019;31(3):330–335.
18. Fava LR. A comparison of one versus two appointments endodontic therapy in teeth with non-vital pulps. Int Endod J 1989;22:179–83.
19. Rudner WL, Oliet S. Single-visit endodontics: A concept and a clinical study. Compend Contin Educ Dent 1981;2:63–8.
20. Dodge JS. Single visit endodontics a clinical study. J Endod 1983;9:35–40.
21. Clem WH. Post-treatment endodontic pain. J Am Dent Assoc 1981; 116:533–6.
22. Sjögren U, Figdor D, Persson S, Sundqvist G. Influence of infection at the time of root filling on the outcome of endodontic treatment of teeth with apical periodontitis. Int Endod J 1997;30:297–306.

Original Article

Prediction of Oral Cancer Survival Utilizing Micro RNA 21 and Clinicopathological Variables

Nosheen Mehmood[1], Humera Akhlaq[2], Qamar Jamal[1], Isma Sajjad[3] and Sajid Hanif[2]

ABSTRACT

Objective: To investigate the impact of various socio demographic, clinical/pathological and novel miRNA biomarkers on oral cancer survival.

Study Design: Prospective cohort study

Place and Duration of Study: This study was conducted at the Department of Pathology, Ziauddin Hospital, Karachi, Pakistan from January 2014 to January 2020.

Materials and Methods: The data were obtained from 146 consecutive biopsy proven oral squamous cell carcinoma patients falling in an age bracket of 20 to 80 years. Association of variables with the survival was made through student's t test for continuous variables and chi square test for qualitative variables. Survival analysis was done via cox regression. Survival curves were plotted via Kaplan-Meier method using the Log-rank test. All statistical analysis was carried out on SPSS version 24.

Results: Overall survival was 43.8%. Cox regression analysis demonstrated miRNA 21 overexpression was linked to poor survival with a Hazard risk (HR) of 0.929, P<0.005. Other significant predictors included tumor grade (HR of 1.77, P< 0.001), nodal metastasis (HR of 9.4, p<0.01), advance stage (HR of 2.8, P<0.001 and age in years (HR of 1.02, p<0.01)

Conclusion: In this cohort we observed overexpression miRNA-21 was an independent prognostic factor suggesting it as a potential biomarker predicting poor survival. Furthermore, advancing age, nodal metastasis, poor grade, and advanced stage impacted poor survival in Oral Squamous cell carcinoma.

Key Words: Oral cancer, survival analysis, prognostic factors, miR-21

Citation of article: Mehmood N, Akhlaq H, Jamal Q, Sajjad I, Hanif S. Prediction of Oral Cancer Survival Utilizing Micro RNA 21 and Clinicopathological Variables. Med Forum 2021;32(10):20-24.

INTRODUCTION

Oral cancer is one of the frequently diagnosed malignancies in Southeast Asia with around 66 % of global burden borne by developing countries (Gupta et al, 2014).[1] Being the most common cancer amongst men and second only to breast cancer amongst women it remains a significant contributor of cancer associated morbidity and mortality in Pakistan. A significant rise is observed in incidence of oral cancer from 12761(8.6%) in 2012 to 18,881(12.9%) in 2020 (IARC Globocan., 2020). [2]

Despite maintaining a stable rank as second most common cause of cancer related deaths in Pakistan, proportion of people dying of it is increasing as evident by IARC GLOBOCAN report endorsing a rise from 7.2.% (7266) in 2012 to 9.1% (13351) in 2020.[2,3]

To improve survival, advances in treatment strategies have been introduced but despite all these efforts survival remains unchanged for several decades.[4] Achieving a high cure rate in any cancer with minimal side effects of treatment is a very challenging task. This is especially true for oral cancers where surgeries can be extremely disfiguring owing to the anatomical location while chemo and radiotherapy is also not free of toxicities. Moreover, oral cancers are more common in low socioeconomic group patients and majority of them find it very difficult to bear the cost of treatment. On an average the cost of Cancer treatment exceeds the monthly income of these patients hence exploring the prognostic factors will help in streamlining the treatment guidelines for individual patient.[5] Tumor staging using TNM is well established prognostic indicator however its utility becomes limited as majority of patients present at advance stage[6]

It can be concluded from researches carried out in other countries that socio demographic and Clinicopathological factors including old age, poor socioeconomic status, tobacco smoking, T stage, nodal metastasis, local invasion , positive tumor margins, and presence of extra capsular spread of tumor cells have been observed to impart poor survival.[7] Inflammation in

[1.] Department of Pathology, Ziauddin University, Karachi.
[2.] Department of Oral Pathology / Operative Dentistry[3], Jinnah Sindh Medical University, Karachi.

Correspondence: Dr. Humera Akhlaq, Department of Oral Pathology, Jinnah Sindh Medical University, Karachi.
Contact No: 0321 8912767.
Email: humeraakhlaq@ymail.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

tumor microenvironment has been linked to survival as it contributes to local invasion reflected by rising levels of proinflammatory cytokines.[8]

This study is the first step taken to determine overall survival and impact of various factors on survival in subjects with oral cancer in Karachi, Pakistan. Sizeable research is published on risk factors, but research specific to survival analysis and prognostic factors is sparse.

MATERIALS AND METHODS

This prospective cohort study was carried out with the approval of the Ethics Research Committee of Ziauddin University, Karachi, Pakistan. Subjects were selected via Purposive nonprobability sampling. Sample size of 144 was calculated through raosoft sample size calculator with an expected margin of error of 8%.[9] Patient recruitment was started in Jan 2014. During this period, we recruited 146 biopsy proven cases of Squamous cell carcinoma of Oral cavity. Cases with a history of any other malignancy were excluded. Data was collected on age, gender, ethnicity, chewing habits, smoking, alcohol intake and family history of oral cancer through a structured questionnaire. Pathological features including tumor site, nodal status, tumor recurrences and histologic classification were recorded after physical examination and careful review of patient's file. Recurrences were detected by history, physical examinations and imaging and confirmed by histopathological examinations.

Tumors were classified according to American Joint Committee on Cancer (AJCC) seventh edition system. Survival was taken as the primary outcome. End were death related to oral cancer or January 2020 considered as last day of follow up. Overall survival (OS) was defined as the time between the date of diagnosis of primary OSCC and the date of death due to any cause or date of the last follow-up or date of end of study which was 1st January 2020.

For miRNA21 expression, miRNA was extracted, CDNA was synthesized, and qRT-PCR was carried out to quantitatively detect miR-21 expression. miR-16 was used as a normalizer detailed methodology explained by Mahmood and colleagues.[10.]

Statistical analysis was performed using the SPSS software package SPSS (Version 24.0; SPSS Inc. Chicago, IL, USA). Chi- square was used for comparison of nominal and ordinal variables between the groups. Continuous variables were examined using Students t test. Survival estimates were calculated for the period Jan 2014– Jan 2020. Survival curves were generated through Kaplan-Meier and compared by log-rank test. For multivariate analysis of significant variables ($p< 0.05$) Cox regression models were created. Statistical significance was set at $P<0.05$.

RESULTS

A total of 146 cases fulfilled our criteria. Subjects included fell in an age range of 20 to 80 years with a mean of 43.7± 11.9 years. Most of the patients, 126(86%) were diagnosed in the age bracket of 15 to 54 years. When subjects were distributed according to International Cancer Survival Standards (ICSS) age groups there were 76(52%) subjects between 15-44 years, 50(34.2%) between 45-54 years, 14 (9.6%) between 55-64 years,4 (2.7%) between 65-74 years and only 2(1.4%) above 75.[9] There were 107 (73%) males and 39(26.7%) females making a male to female ratio of 2.7 :1. A positive family history of oral cancer was reported in 9 (6.2%) subjects whereas remaining 137 (93.8%) did not report any family history of oral cancer.

Majority of patients 121(82.9%) had a tumor in oral cavity, tongue was the second commonest site with 15 cases (10.3%) and 10(6.8%) subjects had a lip cancer. Majority of subjects 94 (64.4%) had a moderately differentiated tumor whereas in 29(19.9%) subjects a well differentiated histology was observed and 23(15.8%) reported poorly differentiated histology. Distant metastasis was seen in 8(5.5%) subjects. A tumor recurrence was observed in 7(4.8%) cases however 139(95.2%) did not report any recurrence.

To compare the variables subjects were allocated into survivors and non survivors. miRNA 21 expression was checked in 100 subjects including 56 who did not survive and 44 alive or censored. Circulating miR21 was up regulated in the non-survivor group (27.6± 5.8 vs. 30.8± 4.3, p-0.002 Figure 1. Moreover, a significant difference in the two groups was observed in age at presentation, tumor grade, nodal involvement, and stage. In contrast we did not observe any difference between the two groups in gender, ethnicity, site of tumor and tumor recurrence (Table 1).

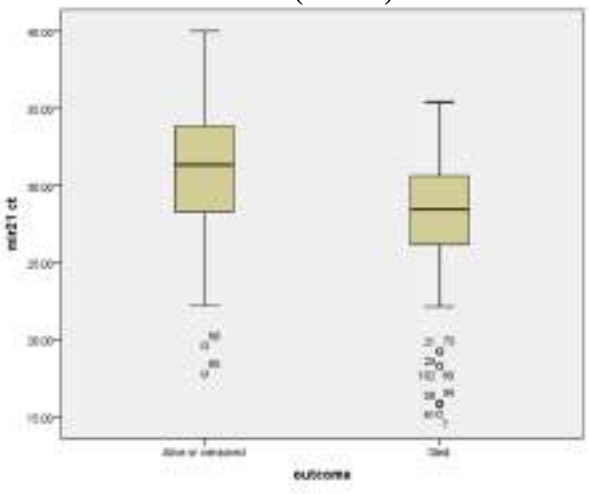


Figure No.1: miRNA 21 expression between survivors and non survivors

Table No.1: Comparison of Sociodemographic and clinic Pathologic variables between Survivors and Non-Survivors.

Variable	Category	Survival Status		*P* value
		Survivors (N= 64)	**Non-Survivors (N=82)**	
Age in years	< 40 years	35 (55.6%)	28(44.4%)	**0.013***
	>40 years	29 (34.9%)	54 (65.1%)	
Gender	Male	44(41%)	63(58.9%)	0.27
	Female	20(51.3%)	19(48.7%)	
Anatomic site	Tongue	5(33%)	10(66.7%)	0.17
	Lip	7(70%)	3(30%)	
	Buccal cavity	52(43%)	69(57%)	
Histological Differentiation	I	20(69%)	9(31%)	**0.009****
	II	36(38.3%)	58(61.7%)	
	III	8(34.8%)	15(65.2%)	
Recurrence	Yes	1(14.3%)	6(85.7%)	0.108
	No	63(45.3%)	76(54.7%)	
Nodal Metastasis	No	18(85.7%)	3(14.3%)	**<0.0001****
	Yes	46(36.8%)	79(63.2%)	
Stage	I	2(100%)	0(0%)	**0.001****
	II	13(81.2%)	3(18.8%)	
	III	19(48.7%)	20(51.3%)	
	IV	30(33.7%	59(66.3%)	

N; Number of cases, *; p<0.05, **; p<0.01

Table No.2: Cox regression analysis between variables and survival

Variable	HR	95%CI		*P* value
		Lower	Upper	
Age	0.72	0.571	0.910	.006*
Ethnicity	0.957	0.822	1.113	0.566
Site	1.09	0.755	1.558	.667
Recurrence	0.306	0.131	0.718	0.007
Grade	1.77	1.770	2.5	0.001**
Local Invasion	0.709	0.409	1.227	0.219
Tumor size	1.52	1.187	1.970	.001**
Nodal status	2.3	1.609	3.26	<0.001**
Mets	0.5	0.216	1.154	.104
Stage	2.28	1.583	3.283	<0.001**
miR-21	0.929	0.887	0.973	<0.001**

HR; hazard ratio, SE; Standard error, *; p<0.05, **; p<0.01

Survival Analysis: The Overall survival was 43.8% at the end of study. Median survival was 37 months with 95 % CI (32.2-41.7). At 20 months of follow up 112 (77%) patients were alive which dropped to 42(31%) at 40 months. Table 2 shows cox regression analysis between variables and overall survival. A significantly higher Hazard risk was observed among subjects above 40 years, having poor tumor grade, nodal involvement and advancing stage. Figure 2 shows survival curves for different tumor grades. Subjects with poor grade had poor overall survival, Log rank value of 13.1, p<0.01.

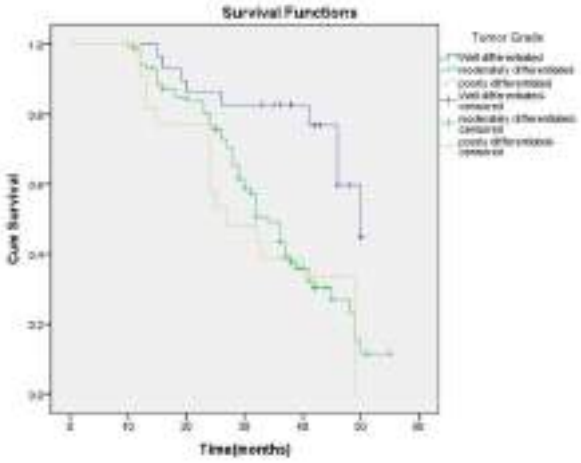


Figure No.2: Survival of subjects among different grades, Kaplan-Meier test was applied (Log rank= 13.1, p<0.01)

DISCUSSION

Despite being the second most common cancer in Pakistan research targeted at exploring potential predictors is scarce. Only two studies have reported contributors of survival in oral cancer patients. Abbas et al conducted a retrospective study to explore predictors of survival among oral cancer patients in a tertiary care hospital of Karachi and Hussain et al studied survival cancer among Tongue squamous cell carcinoma at Shaukat Khanum cancer hospital.[11,12.]

We report an overall survival of 43% in our subjects. Matching to our findings Hussain et al observed an overall survival of 50% in Stage III &IV Tongue cancers recruited at Shaukat Khanum Cancer Hospital. Selection of subjects from a cancer hospital makes it likely to recruit advanced cases and hence a poor survival. However, in contrast to our study they only followed T1 and T2 Tongue cancer. [12]

Our findings are in agreement with the findings of Centeless et al who recorded a survival rate of 44%.[13] Rao et al reported a 5 year survival of 38-42% in India.[14] Listl et al also reported a 5 year survival of 51.7% for tumors of oral cavity.[15] Whereas, a survival rate of 28.7% was reported by komolmalai et al in their subjects in Thailand.[16] Rich lymphovascular supply of oral cavity allows early nodal involvement and hence advanced stage irrespective of tumor size or grade.

We observed a better overall survival in our younger patients which agrees with other reports. A decline in survival from 61.1% in 15-44 years old to 43.9% in 65-74 years old was observed by Listl et al in German subjects.[15] The observed difference may be the result of more aggressive adherence to treatment and regular follow ups by younger patients.

We observed a poor survival in our subjects with up regulation of miRNA-21. These findings agreed with the report by Hedback et al who also observed a higher miRNA 21 expression as an independent factor predicting survival. They checked expression on tissue samples and found an up regulation of miR-21 in tumor stroma. After adjusting for clinical variables, multivariate regression analysis confirmed role of miRNA-21 in predicting disease free survival. [17]

We observed a significant association between tumor grade and survival. Analogous findings are reported by Listl et al; they observed an association of tumor grade with survival and reported a drop in survival from 65.2% to in Grade 1 cancers to 41.1% in Grade III& IV.[15] Liu et al observed a progressive decline in survival from 67.63% in well differentiated to 63% in moderately differentiated and 51.66% in poorly differentiated tumors.[18] Thomas et al also observed a strong impact of Tumor grade on survival. They found an association of poorly differentiated histology with increased risk of death in only Stage I and II subjects. Moreover, they observed increased death risk with moderately differentiated histology only in subjects who were older than 65 years.[19]It is quite possible that the observed increased risk in moderately differentiated group could have been attributed by the advancing age and not the tumor grade.

We found lymph node metastasis to impact poor survival among our subjects. Lymphatic involvement is linked to advanced stage and thus poor survival. Like us Abbas et al also observed poor survival among the subjects having lymph node involvement.[11]

We did not observe an effect of tumor location on overall survival which agrees with findings of Liu et al who also did not observe any association between tumor location and survival.[20]

No statistically significant difference was observed in different socioeconomic groups. Majority of our subjects were from low or low middle socioeconomic group, so it was not possible to evaluate its impact on overall survival. Komolamai et al observed a poor prognosis in their subjects from a low socioeconomic status.[16]

CONCLUSION

In conclusion, advancing age, poor histological grade, nodal metastasis, advanced stage, and up regulation of miR-21 predict poor prognosis. Future multicenter studies validating these findings might enable the development of prognostic scores and thus treatment guidelines.

Acknowledgments: We express our appreciation for Dr. Javed Malik for his kind guidance in recruiting patients of Oral Cancer from Ziauddin Hospital Oncology Department.

Author's Contribution:

Concept & Design of Study:	Nosheen Mehmood
Drafting:	Humera Akhlaq, Qamar Jamal
Data Analysis:	Isma Sajjad, Sajid Hanif
Revisiting Critically:	Nosheen Mehmood, Humera Akhlaq
Final Approval of version:	Nosheen Mehmood

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Gupta B, Johnson NW. Emerging and established global life-style risk factors for cancer of the upper aero-digestive tract. Asian Pac J Cancer Prev 2014;15(15):5983-91.
2. https://gco.iarc.fr/today/data/factsheets/populations/900-world-fact-sheets.pdf
3. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in Globocan 2012. Int J Cancer 2015;136(5).
4. Li K, Guo Q, Zhang X, Dong X, Liu W, Zhang A, et al. Oral cancer-associated tertiary lymphoid structures: gene expression profile and prognostic value. Clin Exp Immunol 2020;199(2):172-81.
5. Zaidi AA, Ansari TZ, Khan A. The financial burden of cancer: estimates from patients undergoing cancer care in a tertiary care hospital. Int J Equity in Health 2012;11(1):60.

6. Bao X, Liu F, Lin J, Chen Q, Chen L, Chen F, et al. Nutritional assessment and prognosis of oral cancer patients: a large-scale prospective study. BMC Cancer 2020;20(1):1-8.
7. Lin NC, Hsu JT, Tsai KY. Survival and clinicopathological characteristics of different histological grades of oral cavity squamous cell carcinoma: A single-center retrospective study. PloS One 2020;15(8): e0238103.
8. Lee S, Kim DW, Kwon S, Kim HJ, Cha IH, Nam W. Prognostic value of systemic inflammatory markers for oral cancer patients based on the 8th edition of AJCC staging system. Scientific Reports 2020;10(1):1-9.
9. http://www.raosoft.com/samplesize.html
10. Mahmood N, Hanif M, Ahmed A, Jamal Q, Mushtaq S, Khan A, et al. Circulating miR-21 as a prognostic and predictive biomarker in oral squamous cell carcinoma. Pak J Med Sci 2019;35(5):1408-1412.
11. Abbas SA, Saeed J, Tariq MU, Baksh AR, Hashmi S. Clinicopathological prognostic factors of oral squamous cell carcinoma: An experience of a tertiary care hospital. J Pak Med Assoc 2018; 68(7):1115-1119.
12. Hussain R, Jamshed A, Iqbal H, Usman S, Irfan M, Bhatti AB. Long term survival and impact of various prognostic factors in T1, T2 oral tongue cancer in Pakistan. JPMA. J Pak Med Assoc 2016; 66(2):187-93.
13. Varela-Centelles PI, Fernández EV, Asenjo JG. Survival to oral cancer. A study of clinical risk markers with independent prognostic value. Bulletin du Groupement International pour la Recherche Scientifique en Stomatologie et Odontologie 2008;44(2):46-51.
14. Rao SV, Mejia G, Roberts-Thomson K, Logan R. Epidemiology of oral cancer in Asia in the past decade-an update (2000-2012). Asian Pacific J Cancer Prevention 2013;14(10):5567-77.
15. Listl S, Jansen L, Stenzinger A, Freier K, Emrich K, Holleczek B, et al, GEKID Cancer Survival Working Group. Survival of patients with oral cavity cancer in Germany. PLoS One 2013;8(1): e53415.
16. Komolmalai N, Chuachamsai S, Tantiwipawin S, Dejsuvan S, Buhngamongkol P, Wongvised C, et al. Ten-year analysis of oral cancer focusing on young people in northern Thailand. J Oral Sci 2015;57(4):327-34.
17. Hedbäck N, Jensen DH, Specht L, Fiehn AM, Therkildsen MH, Friis-Hansen L, et al. MiR-21 expression in the tumor stroma of oral squamous cell carcinoma: an independent biomarker of disease-free survival. PLoS One 2014;9(4):e95193.
18. Liu SA, Tsai WC, Wong YK, Lin JC, Poon CK, Chao SY, Hsiao YL, Chan MY, Cheng CS, Wang CC, Wang CP. Nutritional factors and survival of patients with oral cancer. Head Neck 2006;28(11):998-1007.
19. Thomas B, Stedman M, Davies L. Grade as a prognostic factor in oral squamous cell carcinoma: a population- based analysis of the data. Laryngoscope2014;124(3):688-94.
20. Liu F, Chen F, Huang J, Yan L, Liu F, Wu J, et al. Prospective study on factors affecting the prognosis of oral cancer in a Chinese population. Oncotarget 2017;8(3):4352.
21. Fan Y, Zheng L, Mao MH, Huang MW, Liu SM, Zhang J, et al. Survival analysis of oral squamous cell carcinoma in a subgroup of young patients. Asian Pac J Cancer Prev 2014;15(20):8887-91.

Original Article

Adapting Health Literacy Tool for Use in Hospital: Experience of Holy Family Hospital Rawalpindi, Pakistan

Health Literacy Tool for Use in Hospital

Aashi Ahmed, Bushra Anwar, Nadia Nisar, Saima Omair, Salma Ambreen and Bilal Ahmed

ABSTRACT

Objective: To adapt HL-SF12 for measurement of literacy regarding disease prevention, health care and health promotion in patients visiting tertiary care hospital, Rawalpindi, Pakistan.
Study Design: Cross sectional study
Place and Duration of Study: This study was conducted Department of Community Medicine, HITEC-IMS, Taxila during the year January to June 2021.
Materials and Methods: Data was collected in three public sector tertiary care hospitals including Holy Family Hospital Rawalpindi during the year 2018. We translated the HL-SF12 (short-form health literacy 12 items questionnaire) for Pakistani population in Urdu language. Face validity was assessed by 5 patients resembling target population. For content validity, 7 public health experts were consulted. Construct validity was assessed by administering questionnaire to patients and analyzing its results by exploratory factor analysis and correlation analysis. A total of 450 adults of either gender with age > 18 years, able to communicate in Urdu were selected from outpatient and emergency departments of three public sector hospitals.
Results: Health literacy questionnaire adapted by translating a 12 item pre-validated tool by European Consortium was accepted by subject experts as feasible. Some change in order of questions was advised by experts that were followed by researcher. Patients responded well to the questionnaire and didn't require any help of data collectors for understanding of questions. Exploratory Factor analysis of this data identified three components. Construct validity assessed by correlation analysis was reasonably high.
Conclusion: Health literacy questionnaire by European Consortium was adapted by translation in Urdu language and was successfully applied with reasonable validity.
Key Words: Health literacy; HL-SF12; health promotion; delivery of health care; prevention and control

Citation of article: Ahmed A, Anwar B, Nisar N, Omair S, Ambreen S, Ahmed B. Adapting Health Literacy Tool for Use in Hospital: Experience of Holy Family Hospital Rawalpindi, Pakistan. Med Forum 2021;32(10): 25-29.

INTRODUCTION

'Health literacy' is the ability of individuals to access, understand and utilize health related information which is necessary to maintain good health.[1] Low health literacy is associated with risky health behaviors leading to diseases.[2]

Health literacy has been assessed by different researchers across the globe using different methods. These methods vary from assessment using document literacy, and quantitative literacy to validated tools. Tools for health literacy assessments include Rapid Estimate of Adult Literacy in Medicine (REALM), Test of Functional Health Literacy in Adults (TOFHLA), some validated self-report scales and a tool designed by European Union (EU). These have been used in different countries for health literacy measurement for patients and general population.[3]

A Health Literacy tool was designed by European Union and survey done in 2009-2012. It was supported and funded by the European Commission. The aims included to measure health literacy in Europe, to establish networks, at national and European level and to promote health literacy in Europe. This Health Literacy Survey (HLS) tool comprised questions that further helped to design a model around concepts of health literacy.[4] In first phase a comprehensive questionnaire with 47 items was made and used in 2011 for health literacy survey in eight member states of European Consortium. Shorter versions of this tool (12 item and 6 item questionnaires) were developed and validated in the same project after testing comprehensive one.[5]

Pakistan continues to struggle with low health literacy that often results in late presentation of disease, poor adherence to treatment and meagre understanding of

Department of Community Medicine, HITEC-IMS, Taxila.

Correspondence: Nadia Nisar, Assistant Professor of Community Medicine, HITEC,IMS, Taxila.
Contact No: 0334-5663255
Email: nadia.nisar15@yahoo.com

Received: July, 2021
Accepted: August, 2021
Printed: October, 2021

wellness and disease prevention. In a country burdened by diseases of the developing and the developed world, with poor healthcare infrastructure and low literacy levels improving healthcare literacy could have major influence on health and wellness of our masses.[6] In Pakistan, there is scarcity of evidence regarding the role of health literacy on treatment outcomes, medication adherence or use of health care services. Sulehri MA et al studied commonly reported health literacy factors including information regarding balanced diet, injury prevention during traveling, hand-washing and hygiene, safety, use of drugs, behavior in schools, family and community.[7] Another study done in Karachi assessed health literacy using Health Literacy Survey Questionnaire (HLS-Asia-Q) and reported low levels of literacy.[8] In Rawalpindi, health literacy levels were measured using a validated tool designed by European Consortium and was found to be low.[9] However to our best knowledge, no study was found published on validation of health literacy questionnaires or adaptation of any valid tool with local context. Our objective is to adapt HL-SF12 Tool for measurement of Health Literacy regarding disease prevention, health care and health promotion in patients visiting tertiary care hospital, Rawalpindi, Pakistan. This tool is validated in many countries and is a highly reliable tool. It has been adapted in other languages also. This study aims to adapt this tool in Urdu language and provide researchers a validated tool for measuring health literacy levels for Pakistani population speaking Urdu. This will help acquiring epidemiological information related to health literacy in Pakistan and help in planning strategies for improving health literacy which is important to reduce the burden of communicable and non-communicable diseases.

MATERIALS AND METHODS

A cross sectional study was conducted in year 2018 in a period of four months from March to June to assess health literacy levels in patients visiting medical outdoor department of three tertiary hospitals. Current study conducted in 2021 was another analysis of this previously published larger study.[9]

Patients visiting medical Outdoor Patients Department (OPD) and medical emergency departments of three tertiary care hospitals were included in the study. Sample size was 450 patients in this study based on the number of patients available during one week of data collection. This sample size was sufficient as the minimum sample size requirement for factor analysis is 20 subjects per variable. We had 12 variables in our questionnaire and so minimum sample size required was 240. Patients were selected from OPD and emergency department using purposive sampling technique. Patients were included in sample if they were adults, of either gender, clinically stable patients, and able to communicate in Urdu language. Patients were excluded from sample if they were incapable of providing informed consent.

Data collection procedure: A pre-validated questionnaire[10] was adapted to collect information regarding health literacy of patients after taking permission from developers of this tool. The questionnaire included 12 questions from a short version of health literacy questionnaire designed and validated by European Consortium under European Health Literacy (HLS-EU) project.[9] We translated the 12 item questionnaire (more detail of translation, back translation) into Urdu and pilot tested it among 50 patients. Face validity of final questionnaire was assessed by 5 persons resembling target population. For assessing content validity, questionnaire was sent to 7 public health experts and their opinions were taken. These experts belonged to different institutes and all had more than three years' experience in public health. The panel of experts determined whether the contents of the questionnaire were relevant to the conceptual framework and the local context. Reliability of this translated questionnaire was determined by calculating Cronbach's Alpha in SPSS, which came out to be 0.806, showing that the tool was highly reliable. Therefore, questionnaire was approved for final study. The 12 questions included in it were related to assessment of health literacy levels in three domains, including health promotion, disease prevention and health care. Patients were asked questions to assess their ability to 'access', 'understand' and 'use' health related information in these three domains of health. Data was collected from the patients by trained data collectors and answers were recorded on a Likert scale from very easy to very difficult. Informed consent was taken from the patients before their interview. Confidentiality of their data was ensured.

Statistical analysis: The data was entered and analyzed using SPSS version 21. Data from pilot study was not included in the final analysis. Data was analyzed by exploratory factor analysis (EFA), internal consistency analysis. Principal component analysis was run in SPSS for confirming constructs in adapted questionnaire. KMO and Bartlett's test was performed and orthogonal rotation was used. KMO value >0.6 was considered acceptable. Components were extracted based on Eigen value >1. Items were grouped in a component based on loading in component matrix. For construct validity, convergent validity was assessed based on correlation >0.5. Internal consistency of items was assessed by calculating Cronbach alpha. Acceptable level of cronbach was 0.7.

RESULTS

A total of 450 participants gave consent to fill data. The mean age of 450 respondents was 37.6 years (SD + 13.1Years). Majority respondents had 1-10 years of education. Socio-demographic characteristics have been summarized in table 1.

Table No.1: Socio-demographic characteristics of respondents (n=450)

Characteristics		Findings*
Age in years		37.6 + 13.1
Gender	Male	195 (43.3%)
Employment	Employed	202 (44.9%)
	Unemployed	242 (53.8%)
	Student	5 (1.1%)
	Retired	1 (0.2%)
Nature of job	Business	38 (21.1%)
	Govt. job	19 (10.6%)
	Private job	77 (42.8%)
	Related to health	0 (0.0%)
	Education	31 (17.2%)
	Commerce	2 (1.1%)
	Any other	13 (7.2%)
Educational Status	Illiterate	16 (3.6%)
	1-10 years of education	191 (42.5%)
	>10-12 years of education	106 (23.6%)
	13-16 years of education	122 (27.2%)
	> 16 years of education	13 (2.9%)
	7 years of education	1 (0.2%)
Monthly income in Rupees	< 10,000	129 (30.4%)
	10,000-20,000	149 (35.1%)
	>20,000-30,000	92 (21.6%)
	>30,000-40,000	34 (8.0%)
	>40,000-50,000	7 (1.6%)
	>50,000	14 (3.3%)
Watch health related programs on TV	Never	169 (37.6%)
	Often	240 (53.3%)
	Mostly	41 (9.1%)

*Findings are mean +SD or count (percent) as applicable.

HLQ by European Consortium was translated into Urdu language with 12 questions for adaptation with local context. This tool's content validity was assessed by taking feedback from 7 experts. They all considered questions relevant and appropriate to assess health literacy. One expert advised some change in order that was not considered feasible.

Factor analysis was performed on data for arranging items under constructs using principal component analysis. KMO value was >0.6 and considered acceptable. Three components were extracted based on Eigen value >1. Items were identified based on their loading on one construct as shown in table 2. Items with higher commonality were considered relevant to one construct and were arranged under that construct as shown in table 3.

One item related to joining sports club was arranged under health promotion construct in original HL-SF-12. Whereas in our factor analysis results, this item was found to have higher commonality with construct of disease prevention and was therefore considered an item under that component (table 3).

Construct validity assessed by convergent validity was fulfilled by correlations between items in one construct and items were found to be having high correlations of >0.5 for all items. Only one item "find information on how to manage mental health problems" had <0.5 correlation with its construct of disease prevention.

Internal consistency of each component's items were assessed with Cronbach alpha that came out to be more than 0.7 and was considered reliable (refer to table 4). Cronbach alpha of all 12 items in questionnaire was 0.882 and thus found to be highly reliable.

Table No.2: Items loading on constructs

Items		Constructs*		
		Disease Prevention	Health care	Health promotion
1	To find information on treatments of illnesses that concern you?		.848	
2	To understand the leaflets that come with your medicine?		.738	
3	To judge the advantages and disadvantages of different treatment options?		.810	
4	To call an ambulance in an emergency?		.634	
5	To find information on how to manage mental health problems like stress or depression?	.457	.375	
6	To understand why you need health screenings (such as breast exam, blood sugar test, blood pressure)?	.808		
7	To decide how you can protect yourself from illness based on advice from family and friends?	.739	-.106	
8	To assess the need of vaccination	.726		-.148
9	To find out about activities (such as meditation, exercise, walking, Pilates etc.) that are good for your mental well-being?	.324		-.653
10	To understand information in the media (such as Internet, newspaper, magazines) on how to get healthier?		.189	-.840
11	To judge which everyday behavior (such as drinking and eating habits, exercise etc.) is related to your health?			-.860
12	To join a sports club or exercise class if you want to?	.589	.259	.174

*Constructs extracted by Principal Component analysis using Oblique rotation

Table No.3: Items relevance to all three constructs

Health care	Disease Prevention	Health promotion
1. To find information on treatments of illnesses that concern you? 2. To understand the leaflets that come with your medicine? 3. To judge the advantages and disadvantages of different treatment options? 4. To call an ambulance in an emergency?	1. To find information on how to manage mental health problems like stress or depression? 2. To understand why you need health screenings (such as breast exam, blood sugar test, blood pressure)? 3. To decide how you can protect yourself from illness based on advice from family and friends? 4. To assess the need of vaccination 5. To join a sports club or exercise class if you want to?	1. To find out about activities (such as meditation, exercise, walking, Pilates etc.) that are good for your mental well-being? 2. To understand information in the media (such as Internet, newspaper, magazines) on how to get healthier? 3. To judge which everyday behavior (such as drinking and eating habits, exercise etc.) is related to your health?

Table 4: Reliability coefficient

Domain	Cronbach alpha
Health care	0.806
Disease prevention	0.789
Health promotion	0.819

HL-SF12 questionnaire translated and adapted in Urdu has been added in supplemental section.

DISCUSSION

Health literacy remains a confusing concept and its measurement is not done in Pakistan to our best knowledge. The current lack of consensus of measurement of health literacy needed to be overcome in our setting.[11] This study aims to fill this gap by adapting a pre-validated health literacy questionnaire with local context. The main findings were extraction of three components that were in line with the components as in original questionnaire. They were named as health care, disease prevention and health promotion. Internal consistency of items was moderately high. Results of a European study revealed that patients' health literacy assessed with the HL-SF12 was shown with high internal consistency (Cronbach $\alpha = .87$), and moderately correlated with the single-item from Chew's Set of Brief Health Literacy Question, with satisfactory item-scale convergent validity (item-scale correlation $\geq .40$).[12]

Items retained in our questionnaire were related to information processing stages of health. One item for each stage of health care information processing (access, understanding, appraise, apply) was included. One aspect for understanding disease prevention, two items for accessing disease prevention information and one for applying it were included. Regarding health promotion, one item for each aspect (access, understand, appraise) was included. This totaled as 12 items in questionnaire. Comprehensive tool by European Consortium was finalized with 47 items in total. This included three to five items for each stage of information processing in the three domains.[13] In contrast with EU questionnaire, in our study one item regarding joining a sports club was found to have low commonality with a single construct. This difference maybe because in Pakistani culture sports is not considered important for health.

This study used a robust statistical approach for assessing validity of an adapted questionnaire. Sample size was sufficient. Data collectors were trained well and a pilot study was also done to check the efficacy of questionnaire. However, there were a few limitations. Correlation analysis for comparing scores on adapted questionnaire and gold standard was not done. Content analysis feedback was also not adequately incorporated. We advocate for more research in literacy and validating tools by translating in other local languages in Pakistan. Meanwhile, strategies for enhancing health literacy should be used. Nejatian recommended that ability to recognize disorders, knowledge of self-treatment and knowledge of risk factors and causes should also be included while measuring health literacy.[14] These items can be added if further adaption of this tool is to be considered.

CONCLUSION

The adapted HL-SF12 was a valid and easy to use tool for assessing patients' health literacy in the hospitals to facilitate healthcare providers in enhancing patients' health literacy and healthcare qualities. This can be used by researchers in Pakistan for conducting more surveys to identify gaps. However, it should be adapted in other languages in Pakistan also.

Author's Contribution:

Concept & Design of Study:	Bushra Anwar
Drafting:	Aashi Ahmed, Nadia Nisar
Data Analysis:	Saima Omair, Salma Ambreen, Bilal Ahmed
Revisiting Critically:	Bushra Anwar, Aashi Ahmed
Final Approval of version:	Bushra Anwar

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Cąllşkan C, Üner S. Disaster Literacy and Public Health: A Systematic Review and Integration of Definitions and Models. Disaster Med Public Health Prep. Published online 2020. doi:10.1017/dmp.2020.100.
2. Intarakamhang U, Macaskill A. Effectiveness of a health literacy intervention based on transformative learning and incorporating positive psychology on health behavior and well-being of Thai families with NCDs risk. J Public Health Res 2021 May 26. doi: 10.4081/jphr.2021.1935. Epub ahead of print. PMID: 34092070.
3. Zhang NJ, Terry A, McHorney CA. Impact of Health Literacy on Medication Adherence: A Systematic Review and Meta-analysis. Ann Pharmacother 2014;48(6):741-751.
4. HLS-EU-Consortium. HLS-EU-Q Measurement of Health Literacy in Europe: HLS-EU-Q47; HLS-EU-Q16; and HLS-EU-Q86. Exec Agency Heal Consum. Published Online 2012:1-14.
5. Pelikan JM, Ganahl K. Measuring Health Literacy in General Populations: Primary Findings from the HLS-EU Consortium's Health Literacy Assessment Effort. Stud Health Technol Inform 2017;240: 34-59.
6. Sabzwari SR. Short Review Health literacy in Pakistan : Exploring new ways of addressing an old challenge Present State of Healthcare in Pakistan. J Pak Med Assoc 2017;67(12):1901-1904.
7. Sulehri MA, Anwar R, Madiha AS. Role of health literacy through schools in achievement of health education and public health promotion in Pakistan. J Sharif Med Dent Coll 2016;2(01):17-21.
8. Ahmed W, Shaikh ZN, Soomro JA, Qazi HA, Soomro AK. Assessment of health literacy in adult population of Karachi: a preliminary investigation for concept-based evidence. Int J Heal Promot Educ 2018;56(2):95-104.
9. Ahmed A, Anwar B, Qureshi M, Asim M, Nisar N. Assessment of Health literacy and its determinants in patients visiting tertiary care hospital, Rawalpindi, Pakistan. Pak J Public Health.2020;10(4), 220-225.
10. Conceptual based short-form health literacy questionnaire (HL-SF12):12.
11. Jabeen R, Rehman M, Masood S, Mahmood H, Mashhadi SF. Assessment of functional health literacy among adolescents of model schools of Islamabad. Pak Armed Forces Med J 2018;68(3):545-49.
12. Duong T Van, Chang PWS, Yang SH, et al. A New Comprehensive Short-form Health Literacy Survey Tool for Patients in General. Asian Nurs Res (Korean Soc Nurs Sci) 2017;11(1):30-35.
13. Health Literacy Consortium. Health Literacy Questionnaire. Published online 2015:1-2.
14. Nejatian M, Tehrani H, Momeniyan V, Jafari A. A modified version of the mental health literacy scale (MHLS) in Iranian people. BMC Psychiatr 2021; (1):53.

Original Article

Histopathology of Corona virus

Clinical Characteristics and Histopathology of Corona Virus Disease 2020

Momina Khadija Abbasi[1], Nabeela Naeem[1], Shameela Majeed[1], Mehreen Fatima[3], Amatul Naval[1] and Anum Ashfaq[2]

ABSTRACT

Objective: To investigate the clinical and histopathological characteristics of corona virus disease.
Study Design: Systamatic Review
Place and Duration of Study: This study was conducted at the Watim Medical and Dental College from Jan 2021 to June 2021.
Materials and Methods: All the articles published in 2020 at Google Scholar and PubMed were searched from to gather the information about the clinical and histopathological characteristics of corona virus disease. The articles published in English language only were included in this study. The terms like "clinical features of COVID-19", "COVID-19", "Histopathology of corona virus" and "Histology of COVID-19" were searched. I^2 and Egger's test was used to analyze the data about the clinical characteristics of the patients.
Results: The most common comorbidities related to COVID-19 are hypertension in 16 % cases and cardiovascular and cerebrovascular diseases in 12 % of the cases. The histopathological changes were most evident in the lungs. According to the percentage the most common lungs findings were congestion and diffused alveolar damage with 97.8 %. Corona virus disease also effects other organs and systems like CVS; myocardial hypertension, nervous system; hypoxic injury, digestive system; segmental dilatation and stenosis, liver; steatosis, kidney; acute tubular injury, immune system; coagulation abnormalities among many other.
Conclusion: TMultiple dysfunction caused by corona virus disease can occur due one of the following reasons: to direct viral attack, systemic inflammation, injury to the immune system or shock.
Key Words: COVID-19, Clinical features, Histopathology, Histopathological features, corona virus disease.

Citation of article: Abbasi MK, Naeem N, Majeed S, Fatima M, Naval A, Ashfaq A. Clinical Characteristics and Histopathology of Corona virus Disease 2020. Med Forum 2021;32(10):30-34.

INTRODUCTION

The COVID-19 virus that causes the corona virus disease was first identified in China, Wuhan, in December of 2019. This variant was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV–2). This virus effected the people worldwide to such an extent that it was declared pandemic by World Health Organization [1]. Currently this virus has caused almost 4.3 million deaths worldwide.
We had encountered the virus of this family previously also. In 2002, SARS-CoV caused an outbreak and infected over 8 thousand people[2].

[1.] Department of Pathology / Community Dentistry[2], Watim Medical and Dental College, Rawalpindi.
[3.] Department of Pathology, Rawalpindi Medical University, Rawalpindi.

Correspondence: Dr. Momina Khadija Abbasi, Assistant Professor of Pathology, Watim Medical and Dental College, Rawalpindi.
Contact No: 0300-9558661
Email: mominaabbasi@hotmail.com

Received: July, 2021
Accepted: August, 2021
Printed: October, 2021

Then in 2012, MERS-CoV cause another outbreak [3]. But the outbreak of 2019 has been more severe and dangerous than the previous two outbreaks. This variant of the corona virus is highly contagious and difficult to deal with [4]. It rapidly spreads from the infected person to the non-infected and increases the number of infected people further [5].
The research on the clinical features of this virus is in progress. In one of such researches, meta-analysis was done to sum up the clinical features of COVID-19[6]. This study reported that the most common symptoms of COVID-19 were fever, myalgia, sore throat and fatigue. The case fatality rate was 4.3 %. This study also reported 96.6 % prevalence of abnormal chest CT scan.[6] Some of the studies indicated that the geographical region can cause a difference in the clinical outcomes of the COVID-19 virus. One of the study reported that the patients in Wuhan endured more severe illness and abnormalities than the patients outside Wuhan. [7]
On the other hand, the histopathological features of this virus are also not fully known yet. This is because the autopsies and biopsies of the cases of COVID-19 patients are not sufficient. Even though the clinical features of the disease shows that it mainly effects the

lungs and the respiratory tract, there are indications present that this virus can cause multiple organ dysfunction which can then cause death of the patient. [8]
In the light of the above mentioned information, it is important that we investigate the clinical and histopathological characteristics of corona virus disease to treat and control it in a better way.

MATERIALS AND METHODS

Google Scholar and PubMed were searched to gather the information about the clinical and histopathological characteristics of corona virus disease. The articles published in English language only were included in this study. The terms like "clinical features of COVID-19", "COVID-19", "Histopathology of corona virus" and "Histology of COVID-19" were searched. I^2 test was used to analyze the heterogeneity of different studies related to the clinical features of COVID-19. 25 % value meant low heterogeneity, 50 % meant moderate heterogeneity and 75% meant high heterogeneity. If the heterogeneity was more than 75%, subgroup analysis was done. Age, region, sex and comorbidity variables were included in subgroup analysis. Egger's test was used to analyze the publication bias, if more than three studies are used to analyze the data related to the clinical characteristics. Histopathological features were observed after either autopsy or biopsy of the COVID-19 patient.

RESULTS

In this study, 26 articles with the total number of 2100 patients were included. 1100 were male and 1000 were females. 89 % of the patients had fever, 69 % had non-productive cough and 35 % had fatigue.

Table No.1: Analysis of the clinical characteristics of corona virus disease

Clinical characteristic	Prevalence %	I^2 %	Egger's test
Fever	89 %	96 %	< 0.001
Non-productive cough	69 %	80 %	0.147
Fatigue	35 %	86 %	0.971
Myalgia	29 %	90 %	0.008
Productive cough	27 %	92 %	0.561
Dyspnea	25 %	84 %	0.158
Chills	15.5 %	76 %	0.396
Chest pain	15 %	89 %	0.155
Headache	14.8 %	74 %	0.452
Sore throat	13.4 %	67 %	0.558
Diarrhea	9.5 %	83 %	0.006
Dizziness	8.7 %	51 %	0.239
Nausea / vomiting	4.7 %	49 %	0.873
Rhinorrhea	4.6 %	0 %	0.025
Hemoptysis	3 %	64 %	0.047
Nasal congestion	2.8 %	3 %	0.228

Myalgia was present in 29 % of the patients, dyspnea in 25 % of the patients, chest pain in 15 % patients, chills in 15.5 % patients, headache in 14.8 % patients, sore throat in 13.4 % patients, productive cough in 27 % patients, dizziness in 8.7 % patients, diarrhea in 9.5 % patients, rhinorrhea in 4.6 % patients, nausea/ vomiting in 4.7 % patients, hemoptysis in 3 % patients and nasal congestion in 2.8 % patients. This analysis of the clinical characteristics of corona virus disease is shown in Table 1.
Table 1 also showed the results of Egger's test. Publication bias was present in fever, diarrhea, hemoptysis, myalgia and rhinorrhea.
The most common comorbidities related to COVID-19 are hypertension in 16 % cases and cardiovascular and cerebrovascular diseases in 12 % of the cases. Diabetes mellitus was present in 10 % of the patients, infections like hepatitis and HIV in 1.7 % of the patient, cancer in 1.7 % of the patients, respiratory disorders in 1.6 % of the patients, renal disorders in 0.7 % of the patients and immunodeficiency disorders in 0.02 % of the patients. These results are shown in Table 2.

Table No.2: Comorbidities related to corona virus disease

Comorbidities	Percentage
Hypertension	16 %
Cardiovascular and Cerebrovascular diseases	12 %
Diabetes mellitus	10 %
Infections i.e. hepatitis	1.7 %
Cancer	1.7 %
Respiratory disorders	1.6 %
Renal disorders	0.7 %
Immunodeficiency disorders	0.02 %

Table 3 shows the histopathological finding in lungs. Lungs are most commonly affected organ in case of corona virus disease [8]. This table 3 shows that congestion was described in 97.8 % patients, diffused alveolar damage was described in 97.8 % patients, microthrombi in 82.6 % patients, pneumocyte changes in 95.6 % patients, superimposed pneumonia in 91.3 % patients, vasculitis in 60.9 % patients, paucity of lymphoid cells in 69.6 % patients and proteinaceous exudate in 32.6 % patients. According to the percentage the most common lungs finding is congestion and diffused alveolar damage with 97.8 %.

Table No.3: Histopathological finding in lungs

Histological changes	Percentage
Congestion	97.8
Diffuse alveolar damage	97.8
Microthrombi	82.6
Pneumocyte change	95.6
Superimposed pneumonia	91.3
Vasculitis	60.9
Paucity of lymphoid cells	69.6
Proteinaceous exudate	32.6

Table 4 shows the histopathological findings in different organs and systems of the human body. Diffused alveolar damage is the most common histopathology of lungs in corona virus disease. Histological observation in many studies have reported vascular congestion, diffused alveolar damage, microthrombi, pulmonary embolism, mononuclear inflammation and pneumonia[9-16]. Effects on nervous system included mild hypoxic injury[14]. Liver's pathology included steatosis, nuclear granulation, mild lobular mononuclear inflammation, mild lobular and portal activity and sinusoidal dilatation[10,12,13,16]. Myocardial hypertension, fibrosis, mild mononuclear inflammation and edema was observed in the histology of cardiovascular system[10,14,16]. Effects on the digestive system included segmental stenosis and dilatation, focal/mild edematous mucosa infiltrated by mononuclear inflammatory cells, ACE2 receptors down regulation and esophageal mucous lesion [17, 18]. Immune system also showed histopathological changes i.e. T cell lymphopenia, increased neutrophil- lymphocyte ratio, coagulation abnormalities, high level of cytokines and tissue infiltration by macrophages[19-21]. Corona virus effected the kidneys in many ways: diffuse proximal tubular injury, up regulation of ACE2 receptors, collapsing glumerulopathy, focal interstitial mononuclear inflammation, loss of brush borders, hemosiderin granules, distal tubules and collecting ducts cellular swelling, cystic tubules, fibrosis, tubular atrophy, necrosis, microthrombi, epithelial detachment and pigmented casts.

Table No.4 Histopathological findings in different organs and systems

System	Reported findings	Source
Respiratory	Vascular congestion	16, 12, 15, 9, 14, 10, 13
	Diffused alveolar damage	16, 12, 15, 9, 14, 10, 13
	Microthrombi	16, 12, 15, 14
	Pulmonary embolism	16, 14
	Mild mononuclear inflammation	16, 12, 15, 9, 14, 10, 13
	No mucus plug	16, 12, 15, 9, 14, 10, 13
	Secondary bacterial pneumonia	16, 12, 14, 10
	No eosinophilic or neutrophilic infiltration	16, 12, 15, 9, 14, 10, 13
Nervous system	No inflammation	14
	Mild hypoxic injury	14
	No necrosis	14
Liver	Steatosis	16, 12, 10, 13
	Nuclear granulation	10
	Mild lobular mononuclear inflammation	10
	Mild lobular and portal activity	13
	Sinusoidal dilatation	10
	Myocardial hypertension	16, 14, 10
Cardiovascular system	Fibrosis	10
	Mild or absent mononuclear inflammation	16, 12, 13
	Edema	10
Digestive system	Segmental stenosis and dilatation	18
	Focal/mild edematous mucosa infiltrated by mononuclear inflammatory cells	17
	ACE2 receptors down regulation	17
	Esophageal mucous lesion	17
Immune system	T cell lymphopenia	20, 21
	Increased neutrophil-lymphocyte ratio	20, 21
	Coagulation abnormalities	20, 21
	High level of cytokines	19, 20, 21
	Tissue infiltration by macrophages	20, 21
Kidney	Diffuse proximal tubular injury	14, 22, 23
	Up regulation of ACE2 receptors	23
	Collapsing glumerulopathy	22
	Focal interstitial mononuclear inflammation	14, 22, 23
	Loss of brush borders	23
	Hemosiderin granules	23
	Distal tubules and collecting ducts cellular swelling	23
	Cystic tubules	14, 22
	Interstitial edema or fibrosis	14, 22
	Tubular atrophy	14
	Acute pyelonephritis	23
	Necrosis	23
	Microthrombi	14, 23
	Epithelial detachment	23
	Pigmented casts	23
System	Reported findings	Source
Respiratory	Vascular congestion	16, 12, 15, 9, 14, 10, 13

DISCUSSION

In this study, the clinical characteristics of corona virus disease included fever, non-productive cough, fatigue, myalgia, productive cough, dyspnea, chills, chest pain, headache, sore throat, diarrhea, dizziness, nausea / vomiting, rhinorrhea, hemoptysis and nasal congestion. The major symptoms were fever, non-productive cough and fatigue. In another study, the major symptoms of corona virus disease were fever, cough and dyspnea. One of the study reported that fever, cough and vomiting were the most common clinical characteristics.

The most common comorbidities related to COVID-19 were hypertension and cardiovascular and cerebrovascular diseases in our study. Another study reported hypertension, diabetes mellitus and cardiovascular disorders as some of the risk factors of

corona virus disease. A different study also established that comorbidities i.e. hypertension, diabetes mellitus, increased the risk of severe illness due to COVID-19 virus.

Our study also established that this virus induced histological changes in lungs, digestive system, cardiovascular system, respiratory system, liver, kidneys and nervous system. The histopathological changes were most evident in the lungs. These results are similar to some of the other studies[8].

In our study the microthrombi was majorly observed in kidney and lungs. This is similar to many other studies[24-26]. This indicates that the COVID virus attacks endothelial cells more than other cells. It can cause complications like hypoxemia.

The main strength of this study is that it provides a comprehensive review of clinical and histopathological characteristics of corona virus disease. At the same time, this study has some limitations. Details of the clinical characteristics and histopathological findings is not given. The prevalence of histopathological findings is also not included in this study. Duration of illness and autopsy and biopsy details are also absent in this study.

As the pandemic caused by the corona virus disease continues, it is very import to understand its clinical and histopathological features to understand it in a better way. Doing research on this virus is our only solution right now.

CONCLUSION

The most common symptoms of COVID-19 are fever, non-productive cough, fatigue, myalgia and dyspnea among many other. Patients who suffer from hypertension, cardiovascular and cerebrovascular diseases, diabetes mellitus, infections, cancer, respiratory disorders, renal disorders and immunodeficiency disorders are at higher risk of COVID-19. The most common histopathological characteristic of corona virus disease is mild mononuclear inflammatory cell infiltration. In lungs and kidneys microthrombi was majorly observed. Diffused alveolar damage is the most common histopathology of lungs in corona virus disease. Multiple dysfunction caused by corona virus disease can occur due one of the following reasons: to direct viral attack, systemic inflammation, injury to the immune system or shock.

Author's Contribution:

Concept & Design of Study:	Momina Khadija Abbasi
Drafting:	Nabeela Naeem, Shameela Majeed
Data Analysis:	Mehreen Fatima, Amatul Naval, Anum Ashfaq
Revisiting Critically:	Momina Khadija Abbasi, Nabeela Naeem
Final Approval of version:	Momina Khadija Abbasi

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Omrani-Nava, V, Maleki I, Ahmadi A, Moosazadeh M, Hedayatizadeh-Omran A, Roozbeh F, et al. Evaluation of hepatic enzymes changes and association with prognosis in COVID-19 patients. Hepatitis Monthly 2020;20(4).
2. How SARS. terrified the world in 2003, infecting more than 8,000 people and killing 774. Business Insider 2020;20.
3. World Health Organization. Middle East respiratory syndrome coronavirus (MERS-CoV) 2019.
4. Negahdaripour M. The battle against COVID-19: where do we stand now?. Iranian J Med Sci 2020;45(2):81.
5. Chan JF, Yuan S, Kok KH, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet 2020; 395 :514–23 .
6. Sun P, Qie S, Liu Z, et al. Clinical characteristics of hospitalized patients with SARS-CoV-2 infection: a single arm meta-analysis. J Med Virol 2020 doi: 10. 1002/jmv.25735.
7. Xu XW, Wu XX, Jiang XG, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retro- spective case series. BMJ 2020;368: m606.
8. Al Nemer A. Histopathologic and autopsy findings in patients diagnosed with coronavirus disease 2019 (COVID-19): what we know so far based on correlation with clinical, morphologic and pathobiological aspects. Advances in Anatomic Pathol 2020;27(6):363-70.
9. Tian S, Hu W, Niu L, et al. Pulmonary pathology of early phase 2019 novel coronavirus (COVID-19) pneumonia in two patients with lung cancer. J Thorac Oncol 2020;15:700–704.
10. Tian S, Xiong Y, Liu H, et al. Pathological study of the 2019 novel coronavirus disease (COVID-19) through postmortem core biopsies. Mod Pathol 2020;33:1007–1014.
11. Zeng Z, Xu L, Xie XY, et al. Pulmonary pathology of early phase COVID-19 pneumonia in a patient with a benign lung lesion. Histopathol 2020.
12. Barton LM, Duval EJ, Stroberg E, et al. COVID-19 autopsies, Oklahoma, USA. Am J Clin Pathol 2020;153:725–733.
13. Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory

distress syndrome. Lancet Respir Med 2020;8: 420–422.
14. Menter T, Haslbauer JD, Nienhold R, et al. Post-mortem examination of COVID19 patients reveals diffuse alveolar damage with severe capillary congestion and variegated findings of lungs and other organs suggesting vascular dysfunction. Histopathol 2020.
15. Yao XH, Li TY, He ZC, et al. A pathological report of three COVID-19 cases by minimally invasive auyopsies. Zhonghua Bing Li Xue Za Zhi 2020;49:411–417.
16. Wichmann D, Sperhake JP, Lütgehetmann M, et al. Autopsy findings and venous thromboembolism in patients with COVID-19. Ann Intern Med 2020; M20–M2003.
17. Xiao F, Tang M, Zheng X, et al. Evidence for gastrointestinal infection of SARS-CoV-2. Gastroenterol 2020;158:1831.e3–1833.e3.
18. Liu Q, Wang RS, Qu GQ, et al. Gross examination report of a COVID-19 death autopsy. Fa Yi Xue Za Zhi 2020;36:21–23.
19. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497–506.
20. Wu C, Chen X, Cai Y, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med 2020:e200994.
21. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054–1062.
22. Nasr SH, Kopp JB. COVID-19-associated collapsing glomerulopathy: an emerging entity. Kidney Int Rep 2020;5:759–761.
23. Su H, Yang M, Wan C, et al. Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China. Kidney Int 2020;98:219–227.
24. Ackermann M, Verleden SE, Kuehnel M, et al. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in Covid-19 N Engl J Med 2020;383(2):120-128.
25. Antinori S, Rech R, Galimberti L, et al. Invasive pulmonary aspergillosis complicating SARS-CoV-2 pneumonia: a diagnostic challenge [Published online ahead of print May 26, 2020] Travel Med Infect Dis 2020;10.1016/j.tmaid.2020.101752.
26. Carsana L, Sonzogni A, Nasr A, et al. Pulmonary post-mortem findings in a series of COVID-19 cases from northern Italy: a two-centre descriptive study Lancet Infect Dis 2020;20(10):1135-1140.

Original Article

Effect of Cataract Surgery (Phaco and Manual Small Incision Cataract Surgery) on the Corneal Endothelium

Darikta Dargahi Shaikh[1], Rizwana Dargahi Shaikh[2], Fayaz Ali Kalhoro[2], Allah Dino Tunio[2] and Muhammad Yaqoob Shahani[3]

ABSTRACT

Objective: This study will investigate the relationship between phacoemulsification (active removal of cataracts) and manual tiny incision (passive removal of cataracts) on the corneal endothelial cell count.

Study Design: Prospective Comparative study

Place and Duration of Study: This study was conducted at the Department of Ophthalmology, Chandka Medical College & Shaheed Mohtarma Benazir Bhutto Medical University Larkana, from 1st August 2020 to 30th April 2021.

Materials and Methods: The researchers investigated the effect of phacoemulsification, SICS, and cataract surgery on 100 patients who underwent this procedure using manual small incision cataract surgery (SICS). In order to investigate the correlation between nuclear cataracts and senile cortical cataracts, participants age 30 to 70 years were enrolled. Approximately 70% of the surgeries done by a single surgeon were collected for the study. The data were analyzed in SPSS version 21.0

Results: Phacoemulsification was utilised on a total of 100 patients. In the case of the SICS method, 50 patients received phacoemulsification and 50 patients did not. Lower endothelial count loss was detected with manual SICS, with 22 eyes showing a count lossiofibetweeni100-500icells, and an increase of over 1500 cells was found in 8 eyes (4 eyes). was shown to be at 18% of endothelial cell loss with fewer than 100 endothelial cells lost (9 eyes). When looking at the data in phacoemulsification, it was revealed that theiendothelialicellicountilossiofiunderi100icellsiwas highest at 46% (23 eyes), and greater than 1500 cells was undetected in this study.

Conclusion: In this study, endothelial cell count loss after phacoemulsification surgery was found to be smaller than SICS. After phacoemulsification surgery was found to be super or to manual SICS because it prevented the endothelial cells from receiving extensive injury, which helped to ensure that patients immediately post-surgery would have a good BCVA, as opposed to a lesser-than-desired BCVA experienced by patients who received manual SICS.

Key Words: Corneal Endothelium, Manual Small Incision Cataract Surgery, Phacoemulsification

Citation of article: Shaikh DD, Shaikh RD, Kalhoro FA, Tunio AD, Shahani MY. Effect of Cataract Surgery (Phaco and Manual Small Incision Cataract Surgery) on the Corneal Endothelium. Med Forum 2021;32(10):35-38.

INTRODUCTION

[1.] Department of Ophthalmology, Chandka Medical College & Shaheed Mohtarma Benazir Bhutto Medical University, Larkana.
[2.] Department of Ophthalmology, Civil Hospital Larkana, Larkana.
[3.] Department of Anatomy, Liaquat University of Medical & Health Sciences, Jamshoro.

Correspondence: Dr. Muhammad Yaqoob Shahani, Senior Lecturer of Anatomy, Liaquat University of Medical & Health Sciences, Jamshoro.
Contact No: 033368506956
Email: muhammad.yaqoob@lumhs.edu.pk

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

The cornea is a transparent, avascular outermost layer of the eye which has further six layers namely the epithelium, bowman's membrane, stroma, pre-Descemet's layer, Descemet's membrane, and the endothelium[1].

Small-incision cataract surgery (SICS) is one of the cataract surgical techniques commonly used in developing countries[2]. It is a low-cost, small-incision form of extra capsular cataract extraction (ECCE)[2].

Finally, we expect that this corneal endothelial study aids us in choosing the most optimal extraction approach for Catatractous lens in order to provide good postoperative vision rehabilitation as discussed by our pioneer. 75% of the refractive power of the eye is provided by the cornea, yet to obtain clear vision, a highly transparent cornea is required. The corneal endothelium is a single layer of cells lining the inner surface of the cornea and is responsible for the normal, continuous function of the cornea. The endothelial cell

density in the typical cornea at birth is high.[7] Cell counts range from 1500 cells per millimetre to 3500 cells per mm.[7] To better understand the effects of phacoemulsification cataract surgery and manual small incision cataract surgery on the corneal endothelial cell count, we performed this research. Phacoemulsification outcomes play a critical role in our understanding of how phacoemulsification surgery affects the morphology and central corneal thickness of habitual corneal endothelial cells.

MATERIALS AND METHODS

The researchers carried out a prospective study of 100 patients who had cataract surgery done by SICS and phacoemulsification in Larkana, the city of Larkana, from August 1st, 2020 to April 30th, 2021. The research work done on surgeries performed by a single surgeon is taken as the study. Inclusion criteria include senile cortical cataract and nuclear cataract, which must occur in adults between the ages of 30 and 70. Any pre-existing corneal disease, any complicated cataracts, cataracts with glaucoma, posterior segment lesions, or systemic illness, and insufficiently consistent follow-up are all part of the exclusion criteria. Preoperative evaluation includes a detailed history and routine medical tests, such as measurement of the corrected distance visual acuity (BCVA) using a Snellen chart or an E-chart recording tension with a Schiotz tonometer assessing the patency of the duct, an A-scan, and calculation of IOL power using the SRK II formula.

Special surgical procedures: Before surgery, the use of tropicamide and 10% phenylephrine was done one hour before surgery, to promote adequate pupil dilation. It was employed in all instances of circumilbar anaesthesia. Digital compression was used to achieve anisometropia. A No.11 blade was used to cut a 1 mm wide linear incision that was positioned about 2 mm from the limbus. A fornix-based conjunctival flap was utilised in creating a 5.5 mm (phaco) or 6 mm (manual SICS) long sclera incision. A 1.5 mm-thick crescent blade was embedded into a clear cornea, forming a tunnel. To enter AC, they started out with a 3.2 mm keratome, and later expanded the size.[8] The following types of cataract surgery were used in manual small incision cataract surgery: 1)can opener capsulotomy, 2)continuous curvilinear capsulorhexis, and 3) 26G needle cystectomy. The nucleus was withdrawn with Vectis irrigating device after hydrodissection and hydraulic expression. Everything was done using viscous substances such as viscoelasticity enhancers. Simcoe cannula was used to aspirate the cortex. A 6 mm PMMA single-piece IOL was inserted into the capsular bag, and it was centred correctly. This established the anterior chamber and allowed the incision to close itself. During the surgery, a small (0.5mL) dose of dexamethasone was injected in the conjunctival sac, along with repositioning of the conjunctiva to the wound. After introduction into AC via a 3.2 mm keratome phaco probe, a lens entry procedure known as phacoemulsification was then used to reach the lens tissue. The soft cataracts were treated with phaco aspiration and in the other type of cataracts, the nucleus was emulsified with the divide and conquer technique. As the wound self-sealed, the AC had been formed. A injection of 0.5mL of dexamethasone 4 mg was performed through the conjunctiva.[9] They received topical steroids, antibiotic drops, and 1% cyclopentolate eye drops after the operation.[10] Patients were examined with a microscope that is able to visualise specular particles on the fourth postoperative day.[11] The V/A is ready to be recorded. The corneal endothelial count was taken. Using a specially prepared form, the findings were recorded and various variables were measured.

RESULTS

Table No.1: Frequency of Different Phaco Parameters (n = 100)

Phaco	Power %	Vacuum (mm/H)	Flow rate (cc/mt)
Trenching	70-80	50	10-20
Quadrant emulsification	50-60	200	25-30
Colour of Nucleus			
Grade	Colour of Nucleus	Number of Eyes	Percentage
Grade I	White or green and yellow	22i	22i
Grade II	Yellow	44	44
Grade III	Amber	22	22
Grade IV	Brown	0	0
MC	White	12	12
Age Group Vs. % of Cataract			
Grade of Nucleus	Number of Eyes		Percentage
I	2		4
II	18		36
III	20		40
Mature cataract	10		20
Endothelial Cell Count			
<100	23		46
100-500	15		30
500-1000	7		14
>1000	5		10
BCVA on Fourth Postoperative Day			
6/6	20		40
6/9	16		32
6/12	9		18
6/18	5		10

In the 20 eyes (40%) in which grade III cataracts were found, they were the most common. One of the commonest problems among the preoperative patients was rupture of the posterior capsule and premature entry, with frequency ofi4% and 6%, respectively. As the rating of nuclear sclerosis grew, the incidence of complications rose. In cases where endothelial cell count loss of between 100-500 cells occurred, 44% of the eyes showed a loss of between 100-500 cells, and in those with counts loss >1500 cells, 8% of the eyes had a loss of this amount (4 eyes). Decrease in the number of endothelial cells was reported to be 18% (9 eyes). Half of the 60 people who participated in the study had a corrected visual acuity of 6/96/18.

Nuclear sclerosis (Grade 2) was the most commonly performed cataract surgery in phacoemulsification surgery, with an incidence of 52 percent (26 eyes). Rupture of the posterior capsule is found to be the most prevalent complication, occurring in 10% of cases. Eighty-three percent of those who developed nuclear sclerosis had a loss of <100 endothelial cells, while the remaining 17% had a loss of >1500 endothelial cells. 72% of the participants saw that the cell density before and after phaco was significantly different, as shown by a p-value of <0.018 (5 percent level).

Table No.2: Frequency of Preoperative Complications (n = 100)

Preoperative Complications	Number of Eyes	Percentage
P.C.R.	2i	4i
Premature entry	3i	6i
Difficulty in delivering nucleus	2i	4i
Vitreous disturbance	5i	10i
Increased irritation	3i	6i
Increased phacoitime	3i	6i

DISCUSSION

In order to keep the cornea clear and dehydrated, the corneal endothelium is essential. When it comes to cataract surgery, some endothelial cell loss is unavoidable, although the amount depends on the surgical approach.[13–15] For diagnostic reasons, two key characteristics in the functional assessment of cornea are the thickness of the central cornea and the density of corneal endothelial cells. To compensate for lost cells, corneal endothelial cells use cell enlargement and cell spread to increase their size. This causes an overall drop in endothelial cell density, which may affect the cells' ability to perform their activities.[15,16]

There were 100 patients included in this study. One hundred and six of them were women, while the other forty-four were men. Between 30 and 70 years old was the average age of the patients that came to the clinic. A total of 52.18 years of patient experience were gathered to calculate the mean age. Using a S/L examination of the nucleus colour, the clinical hardness of the lens was determined.

50 individuals who had manual SICS had a self-sealing and suture less superior scleral incision and a superotemporal defect. When phaco surgery was performed on 50 patients, only 17 of those individuals had a superotemporal incision.[17]

Phaco Surgery: This operation was performed on 50 people. In total, there were 40 people, with 20 of them being men and 30 of them being women. People in the study ranged in age from thirty to seventy years old. In general, people were between the ages of 52 and 53. Two of the nuclear graders had fully developed cataracts, ranging in age from grades I-III.

Cataracts of grade II were the most common, with 26 of the eyes examined having this condition (52 percent). In all cases, the incision was linear and CCC was performed.

PC rupture, which occurred in 10% of patients, was the most common intraoperative complication. We counted the endothelial cells in all of the eyes with noncontact specular microscopy, and the average number of cells was 30. Endothelial cell count is shown in Table 5 for your convenience.

Researchers believe theiendothelialicellilossiofi500-1000ior more was caused by problems such PCR, longer phaco times, and more fluids in the AC (prolonged irrigation).[10]

Nearly half (46 percent) of patients who underwent phaco surgery had an endothelial loss of 100 cells or more.

Patients who underwent phaco surgery in the immediate post-operative period (4thPOD) had 6/6-6/9 vision in 36 of 50 eyes (72%), and the 'p-value for BCVA was not statistically significant.

MSICS (Multi-State Information and Communications Systems (manual small incision cataract surgery) This operation was performed on 50 people. In total, there were 42 individuals, with 22 being men and 28 being women. The patients' ages ranged from 35 to 70 years in this clinic. Among the participants, 55.58 years of age was found to be common. This group's nuclear classification ranged from I to III, with 10 people having MC.

Grade III cataract was the most common, with incisions and capsulorhexis extending continuously in 20 of the eyes (40 percent).[18]

In all eyes, an average of 30 endothelial cells were counted using non-contact specular microscopy.

In 23 (46%) of the eyes that underwent manual SICS tunnel surgery, an endothelial cell loss of 100-500 was discovered.[19]

Nine eyes (8 percent) had a cell loss of more than 1500 after non-phaco cataract surgery, while this incidence was very low after phaco surgery and the 'p-value was

statistically significant at the 1 percent level (p-value 0.001). Patients with reduced vision of 6/24-6/60 had a 40% recovery rate of improved vision of 6/6 and 6/9 after a few weeks following surgery. When looked at on a 1% scale, the p-value for BCVA was significant.

CONCLUSION

This study indicated that the loss of endothelial cells was less with phaco surgery than with manual SICS. An endothelial cell loss associated with phaco surgery was discovered in this study to be most often the result of intraoperative difficulties, such as post capsular rupture with vitreous disturbance, higher irrigation in the anterior chamber, and longer total phaco duration in a few patients.[20] The cornea's optical property can be preserved by protecting the endothelium and using good technique during the entire procedure, from incision to IOL implantation. Using phaco surgery instead of manual SICS resulted in less damage to the endothelial cells and, as a result, a higher BCVA immediately after the surgery, allowing patients to see more clearly sooner.

Author's Contribution:

Concept & Design of Study:	Darikta Dargahi Shaikh
Drafting:	Rizwana Dargahi Shaikh, Fayaz Ali Kalhoro
Data Analysis:	Allah Dino Tunio, Muhammad Yaqoob Shahani
Revisiting Critically:	Darikta Dargahi Shaikh, Rizwana Dargahi Shaikh
Final Approval of version:	Darikta Dargahi Shaikh

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Chauhan R, Rathi A, Chugh J, Bhutia T, Goel A. Comparative Study of Corneal Endothelial Cell Loss in Phacoemulsification and Manual Small Incision Cataract Surgery (MSICS) 2019;2.
2. Ahmed MS. Postoperative astigmatism after small-incision cataract surgery with sclera tunnel suturing and without scleral tunnel suturing: A comparative study. J Med Sci Res 2021;4(2):137.
3. Mazhar SA, Zahid S, Hanif J, Arshad MA, Iqbal RN. Mean Corneal Endothelial Cell Loss in Type 2 Diabetic Cataract Patients After Phaco-emulsification. Pakistan J Ophthalmol 2020;36(1).
4. Toygar O, Sizmaz S, Pelit A, Toygar B, Kiziloğlu ÖY, Akova Y. Central corneal thickness in type II diabetes mellitus: is it related to the severity of diabetic retinopathy? Turkish J Med Sci 2015;45(3):651–4.
5. Lee CM, Afshari NA. The global state of cataract blindness. Curr Opin Ophthalmol 2017;28(1): 98–103.
6. Rosado-Adames N, Afshari NA. The changing face of the corneal endothelium in cataract surgery. Curr Opin Ophthalmol 2012;23(1):3–6.
7. Kanski JJ, Bowling B. Clinical ophthalmology: a systematic approach. Elsevier Health Sciences; 2011.
8. Finkelstein E. Textbook of Phacoemulsification. Arch Ophthalmol 1990;108(5):652.
9. Legro MW. Quality of life and cataracts: a review of patient-centered studies of cataract surgery outcomes. Ophthalmic Surgery, Lasers Imaging Retin 1991;22(8):431–43.
10. Huq SMM, Vazeen M. Cataract surgery and phacoemulsification for the beginning surgeons. Author House; 2014.
11. Zetterström C, Laurell CG. Comparison of endothelial cell loss and phacoemulsification energy during endocapsular phacoemulsification surgery. J Cataract Refract Surg 1995;21(1):55–8.
12. Fernández-Muñoz E, Zamora-Ortiz R, Gonzalez-Salinas R. Endothelial cell density changes in diabetic and nondiabetic eyes undergoing phacoemulsification employing the phaco-chop technique. Int Ophthalmol 2019;39(8):1735–41.
13. Gogate P. Commentary: Corneal endothelial cell changes in diabetics versus age-group matched nondiabetics after manual small incision cataract surgery (SICS). Ind J Ophthalmol 2020;68(1):77.
14. Islam QU, Saeed MK, Mehboob MA. Age-related changes in corneal morphological characteristics of healthy Pakistani eyes. Saudi J Ophthalmol 2017;31(2):86–90.
15. Arıcı C, Arslan OS, Dikkaya F. Corneal endothelial cell density and morphology in healthy Turkish eyes. J Ophthalmol 2014;2014.
16. Ewete T, Ani EU, Alabi AS. Normal corneal endothelial cell density in Nigerians. Clin Ophthalmol (Auckland, NZ) 2016;10:497.
17. Arthur E, Sadik AA, Kumah D Ben, Osae EA, Mireku FA, Asiedu FY, et al. Postoperative corneal and surgically induced astigmatism following superior approach manual small incision cataract surgery in patients with preoperative against-the-rule astigmatism. J Ophthalmol 2016.
18. Gogate PM, Kulkarni SR, Krishnaiah S, Deshpande RD, Joshi SA, Palimkar A, et al. Safety and efficacy of phacoemulsification compared with manual small-incision cataract surgery by a randomized controlled clinical trial: six-week results. Ophthalmol 2005;112(5):869–74.
19. Sugar J, Mitchelson J, Kraff M. The effect of phacoemulsification on corneal endothelial cell density. Arch Ophthalmol 1978;96(3):446–8.
20. Bourne RRA, Minassian DC, Dart JKG, Rosen P, Kaushal S, Wingate N. Effect of cataract surgery on the corneal endothelium: modern phacoemulsification compared with extracapsular cataract surgery. Ophthalmol 2004;111(4):679–85.

Original Article

Optimal Hematocrit during Cardiopulmonary Bypass to Minimize Post-Operative Renal Dysfunction in Cardiac Surgery

Abdul Wasay, Muhammad Asad Bilal Awan, Asmatullah Achakzai, Muhammad Mansoor, Muhammad Ishaq Khan and Muhammad Arif

ABSTRACT

Objective: The aim of our study is to identify the ideal hematocrit which must be maintained on CPB to minimize hemodilution induced renal dysfunction after cardiac surgery in our population.

Study Design: Prospective observational study.

Place and Duration of Study: This study was conducted at the Department of Cardiac surgery National Institute of Cardiovascular Diseases (NICVD) Karachi. Duration was 6 months from December 2020 to May 2021.

Materials and Methods: All patients with age between 18 and 80 years undergoing cardiac surgery(CABG, valvular, adult congenital) using CPB were included in study. Patients with preoperative renal failure ,Unstable hemodynamic state and Complex cardiac surgeries were excluded.

Patient's demographic data was obtained such as age (years), gender, height (cm), weight (kg), and BMI (kg/m^2). Hematocrit was recorded and all the patients were observed during their post-operative hospital stay and incidence of post-operative renal dysfunction was recorded. Data was entered and analysis using SPSS version-21.The receiver operating characteristic (ROC) curve analysis was performed to determine the optimal cutoff value of hematocrit. Two sided p-value of ≤ 0.05 was taken as criteria of statistical significance.

Results: Total number of patients were 259 which were included in study. In our study mean age was 50.79 ± 13.31 years and mean body mass index was 25.3 ± 5.1 kg/m^2. Preoperative mean creatinine was 0.9 ± 0.2 ng/dL.The mean cardiopulmonary bypass time was 120.3 ± 32.6 minutes. Mean hematocrit maintained on pump was 26 ± 3.7. Post operatively only 3(1.2%) patients developed renal dysfunction and mean post-operative creatinine was 1 ± 0.3 ng/dL. Overall mortality was 1.2% (3). The area under the curve on ROC analysis was found to be 0.839 [0.691 to 0.986] and the optimal hematocrit level of 27.85 had sensitivity of 100% and specificity of 73% for the prediction of post-operative renal dysfunction.

Conclusion: Hematocrit during CPB affects the outcome after cardiac surgery. It has a direct effect on post-operative renal function. Further larger studies need to be carried out to find out the optimal hematocrit levels needed for best results in cardiac surgery patients.

Key Words: Hematocrit, CardioPumonary Bypass CPB, Renal Dysfunction

Citation of article: Wasay A, Awan MAB, Achakzai A, Mansoor M, Khan MI, Arif M. Optimal Hematocrit during Cardiopulmonary Bypass to Minimize Post-Operative Renal Dysfunction in Cardiac Surgery. Med Forum 2021;32(10):39-44.

INTRODUCTION

Cardiovascular diseases are the leading cause of death worldwide, with annual deaths of 17.9 million people. [1] Despite of recent advances in medical management and percutaneous interventions, many of these patients undergo open heart surgery using cardiopulmonary bypass. CPB is unique because blood exposed to foreign, non-endothelial surfaces is collected and continuously recirculated throughout the body. This contact with synthetic surfaces within the perfusion circuit, as well as open tissue surfaces within the wound trigger inflammatory response which initiates a powerful thrombotic stimulus and production, release and circulation of vasoactive and cytotoxic substances that affect every organ and tissue within the body.[2] Renal injury after CPB is one of the adverse outcome manifest as subclinical injury to established renal failure requiring dialysis.[3]

Renal blood and plasma flow, free water clearance, creatinine clearance and urine volume decreases without hemodilution.[4] Hemodilution dilutes plasma hemoglobin; improves flow to the outer renal cortex;

Department of Cardiac Surgery, NICVD, Karachi.

Correspondence: Muhammad Asad Bilal Awan, Associate Professor of Cardiac Surgery, NICVD, Karachi.
Contact No: 0300-8287242
Email: drasadawan@live.com

Received: June, 2021
Accepted: July, 2021
Printed: October, 2021

improves total renal blood flow; increases creatinine, electrolyte and water clearance; and increases glomerular filtration and urine volume.[5] Furthermore, hemodilution during CPB decreases chances of red blood cell injury[6] which is an independent cause of renal injury.[7] Hemodilution also reduces the risk of hemoglobin precipitation in renal tubules during extracorporeal perfusion.[8]

Hemodilution during CPB results in reduced oxygen carrying capacity of blood and therefore put kidney at risk of ischemic injury.[9] However, due to hemodilution blood viscosity decreases which results in increased blood flow in both micro and macrocirculation which compensates for the reduced oxygen carrying capacity.[10] However optimal hematocrict level below which further hemodilution causes reduced oxygen delivery to tissues is indeterminate. On the other hand increasesd blood flow increase microembolic load to the kidney during CPB and hence raises possibility of renal injury.[9]

The optimal level of hemodilution on CPB for open heart surgery patients is an important question that need careful assessment. Although it is a known fact that severe hemodilution increases the risk of adverse renal outcomes but on the other hand several above discussed benefits necessitates low hematocrict on CPB. The proposed nadir hematocrit necessary to prevent hemodilution-induced renal dysfunction differ greatly, and different values of 22%, 24%, and 26% have all been reported.[11-13] A considerable dispute is still present regarding the optimal level of hematocrict to be maintained on CPB to minimize renal injury.

MATERIALS AND METHODS

This prospective observational study was conducted at the Department of Cardiac surgery National Institute of Cardiovascular Diseases (NICVD) Karachi for 6 months from December 2020 to May 2021.

Sample size: A study conducted by Karkouti K et al. [9] reported that the adjusted odds ratio for acute renal failure necessitating dialysis support with severe hemodilution (nadir hematocrit concentration <21%) was 2.34, and for mild hemodilution (nadir hematocrit concentration >25%) it was 1.88 (95% confidence interval, 1.02-3.46). At 5% level of significance, 80% power of test, with an expected frequency of acute renal failure in high risk patients as 10% and taking odds ratio of 1.8 the minimum required sample size for the study was calculated to be n=247. Sample size for the study was calculated using G*Power 3.1.9.2.

Sample selection:

- **Inclusion criteria**
  1. All patients with age between 18 and 80 years
  2. Either male or female
  3. Patients undergoing cardiac surgery(CABG, valvular, adult congenital) using CPB
  4. CPB time up to 180 minutes
- **Exclusion criteria**
  1. Patients with age above 80 years
  2. Preoperative renal failure
  3. Anemia
  4. Unstable hemodynamic state (IABP, Inotropes, hypotensive (mAP <60 mmHg))
  5. Redo cardiac surgeries
  6. Complex cardiac surgeries
  7. LVEF <30%

Study Variables and Operational Definition

Pre-Operative Renal Failure: Preoperative renal failure is considered when preoperative creatinine level is above 1.4mg/dl.

Post-Operative Renal Injury: Patients was labelled As renal injury when meeting the following criteria:

Creatinine = 2 Times normal.

Urine output= < 0.5 ml /Kg/hour For 12 hours.

Comorbids:

Diabetic Mellitus (DM): patient with documented history of DM and on anti-diabetic medication for at least 6 months

Hypertension (HTN): patient with documented history of HTN and on anti-hypertensive medication for at least 6 months

Smoking: patient currently or has history of smoking 10 or more cigarettes per day for at least 1 year.

Data Collection: The study was started after approval of the ethical review committee of NICVD. For this study we included consecutive patients undergoing cardiac surgery (CABG, valvular, adult congenital) using CPB criteria at cardiac surgery department of NICVD and fulfill the inclusion. Prior to inclusion the purpose, and benefits of the study was explained and verbal informed consent regarding their inclusion in research study and publication of their data while maintaining confidentiality along with written informed consent for the surgery was obtained. Patient's demographic data was obtained such as age (years), gender, height (cm), weight (kg), and BMI (kg/m^2). History of the patients was taken regarding comorbid conditions such as diabetic mellitus, hypertension, and smoking was taken. All the surgeries was performed by cardiac surgeons. Patients with above 80 years of age, preoperative renal failure, anemia, unstable hemodynamic state (IABP, Inotropes, hypotensive (mAP <60 mmHg)), and LVEF <30% were excluded. Patients undergoing redo cardiac surgeries or complex cardiac surgeries was also excluded. Hematocrit was recorded and all the patients were observed during their post-operative hospital stay and incidence of post-operative renal dysfunction was recorded as per the operational definition.

All the collected data was recorded on predesigned proforma. Patient information was kept secured and available to authorized person only. And no patient identification such as name, MR number, CNIC

number, or mobile number etc. was not disclosed during the reporting and publication of results.

Data Analysis: Data was entered and analysis using SPSS version-21 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp). Quantitative (continuous) variables were expressed using appropriate descriptive statistics such as mean ± SD, median (IQR), maximum and minimum. Frequency and percentages were calculated for categorical variables. Patients were categorized into two groups based on post-operative renal dysfunction and appropriate t-test or Mann-Whitney and chi-square test or fisher exact test was applied to assess the differences and associations. Post-operative renal dysfunction was assessed for the various levels of hematocrit. A U-shaped relationship between the hematocrit and post-operative renal dysfunction has been reported in some of the past studies, hence, incidence of post-operative renal dysfunction was assessed by three groups namely low, moderate, and high hematocrit. Logistic regression analysis was performed taking post-operative renal dysfunction as dependent and other characteristics, including hematocrit, as independent variables and adjusted and unadjusted odds ratio (OR) and 95% confidence interval was reported. The receiver operating characteristic (ROC) curve analysis will be performed to determine the optimal cutoff value of hematocrit. Two sided p-value of ≤ 0.05 was taken as criteria of statistical significance.

RESULTS

Total number of patients were 259 which were included in study. In our study male ratio was predominant 69.5% (180) while there were 30.5% (79) females. Mean age was 50.79 ± 13.31 years and mean body mass index was 25.3 ± 5.1 kg/m^2. Most of the patients were in NYHA class II 55.2% (143). Type of cardiac surgery ; CABG were 69.9% (181), valvular were 23.9% (62) and adult congenital were 6.2% (16). Preoperative Left ventricle ejection fraction (LVEF) of these patients was 50.4 ± 8.6%. Preoperative mean creatinine was 0.9 ± 0.2 ng/dL. All pre-existing co- morbid conditions are also shown in Table 1. The mean cardiopulmonary bypass time was 120.3 ± 32.6 minutes. Mean hematocrit maintained on pump was 26 ± 3.7. Post operatively only 3(1.2%) patients developed renal dysfunction and mean post-operative creatinine was 1 ± 0.3 ng/dL. Overall mortality was 1.2% (3). Post-operative stay in ICU and hospital is shown in Table 1. The analysis of patient pre-operative and per-operative characteristics with post-operative renal dysfunction showed significant relationship with hematocrit and post-operative creatinine (p<0.001) as shown in Table-2.

Table No.1: Baseline clinical characteristics and post-operative outcomes

Characteristics	Total
Total (N)	259
Gender	
Male	69.5% (180)
Female	30.5% (79)
Age (years)	50.79 ± 13.31
≤ 50 years	40.9% (106)
50 to 70 years	56% (145)
>70 years	3.1% (8)
Body mass index(kg/m^2)	25.3 ± 5.1
NYHA	
I	39% (101)
II	55.2% (143)
III	5.8% (15)
IV	0% (0)
Type of surgery	
CABG	69.9% (181)
Valvular	23.9% (62)
Adult Congenital	6.2% (16)
Co-morbids	
Diabetes mellitus	50.2% (130)
Hypertension	49.6% (128)
Smoking	34.4% (89)
Obesity	6.2% (16)
AF	7.8% (20)
Cardiopulmonary bypass time (minutes)	120.3 ± 32.6
LVEF (%)	50.4 ± 8.6
Pre-operative creatinine	0.9 ± 0.2
Hematocrit	26 ± 3.7
Post-operative creatinine	1 ± 0.3
Outcomes	
Renal dysfunction	1.2% (3)
Mortality	1.2% (3)
Intensive care unit stay (hours)	72.6 ± 20.7
< 72 hours	30.1% (78)
≥ 72 hours	69.9% (181)
Length of hospital stay (days)	9.99 ± 4.33
< 7 days	13.1% (34)
≥ 7 days	86.9% (225)

The receiver operating characteristic (ROC) curve analysis of hematocrit for the prediction of post-operative renal dysfunction is shown in Figure 1. The area under the curve on ROC analysis was found to be 0.839 [0.691 to 0.986] and the optimal hematocrit level of 27.85 had sensitivity of 100% and specificity of 73% for the prediction of post-operative renal dysfunction.

Table No.2: Baseline clinical characteristics and post-operative outcomes stratified by the post-operative renal dysfunction

Characteristics	Renal Dysfunction		P-value
	Yes	No	
N	3 (1.2%)	256 (98.8%)	-
Gender			
Male	66.7%(2)	69.5% (178)	>0.999
Female	33.3% (1)	30.5% (78)	
Age (years)	48.67 ± 19.63	50.81 ± 13.27	0.782
≤ 50 years	33.3% (1)	41% (105)	0.906
50 to 70 years	66.7% (2)	55.9% (143)	
>70 years	0% (0)	3.1% (8)	
Body mass index	25.31 ± 3.09	25.29 ± 5.1	0.993
NYHA			
I	100% (3)	38.3% (98)	0.093
II	0% (0)	55.9% (143)	
III	0% (0)	5.9% (15)	
IV	0% (0)	0% (0)	
Type of surgery			
CABG	66.7% (2)	69.9% (179)	0.113
Valvular	0% (0)	24.2% (62)	
Adult Congenital	33.3% (1)	5.9% (15)	
Co-morbids			
Diabetes mellitus	33.3% (1)	50.4% (129)	0.622
Hypertension	66.7% (2)	49.4% (126)	0.621
Smoking	0% (0)	34.8% (89)	0.553
Obesity	0% (0)	6.3% (16)	>0.999
AF	0% (0)	7.9% (20)	>0.999
Cardiopulmonary bypass time (minutes)	89 ± 30.45	120.64 ± 32.46	0.094
LVEF (%)	50 ± 17.32	50.44 ± 8.56	0.931
Pre-operative creatinine	1 ± 0.3	0.9 ± 0.2	0.412
Hematocrit	30.45 ± 3.61	26 ± 3.67	0.038*
Post-operative creatinine	1.72 ± 0.73	1.02 ± 0.27	<0.001*
Intensive care unit stay (hours)	64 ± 13.86	72.75 ± 20.75	0.468
< 72 hours	33.3% (1)	30.1% (77)	>0.999
≥ 72 hours	66.7% (2)	69.9% (179)	
Length of hospital stay (days)	14.33 ± 4.62	9.94 ± 4.31	0.081
< 7 days	0% (0)	13.3% (34)	>0.999
≥ 7 days	100% (3)	86.7% (222)	

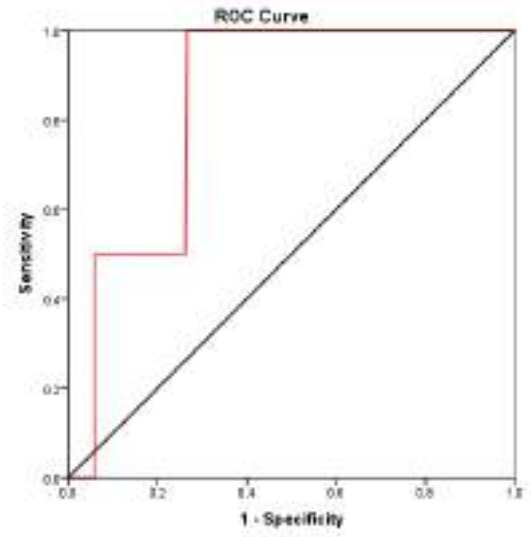


Figure No.1: The receiver operating characteristic (ROC) curve analysis of hematocrit for the prediction of post-operative renal dysfunction

DISCUSSION

It is still unclear that what should be the best value of hematocrit during cardiopulmonary bypass (CPB) to avoid the complications related to hemodilution during cardiac surgery. A study conducted by Ravi Ghatanatti in India on 200 patients documented effects of hemodilution on kidney function. Ravi divided patients according to degree of hemodilution into mild (>25%), moderate (21%–25%), and severe (<21%) and concluded that severe hemodilution(hematocrit of< 21%) is critical during CBP and is associated with significant decrease in creatinine clearance($P \leq 0.0001$) , while there was no significant decrease in creatinine clearance in mild and moderate group[3].This study results indirectly support our study which showed optimal hematocrit of 27.85% to avoid renal dysfunction.

Ranucci et al in a single-center retrospective cohort study analyzed data between 2000 to 2013. He included all patients (20,368 patients) undergoing cardiac operations on pump, and concluded that hemodilution during CPB is an independent risk factor for acute kidney injury (AKI). During these years, changes were made to CPB management to decrease the level of hemodilution by reducing the length of the circuit and by reducing priming volume. He also mentioned other independent risk factors causing AKI which include eGFR, left ventricular ejection fraction, diabetes, redo operations, non-elective operations, nonisolated coronary operations, preoperative IABP use, age, duration of CPB, the timing of angiography, and the HCT value during CPB[14].Where as in our study we could not find any significant relationship between post-operative renal dysfunction and factors like CPB time, age, diabetes mellitus and LVEF.

The association between the degree of hemodilution during CPB and renal dysfunction leading to acute renal failure (ARF) and requiring dialysis is supported by literature. In postmortem findings, most common etiologies for ARF after CPB are acute tubular necrosis(ATN) which is caused by insufficient oxygen delivery and renal infarctions due to microemboli.[15,7] A study done on 9080 patients showed that 1.5% patients (n = 134) developed acute renal failure requiring dialysis. This study showed independent, nonlinear relationship between hematocrit concentration during cardiopulmonary bypass and acute renal failure requiring dialysis .This showed hematocrit concentration 21%-25% was associated with the lowest risk of acute renal failure requiring dialysis. Compared with this the adjusted odds ratio for acute renal failure requiring dialysis was higher in hematocrit concentration <21% and >25%. Conclusion of this study was same as all above studies supporting an independent association between the degree of hemodilution during cardiopulmonary bypass and perioperative acute renal failure requiring dialysis. It also suggested that during cardiopulmonary bypass hematocrit should be kept within optimal range[9].

CPB management updates suggest that if Hb <7.5 g/dL (or hematocrit <22 percent), it should be managed by removal of fluid by ultrafiltration (hemoconcentration) [16]. Packed red blood cells (RBCs) transfusion is another option[17]. The decision to transfuse RBCs should be made based on individual characteristics of the patient[18,19]. In cases of severe anemia, first step is transfusion of available salvaged blood , second step is reinfusion of blood units harvested via normovolemic hemodilution, and as a last option allogenic RBCs should be transfused to maintain optimal hematocrit.In our study Optimal Hct is 27.85%, and has sensitivity of 100% and specificity of 73% to avoid from renal dysfunction in all those patient who are undergoing on-pump cardiac surgery. It include all types of cardiac surgeries i-e CABG, Valvular and Adult congenital surgeries.

CONCLUSION

Hematocrit during CPB affects the outcome after cardiac surgery. It has a direct effect on post-operative renal function. Further larger studies need to be carried out to find out the optimal hematocrit levels needed for best results in cardiac surgery patients.

Author's Contribution:

Concept & Design of Study:	Abdul Wasay
Drafting:	Muhammad Arif
Data Analysis:	Muhammad Mansoor, Muhammad Ishaq Khan
Revisiting Critically:	Asmatullah Achakzai
Final Approval of version:	Muhammad Asad Bilal Awan

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. https://www.who.int/news-room/fact-sheets/ detail /cardiovascular-diseases-(cvds). World Health Organization 06 February 2020 Cardiovascular diseases (CVDs).
2. Sarkar M, Prabhu V. Basics of cardiopulmonary bypass. Ind J Anaesthesia 2017;61(9):760.
3. Ghatanatti R, Teli A, Narayan P, Chowdhuri KR, Mondal A, Bhattacharya S, et al. Ideal hematocrit to minimize renal injury on cardiopulmonary bypass. Innovations 2015;10(6):420-4.
4. Clyne DH, Kant KS, Pesce AJ, Pollak VE. Nephrotoxicity of low molecular weight serum proteins: physicochemical interactions between myoglobin, hemoglobin, bence-jones proteins and tamm-horsfall mucoprotein. Current Problems in Clin Biochem 1979;(9):299-308.
5. Abel RM, Buckley MJ, Austen WG, Barnett GO, Beck Jr CH, Fischer JE. Etiology, incidence, and prognosis of renal failure following cardiac operations: results of a prospective analysis of 500 consecutive patients. J Thoracic Cardiovascular Surg 1976;71(3):323-33.
6. Chen Y, Belboul A, Berglin E, Roberts D. A mathematical analysis of hemorheological changes during heart valve replacement. J Cardiovascular Surg 2000;41(1):37.
7. Krian A. Incidence, prevention, and treatment of acute renal failure following cardiopulmonary bypass. Int Anesthesiol Clin 1976;14(3):87-102.
8. Hellberg PO, Bayati A, Källskog Ö, Wolgast M. Red cell trapping after ischemia and long-term kidney damage. Influence of hematocrit. Kidney Int 1990;37(5):1240-7.
9. Karkouti K, Beattie WS, Wijeysundera DN, Rao V, Chan C, Dattilo KM, et al. Hemodilution during cardiopulmonary bypass is an independent risk factor for acute renal failure in adult cardiac surgery. J Thoracic Cardiovascular Surg 2005; 129(2):391-400.
10. Chen Y, Berglin E, Belboul A, Roberts D. A mathematical analysis of haemorheologic factors during cardiopulmonary bypass for congenital heart disease. Perfusion 1995;10(6):431-8.
11. Vermeer H, Teerenstra S, De Sevaux RG, Van Swieten HA, Weerwind PW. The effect of hemodilution during normothermic cardiac surgery on renal physiology and function: a review. Perfusion 2008;23(6):329-38.
12. Habib RH, Zacharias A, Schwann TA, Riordan CJ, Durham SJ, Shah A. Adverse effects of low hematocrit during cardiopulmonary bypass in the adult: should current practice be changed? J

Thoracic Cardiovascular Surg 2003;125(6): 1438-50.

13. Ranucci M, Romitti F, Isgrò G, Cotza M, Brozzi S, Boncilli A, et al. Oxygen delivery during cardiopulmonary bypass and acute renal failure after coronary operations. Annals Thoracic Surg 2005;80(6):2213-20.
14. Ranucci M, Aloisio T, Carboni G, Ballotta A, Pistuddi V, Menicanti L, et al. Acute Kidney Injury and Hemodilution During Cardiopulmonary Bypass: A Changing Scenario, Ann Thorac Surg 2015;100:95–100.
15. Yeboah ED, Petrie A, Pead JL. Acute renal failure and open heart surgery. Br Med J 1972;415-418.
16. Timpa JG, O'Meara LC, Goldberg KG, Phillips JP, Crawford JH, Jackson KW, et al. Implementation of a Multidisciplinary Bleeding and Transfusion Protocol Significantly Decreases Perioperative Blood Product Utilization and Improves Some Bleeding Outcomes. J Extra Corpor Technol 2016;48(1):11-8.
17. Mazer CD, Whitlock RP, Fergusson DA, et al. Restrictive or liberal red-cell transfusion for cardiac surgery. N Engl J Med 2017;377:2133.
18. Ferraris VA, Ferraris SP, et al. Perioperative blood transfusion and blood conservation in cardiac surgery: the Society of Thoracic Surgeons and The Society of Cardiovascular Anesthesiologists clinical practice guideline. Ann Thorac Surg 2007; 83:S27.
19. Ferraris VA, Brown JR, et al. Society of Thoracic Surgeons Blood Conservation Guideline Task Force, 2011 update to the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists blood conservation clinical practice guidelines. Ann Thorac Surg 2011; 91:944.

Original Article

Frequency of AmpC β-Lactamases in Multi-Drug Resistant Isolates of Escherichia Coli at Tertiary Care Hospital

Whied ul Hussan Shahzad[1], Ali Abuzar Raza[2], Mehvish Javeed[1], Sajida Zafar[2], Muhammad Ibrahim[3] and Ahsanullah M Mirbahar[1]

ABSTRACT

Objective: To determine the frequency of plasmid mediated AmpC beta-lactamases (PABLs) in multi-drug resistant isolates of E.coli.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted in a 450- bed Tertiary Care Hospital of Lahore, (Ittefaq Hospital, Lahore), Pakistan from January 2014 to December 2014.

Materials and Methods: Total 2610 clinical specimens were obtained from different wards and outdoor patient department (OPD) of hospital. Out of 2610 cultured samples only 1200 specimen showed significant growth of pathogens. These isolates were further proceeded for identification through colonial characters, gram staining and biochemical reactions. Standards protocols were used for inoculation, identification and isolation of E.coli. Cefoxitin resistance was used as a primary screening protocol for AmpC enzyme production. AmpC disk test (EDTA disk) was used as a confirmatory test for AmpC enzyme production.

Results: Out of 2610 culture samples only 1200 specimen showed significant growth of pathogens. Out of 1200 positive cultures, 421 (35.08%) isolates were identified as E.coli. Male patients 230 (54.63%) and 191 (45.37 %) female patients having mean ages 44.23 + 10.89 years. AmpC producing strains were more prevalent in surgical specimens than others. Out of 421 E.coli isolates, only 19.95% (n=84) E.coli were selected as plasmid mediated AmpC β-lactamase (PABLs) producers. After the confirmatory AmpC disk test only 8.07% (n=34) E.coli were isolated as PABLs producers and 47.05% (n=16) as ESBL producers. Total 20% (n=84) cefoxitin resistant was detected and 40.48% (n=34) of E.coli were isolated as PABLs producers from cefoxitin resistant. Out of (n=34) the percentage of PABLS and ESBLs co-producers was 26.47 % (n=9).

Conclusion: The isolates that involved in coproduction of PABLs and ESBL showed increased MICs against the applied cephalosporin drugs. This study noted high frequency of PABLs producing bacteria from hospital that may contribute to serious therapeutic problems.

Key Words: Hospital acquired infection (HAI), E.coli, Antimicrobial sensitivity testing, PABLs, ESBLs

Citation of article: Shahzad WH, Raza AA, Javeed M, Zafar S, Ibrahim M, Mirbahar AM. Frequency of AmpC β-Lactamases in Multi-Drug Resistant Isolates of Escherichia Coli at Tertiary Care Hospital. Med Forum 2021;32(10):45-49.

INTRODUCTION

Family of Enterobacteriaceae is the major cause of hospital acquired infections (HAI) and the microorganisms present in this family are acquiring multidrug resistance against the routinely used drugs by the production of AmpC β-lactamases[1,2]. These are worldwide distributed.

[1.] Department of Microbiology / Pathology[2] / Biochemistry[3], Nishtar Medical University, Multan..

Correspondence: Mr. Whied ul Hussan Shahzad, Ph.D. Scholar Dept. of Microbiology, Institute of Industrial Biotechnology GCU Lahore.
Contact No: 0333-5545995
Email: waheed.microbiologist@gmail.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

The AmpC β-lactamases could be either plasmid mediated or chromosomal mediated. No doubt the development of drug resistance in bacteria is a major threat to antimicrobial chemotherapeutic interventions[3,4]. Generally, three categories of antibiotic resistance are presented by bacteria; Intrinsic, acquired and adaptive. The important mechanism of drug resistance to drugs that contain β-lactam ring structure, is the synthesis of β-lactamases. The β-lactamases are AmpC β-lactamases and ESBLs[5]. The genes involved in the synthesis of AmpC β-lactamases are mainly chromosomal mediated. However, in addition to these chromosomal mediated genes, plasmid mediated AmpC β-lactamases (PABLs) have been arisen by chromosomal gene transfer to plasmids and can lead to spreading of antibiotic resistance in different bacterial populations such as E. coli, Klebsiella spp, Proteus mirabilis and Salmonella spp[6,7]. The diagnostic and therapeutic challenges are being offered by PABLs and

ESBLs to the health care experts. The detection of PABLs and ESBLs can play an important role in several surveillance and epidemiological studies[8,9]. It is also important for infection control because may be all these types of resistant genes transfer from one organism to another organism in hospital environment[10].

The present study was carried out to disclose the prevalence of PABLS that have been produced by E.coli in a tertiary care hospital of Lahore. The AmpC disk test is a specified test which performed for detection of PABLs production. PABLs producing bacteria were further tested for antibiotic susceptibility and ESBLs production. This study will help out for the adaptation of better and effective hospital antibiotic policy against the pathogens that are involved in production of PABLs. The results of this study will help to create awareness among healthcare professionals for effective management of such pathogens in their clinical practice which will reduce burden of antimicrobial resistance in our population owing to rational drug therapy.

MATERIALS AND METHODS

The study was executed from January 2014 to December 2014 in a 450- bed tertiary care hospital of Lahore, (Ittefaq Hospital, Lahore), Pakistan. Total 2610 clinical specimens such as catheter tips, sputum, pus, blood, tracheal tips, tracheal secretions, sputum, swabs from wounds, urine and body fluids were obtained from different wards and OPDs of hospital. All pathological specimens were inoculated on Blood agar and MacConkey except urine samples which were inoculated on CLED medium and plates were incubated aerobically at 35 + 2 ºC for 18 hours. Out of these samples only 1200 specimen showed significant growth of pathogens. These isolates were further proceeded for identification through, colonial characters, gram staining and biochemical reactions using API 20E (BioMerieux France). Confirmed isolates were further tested for production of PABLs and ESBLs. Mueller-Hinton agar was used to test the bacterial susceptibility against cefoxitin disk (30μg) by following the standard disc diffusion protocol[11].The isolates which showed resistance or <18mm zone diameter were further analyzed for PABLs production[12-13].The E.coli strain ATCC 25922 was applied as negative control which was phenotypically β-lactamase negative.

PABLs producing isolates were further investigated for ESBLs production by following the double-disk diffusion synergy technique[11-14]. The isolates were swabbed on Mueller-Hinton MHA ager after making 0.5 McFarland dilution of isolates in nutrient broth. A Amoxicillin/clavulanic (AMC 20/10 μg) disk was positioned in the center of MHA plate while the disk of ceftriaxone CRO (30μg), Aztreonam ATM (30μg), ceftazidime CAZ (30μg), cefepime FEP (30μg) and cefpodoxime CPD (10μg) were placed in a close proximity of 20-30 mm distance. The results were interpreted as ESBL production by the clear extension of zone of inhibition of cephalosporin towards Amoxicillin/clavulanic (AMC 20/10 μg) disk.

Kirby-Bauer method was used to determine antimicrobial susceptibility pattern of E.coli. Mueller-Hinton ager plates were used with 0.5 McFarland dilution of already refreshed cultures[11]. Different antibiotics of known concentration were applied on Mueller-Hinton (MHA) for checking the susceptibility. These plates were further incubated at 35 + 2ºC for overnight under aerobic conditions[15]. Following drugs were employed to observe their susceptibility; "Ampicillin 10ug, Amoxicillin/Clavulanic acid 20/10μg, Amikacin 30μg, Aztreonam 30μg, Ceftazidime 30μg, Cefpodoxime 10μg, Chloramphenicol 30μg, Ceftriaxone 30μg, Cefepime 30μg, Cefoxitin 30μg, Ciprofloxacin 5μg, Cefoperazone/Sulbactam 95/10μg, Imipenem 10μg, Norfloxacin 10ug, Nitrofurantoin 300μg, Piperacillin 100μg, Trimethoprim-sulfamethoxazole 1.25/23.75μg, Piperacillin/Tazobactam 100/10μg , Tetracycline 30μg, and Tigecycline 15μg discs (Oxoid)"[16]. Antibiotics zone of inhibition were measured and interpreted by following the guidelines of Clinical Standard Laboratory Institute (CLSI)[17]. The isolate were considered as susceptible to an antimicrobial agent concentration when the zone of growth inhibition was in the range displayed by wild-type strain. Similarly, the isolates were considered as resistant to an antimicrobial agent when zone of growth inhibition was higher than that of wild-type strain. Two-fold agar dilution plate method was used to determine the minimum inhibitory concentrations of different drugs such as Imipenem, Cefepime, Cefoxitin and ceftazidime[18].

RESULTS

Out of 2610 culture samples only 1200 specimen showed significant growth of pathogens. These isolates were further proceeded for identification through Gram staining and biochemical reactions. Out of 1200 positive cultures, 421 (35.08%) isolates were identified as E.coli from 230 (54.63%) male patients and 191 (45.37 %) female patients having mean ages 44.23 + 10.89 years. From surgical specimens 20.1% (n=85), from non-surgical samples 60.80% (n=256) and from OPD 19% (n=80) E.coli were isolated from total (n=421) isolates. Out of total (n=34) AmpC producing strains were isolated from surgical specimens at the frequency of 44.12% (n=15), from OPDs 20.58% (n=7) and from non- surgical specimens 35.29% (n=12). AmpC producing strains were more prevalent in surgical specimens than others. Frequency of 421 E. coli was observed from different types of samples such

as sputum 4.75% (n=20), fluid 2.37 % (n=10), pus 30.87% (n=130), tissue 0.5% (n=2), urine 48.93% (n=206), blood 3.33% (n=14), tracheal secretions (n=7) 1.66%.

Out of 421 E.coli isolates, only 19.95% (n=84) E.coli were selected as plasmid mediated AmpC β-lactamase (PABLs) producers. After the confirmatory AmpC disk test only 8.07% (n=34) E.coli were isolated PABLs producers. Moreover 26.47 (n=9) of E.coli were ESBL producers. Almost 26.47 % (n=9) of E.coli were producing both ESBLs and PABLs. Out of n=34 AmpC producing strains of E.coli recovered from pathological specimens at the frequency of blood 8.82% (n=3), urine 17.64% (n=6), pus 52.94% (n=18) tips 8.82 (n=3), fluids 8.82 (n=3) and tracheal secretions 2.94% (n=1). AmpC producing strains of E.coli had been isolated from 21 (61.76%) male out of 34. AmpC producing strains were more prevalent in males than females.

PABLs producing strains of E.coli were resistant to Ampicillin, Piperacillin, Tetracycline, Amoxicillin/ Clavulanic acid, Aztreonam, Ceftriaxone, Ceftazidime and Cefpodoxime. PABL and ESBL co-producing E.coli were resistant to Cefepime. E. coli showed the susceptibility to Ciprofloxacin 17.64%, Amikacin 67.64%, Chloramphenicol 26.47%, Cotrimoxazole 20.58%, Imipenem 100%, Tigecycline 100%, Cefepime 67.6%, Cefoperazone/sulbactam 29.41%, Piperacillin /Tazobactam 41.17% (Fig.1). Norfloxacin and Nitrofurantoin were applied on isolates from urine samples. Nitrofurantoin was 71.42%and 100% susceptible and Norfloxacin was 100% resistant against isolates from urine. Cefepime was less susceptible; Imipenem and Tigecycline were susceptible against all isolates.

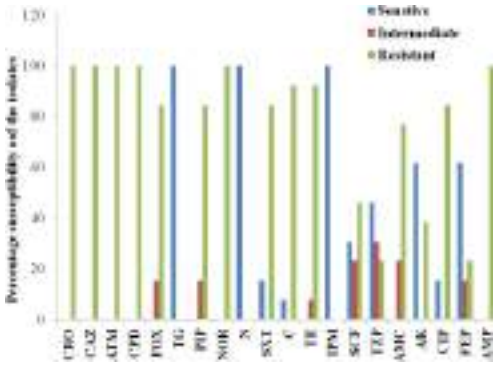


Figure No.1: Percentage Susceptibility pattern of PABLs producing E. coli.

Cefoxitin minimum inhibitory concentration for E.coli were 256 to ≥512 µg/ml. PABLs and ESBLS Co-producer showed increased MICs for Cefoxitin. High Ceftazidime MICs, 512 to ≥512 µg/ml were observed against AmpC producing strains. Cefepime MICs ranges from 4 to256 µg/ml against the isolates and is considered effective. High MICs Values were observed against ESBLs and PABLs co-producers and few of co-Producers showed intermediate to resistant MIC results (16 µg/ml to32 µg /ml) for cefepime. Imipenem MICs ranges from 0.5 to 2µg/ml were observed against all the isolates.

DISCUSSION

The current study detect the frequency of plasmid-mediated AmpC β-lactamases among the E.coli isolates from the hospital sites. Enterobacteriaceae play a major role in causing the hospital acquired infection and emergence of resistance in these organisms is a great challenge for health-care professionals[9]. The plasmid mediated AmpC beta-lactamases producing organism are very problematic in clinical point of view as they inhibit the action of most of the β-lactam drugs and make them ineffective. The mechanism of emergence of resistance in these organism is the production of ESBLs and PABLs[19].

In current study 8.07% (n=34) E.coli were isolated as AmpC producers. A similar study was carried out in a hospital of Pakistan, where 40.74% (n = 33) E. coli were PABL producers[9]. A study reported 39.3% AmpC β-lactamase producers in E.coli[20]. Another study reported 28.5 % AmpC producers in the E.coli isolates[21]. PABL producing strains were isolated from surgical specimens at the frequency of; 44.12% (n=15) E.coli. The frequency of PABL producers was high from surgical sites[22]. From OPDs 20.58% (n=7) E.coli had been isolated. From non- surgical specimens 35.29% n=12 E.coli were isolated. This may represent referral cases from other hospitals that indicate the frequency of PABL producers in community[23].

Almost 26.47 % (n=9) of E.coli were producing both ESBLs and PABLs. These findings were consistent with the previous study which reported PABLs and ESBLs in E. coli (24.24%)[17]. In my study 19.95% E. coli were observed as showing resistance to cefoxitin[24]. Another study demonstrated that 1.6 % of E.coli had been resistant to Cefoxitin. In my study 67.75% E.coli were sensitive to cefepime. 22.4% susceptibility was reported to Cefepime by the ESBL and AmpC producing strains[25]. All ESBL and AmpC β-lactamase co-producing isolates had been resistant to cefepime. Intermediate susceptibility to cefepime was exhibited by 8.24% of E.coli. Only two of the AmpC β-lactamase producing isolates of E.coli showed resistant to cefepime.

In our study, Ampicillin, piperacillin, tetracycline, Amoxicillin/Clavulanic acid, Aztreonam, ceftriaxone, Ceftazidime and cefpodoxime had no susceptibility against AmpC producing isolates. 94.3%, 80.2%, 77.6%, 78.6%, 8.6%, 10.2% resistant was reported to amoxicillin/clavulanic acid, Aztreonam, Cefepime, ampicillin/sulbactam, imipenem, piperacillin/ Tazobactam respectively by the ESBL and AmpC producing isolates[25]. 96%, 92%, 83%, 77%, 71% and 69% resistance to cefoxitin, ampicillin, ceftriaxone, ceftazidime, Cotrimoxazole and ciprofloxacin was

reported in isolates of E.coli respectively[21]. A study reported 59.7%, 92.7%, 90.72%, 86.6%, 39% and 79.3% resistant to Cefoxitin, Ceftriaxone, Ceftazidime, Aztreonam, Imipenem and Cefepime respectively among the members of the Enterobacteriaceae family. In my study, Ampicillin, piperacillin, tetracycline, Amoxicillin/Clavulanic acid, Aztreonam, ceftriaxone, Ceftazidime and cefpodoxime had no susceptibility against AmpC producing isolates. 94.3%, 80.2%, 77.6%, 78.6%, 8.6%, 10.2% resistant was reported to amoxicillin/clavulanic acid, Aztreonam, Cefepime, Ampicillin/Sulbactam, Imipenem, Piperacillin/ Tazobactam respectively by the ESBL and AmpC producing isolates[26]. 96%, 92%, 83%, 77%, 71% and 69% resistance to Cefoxitin, Ampicillin, Ceftriaxone, Ceftazidime, Cotrimoxazole and Ciprofloxacin was reported in isolates of E.coli respectively[20]

In our study isolates showed 100% susceptibility to Imipenem, and Tigecycline Worldwide studies also authenticate the imipenem efficiency against these most challenging organisms and even in serious infections, it was recommended as a drug of choice[25]. No resistance was reported to Imipenem by AmpC producers[20].

CONCLUSION

This study shows the high frequency of plasmid mediated AmpC beta-lactamases (PABLs) producing isolates. The important aims of study were to detect the possible source of emergence of these PABLs producing strains for the prevention and treatment of infections. It is required to establish the standard procedures in order to overcome the controversies in susceptibility reporting of PABLs producers. Indiscriminate use of antibiotics should be discouraged to control the development of multi-drug resistant microorganisms.

Author's Contribution:

Concept & Design of Study:	Whied ul Hussan Shahzad
Drafting:	Ali Abuzar Raza, Mehvish Javeed
Data Analysis:	Sajida Zafar, Muhammad Ibrahim, Ahsanullah M Mirbahar
Revisiting Critically:	Whied ul Hussan Shahzad, Ali Abuzar Raza
Final Approval of version:	Whied ul Hussan Shahzad

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Abdalhamid B, Albunayan S, Shaikh A, Elhadi N, Aljindan R. Prevalence study of plasmid-mediated AmpC β-lactamases in Enterobacteriaceae lacking inducible ampC from Saudi hospitals. J Med Microbiol 2017;66(9):1286-90.
2. Maleki A, Khosravi A, Ghafourian S, Pakzad I, Hosseini S, Ramazanzadeh R, et al. High Prevalence of AmpC β-Lactamases in Clinical Isolates of Escherichia coli in Ilam, Iran. Osong Public Health Res Perspect 2015;6(3): 201-4.
3. Poirel L, Madec JY, Lupo A, Schink AK, Kieffer N, Nordmann P, et al. Antimicrobial Resistance in Escherichia coli. Microbiol Spectr 2018;6(4): 289-316.
4. Parsonage B, Hagglund PK, Keogh L, Wheelhouse N, Brown RE, Dancer SJ. Control of Antimicrobial Resistance Requires an Ethical Approach. Front Microbiol 2017;2(8): 2124.
5. Gupta V, Singh M, Datta P, Goel A, Singh S, Prasad K et al. Detection of various beta-Lactamases in Escherichia coli and Klebsiella sp.: A study from Tertiary Care Centre of North India. Ind J Med Microbiol 2020;38(3 & 4): 390-6.
6. Rizi KS, Mosavat A, Youssefi M, Jamehdar SA, Ghazvini K, Safdari H, et al. High prevalence of blaCMY AmpC beta-lactamase in ESBL co-producing Escherichia coli and Klebsiella spp. clinical isolates in the northeast of Iran. J Glob Antimicrob Resist 2020;22: 477-82.
7. Zorgani A, Daw H, Sufya N, Bashein A, Elahmer O, Chouchani C. Co-Occurrence of Plasmid-Mediated AmpC β-Lactamase Activity Among Klebsiella pneumoniae and Escherichia. Coli Open Microbiol J 2017;26(11): 195-202.
8. Yilmaz NO, Agus N, Bozcal E, Oner O, Uzel A. Detection of plasmid-mediated AmpC β-lactamase in Escherichia coli and Klebsiella pneumoniae. Ind J Med Microbiol 2013;31(1): 53-9.
9. Shafiq M, Rahman H, Qasim M, Ayub N, Hussain S, Khan Jet al. Prevalence of plasmid-mediated AmpC β-lactamases in Escherichia coli and Klebsiella pneumonia at tertiary care hospital of Islamabad, Pakistan. Eur J Microbiol Immunol 2013;3(4): 267-71.
10. Coşkun S, Altanlar N, Sefoksitine D. Escherichia coli ve Klebsiella pneumoniae Klinik İzolatlarında Plazmid Aracılı AmpC Beta-Laktamaz Tespiti [Detection of plasmid-mediated AmpC beta-lactamase in clinical isolates of cefoxitin-resistant Escherichia coli and Klebsiella pneumoniae]. Mikrobiyol Bul 2012;46(3): 375-85.
11. Kirby WM, Yoshihara GM, Sundsted KS, Warren JH. Clinical usefulness of a single disc method for antibiotic sensitivity testing. Antibiot Annu 1956;892-7.
12. Zhang H, Zhou Y, Guo S, Chang W. Multidrug resistance found in extended-spectrum beta-lactamase-producing Enterobacteriaceae from rural water reservoirs in Guantao, China. Front Microbiol 2015;**31**; 6:267.

13. Reuland EA, Hays JP, de Jongh DM, Abdelrehim E, Willemsen I, Kluytmans JA, et al. Detection and occurrence of plasmid-mediated AmpC in highly resistant gram-negative rods. PLoS One 2014;9(3): e91396.
14. Thomson KS. Extended-spectrum-beta-lactamase, AmpC, and Carbapenemase issues. J Clin Microbiol 2010;48(4):1019-25.
15. Prakash D, Saxena RS. Distribution and antimicrobial susceptibility pattern of bacterial pathogens causing urinary tract infection in urban community of meerut city, India. ISRN Microbiol 2013;29:749629.
16. Martin D, Fougnot S, Grobost F, Thibaut-Jovelin S, Ballereau F, Gueudet T, et al. Prevalence of extended-spectrum beta-lactamase producing Escherichia coli in community-onset urinary tract infections in France in 2013. J Infect 2016;72(2):201-6.
17. CLSI, Clinical and Laboratory Standards Institute; Quality control minimal inhibitory concentration (MIC) limits for broth micro dilution and MIC interpretive breakpoints. Clinical and Laboratory Standards Institute (CLSI) CLSI document M27-S2. Wayne, PA 2017.
18. Wiegand I, Hilpert KH. RE. Agar and broth dilution methods to determine the minimal inhibitory concentration (MIC) of antimicrobial substances. Nat Protoc 2015;**2**(3): 163-75.
19. Conen A, Frei R, Adler H, Dangel M, Fux CA, Widmer AF. Microbiological screening is necessary to distinguish carriers of plasmid-mediated AmpC beta-lactamase-producing enterobacteriaceae and extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae because of clinical similarity. PLoS One 2015;10(3): e0120688.
20. Koshesh M, Mansouri S, Hashemizadeh Z, kalantar-Neyestanaki D. Identification of Extended-Spectrum β-Lactamase Genes and AmpC-β-Lactamase in Clinical Isolates of Escherichia coli Recovered from Patients with Urinary Tract Infections in Kerman, Iran. Arch Pediatr Infect Dis 2017;5(2): e37968.
21. Dutta H, Nath R, Saikia L. Multi-drug resistance in clinical isolates of Gram-negative bacilli in a tertiary care hospital of Assam. Ind J Med Res 2014;139(4): 643-5.
22. Chen FC, Ho YN, Cheng HH, Wu CH, Change MW, Su CM. Does inappropriate initial antibiotic therapy affect in-hospital mortality of patients in the emergency department with Escherichia coli and Klebsiella pneumoniae bloodstream infections? Int J Immunopathol Pharmacol 2020;34:2058738420942375.
23. Mita Y, Shigemura K, Osawa K, Kitagawa K, Kotaki T, Shirakawa T, et al. Clinical Risk Factors for Death Caused by Extended-Spectrum Beta-Lactamase: Producing Bacteria. Urol Int 2019; 102(2): 205-11.
24. Rensing KL, Abdallah HM, Koek A, Elmowalid GA, Vandenbroucke-Grauls CMJE, Al Naiemi N, et al. Prevalence of plasmid-mediated AmpC in Enterobacteriaceae isolated from humans and from retail meat in Zagazig, Egypt. Antimicrob Resist Infect Control 2019;26(8): 45.
25. Khashei R, Edalati Sarvestani F, Malekzadegan Y, Motamedifar M. The first report of Enterobacter gergoviae carrying blaNDM-1 in Iran. Iran J Basic Med Sci 2020;23(9): 1184-90.

Original Article

Assessment of Coagulation Profile of Patients with Pregnancy Induced Hypertension Visiting Tertiary Care Hospital

Coagulation Profile with Pregnancy Induced Hypertension

Huda Abbas[1], Sadia Bashir[2], Hamad Masood[1], Wajahat Hussain[1], Arif Ahmed Zaidi[1] and Sadaf Mushtaq[1]

ABSTRACT

Objective: To assess abnormalities in platelet count, PT (prothrombin time) and APTT (activated partial thromboplastin time) in patients with PIH.

Study Design: Cross sectional analytical study

Place and Duration of Study: This study was conducted at the department of Pathology in collaboration with Gynecology and Obstetrics Department of Bahawal Victoria Hospital from January, 2021 to June 2021 for a period of six months.

Materials and Methods: After approval from Institutional ethics review committee. All the women more than 28 weeks gestation having uncomplicated pregnancy with pregnancy induced hypertension visiting the hospital were included in the study. Pregnancy induced hypertension was defined as blood pressure at or above 140/90 mm of Hg on at least two occasions, six or more hours apart together with or without proteinuria, edema, convulsions and coma. Investigation done were platelet count, PT and APTT. Data entry was done in SPSS version 22.0. An independent sample t-test was used to check for differences in mean platelet count, PT & APTT between women with pregnancy induced hypertension (PIH) and without PIH and p-value <0.05 was set for statistical significance.

Results: Out of total 372 women 186 were cases of pregnancy induced hypertension while remaining 186 had no PIH. Maximum number of women in both groups were between 25 to 30 years of age. The mean age of women with PIH was 27.43±6.82 and women without PIH is 29.72±7.43 years. PIH was more common in primigravida women. The differences of prothrombin time ($p<0.001$) and Activated partial thromboplastin time ($p<0.001$) between two groups was statistically significant.

Conclusion: Patients with pregnancy-induced hypertension showed reduction in platelet count with increase PT and APTT in women with pregnancy induced hypertension.

Key Words: Platelet count, preeclampsia, Prothrombin Time, Platelet count

Citation of article: Abbas H, Bashir S, Masood H, Hussain W, Zaidi AA, Mushtaq S. Assessment of Coagulation Profile of Patients with Pregnancy Induced Hypertension Visiting Tertiary Care Hospital. Med Forum 2021;32(10):50-53.

INTRODUCTION

Pregnancy is a physiological process that can pose a number of health concerns to both the mother and the fetus. Pregnancy-induced hypertension (PIH) is one of the most frequent illnesses linked with high blood pressure that starts after 20 weeks of pregnancy and disappears after birth.[1,2]

[1.] Department of Community Medicine / Pathology[2], Quaid-e-Azam Medical College, Bahawalpur.

Correspondence: Dr. Huda Abbas, Assistant Professor of Community Medicine, Quaid-e-Azam Medical College, Bahawalpur.
Contact No: 0300 2371093
Email: hudaarshad@yahoo.com

Received: July, 2021
Accepted: August, 2021
Printed: October, 2021

Pregnancy-induced hypertension (PIH) is a common medical disorder during pregnancy that causes multi-organ failure and contributes significantly to maternal morbidity and death.[1] It is more common in primigravida than in multiparous women.[3] Preeclampsia is a hypertensive disorder that affect 2-8% pregnancies globally and associated with maternal morbidity and mortality. It is characterized by high blood pressure and significant amount of protein in the protein. Many body systems are involved including the presence of decreased blood platelet count (Thrombocytopenia), deranged liver functions, renal functions impairment, fluid retention in the lungs (Pulmonary edema), visual disturbances and if left untreated can develop eclampsia, a life threatening condition during pregnancy[3].

Eclampsia is a severe form of pregnancy-induced hypertension that is accompanied by seizures.[4] The majority of these illnesses can be prevented and treated with good antenatal care, but due to a lack of health

facilities in developing countries, this is not always possible.[5,6] During normal pregnancy, profound alterations in the coagulation and fibrinolytic systems occur, resulting in a hypercoagulable state. In PIH, there are a range of hematological abnormalities, with thrombocytopenia being the most common aberration due to increased consumption during low-grade intravascular coagulation.[7,8] The underlying coagulation problem raises the risk of bleeding issues, particularly during birth and the insertion of an epidural catheter for regional anesthesia. Preventing these coagulation abnormalities in pre-eclampsia patients can save lives and reduce maternal morbidity and mortality.[9-11] The coagulation system plays vital role in maintaining the integrity and patency of the vascular compartment. Extensive physiological changes during pregnancy are induced in coagulation system. In women preeclampsia and eclampsia there is evidence of intravascular coagulation shown by decrease in platelet counts and increase in prothrombin and activated partial thromboplastin time.

This study was undertaken to assess the coagulation profile of women with PIH and coagulopathy related adverse effects by using hematological/coagulation parameters which are rapid, cheaper and easily available, that also guide us for management before the patient goes into a complication.

MATERIALS AND METHODS

It was cross sectional analytical study conducted from January to June 2021 in department of Pathology Quaid-e-Azam Medical college Bahawalpur in collaboration with Gynecology and Obstetrics Department of Bahawal Victoria Hospital, Bahawalpur after taking approval from Institutional ethics review committee. All the primigravida women more than 28 weeks gestation having uncomplicated pregnancy with pregnancy induced hypertension visiting the department of Obstetrics and gynecology were included in the study through non probability consecutive method. Pregnancy induced hypertension was defined as blood pressure at or above 140/90 mm of Hg on at least two occasions, six or more hours apart together with or without proteinuria, edema, convulsions and coma. Similar number of pregnant women in 3rd trimester with normal blood pressure, no proteinuria or edema were also included. Known cases of hemorrhagic disorder, Epilepsy, Hepatic or renal disorder, diabetes mellitus and hypertension were excluded from the study. Routine antenatal investigations like blood group, CBC, BT, CT, blood sugar, HIV, VDRL, HBs-Ag and anti HCV were done. Additional investigation done in both groups were manual platelet counts, prothrombin time (PT), activated partial thromboplastin time (APTT) and ultrasonography (USG). Sample of 5ml of blood was collected in an EDTA and sodium citrate vacutainer. Coagulation parameters were carried out by ERBA ECL 412 series coagulometer. Platelet count was estimated by hematology analyzer Sysmex XN-330 and manual method by peripheral blood smear. Data entry was done in SPSS version 22.0. Data cleaning and validation were done. An independent sample t-test was used to check for differences in mean parameter values like platelet count, PT, APTT between women with pregnancy induced hypertension (PIH) and without PIH. P-value <0.05 was set for statistical significance.

RESULTS

A total of 372 pregnant females visiting Obstetrics & Gynecology outpatient department of Bahawal Victoria Hospital Bahawalpur were enrolled in the study. Out of total 372 women 186 were cases of pregnancy induced hypertension while remaining 186 had no PIH. Age distribution showed that maximum number of cases in both the groups were between 25 to 30 years of age. The mean age of women with PIH was 27.43±6.82 and women without PIH is 29.72±7.43 years.

Table No.1: Age distribution of the patients with and without pregnancy induced hypertension (PIH)

Age in years	Patients with PIH (n=186)	Patients with no PIH (n=186)
18-24	58 (31.2%)	44 (23.6%)
25-30	97 (52.1%)	85 (45.7%)
31-35	31 (16.7%)	57 (30.7%)
Total	186 (100%)	186 (100%)

In the present study PIH was more in primigravida women as compared to multigravida. Out of total 186 women with pregnancy induced hypertension 125 (67.2%) were primigravida while 104 (55.9%) women without PIH were multigravida (Table II).

Table No.2: Distribution of the patients by gravidity

Gravidity	Patients with PIH (n=186)	Patients with no PIH (n=186)
Primigravida	125 (67.2%)	082 (44.1%)
Multigravida	061 (32.8%)	104 (55.9%)
Total	186 (100%)	186 (100%)

The mean and standard deviation of platelet count (lacs/cu mm) in women with no PIH was 2.73±0.54(lacs/cu mm) as compared to 1.54±0.46 (lacs/cu mm) in women with pregnancy induced hypertension and the difference between two groups is statistically significant (p<0.001). The mean and standard deviation of prothrombin time (in seconds) in women with no PIH was 12.54±1.32 (sec) as compared to the 17.62±0.54 (sec) in women which had pregnancy induced hypertension. The mean and standard deviation of Activated partial thromboplastin time (sec) in females with no PIH was 33.14±2.41 (sec) as compared to the 26.24±3.34 (sec) in women which were diagnosed cases of PIH. The differences of prothrombin time (p<0.001) and Activated partial thromboplastin

time (p<0.001) between two groups was statistically significant as shown in Table III.

Table No.3: Comparison of Coagulation profile between patients with and without pregnancy induced hypertension (PIH)

Age in years	Patients with PIH (n=186) Mean±S.D	Patients with no PIH (n=186) Mean±S.D	p-value
Platelet count	1.54±0.46	2.73±0.54	<0.001
PT	17.62±1.79	12.54±1.32	<0.001
APTT	26.24±3.34	33.14±2.41	<0.001

DISCUSSION

Women with Pregnancy-Induced Hypertension may develop various haematological changes and thrombocytopenia is the most commonly observed change. In third trimester of pregnancy there is hemodilution and platelet consumption is increased. Endothelial changes during pre-eclampsia also results in altered level of fibrinogen, activated partial thromboplastin time and prothrombin time. This study was conducted to assess the changes in coagulation profile of women that were diagnosed as cases of pregnancy induced hypertension and these changes were also compared with the coagulation profile of women which has no pregnancy induced hypertension.

Out of total 186 cases of pregnancy-induced hypertension was more common in primigravida. Similar findings have been reported in the study conducted by Xiong et al.[12] in which the frequency of preeclampsia was significantly lower in multiparous women as compared to primigravida women.

Our study findings showed that mean platelet count was 2.73±0.54 lacs/mm^3 in women which had no pregnancy induced hypertension and in the group with pregnancy induced hypertension it was 1.52±0.46 lacs/mm^3 and difference in mean platelet count between the groups was statistically significant (p<0.001). Our findings are in accordance with the results of study conducted by Halder et al.[13] which revealed mean platelet 1.21 lac/mm^3 in women that were diagnosed cases of eclampsia. Sharma et al.[14] in their study also found the decrease in mean platelet count in cases of preeclampsia. In a study done by Sultan R et al.[15] on platelet count in women which had preeclampsia and found that preeclampsia is associated with low platelet count. Our findings are also consistent with the results of studies done by Leduc l, et al[16] and Shete AN et al.[17] which showed decrease in mean platelet count in women with pregnancy induced hypertension as compared to the control group.

The findings of our study showed increased prothrombin time (sec) in women with pregnancy induced hypertension as compared to prothrombin time in group of women which were normotensive. Similarly, an increase in Activated partial thromboplastin time (sec) in group of women with PIH was increased as group with no PIH. The difference in prothrombin time (p<0.001) and Activated partial thromboplastin time (p<0,001) between two groups was statistically significant. These findings were in line with the results of study done by Lakshmi et al. [18] which revealed increased prothrombin time (PT) and activated partial thromboplastin time (APTT) in women that have preeclampsia and eclampsia. Similar findings were also shown by the study conducted by Joshi SR et al.[8] which showed coagulation abnormalities particularly an increase in APTT.

Currently there is no screening test available that may help to identify the severity and complications associated with pregnancy-induced hypertension. It is necessary to evaluate the women with pregnancy induced hypertension early for prevention of complications, morbidity and mortality. This study assessed the coagulation profile of women with PIH by easily available, cheaper and rapid method so that management should be started before onset of complications. The present study reveals that platelet count is cost effective, rapid, reliable and easily available method that may be used as useful of screening for early detection of complications in women with PIH even in the rural areas. It was a cross sectional study and has certain limitations and is potentially subject to many biases and variations. Further analytical studies are necessary to clarify the role of early assessment of coagulation as screening tool for detection of complication in women with preeclampsia.

CONCLUSION

Patients with pregnancy-induced hypertension showed reduction in platelet count with increase PT and APTT in women with pregnancy induced hypertension.

Author's Contribution:

Concept & Design of Study:	Huda Abbas
Drafting:	Sadia Bashir, Hamad Masood
Data Analysis:	Wajahat Hussain, Arif Ahmed Zaidi, Sadaf Mushtaq
Revisiting Critically:	Huda Abbas, Sadia Bashir
Final Approval of version:	Huda Abbas

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Ekun OA, Ogidi NO, Lawal RA, Ogunmuyiwa OA, Umewune MC, Adefolaju FO, et al. Interrelationship between markers of oxidative stress, inflammation and hematological parameters

among preeclamptic Nigerian women. Med Sci Monitor Basic Res 2018;24:225.
2. Feldstein O, Kovo M, Tal O, Braunstein M, Grinstein E, Schreiber L, et al. The association between abnormal coagulation testing in preeclampsia, adverse pregnancy outcomes, and placental histopathology. Hypertens Pregnancy 2019;38(3):176-83.
3. Swetha AG, Puranik N, Kammar KF. A comparative study on coagulation profile and neutrophil-lymphocyte ratio in pregnancy-induced hypertension. National J Physiol Pharm Pharmacol 2018;8(3):400-5.
4. Naaz A, Padugupati S, Sarma, Sushma P. A Study on Coagulation Profile in Pregnancy Induced Hypertension Cases. IOSR J Biotechnol Biochem 2015;1(6): 82-8.
5. Prakash J, Ganiger VC, Prakash S, Iqbal M, Kar DP, Singh U, et al. Acute kidney injury in pregnancy with special reference to pregnancy-specific disorders: a hospital based study (2014–2016). J Nephrol 2018;31(1):79-85.
6. Prakash J, Pandey LK, Singh AK, Kar B. Hypertension in pregnancy: Hospital based study. J Assoc Physicians Ind 2006;54:273.
7. Priyadarshini G, Mohanty RR. Assessment of Coagulation Profile and its Correlation with Severity of Preeclampsia in Women of Odisha. Int J Physiol 2014;3(1):135-40.
8. Kumar PL, Nirmala T, Vani BR, Srinivasa MV, Geetha RL. Study of coagulation profile in pregnancy induced hypertension (PIH). Indian J Pathol Oncol 2015;2(1):1-6.
9. Steegers EA, von Dadelszen P, Duvekot JJ, Pijnenborg R. Pre-eclampsia. Lancet 2010; 376(9741):631-44.
10. Duley L. The global impact of pre-eclampsia and eclampsia. Semin Perinatol 2009;33(3):130-7.
11. Pankiewicz K, Szczerba E, Maciejewski T, Fijałkowska A. Non-obstetric complications in preeclampsia. Prz Menopauzalny 2019;18(2):99-109.
12. Xiong X, Fraser WD, Demianczuk NN. History of abortion, preterm, term birth, and risk of preeclampsia- a population-based study. Am J Obstet Gynecol 2002;187(4):1013-8.
13. Haldar, B, Barui G. Study of coagulation profile and platelet indices in pregnancy induced hypertension with special reference to preeclamptic and eclamptic patients. Int J Res Med Sci 2020;8(3):1114-8.
14. Sharma UP, Kouli R, Sonowal R, Saikia P. Coagulation Parameters in Pre- eclamptic and Eclamptic Patients- A Comparative Study of 90 Cases. Int J Contem Med Res 2016;3(8):2235-8.
15. Sultana R, Karim SF, Atia F, Ferdousi S, Ahmed S. Platelet count in preeclampsia. J Dhaka National Med Coll Hosp 2012;18(2):24-26.
16. Leduc L, Wheeler JM, Kirshon B, Mitchell P, Cotton DB. Coagulation profile in severe preeclampsia. Obstet Gynecol 1992;79(1):14-8.
17. Shete AN, Garkal KD, Deshmukh PR. Physiological parameters in pregnancy induced hypertension. Int J Recent Trends Sci Technol 2249-8109. 2013;7:3-5.
18. Lakshmi CV. Comparative Study of Coagulation Profile in Mild Pre-eclampsia, Severe Pre-eclampsia, and Eclampsia. Int J Scientific Study 2016;4(4):180-183.

Original Article

Role of Dexamethasone Therapy in Preventing Transient Hypocalcemia after Total Thyroidectomy

Nasir Wakeel[1], Asma Tariq[1], Iqra Gul[3] and Wajahat Hussain[2]

ABSTRACT

Objective: To see the effect of dexamethasone therapy in preventing transitory hypocalcemia after total thyroidectomy.

Study Design: Cross sectional analytical study

Place and Duration of Study: This study was conducted at the department of ENT, Bahawal Victoria Hospital, Bahawalpur from March 2020 till April 2021 for a period of one year.

Materials and Methods: Total 62 participants had complete thyroidectomy. Participants were randomly allocated to every one of 2 groups: control (n=32) and dexamethasone group (n=32) in which injected Intravenous dexamethasone 8 mg dose 45 minutes prior to skin incision procedure. All participants were screened for purpose of clinical and laboratory hypocalcaemia next to surgery.

Results: While adjusting of baseline factors, post-operative transitory biochemical hypoparathyroidism as well as hypocalcaemia was not occurred more commonly with in control study group and in those participants in the dexamethasone group. However, the dexamethasone & control groups had a big variation for phosphorus levels (P=0.028). Following surgery, a total of 17 patients (53.1%) had hypocalcemia. Furthermore, the control group 23 (71.9%) had symptomatic hypocalcemia following the operation frequently than the dexamethasone group 9 (28.1%), But statistically this difference was not significant (P=0.592).

Conclusion: Due to Pre-operative dexamethasone treatment, it caused decrease in the frequency of hypocalcemia post-operatively. For improved findings, further research must be conducted using validated approaches.

Key Words: Parathyroid hormone, Hypocalcemia, Dexamethasone

Citation of article: Wakeel N, Tariq A, Gul I, Hussain W. Role of Dexamethasone Therapy in Preventing Transient Hypocalcemia after Total Thyroidectomy. Med Forum 2021;32(10):54-58.

INTRODUCTION

Complete thyroidectomy has become a widely used surgical procedure for both benign as well as malignant conditions related to thyroid.[1,2,3] However, perhaps it would increase post-operative problems risks prior to substantial resection.[4] Thyroidectomy for transitory hypoparathyroidism has a problem related risk of 6.9-46 percent,[5,6,7] which results hypocalcemia post-operatively with a 1.6-50 percent occurrence rate.[8,9]

After a complete thyroidectomy, hypocalcemia seems to be the most common and occasionally the most severe consequence[10]. Hypocalcemia is most commonly caused by devascularization, the unexpected loss with one or even more parathyroid glands performing the surgery after hypothyroidism, or parathyroid glands can be injured during procedure of lymphadenectomy.[10,11]

As a result, using the right surgical approach during a complete thyroidectomy might avert problems, especially those involving the parathyroid glands.[12] On the other hand, after few Days to weeks prolonged hospital stay post-operative transitory hypocalcaemia usually responds positively to supplements provides for vitamin D and calcium. When individuals have calcium level at normal range but prophylactic consumption is given to them, it has the potential to cause hypercalcemia,[11] which is necessitating alternate treatment method. Prior to operation many potentially essential biological consequences of inflammatory responses are changed by pre-treatment by a glucocorticoid single dose, as found in several clinical investigations during various major and small procedures of surgery. This dose cause reduction in inflammatory response after surgery, as well as the complications numbers plus duration of stay in the hospital.[13,14] There are some well know actions of glucocorticoids like Antiemetic, immune-modulating, and analgesic effects.[15]

Dexamethasone is presented as an effective and safe corticosteroid medicine, when it is administrated in a single dose prior to operation it provides relief from

[1.] Department of ENT / Community Medicine[2], Quaid-e-Azam Medical College, Bahawalpur.
[3.] Department of ENT, THQ Hospital, Khair Pur Tamewali, Bahawalpur.

Correspondence: Dr. Nasir Wakeel, Assistant Professor of ENT, Quaid-e-Azam Medical College, Bahawalpur.
Contact No: 0308-6110710
Email: revire140@yahoo.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

post-operative conditions such as nausea, pain and vomiting.[16,17,18] Post-operative use of dexamethasone was recently found to reduce the prevalence and severity of sore throat when ingesting post thyroidectomy during a double-blind randomized study.[19] Yet in case of hypoparathyroidism there really are limited studies present in literature about the use of dexamethasone in post-operative duration.

Only one research concluded that single dexamethasone prior to thyroidectomy might impact transitory hypoparathyroidism after operation.[16] Therefore, the aim of this study was to see if use of dexamethasone prior to operation may help to prevent transitory hypocalcemia after total thyroidectomy.

MATERIALS AND METHODS

During March 2020 till April 2021, cross sectional analytical study was conducted at Bahawalpur Victoria hospital, after of institutional ethics review committee. A number of 64 individuals were included in the study in which complete thyroidectomy was done. The patients having a history of renal failure, parathyroid illness, or one-sided thyroid lobectomy were not included in the study. All surgical procedures were performed by experienced surgeons (with at least 5 years' experience after post-graduation).

Informed consent was taken from all the participants before data collection. All participants' demographic information was gathered including histological diagnosis, gender, age, plus pathology findings (specimen information about the existence of parathyroid tissues). The capsular dissection method was used to conduct the procedure of total thyroidectomy. The ENT specialist also a competent surgeon established the need for surgery. Clinical results and thyroid operations reference criteria were used to make the decision to have surgery.

The patients in this research were randomly assigned to one of two groups: control (n=32) or treatment (n=32). The participants in groups were matched in relations of gender and age to avoid duplication. Patients were randomly assigned to receive an intravenous 8 mg dexamethasone 45 minutes before going to procedure of skin incision. All of the participants were given general anaesthesia in the same way. The typical procedure lasted about 75 minutes. Vital signs (pulse oximetry, blood pressure, respiration, pulse, and appropriate answering) were checked within every 15 minutes when patients were in post-operative anesthesia care unit by an experienced person. Once vitals became controlled and steady, patients were shifted to ENT ward. Following surgery, all subjects were evaluated for hypocalcaemia during clinical plus analytical condition. Patients were also instructed to begin taking oral supplements for vitamin D analogue and calcium in case of appearance of symptoms or signs regarding hypocalcaemia. Patients who had circumoral numbness, paresthesia, sense of tingling spreading in fingers plus toes, muscular irritability or a positive Chvostek sign were considered to have symptomatic hypocalcemia. In individuals experiencing clinical hypocalcemia, oral supplements for vitamin D analogues and calcium were started. A minimum one serum calcium reading under 8.1 mg/dL (range for reference is 8.1-10.4 mg/dL) was defined as laboratory related hypocalcemia. If participants had symptomatic hypocalcemia or had a serum level for calcium less from 8.1 mg/dL, oral supplements for calcium were suggested.

For severe hypocalcemic symptoms or till oral treatment was not sufficient, an iv-calcium gluconate with 10% infusion was administered. When the levels of calcium serum were more than 8.1 mg/dL, the participants were discharged from facility. In addition, laboratory measurements including serum calcium, serum phosphorus, plus serum level of parathyroid hormone (PTH) were examined before to surgery, as well as after operation PTH and calcium levels at duration of 1, 6, and at the 24 hours.

Quantitative data was expressed using terms of mean whereas categorical data by frequency (percentage). Between groups quantitative data was compared by the use of independent t-test and for categorical data, Fisher test or Chi-square test was used. SPSS was used to perform all statistical computations (version 22.0).

RESULTS

There was a total of 64 participants included in the study analysis. Our dexamethasone group had 32 patients, whereas control group also had 32 (No dexamethasone treatment was given to these participants). In Table 1 the demographic features of participants in the dexamethasone versus control groups are shown. The only substantial difference between groups was the level of PTH before surgery (P<0.003).

Table No.1: Characteristics of the patients in dexamethasone and control group

Characteristics	Dexamethasone group (n=32)	Control group (n=32)	p-value
Gender Male Female	 25 (78.1%) 07 (21.9%)	 23 (71.9%) 09 (28.1%)	0.45
Age (Mean±S.D)	44.83±11.52	44.83±11.52	0.43
PTH pre-operative	35.53±20.51	57.6±24.25	0.003
Phosphor(mg/dL) pre-operative	7.0±0.50	8.23±0.54	0.80
Ca (mg/dL) pre-operative	2.9±0.61	2.50±0.47	0.79

There was a significant difference among two groups when level of PTH plus calcium were compared in pre- and post-operative condition (P<0.001; (Table.2). However, once baseline values were taken into account, there was no significant difference in between the two

groups. The differences for phosphorus levels in between the dexamethasone plus control groups seemed significant. The dexamethasone group and control group exhibited a significant variation in pre-operative PTH levels, but once correcting for the baseline values, the significant difference between the two groups was not found.

Table No.2: Calcium, phosphorus, and parathyroid hormone levels in the dexamethasone & control groups before and after Operation

Group	Parameter	Pre-operative Mean ±SD	Post-operative Mean ±SD	p-value
Dexamethasone group	PTH	37.93±21.80	16.62±12.65	<0.001
Control group		56.8±22.36	17.9±15.92	<0.001
Dexamethasone group	Calcium	9.0±0.52	8.7±0.69	0.854
Control group	(mg/dL)	8.20±0.51	8.50±0.29	<0.001
Dexamethasone group	Phosphorous	3.1±0.61	3.7±0.6	0.48
Control group	(mg/dL)	2.93±0.46	3.0±0.43	0.089

After surgery, 51% patients had hypocalcaemia. The control group had greater symptomatic hypocalcemia than the dexamethasone group after operation; although, statistically this difference was not the significant (P=0.54). Additionally, dexamethasone treatment further divided into subgroups and analyzed depending on the presence or absence for symptomatic hypocalcemia. There was a significant difference in PTH and calcium levels between prior and after operative procedure levels, for individuals having or not symptomatic hypocalcaemia. The post-operative serum level of calcium fell more often in individuals who had symptomatic hypocalcaemia than in individuals who did not develop symptomatic hypocalcaemia with (P=0.05).

DISCUSSION

When compared to the dexamethasone group, post-operative transitory biochemical hypoparathyroidism as well as hypocalcaemia did not happen more frequently with in control group during this study. Moreover, by comparing control group, the dexamethasone group had a non-significant low rate of post-operative symptomatic hypocalcemia occurring. Clinically evident hypoparathyroidism after operation is a serious consequence following complete thyroidectomy.[9,10] Although the exact cause of transitory hypoparathyroidism is unknown, the most widely accepted theory is that it is caused by the partial disruption of blood supply for the parathyroid gland, resulting in transitory hypocalcaemia.[10,12]

A large drop in blood calcium level in post-operative condition is an obviously strong indicator for hypocalcaemia. The prevention of symptomatic hypocalcaemia and a considerable decrease in days of stay in hospital and hospitalization expenditures can be achieved by earlier detection for hypocalcaemia plus prophylactic treatment.[11] There is insufficient information to draw definitive results about the drug's efficacy in reducing post-operative transitory hypocalcaemia.

However, it was discovered in one research that preventive therapy by one dose of dexamethasone (8 mg IV) might affect post-operative transitory hypoparathyroidism.[16] To the best of the authors' understanding, this is the first trial to show that dexamethasone is effective in preventing transitory hypoparathyroidism in individuals who have just had a complete thyroidectomy. During surgery, the risk of traumatic edema or vasospasm, which may have produced edema and/or transient hypoparathyroidism, may rise. Steroid treatment may avoid or decrease edema caused by surgical trauma, according to investigational and clinical studies.[16,17]

In other words, there is a role of Glucocorticoids as physiologic modifiers for response of inflammation after operation by the mean of reducing activity of vessels by constriction and persuaded response of cellular immunity which is controlled by function of cytokine.[15,18] Cytokines have an important role in post-operative immunological response.[19] In this study, it appears that dexamethasone decreased the induced immune response in parathyroid gland surgery, producing no major decrease there in dexamethasone group's transitory hypocalcaemia ratio. Research by Nasiri et al. showed that the preventive therapy with dexamethasone reduces vocal dysfunction at the day 1st following thyroidectomy and their study was line with the outcomes of this ongoing investigation.[20] Dexamethasone can be concluded to impact on results of thyroid surgery temporarily.

PTH and calcium levels were measured many times before and after surgery. The assessment of PTH and calcium levels before and after operation indicated a substantial difference between the dexamethasone and control groups without adjustment for baseline values. PTH levels fell more quickly in hypoparathyroidism patients than blood calcium levels did.[21] PTH levels changed significantly four hours after complete thyroidectomy, which guiding clinicians as a helpful predictor of hypocalcemia post-operatively for providing treatment to patients at high-risk as well as reduce the danger of hypocalcemia and early hospital release. There is no apparent link between pre-operative

level of blood calcium with post-operative hypocalcemia.[22,23] A meta-analysis which is recent stated that, there has been no clear link between pre-operative level of blood calcium with post-operative hypocalcemia.[24] On the one side, hypocalcemia played an important role in the diagnosis and treatment of hypocalcemia post-operatively. Consequently, measurement of calcium and PTH for appropriate hypocalcemia treatment looked reasonable before and after operation. While the administration time must be taken into account. According to a 2015 meta-analysis, the efficacy of a single dosage of pre-operative dexamethasone and the timing for administration of that dose are yet unclear.[25]

However, during the majority of trials, this medication was given 20-45 minutes before to anesthetic induction. Because glucocorticoids bound to receptor molecules and administration routs affect the commencement of biological action, it generally action within one or two hrs.[26]

In accordance all of these findings, we gave dexamethasone 45 minutes before to surgery to maximize the treatment's post-operative benefits. In conclusion, we weighed transitory hypoparathyroidism in patients following total thyroidectomy also these findings are based on prior researches and the efficacy and safety of dexamethasone (8 mg IV) for voice dysfunction, vomiting, pain, and tiredness.[17,27] When we compared the control group, with dexamethasone group and it had a lower rate of non-significant symptomatic hypocalcemia after operation. Dexamethasone dosing appears to be less important than careful surgical care.

CONCLUSION

Pre-operative dexamethasone dose decreased the incidence of hypocalcemia after operation. For better results, it is suggested that the investigation of study be enlarged with analytical methods.

Author's Contribution:

Concept & Design of Study:	Nasir Wakeel
Drafting:	Asma Tariq, Iqra Gul
Data Analysis:	Iqra Gul, Wajahat Hussain
Revisiting Critically:	Nasir Wakeel, Asma Tariq
Final Approval of version:	Nasir Wakeel

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Bron L, O'Brien C. Total thyroidectomy for clinically benign disease of the thyroid gland. Br J Surg 2004;91(5):569-74.
2. Rosato L, Avenia N, Bernante P, De Palma M, Gulino G, Nasi PG, et al. Complications of thyroid surgery: analysis of a multicentric study on 14,934 patients operated on in Italy over 5 years. World J Surg 2004;28(3):271-6.
3. Dener C. Complication rates after operations for benign thyroid disease. Acta oto-laryngologica 2002;122(6):679-83.
4. Falk SA, Birken EA, Baran DT. Temporary post thyroidectomy hypocalcemia. Archives of Otolaryngology-Head Neck Surg1988;114(2): 168-74.
5. Percival RC, Hargreaves AW, Kanis JA. The mechanism of hypocalcaemia following thyroidectomy. Acta endocrinologica 1985;109 (2): 220-6.
6. See A, Soo K. Hypocalcaemia following thyroidectomy for thyrotoxicosis. Br J Surg 1997;84(1):95-7.
7. Falk S. Complications of Thyroid Surgery: Hypocalcemia, Hypoparathyroidism. Thyroid disease: Endocrinology, Surgery, Nuclear Medicine, Radiotherapy-Raven Press, New York 1990;609-20.
8. Reeve T, Thompson NW. Complications of thyroid surgery: how to avoid them, how to manage them, and observations on their possible effect on the whole patient. World J Surg 2000; 24(8):971-5.
9. Asari R, Passler C, Kaczirek K, Scheuba C, Niederle B. Hypoparathyroidism after total thyroidectomy: a prospective study. Arch Surg 2008;143(2):132.
10. Tredici P, Grosso E, Gibelli B, Massaro M, Arrigoni C, Tradati N. Identification of patients at high risk for hypocalcemia after total thyroidectomy. Acta Otorhinolaryngologica Italica 2011;31(3):144.
11. Cavicchi O, Piccin O, Caliceti U, De Cataldis A, Pasquali R, Ceroni AR. Transient hypoparathyroidism following thyroidectomy: a prospective study and multivariate analysis of 604 consecutive patients. Otolaryngol-Head Neck Surg 2007;137(4):654-8.
12. Srinivasa S, Kahokehr AA, Yu T-C, Hill AG. Pre-operative Glucocorticoid Use in Major Abdominal Surgery: Systematic Review and Meta-Analysis of Randomized Trials. Annals Surg 2011;254(2): 183-91.
13. Holte K, Kehlet H. Perioperative single-dose glucocorticoid administration: pathophysiologic effects and clinical implications. J Am Coll Surg 2002;195(5):694-712.
14. Sapolsky RM, Romero LM, Munck AU. How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions 1. Endocrine Reviews 2000; 21(1):55-89.

15. Schietroma M, Cecilia EM, Carlei F, Sista F, De Santis G, Lancione L, et al. Dexamethasone for the prevention of recurrent laryngeal nerve palsy and other complications after thyroid surgery: a randomized double-blind placebo-controlled trial. JAMA Otolaryngology–Head Neck Surg 2013;139(5):471-8.
16. Feroci F, Rettori M, Borrelli A, Lenzi E, Ottaviano A, Scatizzi M. Dexamethasone prophylaxis before thyroidectomy to reduce post-operative nausea, pain, and vocal dysfunction: a randomized clinical controlled trial. Head Neck 2011;33(6):840-6.
17. Lachanas VA, Exarchos S, Tsiouvaka S, Tsea M, Hajiioannou JK, Skoulakis CE, et al. Does perioperative dexamethasone affect voice-related quality of life after thyroidectomy? European Arch Oto-Rhino-Laryngol 2014; 271 (11):3073-6.
18. Yang C, Jung SM, Bae YK, Park SJ. The effect of ketorolac and dexamethasone on the incidence of sore throat in women after thyroidectomy: a prospective double-blinded randomized trial. Korean J Anesthesiol 2017;70(1):64-71.
19. Nasiri S, Shafag S, Khorgami Z, Sodagari N, Aminian A, Hedayat A. Does corticosteroid have any beneficial effect on voice change after thyroidectomy? The Am Surg 2013; 79(12): 1258-62.
20. Hermann M, Ott J, Promberger R, Kober F, Karik M, Freissmuth M. Kinetics of serum parathyroid hormone during and after thyroid surgery. Bri J Surg 2008; 95(12): 1480-7.
21. Mazotas IG, Wang TS. The role and timing of parathyroid hormone determination after total thyroidectomy. Gland Surg 2017;6(Suppl 1): S38.
22. Edafe O, Balasubramanian SP. Incidence, prevalence and risk factors for post-surgical hypocalcaemia and hypoparathyroidism. Gland Surg 2017;6(Suppl 1):S59.
23. Edafe O, Antakia R, Laskar N, Uttley L, Balasubramanian SP. Systematic review and meta-analysis of predictors of post-thyroidectomy hypocalcaemia. Br J Surg 2014;101(4):307-20.
24. Cheng SP, Liu TP, Yang PS, Lee KS, Liu CL. Effect of perioperative dexamethasone on subjective voice quality after thyroidectomy: a meta-analysis and systematic review. Langenbeck's Arch Surg 2015;400(8):929-36.
25. Donnelly LE, Newton R, Kennedy GE, Fenwick PS, Leung RH, Ito K, et al. Anti-inflammatory effects of resveratrol in lung epithelial cells: molecular mechanisms. Am J Physiol-Lung Cellular Molecular Physiol 2004;287(4):L774-L83.
26. Zou Z, Jiang Y, Xiao M, Zhou R. The impact of prophylactic dexamethasone on nausea and vomiting after thyroidectomy: a systematic review and meta-analysis. PLoS One 2014;9(10):e109582.

Original Article

Potential Protective Effect of Melatonin on Acetaminophen-Induced Hepatotoxicity in Albino Rats

Hina Mawani[1], Abdul Majid[2], Asim Mehmood[4], Rashed Ahmed Soomro[5], Samreen Pandhiani[6] and Aftab Abbasi[3]

ABSTRACT

Objective: To determine the potential protective effect of melatonin on acetaminophen (APAP) induced hepatotoxicity in male Wistar albino rats.

Study Design: Experimental study

Place and Duration of Study: This study was conducted at the Department of Anatomy, Pharmacology, and Pathology, SRMC, Tando Adam from March 2019 to January 2020 for a period of 10 months.

Materials and Methods: 100 adult male rats were divided into five groups; Group A – negative control, Group B (positive control), C, D and E were given APAP (2 gram/Kg daily orally). Groups C, D and E received melatonin therapy 5, 10 and 15 mg/dl daily orally for six weeks. Blood samples were collected and sera separated by centrifugation. Sera were used for the liver functions tests and natural anti – oxidant enzymes. Data was analyzed on statistical SPSS package (ver. 21.0 at $p \leq 0.05$ (Confidence interval 95%).

Results: Six weeks melatonin therapy shows significant improvement in serum bilirubin, Prothrombin time (PT), alanine transaminase (ALT), aspartate transaminase (AST) and G-glutamyl transferase (GGT) and significant boosting effect on the superoxide dismutase (SOD), glutathione peroxidase (GPX) and catalase (CAT) ($P \leq 0.0005$) was noted.

Conclusion: The present study reports potential protective effect of melatonin in acetaminophen (APAP) induced hepatotoxicity in male Wistar albino rats.

Key Words: Melatonin, Acetaminophen, Liver toxicity, Rats

Citation of article: Mawani H, Abdul Majid, Mehmood A, Soomro RA, Pandhiani S, Abbasi A. Potential Protective effect of Melatonin on Acetaminophen-Induced Hepatotoxicity in Albino Rats. Med Forum 2021;32(10):59-63.

INTRODUCTION

Melatonin is secreted by the pineal gland during night time. Melatonin is a derivative of tryptophan through serotonin. Serotonin is methylated to yield melatonin. Melatonin is stored in pienalocytes of pineal gland and released into blood capillaries at night time during sleep.[1,2] Pineal gland melatonin regulates the sleep cycle through circadian rhythm. Secretion of melatonin is controlled by the light – dark cycles.

[1.] Department of Anatomy, Indus Medical College,, Tando Muhammad Khan, Sindh.
[2.] Department of Pathology / Anatomy[3], Isra University, Hyderabad, Sindh.
[4.] Department of Anatomy / Pathology[5] / Pharmacology[6], Suleman Roshan Medical College, Tando Adam, Sindh.

Correspondence: Dr. Samreen Pandhiani, Assistant Professor of Pharmacology, Suleman Roshan Medical College, Tando Adam, Sindh.
Contact No: 0333-7103324
Email: mailboxKxm@gmail.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

Melatonin is secreted in nighttime during sleep. It induces biological changes in body systems during sleep. It is sleep inducer that decreases metabolism, body temperature and breathing rats during sleeping. Beside Pineal gland, the melatonin is found in multiple cell and organs in particular the gastrointestinal tract.[1,2] Extra – pineal gland melatonin plays role of anti – oxidant and immunomodulation in local tissues. Melatonin functions in autocoid and paracoid pattern in tissues.[1,3] Melatonin has receptors on target cells present on cell membrane. Melatonin cell membrane receptors are of two types – the MT1 and MT2 that belong to the G-protein coupled receptor family.[1,4] Melatonin protects against oxidative stress as it is part of antioxidant defense system. Melatonin stimulates anti – oxidant enzyme systems and helps scavenge free radicals. Anti – oxidant activity of melatonin is observed in different cell compartments such as the membrane, cytosol, and nucleus. Studies suggest the melatonin exerts direct free radical scavenging activity against the oxygen derived free radicals.[1,3] Its anti – oxidant potential is more effective than glutathione, α – tocopherol, and mannitol[1] hence its protective role against proliferative and degenerative injuries is noticeable. Melatonin protects the macro – and micro – molecules such as the DNA from oxidative injuries.[1,5]

Melatonin shows anti – oxidant potential at very high peak concentrations higher than nighttime peak levels. Thus anti –oxidant activity is noticeable at high pharmacological doses.[6,7] Melatonin stabilizes the inner mitochondria membrane protecting against the electron transport chain (ETC) derived oxygen free radicals.[1,7] Melatonin protects against reactive oxygen species (ROS) and reactive nitrogen species (RNS) especially in the inner cell compartments.[1,7] Melatonin increases the physiological functioning of natural anti – oxidant enzymes such as the superoxide dismutase (SOD), glutathione peroxidase (GPX) and catalase (CAT) that maintain normal physiological homeostasis in different organs for example liver, that is the seat of free radical formations.[1,7] As the liver is active in performing different biochemical reactions throughout the clock hence it is vulnerable to oxidative injuries if exposed by chance resulting in hepatocellular necrosis.[1] Liver is major organs of biochemical reactions and injuries and acetaminophen (N-acetyl-para-aminophenol) (APAP) is a common hepatotoxin.[8,9] Accidental acetaminophen[9] injury is common toxicological problem in the patients presenting in the emergency room. Hence the present experimental study was conducted to determine the potential protective effect of melatonin on acetaminophen-induced hepatotoxicity in male Wistar albino rats.

MATERIALS AND METHODS

The present experimental study was conducted at the Department of Anatomy, Pharmacology, and Pathology, SRMC, Tando Adam in collaboration with Sindh Agriculture University. The study was approved by the Ethics committee of institute and carried out from March 2019 to January 2020. Ethical permission was also taken from the animal house of Sindh Agriculture University for conducting animal research. Protocol of Animal house was maintained strictly and animals handling was in accordance to the ethics regulations. One hundred adult male Wistar rats were purchased from the animal house and selected according to the inclusion criteria of study protocol. A rat of 150 – 200 grams, male gender and Wistar albino strain were inclusion criteria. Rats moving actively around cages, feeding and drinking water well were also inclusion criteria. Any rat found not feeding and drinking well, and moving lazy were excluded. Female rats, sick male with limited mobility in cages were also excluded. Animal house is well equipped with proper ventilation. Animals were housed in 12/12 dark/light cycle. Rats were divided into five groups; 20 rats in each group. Negative control (group A) – no intervention and given Normal saline as placebo therapy. Positive control (group B) was given acetaminophen (APAP) (2g/Kg) – only APAP was given to induce hepatotoxicity not given drug therapy. Group B was taken as positive control for comparison with experimental melatonin treated groups. Experimental groups C – E received APAP+ melatonin therapy as; Group C- was received APAP (2g/Kg)[10] + 5 mg melatonin[11] daily orally, Group D- received APAP (2g/Kg)[10] + 10 mg melatonin [11] daily orally, and experimental Group E- received APAP (2g/Kg)[10] + 15 mg melatonin[11] daily orally. Melatonin was given for six weeks. At the end of experiment, the rats were anesthetized with chloral hydrate and blood samples were taken from the retro – orbital venous plexus using a capillary tube put behind the eyeballs. Blood was taken into disposable syringes (BD, USA) collected in gel tubes. Centrifuged carried at 4000 rpm for 10 minutes get sera that were stored at -20^{0}C. Biochemical analysis was performed on sera for the liver function tests (spectrophotometric). Natural anti – oxidant enzymes (SOD, GPX, CAT) were detected by ELISA assay kit (Fortress Diagnostics). Laboratory findings were entered in a pre – structured proforma and kept in lockers confidential. Statistical analysis was performed on SPSS package (ver. 21.0, IBM, incorporation, USA) using one – way analysis variance (1- ANOVA) post – Hoc Benforinni test. Results significance was analyzed at $p \leq 0.05$ (Confidence interval 95%).

RESULTS

We observed highly significant effects of melatonin against the acetaminophen induced hepatotoxicity in male rats. The present study observed significant improvement of serum bilirubin, Prothrombin time (PT), alanine transaminase (ALT), aspartate transaminase (AST) and G-glutamyl transferase (GGT) ($P \leq 0.0005$) as shown in table –1. Melatonin therapy in acetaminophen treated rats a significant boosting effect on the superoxide dismutase (SOD), glutathione peroxidase (GPX) and catalase (CAT) ($P \leq 0.0005$) as shown in table – 2.

Table No.1: Liver function tests in control and experimental rats (n=100)

		Mean	SD	P-value
Total Bilirubin (mg/dL)	Group. A- Negative Control	0.57	0.11	≤0.0002
	Group B. APAP (Positive control)	2.75	0.72	
	Group C. APAP+ Melatonin (5 mg)	1.50	0.74	
	Group D. APAP+ Melatonin (10 mg)	1.17	0.28	
	Group E. APAP+ Melatonin (15 mg)	1.01	0.03	
	Group. A- Negative Control	7.19	1.54	
	Group B. APAP (Positive control)	13.70	1.09	

PT (sec)	Group C. APAP+ Melatonin (5 mg)	11.54	3.17	≤0.0001
	Group D. APAP+ Melatonin (10 mg)	9.32	2.54	
	Group E. APAP+ Melatonin (15 mg)	9.01	1.13	
ALT (U/L)	Group. A- Negative Control	32.70	6.39	≤0.0001
	Group B. APAP (Positive control)	69.82	13.19	
	Group C. APAP+ Melatonin (5 mg)	57.5	8.21	
	Group D. APAP+ Melatonin (10 mg)	53.13	7.66	
	Group E. APAP+ Melatonin (15 mg)	52.2	7.2	
AST (U/L)	Group. A- Negative Control	31.60	6.51	≤ 0.0005
	Group B. APAP (Positive control)	42.90	19.21	
	Group C. APAP+ Melatonin (5 mg)	36.53	10.71	
	Group D. APAP+ Melatonin (10 mg)	35.51	8.30	
	Group E. APAP+ Melatonin (15 mg)	33.1	3.12	
ALP (U/L)	Group. A- Negative Control	79.53	17.34	≤0.0001
	Group B. APAP (Positive control)	139.50	32.34	
	Group C. APAP+ Melatonin (5 mg)	115.70	41.57	
	Group D. APAP+ Melatonin (10 mg)	97.35	31.43	
	Group E. APAP+ Melatonin (15 mg)	91.34	11.03	
LDH (U/L)	Group. A- Negative Control	109.11	16.16	≤0.0005
	Group B. APAP (Positive control)	161.34	31.12	
	Group C. APAP+ Melatonin (5 mg)	139.51	31.11	
	Group D. APAP+ Melatonin (10 mg)	130.15	19.61	
	Group E. APAP+ Melatonin (15 mg)	119.31	10.31	
GGT (U/L)	Group. A- Negative Control	35.15	4.91	≤0.0001
	Group B. APAP (Positive control)	71.15	17.53	
	Group C. APAP+ Melatonin (5 mg)	57.25	18.81	
	Group D. APAP+ Melatonin (10 mg)	47.35	19.21	
	Group E. APAP+ Melatonin (15 mg)	41.18	11.00	

Table No.2: Anti – oxidant enzymes in control and experimental rats (n=100)

		Mean	SD	P-value
Superoxide Dismutase (U/ml)	Group. A- Negative Control	136.05	33.80	≤0.0001
	Group B. APAP (Positive control)	75.35	15.34	
	Group C. APAP+ Melatonin (5 mg)	112.70	19.27	
	Group D. APAP+ Melatonin (10 mg)	121.75	13.25	
	Group E. APAP+ Melatonin (15 mg)	131.43	11.31	
Glutathione peroxidase (nM/mL)	Group. A- Negative Control	137.10	31.23	≤ 0.0005
	Group B. APAP (Positive control)	87.14	21.35	
	Group C. APAP+ Melatonin (5 mg)	117.13	15.72	
	Group D. APAP+ Melatonin (10 mg)	121.35	11.08	
	Group E. APAP+ Melatonin (15 mg)	129.78	15.76	
Catalase (nM/mL)	Group. A- Negative Control	307.35	30.32	≤0.0001
	Group B. APAP (Positive control)	133.68	52.44	
	Group C. APAP+ Melatonin (5 mg)	201.35	71.19	
	Group D. APAP+ Melatonin (10 mg)	276.15	62.35	
	Group E. APAP+ Melatonin (15 mg)	187.91	78.19	

DISCUSSION

Human beings are constantly exposed to chemical pollutants and toxic drugs in the modern era. Many of chemicals are deleterious to the liver producing acute or chronic liver injury. Effects of melatonin against the chemical induced liver injuries have been studied widely.[1,2] The present study is the first experimental research conducted to clarify the effects of melatonin administration in acetaminophen induced liver toxicity in rat model. Ameliorative effects of melatonin against the APAP induced liver toxicity were observed in terms of liver function tests and natural anti – oxidant enzymes. In present study, the six weeks melatonin therapy improved the liver function test markers (Bilirubin, PT, ALT, AST & GGT) and anti – oxidant enzymes (SOD, GPX & CAT). We observed highly significant effects of melatonin against the

acetaminophen induced hepatotoxicity in male rats. Serum bilirubin and PT were improved; ALT, AST and GGT were decreased compared to positive control group B. The findigns of present study are in line keeping full concordant to previous studies.[1-3] We observed the melatonin therapy boosted natural anti – oxidant enzyme (SOD, GPX, CAT) significantly. We suggest the melatonin exerts effects through direct anti – oxidant activity and through inductions of natural anti – oxidant enzymes. It is explained the acetaminophen is converted to N – acetyl – benzoquinone – imine (NAPQI), an electrophilic metabolite. NAPQI is activated by the cytochrome P- 450 system that depletes the hepatic glutathione concentration resulting in ultimately in liver toxicity.[12] In present experimental rat model study, the acetaminophen treated positive control group B revealed peak rise in the liver parenchyma injury as marked by significant rise in the serum bilirubin ALT, AST and GGT that were ameliorated by melatonin therapy in experimental groups C, D and E. Acetaminophen overdose produces liver injury in both humans and animal equally.[12] Complete mechanism of APAP induced liver injury remains not well known but the NAPQI is involved with free radical mediated injury. [12] Several experimental models have shown drug induced liver toxicity with acetaminophen, albendazole, co-amoxiclav, labetaol, etc.[13,14] Many foods are reported to induce hepatotoxicity. Administration of melatonin in animal have shown increase GPX, GSSH, SOD, CAT NADP-dependent - isocitrate dehydrogenase, and glucose-6-phosphate dehydrogenase. A previous study[15] observed hepatic GSH concentration was decreased after melatonin therapy and concluded this was consumed in eradicating the free radical oxidation. In present study, we observed the melatonin therapy induced the natural anti – oxidant enzyme (SOD, GPX, CAT) significantly. We suggest the melatonin exerts effects through direct anti – oxidant activity and through inductions of natural anti – oxidant enzymes. A previous study[16] has shown anti – inflammatory effects of melatonin in experimental rabbits. It was concluded that the melatonin decreased liver injury by reducing apoptosis through attenuating endoplasmic reticulum stress.[17] Previous studies[18,19] investigated the potential of melatonin for treating the nonalcoholic steatohepatitis (NASH). Melatonin therapy was continued for three months and a significant improvement was observed in the liver function tests without any side effects.[18,19] The findings of above study are in agreement with our present study indicating the hepatoprotective efficacy of melatonin. A previous experimental study induced liver fibrosis by carbon tetrachloride (CCl_4) and investigated the melatonin effects against liver injury and fibrosis. Attenuation of CCl_4-induced liver fibrosis was observed with melatonin therapy. [20,21] This shows the hepatoprotective potential of melatonin similar to our present study. Findings of present study of melatonin against acetaminophen induced liver injury, in light of available literature, shows the drug may prove clinically effective in acetaminophen toxicity.

CONCLUSION

The present study reports potential protective effect of melatonin in acetaminophen (APAP) induced hepatotoxicity in male Wistar albino rats. It improves liver function tests through boosting of anti – oxidant enzymes; the superoxide dismutase, glutathione peroxidase and catalase. Further animal studies are warranted and similarly the clinical trials be conducted to make melatonin convenient for clinical use in different groups of patients with drug induced liver injury.

Author's Contribution:

Concept & Design of Study:	Hina Mawani
Drafting:	Abdul Majid, Asim Mehmood
Data Analysis:	Rashed Ahmed Soomro, Samreen Pandhiani, Aftab Abbasi
Revisiting Critically:	Hina Mawani, Abdul Majid
Final Approval of version:	Hina Mawani

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Oleshchuk O, Ivankiv Y, Falfushynska H, Mudra A, Lisnychuk N. Hepatoprotective Effect of Melatonin in Toxic Liver Injury in Rats. Medicina 2019;55 (304):1-11.
2. Oleshchuk OM, Ivankiv YI. Melatonin as hepatoprotector at diabetes. Bull Sci Res 2015;1:10–14.
3. Ivankiv YI, Oleshchuk OM. Indicators of prooxidant-antioxidant homeostasis of healthy animals under the introduction of melatonin. Med Clin Chem 2015;17:39–42.
4. Jaworek J, Konturek SJ, Leja-Szpak A. Role of endogenous melatonin and its MT2 receptor in the modulation of caerulein-induced pancreatitis in the rats. J Physiol Pharmacol 2002;53:791–804.
5. Aydogan S, Yerer MB, Goktas A. Melatonin and nitric oxide. J Endocrinol Investig 2006;29:281–287.
6. Galano A, Medina ME, Tan DX, Reiter RJ. Melatonin and its metabolites as copper chelating agents and their role in inhibiting oxidative stress: A physicochemical analysis. J Pineal Res 2015;58:107–116.
7. Li B, He X, Zhuang M, Niu B, Wu C, Mu H. Melatonin ameliorates busulfan-induced

spermatogonial stem cell oxidative apoptosis in mouse testes. Antioxid Redox Signal 2018;28(5):385-400.

8. Mahmood ND. Mamat SS, Kamisan FH, Yahha F, Kamarolzaman MFF, Nasir N, et al. Amelioration of Paracetamol-Induced Hepatotoxicity in Rat by the Administration of Methanol Extract of Muntingia calabura L. Leaves. BioMed Res Int`l 2014;Article ID 695678:1–10.
9. Al – Doaiss AA. Hepatotoxicity-induced by the therapeutic dose of acetaminophen and the ameliorative effect of oral co-administration of selenium / Tribulus terrestris extract in rats. Int`l J Morphol 2020; 38(5):1444-1454.
10. Bunchorntavakul C, Reddy KR. Acetaminophen related hepatotoxicity. Clin Liver Dis 2013; 17:587-607.
11. Wang TY, Li Y, Wu X, Yang XL, Wang Y, Wang D. Protective Effects of Melatonin on CCl4-induced Acute Liver Damage and Testicular Toxicity in Rats. Indian J Pharm Sci 2018; 80(6):1100-1107.
12. El – Gendy AA. Potential Protective Effect of Melatonin on Acetaminophen-Induced Hepatotoxicity in Albino Rats. Int J Med Phys 2020;13:1-12.
13. Liu YQ, Dai J, Hu K, Cai L, Lin L et al. Metformin alleviates acetaminophen-induced toxic hepatitis. Genom Appl Biol 2016;35:1633–1637.
14. Kurtgoz PO, Tunay H, Kurban F, Kurtgoz S, Demir K, Acarturk, G. Toxic hepatitis associated with amoxicillin-clavulanic acid in a chronic viral hepatitis B patient: A case report. Med J Bakirkoy 2016; 12:92–95.
15. Pashkov AN, Popov SS, Semenikhina AV, Rakhmanova TI. Glutathione system and activity of NADPH-generating enzymes in the liver of intact rats and animals with toxic hepatitis receiving melatonin. Bull Exp Biol Med 2005;139:565–568.
16. Laliena A, San Miguel B, Crespo I, Alvarez M, Gonzalez-Gallego J, Tunon MJ. Melatonin attenuates inflammation and promotes regeneration in rabbits with fulminant hepatitis of viral origin. J Pineal Res 2012;53:270–278.
17. Tunon MJ, San-Miguel B, Crespo I, Laliena A, Vallejo D, Alvarez M, Prieto J, Gonzalez-Gallego J. Melatonin treatment reduces endoplasmic reticulum stress and modulates the unfolded protein response in rabbits with lethal fulminant hepatitis of viral origin. J Pineal Res 2013;55:221–228.
18. Gonciarz M, Gonciarz Z, Bielanski W, Mularczyk A, Konturek PC, Brzozowski T, et al. The pilot study of 3-month course of melatonin treatment of patients with nonalcoholic steatohepatitis: Effect on plasma levels of liver enzymes, lipids, and melatonin. J Physiol Pharmacol 2010;61:705–710.
19. Gonciarz M, Gonciarz Z, Bielanski W, Mularczyk A, Konturek PC, Brzozowski T, Konturek SJ. The effects of long-term melatonin treatment on plasma liver enzymes levels and plasma concentrations of lipids and melatonin in patients with nonalcoholic steatohepatitis: A pilot study. J Physiol Pharmacol 2012; 63: 35–40.
20. Choi HS, Kang JW, Lee SM. Melatonin attenuates carbon tetrachloride-induced liver fibrosis via inhibition of necroptosis. Transl Res 2015;166:292–303.
21. Mortezaee K, Sabbaghziarani F, Omidi A, Dehpour AR, Omidi N, Ghasemi S, et al. Therapeutic value of melatonin post-treatment on CCl_4-induced fibrotic rat liver. Can J Physiol Pharmacol 2016; 94:119–130.

Original Article

A Study of Asymmetry in Foot Length in Adult Males

Syed Zia Uddin[1], Roman Ashraf[2], Sarba Khalid[3], Pervaiz Zarif[3] and Mazhar Murtaza[3]

ABSTRACT

Objective: Aim of the study was to find any dissimilarity in right and left foot length.
Study Design: Cross-sectional study
Place and Duration of Study: This study was conducted at the Lahore General Hospital, Lahore and duration of study is Jan, 2020 to Dec, 2020 for period of one year.
Materials and Methods: Non-probability Convenience sampling technique was used in this study. Statistical analysis was done by using SPSS 23.
Results: Mean RFL was 26.12 cm and mean LFL was 26.10 cm. Mean difference in right and left foot length was 0.013 cm with p value 0.139 indicating statistically insignificant difference
Conclusion: This study will be beneficial to orthopedic and forensic departments

Key Words: RFL (right foot length), LFL (left foot length), Asymmetry, Lahore General Hospital

Citation of article: Zia Uddin S, Ashraf R, Khalid S, Zarif P, Murtaza M. A Study of Asymmetry in Foot Length in Adult Males. Med Forum 2021;32(10):64-66.

INTRODUCTION

Dissymmetry is an absence of mirror image of an organ or part of the body on both sides of the body[1]. Human foot is one of the organs and parts of the body which shows dissimilarity in its length and other dimensions on both sides of the body. This variation in size differs not only in different ethnicities but also in different ages[2]. It may be due to combined impact of heredity, cultural, social and climatic factors[3]. Same physical factors affecting on movements of different individuals result in different levels of dissymmetry. Right sided dissymmetry is more noticeable in arms[4]. Dissymmetry of organs or part of body has been studied a lot. Many authors say that right foot length is more than left one[5,6]. Some of the studies show that LFL is more than RFL[7,8,9]. Mean foot length of males was more than that of females. LFL is more than RFL in both sexes[10]. A study has shown that there is a significantly higher mean value of foot length and foot breadth in males than females[5]. Litrature review is silent with respect to work on this topic in Pakistan.

[1.] Al-Aleem Medical College, Lahore.
[2.] Lahore Medical and Dental College, Lahore.
[3.] PGMI, Lahore.

Correspondence: Dr. Muhammad Asif, Assistant Professor, Sialkot Medical College, Sialkot.
Contact No: 0333-4272575
Email: drasif_hameed@hotmail.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

MATERIALS AND METHODS

It is cross-sectional study in nature conducted in Lahore General Hospital, Lahore and duration of the study is Jan-Dec 2020. A 200 sample size was taken of men with age between 20-25 years. Non-probability convenience sampling technique was used. Informed consent was taken. Every person was requested to show N.I.D., to confirm stated age. Both feet length was taken. Samples were asked to place their feet turn by turn on wooden board with steel scale fixed on its floor Distance between tip of the maximum projected portion of back of foot to the maximum forward projected portion at first toe was taken by measuring tape. Length was measured from most posterior part of heel to the tip of big toe after cutting the nail where required. Statistical Analysis was done by using SPSS 21.

RESULTS

Mean RFL was 26.12 cm and mean LFL was 26.10 cm. Mean difference in right and left foot length was 0.013 cm with p value 0.139 indicating statistically insignificant difference.

Data was gathered, arranged and put in to SPSS version 23. After collection of data, it was subjected to statistical analysis using Statistical Package for the Social sciences (SPSS) version 21.

Descriptive statistics of RFL and LFL: Minimum RFL and LFL is 23.00 cm. Maximum right foot length is 30.00 cm. Mean right foot length is 26.12 cm. The standard deviation is 1.44. Mean LFL is 26.10 cm. Maximum LFL is 30.00 cm. Minimum LFL is 23.00 cm. The standard deviation of left foot length is 1.44. As shown in table 1.

Table No.1: Paired difference between RFL and LFL

Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference		upper	T	Df	Sig. (2-tailed)
			lower					
0.013	0.1404	0.0091	-.0044		0.03157	1.48	199	0.139

Table No 2: Descriptive Statistics of RFL and LFL.

	Minimum	**Maximum**	**Mean**	**Std. Deviation**
RFL	23.00	30.00	26.122	1.443
LFL	23.00	30.00	26.108	1.445

In this study, there is the difference in mean lengths of right and left foot. Mean right foot length (26.122 cm) is more than mean left foot length(26.108 cm). Difference between mean length of right and left foot was 0.013 cm with an insignificant p-value (> 0.05). 0.139 was value of p which is more than 0.05 not rejecting the null hypothesis that there is no significant difference between right and left foot length. It means that difference between lengths of feet is not statistically significant. This is consistent with the studies which were carried out by different researchers as depicted in table 3. Various researches carried out in different areas of the world has denoted that average length of the right foot was greater than that on opposite side. Contrary to this a few other studies has shown opposite results. The current study also belongs to the second type of studies which are summerized in table no 4.

Table No. 3: Difference between feet lengths

Sr#	**Researcher**	**Country**	**Mean RFL**	**Mean LFL**
1	Bharati et al.[14]	Karnataka India	23.37	23.18
2	Agarwal et al.[15]	India	24.94	24.93
3	Jakhar et al.[16]	India	25.445	25.442
4	This study	Punjab, Pakistan	26.05	26.04
5	Ewunonu et al.[5]	Nigeria	26.40	26.28

Table No. 4: Difference between feet lengths

Sr#	**Researcher**	**Country**	**Mean RFL**	**Mean LFL**
1	Hemy et al.[13]	Western Australia	27.34	27.42
2	Abhilasha1, Ajitpal Singh[17]	India	26.71	26.64
3	Zhao X et al.[18]	Japan	24.24	24.18

DISCUSSION

Although the current study shows negligible difference between feet length yet a study carried out in Egypt has denoted large difference between feet length [6]. One of the reasons leading to this difference was due to over utilization of certain foot[11]. Another reason may be when during upbringing a person is repeatedly affected by diseases [12]. When a person goes on over utilizing a certain foot than the other the gap between both feet lengths also enlarges [13].

In a study it was found that mean foot length in Nigerian males was more than the feet length of individuals living in advance countries. As Nigeria is hotter than most of the advanced countries so the people will have to lose additional heat [19].

CONCLUSION

This study resulted that there is no statistically significant difference between right and left foot length. It will not only give information about normal asymmetry in organs and parts of body but will also help in orthopedic and forensic departments. It will also save the time of future scholars in studying both feet length. Shoe making may also be benefited by this study.

Author's Contribution:

Concept & Design of Study:	Syed Zia Uddin
Drafting:	Roman Ashraf, Sarba Khalid
Data Analysis:	Pervaiz Zarif, Mazhar Murtaza
Revisiting Critically:	Syed Zia Uddin, Roman Ashraf
Final Approval of version:	Syed Zia Uddin

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Valdez, D. Bilateral asymmetries in flexibility, stability, power, strength, and muscle endurance associated with preferred and nonpreferred leg. Doctoral dissertation, University of Florida 2003.
2. Rout N, Zhang YF, Khandual A, Luximon A. 3D foot scan to custom shoe last. Special Issue of Int J Computer and Communication Technol 2010;1: 14-18.
3. Alabi A, Oladipo G, Didia B, Aigbogun E, Akintunde K. Homo sapiens are bilaterally symmetrical but not with toe length and toe-length ratios among Nigerians. Anatomy J Africa 2017;6:1024-1032.
4. Auerbach BM, Ruff CB. Limb bone bilateral asymmetry: variability and commonality among modern humans. J Human Evolution 2006;50: 203-218.

5. Ewunonu E, Egwu A, Eteudo A, Ajoku K. Bilateral foot asymmetry and sexual dimorphism in young adult Igbo people of South-Eastern Nigeria. Eur J Biotechnol Biosci 2014;1(4):1-5.
6. Fawzy IA, Kamal NN. Stature and body weight estimation from various footprint measurements among Egyptian population. J Forensic Sci 2010;55(4): 884-888.
7. Uhrová P, Beňuš R, Masnicová S, Obertová Z, Kramárová D, Kyselicová K, et al. Estimation of stature using hand and foot dimensions in Slovak adults. Legal Med 2015;17(2): 92-97.
8. Hemy N, Flavel A, Ishak NI. Franklin D. Estimation of stature using anthropometry of feet and footprints in a Western Australian population. J Forensic Legal Med 2013;20:435-441.
9. Khairulmazidah M, Nadiah AN, Rumiza A. Stature Estimation Using Foot and Shoeprint Length of Malaysian Population.Int J Med Health Sci 2013; 7(7):365-368.
10. Alabi A, Oladipo G, Didia B, Aigbogun E. Foot Length and Preference: Implication in Footwear Design. Global J Anthropol Res 2016;3:25-30.
11. Krishan K, Kanchan T, Dimaggio JA. A study of limb asymmetry and its effect on estimation of stature in forensic case work. Forensic Sci Int 2010;200:181. e1-181. e5.
12. Anzellini A. Developing Methods for the Estimation of Stature and their Use as a Proxy for Health among the Ancient Chachapoya of Peru.M.A.thesis, University of Central Florida Orlando. Florida 2016;1-143.
13. Riskowski J, Hagedorn T, Dufour A, Hannan M. Functional foot symmetry and its relation to lower extremity physical performance in older adults: the Framingham Foot Study. J Biomechanics 2012;45: 1796-1802.
14. Bharati AS, Kumari S, Rani VS. Study of Correlation between Human Height and Foot Length in North-East Karnataka Population (Gulbarga and Bidar). Ind J Anatomy 2016;5(3): 299-302.
15. Agarwal S, Zaidi SHH, Agarwal SK. Correlation of Body Height By Foot Length and Knee Height Measurements in Population of North India. Int J Anatomy Res 2015; 3(3):1225-1229.
16. Jakhar JK, Pal V, Paliwal P. Estimation of height from measurements of foot length in Haryana Region. J Ind Acad Forensic Med 2010; 32(3):231-233.
17. Males OY. Bilateral Variations in the Foot Anatomy: Morphometric Analysis 2019;7(1): 399-404.
18. Zhao X, Tsujimoto T, Kim B, Katayama Y, Tanaka K. Characteristics of foot morphology and their relationship to gender, age, body mass index and bilateral asymmetry in Japanese adults. J Back and Musculoskeletal Rehabilitation 2017;30(3):527-35.
19. Chiroma SM, Philip J, Attah OO, Dibal NI. Comparison of the Foot Height, Length, Breadth and Foot Types between Males and Females Ga'anda People, Adamawa, Nigeria. IOSR J Dent Med Sci 2015;14(8): 89-93.

Original Article

Frequency of Low HDL in Young Patients in Acute Myocardial Infarction

Kashif Ali Hashmi, Muhammad Saeed Khalid and Hafiz Abdul Kabir

ABSTRACT

Objective: To evaluate the frequency of low HDL in young patients in acute myocardial infarction.
Study Design: Cross-sectional study
Place and Duration of Study: This study was conducted at the Department of Cardiology Ch. Pervaiz Elahi Institute of Cardiology, Multan from Sep, 2019 to Feb, 2020 for a period of 05 months.
Materials and Methods: Patients with acute myocardial infarction admitted within 24 hours were included. Lipid-lowering therapy, diabetes mellitus, and hypothyroidism were regarded as exclusion criteria. Demographic variables and the complete history of the patients were taken. 5 mL of venous blood was taken from patients during 24 hours of AMI and was immediately transferred to plain tubes. The samples were analyzed using calorimetric kit methods for the detection of High-density lipoprotein (HDL). HDL was considered deranged if found <40mg/dL in males or <50mg/dL in females.
Results: The age of the patients ranges from 20 to 35 years with the mean age of 28 ± 6.32 years. Among these 56.6% were males and 43.4% were females. Blood serum of 28 patients 46.6% out of 60 revealed low levels of high-density lipoprotein. Among these 28 patients, 20% were females and 26.6% were females. The comparison of percentages using chi-square revealed no statistically significant difference in the male and female groups ($p>0.05$). However, the overall percentage analysis shows significantly low levels of HDL in a study population of Acute myocardial infarction ($p<0.05$).
Conclusion: There is a high frequency of low HDL in young patients presenting with acute myocardial infarction.

Key Words: Acute myocardial infarction, Dyslipidemia, High-density lipoprotein

Citation of article: Hashmi KA, Khalid MS, Kabir HA. Frequency of Low HDL in Young Patients in Acute Myocardial Infarction. Med Forum 2021;32(10):67-70.

INTRODUCTION

Cardiovascular disease (CVD) has become a leading cause of morbidity and mortality in recent years. It has been estimated that cardiovascular disease is the cause of more than 100,000 deaths annually [(1)]. An epidemic of CVD in South Asians has been reported, hence Pakistan also has a high incidence of coronary artery disease[(2)]. With the increase in the incidence of coronary artery disease, cardiovascular disease has been regarded as a multifactorial disease [(3)]. The risk factors associated with cardiovascular disease include smoking, drinking, diabetes, and dyslipidemia. These risk factors also attribute to acute myocardial infarctions [(4)].
Among these factors, dyslipidemia is considered a strong indicator of cardiovascular outcomes following acute myocardial infarction [(5)].

Department of Cardiology Ch. Pervaiz Elahi Institute of Cardiology, Multan.

Correspondence: Kashif Ali Hashmi, Associate Professor of Cardiology, Ch Pervaiz Elahi Institute of Cardiology Multan.
Contact No: 0306-7302600
Email: drkash226@gmail.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

Dyslipidemia is a disorder of lipid metabolism resulting in premature atherosclerosis [(6)]. Dyslipidemia can be assessed by lipid profile evaluation. The lipid profile includes total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides (TG) [(7)]. Decreased levels of high-density lipoprotein and increased levels of triglycerides, total cholesterol, low-density lipoprotein result in the development of atherosclerosis and consequently coronary artery disease and events like acute myocardial infarction[(8)]. Lipid profile is evaluated differently depending upon age and gender. Recent evidence reveals that different lipid levels are associated with AMI patients belonging to different age groups and gender[(9)]. However, despite being modifiable risk factors of acute myocardial infarction, it is important to understand age-related differences in post-AMI characteristics of dyslipidemia [(10)].
It has been reported that the lipid profile is no longer valid after 24 hours following AMI. The Rapid decline occurs during the first 24 hours of presentation with AMI, however, there is no clear mechanism yet identified that can explain this[(11)]. A sigmoid relationship has been observed between total serum cholesterol and the prevalence of CAD in some studies done on the middle-aged group [(12)]. Along with the high frequency of dyslipidemia, there is also a particular pattern reported that has been termed as atherogenic lipid triad [(13)]. The pattern is associated with increased

levels of very low-density lipoprotein (VLDL), low-density lipoprotein, triglycerides, and reduced levels of high-density lipoprotein [14]. One of the important parameters in this triad is High-density lipoprotein. HDL is known to perform various atheroprotective functions. These functions include the removal of macrophages foam cells present inside arterial walls i.e., cholesterol efflux [15]. HDL also has anti-oxidative and anti-inflammatory potential for example it inhibits the expression of inflammation-induced adhesion molecules. Therefore HDL is involved in the inhibition of the prime events in the initiation of coronary artery disease [16]. It is now a well-established fact that populations with low levels of serum HDL are at higher risk of developing atherosclerosis that ultimately can lead to AMI [17]. The objective of the study was to evaluate the frequency of low HDL in young patients in acute myocardial infarction.

MATERIALS AND METHODS

This cross-sectional study was done from 7th Sep 2019 to 7th Feb 2020 at Department of Cardiology Ch. Pervaiz Elahi Institute of Cardiology Multan. 60 patients between age 20 to 35 years with acute myocardial infarction admitted within 24 hours onset of the chest pain and ST elevation was included in the study. All patients that were admitted later than 24 hours after the development of myocardial infarction or a diagnosed case of hypothyroidism, diabetes mellitus on history were excluded from the study. Besides this, the patients who were on lipid-lowering therapy such as statins and fibrates were also excluded from the study. Demographic variables and the complete history of the patients were taken. The study was conducted after taking written approval from the Institutional Review Board and Ethical Committee.

5 mL of venous blood was taken from patients during 24 hours of AMI and was immediately transferred to plain tubes. The samples were allowed to clot. The serum was then separated by centrifugation and stored until analysis. The samples were analyzed using calorimetric kit methods for the detection of High-density lipoprotein (HDL). HDL was considered deranged if found <40mg/dL in males or <50mg/dL in females.

Data Analysis: The data was collected and analyzed using the Standard package for the Social Sciences (SPSS version 16.0). Demographic variables were expressed as mean and standard deviation using descriptive statistics. A Frequency and percentage analysis of the obtained HDL results was done. Chi-square test was used and a p-value <0.05 was considered significant.

RESULTS

60 young participants were included in the study. The age of the patients ranges from 20 to 35 years with a mean age of 28 ± 6.32 years. Among these 34 (56.6%) were males and 26 (43.4%) were females. The mean BMI of the patients was calculated with a mean value of 25 ± 4.1. Total 18 patients (30%) were hypertensive based on the recorded history while no patient showed deranged glucose levels as expected following exclusion criteria. 10 of the patients with a history of high blood pressure were males and 8 were females.

Blood serum of 28 patients (46.6%) out of 60 revealed low levels of high density lipoprotein (Table II). Among these 28 patients, 12 (20%) were females and 16 (26.6%) were females (Table III). The comparison of percentages using chi square revealed no statistically significant difference in the male and female groups ($p>0.05$). However, the over-all percentage analysis shows significantly low levels of HDL in a study population of Acute myocardial infarction ($p<0.05$).

Table No.1: Demographic and clinical characteristics of Patients (n=60)

Variable	Variable	Value (Mean ± SD)
Age (years)	Mean SD	28 ± 6.32
Gender	Male (n) Female (n)	56.6% (34) 43.3% (26)
BMI (Kg/m2)	Mean SD	25± 4.1
Hypertensive	Male (n) Female (n)	16.6% (10) 13.3% (8)

Table No.2: Frequency of low HDL in Acute MI Patients

HDL	Frequency	% age
Low HDL	28	46.7%
Normal HDL	32	53.3%

Table No.3: Frequency of low HDL with respect to genders

Age (20-35 years)	Low HDL	Normal HDL
Male		
Frequency	16	18
%age	26.7%	30%
Female		
Frequency	12	14
%age	20%	23.3%

DISCUSSION

Being a part of the ethnic region where coronary artery disease is prevalent it has been estimated that around 100,000 people suffer from acute myocardial infractions annually in Pakistan [18]. Several studies have been done to date to correlate lipid profile with the incidence of acute myocardial infarction. However, there are no reports that particularly focus on High density lipoprotein and its link with acute myocardial infarction among the young population [19].

Significantly high levels of triglycerides and low levels of HDL are suggestive of atherosclerosis and its related cardiovascular events [20]. The low levels of HDL in

patients with acute myocardial infarction have also been reported in other Asian countries. The etiology behind this can be the genetic predisposition and the dietary habits [21].

Our study showed that there can be a relation of hypertension on serum levels of HDL as 30% of the patients showed a history of high blood pressure.

21 patients showed HDL cholesterol levels of less than 40mg/dl which is below normal as recommended by the National Cholesterol Education Program [22]. As these results are significant so there can be an association of low HDL levels with underlying coronary artery disease that led to the incidence of acute myocardial infarction in the study group [23]. There are shreds of evidence, particularly that a reduced Low density lipoprotein or high levels of High density lipoprotein can act against atherosclerosis, hence preventing the occurrence of cardiovascular events [24].

Another related factor found in literature is Human serum paraoxonase. It is an HDL bound enzyme, synthesized by the liver having antiatherogenic potential[25]. As this enzyme prevents oxidation of HDL it is considered a protective agent against coronary heart disease [26]. Therefore it can be inferred that the populations that show low levels of serum paraoxonase and HDL are at higher risk of developing myocardial infarction [27].

Countless epidemiological studies show that a higher concentration of HDL cholesterol in plasma is associated with a lower risk of coronary heart disease. The correlation of two variables alone cannot imply that one causes the other [28]. As there are other genetic and environmental factors that can influence these variables.

Furthermore, several clinical studies emerged with the concept that HDL function might be a better indicator in comparison to HDL cholesterol levels [28]. Similarly, it has been demonstrated among patients of acute myocardial infarction that HDL is defective in its antioxidative activity. Moreover, the severity of AMI events is also thought to have an impact on HDL function, AMI is a pro-inflammatory state which causes a decrease in cholesterol efflux potential of HDL [29].

Interestingly the decrease in anti-inflammatory properties of HDL results in high plasma myeloperoxidase levels which in turn is a strong predictor for future cardiovascular events in patients with AMI [30]. However, there are very few reports that investigated different functions of HDL relative to CVD.

All researchers have agreed with the concept that serum HDL rise and serum TGs fall right after acute MI. However, there is ambiguity in understanding of the events that causes the maximum change and later on causes the serum levels return to baseline. The serum HDL levels reach their maximum in 4 to 7 days and then return to normal in few months.

Besides this, there are methodological limitations to the interpretations of all HDL studies as till now no gold standard has been established for HDL isolation. Therefore, all available methods have their associated advantages and disadvantages [31].

CONCLUSION

The study concluded that there is a high frequency of low HDL in young patients presenting with acute myocardial infarction. It can be due to their genetic makeup and nutritional habits involving high consumption of saturated fats.

Author's Contribution:

Concept & Design of Study:	Kashif Ali Hashmi
Drafting:	Muhammad Saeed Khalid, Hafiz Abdul Kabir
Data Analysis:	Hafiz Abdul Kabir, Muhammad Saeed Khalid
Revisiting Critically:	Kashif Ali Hashmi, Muhammad Saeed Khalid
Final Approval of version:	Kashif Ali Hashmi

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Hedayatnia M, Asadi Z, Zare-Feyzabadi R, Yaghooti-Khorasani M, Ghazizadeh H, Ghaffarian-Zirak R, et al. Dyslipidemia and cardiovascular disease risk among the MASHAD study population. Lipids Health Dis 2020;19(1):1-11.
2. Martinez-Amezcua P, Haque W, Khera R, Kanaya AM, Sattar N, Lam CS, et al. The upcoming epidemic of heart failure in South Asia. Circulation: Heart Failure 2020;13(10):e007218.
3. Safai N, Carstensen B, Vestergaard H, Ridderstråle M. Impact of a multifactorial treatment programme on clinical outcomes and cardiovascular risk estimates: a retrospective cohort study from a specialised diabetes centre in Denmark. BMJ Open 2018;8(3):e019214.
4. Khunti K, Kosiborod M, Ray KK. Legacy benefits of blood glucose, blood pressure and lipid control in individuals with diabetes and cardiovascular disease: time to overcome multifactorial therapeutic inertia? Diabetes, Obesity and Metabolism 2018;20(6):1337-41.
5. Lu S, Bao MY, Miao SM, Zhang X, Jia QQ, Jing SQ, et al. Prevalence of hypertension, diabetes, and dyslipidemia, and their additive effects on myocardial infarction and stroke: a cross-sectional study in Nanjing, China. Annals Translational Med 2019;7(18).
6. Kurdi A, Martinet W, De Meyer GR. mTOR inhibition and cardiovascular diseases:

dyslipidemia and atherosclerosis. Transplantation 2018;102(2S):S44-S6.
7. Kopin L, Lowenstein CJ. Dyslipidemia. Annals Internal Med 2017;167(11):ITC81-ITC96.
8. Jialal I, Singh G. Management of diabetic dyslipidemia: An update. World J Diabetes 2019;10(5):280.
9. Chandrasekhar J, Gill A, Mehran R. Acute myocardial infarction in young women: current perspectives. Int J Women's Health 2018;10:267.
10. Yandrapalli S, Nabors C, Goyal A, Aronow WS, Frishman WH. Modifiable risk factors in young adults with first myocardial infarction. J Am Coll Cardiol 2019;73(5):573-84.
11. Kumar N, Kumar S, Kumar A, Shakoor T, Rizwan A. Lipid profile of patients with acute myocardial infarction (AMI). Cureus 2019;11(3).
12. Calling S, Johansson SE, Wolff M, Sundquist J, Sundquist K. The ratio of total cholesterol to high density lipoprotein cholesterol and myocardial infarction in Women's health in the Lund area (WHILA): a 17-year follow-up cohort study. BMC Cardiovascular Disorders 2019;19(1):1-9.
13. Wang FH, Liu J, Deng QJ, Qi Y, Wang M, Wang Y, et al. Association between plasma essential amino acids and atherogenic lipid profile in a Chinese population: A cross-sectional study. Atherosclerosis 2019;286:7-13.
14. Horlenko O, Arkhiy E, Prylypko L, Moscal O, Derbak M, Halay B. P335 'Lipid triad 'in patients with chronic pancreatitis in combination with arterial hypertension. BMJ Publishing Group Ltd; 2019.
15. Ito F, Ito T. High-density lipoprotein (Hdl) triglyceride and oxidized HDL: new lipid biomarkers of lipoprotein-related atherosclerotic cardiovascular disease. Antioxidants 2020; 9(5):362.
16. Gordon SM, Chung JH, Playford MP, Dey AK, Sviridov D, Seifuddin F, et al. High density lipoprotein proteome is associated with cardiovascular risk factors and atherosclerosis burden as evaluated by coronary CT angiography. Atherosclerosis 2018;278:278-85.
17. Kontush A. HDL and Reverse Remnant-Cholesterol Transport (RRT): Relevance to Cardiovascular Disease. Trends in Molecular Med 2020.
18. Rehman S, Li X, Wang C, Ikram M, Rehman E, Liu M. Quality of Care for Patients with Acute Myocardial Infarction (AMI) in Pakistan: A Retrospective Study. Int J Environmental Research Public Health 2019;16(20):3890.
19. Kheraj Mal RK, Mishal Ejaz KF. Comparison of lipid profile in patients with and without acute myocardial infarction. Cureus 2019;11(12).
20. Winter MP, Wiesbauer F, Blessberger H, Pavo N, Sulzgruber P, Huber K, et al. Lipid profile and long term outcome in premature myocardial infarction. Eur J Clin Investigation 2018; 48(10):e13008.
21. Gupta MD, Gupta P, Girish M, Roy A, Qamar A. Risk factors for myocardial infarction in very young South Asians. Current Opinion in Endocrinology, Diabetes and Obesity 2020; 27(2):87-94.
22. Khan SH, Asif N, Ijaz A, Manzoor SM, Niazi NK, Fazal N. Status of non-HDL-cholesterol and LDL-cholesterol among subjects with and without metabolic syndrome. Group 2018;2(14):15.
23. Kosmas CE, Martinez I, Sourlas A, Bouza KV, Campos FN, Torres V, et al. High-density lipoprotein (HDL) functionality and its relevance to atherosclerotic cardiovascular disease. Drugs in context 2018;7.
24. Poorzand H, Tsarouhas K, Hozhabrossadati SA, Khorrampazhouh N, Bondarsahebi Y, Bacopoulou F, et al. Risk factors of premature coronary artery disease in Iran: A systematic review and meta-analysis. Eur J Clin Investigation 2019; 49(7):e13124.
25. Ikhlef S, Berrougui H, Kamtchueng Simo O, Zerif E, Khalil A. Human paraoxonase 1 overexpression in mice stimulates HDL cholesterol efflux and reverse cholesterol transport. PLoS One 2017; 12(3):e0173385.
26. Ebtehaj S, Gruppen EG, Parvizi M, Tietge UJ, Dullaart RP. The anti-inflammatory function of HDL is impaired in type 2 diabetes: role of hyperglycemia, paraoxonase-1 and low grade inflammation. Cardiovascular Diabetol 2017;16(1):1-9.
27. Saber SI. Evaluating The Activity Of Paraoxonase 1 In Myocardial Infarction. Mosul J Nursing 2021;9(1):46-57.
28. Wongcharoen W, Sutthiwutthichai S, Gunaparn S, Phrommintikul A. Is non-HDL-cholesterol a better predictor of long-term outcome in patients after acute myocardial infarction compared to LDL-cholesterol?: a retrospective study. BMC Cardiovascular Disorders 2017;17(1):1-7.
29. Pirillo A, Catapano AL, Norata GD. Biological consequences of dysfunctional HDL. Current Med Chem 2019;26(9):1644-64.
30. Ramachandra CJ, Ja KMM, Chua J, Cong S, Shim W, Hausenloy DJ. Myeloperoxidase as a multi-faceted target for cardiovascular protection. Antioxidants Redox Signaling 2020;32(15): 1135-49.
31. Peng L, Qin J, Tang W, Li C. GW28-e0589 HDL function is impaired in acute myocardial infarction independent of plasma HDL cholesterol levels. J Am Coll Cardiol 2017;70(16S):C97-C.

Original Article

Role of Calcium Supplementation in Prevention of Preeclampsia in High Risk Women

Diana Kumari[1], Aruna Kumari Hira[1], Urooj Naz[1], Nusrat Jafri[2], Sarah Kazi[1] and Farhat Jafri[3]

ABSTRACT

Objective: To determine the efficacy of calcium supplementation in prevention of preeclampsia in high risk women.
Study Design: Quasi experimental
Place and Duration of Study: This study was conducted at the Department of Obstetrics and Gynecology, Civil Hospital, Karachi from June, 2019 to December, 2019 for a period of six months.
Materials and Methods: All pregnant women were given 2-gram calcium sachets to take with water after breakfast until delivery. These patients were monitored until they gave birth to check their blood pressure and assess the medication's effectiveness. They were followed up on in the OPD on a regular basis until delivery. SPSS-21 was used to analyze the data. The mean and standard deviation were used to present quantitative data, while frequency and percentage were used to present qualitative data.
Results: One hundred and forty-eight patients were included in this research. The patients' average age was 27.2±6.01 years. Calcium supplementation was found to be effective in preventing preeclampsia in 79.05% of high-risk women.
Conclusion: Calcium supplementation during pregnancy lowers systolic and diastolic blood pressure and prevents preeclampsia. While calcium supplementation is recommended for pregnant women at risk of preeclampsia, more patient data is needed to confirm calcium's effect on maternal and foetal morbidity.

Key Words: Calcium supplementation, Micronutrient supplements, Maternal nutrition, Maternal health, Preeclampsia

Citation of article: Kumari D, Hira AK, Naz U, Jafri N, Kazi S, Jafri F. Role of Calcium Supplementation in Prevention of Preeclampsia in High Risk Women. Med Forum 2021;32(10):71-75.

INTRODUCTION

Prematurity and enhanced perinatal mortality are linked to hypertension during gestation, which is currently one of the leading causes of maternal mortality and morbidity [1].

Pregnancy-induced hypertension (PIH) is defined as blood pressure metrics taken 6 hours apart that are equal to or greater than 140/90mmHg in previously normotensive women after the 20th week of pregnancy and without proteinuria [2].

1. Department of Obstetrics and Gynecology, Civil Hospital, Karachi.
2. Department of Obstetrics and Gynecology, Abbasi Shaheed Hospital, Karachi
3. Department of Community Health Sciences, KMDC, Karachi.

Correspondence: Dr. Urooj Naz, Senior Registrar, Department of Obstetrics and Gynecology, Civil Hospital, Karachi.
Contact No: 0332-2529126
Email: dr_uroojnaz@hotmail.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

Preeclampsia is a clinical syndrome with an unknown aetiology that manifests as hypertension and proteinuria after 20 weeks of pregnancy in previously healthy women. Calcium necessities are elevated during pregnancy and lactation to maintain calcium balance and maternal bone density, as well as to meet foetal growth requirements. A sufficient maternal nutritional status, as well as a sufficient daily intake of micronutrients such as folic acid, vitamins, and minerals, are required for a normal pregnancy outcome[3,4]. Several studies have shown that calcium supplementation during pregnancy has beneficial effects on bone mineralization, foetal growth, and the prevention of maternal osteopenia [5].

Preeclampsia can be prevented by taking calcium supplements regularly during pregnancy, according to WHO guidelines.[6] The effectiveness of calcium supplementation for the prevention of preeclampsia in populations with low dietary intake and a high risk of preeclampsia has also been questioned by prominent obstetrics professional organizations. [7]

According to the WHO, "Calcium supplementation as part of antenatal care is recommended for the prevention of preeclampsia among pregnant women, particularly among those at higher risk of hypertension, in populations where calcium intake is low." [6] This strong recommendation is based on moderate-quality

evidence from meta-analyses of randomized clinical trials, which found that calcium supplementation prevented roughly half of all cases of preeclampsia. [8]
Calcium supplementation has a 59 percent efficacy in preventing preeclampsia in high-risk females, according to Imdad A, et al [9]. Calcium supplementation has a 31.6% effect in treating preeclampsia in high-risk women, according to Khaing W, et al. [10]
The goal of this study is to see how effective calcium supplementation is at preventing preeclampsia in high-risk pregnant women. Even after the WHO's recommendations, there is no local evidence on this crucial topic. The majority of these studies were conducted on a global scale, and because our environment, genetics, diet, and habits differ from theirs, local data on their significance is inconclusive. The findings of my research will not only provide local evidence, but will also pave the way for future research on this topic.

MATERIALS AND METHODS

This research took place over a six-month period, from June to December 2019. On Doppler ultrasound, a total of 148 patients had a uterine artery pulsating index greater than 1.1 and at least one of the following factors: h/o preeclampsia in previous pregnancies on medical record or Chronic hypertension on medical record or BMI > 30 Kg/m^2 or Family history of hypertension were included in the study using a non-probability consecutive sampling technique if the eligibility criteria were met. If the incidence efficacy of calcium supplementation in preventing preeclampsia in high-risk women is 31.6%[10], the margin of error is 5%, and the level of confidence is 95%, then a sample of at least 148 patients is required. Women between the ages of 18 and 40, gestational age of 20 weeks on LMP, and parity of 0 to 4 were eligible. Women with h/o diabetes on medical records, h/o renal disease on medical records, or h/o parathyroid disorder on medical records were excluded.
A detailed history was taken, including age, parity, current history, and previous history of any medical disorder. During the examination, the patient's weight, height, and blood pressure were measured. Every visit, a standard manual sphygmomanometer was used to check blood pressure. Any woman who had a BP reading of more than 140/90 mm hg six hours apart was offered a 24-hour proteinuria test to quantify protein in urine through laboratorial analysis. All pregnant women were given 2-gram calcium sachets to take with water after breakfast until delivery. These patients were monitored until delivery to ensure that the medication was working properly. They were followed up on in the OPD on a regular basis until delivery.
Blood pressure of 140/90 mmHg (on two occasions at least 6 hours apart) and proteinuria of 300 mg/24 hours were considered positive signs of preeclampsia. No preeclampsia during pregnancy was defined as efficacy. For quantitative variables such as age, parity, weight, height, and BMI, the mean and standard deviation were presented. For qualitative variables like history of chronic hypertension, family history of hypertension, or previous history of pre-eclampsia, and efficacy, frequency and percentage were calculated. Stratification was used to control effect modifiers such as age, parity, BMI, history of hypertension, family history of hypertension, or previous history of pre-eclampsia. The chi square test was used after stratification, and p 0.05 was considered statistically significant.

RESULTS

A total of 148 high risk patients were included in this study. The average age of the patients was 27.21±6.01 years. Similarly mean parity, weight, height and BMI of the patients are also reported in table 1. History of hypertension was observed in 53.38% women figure 1. Family history of pre-eclampsia was found in 75(50.68%) as shown in figure 2. Family history of hypertension was also observed in 99(66.89%) as presented in figure 3. Efficacy of calcium supplementation in prevention of preeclampsia in high risk women was 79.05% (117/148) as presented in figure 4. Efficacy of calcium supplementation was not statistically significant with respect to age groups, parity, patients who had history of hypertension and history of pre-eclampsia but it was statistically significant with family history of hypertension table 2.

Table No.1 Descriptive Statistics of the Patients (N=148)

Variables	Mean	Std. Deviation
Age (Years)	27.21	6.01
Parity	1.61	1.27
Weight (kg)	70.04	12.11
Height (cm)	161.84	9.72
BMI (kg/m^2)	26.83	4.79

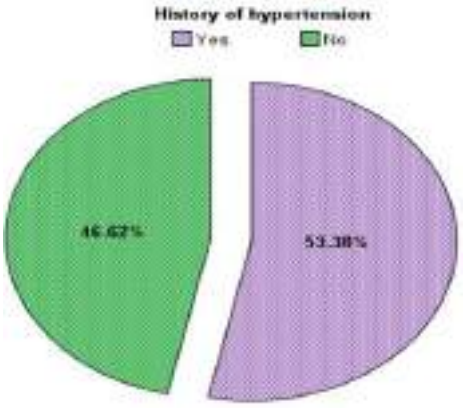


Figure No.1: History of Hypertension of Patients (N=148)

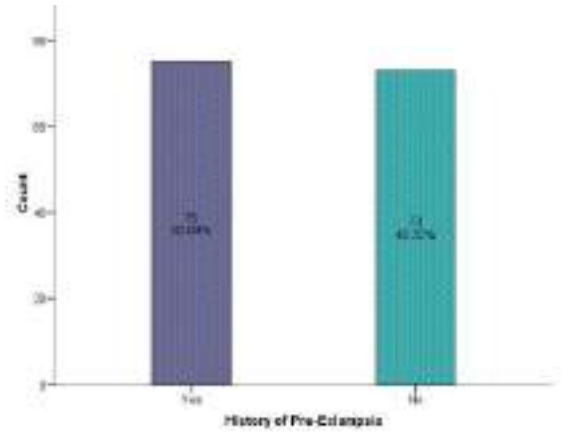


Figure No.2: Family History of Preeclampsia (N=148)

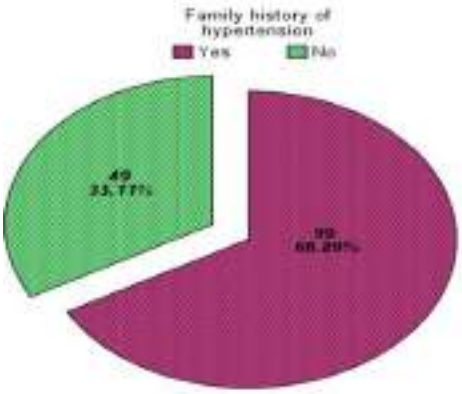


Figure No.3: Family History of Hypertension (N=148)

Table no.2: Efficacy of calcium supplementation in prevention of Preeclampsia in high risk women

Effect Modifiers	Efficacy of Calcium Supplementation		P-value
	Yes	No	
Age Groups (Years)			
≤ 20 Years	26(86.7%)	4(13.3%)	
21-30 Years	55(83.3%)	11(16.7%)	
>30 Years	36(69.2%)	11(16.7%)	0.09
Parity			
0	28(80%)	7(20%)	
1-2	62(80.5%)	15(19.5%)	0.788
3-4	27(75%)	9(25%)	
H/o Hypertension			
Yes	64(81%)	15(19%)	
No	53(76.8%)	16(23.2%)	0.53
H/o Preeclampsia			
Yes	59(78.7%)	16(21.3%)	
No	58(79.5%)	15(20.5%)	0.907
Family H/o Hypertension			
Yes	85(85.9%)	14(14.1%)	
No	32(65.3%)	17(34.7%)	0.004

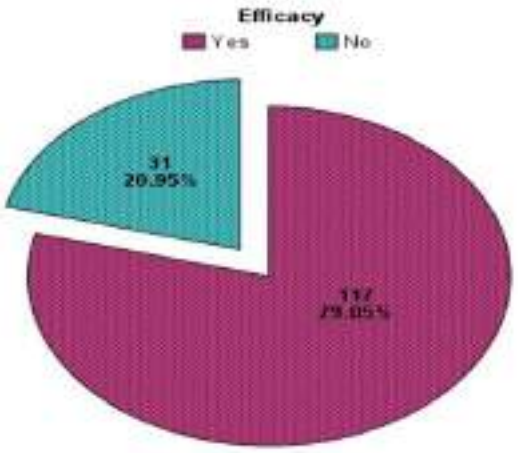


Figure No.4: Efficacy of Calcium Supplementation in Prevention of Preeclampsia in High Risk Women (N=148)

DISCUSSION

After 20 weeks of pregnancy, preeclampsia is defined as a new onset of high blood pressure with proteinuria and/or end-organ or utero-placental dysfunction. It's one of the leading causes of maternal-fetal morbidity and mortality all over the world [11]. Preeclampsia and eclampsia affected 4.6 percent and 1.4 percent of all pregnancies, respectively[12]. In developed countries, the incidence was around 3.4 percent [13], whereas in developing countries, it ranged from 1.8 percent to 16.7 percent[13,14]. In low and middle-income countries, preeclampsia or eclampsia is responsible for 10% to 15% of maternal deaths [15], whereas in developed countries, it is responsible for one in every 100,000 live births[16]. It was also linked to life-threatening adverse outcomes in both the mother and the foetus (e.g., placental abruption, preterm delivery and hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome, etc.) [17].

High blood pressure and calcium intake have been shown to have an inverse relationship in the past [18, 19]. This link has also been shown in a number of epidemiological and clinical studies [18-21], as well as a series of systematic reviews [22-25]. Their findings suggest that calcium supplements (1g/day) may reduce the risk of preeclampsia[26].

As a result, the World Health Organization (WHO) recommends calcium supplementation for pregnant women, particularly those in high-risk populations who consume a low-calcium diet[27].

There has been one previous study of calcium supplementation in early pregnancy[28]. This small RCT assessed calcium and antioxidant supple-mentation initiated at 8–12 weeks' gestation paralleled with placebo and found declines in pre-eclampsia (two of 29 in the calcium group *vs* nine of 31 in the placebo group) and miscarriage (zero of 29 *vs* eight of 31) with the intervention; the outcomes are indicative of a calcium

effect since antioxidants have not been establish to lessen pre-eclampsia [29].

Calcium supplementation was found to be 79.05% effective in preventing preeclampsia in high-risk women. Calcium supplementation has a 59 percent efficacy in preventing preeclampsia in high-risk women, according to Imdad A, et al. [8] Calcium supplementation has a 31.6% efficacy in preventing preeclampsia in high-risk women, according to Khaing W, et al. [9,10]

Vitamin D is involved in bone metabolism, calcium and phosphate absorption, and muscle function maintenance [30]. As a result, vitamin D supplementation may be beneficial in preventing preeclampsia. However, systematic reviews of randomized controlled trials (RCTs) [31,32] found no benefit in preeclampsia prevention, whereas two systematic reviews of observational studies [33,34] did. This disparity could be due to confounding bias in the latter or a lack of power in the former. Tang et al. found that calcium supplementation had the same effect in high-risk pregnancy, but not in low-risk pregnancy [35]. Furthermore, the effect of calcium supplementation was significantly beneficial in developing countries but not in developed countries, which was consistent with Imdad et al. [36], who discovered that calcium supplementation was beneficial in developing countries with low calcium intake. As a result, the WHO has recommended that high-risk pregnant women with low calcium intake receive calcium supplementation as part of routine antenatal care to prevent preeclampsia. The results of vitamin D supplementation and calcium plus vitamin D supplementation are also consistent with the findings of the most recent Cochrane review [30]. Although the effects of these supplements may reduce the risk of preeclampsia, more high-quality RCTs are needed to confirm the findings. For preventing preeclampsia, vitamin D may be preferable. The following are some possible explanations for this result: to begin with, adequate vitamin D intake may help to maintain calcium homeostasis, which has an inverse relationship with blood pressure [20], or it may directly suppress vascular smooth muscle cell proliferation [37]. Second, vitamin D may act as an endocrine suppressor of renin biosynthesis and regulate the renin-angiotensin system, which is important in blood pressure regulation. Third, vitamin D may modulate the immune system by balancing T helper cells [37].

CONCLUSION

Calcium supplementation during pregnancy lowers systolic and diastolic blood pressure and prevents preeclampsia. While calcium supplementation is recommended for pregnant women at risk of preeclampsia, more patient data is needed to confirm calcium's effect on maternal and foetal morbidity.

Author's Contribution:

Concept & Design of Study:	Diana Kumari
Drafting:	Aruna Kumari Hira
Data Analysis:	Nusrat Jafri, Urooj Naz
Revisiting Critically:	Sarah Kazi, Farhat Jafri
Final Approval of version:	Farhat Jafri

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Jabeen M, Yakoob MY, Imdad A, Bhutta ZA. Impact of interventions to prevent and manage preeclampsia and eclampsia on stillbirths. BMC Public Health 2011;11 Suppl 3:S6.
2. Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY. Williams Obstetrics. 23rd ed. New York: McGraw-Hill; 2010.
3. Simpson JL, Bailey LB, Pietrzik K, Shane B, Holzgreve W. Micronutrients and women of reproductive potential: required dietary intake and consequences of dietary deficiency or excess. Part I–Folate, Vitamin B12, Vitamin B6. J Matern Fetal Neonatal Med 2010;23:1323–43.
4. Simpson JL, Bailey LB, Pietrzik K, Shane B, Holzgreve W. Micronutrients and women of reproductive potential: required dietary intake and consequences of dietary deficiency or excess. Part II–vitamin D, vitamin A, iron, zinc, iodine, essential fatty acids. J Matern Fetal Neonatal Med 2011;24:1–24.
5. Hofmeyr GJ, Mlokoti Z, Nikodem VC, Mangesi L, Ferreira S, Singata M, Jafta Z, et al. WHO Calcium Supplementation for the Prevention of Pre-eclampsia Trial Group. Calcium supplementation during pregnancy for preventing hypertensive disorders is not associated with changes in platelet count, urate, and urinary protein: a randomized control trial. Hypertens Pregnancy 2008;27:299–304.
6. World Health Organization. Guideline: calcium supplementation in pregnant women; World Health Organization: Geneva, Switzerland, 2013.
7. Tranquilli AL, Dekker G, Magee L, Roberts J, Sibai BM, Steyn W, et al. The classification, diagnosis and management of the hypertensive disorders of pregnancy: a revised statement from the ISSHP. Pregnancy Hypertens 2014;4:97–104
8. Omotayo MO, DickinKL,O'Brien KO, Neufeld LM, De Regil LM, Stoltzfus RJ. Calcium supplementation to prevent preeclampsia: translating guidelines into practice in low-income countries. Adv Nutr 2016;7(2):275–8.
9. Imdad A, Jabeen A, Bhutta ZA. Role of calcium supplementation during pregnancy in reducing risk of developing gestational hypertensive disorders: a meta-analysis of studies from developing countries. BMC Public Health 2011;11(Suppl 3):S18.
10. Khaing W, Vallibhakara SAO, Tantrakul V. Calcium and vitamin D supplementation for prevention of preeclampsia: a systematic review

and network meta-analysis. Nutrients 2017;9(10):1141-45.
11. Tranquilli AL, Dekker G, Magee L. The classification, diagnosis and management of the hypertensive disorders of pregnancy: A revised statement from the ISSHP. Pregnancy Hypertens 2014;4:97-99.
12. Abalos E, Cuesta C, Grosso AL. Global and regional estimates of preeclampsia and eclampsia: a systematic review. Eur J Obstet Gynecol Reprod Biol 2013;170:1-5.
13. Ananth CV, Keyes KM, Wapner RJ. Pre-eclampsia rates in the United States, 1980–2010: Age-period-cohort analysis. BMJ 2013;347:f6564.
14. Osungbade KO, Ige OK. Public health perspectives of preeclampsia in developing countries: Implication for health system strengthening. J Pregnancy 2011;2011:1–6.
15. Abalos E, Cuesta C, Carroli G, Qureshi Z, Widmer M, Vogel, et al. WHO Multi country Survey on Maternal and Newborn Health Research Network. Pre-eclampsia, eclampsia and adverse maternal and perinatal outcomes: A secondary analysis of the world health organization multi country survey on maternal and newborn health. BJOG Int J Obstet Gynaecol 2014;121:14–24.
16. MacKay AP, Berg CJ, Atrash HK. Pregnancy-related mortality from preeclampsia and eclampsia. Obstet Gynecol 2001;97:533–38.
17. Berzan E, Doyle R, Brown CM. Treatment of preeclampsia: Current approach and future perspectives. Curr Hypertens Rep 2014;16:473.
18. Cunningham FG, Roberts JM, Taylor RN. The clinical spectrum of preeclampsia. In Chesley's Hypertensive Disorders in Pregnancy, 4th ed.
19. Taylor RN, Roberts JM, Cunningham FG, Lindheimer MD, editors. Elsevier Science: Amsterdam, the Netherlands; 2014.p.25–36.
20. Belizán JM, Villar J, Repke J. The relationship between calcium intake and pregnancy-induced hypertension: Up-to-date evidence. Am J Obstet Gynecol 1988;158:898–902.
21. Villar J, Belizan JM, Fischer PJ. Epidemiologic observations on the relationship between calcium intake and eclampsia. Int J Gynaecol Obstet 1983;21:271–78.
22. Villar J, Repke J, Belizan JM, Pareja G. Calcium supplementation reduces blood pressure during pregnancy: Results of a randomized controlled clinical trial. Obstet Gynecol 1987;70:317–22.
23. Hofmeyr GJ, Atallah AN, Duley L. Calcium supplementation during pregnancy for preventing hypertensive disorders andrelated problems. Cochrane Database Syst Rev 2006;CD001059.
24. Hofmeyr GJ, Duley L, Atallah A. Dietary calcium supplementation for prevention of pre-eclampsia and related problems: A systematic review and commentary. BJOG Int J Obstet Gynaecol 2007;114:933–43.
25. Hofmeyr GJ, Lawrie TA, Atallah AN, Duley L. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database Syst Rev 2010;CD001059.
26. Hofmeyr GJ, Lawrie TA, Atallah AN, Duley L, Torloni MR. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database Syst Rev 2014;6:CD001059.
27. World Health Organization. Guideline: Calcium Supplementation in Pregnant Women; World Health Organization: Geneva, Switzerland, 2013.
28. Rumiris D, Purwosunu Y, Wibowo N, Farina A, Sekizawa A. Lower rate of preeclampsia after antioxidant supplementation in pregnant women with low antioxidant status. Hypertens Pregnancy 2006;25:241–53.
29. Hofmeyr GJ, Manyame S. Calcium supplementation commencing before or early in pregnancy, or food fortification with calcium, for preventing hypertensive disorders of pregnancy. Cochrane Database Syst Rev 2017;9: CD011192.
30. Pérez-López FR. Vitamin D. The secosteroid hormone and human reproduction. Gynecol. Endocrinol 2007;23:13–24.
31. Pérez-López FR, Pasupuleti V, Mezones-Holguin E, Benites-Zapata VA, Thota P, et al. Effect of vitamin D supplementation during pregnancy on maternal and neonatal outcomes: A systematic review and meta-analysis of randomized controlled trials. Fertil Steril 2015;103:1278–88.
32. De-Regil LM, Palacios C, Lombardo LK, Pena-Rosas JP. Vitamin D supplementation for women during pregnancy. Cochrane Database Syst Rev 2016;CD008873.
33. Aghajafari F, Nagulesapillai T, Ronksley PE, Tough SC, O'Beirne M, Rabi DM. Association between maternal serum 25-hydroxyvitamin d level and pregnancy and neonatal outcomes: Systematic review and meta-analysis of observational studies. BMJ 2013;346:f1169.
34. Tang R, Tang IC, Henry A, Welsh A. Limited evidence for calcium supplementation in preeclampsia prevention: A meta-analysis and systematic review. Hypertens. Pregnancy 2015;34:181–203.
35. Imdad A, Bhutta ZA. Effects of calcium supplementation during pregnancy on maternal, fetal and birth outcomes. Paediatr Perinat Epidemiol 2012;26:138–52.
36. Cardus A, Parisi E, Gallego C, Aldea M, Fernandez E, Valdivielso J. 25-dihydroxyvitamin D3 stimulates vascular smooth muscle cell proliferation through a vegf-mediated pathway. Kidney Int 2006;69;1377–84.
37. Evans KN, Bulmer JN, Kilby MD, Hewison M. Vitamin D and placental-decidual function. J Soc Gynecol Investig 2004;11:263–71.

Original Article

Glycemic Control Among Children with Type 1 Diabetes Mellitus in Northern Areas of Pakistan

Saima Gillani[1], Muhammad Junaid Khan[2], Zaheer Abbas[1], Abdur Razzaq[1], Ijaz Ahmed and Shazia Sadaat[1]

ABSTRACT

Objective: To find the glycemic control in type 1 diabetes mellitus (T1DM) children and highlight the factors associated with its poor control.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Ayub Teaching Hospital, Pediatrics ward for a duration of two years from January 2019 to April 2021.

Materials and Methods: By convenient sampling technique, total 53 patients were included in the study. After ethical approval from institutional ethical review committee, and ensuring the inclusion/exclusion criteria, HbA1C was measured in all patients. Children with glycated haemoglobin (HbA1C) equal to 8.0% or less were categorized as having good control. Data were recorded on a proforma and then entered in IBM SPSS (Version 21). For seeing the association between dependent (glycemic control) and independent variables (age, gender, anthropometric variables and) chai square test was used. A P-value less than 0.05 was considered significant.

Results: Total 53(100%) children of mean age 10.18 ± 5.278 years with a mean height of 123.01 ± 25.909 centimeters, the weight of 25.22±14.066 kilograms were included in the study. Their mean HbA1C level was 10.90±2.475%. The incidence of poor glycemic control (PGC) appeared alarming i.e., 46(86.8%). While comparing glycemic controls of T1DM patients with gender, socioeconomic status, parents' literacy etc., none of the p-values was significant. The majority of patients i.e.,22(41.5%) with PGC presented with diabetes ketoacidosis.

Conclusion: The PGC with a high level of HbA1c in the Northern area of Pakistan is perturbing. Educating caregivers especially about recognizing early clinical presentation and adhering to strict glycemic control is required.

Key Words: Glycemic Control, Children, Diabetes Mellitus, Northern Areas

Citation of article: Gillani S, Khan MJ, Abbas Z, Razzaq A, Ahmed I, Sadaat S. Glycemic Control Among Children with Type 1 Diabetes Mellitus in Northern Areas of Pakistan. Med Forum 2021;32(10):76-80.

INTRODUCTION

Diabetes mellitus is as emerging as an epidemic and affects almost all ages and ethnicity. [1, 2] It is a chronic metabolic disease of the pancreas and is either insulin-dependent or not. The former is type 1 diabetes mellitus (T1DM) which presents earlier in life and constitutes about 5-10% of all cases of diabetes.[3] Insulin is a hormone that regulates blood glucose level i.e. glycosylated hemoglobulin (HbA1c) and plasma glucose level. Uncontrolled T1DM pose serious complications and increase the rate of morbidity and earlier age mortality. This appears as a dilemma for the younger population especially in developing countries like Pakistan. What are the reasons behind poor glycemic control (PGC) of T1DM in the Northern area of Pakistan, prompted pediatricians for conducting the study?

The incidence of T1DM varies worldwide. Worldwide it is 15/100000, in Africa 8/100000 and America as 20/100000. [3] In Pakistan, it lies between 1/100000 per year and 8/100000 per years in Egypt with the highest incidence rate in European regions.[4,5] Good glycemic control (GGC) is the key to offsetting short- and long-term complications.[6] and requires compliance to insulin regimen as well as dietary compliance. Measuring the HbA1c levels gives a good idea of the glycemic control over the previous 120 days.[7] Ideal average HbA1c in children is taken as 7.5% or less.[8] In our study we kept it at 8.0%.

The association of personal and family attributes with T1DM is not documented for the Northern area of Pakistan. This makes the current study unique and will highlight an important personal and sociocultural aspect

[1.] Department of Paediatrics and Neonatology, Medical Education, Ayub Medical College, Abbottabad, KPK, Pakistan.

Correspondence: Saima Gillani, Chairperson and Associate Professor Department of Paediatrics and Neonatology, Medical Education, Ayub Medical College, Abbottabad, KPK, Pakistan.
Contact No: 03208512073
Email: drsaimagillani@gmail.com

Received: June, 2021
Accepted: July, 2021
Printed: October, 2021

of T1DM. Thereby, the current study aims to documents the occurrence of T1DM over 2 years period of clinical practice and find the association of PGC with certain personal and socio-cultural attributes among the paediatric population of Northern area of Pakistan.

MATERIALS AND METHODS

This cross-sectional study was conducted at Ayub Teaching Hospital Abbottabad from January 2019 to April 2021. By convenient sampling technique, total 53 patients were included in the study. Children of age less than 18 years, of either gender and those who had clinical symptoms of T1DM or already diagnosed were included in the study. However, any child with T2DM, any metabolic disorders or with any congenital anomaly or urinary-genital tract disease were excluded. After ethical approval from the same institutional ethical review committee, HbA1C was measured in all patients. Children with HbA1C equal to 8.0% or less were categorized as having good control while those with HBA1C levels above 8.0% were taken poorly controlled diabetics. Data were recorded on a proforma and then entered in IBM SPSS (Version 21). Quantitative variables are presented in frequencies and percentages with mean ±standard deviation. For seeing the association between dependent (glycemic control) and independent variables (age, gender, anthropometric variables and) chai square test was used. A P-value less than 0.05 was considered significant.

RESULTS

Total 53(100%) children of mean age 10.18 ± 5.278 years with a mean height of 123.01 ± 25.909 centimeters, the weight of 25.22±14.066 kilograms was included in the study. Their mean glycated haemoglobin level was 10.90±2.475. table 1

Among the total, 24(45.3%) were males and 7-12 years of age was most common presentation 25(47.2%). The majority were with poor socioeconomic status i.e 38(71.7%) and were having illiterate parents i.e.29(54.7%). The incidence of PGC appeared alarming i.e., 46(86.8%). Table 2

While comparing glycemic controls of T1DM patients with gender, socioeconomic status, parents' literacy etc., none of the p-values was significant. However, percentages show that POC was greater in females 20(37.7%) than males, among the age group of 7-12 years 24(45.3%), underweight 26(49.1%). Table 3.

Among total 53 cases, the majority of patients i.e., 22(41.5%) with POC presented with DKA. Figure 1. Among 46(86.8%) patients with PGC, the majority used BID 70:30 insulin regime, family history of diabetes were negative 22(41.5%) and mothers appeared the primary caregivers 14(26.4%). None of the p-values were significant. Table 4.

Table No.1: Characteristics of T1DM patients included in the study. (n=53)

Characteristics	Min.	Max.	Mean	Std. Deviation
Age of patient in years	1.5	20.0	10.184	5.278
Height of patient in centimeters	75.00	174.0	123.90	25.910
Weight of patient in kilograms	8.00	85.0	25.22	14.066
Body mass index	7.90	30.2	15.88	4.620
Glycated hemoglobin Level (%),	7.5	17.0	10.90	2.474
Total duration of illness in years after first diagnosis	0.00	7.0	2.75	2.213

Table No.2: Frequencies and percentages of patients' demographics and dependent variables

Variables	Categories	Frequency	Percentage
Gender	Male	24	45.3
	Female	29	54.7
Age group	1-6 years	14	26.4
	7-12 years	25	47.2
	≥ 13 years	14	26.4
socioeconomic status	Well	15	28.3
	Poor	38	71.7
Parent's literacy	Illiterate	29	54.7
	Literate	23	45.3
BMI classification	Underweight	30	56.6
	Ideal	19	35.8
	Obese	4	7.5
Family history of diabetes and other illness	None	25	47.2
	Diabetes	16	30.2
	Hypertension	8	15.1
	Misc	4	7.5
Status of T1DM	New cases	8	15.1
	Old cases	45	84.9
Glycemic control	Poor (HbA1c ≥ 8.0)	46	86.8
	Good (HbA1c < 8.0)	7	13.2
Total		53	100

Table No.3: Comparison of glycemic control with patients' characteristics

Independent variables	Categories	Glycemic control		P value
		Poor (HbA1c ≥ 8.0)	Good (HbA1c < 8.0)	
Gender	Male	20(37.7)	4(7.5)	0.499
	Female	26(49.1)	3(5.7)	
Age group	1-6 years	12(22.6)	2(3.8)	0.093
	7-12 years	24(45.3)	1(1.9)	
	≥ 13 years	10(18.9)	4(7.4)	
socioeconomic	Poor	34(64.2)	4(7.5)	0.359

status	Well	12(22.6)	3(5.7)	
Parents literacy	Illiterate	25(47.1)	4(7.5)	0.499
	Literate	20(37.7)	3(5.6)	
BMI classification	Underweight	26(49.1)	4(7.5)	0.698
	Ideal	16(30.2)	3(5.7)	
	Obese	4(7.5)	0(0.0)	
Status of T1DM	Old	39(73.6)	6(11.3)	0.949
	New	6(11.3)	1(1.9)	
Presentation with DKA	No	24(45.3)	3(5.7)	0.646
	Yes	22(41.5)	4(7.5)	
Total		46(86.8)	7(13.2)	

p-value <0.005 significant

Figure No.1: Frequencies of clinical presentation of patients' with T1DM

Table No.4: Different questions about glycemic control and their response by 53 T1DM patients

Questions	Categories	Glycemic control		Total	P-value
		Poor Control (HbA1c more than 8.0)	Good Control (HbA1c 8.0 or less)		
Types of insulin regimen in use	none	4(7.5%)	1(1.9%)	5(9.4%)	0.061
	bid 70:30	39(73.6%)	5(9.4%)	44(83.0%	
	long-acting glargine	3(5.7%)	0(0.0%)	3(5.7%	
	others	0(0.0%)	1(1.9%)	1(1.9%)	
Family history of diabetes and other illness	None	22(41.5)	3(5.7)	25(47.2)	0.113
	Diabetes in family	14(26.4)	2(3.8)	16(15.1)	
	Hypertension in family	8(15.1)	0(0.0)	8(15.1)	
	Misc. T.B. CARDIAC etc.	2(3.8)	2(3.8)	4(7.5)	
Administration of insulin by	Self	6(11.3)	0(0.0)	6(11.3)	0.865
	Mother	14(26.4)	2(3.8)	16(30.2)	
	New	7(13.2)	1(1.9)	8(15.1)	
	Father	5(9.4)	1(1.9)	6(11.3)	
	others/siblings/staff	14(26.4)	3(5,7)	17(32,1)	
Presence of electricity at home	No	5(9.4)	1(1.9)	6(11.3)	0.790
	Yes	41(77.4)	6(11.3)	47(88.7)	
Awareness among family about Diabetes	Poor	15(28.3)	3(5.7)	18(34.0)	0.594
	Good	31(58.5)	4(7.5)	35(66.0)	
Willingness on part of parents and patient to treat disease	Poor	6(11.3)	2(3.8)	8(15.1)	0.285
	Good	46(75.5)	5(9.4)	45(84.9)	
Knowledge about insulin regimen and method of injecting	Poor	15(28.3)	2(3.8)	17(32.1)	0.831
	Good	31(58.5)	5(9.4)	36(67.9)	
Knowledge and understanding about insulin injection site	Poor	8(15.1)	2(3.8)	10(18.9)	0.481
	Good	38(71.7)	5(9.4)	43(81.1)	
Knowledge about dietary compliance of diabetes	Poor	21(39.6)	1(1.9)	22(41.5)	0.117
	Good	25(47.2)	6(11.3)	31(58.5)	
Availability of fridge/cold storage at home	Not available	9(17.0)	2(3.8)	11(20.8)	0.584
	Available	37(69.8)	5(9.4)	42(79.2)	
Total		46(86.8)	7(13.2)	53(100)	
p-value <0.005 significant.					

DISCUSSION

T1DM is the most common type of diabetes mellitus in people younger than 20 years.[9] Its association with health determinants, early diagnosis and prompt management reduces the early as well as a late-onset complication in a younger population.[5] Furthermore, GGC with optimal HbA1c is the key factor in controlling T1DM. This study explored different factors and association of demographic variants among T1DM children of the Northern area of Pakistan. Circumstantially, the study revealed a very high rate of PGC i.e., 86.8% with a mean value of HbA1c equaled to 10.90±2.475%.

In the current study, a very low rate of GGC and high levels of HbA1c in the majority of patients put the

pediatric population at risk. This statement is supported by a WHO report stating that T1DM cases with PGC and high level of HbA1c in low and middle-income countries is staggering.[10] Moreover, Djonou C et al,. from Cameroon and Taha Z et al,. from Sudan mentioned a close percentage of PGC as 67.4% and 76% respectively.[11-12] The closest HbA1c (10.90± 2.475%) level of the current study is reported by other authors as 9.2±2.5%, 12.5±2.7% and 13±5.9%. [13] Contrary to this, Patitti DB et al,. from the US ensued 17%.[14] This is obvious that a resource-restricted country and socio-economically staggered area like Northern Pakistan has a high value of HbA1c.

Demographic attributes like age and gender may or may not be associated with PGC. In the current study, no such association was found for both variables. This is supported by Mark AC's study, done in the Midwest of USA.[15] Besides, the percentages among female 54.7% and mean age of 10.18-±5.2 years were high among PGC. This is in accordance with 51.5%, 63% among females and with mean age of 13±5.7 and 12±2.7 years respectively.[12, 13] A very close mean age of 9.2±2.5 years is resulted by Djonou C et al,. [11] The possible reason for late years of the first decade are probably due to late diagnosis of the disease or more parental supervision of the sick child.

For a resource-restricted country, the total duration of illness since initial diagnosis and presentation of T1DM to a tertiary care hospital, seeking specialist care is also subtle. The mean duration since diagnosis of T1DM in Northern areas of Pakistan appeared as 2.75±2.2 years. This lies in close proximity to a study done by Noorani M et al,. i.e. 3.74 years.[9] Moreover, Djonou C et al,. mentioned 4.1 years and Clements MA et al,. from the US reported 5.2 years. [11, 15] This is even more concerning, the earlier presentation of T1DM in the first decade of life.

As younger aged children are more dependent on caregivers and parents are sole caregivers in the present setup. Therefore, their literacy rate and awareness about diabetes are among the other factors which affect glycemic control. Literate parents and good awareness about insulin storage and the regime should ensue better outcomes with less complication of the disease. Despite negative correlation of such attributes in current study, illiterate parents with good awareness had more cases of PGC. This conforms with other studies. [15, 16] About 66% of parents of the current study had good awareness about T1DM which is close to 70% of children studied in Tanzania. [9]

When comparing socioeconomic status, 64.2% of families with PGC belonged to poor background. In spite of their non-significant association (p-value>0.005), other studies found a positive relation of low socioeconomic status with glycemic control. [17,18] Another important determinant i.e., family history with positive T1DM in our study came out 30.2%. Not very close yet this also appeared comparable with that of another study, 21%. [12]

T1DM decreases the life expectancy by 10-20 years and this is even more with children presenting with complication.[19] It is worth noting that earlier detection or proper management of T1DM will lessen mortality. In the current study, DKA resulted as the top presenting complication, 41% among all which is staggering. Similarly, most of the cases reported by Taha Z[12] et al,. had DKA 80% and 81% by Eliadarous H. [18] Ziegler R et al,. mentioned 21.1% of children and adolescents and resulted in a low rate of 4.9% had presented with DKA.[23] In addition to this, hypoglycemia is associated with unexpected dead by 4-10% and children with age less than 5 years are more prone to hypoglycemia than any other age group. [20]

Proper use of insulin syringes and timely rotation of injectable site decreases another serious complication like lipohypertrophy. It is the most occurring issue especially among younger patients of T1DM. [21] The percentage of lipohypertrophy, 7.5% were observed in the current study. In contrast to the current study, Gupta SS reported it as 69.8% cases among adults. [22] Despite less occurrence in our setup, it could not be overlooked and seek special attention for education of caregivers. Up to the best knowledge of the author, literature lacks any data for comparing other complications like sepsis, hypoglycemia.

The study does not evade the limitation. Inspite of 2 years of data collection in only tertiary care facility of the Northern area of Pakistan, the sample size of study is small and the results cannot be generalized over the diabetic pediatric population. The socioeconomic determinants are prone to recall biased. This could be minimized by indept interview of caregiver with qualitative approaches. Moreover, further research with a systematic approach to acute and chronic complication of T1DM is needed with a random sampling technique.

CONCLUSION

Owing to lesser life expectancy and more morbidity and mortality of T1DM among the pediatric population, the poor glycemic control with a high level of HbA1c in the Northern area of Pakistan is perturbing. Educating caregivers especially about recognizing early clinical presentation and adhering to strict glycemic control is required. Governmental actions with an epide-miological approach and caregiver's awareness training can ensure a better life with less mortality among such population.

Author's Contribution:

Concept & Design of Study:	Saima Gillani
Drafting:	Muhammad Junaid Khan, Zaheer Abbas
Data Analysis:	Abdur Razzaq, Ijaz

	Ahmed, Shazia Sadaat
Revisiting Critically:	Saima Gillani, Muhammad Junaid Khan
Final Approval of version:	Saima Gillani

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Passa P.Diabetes trends in Europe. Diabetes Metab Res Rev 2002; 18: S3-8.
2. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025 - prevalence, numerical estimates, and projections. Diabetes Care 1998;21: 1414-31.
3. Mobasseri M, Shirmohammadi M, Amiri T, Vahed N, Hosseini Fard H, Ghojazadeh M. Prevalence and incidence of type 1 diabetes in the world: a systematic review and meta-analysis. Health Promot Perspect 2020;10(2):98-115.
4. The diamond project group. Incidence and trends of childhood type 1 diabetes worldwide 1990-1999. Diabet Med 2006: 23: 857– 866.
5. Soltész G, Patterson C, Dahlquist G. Global trends in childhood type 1 diabetes. In Diabetes Atlas. chapter 2.1, 3rd ed. Int Diabetes Federation 2006; 153– 190.
6. Nordwall M, Arnqvist HJ, Bojestig M, Ludvigsson J. Good glycemic control remains crucial in prevention of late diabetic complications--the Linköping Diabetes Complications Study. Pediatr Diabetes 2009;10(3):168-76.
7. William HL, Mary LW, George PC, Sasigran AB. What is the role of HbA1c testing in workup of pediatric type1 diabetes mellitus (DM)? Medscape. [cited 2021 May 26]. Available from: https://www.medscape.com/answers/919999-120981/what-is-the-role-of-hba1c-testing-in-the-workup-of-pediatric-type-1-diabetes-mellitus-dm
8. Gerich JE. The importance of tight glycemic control. The Am J Med 2005;118(9):7–11.
9. Noorani M, Ramaiya K, Manji K. Glycaemic control in type 1 diabetes mellitus among children and adolescents in a resource limited setting in Dar-es-Salaam-Tanzania. BMC Endocr Disord 2016; 16(1):1–8.
10. Aanstoot HJ, Anderson BJ, Daneman D, Danne T, Donaghue K, Kaufman F, et al. The global burden of youth diabetes: perspectives and potential. Pediatr Diabetes 2007;8(Suppl 8):1–44.
11. Djonou C, Tankeu AT, Dehayem MY, Tcheutchoua DN, Mbanya JC, Sobngwi E. Glycemic control and correlates in a group of sub-Saharan type 1 diabetes adolescents. BMC Res Notes 2019;12(1):50.
12. Taha Z, Eltoum Z, Washi S. Predictors of glucose control in children and adolescents with type 1 diabetes: Results of a cross-sectional study in Khartoum, Sudan. Open Access Maced J Med Sci 2018;6(11):2035–9.
13. Mostofizadeh N, Hashemipour M, Roostazadeh M, Hashemi-Dehkordi E, Shahsanai A, Reisi M. The impact of poor glycemic control on lipid profile variables in children with type 1 diabetes mellitus. J Educ Health Promot 2019;8:6.
14. Petitti DB, Klingensmith GJ, Bell RA, Andrews JS, Dabelea D, Imperatore G, et al. Glycemic control in youth with diabetes: the SEARCH for diabetes in Youth Study. J Pediatr 2009;155(5):663–8.
15. Clements MA, Lind M, Raman S, Patton SR, Lipska KJ, Fridlington AG, et al. Age at diagnosis predicts deterioration in glycaemic control among children and adolescents with type 1 diabetes. BMJ Open Diabetes Res & Care 2014;2(1): e000039.
16. Archinkova M, Konstantinova M, Savova R, Iotova V, Petrova C, Kaleva N, et al. Glycaemic control among Bulgarian children and adolescents with type 1 diabetes–an impact of the social status and the educational level of the parents. Biotechnol Biotechnol Equip 2018;32(2):535–41.
17. Eliadarous H. Exploring the impact of diabetes in Sudan: Out-of- pocket expenditure and social consequences of diabetes on patients and their familie. Stockholm, Sweden : Karolinska Institutet; 2017.
18. Mikkonen J, Raphael D. Social determinants of health: the Canadian facts. Toronto: York University School of Health Policy and Management; 2010.
19. Los E, Wilt AS. Diabetes Mellitus Type 1 In Children. In Treasure Island (FL); 2021.
20. Ziegler R, Neu A. Diabetes in Childhood and Adolescence. Dtsch Arztebl Int 2018;115(9): 146–56.
21. Omar MA, Christopher L, Motala AA, Jialal I, Seedat MA. Management of diabetes mellitus. S Afr Med J 1987;71(9):580-4.
22. Gupta SS, Gupta KS, Gathe SS, Bamrah P, Gupta SS. Clinical Implications of Lipohypertrophy Among People with Type 1 Diabetes in India. Diabetes Technol Ther 2018;20(7):483–91.

Original Article

Evaluate the Levels of Cardiac Troponin I in Saliva and Serum of Acute Myocardial Infarct Patients

Bhunesha Devi[1], Shazia Akbar[1], Sana Mubarak[1] and Syed Faraz Moin[2]

ABSTRACT

Objective: The objective of this research was to evaluate the levels of cTnI in saliva between 12-24 hours and correlate the levels of saliva and serum cardiac Troponin I in AMI patients.

Study Design: A cross sectional analytical study

Place and Duration of Study: This study was conducted at the Departments of Cardiology Civil Hospital and Ojha campus Karachi from April, 2021 to August, 2021.

Materials and Methods: Sixty Myocardial infarct patients between the age of thirty to seventy were included in this research. Participants were clinically examined for cardiac and dental complications. Blood and saliva samples were collected between 9 -11 am between 12-24 hours and analyzed by sandwich ELISA technique.

Results: The cTnI was significantly increased in saliva and serum with mean values (0.1609 ng/dl and 14.494 ng/dl in serum) in patients with acute MI. We have positive statistical correlation i.e. spearman roh (r= 0.647) with p-value .001.

Conclusion: Present results reveals positive correlation of Troponin I in saliva and serum which indicates a constant release of troponin I in saliva. Hence, saliva can be used as a noninvasive approach for detection of troponin I at low value in myocardial infarct patients as point of care testing for early and rapid diagnosis.

Key Words: Myocardial infarction, Cardiac troponin-I, Saliva, Serum, ELISA

Citation of article: Devi B, Akbar S, Mubarak S, Moin SF. Evaluate the Levels of Cardiac Troponin I in Saliva and Serum of Acute Myocardial Infarct Patients. Med Forum 2021;32(10):81-85.

INTRODUCTION

Heart diseases are increasing progressively in the world population due to excessive food consumption or genetic background. It is the primary source of morbidity and mortality in different parts of the world [1]. Pakistan is a growing South Asian country with four major territories, and its evaluated population is more than 200 million. Cardiovascular hazard for example, hypertension, diabetes mellitus, and weight[2] are expanding in Pakistan and are the leading cause of morbidity and mortality[3]. The most frequent type of CHD is myocardial infarction (MI).

It is responsible for over 15% of mortality consistently, in which the majority of people experiencing a non-ST-segment elevated myocardial infarction (NSTEMI) than ST-segment elevation myocardial infarction (STEMI) [4]. In the emergency setting, patients associated with having an AMI get an electrocardiogram (ECG) and proportions of serum biomarkers to recognize or exclude myocardial necrosis. For MI, cardiac Troponin-T (cTnT) and cardiac troponin-I (cTnI) are observed as sensitive whereas Cardiac troponin-I (cTnI) is considered a gold standard biomarker and ultimate laboratory analysis for the diagnosis of acute MI. The cardiac troponin-I could be detected within 4 to 12 hrs. in serum after the beginning of myocardial ischemia and acheive its peak from 12 hours to 2 days. It can remain high up to two weeks after myocardial injury[5]. Currently, various devices have become available for point-of-care testing for most established cardiovascular markers that takes less than 20 minutes. Whole blood, plasma as well as the serum is being tested as a specimen, but novel Nano-biochip technology which is based on saliva testing consisting of 21 biomarkers, revealed another enormous capability to diagnose acute MI[6]. Body fluids such as serum, sputum, saliva are likewise being utilized for the appraisal of these biomarkers[7]. These biological markers are being determined and checked for their levels through different strategies like enzyme-linked immunosorbent assay (ELISA), immuno-histochemistry (IHC), western blot, and others. Out of these methods, ELISA and IHC are ordinarily utilized techniques to identify proteins in body fluids and tissues separately due to their reasonable, reproducible, and cost-effective properties [8]. For early diagnosis and

[1.] Department of Oral Pathology, Dow University of Health Sciences, Karachi.
[2.] National Center for Proteomics, University of Karachi, Karachi.

Correspondence: Dr. Bhunesha Devi, Department of Oral Pathology, Dow University of Health Sciences, Karachi.
Contact No: 0333-3934163
Email: bhunesha.devi@gmail.com

Received: September, 2021
Accepted: September, 2021
Printed: October, 2021

to reduce the stress level of the patients, early sample collection for detection of biomarkers is mandatory, and for that reason, saliva collection is the fundamental focal point of testing which incorporates its ease, inexpensive, non-intrusiveness, and non-clotting nature, unlike blood and negligible danger of cross-contamination[9]. Oral saliva is a unique bio-fluid containing various components secreted from three major (paired) salivary glands named parotid, submandibular and sublingual glands, and hundreds of minor salivary glands distributed all over the oral cavity[10]. For such reasons saliva is gaining attention as a fluid of choice in the detection of multiple diseases like inflammatory conditions, metabolic disorders, cardiac myopathies, neurological and malignant conditions [11,12].

MATERIALS AND METHODS

2.1. Study Participants: A total of 60 patients between the ages of 30-70 years in the emergency department of cardiology having complained of chest pain, shortness of breathing, history of diabetes, and hypertension went through ECG and lab investigations. Standard clinical records were collected from all participants on questionnaire about their biographic data, medical history, oral hygiene status, medication, and other health issues. OPD, CCU, ICU, unstable critical patients, and patients on the ventilator were excluded from the study.

2.2. Serum and Saliva Sample Collection: Saliva sampling was collected between 9-11 am. Participants were asked to refrain from anything at least two hours prior sampling and then allowed to rinse their mouth with water and swallow saliva for 2- 3 minutes. Later they were asked to collect 3-5 mL unstimulated saliva for 10 minutes into 15 mL sterile plastic falcon tube placed on ice. After saliva collection, immediately 3cc blood was drawn by a phlebotomist and stored in vacutainers. All samples were centrifuged at 4000 rpm for 15 minutes, and aliquots were stored at -20 ˚C for further analysis. ELISA (ELISA Kit (Cloud-clone Crop.SEA478Hu) was performed to analyze cardiac Troponin-I in the laboratory of the National Center for Proteomics, University of Karachi to measure the concentration of cTnI in samples of saliva and serum according to the manufacturer's guideline.

2.4. Statistical Analyses: The data was entered and analyzed in SPSS version 21. The frequencies were analyzed and correlation of serum and saliva samples, was established accordingly. The nonparametric test of spearman roh was applied. p-value=0.05 were considered significant. Chi-square was applied to determine the association of gender with risk factors (hypertension, DM, smoking and stress).

RESULTS

The number of patients calculated for the study was (n=60). Four (n=4) patients were dropped due to dry months and inability to give the required quantity of saliva. Therefore, the total samples analyzed were (n=56). About 80% of the subjects were male with mean age was 55 years. Participants (n=36) showed non-ST elevation on ECG readings, whereas only (n=20) showed ST elevation as shown in Fig.1. The frequency of mild to moderate gingivitis was 98.2% of the patients and 83.9% of patients have mild to moderate periodontitis, while only 32% of patients presented carious teeth (Fig. 1 and Fig. 2).

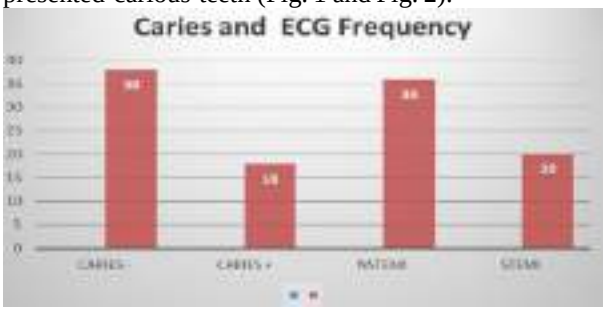


Figure No.1: Statistical presentation of presence (+) and absence (-) of caries and non-ST/ST elevation myocardial infarction by ECG readings

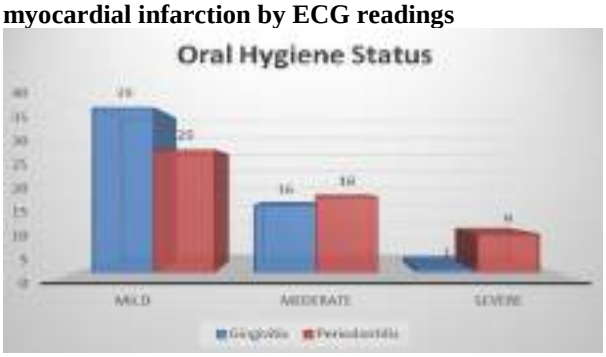


Figure No.2: Statistical presentation of mild, moderate and severe levels of gingivitis and periodontitis

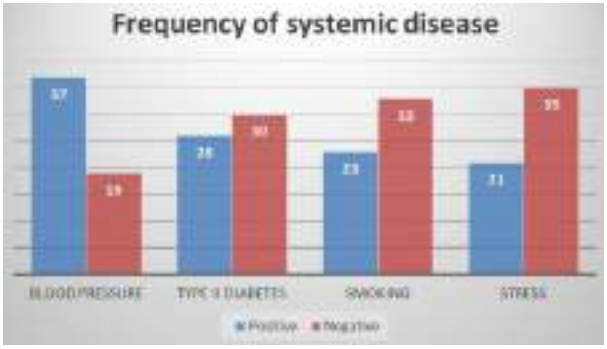


Figure No.3: Statistical presentation of systemic diseases with occurrence (positive) and absence (negative) of the respective disorder

The risk factor found in the study group was blood pressure (BP) which was analyzed to be 66% followed by diabetes at 46%, smoking at 39% and stress was 37%.as shown in fig 3.

When the saliva troponin-I level was correlated with risk factors, a weak positive correlation (r=0.112) was observed between salivary troponin-I and diabetes only. When the troponin-I was statistically analyzed, the patients were having different values in serum from a lower limit of 0.18 ng/ml up to 45 ng/dl (the cutoff value in serum is 0.04 ng/dl), while the lowest value to be found in saliva was from 0 to 0.45 ng/dl.

Table No.1: Statistical analysis of cardiac troponin-I values obtained in serum and saliva of myocardial infarction patients (N= 56 cases)

Samples	N	Minimum	Maximum	Mean	Std. Deviation
Serum Troponin I	56	0.18	45.00	14.0188	9.93341
Saliva troponin I	56	0.00	0.45	0.1609	0.14806
Valid N (listwise)	56				

The mean value of cTnI in saliva was 0.16 ng/dl and in serum was 14.01 ng/dl with a standard deviation of 9.93 and 0.14 in serum and saliva, respectively (Table 1). The Spearman correlation between the values in salivary and serum troponin I and the correlation was found to be positive (r=0.647) with a significant p-value of 0.001.

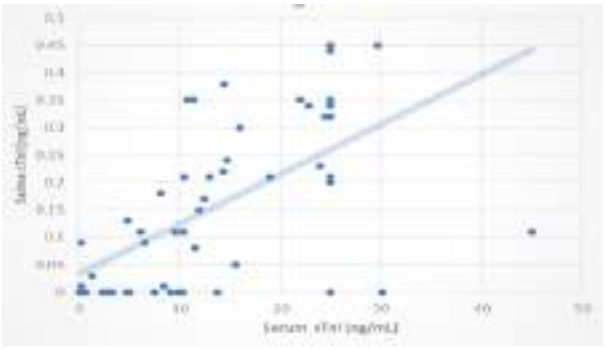


Figure No.4: Serum levels of cardiac Troponin-I in correlation with saliva levels demonstrate a moderate positive relation (r=0.643)

DISCUSSION

In this study, we analyzed cardiac troponin-I in acute myocardial infarct patients by using the ELISA technique. We tested the troponin-I cardiac marker in saliva and correlated its results with serum troponin-I. The correlation between serum and saliva was found to be (r=0.647) according to non-probability test of the Spearman correlation which depicts a moderate positive correlation. This finding is in agreement with a previously reported study that showed a positive correlation between serum and saliva troponin concentrations (r=0.56)[13]. This also indicates the presence and continuous release of the troponin-I biomarker in saliva as well. Another study conducted in 2013 by Iraj Mirzaii-Dizgah also found a positive correlation (r=0.45) of cardiac troponin-I that suggested point of care testing at the preclinical stage, which is time-saving and helpful to start immediate treatment. The evaluation of troponin-I with high sensitivity assay in acute myocardial patients showed that the value of troponin-I increases in saliva with respect to the increase in serum levels in 24 hours. However, the value drops but remain significant in the 24 to 48 hour period[14]. The evaluation of different biomarkers including troponin-I from saliva was reported by CS Miller and co-workers who concluding that the serum markers are more sensitive than saliva. However, combining the salivary biomarker such as c-reactive protein (CRP) detection with clinical information such as an ECG, can provide sensitivity of 80% with 100% specificity for acute myocardial infarction[6]. As mentioned above that we have found a moderate positive correlation of cTnI values in saliva and serum samples taken within 24 hours of MI, whereas, Vaibhav Mishra and associates found a strong positive relation between the levels of cTnI in serum and saliva samples taken during the same time[15]. During the analysis of saliva, it is important to have an idea related to the oral disorders that may or may not interfere with the sample analysis. The percentages of diseases such as gingivitis, periodontitis and caries have already been mentioned in our results (Fig. 1 and 2). These conditions may develop as a result of the negligence of oral hygiene by MI patients. All of the patients in the study were affected by gingivitis and periodontitis at different severity levels. Therefore, it is contributory to discuss briefly about these oral conditions with respect to cardiovascular disease. Generally, periodontal disease (PD) seems to be associated with no more than a modest increase (~20%) in cardiovascular risk in the overall population[16]. The underlying mechanism might be the signaling pathways in human gingival fibroblasts leading to periodontal disease, which in turn offers a biological burden of endotoxin and inflammatory cytokines such as thromboxane A2, prostaglandin E2, interleukin (IL), and tumor necrosis factor-β. These factors may lead to thrombus formation as well as towards atherogenesis[17,18]. Systematically, diabetes and hypertension were noted to be the two main disorders present in the study subjects. In Pakistan there is an increasing trend of hypertension in both urban and rural areas and in both genders with respect to time. The urban areas have higher prevalence[19]. Our analysis showed that 66% of the patients were suffering from hypertension. For diabetes mellitus it is known to have a direct association with coronary artery disease and the risk of coronary death is higher in women as

compared to men [20, 21]. Our data showed 46% of the cases were diabetic, the second prevailing systemic complaint. This is the first report of cTnI evaluation in the saliva samples from local population. Several modified approaches can be adopted for further evaluation and validation of this study in the future starting from adopting a standard method of saliva collection rather than the classical method of passive drooling. This is necessary for keeping the consistency of saliva samples which is altered from one individual to another and negatively impacts when analyzing secreted biomarkers in nano measuring levels like in this study. Additionally, thermo-sensitivity of saliva proteins, saliva secretion and its flow rates[22,23] are also few parameters to be considered. To establish saliva as an alternative medium of diagnosis to various other biological fluid such as plasma, is a highly attractive research topic. Our study also presents an idea that saliva has the potential to detect biomarkers and by developing a highly sensitive tool through available molecular technologies a saliva based assay can be developed for cTnI detection in MI patients, a direction that has started to be explored [24].

CONCLUSION

Myocardial infarction is a life-threatening condition and needs to be diagnosed very quickly and accurately. In this analytical study, most saliva samples showed a significant association between the unstimulated saliva and blood serum concentrations of cardiac troponin-I. Although collecting saliva is non-invasive and a less stressful tool but an important cardiac biomarker such as troponin-I, is detected in minimal values during our analysis as compared to serum. However, saliva based assay can be developed for cTnI detection requiring a large sample size and a high sensitive cTnI assay.

Acknowledgement: Author thanks Dr. Nawaz Lashari, Kelash Chandar, and coworkers from the Cardiology Department Civil Hospital Karachi for their support.

Author's Contribution:

Concept & Design of Study:	Bhunesha Devi
Drafting:	Shazia Akbar, Sana Mubarak
Data Analysis:	Sana Mubarak, Syed Faraz Moin
Revisiting Critically:	Bhunesha Devi, Shazia Akbar
Final Approval of version:	Bhunesha Devi

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Bahbah EI, Noehammer C, Pulverer W, Jung M, Weinhäusel A. Salivary biomarkers in cardiovascular disease: An insight into the current evidence. The FEBS J 2020.
2. Khowaja S, Karim M, Zahid M, Zahid A, Ahmed S, Kazmi K, et al. Impact of Temperature Variation on Acute Myocardial Infarction in Karachi, Pakistan. Cureus 2019;11(10).
3. Rehman S, Li X, Wang C, Ikram M, Rehman E, Liu M. Quality of Care for Patients with Acute Myocardial Infarction (AMI) in Pakistan: A Retrospective Study. Int J Environmental Research and Public Health 2019;16(20):3890.
4. Anderson JL, Morrow DA. Acute myocardial infarction. New England J Med 2017;376(21): 2053-64.
5. Bavia L, Lidani KCF, Andrade FA, Sobrinho MIAH, Nisihara RM, de Messias-Reason IJ. Complement activation in acute myocardial infarction: An early marker of inflammation and tissue injury? Immunol Letters 2018;200:18-25.
6. Miller C, Foley III J, Floriano P, Christodoulides N, Ebersole J, Campbell C, et al. Utility of salivary biomarkers for demonstrating acute myocardial infarction. J Dental Research 2014;93(7_suppl): 72S-9S.
7. Csősz É, Kalló G, Márkus B, Deák E, Csutak A, Tőzsér J. Quantitative body fluid proteomics in medicine—A focus on minimal invasiveness. J Proteomics 2017;153:30-43.
8. Comakli S, Sağlam YS, Timurkan MÖ. Comparative detection of bovine herpesvirus-1 using antigen ELISA, immunohistochemistry and immunofluorescence methods in cattle with pneumonia. Turkish J Veterinary Animal Sciences 2019;43(3).
9. Ngamchuea K, Chaisiwamongkhol K, Batchelor-McAuley C, Compton RG. Chemical analysis in saliva and the search for salivary biomarkers–a tutorial review. Analyst 2017;143(1):81-99.
10. Khurshid Z, Warsi I, Moin SF, Slowey PD, Latif M, Zohaib S, et al. Biochemical analysis of oral fluids for disease detection. In Advances in Clinical Chemistry; Elsevier: London, UK;2021.p.205–253.
11. Meleti M, Cassi D, Vescovi P, Setti G, Pertinhez TA, Pezzi ME. Salivary biomarkers for diagnosis of systemic diseases and malignant tumors. A systematic review. Medicina Oral, Patología Oraly Cirugía Bucal 2020;25(2):e299.
12. Khurshid Z, Zafar MS, Khan RS, Najeeb S, Slowey PD, Rehman IU. Role of salivary biomarkers in oral cancer detection. Advances Clin Chem 2018;86:23-70.
13. Haybar H, Yousefimanesh H, Ahmadzadeh A, Malekzadeh H, Assare A. Relation of saliva and blood troponin levels in patients with myocardial infarction: cross-sectional clinical study. Int J Cardiovasc Res 2012;1(5):8602:2.
14. Mirzaii-Dizgah I, Riahi E. Salivary troponin I as an

indicator of myocardial infarction. Ind J Med Res 2013;138(6):861.
15. Mishra V, Patil R, Khanna V, Tripathi A, Singh V, Pandey S, et al. Evaluation of Salivary Cardiac Troponin-I as Potential Marker for Detection of Acute Myocardial Infarction. J Clin Diagnostic Research 2018;12(7).
16. Pattnaik NK, Das SN, Biswal BN. Cardiovascular Diseases and Periodontal Diseases: Review and Update. Int J Scientific Study 2017;5(1):239-44.
17. Brinson CW, Lu Z, Li Y, Lopes-Virella MF, Huang Y. Lipopolysaccharide and IL-1β coordinate a synergy on cytokine production by upregulating MyD88 expression in human gingival fibroblasts. Molecular Immunol 2016;79:47-54.
18. Moss JW, Ramji DP. Cytokines: roles in atherosclerosis disease progression and potential therapeutic targets. Future Med Chem 2016;8(11):1317-30.
19. Mahendra J, Rao AN, Mahendra L, Fageeh HN, Fageeh HI, Balaji TM, et al. Genetic Polymorphisms of NLRP3 (rs4612666) and CARD8 (rs2043211) in Periodontitis and Cardiovascular Diseases. Biol 2021;10(7):592.
20. Fuchs FD, Whelton PK. High blood pressure and cardiovascular disease. Hypertension 2020; 75(2):285-92.
21. Mendis S, O'Brien E, Seedat YK, Yusuf S. Hypertension and diabetes: entry points for prevention and control of the global cardiovascular epidemic. Int J Hypertens 2013;1-3.
22. Criado C, Chaya C, Fernández-Ruíz V, Álvarez MD, Herranz B, Pozo-Bayón MÁ. Effect of saliva composition and flow on inter-individual differences in the temporal perception of retronasal aroma during wine tasting. Food Research Int 2019;126:108677.
23. Pedersen AML, Sørensen CE, Proctor G, Carpenter G, Ekström J. Salivary secretion in health and disease. J Oral Rehabilitation 2018; 45(9):730-46.
24. Westreich R, Neumann Y, Deutsch O, Krief G, Stiubea-Choen R, Zager D. Development of saliva-based cTnI point-of-care test: a feasibility study. Eur Heart J 2020 Nov;41(Supplement_2):ehaa946-1693.

Original Article

Awareness About Unsafe Plastic Utensils and Linked Health Hazards Amongst Doctors

Bushra Anwar[1], Khushbakht Anwar[2], Aashi Ahmed[1], Nadia Nisar[1], Saima Omair[1] and Warda Wazir[1]

ABSTRACT

Objective: To assess the awareness about plastic utensils in doctors of Rawalpindi and Islamabad.
Study Design: Cross-sectional study
Place and Duration of Study: This study was conducted at two medical colleges of Rawalpindi and Islamabad in a period of six months in year 2017.
Materials and Methods: Data was collected from 228 doctors selected using simple random sampling technique in three medical colleges and hospitals. Their knowledge about different qualities of plastic, the number allocation of plastics, and which plastic numbers to avoid as utensils was assessed. Also, their awareness about the leaching of chemicals from plastic utensils, factors increasing this leaching, and diseases associated with the use of plastic, was assessed.
Results: Only 27.2% of doctors in our study sample were aware of plastic safety as measured using our awareness scale. Lowest awareness was found for the question about which plastic numbers to avoid (1.3% awareness). The highest awareness was found for the question about the leaching of chemicals from plastics into food (93.4%)
Conclusion: According to our results, the majority of the doctors were unaware of plastic safety
Key Words: Awareness, Plastic safety, leaching of chemicals

Citation of article: Anwar B, Anwar K, Ahmed A, Nisar N, Omair S, Wazir W. Awareness About Unsafe Plastic Utensils and Linked Health Hazards Amongst Doctors. Med Forum 2021;32(10):86-90.

INTRODUCTION

Different types of plastics are available in the market, based on the resin identification coding (RIC) system. Each plastic type is allotted a specific number that is written on the bottom of plastic bottles and containers.[1,2] It consists of a triangular design of arrows with a number inside and an abbreviation of the resin type.[3] It is anticipated that almost half of plastic containers have chemicals that can be poisonous for humans.[4]

The different resins used in synthesizing plastics are mostly linked with estrogenic and carcinogenic activity.[5] Some examples are bisphenol-A (BPA), polycarbonate (PC), non-BPA-based polypropylene (PP) and Phthalates. BPA and Phthalates are especially harmful for children and women of reproductive age.[6]

[1.] Department of Community Medicine, HITEC IMS, Taxila.
[2.] Msph student, London School of Hygiene and Tropical Medicine

Correspondence: Bushra Anwar, Lecturer, Community Medicine Department, HITEC IMS, Taxila
Contact No: 0300-4466885
Email: bushra.anwar@live.com

Received: March, 2021
Accepted: July, 2021
Printed: October, 2021

Most plastic items release these chemicals in the liquid contained in them, even without any physical stress. This leaching is frequent if the liquid contains both polar and non-polar components such as in milk, and is further increased in the presence of heat, sunlight, or microwave heating.[5]

Recet studies show that some of these seven types of plastics contain higher amounts of endocrine disruptors and are considered highly unsafe for health.[5,7] These unsafe plastics are indicated by numbers 3, 6, and 7 and are made up of Polyvinyl chloride or PVC (no. 3 plastic), Polystyrene or PS (no. 6), and Polycarbonate (no. 7), which contains Bisphenol A (BPA). Other plastics that are safer are Polyethylene Terephthalate or PET (no.1), High-Density Polyethylene or HDPE (no. 2), Low-Density Polyethylene or LDPE (no. 4), and Polypropylene or PP (no.5).[7,8]

On a global scale, despite being notorious for its harmful effects, plastic is still being used on a large scale in everyday life because of its convenience in eating, drinking, and use in everyday household items like baby bottles, teethers and toys, which can expose us to destructive chemicals of plastic.[7] A study in Korea evaluated the levels of BPA in the urine of infants and found BPA in all samples, which was higher in those infants who were bottle-fed (P=0.014).[10] BPA affects fertility, reproductive, immune, developmental, renal and nervous systems by its cytotoxic and mutagenic actions.[11]

There are gaps in public awareness about these issues. A Nigerian study showed that majority people did not know the meaning of the label 'BPA free' written on bottles. Most policymakers are also unaware of its meaning. The lack of awareness about plastic safety suggests a high level of exposure to these chemicals.[12]

To date, there are no statistics or studies available about the awareness of unsafe plastic utensils in doctors internationally or nationally. To fill this gap, we conducted a pilot study first, on doctors of Rawalpindi Medical College, to calculate the desired sample size, which revealed 0% overall awareness. Current research aimed to assess awareness about unsafe plastic utensils in doctors as they are supposed to be well aware with any kind of health hazards. Its results will be valuable for health-sector authorities to focus on this neglected issue by increasing research, health education, and regulating the sale and use of unsafe plastics.

MATERIALS AND METHODS

This is a descriptive cross-sectional study conducted in six months period during the year 2017. Sampling was done from two selected medical colleges with their affiliated hospitals namely, Rawalpindi Medical College and its Allied hospitals, Shifa College of Medicine, Islamabad and its affiliated hospital. A total of 228 doctors were surveyed. Sample size was calculated after conducting a pilot study on 20 doctors from Rawalpindi Medical College. The proportion used for calculating sample size was of awareness about the numbering system of plastics in the pilot study, which was 6.66%. Taking margin of error (e) as 3.3%, with confidence level of 95%, the sample size came out to be 228. Sample was selected using consecutive sampling technique. Both genders of age 25 to 65 years were included. Doctors who had attained some degree related to environmental sciences were excluded from the study. Data was collected by using questionnaires made in English with close-ended questions.

In this study, awareness about unsafe plastic utensils was defined as knowledge that should be possessed to ensure the safe use of plastics. Information was collected regarding age, gender, clinical/ basic sciences department, highest qualification, years of experience, and knowledge about unsafe plastic utensils. Seven variables were included to judge their knowledge. Questions included knowledge about leaching of chemicals from plastic utensils, higher toxicity of certain plastics, seven types of plastics, numbering system of plastics, number of unsafe plastic utensils (3, 6 and 7), factors increasing leaching and diseases linked with unsafe plastic utensils. Those who answered four or more questions correctly were labeled as 'aware,' and those answering less than four questions correctly were labeled as 'unaware'.

Data was collected after obtaining informed consent from the doctor. Confidentiality of information was maintained, and due respect was given to them. Data was entered and analyzed in SPSS version 21. For effect modifiers like field of doctors (clinical/ basic sciences and qualification, stratification was done during the analysis of results, and awareness was compared among these groups using chi-square test.

RESULTS

A total of 228 doctors were recruited in this study. Majority were young female doctors with MBBS as their qualification and 1-10 years of experience. The demographic and professional characteristics of the sample are shown in table 1.

Table No.1: Demographic and professional characteristics of doctors (n=228)

Characteristics	Frequency	Percent
Age groups in years		
25-35 years	190	83.3
36-45 years	23	10.1
46-55 years	7	3.1
56-65 years	8	3.5
Gender		
Male	65	28.5
Female	163	71.5
Clinical/ Basics		
Clinical sciences	188	82.5
Basic sciences	40	17.5
Highest Qualification		
MBBS	196	86.0
Postgraduate diploma	5	2.2
MCPS or equivalent	11	4.8
FCPS or equivalent	16	7.0
Professional Experience Of Doctors In Years		
<1 year	29	12.7
1-10 years	178	78.1
11-20 years	12	5.3
>20 years	9	3.9
Total	**228**	**100.0**

Most doctors were aware about leaching of chemicals from plastics and higher toxicity of certain plastics. Lowest awareness was found regarding numbers of unsafe plastic type. Table 2 shows knowledge about plastic safety and percentage of correct and incorrect responses to each question.

Table No.2: Awareness of doctors about questions asked about plastic use (n=228)

Question asked	Correct answer (%)	Incorrect answer (%)	Total (%)
Do you know plastic utensils release chemicals in the food they contain?	93.4	6.6	100
Do you know certain types of plastics release more toxic	78.9	21.1	100

chemicals than other types?			
How many types/ qualities of plastic are available?	3.1	96.9	100
Do you know each plastic type is allocated a specific number?	43	57	100
Which plastic numbers one should avoid to be used as utensils	1.3	98.7	100
Which factors increase the rate of release of chemicals from plastic?	42.5	57.5	100
Which diseases you know to be linked with use of plastic?	14.9	85.1	100

Those who answered four or more questions correctly were labeled as 'aware' and those answering less than four questions correctly were labeled as 'unaware'. Overall awareness calculated using this scale was only 27.2%.

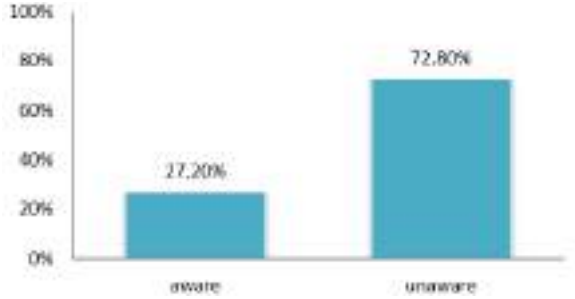


Figure No.1: Overall Awareness about plastic safety (n=228)

Overall awareness was compared among groups of doctors according to their field. Doctors working in clinical departments were more aware as compared to basic sciences doctors (p-value= 0.021). Also doctors having higher qualification had higher level of awareness with significant p-value of 0.043 (refer to table 3).

Table no.3:

Effect modifier	Aware	Unaware	p-value
Clinical/ basic department			
Clinical sciences	57 (30.3%)	131 (69.7%)	0.021
Basic sciences	5 (12.5%)	35 (87.5%)	
Qualification			
MBBS	49 (25%)	147 (75%)	0.043
Postgraduate diploma	2 (40%)	3 (60%)	
MCPS or equivalent	2 (18.2%)	9 (81.8%)	
FCPS or equivalent	9 (56.3%)	7 (43.8%)	

Data are shown as N (%) and p-value calculated using chi-square test.

DISCUSSION

This study aimed to assess the awareness of doctors about the unsafe plastic utensils. According to results, majority doctors (93.4%) were aware that leaching occurs from plastics into the food they contain. Lowest awareness was found regarding which plastic numbers to be avoided for use as utensils; the correct answer was given by only three doctors (1.3%). Overall 62 doctors (27.2%) were aware of unsafe plastic utensils according to the scale used, while the majority of 166 (72.8%) doctors were unaware of it. This highlights the lack of awareness, and the need thereof, of raising public awareness of the hazards of plastic materials on a large scale to address the rising issue of plastic safety.[13] In the past few years, there has been an increase in concern about the possible health problems linked with exposure to phthalates, a chemical in plastics.[14] Only a few years back, there were limited studies available which studied the relationship between BPA and effects on human health.[15] The first such study got published in 1997, and after that, more than 100 such studies have been published.[16, 17] More researches are now available for PBDEs as well.[18]

In current study, only 15% doctors were aware of the diseases linked with the use of plastic utensils. This level of awareness is considered very low as doctors are supposed to be knowledgeable regarding health risks in environment. Similar results were shown by a survey done on experts' opinions about phthalates, an important chemical of plastics, in Norway. This survey revealed a high gap in knowledge. None of the six experts (0%) agreed that they have a high level of knowledge about phthalates toxicokinetics.[19] This low level of awareness is probably due to lack of consensus on hazards of plastics among plastic industry and scientists coupled with lack of political will in curbing its use. Therefore, our current trend of plastic use and manufacture is rising at a fast rate.[20] A survey done in the US also showed that people were confused about banning BPA due to the opposing claims of scientists and the plastic industry.[21] In California, a bill named 'AB319' was started in 2005 on banning BPA, which was actively opposed by industries making plastics, chemicals, grocery and baby products. Uncertainty was spread by contradictory statements and obscuring real information from the public, especially by those interested in BPA production.[22]

Plastic is toxic for infants as well, and its use needs to be regulated. It is banned in many developed countries. Association of Canadian Community Colleges advises elimination of Styrofoam plastics as it is supposed to be a probable carcinogen.[23] In France also, the use of bisphenol A in baby bottles was banned on 30th June 2010, and also banned for use in food packaging made

for children of ages 0 to 3 years, on 1st January 2013.[24] Also, U.S. state governments and European authorities suggested legal actions to limit the use of certain phthalates, as evident by Consumer Product Safety Improvement Act in 2008 by US.[25]

This is an innovative study and to our knowledge is the first study on this topic in our country. Researchers conducted a pilot study to test the check the efficacy of questionnaire and used a sufficient sample size for data collection. However, there were some limitations also in this study. Firstly, no international, national or local study was found on this topic so comparison with other studies was insufficient. Secondly, there is no standard tool available for measuring awareness about plastic safety as this concept is not established in our public and even public health authorities. So we made our own scale of measuring awareness about plastic safety, the validity of which is uncertain**.**

CONCLUSION

In this study, we observed that most doctors were unaware of unsafe plastic utensils and diseases linked with them. However, most of them knew that chemicals leach from plastics in food, and certain plastic types leach more chemicals than other types. This awareness was found to have significant relation with the qualification of doctors.

Recommendations: Seminars should be done to raise awareness of doctors regarding unsafe plastic utensils. Public can benefit from awareness campaigns through public health messages on social media. Policies should be made to cut down manufacture and use of plastics that are more toxic and safe alternatives should be made available. Safe alternatives for plastic include glass and lead. Glass baby bottles since these are an excellent alternative to plastic bottles. It has been found that no detectable lead or cadmium leaches from the glass. The aluminium and stainless-steel bottles are also harmless with respect to leaching of metals in water.

Acknowledgments: The research reported here was made possible through the participation and support of a number of individuals. We are grateful for the support of all our participants and those who facilitated our engagement with the participants. We are pleased to acknowledge here contribution of Dr. Sayema Awais and Dr. Madiha Shafi who supported the research endeavour in terms of data collection and data management processes.

Author's Contribution:

Concept & Design of Study:	Bushra Anwar
Drafting:	Khushbakht Anwar, Aashi Ahmed, Nadia Nisar
Data Analysis:	Saima Omair, Warda Wazir
Revisiting Critically:	Bushra Anwar, Khushbakht Anwar
Final Approval of version:	Bushra Anwar

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Nature Works LLC. Plastic Coding Guidelines in the United States. SPI Coding System Background. [Internet]. 2008 Available from: http://www.natureworksllc.com/~/media/The_Ingeo_Journey/EndofLife_Options/plastic_codes/2008_04_10_plastic_code_guidelines_pdf.pdf
2. American Chemistry Council. Plastics: plastic packaging resin identification codes. [Internet]. Available from: http://plastics.american-chemistry.com/Education-Resources/Plastics-101/Plastic-Packaging-Resin-Identification-Codes.html
3. Federal trade commission. Green guides. Part 260–guides for the use of environmental marketing claims: 24. [Internet]. Available from: https://www.ftc.gov/sites/default/files/attachments/press-releases/ftc-issues-revised-green-guides/greenguides.pdf
4. Rochman CM, Browne MA, Halpern BS, Hentschel BT, Hoh E, Karapanagioti HK. Policy: Classify plastic waste as hazardous. Nature 2013;494:169–71.
5. Yang CZ, Yaniger SI. Most plastic products release estrogenic chemicals: a potential health problem that can be solved. Environ Health Perspect 2011;119:989-96.
6. Koch HM, Calafat AM. Human body burdens of chemicals used in plastics manufacture. Phil Trans R Soc B. 2009;364:2063–78.
7. Edgar D, Edgar RA. Fantastic Recycled Plastic: 30 Clever Creations to Spark Your Imagination. Characteristics and properties of plastics. 1st ed. Lark Books: New York; 2009.
8. Carwile J, Luu H, Bassett L, Driscoll D, Yuan C, Chang J, et al. Polycarbonate bottle use and urinary bisphenol A concentrations. Environ Health Perspect 2009;117(9):1368-72.
9. What Science Should We Really Follow? [Internet]. Mercola.com. 2021 [cited 24 September 2021]. Available from: https://articles.mercola.com/sites/articles/archive/2013/04/11/plastic-use.aspx
10. Rhie YJ, Nam HK, Oh YJ, Kim HS, Lee KH. Influence of bottle-feeding on serum bisphenol A levels in infants. J Korean Med Sci 2014; 29:261-4.
11. Gowder SJ. Nephrotoxicity of bisphenol A (BPA)--an updated review. Curr Mol Pharmacol 2013; 6:163-72.
12. Pouokam GB, Ajaezi GC, Mantovani A, Orisakwe OE, Frazzoli C. Use of Bisphenol A-containing baby bottles in Cameroon and Nigeria and possible

risk management and mitigation measures: community as milestone for prevention. Sci Total Environ 2014;481:296-302.
13. Thompson R, Swan S, Moore C, vom Saal F. Our plastic age. Phil Trans R Soc B 2009;364 (1526):1973-6.
14. Latini G. Monitoring phthalate exposure in humans. Clin Chim Acta 2005;361(1-2):20-9.
15. Rochester JR. Bisphenol A and human health: a review of the literature. Reprod Toxicol 2013;42:132-55.
16. Vom Saal F, Welshons W. Large effects from small exposures. II. The importance of positive controls in low-dose research on bisphenol A. Environmental Res 2006;100(1):50-76.
17. Vom Saal F, Timms B, Montano M, Palanza P, Thayer K, Nagel S, et al. Prostate enlargement in mice due to fetal exposure to low doses of estradiol or diethylstilbestrol and opposite effects at high doses. Proceedings of the National Academy of Sciences 1997;94(5):2056-2061.
18. Welsh L. Polybrominated diphenyl ethers: Causes for concern and knowledge gaps regarding environmental distribution, fate and toxicity. Sci Total Environ 2008;400(1–3):425–36.
19. Zimmer K, Gutleb A, Ravnum S, Krayer von Krauss M, Murk A, Ropstad E et al. Policy relevant results from an expert elicitation on the health risks of phthalates. Environ Health 2012;11(Suppl 1):S6.
20. Ali M, Bhuiyan A, Gayen T. Rise in Single-Use Plastic Pollution Amid COVID-19 Pandemic: Bangladesh Perspective. J Agriculture, Food and Environment 2021;02(02):80-84.
21. Brewer PR, Ley BL. Contested evidence: Exposure to competing scientific claims and public support for banning bisphenol-A. Public Underst Sci 2014;23(4):395-410.
22. Quitmeyer A, Roberts R. Babies, bottles, and bisphenol A: the story of a scientist-mother. PLoS Biol 2007;5(7):e200.
23. Association of Canadian Community Colleges, National Round Table on the Environment and the Economy (Canada). Green Guide: A User's Guide to Sustainable Development for Canadian Colleges. Canada: Alger press; 1992. p. 131.
24. Bisphenol A. A body of evidence supporting exposure reduction. Prescrire Int 2013; 22(141):219-23.
25. Kamrin MA. Phthalate risks, phthalate regulation, and public health: a review. J Toxicol Environ Health B Crit Rev 2009;12(2):157-74.

Original Article

Hypertriglyceridemia in Acute Coronary Syndrome

Frequency of Hypertriglyceridemia in Patients Presenting with Acute Coronary Syndrome in Local Population

Atif ur Rahman[1], Samiullah Khan[2], Sadullah Shah[2], Muhammad Niaz Khan[3], Muhammad Nadeem Khan[2] and Raza Mohammad[2]

ABSTRACT

Objective: To determine the frequency of hypertriglyceridemia in acute coronary syndrome (ACS) patients in local population.

Study Design: Descriptive cross-sectional study

Place and Duration of Study: This study was conducted at the DHQ Teaching Hospital Bannu from January, 2019 to June, 2019 for a period of six months.

Materials and Methods: In this study, a total of 214 patients with acute coronary syndrome (ACS) were observed over a period of 6 months under informed written consent. They were interviewed through a pre-designed research proforma. ECG of the patients was done by Fukuda ME C110 machine present at ECG section and interpretation was done by myself. High sensitive troponin level for confirmation of ACS was measured in District Head Quarter Teaching Hospital (DHQ-TH), Bannu by ROCHE analyzer machine. The fasting serum triglyceride level was taken within 24 hours of admission with ACS. It was measured by ROCHE COBAS 501 chemical analyzer.

Results: In this study, mean age of the patients was 58 ± 12.33, out of which 33% subjects fell in age group 51-60 years, 27% subjects were in age group 30-50 years, and 40% patients were in age group 61-70 years. About 45% subjects were female while 45% were male. The frequency of hypertriglyceridemia was 80% in patients with ACS.

Conclusion: Our study concludes that hypertriglyceridemia was frequently observed among patients presenting with acute coronary syndrome to the coronary care unit of DHQ-TH Bannu.

Key Words: Hypertriglyceridemia, Acute coronary syndrome, DHQ-TH

Citation of article: Rahman A, Khan S, Shah S, Khan MN, Khan MN, Mohammad R. Frequency of Hypertriglyceridemia in Patients Presenting with Acute Coronary Syndrome in Local Population. Med Forum 2021;32(10):91-94.

INTRODUCTION

Coronary Artery disease (CAD) is an international health problem in both gender and also a leading cause of death in the developed countries [(1).] Acute coronary syndrome (ACS) refers to a spectrum of clinical presentations ranging from ST-segment elevation myocardial infarction (STEMI) to non–ST-segment elevation myocardial infarction (NSTEMI) or unstable angina.

[1.] Department of Cardiology, Category D Hospital Razmak, Distt North-Waziristan Agency, Miranshah, KPK.
[2.] Department of Cardiology, Bannu Medical College/ DHQ-TH, Bannu.
[3.] Department of Cardiology, Hayatabad Medical Complex, Peshawar

Correspondence: Dr. Samiullah Khan, Assistant Professor of Cardiology, Bannu Medical College/DHQ-TH, Bannu.
Contact No: 03015151346
Email: drsamee@yahoo.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

CAD being a cause of acute coronary syndrome; its prevalence is equally high in south Asia including Pakistan [(2).]

According to reports, around 17 million people worldwide succumb to death due to coronary artery disease.[(3).] According to the World Health Organization (WHO) the main risk factor of acute coronary syndrome are hypertriglyceridemia, hypertension, cigarette use, hyperglycemia, lack of physical activity, overweight and obesity [(4, 5).]

Hypertriglyceridemia is defined as raised levels of triglycerides in the bloodstream, a condition that increases the risk of CAD[(6).] Hypertriglyceridemia is one of the risk factors for ACS[(4),] characterized by increased levels of LDL cholesterol and decreased HDL cholesterol[(7).] As per numerous studies, triglyceride-rich lipoproteins are an independent risk factor for acute coronary syndrome.[(8,9)] Pathophysiology behind this association include increased pro-inflammatory cytokines, excessive release of free fatty acids, coagulation factors, and deranged fibrinolysis [(10).]

A large randomized controlled trial concluded that in patients with established CAD, twenty years mortality risk increases gradually with increasing triglyceride

levels so that it was increased by 68% with severe hypertriglyceridemia when compared with patients having low triglyceride levels[11]. It was also demonstrated by PROVE-IT TIMI 22 trial that in patients with ACS with each 10mg/dl decrease in triglyceride level lead to lowering of incidence of death, myocardial infarction and recurrent ACS by 1.6%[12]. A study done in Mexico[13] recorded that 50.1% of patients with ACS were suffering from hypertriglyceridemia. A recent study conducted in Pakistan reported that hypertriglyceridemia was present in 83.33% of ACS cases [14].

The previously available studies show significant variation in the frequency of hypertriglyceridemia in ACS necessitating further research to know about actual frequency of hypertriglyceridemia in ACS in our population.

MATERIALS AND METHODS

The present study was conducted at coronary care unit of DHQ-TH Bannu over a period of six months from 1st January 2019 to 1st June 2019. Sample size was calculated using WHO sample size calculator with 95% confidence interval and 5% margin of error. Samples were collected using non probability, consecutive sampling technique. Patients included in the study were of either genders, aged 30-70 years and having ACS as per standard criteria.

Patients excluded from the study were those with Chronic kidney disease having serum creatinine >2.5mg/dl, those with other co-morbidities such as stroke, those denying written informed consent, and those with multi-organ dysfunction.

A total of 214 cases after fulfilling the inclusion and exclusion criteria were enrolled for study purpose from coronary care unit of DHQ-TH Bannu. An informed consent of the patients was obtained with the assurance of confidentiality of their medical records. A detailed history of the patients, their medical records, demographic profile e.g. age, gender, sex, monthly income, home address, and contact No's was obtained and recorded. ECG of the patients was done by Fukuda ME C110 machine present at ECG section followed by myself. High sensitive troponin level for confirmation of ACS was measured in Laboratory by ROCHE analyzer machine at DHQ-TH Bannu. The fasting serum triglyceride level was taken within 24 hours of admission with acute coronary syndrome. It was measured by ROCHE COBAS 501 chemical analyzer machine. Any patient having triglyceride levels >200mg/dl was labelled as having hypertrigly ceridemia. All this information was recorded on Performa and analyzed using Microsoft Excel 2016 and SPSS version-16.

Mean ± S.D were used to assess quantitative variables while Qualitative variables were assessed in the form of frequency and percentage. Data was stratified for gender, age, and BMI (obese and non-obese). Chi-square test was applied after stratification. Statistically significant P value was considered as <0.05.

RESULTS

The Mean age of patients in this study was 58 ± 12.33. About 33% (n, 71) patients were in the age range 51-60 years, 27% (n, 58) patients were in age range 30-50 years, and 40% (n, 85) patients were in age range 61-70 years. (Table 03). About 45% (n, 96) patients were female while 55% (n, 118) patients were male. Status of obesity was analyzed 38% (n, 81) patients were non obese (BMI <30 Kg/m^2 while 62% (n,133) patients were obese (BMI >30 Kg/m^2 (Table No 01). Hypertriglyceridemia was analyzed as 80% (n, 171) patients had hypertriglyceridemia (Table No 02). Stratification of hypertriglyceridemia with age, gender, BMI is given in Table 3, 04 and 05.

Table No.1: BMI (n=214)

BMI	Frequency	Percent
Non obese ≤30 kg/m^2	81	38%
Obese>30 kg/m^2	133	62%
Total	214	100%

Mean BMI was 27 kg/m^2 with SD ± 3.09
Mean height was 1.3 meters with SD ± 0.95
Mean weight was 88 Kg with SD ± 10.71
Mean triglycerides was 242g/dL with SD ± 28.374

Table No.2: Hypertriglyceridemia (n=214)

Hypertriglyceridemia	Frequency	Percent
Yes	171	80%
No	43	20%
Total	214	100%

Table No.3: Age Wise Distribution of Hypertriglyceridemia (n=214)

Hypertriglyceridemia	31-50 years	51-60 years	61-70 years	Total
Yes	46	56	69	171
No	12	15	16	43
Total	58	71	85	214
%age within age gap	27%	33%	40%	100%

Chi square test was applied in which P value was 0.9299

Table No.4: Stratification of Hypertriglyceridemia Within Gender (n=214)

Hypertriglyceridemia	Male	Female	Total
YES	94	77	171
NO	24	19	43
Total	118	96	214

P value: 0.9936

Table No.5: Hypertriglyceridemia Association with Obesity (n= 214)

Hypertriglyceridemia	Obese	Non obese	Total
YES	65	106	171
NO	16	27	43
Total	81	133	214

P value: 0.9014

DISCUSSION

Majority of Patients presented with acute coronary syndrome usually do not usually do not have any information regarding their lipid profile. The early knowledge of lipid status of patients with an ACS might allow an early classification of eventual dyslipidemia and will be helpful in selection of lipid lowering therapy. In this study we used diagnostic criteria for ACS following American Heart Association of Cardiology guidelines.[15]

We observed that the Mean age of patient in the present study was ± 12.33, with slight male dominate [male, 55%] disease as compared to female patients [female, 45%]. This is in consistent with other studies from the region.[16] Adam AM et al [17] had reported mean age of 60± 8.71 years. About 38% patients were female whereas 62% subjects were male.

Our study shows that majority of 40% patients were in age range 61-70 years. This has been proved by previous research that advancing age is a risk factor for CAD and myocardial infarction. [17, 18]

We determine that frequency of hypertriglyceridemia was 80% among patients presenting with acute coronary syndrome and gender has no significant effect [P value, 0.9936] on it.

Malik MN et al[14,] revealed hypertriglyceridemia in 83.33% patients with ACS and raised LDL in 43.30% subjects. Low HDL value was noted in 73.20% ACS patients. P value was not significant (P-value > 0.05) among male and female subjects in terms of comparison for level of dyslipidemia in both genders.

González-Pacheco H et al[13] reported similar frequency of Hypertriglyceridemia about 80.1% in patients with ACS.

We also observed that obesity has no significant effect on hypertriglyecdemia. This is also shown by Lee SY et al that moderate intensity Hypertriglyceridemia in Non-Obese and Non-Diabetic Subjects found due to Altered Plasma Lysophosphatidylcholines and Amides.[19] According to all results this discussion can be concluded that hypertriglyceridemia is a polygenic and environmentally determined metabolic disease that affects the production and clearance of triglyceride (TG)-rich lipoproteins.[20] An elevated level of plasma TG is an independent risk factor for type 2 diabetes (T2D), metabolic syndrome, and atherosclerotic cardiovascular disease (CVD).[21]

So timely admission of ACS patients is beneficial and important for the evaluation of the lipid profile so that most suitable treatment can be chosen for better prognosis.

CONCLUSION

Hypertriglyceridemia is frequently present among patients presenting with acute coronary syndrome in local population.

Author's Contribution:

Concept & Design of Study:	Atif ur Rahman
Drafting:	Samiullah Khan, Sadullah Shah
Data Analysis:	Muhammad Niaz Khan, Muhammad Nadeem Khan, Raza Mohammad
Revisiting Critically:	Atif ur Rahman, Samiullah Khan
Final Approval of version:	Atif ur Rahman

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Okrainec K, Banerjee DK, Eisenberg MJ. Coronary artery disease in the developing world. Am Heart J 2004;148(1):7-15.
2. Qureshi MS, Shah ST, Ali J, Khan SB, Hadi A, Khan A, et al. Frequency of cardiovascular disease risk factors among doctors. Pak Heart J 2012; 44(3-4).
3. Adam AM, Rizvi AH, Haq A, Naseem R, Rehan A, Shaikh AT, et al. Prognostic value of blood count parameters in patients with acute coronary syndrome. Ind Heart J 2018;70(2):233-40.
4. Vedanthan R, Seligman B, Fuster V. Global perspective on acute coronary syndrome: a burden on the young and poor. Circulation Research 2014;114(12):1959-75.
5. Pitsavos CE, Panagiotakos DB, Chrysohoou CA, Skoumas J, Stefanadis C, Toutouzas PK. Education and acute coronary syndromes: results from the CARDIO2000 epidemiological study. Bulletin of the World Health Organization 2002;80:371-7.
6. Pejic RN, Lee DT. Hypertriglyceridemia. J Am Board of Family Med 2006;19(3):310-6.
7. Grundy SM. Hypertriglyceridemia, atherogenic dyslipidemia, and the metabolic syndrome. Am J Cardiol 1998;81(4):18B-25B.
8. Chapman MJ, Ginsberg HN, Amarenco P, Andreotti F, Borén J, Catapano AL, et al. Triglyceride-rich lipoproteins and high-density lipoprotein cholesterol in patients at high risk of cardiovascular disease: evidence and guidance for management. Eur Heart J 2011;32(11):1345-61.
9. Carmena R, Duriez P, Fruchart JC. Atherogenic lipoprotein particles in atherosclerosis. Circulation 2004;109(23 suppl 1):III-2-III-7.
10. Van Gaal LF, Mertens IL, Christophe E. Mechanisms linking obesity with cardiovascular disease. Nature 2006;444(7121):875.
11. Klempfner R, Erez A, Sagit BZ, Goldenberg I, Fisman E, Kopel E, et al. Elevated Triglyceride Level Is Independently Associated With Increased All-Cause Mortality in Patients With Established Coronary Heart Disease: Twenty-Two–Year

Follow-Up of the Bezafibrate Infarction Prevention Study and Registry. Circulation: Cardiovascular Quality and Outcomes 2016;9(2):100-8.

12. Miller M, Cannon CP, Murphy SA, Qin J, Ray KK, Braunwald E, PROVE IT-TIMI 22 Investigators. Impact of triglyceride levels beyond low-density lipoprotein cholesterol after acute coronary syndrome in the PROVE IT-TIMI 22 trial. J Am Coll Cardiol 2008;51(7):724-30.
13. González-Pacheco H, Vargas-Barrón J, Vallejo M, Piña-Reyna Y, Altamirano-Castillo A, Sánchez-Tapia P, et al. Prevalence of conventional risk factors and lipid profiles in patients with acute coronary syndrome and significant coronary disease. Therapeutics and Clinical Risk Management 2014;10:815.
14. Malik MN. Association of Dyslipidaemia and Acute Coronary Syndrome in Patients Admitted to CCU, PIMS. Ann Pak Inst Med Sci 2014; 10(3):155-61.
15. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2019;140:e596–e646.
16. Xavier D, Pais Prem, Devereaux PJ, Xie C, Prabhakaran D. On behalf of the CREATE registry investigators. Treatment and outcomes of acute coronary syndromes in India [CREATE]: a prospective analysis of registry data. Lancet 2008;371:1435-42.
17. Khan S, Asghar Khan M, Khan MN, Shah I, Hassan M ul. Comparison of Risk Factors Profile in Patients Below and Above Forty Years of Age Presenting With Acute Myocardial Infarction. J Postgrad Med Inst 2013;27(4).
18. Dhingra R, Vasan RS. Age as a risk factor. Med Clin North Am 2012;96(1):87-91.
19. Lee SY, Kim M, Jung S, Lee SH, Lee JH. Altered Plasma Lysophosphatidylcholines and Amides in Non-Obese and Non-Diabetic Subjects with Borderline-To-Moderate Hypertriglyceridemia: A Case-Control Study. PLOS One 2015;10(4): e0123306. https://doi.org/10.1371/journal.pone.0123306
20. Sahebkar A, Chew GT, Watts GF. Recent advances in pharmacotherapy for hypertriglyceridemia. Prog Lipid Res 2014;56C:47–66.
21. Miller M, Stone NJ, Ballantyne C, Bittner V, Criqui MH, Ginsberg HN, et al. Triglycerides and cardiovascular disease: a scientific statement from the American Heart Association. Circulation 2011;123: 2292–2333.

Original Article

Spinal Anesthesia in Caesarean Section

Comparison of Crystalloid Preload Rapid Administration after Induction of Spinal Anesthesia in Women Undergoing Elective Caesarean Section

Ravi Kumar[1], Aruna Kumari Hira[3], M. Aneeque Alam Khan[4], Kashif Ali[5], Pavan Kumar[6] and Mukhtiar Begum Noonari[2]

ABSTRACT

Objective: To compare crystalloid preload with prompt administration post induction of spinal anesthesia in women undergoing elective caesarian section.

Study Design: Randomized controlled trial study

Place and Duration of Study: This study was conducted at the Department of Anesthesia, Jinnah Postgraduate Medical Centre, Karachi from July, 2018 to January, 2019 for a period of six months.

Materials and Methods: One hundred and fifty-four patients underwent elective caesarian section under spinal anesthesia were included and divided into two groups, coload and pre load (Group C and Group P). All patients were given bupivacaine. In group P, patients were injected 15 ml/kg ringer lactates solution for over 20 minutes prior to spinal block whereas in group C patients, ringer lactate was injected over 20 min post CSF tapping. Presence of nausea and vomiting were recorded. Maternal hypotension was assessed.

Results: The mean age in Group P was 36.32±6.68 years and Group C was 34.77±5.61 years. In Group P, nausea was 27.3%, vomiting was 37.7% and hypotension was 64.9%. In Group C nausea was 16.9%, vomiting was 9.1% and hypotension was 42.9%. Vomiting and hypotension were significantly association with two study groups but nausea was not found any significance.

Conclusion: Crystalloid preload observed more nausea, vomiting, and hypotension as compared to patients of coload.

Key Words: Crystalloid preload, Rapid administration, Spinal anaesthesia, Elective caesarian section

Citation of article: Kumar R, Hira AK, Khan MAA, Ali K, Kumar P, Noonari MB. Comparison of Crystalloid Preload versus Rapid Administration after Induction of Spinal Anesthesia in Women Undergoing Elective Caesarean Section. Med Forum 2021;32(10):95-98.

INTRODUCTION

Spinal anesthesia is commonly associated with hypotension which is a reaction of cardiovascular system. It occurs as a result of accelerated venous capacity and decline in resistance of systematic vascular supply.[1] Almost 70-80% spinal anesthetized patients developed intra-operative hypotension.[2,3] A large volume of crystalloids is given prior (20-30 min) to spinal anesthesia as a prevention measure against spinal-induced hypotension.[4]

The crystalloids efficiency before deliverance of spinal blockers has been verified as non-beneficial by studies on obstetric patients.[5,6] Injecting intra-venous crystalloids makes patients at a greater risk of pulmonary edema especially in vulnerable patients and also resulting in non-catherized patient to retain urine after surgery.[7] Fluids are given prior to spinal blocker for increasing venous-return so that to conserve central volume of blood in addition to output by the heart. Therefore, studies have evidently proved that deliverance of crystalloids prior to spinal blocker does not assist in incidence reduction of spinal generated hypotension.[8]

[1.] Department of Anesthesiology/Surgery & Allied / Obstet & Gynae[2], Sir Syed College of Medical Sciences for Girls Karachi.
[3.] Department of Obstet & Gynae, Dow University of Health Sciences, Karachi.
[4.] Department of Anaesthesia, Sindh Institute of Urology & Transplantation, Karachi
[5.] Department of Anaesthesia, Hussain Lakhani Hospital/Iqra University, Karachi.
[6.] Department of Anaesthesia, Al-Tibri Medical College Karachi.

Correspondence: Dr. Ravi Kumar, Assistant Professor, Department of Anesthesiology/Surgery & Allied, Sir Syed College of Medical Sciences for Girls Karachi.
Contact No: 0333-7361000
Email: ravi2275000@gmail.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

Crystalloids have minimal intra vascular shelf life.[4] Therefore their deliverance in addition to IV fluids post spinal anesthesia was seemed to be beneficial in reducing cardio related side effects and maintaining arterial pressures.[9]

Hypotension was found in 30(60%) and 23(46%) patients among pre and coload groups respectively. Nausea was found in 19(38%) and 10(20%) patients among pre and coload groups respectively. Vomiting occurred in 14 (28%) and 6 (12%) patients among pre and coload groups respectively.[10]

MATERIALS AND METHODS

This randomized controlled trial was conducted at Department of Anesthesia, Jinnah Postgraduate Medical Centre, Karachi from 8th July 2018 to 7thJanuary 2019 and comprised 154 patients (77 in each group). Age range 18 to 45 years, gestational age 37 to 41 weeks assessed on dating scan, women who underwent elective caesarian through spinal anesthesia and ASA status I & II were included. Patients with chronic hypertension, PIH, cardiovascular or cerebrovascular disease on medications, chronic hypertension, anaemia, eclampsia, PIH, APH, fetal distress or any contra-indication to spinal anesthesia were being excluded.

Patient's allocation into two groups coload and pre load (Group C and Group P) was made. Height was assessed on stadiometer with bare foot and weight was measured in light cloths on bathroom scale with reading nearest to 0.1kg. Ranitidine in addition to metoclopramide was given to each patient on surgery day. Electrocardiography, oxygen saturation, baseline heart rate (HR), systolic (SBP) and diastolic blood pressure (DBP as well as NIBP-instituted and, were recorded. Spinal anesthesia was delivered to each patient through 2.2 milliliter of 0.5 percent hyperbaric bupivacaine inside intervertebral spaces (left lateral location) such as in L3-4 or L2-3 through 23 or 25G Quincke's needle for spine. All preparations were kept aseptic. Ringer lactate (RL) solution was delivered as 15ml/kg in P group before twenty minutes of spinal block administration. In those patients belonging to group C RL was injected around twenty minutes post tapping of CSF. Post blocking and surgery initiation the sensory level of patient was analyzed and T5 levels were aimed to achieve.

Each patient HR, systolic and diastolic blood pressure were monitored after every two minutes until ten minutes followed by five minutes measuring until 30 minutes and finally measurement after every ten minutes until the completion of surgery. Complains of nausea/vomiting were documented. Reduction in systolic blood pressure by a level of ≥20% from the baseline or SBP <90mmHg (absolute estimate) was defined as maternal hypotension. Injection ephedrine three milligram was given to patients with episodes of hypotension in incremental dosage in addition to fluid boluses.

The data was entered and analyzed through SPSS-20. Two groups were compared in terms of nausea, vomiting and hypotension by applying Chi square test. p value ≤0.05 was taken as significant.

RESULTS

The mean age in Group P was 36.32±6.68 years while in Group C was 34.77±5.61 years. The mean parity in Group P was 3.26±1.75 years and in Group C it was 3.25±1.74 years. The mean gestational age in Group P was 39.80±1.19 weeks and in Group C it was 39.73±1.14 weeks. The mean duration of surgery in Group P was 82.31±28.98 min and in Group C it was 86.17±31.58 minutes. The mean weight in Group P was 72.12±9.54 Kg and in Group C it was 72.03±11.15 Kg (Table 7). The mean height in Group P was 1.61±0.12 meters and in Group C it was 1.63±0.08 meters. Mean BMI in Group P was 28.10±5.71 Kg/m^2 and in Group C it was 26.83±3.24 Kg/m^2 (Table 1).

Table No.1: Descriptive statistics of the patients (n=154)

Variable	Group P (n=77)	Group C (n=77)
Age (years)	36.32±6.68	34.77±5.61
Parity	3.26±1.75	3.25±1.74
Gestational age (weeks)	39.80±1.19	39.73±1.14
Duration of surgery (min.)	82.31±28.98	86.17±31.58
Weight (kg)	72.12±9.54	72.03±11.15
Height (m)	1.61±0.12	1.63±0.08
BMI (Kg/m^2)	28.10±5.71	26.83±3.24

Table No.2: Demographic information of the patients (n=154)

Variable	Group P		Group C	
	No.	%	No.	%
ASA Class				
I	37	48.1	36	46.8
II	40	51.9	41	53.2
Diabetes mellitus				
Yes	21	27.3	13	16.9
No	56	72.7	64	83.1

In group P, 48.1% study subjects were found with ASA Class-I, and 51.9% study subjects with ASA class-II. In group C, 46.8% study subjects were found with ASA Class-I, and 53.2% study subjects with ASA class-II. It was observed that in group P, 31.2% were diabetic and in group C, 22.1% study subjects were diabetic (Table 2).

In Group P, nausea was observed by 27.3%, vomiting was observed in 37.7% and hypotension was observed in 64.9% study subjects. While in Group C, nausea was observed by 16.9%, vomiting was observed in 9.1% and hypotension was observed in 42.9%. The results

showed that vomiting (p=0.000) and hypotension (p=0.006) were significantly association with two study groups but nausea (p=0.120) was not found any significance (Table 3).

Table No. 3: Comparison of nausea, vomiting and hypotension among groups (n=154)

Variable	Group P	Group C	P value
Nausea			
Yes	21 (27.3%)	13 (16.9%)	0.120**
No	56 (72.7%	64 (83.1%)	
Vomiting			
Yes	29	7	0.000*
No	48	70	
Hypotension			
Yes	50	33	0.006*
No	27	44	

**Not Significant >0.05 *Significant <0.05 levels

DISCUSSION

Spinal anesthesia is generally used during cesarean sections due to multiple reasons, the most important one is easy to perform[11] and also to avoid other pregnancy related complications. However, it is associated with significant reduction in blood pressure as indicated in various research up to 83%.[12] Hypotension can cause mild problems like nausea and vomiting to deleterious effects like cardiac arrest.[13] Therefore, despite of its advantages, this exacerbated chances of hypotension in women has become the major concern of anesthetist around the globe. Accordingly, several strategies used to prevent hypotension, changing hemodynamic parameters in spinal anesthesia cause sympatholysis.[14]

Sympatholysis causes vasodilation and reduces the pressure on blood vessels. Several studies focused on "filling" the vessels. A study of Muzlifah and Choy[14] compared the effects of two doses of single crystalloid. Result of the study indicated that larger dose is not required to minimize the effect. Another study by Siddik et al[15] compared additional mixture with crystalloid i.e colloid. This study proved that 10% hydroxyethyl starch is better that ringer's lactate in maintaining maternal blood pressure. Findings of another study Tamilselvan et al[16] further elaborate the accurate flow time and cardiac output of the mother. In their study, they used 6% hydroxyethyl starch and ringers lactate. Effect was high but was not enough to maintain normal blood pressure.[17] Another study Teoh and Siah[18] compared the effect of colloid in preload and coload, the result remains the same.

Similarly, another study showed the comparison of various colloid and crystalloid preload with no preload.[19] They still did not observe any difference among all the groups. It concluded that, these are ineffective in attaining normal blood pressure. McDonald et al[20] highlighted that cardiac output of the mother will remain same if she is coloaded either with crystalloid or colloid. However, the major concern with the use of colloids is that, they also have deleterious side effects even including anaphylactic reactions and are also expensive.[21] Likewise, a study of Dyer et al[7] concluded that, despite of the fact, hemodynamic parameters is not effecting hypotension directly but the requirement of the vasopressor was significantly reduced in ringer's lactate coload group.

Mojica et al[9] reported side effects related to this strategy as well. In this study, they made 3 groups on the basis of dosage administration time and compared it with the placebo group. Incidence of hypotension was higher in preloading in contrast to placebo group, but the result was not statistically substantial.

The coloading and placebo had it as similar. Considering cardiovascular side effects, it was observed and concluded by them that coloading is more appropriate. In another study the protocol of preloading was conducted in a group while coloading was performed in the other group.[22]

Post induction the hypotension was recorded at three and five minutes. Their research elaborated no variance between both at three and five minutes. A significant number of patients had hypotension at either three or five minutes gap in the group of preload. The reason behind this could be that within the above mentioned period the deliverance of fluids in preload group were redistributing in comparison to coload group where fluids were constantly delivered. Hypotension frequency was significantly high such as 70% and 84% in the group of preload and coload respectively at three minutes followed by 76% and 86% in preload and coload group respectively at five minutes.[22] These facts emphasizes that both modalities cannot be relied on for hypotension prevention in cases where they are opted alone. Other literature has also stated similar findings that none of the single modality for prevention of hypotension is considered as reliable in cases of spinal anesthesia-induced hypotension.[23]

CONCLUSION

The difference of vomiting and hypotension are significantly associated with the two treatments but difference in nausea had not significant impact. Further, age, parity, gestational age, ASA class, duration of surgery, and BMI are also observed risk factors which can impact on the results.

Author's Contribution:

Concept & Design of Study:	Ravi Kumar
Drafting:	Aruna Kumari Hira, M. Aneeque Alam Khan
Data Analysis:	Kashif Ali, Pavan Kumar, Mukhtiar Begum Noonari,
Revisiting Critically:	Ravi Kumar, Aruna Kumari Hira
Final Approval of version:	Ravi Kumar

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Morgan PJ, Halpern SH, Tarshis J. The effects of an increase of central blood volume before spinal anesthesia for cesarean delivery: a qualitative systematic review. Anesth Analg 2001;92:997-1005.
2. Klöhr S, Roth R, Hofmann T, Rossaint R, Heesen M. Definitions of hypotension after spinal anaesthesia for caesarean section: literature search and application to parturients. Acta Anaesthesiol Scand 2010; 54:909-21.
3. Hartmann B, Junger A, Klasen J, Benson M, Jost A, Banzhaf A, et al. The incidence and risk factors for hypotension after spinal anesthesia induction: an analysis with automated data collection. Anesth Analg 2002; 94:1521-9.
4. Ah-Young OH, Jung-Won Hwang, In-Ae Song, Mi-Hyun Kim, Jung-Hee Ryu, Hee-Pyoung Park, et al. Influence of the timing of administration of crystalloid on maternal hypotension during spinal anesthesia for cesarean delivery: preload versus coload. BMC Anesthesiol 2014;14:36.
5. Lotfy ME, Moustafa AM, El Feky EME, Mowafy IA. Colloid versus crystalloid coload with spinal anesthesia during emergent cesarean section and their effect on hemodynamic changes. J Am Sci. 2014;10:158-63.
6. Langesater E, Dyer RA. Maternal haemodynamic changes during spinal anaesthesia for caesarean section. Curr Opinion Anaesthesiol 2011.
7. Dyer RA, Farina Z, Joubert IA, DU-Toit P, Meyer M, Torr G, et al. Crystalloid preload versus rapid crystalloid administration after induction of spinal anaesthesia (coload) for elective caesarean section. Anaesth Intensive Care 2004; 32:351-7.
8. Tawfik MM, Hayes SM, Jacoub FY, Badran BA, Gohar FM, Shabana AM, et al. Comparison between colloid preload and crystalloid coload in cesarean section under spinal anesthesia: a randomized controlled trial. Int J Obstet Anesth 2014; 23:317-23.
9. Mojica JL, Melendez HJ, Bautista LE. Timing of intravenous crystalloid administration and incidence of cardiovascular side effects during spinal anesthesia: the results from a randomized control trial. Anesth Analg 2002; 94:432-7.
10. Jacob JJ, Williams A, Verghese M, Afzal L. Crystalloid preload versus crystalloid coload for parturients undergoing cesarean section under spinal anesthesia. J Obstet Anaesth Crit Care. 2012 Jan-Jun;2(1):10-5.
11. Ng K, Parsons J, Cyna AM, Middleton P. Spinal versus epidural anaesthesia for caesarean section. Cochrane Database Syst Rev 2004;(2): CD003765.
12. Orbach-Zinger S, Ginosar Y, Elliston J, Fadon C, Abu-Lil M, Raz A, et al. Influence of preoperative anxiety on hypotension after spinal anaesthesia in women undergoing Caesarean delivery. Br J Anaesth 2012; 109(6): 943-9.
13. Hanss R, Ohnesorge H, Kaufmann M, Gaupp R, Ledowski T, Steinfath M, et al.Changes in heart rate variability may reflect sympatholysis during spinal anaesthesia. Acta Anaesthesiol Scand 2007; 51(10): 1297-304.
14. Muzlifah KB, Choy YC. Comparison between preloading with 10 ml/kg and 20 ml/kg of Ringer's lactate in preventinghypotension during spinal anaesthesia for caesarean section. Med J Malaysia 2009; 64(2): 114-7.
15. Siddik SM, Aouad MT, Kai GE, Sfeir MM, Baraka AS. hydroxyethyl starch 10% is superior to Ringer's solution for preloading before spinal anesthesia for cesarean section. Can J Anaesth 2000; 47(7): 616-21.
16. Tamilselvan P, Fernando R, Bray J, Sodhi M, Columb M. The effects of crystalloid and colloid preload on cardiac output in the parturient undergoing planned cesarean delivery under spinal anesthesia: a randomized trial. Anesth Analg 2009; 109(6): 1916-21.
17. Yokoyama N, Nishikawa K, Saito Y, Saito S, Goto F. Comparison of the effects of colloid and crystalloid solution for volume preloading on maternal hemodynamics and neonatal outcome in spinal anesthesia for cesarean section. Masui 2004; 53(9): 1019-24.
18. Teoh WH, Sia AT. Colloid preload versus coload for spinal anaesthesia for Cesarean delivery: the effects on maternal cardiac output. Anesth Analg 2009; 108:1592-8.
19. Kamenik M, Paver-Erzen V. The effects of lactated Ringer's solution infusion on cardiac output changes after spinal anesthesia. Anesth Analg 2001; 92(3):710-4.
20. McDonald S, Fernando R, Ashpole K, Columb M. Maternal cardiac output changes after crystalloid or colloid coload following spinal anaesthesia for elective cesarean delivery: a randomized controlled trial. Anesth Analg 2011;113:803-10.
21. Shah SA, Iqbal A, Naqvi SS. SS: Comparison of crystalloid preloading and crystalloid co-loading for prevention of spinal anesthesia induced hypotension. Pak Armed Forces Med 2015; 65:s231-5.
22. Emmett RS, Cyna AM, Andrew M, Simmons SW. Techniques for preventing hypotension during spinal anaesthesia for caesarean section. Cochrane Database Syst Rev 2002; 3: CD002251.
23. Bailit JL, Garrett JM. Stability of risk-adjusted primary cesarean delivery rates over time. Am J Obstet Gynecol 2004; 190: 395-400.

Original Article

Management and Outcomes in Pregnant Women having Placenta Previa and Placenta Accreta Spectrum Disorders

Placenta Previa and Placenta Accreta Spectrum Disorders

Amna Kazi[1], Jamshed Rahim[2], Nadir Hussain[3], Sana Danish[1], M. Ikram[1] and Sara Munir[1]

ABSTRACT

Objective: To characterize the obstetrical management and maternal outcomes in a series of women presenting with placenta previa and placenta accrete spectrum disorders in pregnancy.

Study Design: Prospective case series

Place and Duration of Study: This study was conducted at the Department of Obstetrics & Gynaecology, Shaikh Zayed Hospital, Lahore from January 2018 to December 2020 for a period of one year.

Materials and Methods: Twenty-five women age between 27-39 years who were prenatally diagnosed with placenta previa with placenta accreta spectrum disorders through ultrasound and/or magnetic resonance imaging were included. All patients underwent caesarean hysterectomy. The hospital stay, post-operative maternal and neonatal outcomes were recorded.

Results: The mean age was 34.9±5.1 years and mean gestational age at delivery was 36.3±1.3 weeks. The average blood loss in women was 3.5 litres. All women had placenta previa but 12 had placenta accreta while rest had placenta increta and percreta. Two previous caesarean histories were noticed in 82.04% and of ≥3 in 5.30% patients.

Conclusion: Massive blood loss, caesarean hysterectomy and pre-term delivery were evident outcomes of placenta previa with placenta accreta spectrum disorder. The incidence of prior caesarean sections was high among these patients.

Key Words: Cesarean deliveries, Placenta previa, Placenta accrete spectrum, Caesarean hysterectomy

Citation of article: Kazi A, Rahim J, Hussain N, Danish S, Ikram M, Munir S. Management and Outcomes in Pregnant Women having Placenta Previa and Placenta Accreta Spectrum Disorders. Med Forum 2021;32(10):99-102.

INTRODUCTION

Placenta accreta spectrum (PAS) is a heterogeneous condition which is associated with increased morbidity and requires challenges in early diagnosis as well as management. In PAS placenta is invaded in the uterus making it un detachable from uterus and resulting in life threatening massive bleeding if forcefully removed.[1,2] Globally ascending caesarean trend is increasing the incidence of PAS.[3,4] The absence of standardized high quality diagnostic tools results in its poor management and understanding. Maternal as well as neonatal life can be saved by high quality imaging and diagnosis of PAS.[5]

[1.] Department of Obstetrics & Gynaecology / Urology[2], Shaikh Zayed Hospital, Lahore.

Correspondence: Dr. Amna Kazi, Assistant Professor of Obstetrics & Gynaecology, Shaikh Zayed Hospital, Lahore.
Contact No: 0321-2250812
Email: amnakazi193@gmail.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

Other reason which results in PAS could include placental removal by manual method, uterine-curettage or due to endometritis.[6]

The overall incidence of PAS is around 1 in 2000 gestational woman, however this can vary among different races and countries depending upon their delivery practices and number of caesarean performed. In developing countries here birth rate is much higher the problem seems to be aggravated.[4,7] Placenta previa is a situation in which placenta is located and covers the cervix. This could also be a major cause for PAS. Additional factors which increase PAS risk are advanced maternal age, in vitro fertilization and PAS history in previous gestation.[8,9]

In a mega research at united states of America it was observed that the prevalence of PAS increased in women with placenta previa by 3%, with one caesarean, 11% with second caesarean, 40% with third caesarean, 61% with fourth caesarean and 67% with fifth or greater than fifth caesarean respectively. The incidence of placenta previa is reported in almost half of PAS cases.[10-14] The present study was designed to categorize PAS management strategies and determine the outcome success with given management in women having placenta previa in addition to PAS.

MATERIALS AND METHODS

It was a prospective case series which was conducted at Department of Obstetrics & Gynecology, Shaikh Zayed Hospital Lahore from 1st January 2018 to 31st December 2020. After a formal written informed consent, the study included 25 women who were prenatally diagnosed either clinically or through sonography/imaging (ultrasound and/or magnetic resonance) with placenta previa with placenta accreta spectrum disorders. Histopathological reports assisted in identifying PAS cases. Those women who were diagnosed incidentally during a caesarean section or those with a false-positive ultrasound (USG) report of a morbidly adherent placenta: which were not seen intraoperatively and planned in exclusion criteria. Obstetric data was retrieved from medical records. The complete demographic and clinical features results were documented on a well-structured questionnaire. The histopathological depth of invasion was recorded. The gestational period was dated by last menstruation period (LMP) assessing length of crown rump earlier than 14 weeks. Estimated weight of foetus and referral percentiles calculation was performed by measuring abdominal circumference. Transvaginal USG was performed for defining placenta as placenta previa. All the study participants underwent planned caesarean hysterectomy in a well-equipped tertiary care hospital, as the uterus could not be salvaged due to the severe invasiveness of the placenta and the massive postpartum haemorrhage.

Data was analyzed by using Chi square and t test tools for qualitative and quantitative variables using SPSS version 24. P value below 0.05 was considered significant.

RESULTS

The mean age of women was 34.9±5.1 years with mean gestational age at delivery as 36.3±1.3 weeks (Table 1). The average blood loss in women was 3.5 litters and all the patients received 4-6 units of packed RBG intraoperatively. There was one exception – a woman with one previous caesarean had only a litter of blood lost, and so she was transfused with one unit of blood only. None of the patients died with only one (4%) patient who was in ICU after surgery for 42 days and suffered from disseminated intravascular coagulation acute, renal failure, septicemia and pneumonia with psychosis was also discharged after complete recovery. Bladder was not separate able in 5 patients and required inverdent cystotomy (Fig. 1).

Out of the total cases there were 82.04% such women who had two cesarean or C-sections while only 5.30% had more than 3 C-sections clinical history p value <0.05 (Fig. 2).

There were 48% PAS with accreta categorization and 52% women had placenta increta or percreta. The mean age, gestation age at delivery and foetus birth weight was insignificantly different between adherent and invasive PAS cases (Table 2).

Table No.1: Clinical features of placenta previa and placenta accrete spectrum

Variables	PP+PAS
Mean age (years)	34.9±5.1
Parity	2.5±3.0
Gestational age(weeks) at delivery	36.3±1.3
Birth weight>90th percentile	4 (16%)
Birth weight<10th percentile	5 (20%)

Table No.2: Comparison of clinical features of PAS severity categories

Variable	Placenta accrete spectrum (n=12)	Increta/ percreta (n=13)	P value
Mean age (years)	35.0±4.8	34.9±5.5	0.92
Parity	2.3±2.0	2.8±4.0	0.07
Gestation age (weeks) at delivery	36.5±1.4	36.1±1.2	0.81
Birth weight >90th percentile	2 (16.6%)	3 (23.07%)	0.82
Birth weight<10th percentile	2 (16.6%)	3 (23.07%)	0.84

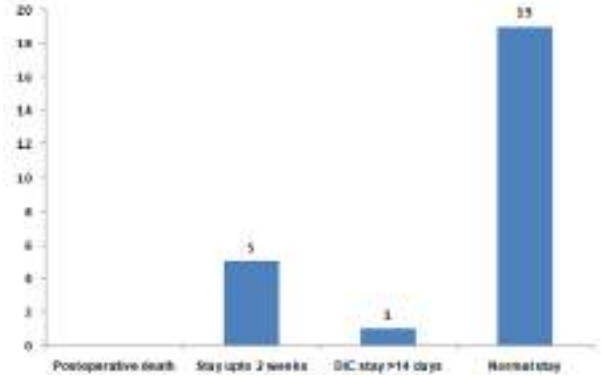


Figure No.1: Frequency of morbidity and hospital stay among PP and PAS cases

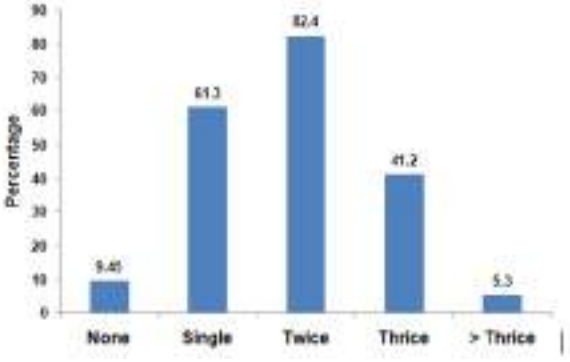


Figure No.2: Frequency of caesarean in PAS cases

DISCUSSION

In the current study, women with placenta previa (in the present pregnancy) and prior caesarean section(s) were at higher risk of placenta accreta spectrum (PAS) disorders. These life-threatening complications result into severe peripartum haemorrhage in women as is evident from present study. In pregnant women, placenta accreta spectrum is considered as the most common reason of caesarean hysterectomy and also the prevalent cause of catastrophic blood loss. The average blood loss in such cases is between 3000-5000 ml and 13% of the females have a blood loss of ≥10,000 ml.[15] Present study reports an average blood loss of ~3500 ml and 3-4 packed red blood cells transfusion per patient. The blood loss associated with placenta accreta spectrum disorder is in accordance with that of trauma surgery and requires proper management for effective treatment.[16]

Caesarean hysterectomy is an important measure for controlling blood loss during surgery. The hysterectomy should be attempted by placenta in situ.[17] Ureter, bladder or bowel may get injured during surgery, consequently, increasing the number of patients in intensive care unit and prolonged hospital stay. The rate of injury to urinary bladder or ureter ranges from 6 to 29% and 7% respectively during this procedure.[18] In cases where the placenta invades the bladder, partial cystectomy by a trained urologist can be a better choice in PAS cases.[19]

This study highlighted the major outcomes of placenta previa with placenta accreta spectrum as difficult and life-threatening delivery which escalates morbidity and mortality in mother and the baby. Pre-term labor, loss of fertility, low birth weight, admission to neonatal intensive care unit are some of the major outcomes of placenta previa with PAS requiring critical care management.[20]

The PAS care bundle comprised of consultant obstetrician, anaesthesiologist, neonataologist, vascular surgeon, urologist, haematologist and well equipped blood bank. Due to limited resources we have omitted interventional radiology from this care bundle.

CONCLUSION

Placenta previa in addition to placenta accreta requires standardized management by a multidisciplinary team in a tertiary care hospital. Higher incidence of caesarean sections and placenta previa increases the chances of placenta accreta spectrum disorder.

Author's Contribution:

Concept & Design of Study:	Amna Kazi
Drafting:	Jamshed Rahim, Nadir Hussain
Data Analysis:	Sana Danish, M. Ikram, Sara Munir
Revisiting Critically:	Amna Kazi, Jamshed Rahim
Final Approval of version:	Amna Kazi

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Jauniaux E, Collins S, Burton GJ. Placenta accreta spectrum: pathophysiology and evidence-based anatomy for prenatal ultrasound imaging. Am J Obstet Gynecol 2018;218(1):75-87.
2. Chantraine F, Braun T, Gonser M, Henrich W, Tutschek B. Prenatal diagnosis of abnormally invasive placenta reduces maternal peripartum hemorrhage and morbidity. Acta Obstetricia et Gynecologica Scandinavica 2013;92(4):439-44.
3. Jauniaux E, Chantraine F, Silver RM, Langhoff-Roos J. FIGO consensus guidelines on placenta accreta spectrum disorders: epidemiology. Int J Gynecol Obstet 2018;140(3):265-73.
4. Morlando M, Collins S. Placenta accreta spectrum disorders: challenges, risks, and management strategies. Int J Womens Health 2020;12:1033-45.
5. Shamshirsaz AA, Fox KA, Salmanian B, Diaz-Arrastia CR, Lee W, Baker BW, et al. Maternal morbidity in patients with morbidly adherent placenta treated with and without a standardized multidisciplinary approach.Am J Obstet Gynecol 2015; 212(2):218.e1-9.
6. Badr DA, Al Hassan J, Salem Wehbe G, Ramadan MK. Placenta - uterine body placenta accreta spectrum: a detailed literature review 2020;95:44-52.
7. Cheng KK, Lee MM. Rising incidence of morbidly adherent placenta and its association with previous caesarean section: a 15-year analysis in a tertiary hospital in Hong Kong. Hong Kong Med J 2015; 21(6): 511–7.
8. Modest AM, Toth TL, Johnson KM, Shainker SA. Placenta accreta spectrum: in vitro fertilization and non-in vitro fertilization and placenta accreta spectrum in a Massachusetts Cohort. Am J Perinatol 2020;5:s-0040-1713887.
9. Salmanian B, Fox KA, Arian SE, et al. In vitro fertilization as an independent risk factor for placenta accreta spectrum. Am J Obstet Gynecol 2020;11: 293-9.
10. Silver RM, Landon MB, Rouse DJ, et al. Maternal morbidity associated with multiple repeat cesarean deliveries. Obstet Gynecol 2006;107(6):1226-32.
11. Thurn L, Lindqvist PG, Jakobsson M, et al. Abnormally invasive placenta-prevalence, risk factors and antenatal suspicion: results from a large population-based pregnancy cohort study in the Nordic countries. BJOG 2016; 123(8):1348-55.
12. Reddy UM, Abuhamad AZ, Levine D, Saade GR; Fetal imaging workshop invited participants. fetal

imaging: executive summary of a joint Eunice Kennedy Shriver National Institute of Child Health and Human Development, Society for Maternal-Fetal Medicine, American Institute of Ultrasound in Medicine, American College of Obstetricians and Gynecologists, American College of Radiology, Society for Pediatric Radiology, and Society of Radiologists in Ultrasound Fetal Imaging Workshop. J Ultrasound Med 2014; 33: 745–57.

13. Collins SL, Ashcroft A, Braun T, Calda P, Langhoff-Ross J, Morel O Stefanovic V, et al. European Working Group on Abnormally Invasive Placenta (EW-AIP). Proposed for standardized ultrasound descriptions of abnormally invasive placenta (AIP). Ultrasound Obstet Gynecol 2016; 47: 271-5.
14. Nicolaides KH, Wright D, Syngelaki A, Wright A, Akolekar R. Fetal medicine foundation fetal and neonatal population weight charts. Ultrasound Obstet Gynecol 2018; 52: 44-51.
15. Wright J, Pri-Paz S, Herzog T, Shah M, Bonanno C, Lewin S, et al. Predictors of massive blood loss in women with placenta accreta. Obstetric Anesthesia Digest 2012;32: 115.
16. Snegovskikh D, Clebone A, Norwitz E. Anesthetic management of patients with placenta accreta and resuscitation strategies for associated massive hemorrhage. Curr Opinion Anaesthesiol 2011;24:274-81.
17. Tjokroprawiro BA. Caesarean hysterectomy in a patient with placenta accreta spectrum disorders. BMJ Case Reports 2021;14: e242044.
18. Eller AG, Bennett MA, Sharshiner M, et al. Maternal morbidity in cases of placenta accreta managed by a multidisciplinary care team compared with standard obstetric care. Obstet Gynecol 2011; 117: 331-7.
19. Shepherd AM, Mahdy H. Placenta accreta. Stat Pearls 2021.
20. Farquhar CM, Li Z, Lensen S, et al. Incidence, risk factors and perinatal outcomes for placenta accreta in Australia and NewZealand: a case control study. BMJ Open 2017;7: e017713.

Original Article

Effect on Mobility and Pain with Collagen Peptides in Knee Osteoarthritis in Pakistani Population

Mehwish Mansoor[1], Muhammad Ali Zubair[1], Shabih Zehra[3], Muhammad Sajid Abbas Jaffri[2], Hina Amjad[1] and Syed Ijaz Hussain Zaidi[1]

ABSTRACT

Objective: To evaluate the effects on mobility and pain with the use of collagen active peptides in knee osteoarthritis patients in Pakistani Population.

Study Design: It is an open label randomized clinical trial study.

Place and Duration of Study: This study was conducted at the Tertiary Care Hospital, Karachi from Sep, 2020 to March, 2021 for a period of six months.

Materials and Methods: One hundred and ten patients were scheduled in the study suffering from knee osteoarthritis. They were divided into three groups; Group I Diacerein (n=37), Group II Collagen active peptides (n=37) and Group III NSAID's (Diclofenac Potassium) (n=36).

Results: One hundred and two patients successfully completed the study with collagen active peptides improving the intensity of pain (VAS) visual analogue score at 6th and 12th weeks ($p > 0.001$) with highly significant results.

Conclusion: Collagen active peptides not only reduces pain and associated joint stiffness with OA but also enhances the functional mobility hence the quality of life improved with the use of collagen active peptides.

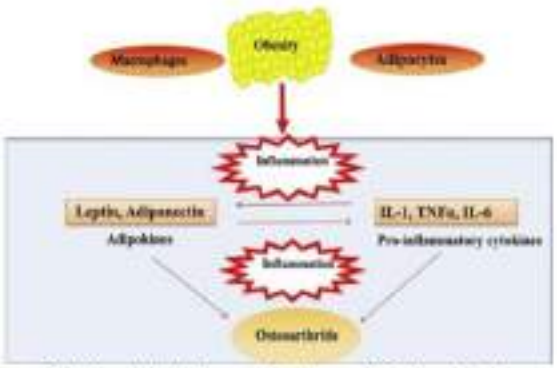
Key Words: Collagen active peptides, mobility, visual analogue score

Citation of article: Mansoor M, Zubair MA, Zehra S, Jaffri MSA, Amjad H, Zaidi SIH. Effect on Mobility and pain with Collagen Peptides in Knee Osteoarthritis in Pakistani Population. Med Forum 2021;32(10):103-107.

INTRODUCTION

Osteoarthritis is described as the slow progressing and degenerative inflammatory disorder of the synovial joints where there is gradual loss of the articular cartilage. It is most commonly found in patients who are above the age of 40 years. Among the various factors involved in disability osteoarthritis stands at the 11th highest number[1]. It can also be considered as a syndrome because it involves various targeted tissues in different areas therefore it becomes quite a challenge to manage patients of OA with a single drug therapy. The incidence of osteoarthritis is approximately 1 in 10 people. It is more common in young males who are less than 45 years of age and more common in older females who are above the age of 45 years. The prevalence of osteoarthritis has been generally observed tobe common in ages between thirty and sixty –five which is approximately 33.6%. In addition to the advancement in age, obesity is another major risk factor associated with osteoarthritis.[2]

Obesity is one of the most contributing and important factor for this disease. In addition to leading a high prevalence of OA in non-weight bearing areas, obesity also increases the mechanical stress on the cartilage of tibia and femur bone.



Relationship between obesity and Osteoarthritis

The relationship between inflammation and increase in weight is evident. Adipose tissues are a source of adipokines which are the metabolically-active mediators including leptin and adiponectin, chemokines and cytokines including interleukin 1- beta and IL-6. Adipokines are known to regulate the immune responses in the cartilage while the regulatory mechanism of cytokines promote lipolysis, modulate

1. Department of Pharmacology / Medicine[2], Bahria University Medical & Dental College, Karachi.
3. Department of Radiology, Al Tibri Medical College & Hospital, Karachi.

Correspondence: Dr. Mehwish Mansoor, Senior Lecturer Pharmacology, Bahria University Medical & Dental College, Karachi
Contact No: 03342988957
Email: mehwish_mansoor@hotmail.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

proliferation and apoptosis of fat cells and inhibit the synthesis of lipids. There-fore an increase in the inflammation in OA is related to the environment of low grade systemic inflammation created by the obesity/adiposity.[3]

Despite there being no cure for the disease the main focus during the management is the reduction of pain and improvement in the physical and functional mobility of the joints.

MATERIALS AND METHODS

This prospective study is a part of an ongoing randomized open prospective clinical trial for MPhil research work. After approval (FRC/BUMDC/ Phar/120) from Faculty Research Committee & Ethical Review Committee (ERC 64/2021) dated: 14.01.2021, of Bahria Univerisity of Medical & Dental College (BUMDC), the study was conducted at National Medical Centre, Karachi from September 2020 to March 2021. It included 110 patients suffering from Knee Osteoarthritis. After a well- written informed consent data collection was started. Basic biophysical parameters were recorded of all the patients. Lab investigations were done before and at the end of the treatment. The parameters were recorded before, at 6th week and at 12th weeks. The patients were divided into 3 groups each consuming capsule Diacerein, Collagen (sachet powder) and NSAID's.

Inclusion Criteria:

Patients who met the following criteria were included in the study:

1. Males and females $\geq$ 40 years of age.
2. Diagnosed cases of knee osteoarthritis on radiological images of the knee.
3. OA patients willing to participate in the study.
4. Patients with co-morbidities.
5. BMI < 30
6. Clinical and X-ray findings according to the criteria of ACR for OA.

Exclusion Criteria:

Patients who had the following features were excluded in the study:

1. Known history of hypersensitivity to patients to the study drugs.
2. Pregnant women.
3. Lactating mothers.
4. Concurrent inflammatory disease such as Rheumatoid arthritis.
5. Overweight BMI (body mass index) > 30.
6. Women on hormonal replacement therapy.
7. Terminal illness.
8. Patients having connective tissue disorders

The drugs included in the study are:

1. Capsule, Diacerein- 50mg (Group I) orally twice daily
2. Bioactive Peptides- Collagen active peptide 10g powder sachet (Group II) orally twice daily
3. NSAID's - (Diclofenac potassium) 50mg (Group III) orally twice daily

A subject evaluation performa was made and filled for each patient that included patient's personal bio-data including patient's identity, age, weight, height, gender, co-morbids, side of knee involvement, duration of pain etc.

RESULTS

Biophysical parameters are shown in Table I. The effects of mobility are shown in Table 2. The effects of pain (VAS at rest and movement) are shown in Table 3.

Table No.1: Bio physical Parameters in the study patients (n = 110)

Variable	Group I Mean ± SD	Group II Mean ± SD	Group III Mean ± SD	p-value
Age (years)	50.94±13.14	51.0±11.93	54.69±7.01	0.259^{ns}
Weight (kg)	84.83±18.84	78.55±15.36	74.94±11.99	0.029*
Height (m)	152.36±5.91	153.11±7.59	158.72±7.53	<0.001**
BMI	37.11±7.41	34.97±9.50	29.28±3.60	<0.001**

Variable		Group I n(%)	Group II n(%)	Group III n(%)	p-value
Gender	Male	9(25.0%)	4(11.1%)	13(36.1%)	0.045*
	Female	27(75.0%)	32(88.9%)	23(63.9%)	0.045*
Type of Knee	Right	11(30.6%)	22(61.1%)	4(11.1%)	<0.001**
	Left	7(19.4%)	5(13.9%)	0(0.0%)	<0.001**
	Both	18(50.0%)	9(25.0%)	32(88.9%)	<0.001**

Table No.2: Effects of mobility in the study patients

Variable		Group I n(%)	Group II n(%)	Group III - n(%)	p-value
Mobility Walking	Yes	31(86.1%)	34(94.4%)	31(86.1%)	0.430 ^{ns}
	No	5(13.9%)	2(5.6%)	5(13.9%)	
Mobility Bending	Yes	32(88.9%)	29(80.6%)	24(66.7%)	0.067 ^{ns}
	No	4(11.1%)	7(19.4%)	12(33.3%)	
Mobility Kneeling	Yes	15(41.7%)	6(16.7%)	19(52.8%)	0.005*
	No	21(58.3%)	30(83.3%)	17(47.2%)	
Mobility	Yes	11(30.6%)	3(8.3%)	7(19.4%)	0.059*

Housecleaning	No	25(69.4%)	33(91.7%)	29(80.6%)	
Mobility Getting In or out of bed	Yes	24(66.7%)	31(86.1%)	32(88.9%)	0.034*
	No	12(33.3%)	5(13.9%)	4(11.1%)	
Mobility Standing up from a Chair	Yes	28(77.8%)	26(72.2%)	32(88.9%)	0.202 ns
	No	8(22.2%)	10(27.8%)	4(11.1%)	
Mobility Lifting	Yes	10(27.8%)	3(8.3%)	34(94.4%)	<0.001**
	No	26(72.2%)	33(91.7%)	2(5.6%)	
Mobility Crepitus	Yes	22(61.1%)	25(69.4%)	11(30.6%)	0.002*
	No	14(38.9%)	11(30.6%)	25(69.4%)	

Table No.3: Effects of pain in the study patients

Day 0

Comparison of Visual Analogue Scale (VAS) in Groups I, II and III Pain at Rest

Variable		Group I n(%)	Group II n(%)	Group III n(%)	p-value
Pain on Visual Analogue Scale	Moderate	16(44.4 %)	14(38.9%)	18(50.0%)	0.638 ns
	Severe	20(55.6 %)	22(61.1%)	1(50.0%)	

Week 6th

Comparison of Visual Analogue Scale (VAS) in Groups I, II and III Pain at Movement

Variable		Group I n(%)	Group II n(%)	Group III n(%)	p-value
Pain at 6th Week	Slight Relief	29(80.6%)	10(27.8%)	27(75.0%)	<0.001**
	Complete Relief	7(19.4%)	23(63.9%)	1(2.8%)	
	No Relief	0(0.0%)	3(8.3%)	8(22.2%)	

Week 12th

Comparison of Visual Analogue Scale (VAS) in Groups I, II and III Pain at Movement

Variable		Group I n(%)	Group II n(%)	Group III n(%)	p-value
Pain at 12th Week	Slight Relief	19(52.8%)	11(30.6%)	19(52.8%)	<0.001**
	Complete Relief	14(38.9%)	20(55.6%)	5(13.9%)	
	No Relief	3(8.3%)	5(13.9%)	12(33.3%)	

DISCUSSION

This study was conducted on 110 patients of knee osteoarthritis who were equal to or above the age of 40 years having primary (idiopathic) osteoarthritis. Idiopathic (primary) osteoarthritis is the most common type of arthritis especially in elderly people. This has been shown in a study conducted in Austria where people having age more or equal to 40 years suffered from knee OA[4,5]. In our study 74.5% of the participants were females as compared to 23.6% males. A Japanese study showed similar results where prevalence of knee OA was more in females (62.4%) than males (42%)[6-10]. Another study conducted in Korea also showed knee OA prevalence to be 28.5% in the female population above 40 years of age. The prevalence being more frequent in females is still unknown.[11] A European study by Turkiewicz et al also reported a prevalence of 25.1% frequent knee pain in females[12].

A double blinded randomized trial was carried out on 218 patients. The participants were assigned to CP-group and Placebo-group randomly. They were assessed using the visual analogue scale pre and post treatment. Specific collagen peptides supplementation of 5g daily intake led to a statistically significant reduction (P- value = 0.024) in knee pain compared to placebo group. These findings were however consistent with the evaluation of the physician (P- value = 0.003)[13-16].

Another similar double blinded randomized trial was conducted in Germany on 139 knee OA patients, with the objective to evaluate the use of specific collagen peptides in reducing pain in athletes with functional knee problems. The patients were randomized to CP and placebo groups. Individual having functional knee pain ingested 5g of collagen peptides supplementation or placebo for about 12 weeks. The physicians then evaluated the primary outcome of the study which was a change in the intensity of pain during activity using visual analogue scale (VAS) before and after the end of the study. No statistically significant group differences could be detected (p = 0.253) at baseline. A marked statistically significant improvement was observed in the individuals taking supplementation of CP compared to placebo (P –value = 0.021) [17].

Another similar study was conducted on patients with functional knee pain where the primary end points were pain during movement(walking) and pain at rest. The intake of BCP showed good results of 38% and 39% improvement respectively. The parameters including joint stiffness, joint pain, movement restriction was however more pronounced in the BCP group compared to placebo group. A statistically significant improvement ($p < 0.05$) after a 12-week BCP supplementation was observed specifically in pain after physical stress(movement-

related) and pain and movement restriction when kneeling or crouching down. These results were hence in accord with our study.[18]

A prospective, multi-centric clinical trial was conducted on 226 patients in India to

Assess the effectiveness of collagen active peptides. The signs and symptoms were assessed for VAS at day 30, day 60 and day 90. Statistically significant reductions were observed in VAS scores at day 90 with P value <0.0001 thus suggesting the effectiveness of collagen active peptides. Hence, it can be concluded that collagen active peptides not only help in reducing pain and associated joint stiffness with OA but also helps in enhancing the functional mobility in patients suffering from knee OA. The results are in accord with our study[7].

A multicenter clinical trial was conducted in 78 patients in Spain to evaluate the effectiveness of dietary supplement containing hydrolyzed collagen in pain reduction and functional capacity in OA patients. The participants consumed the supplementation for 6 months where the primary outcome was measured using the VAS for pain reduction and functional mobility was assessed using the WOMAC score. Patients showed a statistically significant reduction in pain after 3 (1st follow up visit) and 6 (2nd follow up visit) months (P value< 0.0001). In adition marked significant score reduction was observed in physical function after 6 months ((P value< 0.0001).[19].

CONCLUSION

1. Collagen active peptides is clinically effective in management of knee osteoarthritis.
2. Collagen active peptides has better outcome in knee OA in terms of safety profile.
3. The quality of life improved with the use of collagen active peptides.

Recommendations:

1. Multicentre study
2. Using probability sample technique
3. Duration of the study should be 12 months or more
4. Use MRI for diagnosis of knee OA
5. OA without co-morbidities should be included

Author's Contribution:

Concept & Design of Study:	Mehwish Mansoor
Drafting:	Muhammad Ali Zubair, Shabih Zehra
Data Analysis:	Muhammad Sajid Abbas Jaffri, Hina Amjad, Syed Ijaz Hussain Zaidi
Revisiting Critically:	Mehwish Mansoor, Muhammad Ali Zubair
Final Approval of version:	Mehwish Mansoor

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Aae TF, Randsborg PH, Breen AB, Visnes H, Vindfeld S, Sivertsen EA, et al. Norwegican Cartilage Project-a study protocol for a double-blinded randomized controlled trial comparing arthroscopic microfracture with arthroscopic debridement in focal cartilage defects in the knee. BMC Musculoskeletal Disorders 2016;17(1):1-8.
2. Lianzhi Chen Jessica Jun Yi Zheng, et al, Pathogenesis and clinical management of obesity-related kneeosteoarthritis: Impact of mechanical loading. J Orthopaedic Translation 2020;24.
3. Wang T, He C. Pro-inflammatory cytokines: the link between obesity and osteoarthritis, Cytokine and Growth Factor Reviews 2018.
4. Clifford T, Ventress M, Allerton DM, Stansfield S, Tang JC, Fraser WD, et al. The effects of collagen peptides on muscle damage, inflammation and bone turnover following exercise: a randomized, controlled trial. Amino Acids 2019;51(4):691-704.
5. Culvenor AG, Øiestad BE, Hart HF, Stefanik JJ, Guermazi A, Crossley KM. Prevalence of knee osteoarthritis features on magnetic resonance imaging in asymptomatic uninjured adults: a systematic review and meta-analysis. Br J Sports Med 2019;53(20):1268-78.
6. Dar QA, Schott EM, Catheline SE, Maynard RD, Liu Z, Kamal F, et al. Daily oral consumption of hydrolyzed type 1 collagen is chondroprotective and anti-inflammatory in murine posttraumatic osteoarthritis. PloS One 2017;12(4):e0174705.
7. Mehra A, Anand P, Borate M, Pal P, Kamble S, Dev Mehta K, et al. A non-interventional, prospective, multicentric real life Indian study to assess safety and effectiveness of un-denatured type 2 collagen in management of osteoarthritis. Int J Res Orthop 2019;5(2):315.
8. Oesser S, Schulze CH, Zdzieblik D, König D. Efficacy of specific bioactive collagen peptides in the treatment of joint pain. Osteoarthritis and Cartilage 2016;24:S189..
9. Pelletier JP, Raynauld JP, Beaulieu AD, Bessette L, Morin F, de Brum-Fernandes AJ, et al. Martel-Pelletier J. Chondroitin sulfate efficacy versus celecoxib on knee osteoarthritis structural changes using magnetic resonance imaging: a 2-year multicentre exploratory study. Arthritis Research Therapy 2016;18(1):1-2.
10. Sasaki E, Ota S, Chiba D, Kimura Y, Sasaki S, Yamamoto Y, et al. Early knee osteoarthritis prevalence is highest among middle-aged adult females with obesity based on new set of diagnostic criteria from a large sample cohort study in the Japanese general population. Knee Surgery, Sports Traumatology, Arthroscopy 2020;28(3):984-94.

11. Schadow S, Siebert HC, Lochnit G, Kordelle J, Rickert M, Steinmeyer J. Collagen metabolism of human osteoarthritic articular cartilage as modulated by bovine collagen hydrolysates. PLoS One 2013;8(1):e53955.
12. Turkiewicz A, Gerhardsson de Verdier M, Engström G, Nilsson PM, Mellström C, Lohmander LS, et al. Prevalence of knee pain and knee OA in southern Sweden and the proportion that seeks medical care. Rheumatol 2015;54(5):827-35.
13. Verkleij SP, Luijsterburg PA, Koes BW, Bohnen AM, Bierma-Zeinstra SM. Effectiveness of diclofenac versus acetaminophen in primary care patients with knee osteoarthritis:[NTR1485], DIPA-trial: design of a randomized clinical trial. BMC Musculoskeletal Disorders 2010;11(1):1-6.
14. Wang L, Wang Q, Liang Q, He Y, Wang Z, He S, et al. Determination of bioavailability and identification of collagen peptide in blood after oral ingestion of gelatin. J Sci Food Agri 2015;95(13):2712-7.
15. Woo T, Lau L, Cheng N, Chan P, Tan K, Gardner A. Efficacy of oral collagen in joint pain-osteoarthritis and rheumatoid arthritis. J Arthritis 2017;6(2):1-4.
16. Zdzieblik D, Brame J, Oesser S, Gollhofer A, König D. The Influence of Specific Bioactive Collagen Peptides on Knee Joint Discomfort in Young Physically Active Adults: A Randomized Controlled Trial. Nutrients 2021;13(2):523.
17. Zdzieblik D, Oesser S, Gollhofer A, König D. Improvement of activity-related knee joint discomfort following supplementation of specific collagen peptides. Applied Physiology, Nutrition, and Metabolism 2017;42(6):588-95.
18. Alkhawajah, H.A., Alshami, A.M. The effect of mobilization with movement on pain and function in patients with knee osteoarthritis: a randomized double-blind controlled trial. BMC Musculoskelet Disord 2019;20:452.
19. Puigdellivol J, Comellas Berenger C, et al. Effectiveness of a Dietary Supplement Containing Hydrolyzed Collagen, Chondroitin Sulfate, and Glucosamine in Pain Reduction and Functional Capacity in Osteoarthritis Patients. J Diet Suppl 2019;16(4):379-389.

Original Article

Comparison of Severity of COVID-19 Symptoms Between Vaccinated and Unvaccinated Dental Faculty in Lahore

Nasrullah Khan[1], Muhammad Behzad Salahuddin[2], Ehsan Rathore[4], Omair Anjum[5], Waleed Javaid Toosy[3] and Rubbab Zahra[1]

ABSTRACT

Objective: This study aimed to find the differences in severity of COVID-19 symptoms among vaccinated and unvaccinated dental faculty members serving different dental colleges in Lahore.

Study Design: Retrospective Exploratory Cohort study

Place and Duration of Study: This study was conducted at the Avicenna Dental College, Lahore for a period of 2 months from August, 2021 to September, 2021.

Materials and Methods: This study identified 207 COVID-19 affected dental faculty/dentists in Lahore and retrospectively observed the severity of symptoms that included Fever, Cough, Fatigue, shortness of breath. The study divided the participants in two strata namely vaccinated and unvaccinated and statistically ran bivariate analysis on severity of COVID-19 symptoms.

Results: Mean duration among 40 vaccinated dentists between completion of 2 doses and contraction of COVID-19 was 58 days (SD ±6.3). Bivariate analysis between severity of symptoms among vaccinated and unvaccinated dentists showed that the mild and severe cough were significantly (p=0.04) reduced among vaccinated participants. Episodes of dyspnea were significantly (p=0.01) less observed among vaccinated dentists.

Conclusion: Even with the emergence of COVID-19 vaccine breakthrough, vaccine turns out to be protective against severity of symptoms and hence, hospitalization is reduced.

Key Words: COVID-19, COVID-19 Vaccine, Symptoms of COVID-19, Dyspnea in COVID-19, Cough in COVID-19

Citation of article: Khan N, Salahuddin MB, Rathore E, Anjum O, Toosy WJ, Zahra R. Comparison of Severity of COVID-19 symptoms between Vaccinated and Unvaccinated Dental Faculty in Lahore. Med Forum 2021;32(10):108-111.

INTRODUCTION

Covid-19 Pandemic started off from Capital city of Hubei Province of China, Wuhan. It is caused by a species of virus named "severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)". This disease spread swiftly through airborne transmission and spread swiftly internationally.

1. Department of Oral Medicine / Pathology[2] / Prosthodontics[3], Avicenna Dental College, Lahore.
4. Department of Oral Medicine, Faryal Dental College, Lahore.
5. Department of Sciences of Dental Materials, Lahore Medical and Dental College, Lahore.

Correspondence: Dr. Nasrullah Khan, Assistant Professor, Oral Medicine, Avicenna Dental College, Lahore.
Contact No: 0321-9497413
Email: khan_nassar@yahoo.com

Received: September, 2021
Accepted: October, 2021
Printed: October, 2021

In response to COVID-19 outbreak spreading across all regions of earth, WHO announced Global Health Emergency and advised preventive measures to be taken against Viral transmission. Subsequently, development of COVID-19 started and leading pharmaceutical companies began production of vaccine by August, 2020[1]. Another possibility to develop protection against COVID-19 in the population was through herd immunity, which is a natural immunity in a population to resist the transmission of infection[2]. However, this herd immunity failed to give protection to the population in Sweden where 60% of the population was infected with COVID-19. Mortality rate in Sweden was recorded to be 5 times to that of Germany, with devastating disease burden[3]. Hence, achievement of herd immunity was crucially linked to development of vaccine. Mass vaccination programs in the world started with multiple types of vaccine developed with specific pharmaceutical manufacturers including Pfizer and BioNTech and Moderna[4]. Pakistan began its COVID-19 vaccination program in February 2021 with first phase targeted for vaccination of health care workers working as front-liners in battling the pandemic[5]. High acceptance level for COVID-19

vaccine was observed among health care workers in Pakistan. Dentists and dental faculty members working in various dental institutes in Pakistan got vaccinated in early phases of vaccination. With passage of time vaccine breakthrough cases started emerging among dentists[6]. The next possible protective factor of COVID-19 vaccines might be less severity of symptoms[7]. Although studies have shown that vaccine breakthrough in COVID-19 is linked to mutation and emergence of variation in SARS-CoV-2 virus[8], the efficacy of vaccine in protection against hospitalization in COVID-19 infected individuals is also observed[9]. The severity of symptoms of COVID-19 is also stratified into mild, moderate, severe and critical[10]. This study aimed to draw a comparison in severity of symptoms among vaccinated and unvaccinated dental faculty members in Lahore.

MATERIALS AND METHODS

Primary data collection from COVID-19 infected dentists (n=207) from Lahore began with the aim to assess the symptoms of loss of smell and taste. However, it was observed that a considerable number of dentists were already fully vaccinated before contraction of COVID-19. This development led to the conception of this research and the dentists including dental faculty members involved in teaching and dental practice, were contacted with inclusion of a series of new questions about other COVID-19 symptoms in this retrospective study. This study only included the affected patients with confirmed PCR reports of COVID-19 from reliable laboratories of Pakistan. Over a period of one month, data was collected from 207 participants working in different recognized dental institutes in Lahore. We looked into the chronological contraction of COVID-19 with vaccination and its correlation with severity of symptoms among the participants. They were first inquired about the nature of the first appearing symptom. Assessment of severity of symptoms was carried out using different criteria, for example, severity of fever was assessed by low grade fever, high grade fever and/or being asymptomatic. Cough was assessed by categorizing it into mild, moderate and severe. The oxygen saturation monitoring was also inquired for its episodes of going below 94%, remaining constantly above 94%. Other frequent symptoms of COVID-19 including dyspnea and fatigue were investigated among vaccinated and unvaccinated patients retrospectively. The investigators also looked into the comparison of chest radiographs of the patients who at some point of infection, got them done.

Data Analysis: To analyze the obtained data, we used standard descriptive statistics. Continuous variables (Age at the contraction of COVID-19) were statistically expressed in mean while categorical variables were statistically expressed in proportions or percentages. The comparisons of symptoms in two groups i.e. vaccinated and non-vaccinated, were statistically analyzed using Pearson's Chi-Squared test and P value of less than 0.05 was considered to be of standard significance.

RESULTS

From August, 2021 to September, 2021, the data on severity of symptoms was collected from 207 dentists/dental faculty members from various colleges of Lahore who recovered from COVID-19. Collection of data was done by two methods i.e. Face-to-face questionnaire and via phone. Off 207 dentists, 119 (57.48%) were female and 88 (42.51%) were male. From the survey of individuals taking part, it was observed that mean age at which participants contracted COVID-19 infection was a little above 36 years (SD ±2.1). By categorizing the age into 5 categories of 20-30 years, 31-40 years, 41-50 Years, 51-60 years, 61 and Above, this research observed that most the dentists falling in the category of 31-40 years contracted the virus (n=98) while 61 years and Above age category showed only 1 dentist working as General Dental Practitioner.

Table No.1: Patients' Demographics

Patients' Demographics (N=207)		
Gender (N=207)		
	Male	88 (52.51%)
	Female	119 (57.48%)
Age (N=207)		
	Mean Age at the Contraction of Covid-19	36.2 Years (SD ±2.1)
	20-30 Years	58 (28%)
	31-40 Years	98 (47.34%)
	41-50 Years	39 (18.84%)
	51-60 Years	11 (5.31%)
	61 Years & Above	1 (0.5%)
Time Passed Since Contraction of COVID-19 (N=207)		
	3 Months	34 (16.42%)
	4-6 Months	25 (12%)
	7-9 Months	59 (28.50%)
	10 Months & Above	89 (42.99%)
Average Duration between Full Vaccination and Contraction of COVID-19 (N=40)		
	58 Days (SD ±6.3)	

The researchers obtained the data on time duration between completion of 2 doses of vaccine and contraction of COVID-19. The mean duration among 40 vaccinated dentists was recorded to be 58 days (SD ±6.3). Bivariate analysis of severity of symptoms between vaccinated and non-vaccinated dentists was carried out and results are shown in table 2. Major and significant difference in appearance of 1st symptom was observed in Loss of smell and taste (p value=0.02). Mild and Severe Cough were observed to be significant

differences among vaccinated and non-vaccinated dental faculty members.

Table No.2: Bivariate analysis of Covariates (Severity of Symptoms of COVID-19) among Vaccinated and Non Vaccinated Dentists: Total Number: 207

Variables	Non Vaccinated	Vaccinated	P-Value
	N (%)	N (%)	(Pearson's Chi Squared Test)
Total 207	167	40	
Gender			
Male	70 (41.91%)	18 (45%)	0.89 (Non-Significant)
Female	97 (58.08%)	22 (55%)	
1st Symptom			
Fever	95 (56.88%)	15 (37.50%)	0.32 (Non-Significant)
Sore Throat & Cough	39 (23.35%)	25 (62.50%)	0.96 (Non-Significant)
Loss of Smell & Taste	33 (19.76%)	0	0.02 (Significant)
Malaise & Fatigue	0	0	
Shortness of Breath	0	0	
Fever			
Low Grade Fever	95 (56.88%)	33 (82.50%)	0.25 (Non-Significant)
High Grade Fever	72 (43.11%)	7 (17.50%)	0.82 (Non-Significant)
No Fever	0	0	
Cough			
Mild	25 (14.97%)	`35(87.50%)	0.04 (Significant)
Moderate	88 (52.69%)	5 (12.50%)	0.77 (Non-Significant)
Severe	54 (32.33%)	0	0.04 (Significant)
Oxygen Saturation			
Going below 94%	45 (26.94%)	4 (10%)	0.70 (Non-Significant)
Constant above 94%	122 (73.05%)	36 (90%)	0.02 (Significant)
Episodes of Dyspnea (Shortness of Breath)			
Yes	23 (13.77%)	1 (2.50%)	0.01 (Significant)
No	144 (86.22%)	39 (97.50%)	0.01 (Significant)
Fatigue during/after COVID-19 infection			
Yes	122 (73.05%)	39 (97.50%)	0.10 (Non-Significant)
No	45 (26.94%)	1 (2.50%)	0.20 (Non-Significant)

Data obtained on episodes of dyspnea (shortness of breath) during COVID-19 infection that appeared to be significant. Among non-vaccinated, 23 (13.77%) experienced episodes of shortness of breath at least once during infection. However, among vaccinated, only 1 (2.50%) had an experience of shortness of breath. Severity of Fever and experience of fatigue during/after COVID-19 infection were observed to be non-significant in bivariate analysis.

DISCUSSION

COVID-19 is seen as novel disease with extensive on-going research and investigations to understand the disease. Clinical course of COVID-19 disease is also variable and renders different kind of symptoms with different severity levels[11]. Clinical progression of severe disease may lead to hospitalization and death eventually. The vaccination of COVID-19 is seen to be protective against the virus transmission. However, efficacy of vaccines available is not 100% leading to emerging cases of COVID-19 infection in vaccinated individuals. Our study too, identified such cases of vaccine breakthrough among COVID -19 patients just like previous studies on vaccine breakthrough[11]. A study conducted among vaccinated and COVID-19 positive patients showed that viral load was 2-4 times lower than that in unvaccinated individuals[12]. Another study done on nasal swabs of vaccinated and unvaccinated COVID-19 positive individuals showed that viral load of SARS-CoV-2 was 1.6-2 times lower on nasal swabs of vaccinated participants than those of unvaccinated individuals[13]. This may explain the significant differences of severity of cough in vaccinated and unvaccinated COVID-19 patients observed in our study. Non-significant statistical difference of gender in vaccinated and unvaccinated patients can also be affirmed by another study conducted by Candelli *et al*[14]. Scientific interpretation of differences in episodes of dyspnea among vaccinated and unvaccinated dentists may be explained by the decreased viral load. Three variables relating the most prevalent symptoms of COVID-19 i.e. fever, oxygen saturation and fatigue were not found to be significantly associated with vaccination. The plausible reason behind these non-significance differences may be because of relative young age of vaccinated dental faculty without any comorbidities[15, 16]. Delay in second dose in vaccinated individuals should be assessed in associated with levels of antibodies against COVID-19 via lab testing and its link to severity of symptoms should be determined as it was observed in some of the individuals with comorbidities[17]. Added values and strength of this study was its Cohort nature and comparison of symptoms with a control group (Unvaccinated COVI-19 patients). Limitations of this study included small data size that didn't include old aged individuals and memory bias as participants relied on the memory of past COVID-19 infection. Further work is needed to establish the association of serum levels of antibodies and SARS-CoV-2 viral load with

prospective exploration. However, this study could be replicated on a larger scale among general masses to lead to more promising results on differences in severity of symptoms of COVID-19 among vaccinated and non-vaccinated individuals.

CONCLUSION

Regardless of COVID-19 vaccine breakthrough cases, completion of COVID-19 vaccine is observed to be resulting in less severe symptoms of COVID-19. Assessment and monitoring of serum antibodies against COVID-19 after completion of vaccine doses should be recommended because COVID-19 is novel disease and its vaccines' efficacies in producing adequate protective levels might be affected by multiple variable.

Author's Contribution:

Concept & Design of Study:	Nasrullah Khan
Drafting:	Muhammad Behzad Salahuddin, Ehsan Rathore
Data Analysis:	Omair Anjum, Waleed Javaid Toosy, Rubbab Zahra
Revisiting Critically:	Nasrullah Khan, Muhammad Behzad Salahuddin
Final Approval of version:	Nasrullah Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Sharma O, Sultan AA, Ding H, Triggle CR. A Review of the Progress and Challenges of Developing a Vaccine for COVID-19. Frontiers in Immunol 2020;11:2413.
2. Randolph HE, Barreiro LB. Herd immunity: understanding COVID-19. Immunity 2020; 52(5):737-41.
3. Jung F, Krieger V, Hufert FT, Küpper JH. Herd immunity or suppression strategy to combat COVID-19. Clinical Hemorheol Microcirculation 2020;75(1):13-7.
4. Haynes BF. A new vaccine to battle Covid-19. New Eng J Med 2020.
5. Voa. Covid-19 pandemic [Internet]. VOA. COVID-19 Pandemic; 2021 [cited 2021Sep30]. Available from: https://www.voanews.com/z/6730
6. Siddiqui Qul Ain. Breakthrough infections and vaccine efficacy: Why are vaccinated people still getting the virus? DAWNCOM 2021. https://www.dawn.com/news/1642019 (accessed September 30, 2021).
7. Mehrotra DV, Janes HE, Fleming TR, Annunziato PW, Neuzil KM, Carpp LN, et al. Clinical endpoints for evaluating efficacy in COVID-19 vaccine trials. Annals Internal Med 2021;174(2):221-8.
8. Musser JM, Christensen PA, Olsen RJ, Long SW, Subedi S, Davis JJ, et al. Delta variants of SARS-CoV-2 cause significantly increased vaccine breakthrough COVID-19 cases in Houston, Texas. medRxiv 2021 Jan 1.
9. Roghani A. The Influence of Covid-19 Vaccine on Daily Cases, Hospitalization, and Death Rate in Tennessee: A Case Study in the United States. medRxiv 2021 Jan 1.
10. Verity R, Okell LC, Dorigatti I, Winskill P, Whittaker C, Imai N, Cuomo-Dannenburg G, Thompson H, Walker P, Fu H, Dighe A. Estimates of the severity of COVID-19 disease. MedRxiv 2020 Jan 1.
11. Thompson MG, Burgess JL, Naleway A, Tyner H, Yoon SK, Meece J, et al. Prevention and Attenuation of COVID-19 by BNT162b2 and mRNA-1273 Vaccines. medRxiv 2021 Jan 1.
12. Callaway E. Delta coronavirus variant: scientists brace for impact. Nature 2021;595(7865):17-18.
13. Levine-Tiefenbrun M, Yelin I, Katz R, Herzel E, Golan Z, Schreiber L, Wolf T, Nadler V, Ben-Tov A, Kuint J, Gazit S. Initial report of decreased SARS-CoV-2 viral load after inoculation with the BNT162b2 vaccine. Nature Med 2021;27(5):790-2.
14. Candelli M, Pignataro G, Torelli E, Gullì A, Nista EC, Petrucci M, et al. Effect of influenza vaccine on COVID-19 mortality: A retrospective study. Internal and Emergency Med 2021:1-7.
15. Felsenstein S, Hedrich CM. COVID-19 in children and young people. Lancet Rheumatol 2020; 2(9):e514-6.
16. Phelps M, Christensen DM, Gerds T, Fosbøl E, Torp-Pedersen C, Schou M, et al. Cardiovascular comorbidities as predictors for severe COVID-19 infection or death. European Heart J-Quality of Care Clin Outcomes 2021;7(2):172-80.
17. Chavarot N, Morel A, Leruez-Ville M, Villain E, Divard G, Burger C, et al. Weak antibody response to 3 doses of mRNA vaccine in kidney transplant recipients treated with belatacept. Am J Transplantation 2021.

Original Article

Right Ventricular MI in Inferior Wall MI

Frequency of Right Ventricular Myocardial Infarction in Patients with Presenting Acute Inferior Wall Myocardial Infarction in Local Population

Samiullah Khan[1], Naveed Danish[2], Muhammad Niaz Khan[4], Muhamad Kashif Iltaf[5], Sadullah Shah[1] and Raza Mohammad[3]

ABSTRACT

Objective: To determine the frequency of Right Ventricular Myocardial Infarction **(**RVMI) in patients with presenting with acute Inferior Wall Myocardial Infarction **(**IWMI).

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Cardiology, Coronary Care Unit (CCU) of DHQ Teaching Hospital (DHQ-TH) Nowshera and Qazi Hussain Ahmad Medical Complex (QHMC) Nowshera from Feb, 2017 to Sept, 2017 for a period of 08 months.

Materials and Methods: Patients with acute IWMI were selected for study from CCU under informed written consent. They were interviewed through a pre-designed research proforma.

Two sets of ECGs were performed one each for diagnosis of IWMI and other for RVMI. ECG was done through Fuduka-ME-C110-ECG machine at a standard setting. The ECGs were looked for ST segment elevation in leads II, III, aVF and V3R, V4R, V5R, and V6R for diagnosis of IWMI and RVMI, respectively. Results were analyzed using SPSS 16.

Results: Mean age was 64±8.97. Patients 30-50 years age group was 100 (38.46%) and in 51-70 years age group was 160 (61.53%). There were 141 (54.23%) male and 119 (45.76%) female patients. RVMI was observed in 24.23% (n, 63) patients. RVMI was significantly [p=0.014] more frequent 18.07% (n,47) in age group 31-70 years as compared to 6.15% (n, 16) age group 30-50 years. RVI was insignificantly more frequent in male [37, 14.2%] as compared to female [26, 10%, p=0.410] patients

Conclusion: RVMI is frequently observed in patients presenting with acute inferior wall myocardial infarction in local population.

Key Words: Revascularization, RVMI, IWMI

Citation of article: Khan S, Danish N, Khan MN, Iltaf MK, Shah S, Mohammad R. Frequency of Right Ventricular Myocardial Infarction in Patients with Presenting Acute Inferior Wall Myocardial Infarction in Local Population. Med Forum 2021;32(10):112-115.

INTRODUCTION

Ischemic heart disease is a common clinical entity and has a spectrum ranging from stable angina to unstable angina to Myocardial infarction (MI).[1]

[1.] Department of Cardiology, Nowshera Medical College / QHAMC Nowshera.
[2.] Department of Cardiology / Medicine[3], DHQ Hospital Nowshera.
[4.] Department of Cardiology, Hayatabad Medical Complex, Peshawar.
[5.] Department of Cardiology, Khyber Teaching Hospital, Peshawar.

Correspondence: Dr. Samiullah Khan, Assistant Professor of Cardiology, Bannu Medical College/DHQ-TH, Bannu.
Contact No: 03015151346
Email: drsamee@yahoo.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

Myocardial infarction is the necrosis of myocytes due to interruption of its blood supply[2]. It can be anterior, inferior, lateral or posterior depending upon the area and coronary artery involved.[3]

Worldwide about 15 million people suffered MI in 2015. More than 3 million people have ST elevated MI (STEMI) and 4 million people have non ST elevated MI. The incidence of STEMI is more common in man than women.[4]

Acute IWMI account for about 40% of all MI.[5] Twenty percent of patients with inferior ST elevated MI have significant bradycardia to second degree AV or third degree AV block.[6] The mortality rate of an inferior wall MI is less than 10%. However, several complicating factors that increase mortality, including right ventricular infarction, hypotension, bradycardia heart block, and associated cardiogenic shock.[7]

The prevalence of RVMI in Acute IWMI reported differently. Sawar et.al studied that the prevalence of RVMI is 21.6% in local population[8] while other reported the RVMI frequency of 34%[9] in patients with

acute IWMI. Eighty percent of inferior ST elevated MI is due to obstruction of dominant RCA while in 18% culprit artery is left circumflex.[10] The more proximal the right coronary is occluded the larger is RV infarction.[11]

The aim of study is to find frequency of RVMI in patient who present with acute inferior wall MI. As patients with RV infarction are prone to severe hypotension, leading to cardiogenic shock, therefore early diagnosis and management will help to overcome the complications and reduce morbidity and mortality.

Operational Definitions: Acute inferior wall MI:

Patients complaining of acute severe crushing, burning or constricting chest pain mostly radiating to left arm, lower jaw, back or upper abdomen and not relieved by rest or sublingual nitrates, evident by ST segment elevation in leads II, III and aVF.

RV Myocardial infarction:

RVMI is diagnosed on right sided chest leads ST segment elevation of ≥ 1 mm in any of the right sided chest leads V3R, V4R V5R or VR6 in symptomatic patients.

ST segment elevation on ECG:

ECG to be performed by "FUDUKA ME C110 ECG" machine at standard paper speed of 25mm/sec with 0.1 mV/mm, showing ST segment elevation at the j-point for more than 1mm in at least two inferior leads.

MATERIALS AND METHODS

This study was a hospital based descriptive cross sectional study. It was carried out from 1st February, 2017 to 1st September, 2017, at the Coronary Care Unit of DHQ-TH and QHMC Nowshera.

Sample size: Sample size was 260, using 21.6% frequency of RVIwith patients with acute inferior wall MI, 95% confidence interval and 5% margin of error using WHO sample calculator[8].

Sampling techniques: Non probability consecutive sampling

Sample Selection:

Inclusion criteria:

1. Both gender
2. Age 30 to 70 years
3. Typical chest pain of more than 20 minutes
4. ST segment elevation in lead II, III, aVF (any two leads).
5. ST segment elevation in V3R, V4R, V5R and/or V6R.

Exclusion criteria:

1. Previous MI.
2. ST elevation MI other than RV infarction and inferior wall MI.
3. Valvular heart disease.
4. Chronic heart failure.
5. Pulmonary embolism.
6. Chronic obstructive pulmonary diseases.
7. Idiopathic pulmonary hypertension.
8. Pericarditis and myocarditis.

Data Collection Procedure: The study was conducted after approval from the hospital ethical and research committee. All the patients presented with acute IWMI to cardiology department of DHQ-TH and QHMC Nowshera were enrolled in the study while strictly following inclusion and exclusion criteria. The purpose and benefits of the study were explained to the patients and a written informed consent be obtained. A detailed history was taken and physical examination was done. A proforma was filled showing demographics of the patients. Two sets of ECGs were performed one each for diagnosis of IWMIand other for RV infarction. ECG was done through Fuduka-ME-C110-ECG machine at a standard paper speed of 25mm/sec with 0.1 mV/mm. The ECGs were looked for diagnosis of IWMI and RV infarction in leads II, III, aVF for ST segment elevation and also ST segment elevation in V3R, V4R, V5R, V6R, respectively. Furthermore, the ECGs findings were verified by a team of consultant cardiologists.

Data Aanalysis: Data was analyzed using SPSS 16. Frequencies and percentages were calculated for categorical variables like gender, RV infarction. Mean ± standard deviation was calculated for numerical variables like age. RVMIwas stratified among age, gender to see effect modification. Post stratification chi square test was applied keeping p value less than 0.05 as significant.

RESULTS

A total of 260 patients satisfying the inclusion criteria, were enrolled in this study.

Mean age was 64±8.97. There were 38.46% (n, 100) patients in 30-50 years age group and 61.53% (n, 160) patients in 51-70 years age group. (Table No. 1). The male (n,141, 54.23%) to female (n, 119, 45.76%) ratio was 1:1.81. Frequency of RVMI was 24.23% (n, 63) patients in the present study (Table No. 2). RVMI was significantly [p=0.014] more frequent 18.07% (n, 47) in age group 31-70 years as compared to 6.15% (n, 16) age group 30-50 years (Table No. 3). RVMI was insignificantly [p=0.410] more frequent in male [37, 14.2%] as compared to female [26, 10%,] patients (Table No. 4).

Table No. 1: Frequencies and Percentages for Age (n=260)

Age Groups	Frequencies	Percentages
30-50 Years	100	38.46%
51-70 Years	160	61.53%
Total	260	100%

Table No. 2: Frequencies and Percentages for RVMI (n=260)

Right Ventricle Infarction	Frequencies	Percentages
Yes	63	24.23%
No	197	75.76%
Total	260	100%

Table No. 3: Stratification of RVMI within age group (n=260)

Age	RVI(RVI)	Frequencies	Percentages	P Value
30-50 Years	Yes	16	6.15%	0.014
	No	84	32.30%	
31-70 Years	Yes	47	18.07%	
	No	113	43.46%	

Table No. 4: Stratification of RVMI within gender (n=260)

Gender	RVI(RVI)	Frequencies	Percentages	P Value
Male	Yes	37	14.23%	0.410
	No	104	40%	
Female	Yes	26	105	
	No	93	35.76%	

DISCUSSION

In the present study we observed that majority of patients with Acute IWMI and RVMI were elderly. The mean age was 64±8.97 and the most frequent 160 (61.53%) patients age group was 51-70 years. This is in consistent with previous research[12] that that onset of this disease is mostly common in the older age. We found the male (141, 54.23%) to female (119, 45.76%) ratio about 1:1.2 Khan S has reported even more male (Male: Female, 1:1.9) with Acute Myocardial infarction in local population.[13]

Frequency of RVMI was 24.23% in patients with acute inferior wall myocardial infarction in the present study. There is variable frequency of RVMI in the literature review. Kumar et al reported RVMI 32.9 % of acute inferior wall MI.[7] Our hypothesis generating study[8] has shown 21.6% patients with RVMI in acute IWMI. Memon AG et.al studied that RVMI complicate 48.6% of patients with acute inferior wall MI.[14]

We determine the frequency of RVMI on the basis of elevated ST Segments in right precordial leads i.e. V4R (63, 24.23%). Masami K et al[11] showed ECG evidence of elevated ST Segments in V4R in diagnoses of RVMI as the most accurate, simple and easiest with an incidence of 30-50%. This supports our methods of detection and study outcome for the present study.

Similarly, In patients with IWMI the incidence of RVMI was found to be 30%, based on ECG evidence of ST-Segment elevation in V4R, in the study by Croft CH et al.[15] Recently electrocardiographic evidence of RVMI was proved by four diagnostic procedures i.e. autopsy, coronary angiography, technetium 99m and hemodynamic measurements.[16-18]

CONCLUSION

RVMI was frequently observed in patients with acute inferior wall myocardial infarction. It would be desirable to include right precordial leads specially V4R in the routine ECG in all patients with inferior wall Ml.

Author's Contribution:

Concept & Design of Study:	Samiullah Khan
Drafting:	Naveed Danish, Muhammad Niaz Khan
Data Analysis:	Muhammad Kashif Iltaf, Sadullah Shah, Raza Mohammad
Revisiting Critically:	Samiullah Khan, Naveed Danish
Final Approval of version:	Samiullah Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Sharma LN, Tripathy RK, Dandapat S. Multiscale energy and eigenspace approach to detection and localization of MI. IEEE Trans Biomed Eng Title 2015;62(7):1827-37.
2. Wartman WB, Hellerstein HK. The incidence of heart disease in 2,000 consecutive autopsies. Ann Intern Med 1948;28(1):41-65.
3. Thygesen K, Alpert JS, White HD, Jaffe AS, Apple FS, Galvani M, et al. Universal definition of MI: KristianThygesen, Joseph S. Alpert and Harvey D. White on behalf of the Joint ESC/ACCF/AHA/ WHF Task Force for the Redefinition of MI. Eur Heart J 2007;28(20):2525-38.
4. GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015 [published correction appears in Lancet 2017 Jan 7;389(10064): e1]. Lancet 2016;388(10053):1545-1602.
5. Aydin F, TurgayYildirim O, Dagtekin E, Huseyinoglu Aydin A, Aksit E. Acute Inferior Myocardial Infarction Caused by Lightning Strike. Prehosp Disaster Med 2018;33(6):658-659.
6. Lévy S. Bundle branch blocks and/or hemiblocks complicating acute myocardial ischemia or infarction. J Interv Card Electrophysiol 2018; 52(3):287-292.
7. Kumar V, Sinha S, Kumar P, Razi M, Verma CM, Thakur R, et al. Short-term outcome of acute IWMI with emphasis on conduction blocks: a prospective observational study in Indian population. Anatol J Cardiol: AKD 2017;17(3): 229.
8. Sawar S, Bais MN, Sattar Z, Khan S, Bais N. The prevalence of RV infarct in patients with inferior wall MI. KJMS 2016;9(1):19.
9. Khan S, Kundi A, Sharieff S. Prevalence of right ventricular myocardial infarction in patients with

acute inferior wall myocardial infarction. Int J Clin Pract 2004;58(4):354-7.

10. Balasubramanian K, Ramachandran B, Subramanian A, Balamurugesan K. Combined ST Elevation in a Case of Acute Myocardial Infarction: How to Identify the Infarct-related Artery? Int J Appl Basic Med Res 2018;8(3): 184-186.
11. Masami KA, Gnanavelu G, Subramaniam T, Dorairajan S, Chockalingam V. RV MI: presentation and acute outcomes. Angiol 2005; 56(4):371-6.
12. Roth GA, Johnson C, Abajobir A, Abd-Allah F, Abera SF, AbyuG,etal. Global, regional, and national burden of cardiovascular diseases for 10 causes, 1990 to 2015. J Am Coll Cardiol 2017; 70(1):1-25.
13. Khan S, Asghar Khan M, Khan MN, Shah I, Hassan M ul. Comparison of Risk Factors Profile in Patients Below and Above Forty Years of Age Presenting With Acute Myocardial Infarction. J Postgrad Med Inst 2013;27(4).
14. Memon AG, Shah MI, Devrajani BR, Baloch S. Incidence of RVIin patients with acute inferior wall infarction. J Postgraduate Med Ins (Peshawar-Pakistan) 2015:12;29(3).
15. Croft CH, Goodin J, Phelan B, Kopelman H, Virmani R. Electrocardiographic changes associated with isolated RV infarction. J Am Coll Cardiol 1984:4(3):640-3.
16. Garty I, Barzilay J, Bloch L, Antonelli D, Koltun B. The diagnosis and early complications of RV infarction. Eur J Nucl Med 1984. 9(10):453-60.
17. Giannitsis E, Potratz J, Wiegand U, Stierle U, Djonlagic H, Sheikhzadeh A. Impact of early accelerated dose tissue plasminogen activator on in-hospital patency of the infarcted vessel in patients with acute RV infarction. Heart 1997; 77(6):512-6.
18. Hirsowitz GS, Lakier JB, Goldstein S. RV function evaluated by radionuclide angiography in acute MI. Am Heart J 108(4 Pt 1): 949-54.

Original Article

Frequency of Access Recirculation in Hemodialysis Dependent Patients

Access Recirculation in Hemodialysis

Farman Ullah[1], Irfan Mirza[2], Mufti Baleegh-ur-Raheem Mahmood[1] and Ahmad Zeb Khan[1]

ABSTRACT

Objective: The aim of this study was to find out the health of vascular access in our patients focusing on vascular recirculation as a marker of vascular insufficiency.

Study Design: Descriptive cross-sectional study

Place and Duration of Study: This study was conducted at the department of Nephrology Khyber teaching hospital and Khyber medical college Peshawar for a period of six months from 1st January to 1st July 2020.

Materials and Methods: A total of 104 hemodialysis dependent patients of both genders and all ages were randomly selected, utilizing consecutive non-probability sampling technique. Patients on hemodialysis secondary to Acute Kidney Injury were excluded. Prior Approval of synopsis was obtained from the institutional research evaluation and ethical committee. Informed consent was obtained from each patient before data collection.

Results: A total of 104 patients were studied in this study, of which 53 (51.0%) were males. The Mean age of the group was 39.65 years (SD+-13.84). Mean duration of hemodialysis was 18.78 (SD+-12.93) months. Radio-cephalic AV fistula was the commonest access (45.19%) in this cohort, followed by Brachio-cephalic and Brachio-basilic fistulas. Overall, 46 (44.2%) patients were found to have access recirculation in this study which was statistically significant. The factors involved in access recirculation included inappropriate needle placement (n=51, 49%. p=0.001), Venous stenosis (n=5, 4.8%, p=0.015) and different types of AV fistulas.

Conclusion: This study shows that a high percentage of our patients have access recirculation during hemodialysis. Recirculation is significantly associated with inappropriate needle placement and venous stenosis.

Key Words: Dialysis, Hemodialysis, AV fistula, Dialysis catheter, Recirculation

Citation of article: Farman Ullah, Mirza I, Mahmood MB, Khan AZ. Frequency of Access Recirculation in Hemodialysis Dependent Patients. Med Forum 2021;32(10):116-120.

INTRODUCTION

End Stage Renal disease patients require some form of Renal Replacement Therapy (RRT). This involves either some form of dialysis or renal transplantation. Dialysis can be provided by two major modalities which are Hemodialysis and Peritoneal Dialysis. Hemodialysis is the most commonly employed modality of Renal Replacement Therapy[1].

Vascular access is required to establish a good blood supply to the hemodialysis machine, at an adequate flow rate, to achieve proper dialysis dose. These accesses are commonly in the form of double lumen catheters, arterio-venous fistulas and Polytetrafluoroethylene (PTFE) grafts[2].

Vascular access is the life line of hemodialysis dependent patient. Access related complications are the major cause of morbidity in hemodialysis dependent patients contributing to about 25% hospital admissions and up to 50% of hospitalization costs[3]. Access related problems can result in inadequate blood supply to the hemodialysis machine and thus can substantially reduce the efficiency of dialysis. In a study by SuatUnver, insufficiently functioning AV fistulas were associated with abnormalities of all the patient and dialysis adequacy parameters including serum albumin, hemoglobin, parathyroid hormone levels, and Calcium-Phosphate product[4]. It is proven that inadequate dialysis dose is strongly associated with increased morbidity and mortality of hemodialysis patients[5].

Considering the importance of a properly functioning vascular access for hemodialysis dependent patients, KDOQI guidelines recommend routine monitoring of vascular access for any signs of complications, inadequate functioning and impending failures[6].

Such a strategy can result in early identification of access dysfunction and early salvage in order to prevent the progression to overt access stenosis, thrombosis and

[1.] Department of Nephrology, Khyber Medical College and Khyber Teaching Hospital Peshawar.
[2.] Department of Nephrology, Rehman Medical Institute, Peshawar.

Correspondence: Ahmad Zeb Khan, Associate Professor, Nephrology, Khyber Medical College and Khyber Teaching Hospital, Peshawar.
Contact No: 0301-8575722
Email: ahmad.zeb@hotmail.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

ultimately failure. Monitoring of hemodialysis access includes measures such as clinical examination, sequential measurements of static and dynamic pressures, access flow rates (detected by Duplex Doppler ultrasound and Thermo-dilution method) and access recirculation measurements (detected by urea based method and ultrasound based thermo-dilution techniques)[6].

Access recirculation is one such measure that has been recommended to assess vascular access related problems. It occurs when the dialyzed and purified blood that exits the venous end of the circuit returns back directly into the arterial line and thus to the dialyzer inlet without ever circulating and equilibrating with the systemic circulation. This reduces the solute delivery to the dialyzer causing a reduction in the solute gradient across the dialyzer membrane which ultimately reduces the efficiency of dialysis[7]. A significantly high percentage of recirculation is a marker of problems with access inflow, fistula stenosis and access outflow as occurs in central venous stenosis[8].

There are two common methods of detection of access recirculation. The first involves Doppler ultrasound based Thermo-dilution technique. The second method is urea based techniques. In an Iranian study by JavadSalimi, 19.6% of dialysis dependent patients had significant access recirculation[7]. Akram et al attempted to study level of recirculation only in patients with Double lumen catheters in Pakistani population in Sheikh Zaid hospital Lahore. They found mean percentage of access recirculation to be about 10.3±6.6% (range from 3.6% to 24.8%) [9]In a study by Rafique et al the mean access recirculation of AV fistulas by urea based 2 needle method was found to be 9.55±6.64%[10]. In another study Anees et al found that Access recirculation was less than 10% in all of their patients[11].

Despite that the access recirculation measurement is now recommended by the guidelines to be performed on all hemodialysis dependent patients regularly, such a practice has not taken roots in our setup. So far only a handful studies on access recirculation have been done in Pakistan.

MATERIALS AND METHODS

This was a descriptive cross-sectional study, conducted over a period of six months, at the department of nephrology Khyber teaching hospital and Khyber medical college Peshawar, with the objective to determine the frequency of patients with significant access recirculation (>10% by urea method) among our maintenance hemodialysis patients.

A total of 104 hemodialysis dependent patients of both genders and all ages were randomly selected, utilizing consecutive non-probability sampling technique. Patients on hemodialysis secondary to Acute Kidney Injury were excluded. Prior Approval of synopsis was obtained from the institutional research evaluation and ethical committee. Informed consent was obtained from each patient before data collection.

After recording baseline biodata, Recirculation was calculated according to the standard technique. The sampling for urea based measurement of recirculation done by the 'two needle method' (all three samples taken from the dialysis circuit without giving extra prick to the patient). Considering the ease of sampling, no extra discomfort to the patient and common availability of laboratories for urea measurement, the two needle urea based technique is considered the most practical approach to determine the access recirculation. While using the urea based method a recirculation value of more than 10% is usually taken as significant and warrants further investigation.[7, 8]

Blood samples were collected 30 minutes after starting hemodialysis and after switching off Ultrafiltration (UF). The first two samples labeled arterial (A) and venous (V) were collected directly from the arterial and the venous limbs of the hemodialysis circuit. Then the blood flow was reduced to 120ml/min for 10 seconds. After which the blood pump was switched off, the arterial line was clamped above the sampling port and the third sample obtained from the arterial port. This third sample was the 'systemic sample' (S). The access recirculation was calculated using the standard formula; AR (%) = (S-A) / (S-V) ×100.

Venous stenosis was assessed considering the clinical signs including arm elevation test, presence of collateral vessels, prolonged bleeding after needle withdrawal, and formation of aneurysms in the venous channel. Similarly, clinical signs of arterial insufficiency were absence of palpable thrill over AV fistula and circuit jerking at blood flows of over 250 ml/min. Needle placement was considered inappropriate when lines were reversed, arterial needle was placed less than 2cm from AV fistula, venous needle was placed at less than 5cm from the arterial needle, and when the two needles were directed inappropriately.

All the data was recorded on prescribed proforma and analyzed as under.

Statistical analysis involved application of appropriate statistical tests according to the types of data, in SPSS software version 23. Age of the patients and dialysis vintage were correlated with recirculation values utilizing Pearson's correlation. Fisher's exact test was used for analysis of associations between recirculation status and independent variables such as gender, venous stenosis, inappropriate needle placement and arterial insufficiency. Two independent sample T-test was applied when comparing recirculation values between subcategories of independent variables. A one-way ANOVA was applied looking at the association of recirculation values with different categories of accesses used for hemodialysis. The association of recirculation reached statistical significance with the

presence of venous stenosis, inappropriate needle placement and different access types. Table 2.

RESULTS

A total of 104 patients were studied in this study, of which 53 (51.0%) were males. The mean age of the group was 39.65 years (SD+-13.84). Mean duration of Hemodialysis was 18.78 (SD+-12.93) months. Values of all other descriptive statistics including urea values of venous, arterial and systemic samples and Recirculation are given in table 1.

Radio-cephalic AV fistula was the commonest access (45.19%) in this cohort, followed by Brachio-cephalic and Brachio-basilic fistulas. Fig 1.

Overall, 46 (44.2%) patients were found to have significant access recirculation in this study. figure 2.

Table No.1: Descriptive Statistics

	N	Min.	Max,	Mean	Std. Deviation
Age of Patients (years)	104	20	70	39.65	13.841
Duration of Hemodialysis (months)	104	1	72	18.78	12.938
Arterial Urea (mg/dl)	104	52	204	123.27	38.859
Venous Urea (mg/dl)	104	6	58	24.54	13.814
Systemic Urea (mg/dl)	104	54	211	134.45	39.855
Recirculation (%)	104	1.69	37.50	10.9988	6.30922
Valid N (listwise)	104				

Table No.2. Inferential Statitics

	Recirculation status	Recirculation Values
		Pearson's correlation
Age of patients (years)		Correlation coefficient= -0.22. P=0.826
Dialysis Vintage (moths)		Correlation coefficient= 0.097. P=0.325
	Fisher's exact test	T-test (2 sample)
Gender	Males=53 (51.0%). p=0.693.	p=0.842 (95%CI=-2.71—2.21).
Venous stenosis	n=5 (4.8%). p=0.015.	p=0.014 (95%CI= - 8.769 — -1.444).
Inappropriate needle placement	n=51 (49%). p=0.001.	p=0.034 (95%CI= -5.033 — -0.202).
Arterial insufficiency	n=13 (12.5%). p=0.236.	p=0.146 (95%CI= -6.41 — 0.963).
	Fisher's exact test	ONE WAY ANOVA.
Different types of access	p=0.048.	P=0.006

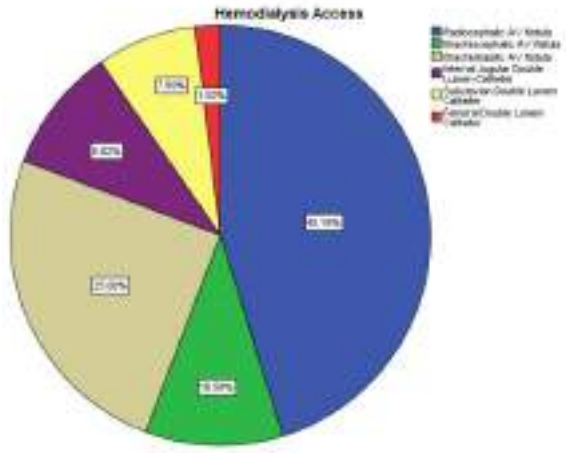


Figure No.1: Hemodialysis Access

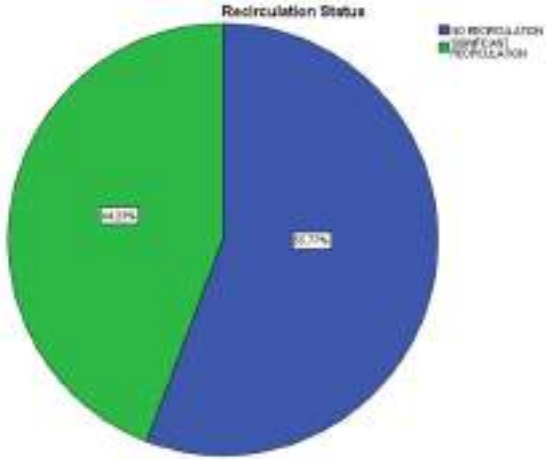


Figure No.2: Recirculation Status

DISCUSSION

Access recirculation can be assessed by multiple methods including ultrasound dilution (transonic device), hematocrit dilution (Crit-line monitor), and differential conductivity (Gambro hemodynamic monitor)[12]. Limited by the availability of expertise and equipment, we chose the conventional urea based method.

The mean value of recirculation was 10.99%, and overall, 44.2% patients were recorded to have significant access recirculation in our study. Literature search reveals a wide pattern of results in different populations. In a study conducted at Sheikh Zayed hospital Lahore, patients undergoing hemodialysis through double lumen catheters had a mean recirculation of 10.3±6.64 %[9]. Another study conducted

at the same institute estimated the mean access recirculation to be around 9.55 ± 6.64%[10]. Both these studies show results similar to our data, however, neither of these studies reported the percentage of patients having significant recirculation. Studies from Iran showed significant access recirculation in around 17% patients with the most common cause being inappropriate needle placement[13,14]. A study from Dhaka produced similar results to our findings with mean recirculation of 8.1 +/- 5.5% (Range 0-66%), and improper needle placement as the most important responsible factor[15]. An international Study estimated recirculation rates ranging from 18 +/- 4% in radial fistulas and 11 +/- 3% in more proximal fistulas[16].

Important factors that cause access recirculation are:

- Improperly placed needles.
- Central or proximal venous obstruction.
- Arterial insufficiency.

In our study the relationship of recirculation was not statistically significant with Age of patients, Dialysis Vintage, Gender and clinical impression of arterial insufficiency. However, access recirculation was found to be significantly associated with the presence of venous stenosis, inappropriate needle placement and different types of access. We found inappropriate needle placement in nearly half of all the cases, by far the commonest cause followed by arterial insufficiency and venous stenosis. These factors are well established, and our study is in concordance with the current literature[17]. Needle placement is the most important factor in determining the access recirculation during hemodialysis. We reviewed an interesting study comparing the recirculation with different patterns of needle cannulation. In this study, recirculation was lowest (8.51 +/- 4.90%) when the needles were placed in the recommended fashion (in opposite directions and 5 cm apart), while it was the highest (20.68 +/- 4.92%) when needles were placed in a single direction, less than 5cm apart. Other patterns of needle placement gave intermediate results[18]. Venous stenosis, producing reverse flow of blood in the veins, is also a frequent underlying cause of recirculation[8]. Arterial insufficiency is an important contributor to access recirculation especially when the access blood flow rate becomes less than the dialyzer blood flow rate suggesting a marked blood flow impairment[19, 20].

Recirculation is not just limited to AV fistulas, but is also observed in patients with temporary or tunneled double lumen catheters. Different sites of double lumen catheters also give different rates of recirculation with internal jugular line giving the least amount of recirculation (2.38 +/- 1.09%), followed by subclavian catheters (3.03 +/- 3.15%) and lastly Femoral lines (9 +/- 6.56%)[21,22]. At any site, the reversal of lines results in a higher value of recirculation, although the dialysis dose may still increase with increasing blood flow rates[23]. Tunneled catheters may similarly show recirculation, which increases with line reversal.[24]

In addition to causing a reduction in the delivered dose of hemodialysis, access recirculation is also considered to be an important clinical marker of AV fistula dysfunction. Research has shown recirculation status to be an important predictor of the need for Av fistula revision if blood flow is found to be < 500ml/min[25]. One study suggested that nearly one quarter of patients with significant access recirculation needed intervention or access revision for vascular access dysfunction[26]. It is therefore recommended that recirculation be measured at regular intervals in all patients on hemodialysis. This is however not practiced in our setup. We find that a significant proportion of our patients have access recirculation. Further study is needed to identify and correct the underlying cause. Considering inappropriate needle placement as the most common cause, we propose re-evaluation and training of dialysis technicians regarding appropriate needle placement. Furthermore, formal assessment of venous and arterial limbs must be undertaken in all patients with access recirculation to identify patients with impending access dysfunction.

CONCLUSION

This study shows that a significant percentage of our patients have access recirculation during hemodialysis, which can be predicted to reduce the efficiency of hemodialysis. Recirculation is significantly associated with inappropriate needle placement and venous stenosis.

There is a need to ascertain and correct the underlying causes of recirculation, to improve the efficiency of hemodialysis and ultimately patient well-being.

Author's Contribution:

Concept & Design of Study:	Farman Ullah
Drafting:	Irfan Mirza, Mufti Baleegh-ur-Raheem Mahmood
Data Analysis:	Ahmed Zeb Khan, Mufti Baleegh-ur-Raheem Mahmood
Revisiting Critically:	Farman Ullah, Irfan Mirza
Final Approval of version:	Farman Ullah

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Kalantar-Zadeh K, et al. Renal Replacement Therapy and Incremental Hemodialysis for Veterans with Advanced Chronic Kidney Disease. Seminars in dialysis 2017;30:251–261.

2. Roy-Chaudhury P, Sukhatme VP, Cheung AK. Hemodialysis Vascular Access Dysfunction: A Cellular and Molecular Viewpoint. J Am Society Nephrol 2006;17**:**1112–1127.
3. Schwab SJ. Vascular access for hemodialysis. Kidney International 1999**;55:**2078–2090.
4. Unver S, Atasoyu EM, Evrenkaya TR. Effects of comorbidity from AV fistula insufficiency on fistula blood flow rate in hemodialysis patients. Dialysis Transplantation 2006;35:682–688.
5. Hakim RM, Breyer J, Ismail N, Schulman G. Effects of Dose of Dialysis on Morbidity and Mortality. Am J Kid Diseases 1994;23**:**661–669.
6. Lok CE, et al. KDOQI Clinical Practice Guideline for Vascular Access: 2019 Update. Am J Kid Dis 2020;**75:** S1–S164.
7. Salimi J, et al. Predicting hemodialysis access failure with the measurement of dialysis access recirculation. Saudi J kidney diseases and transplantation : an official publication of the Saudi Center for Organ Transplantation, Saudi Arabia 2008;19**:**781–4.
8. Zeraati A, BeladiMousavi SS, BeladiMousavi M. A Review Article: Access Recirculation Among End Stage Renal Disease Patients Undergoing Maintenance Hemodialysis. Nephro-Urol Monthly 2013;**5:**728–32.
9. Akram M, Abbas G. Double Lumen Catheters. Profess Med J 2011;18**:**470–474.
10. Rafique Z, Abbas G, Shafi T. Comparison of arteriovenous fistula recirculation by thermo-dilution and urea-based method. Journal of the College of Physicians and Surgeons--Pakistan: JCPSP 2007; 17:603–606.
11. Adequacy of Hemodialysis. J Coll Physicians Surg Pak 2002;12**:**692–5.
12. Lindsay RM, et al. A Comparison of Methods for the Measurement of Hemodialysis Access Recirculation and Access Blood Flow Rate. ASAIO J 1998;44**:**54.
13. Beladi MS, Tavazoe M, Hayati F, Sametzadeh M. Arterio-Venous fistula recirculation in hemodialysis: causes and prevalences 2010.
14. Hayati F, Shayanpour S, Faramarzi M. Access Recirculation in Hemodialysis. Shiraz E Med J 2015;16.
15. Mahbub T, et al. Factors responsible for increased percent recirculation in arterio-venous fistula among the haemodialysis patients. Bangladesh Med Research Council Bulletin 2013**;**39:28–33.
16. Collins DM, et al. Fistula dysfunction: Effect on rapid hemodialysis. Kidney Int 1992;41:1292–1296.
17. Kalinin R, Suchkov I, Egorov A, Klimentova E. Recirculation syndrome in hemodialysis patients. Khirurgiia 2019;24—28.
18. Dias TS, Neto MM, Cardeal da Costa JA. Arteriovenous Fistula Puncture: An Essential Factor for Hemodialysis Efficiency. Renal Failure 2008;30:870–876.
19. Besarab A, Sherman R. The relationship of recirculation to access blood flow. Am J Kid Diseases 1997;29: 223–229.
20. Daniels ID, Berlyne GM, Barth RH. Blood Flow Rate and Access Recirculation in Hemodialysis. Int J Artificial Organs 1992;15**:**470–474.
21. Sefer S, Kes P, Degoricija V, Heinrich B, Vrsalović M. Recirculation of urea and dialysis efficiency using dual-lumen dialysis catheters in various locations: may the venous lumen of the catheter be used as the arterial lumen and vice versa? Lijecnickivjesnik 2003;125:1–5.
22. Leblanc M, Fedak S, Mokris G, Paganini EP. Blood recirculation in temporary central catheters for acute hemodialysis. Clin Nephrol 1996;45**:** 315–9.
23. Kousoula V, et al. Reversed connection of cuffed, tunneled, dual-lumen catheters with increased blood flow rate maintains the adequacy of delivered dialysis despite the higher access recirculation. Int Urol Nephrol 2019;51**:**1841–1847.
24. Sencal L, Saint-Sauveur E, Leblanc M. Blood Flow and Recirculation Rates in Tunneled Hemodialysis Catheters. ASAIO J 2004;50**:**94–97.
25. Wang E, Schneditz D, Ronco C, Levin NW. Surveillance of Fistula Function by Frequent Recirculation Measurements During High Efficiency Dialysis. ASAIO J 2002;48**:**394–397.
26. Vega A, et al. Comparison of urea recirculation and thermodilution for monitoring of vascular access in patients undergoing hemodialysis. J Vascular Access 2018;19:283–290.

Original Article

Assessment of Knowledge, Attitude and Practices Towards Malaria in Rural and Urban Communities of Peshawar and Mardan, Pakistan

Malaria in Rural and Urban Communities of Peshawar and Mardan

Ziauddin, Shah Zeb, Muhammad Abbas

ABSTRACT

Objective: To assess the knowledge, attitude and practices regarding malaria in rural and urban suburbs of Peshawar and Mardan districts, Khyber Pakhtunkhwa, Pakistan.

Study Design: Descriptive study

Place and Duration of Study: This study was conducted at the two major tertiary care hospitals of hospitals of Khyber Pakhtunkhwa from September 2020 to February 2021.

Materials and Methods: A structured questionnaire was used which contained detailed information about the demography, knowledge, attitude and practice of the enrolled inhabitants.

Results: Most study subjects (80% rural, 90% urban) knew facts about malaria. 59% rural, 92% urban knew that mosquitoes were the vectors. 31.5% rural and 43% urban community knew about destruction of mosquito sites. 84% urban while 46.5% rural inhabitants were aware of anti-mosquito sprays. 55% of the rural population and 38% of urban society was not practicing any measures against malarial prevention.

Conclusion: Our community is familiar with the symptoms of malaria and its mode of transmission. The knowledge about preventive measures and vector control was deficient in rural areas. The overall situation needs to be strengthened.

Key Words: Malaria; Knowledge; Attitude; Practice

Citation of article: Ziauddin, Shah Zeb, Abbas M. Assessment of Knowledge, Attitude and Practices Towards Malaria in Rural and Urban Communities of Peshawar and Mardan, Pakistan. Med Forum 2021;32(10):121-126.

INTRODUCTION

Malaria has been recognized as one of the most common diseases affecting the human being worldwide for thousands of years. It is still a severe and life-threatening illness. The major impact of the disease is almost entirely on the developing countries, with the heaviest burden in Africa

Malaria remains one of the most serious health problems in South-East Asia Region. Every year 2.3 million cases and 4200 deaths are reported with an estimation of 18-20 million cases and 100,000 deaths. The vulnerable groups that have greatest risk of deaths due to malaria are children under five years of age, pregnant women and non- immune persons.[1]

[1.] Department of Medicine, Lady Reading Hospital, Peshawar.
[2.] Department of Medicine, Mardan Medical Complex, Mardan.

Correspondence: Dr. Ziauddin, Associate Professor Medicine, Lady Reading Hospital, Peshawar.
Contact No: 0300-5862093
Email: doctorziauddin2011@gmail.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

According to the World Health Organization (WHO), 97% (approximately 150 million) of the Pakistani population is at risk of contracting malaria, with an estimated nationwide burden of 1.6 million cases per year.[2]

Malaria in Pakistan is typically unstable and major transmission period is post monsoon i.e. from August to November. Major vector species are Anopheles culicifacies and A. stephensi, both still susceptible to the insecticides currently being used. The widely distributed causative organisms are Plasmodium falciparum and Plasmodium vivax. Vivax malaria still dominates the transmission though significant rise in the more lethal form, Falciparum malaria is observed in Baluchistan and Sindh provinces.[3]

The malariogenic potential of Pakistan has a negative impact on its socio-economic growth and productivity, as the main transmission season is spiraled with the harvesting and sowing of the main crops (wheat, rice, sugar cane). Seasonal transmission variations, drought, irrigation systems and hydrological changes, population movements, high level anti-malarial drugs and insecticide resistance in the parasite, and vectors are the major determining factors working behind the high endemicity of these districts. Poor access of the population to early diagnosis, effective treatment and effective prevention measures have further compounded the situation.[4]

The objective of our study is to assess knowledge, attitude and practices of community about preventive measures against malaria in rural and urban areas of Peshawar and Mardan, Pakistan.

MATERIALS AND METHODS

Our study is descriptive cross sectional study. The study was conducted in rural and urban areas of Peshawar and Mardan districts of Khyber Pakhtunkhwa province, Pakistan. In rural areas of Peshawar, Palosai and Pishtakhara villages while in urban areas, University Town and Hayatabad were selected. In district Mardan, Takht Bhai was the rural area, while Mardan city was selected as urban area for research purpose. Study duration was from September 2020 to February 2021. Convenient sampling technique was used. Sample size was 400, which included 200 each from urban and rural areas. All males who were permanent inhabitants of above mentioned areas and having age from 15 to 60 years were included in the study. We excluded Afghan nationals from our study.

Data Collection Tool: A structured questionnaire was used covering questions on socio-demographic data, knowledge on transmission, preventive measures against malaria and practices used by community for prevention. The respondents were interviewed according to the questionnaire.

Study Variables: The study variables were age, area of residence, occupation, marital status, education, income, knowledge (about sign and symptoms and mode of transmission of malaria), attitude (community level preventive measures) and practices against prevention of malaria at community level.

Age: Further age-wise categories were made. Individuals having age between 15-30 years, 30-45 years and 45- 60 years were labeled as category 1, 2 and 3 respectively.

Area of Residence: Further two categories were made, a) rural b) urban

Occupation: The participants were asked about their occupation and was recorded

Marital Status: Participants were classified according to their marital status as single or married.

Education: The education status was coded to distinguish between respondents who had received no school education (illiterate), schooling at primary level but had not completed secondary schooling (below matric), those who had completed secondary schooling (matric), those who had completed F. A or F. SC(intermediates), those who had completed B.A or BSC (graduates) and those who had qualification above graduation were coded as post graduates.

Economic Status: The economic status was established by asking about their monthly house hold income in rupees. Those who had income below ten thousand rupees per month were coded as poorest; 10000-25000 were coded as poor, 25000-40000 medium and above 40000 were coded as well off.

Knowledge: In order to evaluate knowledge of respondents about malaria they were asked about the sign and symptoms and mode of transmission of malaria. The effect of education and economic status on knowledge was also established.

Attitude: Both community and personal level attitude towards preventive measures against malaria was recorded. The individuals were asked to specify the methods which they think are better preventive measures at community level and personal level. The effect of education and economic status on attitude was also established.

Practices: In order to know about community level practices, participants were asked about spray in their locality and stagnant water treatment. Spray in locality and/or stagnant water treatment was considered as positive community level practice.

Data Analysis: Data was coded, compiled in statistical package for social sciences (SPSS 22) software for windows 7.

RESULTS

Rural Area: In rural area majority of the respondents (69.5%) were between 15-30years of age, as shown in table 1. 106 respondents (53.0) were single while 94 (47%) were married. Single largest occupation was that of business accounting 31.5%. Table 2. Most of the participants were graduates (26.5%) followed by intermediate pass (22.5%) and illiterates (20%). Table 3. Most of the respondents belonged to poor socioeconomic status (46%) followed by medium class (13.5%) and well off family (4.5%) Graph 1. About 80% of the respondents were aware of the sign and symptoms of malaria and 59% knew that mosquito is the transmitting agent.

Urban Area: In urban area majority of the respondents (78%) were between the age 15-30 years as shown in table 1. Single largest occupation was that of student (80%). Table 2. Most of the participants were graduates (58.2%), intermediate pass (22%) followed by illiterates (1.5%). Table 3. Most of the study subjects belonged to poorest (32%) family. This was followed by medium class (28%) and well (20%) Graph 1. About 94% of the respondents were aware of the sign and symptoms of malaria and 92% knew that mosquito is the transmitting agent.

Table No.1: Age Groups in Rural and Urban Areas

		Rural		Urban	
Sr. No.	Age Groups (years)	Frequency	%age	Frequency	%age
1	15-30	139	69.5	156	72.9
2	31-45	45	22.5	36	16.8
3	46-60	16	8.0	8	3.8
	Total	200	100	200	100

Table No.2: Occupation of Participants in Rural and Urban Areas

		Rural		Urban	
Sr. No	Occupation	Frequ-ency	%age	Frequency	%age
1	Student	41	20.5	160	74.9
2	Laboured	34	17	20	9.3
3	Salaried	27	13.5	12	5.6
4	Businessman	63	31.5	0	0
5	Others	35	17.5	8	3.7
	Total	200	100	200	100

Table No.3: Educational Statuses in Rural and Urban Areas

		Rural		Urban	
Sr. No	Education	Frequ-ency	%age	Frequency	%age
1	Uneducated	40	20	3	1.5
2	Below Matric	26	13	18	8.4
3	Matric	28	14	4	1.9
4	Intermediate	45	22.5	47	22.0
5	Graduate	53	26.5	116	54.2
6	Post-Graduate	8	4.0	12	5.6

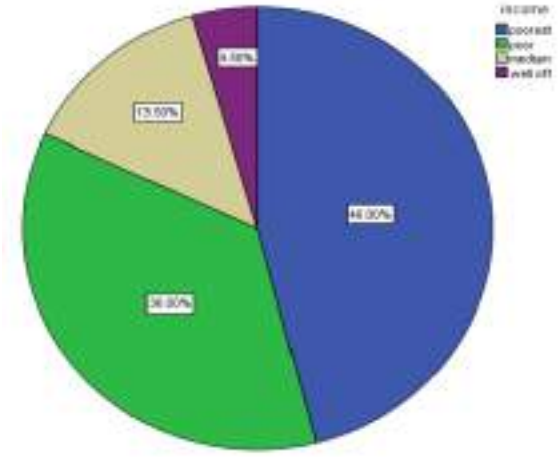


Figure 1.1: Economic Status Rural

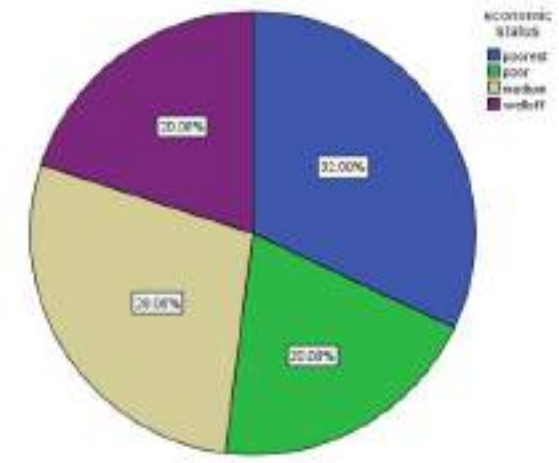


Figure No. 1.2: Economic Status Urban

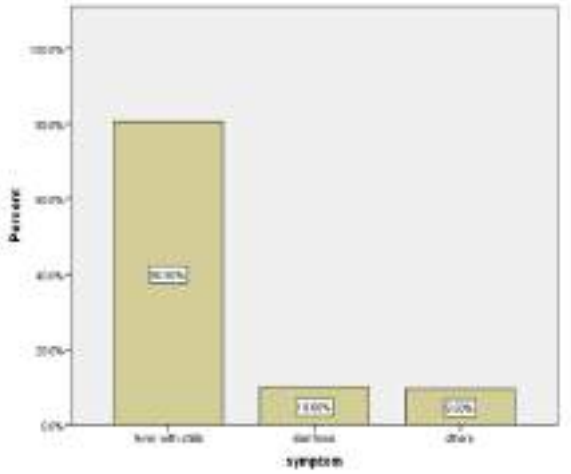


Figure No. 2.1: Sign and Symptoms of Malaria in Rural

Fever with chills is determined by maximum respondents (80.5%), 10% stated diarrhea, 9%stated others (cough, sore throat).

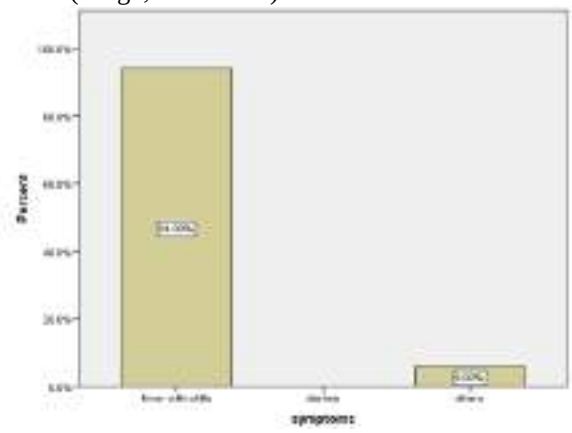


Figure No. 2.2: Sign and Symptoms of Malaria in Urban

Fever with chills is determined by 188 respondents (94%). Other than fever and chills is determined by 12 respondents (6%)

Table No.4: Mode of Transmission

		Rural		**Urban**	
Sr. No.	**Mode of Transmission**	**Frequ-ency**	**%age**	**Frequ-ency**	**%age**
1	Mosquitoes	118	59	184	93.5
2	Flies	15	7.5	0	0
3	Others	67	33.5	16	7.5

Table No.5: Attitudes

		Rural		**Urban**	
Sr. No.	**Attitudes**	**Frequ-ency**	**%age**	**Frequ-ency**	**%age**
1	Destruction of mosquitoes breeding sites	63	31.5	92	43
2	Use of anti-mosquito sprays	93	46.5	84	39.3
3	Others	44	22	24	11.3
4	Total	200	100	200	100

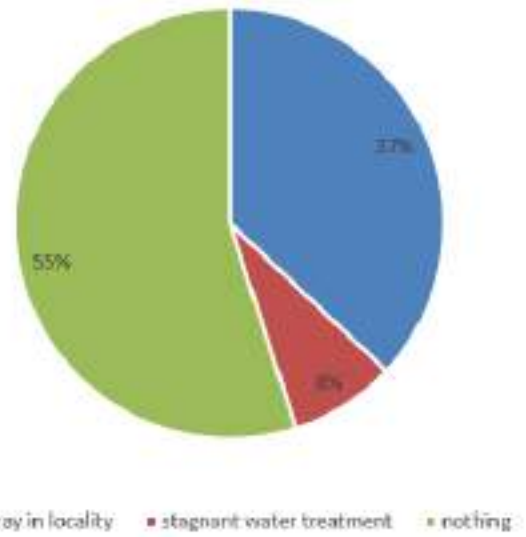


Figure No.3.1: Practices at Community Level

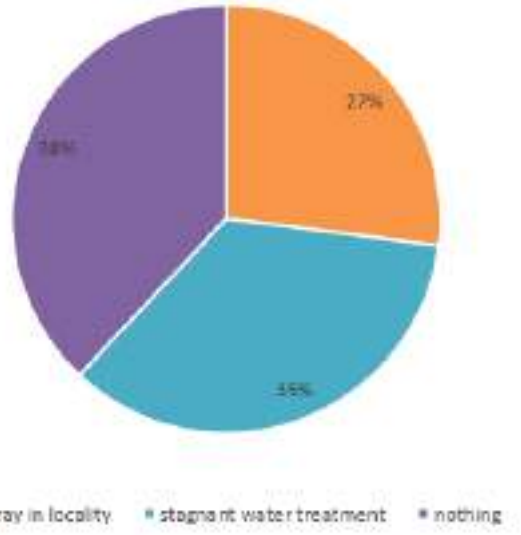


Figure No.3.2: Urban

DISCUSSION

Malaria is a global problem and is the fourth leading cause of death. In Sub-Saharan Africa, malaria is the most important tropical disease, with 1.5 to 2.5 million deaths per year. One of the four childhood death in Africa is caused by malaria and Africa accounts for 80% of malarial morbidity and 90% of malarial mortality.[5]

Findings of our study indicated that the people of urban areas of Peshawar and Mardan city had better knowledge about symptoms and mode of transmission of malaria compared to people of rural areas where knowledge was slightly deficient. This could be explained by the better educational level and increase access to mass media in urban areas compared to rural areas. So efforts to increase the educational level in rural areas and bringing awareness in people through public awareness campaigns and seminars will increase their knowledge level.

In an Ethiopian study it was reported that less than half (47.5%) of the study participants mentioned mosquito bites as a mode of malaria transmission. The knowledge level of respondents about the mode of malaria transmission was very low when compared to the findings in previous studies carried out in Ethiopia which reported awareness levels of up to 93%,[6,7]. Findings in this study are also lower than those reported in other studies across Africa[5,8,9], and in countries like India and Mexico [10,11].

The 2004 NetMark survey did report a slightly lower level of knowledge about modes of transmission (39.5%) [12]. Majority of respondents reported mosquito bites and mosquito disturbance during sleeping as nuisances. However, only a small proportion (29.9%) of the respondents mentioned the role of mosquitoes as a vector for malaria transmission, indicating their limited knowledge of the relationship between mosquitoes and malaria. This lack of awareness may also contribute to misconceptions about causes of malaria.

Similarly, a study from Iran demonstrated that the illiteracy level of the studied population was high (44.2%) and significantly affected the knowledge and practices of the respondents about the route of malaria transmission. 72.1% knew that mosquitoes were the vector.[13]

In the present study, exposure to dirty environments and hot weather, drinking dirty water, poor personal hygiene, eating contaminated foods, and exposures to the sun were identified as possible causes of malaria. Such misconceptions have also been reported from different studies from Ethiopia and other countries.

Results of our study showed that attitude of both rural and urban communities towards preventive measures was positive i.e. they viewed that preventive measures should be adopted against malaria but the attitude of urban community was better compared to rural community.

It might be because of better education in urban area and poor educational level in rural area. Also in rural area some people follow cultural traditions and beliefs which could be responsible for their negative attitude towards preventive measures.

Community members' attitude towards malaria as a disease is important in understanding them health seeking behavior and use of preventive methods. Study from Malaysia showed Promising results about treatment-seeking behavior; almost all the rural participants and two thirds of the aboriginal participants seek treatment at health centers within 24 hours of the onset of symptoms. Previous studies in rural areas in Southeast Asia showed that more than half of the population opts for self-treatment without visiting a

health facility [14, 15]. The better behavior reported by the Malaysian study could be due to the availability of health facilities and access to their services to all Malaysians throughout the country.

It has been observed in our research that community level practices of rural area were poor as compared to urban area. It might be because of the reason that government is giving priority to urban areas where anti mosquito spray is done more frequently. Also the economic status of urban community is better compared to rural population enabling to carry out such projects on self-sustained basis.

The present study revealed that education has impact on malaria knowledge i.e. educated people have more knowledge regarding different aspects of malaria. This corroborates with the evidence of studies in Zambia, Ethiopia and Gambia where high level of education was associated with improved knowledge.[16, 17]

We observed from the present study that economic status affects practices regarding preventive measures of malaria. This might be because of the reason that economically stable people can better afford to buy nets, coils, mats etc.

CONCLUSION

It is concluded that education level affects practices regarding preventive measures of malaria. Subjects of rural area have deficient knowledge compared to that of urban area. Attitude of both rural and urban subjects was positive regarding preventive measures of malaria, but the attitude of urban community is better than rural community.

Recommendations: Based on our study findings we recommend following:

1. Health education should be given through mass communication about the knowledge of malaria, preventive measures, especially those who live in rural areas. This will increase the level of awareness and change the attitude of community.
2. Rural areas should be given proper considerations regarding preventive policies of malaria.
3. Insecticidal house spraying should be done on regular basis.
4. Insecticide treated nets should be provided to people in endemic areas.
5. Health authority should use larvicidal sprays for treating stagnant water in the locality.
6. Measures should be taken for proper drainage of stagnant water.
7. Proper screening of houses should be done.
8. Personal protective measures like use of mosquito repellents should be adopted

Author's Contribution:

Concept & Design of Study:	Ziauddin
Drafting:	Shah Zeb
Data Analysis:	Ziauddin, Muhammad Abbas
Revisiting Critically:	Ziauddin, Shah Zeb
Final Approval of version:	Ziauddin

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. World Health Organization: World Malaria Report 2009. Geneva; 2009.
2. World Health Organization: Strategic plan for malaria control and elimination in the WHO Eastern Mediterranean Region 2006-2010. [http://www.emro.who.int/dsaf/dsa741.pdf]
3. Roll Back Malaria. WHO Eastern Mediterranean Region. Cairo, Egypt; 2002.p.1-14.
4. Asif SA. Departmental audit of malaria control programme 2001-2005 North West Frontier Province (NWFP). J Ayub Med Coll Abbottabad 2008;20:98-102.
5. Adera TD. Beliefs and traditional treatment of malaria in Kishe settlement area, South West Ethiopia. Ethiopian Medical Journal, 2003; 41(1):25-7(2):99-104.
6. Jimma D, Tesfaye G, Deressa W, Woyessa A, Kebede D, Alameraw D. Baseline survey for the implementation of Insecticide –treated mosquito nets in malaria control in Ethiopia. Ethiopian J Health Development 2005;19(1):16-23.
7. Jimma D, Tesfaye G, Deressa W, Woyessa A, Kebede Deressa W, Ali A, et al. Knowledge, Attitude and Practice about Malaria, the Mosquito and Antimalarial Drugs in a Rural Community, Ethiopian J Health Development 2003;1.
8. Adongo PB, Kirkwood B, Kendall C. How local community knowledge about malaria affects insecticide treated net use in northern Ghana. Tropical Medicine and International Health 2005; 10(4):366-378.
9. Tyagi P, Roy A, Malhotra MS. Knowledge, awareness and practices towards malaria in communities of Rural, semi-rural and bordering areas of east Delhi, India. J Vector Borne Disease 2005;42:30- 35.
10. Roderiguez AD, et al. Knowledge and belief about malaria transmission and practices for vector control in southern Mexico. Salud publica de Mexico 2003;45(2).
11. Binka FN, Indome F, Smith T. Impact of spatial distribution of Permethrin-Impregnated bed nets on Child Mortality in Rural Northern Ghana. Am J Tropical Medicine Hygiene 1998;59(1):80-85.
12. NetMark. NetMark 2004 survey on insecticidetreated nets (ITNs) in Ethiopia. A

regional partnership for sustainable malaria prevention; updated; September 2005.
13. Rakhshani F. Ansari Moghadam AR, Alemi R, Moradi A. Knowledge, perceptions and prevention of malaria among women in Sistan va Baluchestan, Islamic Republic of Iran, Revue de Santé de la Méditerranée Orientale 2003;9(3):248-256.
14. Swe KK, Pearson A: Knowledge, attitudes and practices with regard to malaria control in an endemic rural area of Myanmar. Southeast Asian J Trop Med Public Health 2004;35:53-62.
15. Nalongsack S, Yoshida Y, Morita S, Sosouphanh K, Sakamoto J. Knowledge, attitude and practice regarding dengue among people in Pakse, Laos. Nagoya J Med Sci 2009;71:29-37.
16. WHO Fact Sheet on Malaria (No. 94), October 1998
17. Smith LA, Jones C, Meek S, Webster J: Provider practice and user behavior interventions to improve prompt and effective treatment of malaria: do we know what works? Am J Trop Med Hyg 2009;80:326- 335.

Original Article

Frequency of Stress Hyperglycemia and Incident Diabetes Mellitus in Patients Presenting with Acute Coronary Syndrome

Incident Diabetes with Acute Coronary Syndrome

Naveed Danish[1], Samiullah Khan[2], Muhammad Niaz Khan[3], Muhammad Saad Bin Nasir[3], Muhammad Kashif Iltaf[2] and Hammad Shah[4]

ABSTRACT

Objective: To determine the Frequency of stress hyperglycemia and Incident Diabetes Mellitus in patients presenting with Acute Coronary syndrome.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Coronary Care Unit of DHQ Teaching Hospital Nowshera and Qazi Hussain Ahmad Medical Complex (QHMC) Nowshera from January 2017 to June 2018.

Materials and Methods: They were interviewed through a pre-designed research proforma after informed written consent. Random plasma glucose (RPG) and fasting plasma glucose (FPG) were performed. The diagnosis of the sub type of ACS was made using the acute changes of the ECG and Qualitative Cardiac Troponin tests.

Results: A total of 278 ACS patients were enrolled I the present study. There were more male patients (56.8%) with ACS. The frequency of Diabetes was 51.8% (n, 144) as compared to non-diabetics 48.2% (n, 134) in ACS. The Frequency of Stress hyperglycemia using RPG levels was 70.5% (n, 196). Frequency of Incident DM and Pre Diabetes was 13.2% (n, 26) and 9.0% (13), respectively using FPG levels among stress hyperglycemic patients. The Frequency of STEMI, nSTEMI and Unstable angina was 59.7% (n, 166), 19.4% (n, 54) and 21% (n, 58), respectively.

Conclusion: There is higher prevalence of stress hyperglycemia and known diabetes mellitus with small number of incident diabetes in the present study.

Key Words: Acute Coronary Syndrome, Incident Diabetes Mellitus, Stress hyperglycemia

Citation of article: Danish N, Khan S, Khan MN, Nasir MS, Iltaf MK, Shah H. Frequency of Stress Hyperglycemia and Incident Diabetes Mellitus in Patients Presenting with Acute Coronary Syndrome. Med Forum 2021;32(10):127-131.

INTRODUCTION

According to World Health Organization statistics, the prevalence of Diabetes worldwide for all age groups was 2.8% in 2000. This percentage will rise to 4.4% in 2030. From 171 million people in 2000, this disease will affect 366 million individuals in 2030.[1]

[1.] Department of Cardiology, DHQ Hospital, Nowshera.
[2.] Department of Cardiology, Nowshera Medical College/QHAMC Nowshera.
[3.] Department of Cardiology, Hayatabad Medical Complex, Peshawar.
[4.] Department of Cardiology, MRHMS Hospital Pubbi, Nowshera.

Correspondence: Dr. Samiullah Khan, Assistant Professor of Cardiology, Bannu Medical College/DHQ-TH, Bannu.
Contact No: 03015151346
Email: drsamee@yahoo.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

Various risk factors play a role in the occurrence of Acute Myocardial Infarction (AMI) and Diabetes is one of them. An odds ratio of 2.37 was found in a study (the INTERHEART study) when associating diabetes as a risk factor for AMI.[2] Patients often present to the Emergency departments or the Coronary Care Units with an AMI in the presence of hyperglycemia whether it be stress hyperglycemia, an incidental finding of undiagnosed Diabetes or a previously known case of Diabetes Mellitus.[3,4] The TRIUMPH study, having a sample size of 4340 showed that 2854 patients had metabolic data available. Of these, 10.1% had underlying Diabetes which was undiagnosed. In a total of 4193 patients, 6.8% had undiagnosed underlying diabetes which had presented with an AMI.[4] A study carried out in Naples, Italy showed that 29% of their patients who presented with an AMI had no prior history of Diabetes but they presented with a plasma sugar of more than 7 mmol/L.[3] Another study indicated that the prevalence of undiagnosed hyperglycemia was 5.3% and the uncontrolled Glycosylated hemoglobin (HbA1c) lead to more cardiac complications following an MI.[5] A Canadian study showed that the odds ratio for patients without a history of diagnosed diabetes

(135 out of 1078) was 2.44.[6] Diagnosing diabetes mellitus in the presence of Myocardial Infarction can be done by evaluation of Random Blood Sugar on admission followed by Fasting Blood Sugar and the HbA1c levels. Diagnosing diabetes mellitus in the presence of Myocardial Infarction can be done by evaluation of Random Blood Sugar on admission followed by Fasting Blood Sugar and the levels of HbA1c.[7]

Clinical outcomes following an MI have also been divided into subgroups based on the value of plasma glucose on admission. Admission hyperglycemia was a predictor of poor outcome as compared to normoglycemia and hypoglycemia.[8] Another study showed that non-diabetic patients had comparable risk of death to diabetics which presented with a plasma glucose of 200 mg/dl or more. It has been documented that patients who are undiagnosed Diabetics have a much poor outcome as compared to patients with already diagnosed Diabetes once they present with an AMI.[10]

It is evident that stress hyperglycemia does occur with Acute Myocardial Infarction. However, there is no significant data from our country or our province as to how much percentage of this hyperglycemia is indeed stress hyperglycemia or whether it is because of underlying undiagnosed Diabetes Mellitus that presented with AMI. Our aim would be to evaluate the prevalence of undiagnosed diabetes that surfaced due to an AMI which could be the possible complication of DM. Another aim would be finding out the associated diagnosis along with AMI that present with hyperglycemia on admission.

MATERIALS AND METHODS

Study Design: It is a cross sectional study that was carried out from January 2017 to June 2018 at the Coronary Care Unit of DHQ Teaching Hospital Nowshera and QHMC Nowshera.

Participants

Inclusion criteria: All patients presenting to the Coronary Care Unit of DHQ Teaching Hospital and QHMC Nowshera**,** presenting with Acute Coronary Syndrome were enrolled in the study.

Exclusion criteria: Admissions with diagnosis other than ACS were not enrolled into the study. Subjects who were discharged on will or left against medical advice and not consenting were also excluded.

Variables: The diagnosis of the patients was noted. RPG fasting blood sugar (FBS) upon admission was performed regardless their previous status of diabetes. The different diagnosis presenting to the CCU will also show the frequency of the sub-categories of diseases in Acute Coronary Syndrome.

Data Sources/ Measurement: The study was conducted after approval from the hospital ethical and research committee. Author constructed questionnaire was used. It was supplemented by lab results for the tests of RBS, FBS and HBA1c in order to confirm the diagnosis of Diabetes Mellitus. The diagnosis of the sub type of myocardial infarction was made based on the acute changes of the ECG and qualitative troponin kit tests (of Roche Pharmaceuticals**)**.

Sample Size: A total of 278 patients were enrolled into the study to account for an adequate sample size.

Statistical analysis: Data was entered into the latest version of SPSS and analyzed.

RESULTS

The samples taken showed a gender differentiation in which 56.8% (157) were males and 43.2% (120) patients were female. A higher percentage of male population was being affected by Acute Coronary Syndrome. The mean age of the patients was 57.9 ± 10.1 years.

Table 01shows the number of patients who came to the CCU with other known co-morbidities. Patients who were aware of their diabetic status were 144 (51.7%) patients while 134 (48.2%) were either non-diabetics or undiagnosed. On the hand, it is evident that 120 (43.1%) patients were hypertensive.

There were 33 (11.9%) smokers and 245 (88.1%) were non-smokers; while the number of patients who had pertinent family history of ACS was 25 (9%).

Table No.1: Co Morbid Risk Factors and ECG Parton

Sr. No	Co morbid Risk Factor	Yes	No
1.	HTN	120 (43.1%)	158 (56.8%)
2.	DM	144 (51.7%)	134 (48.2%)
3.	Smoker	33 (11.9%)	245 (88.1%)
4.	FH of ACS	25 (9%)	253 (91%)
5.	LBBB	9 (3.2%)	269
6.	RBBB	7 (2.5%)	271

FH=Family History, LBBB=Left bundle branch block, RBBB=Right bundle branch block

Table 02 shows frequency of stress hyperglycemia based on admission RPG that was 70.5% (196) while 82 (29.5%) patients were normoglycemic.

Patients were further sorted into categories based on their admission RPG levels values into normal, pre-diabetic and diabetics. Patients with a normal admission RPG were 82 (29.5%) while patients who had impaired glucose tolerance (IGT) were 69 (24.8%) in number. The admission RPG showed 127 (45.7%) patients having a blood glucose in the range of being a diabetic. Prediabetic Patients and diabetic patients were further subjected to a fasting plasma glucose level as well to rule out stress hyperglycemia.

Table No.2: Frequency of Diabetes, Stress Hyperglycemia & IGT in ACS

Character	Observation	Normoglycemic	Stress Hyperglycemia		Total
Known Diabetic	No	55 (41.00%)	79 (58.95%)		134 (48.2%)
	Yes	27 (18.75%)	117 (81.25%)		144 (51.8%)
	Total	82(29.5%)	196(70.5%)		278
Stress Hyperglycemia			IGT	Diabetes	
			69(24.8%)	127(45.7%)	

IGT=Impaired Hyperglycemia

Table 2 also shows that frequency of Stress Hyperglycemia among known diabetics was 81.25% (117) while among non-diabetics it was 58.95% (n, 79). Patients with an elevated RPG were then subjected to a FBS in order to confirm the diagnosis of underlying diabetes mellitus. This was done to find out the cases which had not been diagnosed and presented to us with one of the complications, i.e ACS, of Diabetes Mellitus as shown in Table 03.

Table No.3: Frequency of Diabetes Mellitus Based On Fasting Blood Sugar

	Observation	Normoglycemic	Pre diabetics	Diabetics by FBS	Missing FBS	Total
Known Diabetics	No	5(3.73%)	5 (3.73%)	26 (19.40%)	98 (73.13%)	134 (48.2%)
	Yes	3(2.08%)	13 (9.0%)	82 (56.94%)	46 (31.94%)	144 (51.8%)
	Total	8(2.87%)	18 (6.47%)	108 (38.8%)	144 (51.79%)	278

It can be seen that out of the 196 (70.5%) patients with stress hyperglycemia, frequency of Incident DM and Pre Diabetes was 13.2% (n, 26) and 9.0% (13), respectively (Table 03). These cases presented with a complication of DM as ACS. There were 56.94% (n, 82) known diabetics having FBS in diabetic range. The total prevalence of Diabetic patients that presented to the CCU with a deranged blood sugar level was 108 (38.8%). These statistics are based on in hospital blood sugar values among patients with ACS.

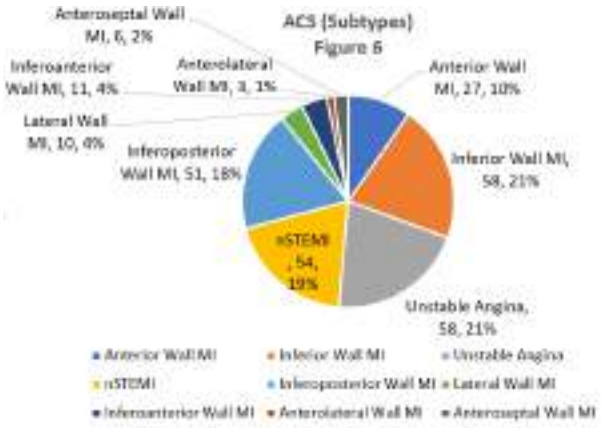


Figure No.1: Prevalence of Sub types of Acute Coronary Syndromes

Taking into account the previously (144) and current cases (26) of Diabetes the total comes down to 170 (61.2%) patients. A total of 144 patients were lost to follow-up and adequate blood sugar measurements which can suggest an underestimated level of undiagnosed diabetics in this study group.

Figure 01 shows the different types of ACS with their respective occurrence. Unstable angina and Inferior wall Myocardial Infarction were the most common ones. There was no significant [P=0.725] association seen between any specific type of ACS and stress hyperglycemia.

DISCUSSION

More male Patients (56.8%) were affected by ACS in this study. The Reykjavik study was entirely conducted on a male population due to the propensity of the disease to affect males more.[11] The disease affected 43.2% of females in our study, a comparatively lower population which is comparable to other studies.[12] The percentage of females being affected by Myocardial infarction is on the rise as shown by our study. The proportion of male patients was still higher as shown in a study conducted over a 25-year period showing hospitalizations due to myocardial infarction.[13]

Global estimates of undiagnosed Diabetes show that the prevalence is 45.8% which is between 24.1% to 75.1% for individual regions.[14] A 13.2% prevalence of undiagnosed diabetes was reported in our study which is underestimated due to loss of follow up of patients.

Trend in the incidence of ACS is also noted in this study which is shown by the increased cases of NSTEMI presenting to the CCU. A similar study carried out showed a rise in the incidence of NSTEMI.[15] Prevalence comparable to another study was seen which showed 61.7% patients with NSTEMI and 38.3% patients with STEMI.[16] Our study showed 59.7% patients showing ST Elevations Myocardial Infarctions.

The Frequency of stress hyperglycemia in our setup was found out to be 70.5%. This percentage is rather high considering the association of mortality with an acute hyperglycemic episode upon admission. In an

American study, the odds ratio of a high glucose level in different diabetic and non-diabetic groups was 2.44 for in-hospital mortality.[16] Similar articles showing a high mortality rate associated with stress hyperglycemia have also been documented which presented with acute myocardial infarction.[18, 19, 20].

CONCLUSION

There is higher prevalence of stress hyperglycemia and known diabetes mellitus with small number of incident diabetes in the present study.

Admission hyperglycemia can be a fatal condition in both diabetics and non-diabetic patients. A small proportion of patients are also undiagnosed diabetics with poor glucose control that present with Acute Myocardial Infarction. Admission hyperglycemia should prompt thorough investigation of underlying Diabetes to diagnose the condition early in order to start glycemic control and to reduce mortality.

Author's Contribution:

Concept & Design of Study:	Naveed Danish
Drafting:	Samiullah Khan, Muhammad Niaz Khan
Data Analysis:	Muhammad Saad Bin Nasir, Muhammad Kashif Iltaf, Hammad Shah
Revisiting Critically:	Naveed Danish, Samiullah Khan
Final Approval of version:	Naveed Danish

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Sarah W, Gojka R, Anders G, Richard S, Hilary K. Global Prevalence of Diabetes: Estimates for the year 2000 and projection for 2030. Diabetes Care 2004;27(5):1047–53.
2. Yusuf S, Hawken S, Ôunpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the Interheart study): case-control study. Lancet [Internet]. 2004 Sep 11 [cited 2018 Oct 1];364(9438):937–52. Available from: https://www.sciencedirect.com/science/article/pii/S0140673604170189
3. Marfella R, Siniscalchi M, Esposito K, Sellitto A, De Fanis U, Romano C, et al. Effects of stress hyperglycemia on acute myocardial infarction: role of inflammatory immune process in functional cardiac outcome. Diabetes Care [Internet]. 2003 Nov 1 [cited 2018 Oct 1];26(11):3129–35. Available from: http://www.ncbi.nlm.nih.gov/pubmed/14578250.
4. Arnold SV., Stolker JM, Lipska KJ, Jones PG, Spertus JA, McGuire DK, et al. Recognition of Incident Diabetes Mellitus During an Acute Myocardial Infarction. Circ Cardiovasc Qual Outcomes 2015 May [cited 2018 Sep 30];8(3):260–7. Available from: https://www.ahajournals.org/doi/10.1161/CIRCOUTCOMES.114.001452.
5. Oswald G, Corcoran S, Yudkin J. Prevalence and risks of hyperglycaemia and undiagnosed diabetes in patients with acute myocardial infarction. Lancet 1984 Jun 9 [cited 2018 Sep 30];323(8389):1264–7. Available from: https://www.sciencedirect.com/science/article/pii/S0140673684924474.
6. Wahab NN, Cowden EA, Pearce NJ, Gardner MJ, Merry H, Cox JL. Is blood glucose an independent predictor of mortality in acute myocardial infarction in the thrombolytic era? J Am Coll Cardiol 2002;40(10):1748–54. Available from: http://dx.doi.org/10.1016/S0735-1097(02)02483-X.
7. Arnold SV, Lipska KJ, Inzucchi SE, Li Y, Jones PG, McGuire DK, et al. The reliability of in-hospital diagnoses of diabetes mellitus in the setting of an acute myocardial infarction [Internet]. Vol. 2, BMJ Open Diabetes Res Care 2014;e000046. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25452878\nhttp://www.ncbi.nlm.nih.gov/pmc/articles/PMC4242083/pdf/bmjdrc-2014-000046.pdf.
8. Goyal A, Mehta SR, Díaz R, Gerstein HC, Afzal R, Xavier D, et al. Differential clinical outcomes associated with hypoglycemia and hyperglycemia in acute myocardial infarction. Circulation 2009;120(24):2429–37.
9. Stranders I, Diamant M, RE van G, et al. ADmission blood glucose level as risk indicator of death after myocardial infarction in patients with and without diabetes mellitus. Arch Intern Med 2004;164(9):982–8. Available from: http://dx.doi.org/10.1001/archinte.164.9.982.
10. Umpierrez GE, Isaacs SD, Bazargan N, You X, Thaler LM, Kitabchi AE. Hyperglycemia: An Independent Marker of In-Hospital Mortality in Patients with Undiagnosed Diabetes. J Clin Endocrinol Metab 2002 Mar 1 [cited 2018 Sep 30];87(3):978–82. Available from: https://academic.oup.com/jcem/article-lookup/doi/10.1210/jcem.87.3.8341
11. Sigurdsson E, Thorgeirsson G, Sigvaldason H, Sigfusson N. Unrecognized Myocardial Infarction: Epidemiology, Clinical Characteristics, and the Prognostic Role of Angina Pectoris: The Reykjavik Study. Ann Intern Med 1995 Jan 15 [cited 2019 Mar 28];122(2):96. Available from: http://annals.org/article.aspx?doi=10.7326/0003-4819-122-2-199501150-00003.
12. Perugini E, Maggioni AP, Boccanelli A, Di Pasquale G. [Epidemiology of acute coronary

syndromes in Italy]. G Ital Cardiol (Rome) [Internet]. 2010 Oct [cited 2019 Mar 28];11(10):718–29. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21246773.

13. Schmidt M, Jacobsen JB, Lash TL, Bøtker HE, Sørensen HT. 25 year trends in first time hospitalisation for acute myocardial infarction, subsequent short and long term mortality, and the prognostic impact of sex and comorbidity: a Danish nationwide cohort study. BMJ 2012 Jan 25 [cited 2019 Mar 28];344:e356. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22279115.
14. Beagley J, Guariguata L, Weil C, Motala AA. Global estimates of undiagnosed diabetes in adults. Diabetes Res Clin Pract [Internet]. 2014 Feb 1 [cited 2019 Mar 28];103(2):150–60. Available from: https://www.sciencedirect.com/science/article/pii/S0168822713003847.
15. Ruff CT, Braunwald E. The evolving epidemiology of acute coronary syndromes. Nat Rev Cardiol [Internet]. 2011 Mar 21 [cited 2019 Mar 28];8(3):140–7. Available from: http://www.nature. com/articles/nrcardio.2010.199.
16. Rizzello V, Lucci D, Maggioni AP, Giampaoli S, Greco C, Pasquale G Di, et al. Clinical epidemiology, management and outcome of acute coronary syndromes in the Italian network on acute coronary syndromes (IN-ACS Outcome study). Acute Card Care [Internet]. 2012 Jun 27 [cited 2019 Mar 28];14(2):71–80. Available from: http://www.tandfonline.com/doi/full/10.3109/17482941.2012.655296.
17. Wahab NN, Cowden EA, Pearce NJ, Gardner MJ, Merry H, Cox JL, et al. Is blood glucose an independent predictor of mortality in acute myocardial infarction in the thrombolytic era? J Am Coll Cardiol 2002 Nov 20 [cited 2019 Mar 29];40(10):1748–54. Available from: http://linkinghub.elsevier.com/retrieve/pii/S07351097020248 3X
18. Ishihara M. Acute Hyperglycemia in Patients With Acute Myocardial Infarction. Circ J 2012;76(3):563–71.
19. Peng XR, Zhao YF, Zou DJ, Gu P. Zhongguo Wei Zhong Bing Ji Jiu Yi Xue 2011;23(6):322-328.
20. Zhao S, Murugiah K, Li N, et al. Admission Glucose and In-hospital Mortality after Acute Myocardial Infarction in Patients with or without Diabetes: A Cross-sectional Study. Chin Med J (Engl) 2017;130(7):767-775.

Original Article

Evaluation of Buccal Corridor Effects on Smile Esthetics Among the Patients Seeking Orthodontic Treatment: A Cross Sectional Study

Abdul Jabbar[1], Nadeem Hussain[3], Irfan Ahmed Shaikh[2], Uzma Bashir[2] and Tariq Aziz[4]

ABSTRACT

Objective: The objective of this study was to determine the effect of buccal corridors preferred by orthodontists and post graduate residents.

Study Design: cross sectional study

Place and Duration of Study: This study was conducted at the Department of Orthodontic, Liaquat University of Medical and health Sciences, Jamshoro from 01-12-2016 to 08-11-2017.

Materials and Methods: Total 58 subjects were included in this study. All subjects were with normal morphology of dentition with the possible exception of 3rd molars. Full face frontal smiling view photographs were taken with Samsung digital camera at standard setting of 10 mega pixels. The buccal corridor was measured as the difference of the visible maxillary dentition and inner commissural width. Each slide of every photograph that was the buccal corridor edited in 5 sub titles such as Broad Buccal Corridor, Medium Broad Buccal Corridor, Medium Buccal Corridor, Narrow Medium Buccal Corridor, and Narrow Buccal Corridor. All photographs were shown by power point through laptop to a consultants and residents of orthodontics for independent evaluation of photographs and aesthetic acceptability. The participants were asked to select preferred buccal corridor. Data was analyzed using SPSS version 18.

Results: The mean age was 30.28±5.251. The medium broad buccal corridor was 19%, medium buccal corridor was 32.8 %. Medium Narrow broad buccal corridor was 10.3% and narrow buccal corridor was 37.9%. The preferred choice is highest in narrow buccal corridor that is 37.92 among others. The preferred choice of area was selected as 50% in LUMHS Jamshoro followed by 45% in University of Lahore. The preferred choice was statistically insignificant with specialty (p-0.308) and gender (p-0.555).

Conclusion: This study concluded that there is no significant difference when judging the effects of buccal corridors on the smile attractiveness between the male and female raters, for both the consultants and residents. Both preferred narrow buccal corridor to medium and broader buccal corridors.

Key Words: Buccal corridor, esthetics, smile perception

Citation of article: Jabbar A, Hussain N, Shaikh IA, Bashir U, Aziz T. Evaluation of Buccal Corridor Effects on Smile Esthetics Among the Patients Seeking Orthodontic Treatment: A Cross Sectional Study. Med Forum 2021;32(10):132-136.

INTRODUCTION

1. Department of Orthodontics / Prosthodontics[2], Liaquat University of Medical and Health Sciences, Jamshoro.
3. Garhi Khuda Bux Bhutto, Larkana.
5. Muhammad Dental College, Mirpurkhas

Correspondence: Dr. Abdul Jabbar, Associate Professor of Orthodontics, Liaquat University of Medical and Health Sciences, Jamshoro
Contact No: 0333-2608489
Email: a_jabbar_lumhs@hotmail.com

Received: February, 2021
Accepted: August, 2021
Printed: October, 2021

Facial esthetics is a subjective and it vary from person to person and with different cultures.[1] The smile is very important for every individual and in every culture and it must be respected and measured, there is literature that smile has the most important role in the facial esthetics.[2]

There are multiple features which are assessed in a smile such as smile arc[3], incisal and gingival show, alignment of dentition, tooth color and shape[4,5,6], and buccal corridor[4]. Out of all these feature buccal corridor has important effect on smile. Buccal corridor also named as lateral dark space or lateral negative space. It is the space that appears during smiles between the maxillary posterior teeth and corners of the mouth and cheeks[7]. The space depends on width of the upper dental arch and the facial soft tissues responsible for the breadth of the smile[8].

The actual size of buccal corridor available in literature is based on clinical observations[9]. In most of studies it is showed that narrow buccal corridor has positive effect on smile esthetics. Some researchers noted that buccal corridor width does not affect the smile attractiveness. A very low significance of transverse features on smile esthetics has been shown by Isiksal et al[10]. While some researchers believe that lateral negative space effects smile esthetics when it becomes excessively wide[4]. In orthodontics there is "paradigm shift" which focus on facial esthetics[11]. Edward Angle believed that ideal occlusion would result in ideal facial esthetics. Despite importance to occlusion on smile there is very little literature on esthetic smile[12]. The perception of smile is very important to orthodontists, orthodontic patients are very anxious about smile along with their static appearance. Literature has shown that importance of smile esthetics has enforced orthodontists to make treatment plan based on facial profile and smile. The purpose of this study was to evaluate the buccal corridor effects on smile esthetics among the patients seeking orthodontic treatment in Jamshoro[13].

MATERIALS AND METHODS

The approval was obtained from ethical review committee of institute. An informed consent was taken from raters which were part of my study. A cross sectional study was conducted from 01-12-2016 to 08-11-2017 at Department of Orthodontics, Institute of Dentistry LUMHS Jamshoro. The patients were recruited with simple random sampling technique. Sample size was calculated using the W.H.O calculator version 2.2 a, by taking the prevalence 76.72% of buccal corridor chosen by the Dentist[10] at 95% confidence interval and 11 % margin of error. The sample size calculated by this statistic was (n=58). The inclusion criteria were participants with age ranges from 20-60 years, both male and female, participants in normal skeletal class 1,SNA =82 Degree, SNB 80 degree ,Dental class 1, normal over jet (2mm) and normal overbite (33.3 %) and the consultants and trainees having minimum experience of 2 years in orthodontics. The exclusion criteria were participants having missed teeth affecting the appearance during smile, those who were not available at the day of visit, those who were not giving consent and orthodontic treatment before study.

Data collection procedure: All participants with normal morphology of dentition with the possible exception of 3rd molars full face frontal smiling view photographs were taken with Samsung digital camera at standard setting of 10 mega pixels, at auto mode, at a distance of 2 feet. A pure white back ground was used for the pictures. The cropping and editing of all the photographs were made using Adobe Photoshop Version 7.0. Calculation of smile fullness was defined as the visible maxillary dentition width divided by the inner commissural width, while buccal corridor is measured as the difference of the visible maxillary dentition and inner commissural width. Each slide of every photograph that was the buccal corridor edited in 5 sub titles such as Broad Buccal Corridor, Medium Broad Buccal Corridor, Medium Buccal Corridor, Narrow Medium Buccal Corridor, and Narrow Buccal Corridor. All (as per operational definition) photographs were shown by power point through laptop to a consultants and residents of orthodontics for independent evaluation of photographs and aesthetic acceptability. The purpose and the procedure of the study were explained to the participants and asked to select preferred buccal corridor. The data of gender, age, qualification and the institute were recorded in proforma.

Data Analysis: The analysis was conducted by using SPSS version 18. Mean and standard deviation were calculated for quantitative variables like age. Frequency and percentages were presented for qualitative variables like gender, type of institute, city, and preferred buccal corridor. Chi-square was applied to check the statistical difference. p value <or equal to 0.05 was considered as significant.

RESULTS

The male and female were 33% and 67% respectively. The medium broad buccal corridor was observed 19%, Medium buccal corridor as 33% Medium narrow buccal corridor as 10% and narrow buccal corridor as 38%.

Table No.1: Descriptive statistics of preferred choices, specialty, Duration of experience and type of institutes

Characteristics	Frequency	Percent
Preferred choice		
Medium Broad Buccal Corridor (MBBC)	11	19.0
Medium Buccal Corridor (MBC)	19	32.8
Medium Narrow Buccal Corridor (MNBC)	6	10.3
Narrow Buccal Corridor (NBC)	22	37.9
Specialty		
Residents	44	75.9
Consultants	14	24.1
Duration of experience of residents and consultants		
Less than 3 year	1	1.7
Less than 5 years	44	75.9
Less than 10 years	9	15.9
Less than 15 years	2	3.4
More than 15 years	2	3.4
Institutes		
University of Lahore	26	44.8
LUMHS Jamshoro	29	50
Bhittai Dental College	3	5.2
Total	58	100

The residents and consultants were 76% and 24% respectively. According to experience the participants having experience less than 3 year (2%) less than 5 year (77%), less than 10 years (16%) and less than 15 years (3%) and more than 15 years (3%). The preferred choice of area was selected as 50% in LUMHS Jamshoro followed by 45% in University of Lahore and 5% in Bhittai Dental College (Table-1).

According to preferred choice of Residents chosen MBC as 34%, MNBC as 11% and NBC as 32%, whereas consultants chosen MBBC (7%), MBC (29%), MNBC (7%) and NBC (57%). The relationship was not statistically significant (p-0.308) as shown in Table-2

According to the gender based preferred choice the male chosen MBC and NBC (37%), whereas the female chosen MBC (31%), NBC (39%). The relationship was not statistically significant (p-0.555) as shown in Table-3.

Table No.2: Specialty based preferred choice

	Preferred Choice				Total	P-Value
Specialty	Medium Broad Buccal Corridor	Medium Buccal Corridor	Medium Narrow Buccal Corridor	Narrow Buccal Corridor		
Resident	10	15	5	14	44	
	22.7%	34.1%	11.4%	31.8%	100.0%	0.308
Consultant	1	4	1	8	14	
	7.1%	28.6%	7.1%	57.1%	100.0%	
Total	11	19	6	22	58	
	19.0%	32.8%	10.3%	37.9%	100.0%	

Table No.3: Gender Base Preferred Choice

	Preferred Choice				Total	P-VALUE
Gender	Medium Broad Buccal Corridor	Medium Buccal Corridor	Medium Narrow Buccal Corridor	Narrow Buccal Corridor		
Male	2	7	3	7	19	
	10.5%	36.8%	15.8%	36.8%	100.0%	0.555
Female	9	12	3	15	39	
	23.1%	30.8%	7.7%	38.5%	100.0%	
Total	11	19	6	22	58	
	19.0%	32.8%	10.3%	37.9%	100.0%	

DISCUSSION

Increasing numbers of adults are seeking orthodontic care[15]. In literature many researchers have compared smiles with different buccal corridor width[15-19] Some researchers customized the same smile by adding or reducing number of teeth,[15,17] changing the mesio-distal diameter of posterior teeth,[20] or modifying the transverse width of posterior teeth.

This study resulted that buccal corridor was altered by modifying tooth position of upper canines, although the dark space can only be shown distal to the canines. The position and angulations of these teeth effect the size and shape of space. This is the reason that canines have important role in forming the dental arch. The study conducted by Nascimento DC et al[4] compared modified pictures in Full-face and close-up of the mouth. Their study revealed no significant difference between the two views (p>0.05). In this research only close-up view of the mouth was assessed. This study noted difference in buccal corridor preference according to gender. Parekh et al[15] and Moore et al[17] also resulted same in comparison to our results. The results of this research confirmed that varying lateral dark space significantly affected smile esthetics. These results were affected by gender, differing with the findings of Moore et al[16] who found that male and female do not hinder with the decision of facial attractiveness. In this study the narrow buccal corridor (38%) was considered the most pleasant. This result was different from studies done by Gracco et al,[21] in which Buccal corridor equivalent to 18.46% of the width of the smile were found more acceptable. Such variations may have occurred due to the fact that in the study by Moore et al[16] the Buccal

corridor was measured on inner commissures and there may also be difference of population. This difference may need further research involving different esthetic parameters for individual. This research studied the effects of buccal corridors on smile attractiveness by orthodontics consultants and residents. Esthetic score did not show significant difference between the male and female raters for the orthodontics consultants and residents, which are in agreement with Moore et al[16] .

In this research, the orthodontics consultants and residents have same inclination in ranking the liking of lateral dark spaces. Parekh et al[15] resulted that lay person and orthodontists have same preferences when smile arcs and buccal corridors are considered together. Krishnan et al[3] also pointed that there was no difference between lay persons and dental specialists on smile evaluation. In this study orthodontics consultants preferred the narrow buccal corridor and residents preferred medium buccal corridor. Hulsey,[22] and Roden-Johnson et al [18] found that buccal corridor was not an important issue for assessing smile attractiveness. This study resulted that effects of buccal corridors on smile esthetics can be evaluated from mouth view. The exact cause of this difference is not clear. The raters may consider a 15% buccal corridor as less attractive. Orthodontists should keep in mind that small change in buccal corridor may considerably effect the perception of smile esthetics. During diagnosis and treatment planning it is important to assess not only the dental arch width but also the alveolar bone width. However, it is important to keep in mind that this study used artificial images and therefore should not be used for all patients.

The findings of this research are guidelines, and should be applied with vigilance, taking into consideration, the individual characteristics of every patient and their esthetic expectations.

CONCLUSION

This study concluded that there is no significant difference when judging the effects of buccal corridors on the smile attractiveness between the male and female raters, for both the consultants and residents. Both preferred narrow buccal corridor to medium and broader buccal corridors.

Author's Contribution:

Concept & Design of Study:	Abdul Jabbar
Drafting:	Nadeem Hussain, Irfan Ahmed Shaikh
Data Analysis:	Uzma Bashir, Tariq Aziz
Revisiting Critically:	Abdul Jabbar, Nadeem Hussain
Final Approval of version:	Abdul Jabbar

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Van der Geld P, Oosterveld P, Heck GV, Kuijpers-Jagtman AM. Smile attractiveness: self-perception and Influence on Personality. Angle Orthod 2007;77(5):759-75.
2. Kokich VO, Kiyak HA, Shapiro PA. Comparing the perception of dentists and lay people to altered dental esthetics. J Esthet Dent 1999 11(6):311-24.
3. Krishnan V, Daniel ST, Lazar D, Asok A. Characterization of posed smile by using visual analog scale, smile arc, buccal corridor measures, and modified smile index. Am J Orthod Dentofacial Orthop 2008;133(4):515-23.
4. Nascimento DC, Santos ER, Machado AW, Bittencourt MAV. Influence of buccal corridor dimension on smile esthetics. Dental Press J Orthod 2012 17(5):145-50.
5. Kokich VO, Kokich VG, Kiyak HA. Perceptions of dental professionals and laypersons to altered dental esthetics: asymmetric and symmetric situations. Am J Orthod Dentofacial Orthop 2006;13(2):141-51.
6. Suzuki L, Machado AW, Bittencourt MAV. An evaluation of the influence of gingival display level in the smile esthetics. Dental Press J Orthod 2011;16(5):37-39.
7. Machado AW, Moon W, Gandini Jr LG. Influence of maxillary incisor edge asymmetries on the perception of smile esthetics among orthodontists and laypersons. Am J Orthod Dentofacial Orthop 2013;143(5):658-64.
8. Correa BD, Bittencourt MAV, Machado AW. Influence of maxillary canine gingival margin asymmetries on the perception of smile esthetics among orthodontists and laypersons. Am J Orthod Dentofacial Orthop 2014;145:55-63.
9. Machado AW, Moon W, Campos E, Gandini Jr LG. Influence of spacing in the upper lateral incisor area on the perception of smile esthetics among orthodontists and laypersons. J World Federation of Orthodontists 2013;25(2): e169e174.
10. Işıksal E, Hazar S, Akyalçın S. Smile esthetics: perception and comparison of treated and untreated smiles. Am J Orthodontics Dentofacial Orthopedics 2006;129(1):8-16.
11. Ackerman JL, Proffit WR, Sarver DM. The emerging soft tissue paradigm inorthodontic diagnosis and treatment planning. Clin Orthod Res 1999;2(2):49-52.
12. Angle E. Malocclusion of the Teeth. 7 ed. Philadelphia: SS White Dental Mfg Co 1907; 132-40.
13. Lombardi RE. The principles of visual perception and their clinical application todenture esthetics. J Prosthet Dent 1973;29(4):358-82.

14. Sarver DM, Ackerman JL. Orthodontics about face: the re-emergence of the esthetic paradigm. Am J Orthod Dentofacial Orthop 2000;117(5): 575-6.
15. Parekh S, Fields HW, Beck FM, Rosenstiel SF. The acceptability of variations in smile arc and buccal corridor space. Orthod Craniofac Res 2007;10(1):15-21.
16. Moore T, Southard KA, Casko JS, Qian F, Southard TE. Buccal corridors and smile esthetics. Am J Orthod Dentofacial Orthop 2005;127(2): 208,13; 261-63.
17. Roden-Johnson D, Gallerano R, English J. The effects of buccal corridor spacesand arch form on smile esthetics. Am J Orthod Dentofacial Orthop 2005;127(3):343-50.
18. Ritter DE, Gardini LG, Pinto A, Locks A. Esthetic influence of negative space in thebuccal corridor during smiling. Angle Orthod 2006;76(2):198-03.
19. Yang IH, Nahm DS, Baek SH. Which hard and soft tissue factors relate withthe amount of buccal corridor space during smiling? Angle Orthod 2008;78(1):5-11.
20. Camara CALP. EstéticaemOrtodontia: Diagramas de ReferênciasEstéticasDentárias (DRED) e Faciais (DREF). R Dental Press OrtodonOrtop Facial. 2006 11(6)1308-56.
21. Gracco A, Cazzani M, D'Elia L, Manfrini M, Peverada C, Siciliani G. The smilebuccal corridors: esthetic value for dentists and laypersons. Prog Orthod 2006;7(1):56-65.
22. SSHulsey CM. An esthetic evaluation of lip-teeth relationships present in the smile. Am J Orthod 1970;57(2):132-44.

Original Article

Chronic Effects of Nicotine on Serum Lipid Profile and Oxidative Stress: An Experimental Study

Shabana Saeed[1], Muhammad Athar Khan[2], Muhammad Azhar Hussain[3], Zunairah Rais[4], Kamal Ahmed[4] and Tabinda Ashfaq[5]

ABSTRACT

Objective: To examine the chronic effect of nicotine on serum lipid profile and oxidative stress in male mice.
Study Design: An Experimental Animal Study
Place and Duration of Study: This study was conducted at the Department of Biochemistry, Liaquat College of Medicine & Dentistry, Karachi from February 2020 to April 2020 for a period of two months.
Materials and Methods: Adult male BALB/C mice weighing 25-30 gm were housed in six cages under light and dark settings at 25ºC and fed lab chow and water ad libitum under regular housing circumstances. Two sets of mice were created (control and test). There were 12 mice in each group. The drug-treated group received nicotine hydrogen tartrate (3.08 mg/ml) in 100 mL of drinking water for 28 days, whereas the control group got tap water.
Results: After chronic nicotine delivery, there was a significant difference in glucose concentration, body weight, and plasma albumin concentration (P<0.01). Between the control and test groups, there was a significant difference in LDL-C and triglycerides (P<0.001). The levels of total cholesterol and HDL-C are unaltered. MDA levels in the liver (P<0.001), reduced glutathione and catalase activity (P<0.01), and brain MDA, reduced glutathione and catalase activity (P<0.01), (P<<0.001), and (P0.001), respectively, were all determined to be significant.
Conclusion: In conclusion chronic administration of nicotine caused change in lipid profile, promoted lipid peroxidation and significantly reduced liver antioxidant enzyme activities in mice. It could be inferred that nicotine users have increased LDL-C and triglycerides which makes them more vulnerable to cardiovascular events.
Key Words: Serum Lipid Profile, Oxidative Stress, Chronic, Tobacco

Citation of article: Saeed S, Khan MA, Hussain MA, Rais Z, Ahmed K, Ashfaq T. Chronic Effects of Nicotine on Serum Lipid Profile and Oxidative Stress: An Experimental Study. Med Forum 2021;32(10):137-140.

INTRODUCTION

Smoking is one of the most important risk factors for the development of coronary atherosclerosis and coronary heart disease. Smoking, which is a known risk factor for the development of ischemic heart disease, can cause a change in the normal plasma lipoprotein pattern.[1] Elevated Total lipid levels are thought to play a role in the progression of atherosclerosis.[2]

[1.] Department of Biochemistry / Community Medicine[2] / Medicine[3], Liaquat College of Medicine & Dentistry, Karachi.
[4.] Department of Medicine, Liaquat National Medical College, Karachi.
[5.] Department of Family Medicine, Jinnah Sindh Medical University, Karachi.

Correspondence: Dr. Muhammad Athar Khan, Department of Community Medicine, Liaquat College of Medicine & Dentistry, Karachi.
Contact No: 0323-2135932
Email: matharm@yahoo.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

Triglyceride levels were also shown to be greater in smokers than in non-smokers. According to recent research, triglyceride levels are the most major element in the development of CHD.[3] Nicotine is one of the most common chemicals found in tobacco smoke. Nicotine raises the levels of triglycerides, cholesterol, and VLDL while lowering the levels of HDL. Cluette Brown found that Long-term oral nicotine intake was also found to raise LDL cholesterol while lowering HDL cholesterol.[4] Nicotine has been demonstrated to increase the circulatory pool of atherogenic LDL by speeding up the transfer of lipids from HDL and hindering LDL clearance from the plasma compartment, resulting in more LDL cholesterol deposition in the arterial wall.[5]

An oxidative stress is defined as a lack of equilibrium between reactive oxygen species (ROS) production and antioxidant defenses, which results in free radicals and, as a result, malondialdehyde (MDA) formation due to membrane lipid peroxidation.[6,7] Nicotine administration has been shown to reduce endogenous antioxidant status, such as superoxide dismutase (SOD) and glutathione peroxidase (GPX) activity.[8]

Previous study has shown that smoking reduces insulin sensitivity, promotes insulin resistance, and increases cardiovascular risk factors such greater plasma triglycerides, decreased HDL-C, and hyperglycemia. A

lot of studies have connected smoking to metabolic abnormalities and metabolic syndrome.[9-11]

Chronic nicotine treatment in forced swim mice fails to alleviate depression-like symptoms, worsens lipid profiles, and impairs glucose homeostasis, which could be linked to a higher risk of cardiovascular disease and depression in chronic smokers, particularly those who live in stressful situations.[12] This experimental study was designed to examine the chronic effect of nicotine on serum lipid profile and oxidative stress in male mice.

MATERIALS AND METHODS

The following animal procedures were carried out in strict accordance with the standards for the care and use of laboratory animals published by the National Research Council (1996). The institutional animal ethics committee at the University of Karachi provided their approval. All efforts were taken to keep the number of animals as low as possible, as well as any pain or anguish they might experience. Adult male BALB/C mice weighing 25-30 gm were kept in six cages at 25ºC, with light and dark settings, and fed lab food and water ad libitum under normal living conditions. There were two sets of mice developed (control and test). Each group consisted of 12 mice. The drug-treated group received nicotine hydrogen tartrate (3.08 mg/ml) in 100 mL of drinking water for 28 days, whereas the control group received tap water. Animals were decapitated after the last treatment. Blood was drawn and centrifuged for 30 minutes at 4000 rpm. The serum was separated as a supernatant and kept at –20°C until further analysis.

Serum Parameters Analysis the O-toluidine technique was used to determine serum glucose concentrations. [13] The dye-binding technique was used to assess serum albumin concentrations. [14] Kit technique was used to calculate serum cholesterol, triglycerides, HDL-C, and LDL-C (Randox®, Private Ltd). Determination of serum Protein by Lowry's Method (1951). Colorimetric Assay of Catalase by Sinha et al., 1972, Estimation of Reduced Glutathione by Ellman (1959) and Determination of Malonaldehyde with Thiobarbituric Acid Test by Uchiyama and Mihara (1977). Drugs and Chemicals Sigma Chemical Co. provided Nicotine Hydrogen (+)-tartrate. The rest of the compounds were of analytical quality.

All data are expressed as the mean minus the standard error of the mean. A two-tailed student t-test was used to determine the significance of the difference between the comparing means. If the accompanying P (probability of error) values were less than 0.05, all values were considered statistically significant.

RESULTS

The effects of nicotine on glucose concentration, body weight, and plasma albumin concentration in mice are shown in Figure 1. After chronic nicotine delivery, there was a significant difference in glucose concentration, body weight, and plasma albumin concentration ($P<0.01$).

The effects of chronic nicotine delivery on the lipid profile in mice are shown in Table 1. Between the control and test groups, there was a significant difference in LDL-C and triglycerides ($P<0.001$). The levels of total cholesterol and HDL-C are unaltered.

Table 2 shows the effects of chronic administration of nicotine on liver oxidative stress parameters in mice. A significant difference was found between MDA levels ($P<0.001$), reduced glutathione and catalase activity ($P<0.01$). Table 2 reveals the impact of prolonged nicotine delivery on the oxidative stress status of mice's brains. MDA, reduced glutathione, and catalase activity were all shown to be substantially different ($P<0.01$, $P<0.001$), ($P<0.001$), and ($P<0.001$), respectively.

Table No.1: Effects of chronic nicotine administration on plasma lipid Profile

Parameter	Control mean ± SEM	Test mean ±SEM	p-value
Total Cholesterol (mg/dl)	163.9±13.01	192.3±14.4	>0.05
HDL-Cholesterol (mg/dl)	36.5±2.95	32.52±1.58	>0.05
LDL-Cholesterol (mg/dl)	49.2±4.43	66.8±3.01	<0.001
Triglycerides (mg/dl)	70.6±2.26	85.5±3.53	<0.001

Table no.2: Effect of Chronic Nicotine Administration on Liver & Brain Antioxidant Status

Parameter		Control mean ± SEM	Test mean ± SEM	p-value
Liver	MDA (nM/g of tissue)	22.4±0.25	25.8±0.46	<0.001
	Reduced Glutathione (µM/g of tissue)	6.3±0.21	4.4±0.88	<0.01
	Catalase (µM/min/mg of protein)	0.1±0.00	0.07±0.00	<0.01
Brain	MDA (nM/g of tissue)	15.8±0.28	18.1±0.65	<0.01
	Reduced Glutathione (µM/g of tissue)	2.3±0.2	5.08±0.47	<0.001
	Catalase (µM/min/mg of protein)	0.13±0.003	0.2±0.01	<0.001

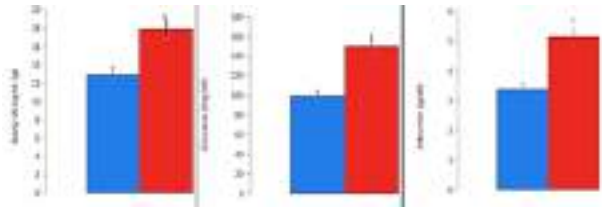


Figure No.1: Effects of Chronic Nicotine Administration on Plasma Glucose Concentration, Body Weight and Plasma Albumin Concentration

DISCUSSION

The current study reveals that giving mice nicotine (3.08 mg/kg/day) for four weeks boosts their body weight and glucose levels. Previous studies suggested that smoking itself may triggers metabolic syndrome by increasing body weight and glucose concentration. Increased glucose concentration causes more glucose to reach pancreatic beta cells, whereas increased glycolysis speeds up insulin secretion. Smoking is likely to promote insulin resistance directly. [15] As a result, smoking raises the risk of metabolic syndrome and diabetes, which, in turn, raises the risk of cardiovascular disease.

Our results indicate that chronic nicotine treatment increases plasma albumin concentration. Recent studies in contrast with our results showed that Plasma albumins are lower in smokers because albumin has an antioxidant characteristic that can be observed by increased oxidative stress.[16,17] Nicotine therapy also elevated triglycerides and LDL-C levels in mice. Serum HDL-C, on the other hand, remained unchanged. These findings are consistent with Bibi et al earlier findings (2011).[18] Our results is consistent with previous studies that cigarette leads to increase in the concentration of serum total cholesterol, triglycerides, LDL-cholesterol, VLDL-cholesterol and fall in the levels of anti atherogenic HDL- cholesterol, as reported by Muscat.[19] Nicotine stimulates adrenaline secretion, which causes glucose to be released from the liver into the bloodstream. We found MDA levels were increased while reduced glutathione and catalase levels were decreased. Our findings are in line with research that show elevated MDA levels cause lipid peroxidation.[20] In nicotine-treated rats, increased lipid peroxidation products are linked to poorer activity of cleaning enzymes such as glutathione and catalase.[21]

In our study brain MDA levels, reduced glutathione and catalase activities were increased in nicotine administered mice. In contrast to our findings, Baskaran et al. found no significant difference in brain MDA levels across rats, implying that nicotine did not promote free radical-mediated tissue damage in the hippocampus. However, our findings are in line with prior research, which found that when 3mg/kg of nicotine was administered, the level of reduced glutathione increased. Furthermore, CAT levels rose considerably.[22] Nicotine administration, according to some, can cause oxidative stress by causing the production of reactive oxygen species in the peripheral and central nervous systems.[23] Furthermore, it has been suggested that nicotine at extremely low doses may function as an antioxidant and play an essential part in its neuroprotective action, but a high dose of nicotine may cause neurotoxicity and induce oxidative stress[24].

CONCLUSION

In mice, chronic nicotine administration changed their lipid profile, accelerated lipid peroxidation, and dramatically lowered liver antioxidant enzyme activity, according to this study. Nicotine smokers are thought to have higher LDL-C and triglycerides, making them more sensitive to cardiovascular problems. Therefore, by quitting smoking and regulating metabolic risk variables reduces the chance of significant adverse cardiovascular events.

Author's Contribution:

Concept & Design of Study:	Shabana Saeed, Muhammad Azhar Hussain, Muhammad Athar Khan
Drafting:	Zunairah Rais, Kamal Ahmad
Data Analysis:	Muhammad Athar Khan, Tabinda Ashfaq
Revisiting Critically:	Zunairah Rais, Kamal Ahmad, Tabinda Ashfaq
Final Approval of version:	Shabana Saeed, Muhammad Azhar Hussain, Muhammad Athar Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Stallones RA. The association between tobacco smoking and coronary heart disease. Int J Epidemiol 2015;44(3):735-43.
2. Linton MRF, Yancey PG, Davies SS, Jerome WG, Linton EF, Song WL, et al. The Role of Lipids and Lipoproteins in Atherosclerosis. [Updated 2019 Jan 3]. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK343489/
3. Upadhyay RK. Emerging risk biomarkers in cardiovascular diseases and disorders. J Lipids 2015;2015:971453.
4. Rao Ch S, Subash YE. The effect of chronic tobacco smoking and chewing on the lipid profile. J Clin Diagn Res 2013;7(1):31-4.

5. Hojnack JM, Cluette-Brown J. Oral nicotine impairs clearance of plasma Low Density Lipoproteins. Proc Soc Exp Biol Med 1986:182;414-18.
6. Betteridge DJ. What is oxidative stress? Metabolism 2000;49(2 Suppl 1):3-8.
7. Srinivasan KN, Pugalendi K. Effect of excessive intake of thermally oxidized sesam oil on lipids, lipid peroxidation and antioxidants status in rats. Ind J Exp Biol 2000:38;777-80.
8. Agarwal P, Bagewadi A, Keluskar V, Vinuth DP. Superoxide dismutase, glutathione peroxidase, and catalase antioxidant enzymes in chronic tobacco smokers and chewers: A case-control study. Ind J Dent Res 2019;30(2):219-225.
9. Benowitz NL. Cigarette smoking and cardiovascular disease: pathophysiology and implications for treatment. Progress in Cardiovascular Diseases 2003;46(1):91–111.
10. Thelle DS, Sharper AG. Blood lipids in middle-aged Britishmen. Br Heart J 1983: 49;205-13.
11. Kim SW, Kim HJ, Min K, Lee H, Lee SH, Kim S, et al. The relationship between smoking cigarettes and metabolic syndrome: A cross-sectional study with non-single residents of Seoul under 40 years old. PLoS One 2021;16(8):e0256257.
12. Facchini FS, Hollenbeck CB, Jeppesen J, Chen YD, Reaven GM. Insulin resistance and cigarette smoking. Lancet 1992; 339:1128-30.
13. Targher G, Alberiche M, Zenere MB, Bonadonna RC, Muggeo M, Bonora E. Cigarette smoking and insulin resistance in patients with noninsulin-dependent diabetes mellitus. J Clin Endocrinol Metab 1997;82(11): 3619-24.
14. Dumas BT, Watson WA, Biggs HG. Albumin standards and the measurement of serum albumin with bromcresol green. 1971. Clin Chim Acta 1997;258(1):21-30.
15. Artese A, Stamford BA, Moffatt RJ. Cigarette Smoking: An Accessory to the Development of Insulin Resistance. Am J Lifestyle Med 2017;13(6):602-605.
16. Roohi N, Mehjabeen, Ashra S. Effect of cigarette smoking on serum proteins profile in male active and passive smokers. Punjab Univ J Zool 2017;32(2): 209-215.
17. Shaika FB, Nagajothi G, Swarnalatha K, Kumar CS, Rajendra W, Maddu N. Correlation between smokeless tobacco (Gutkha) and biomarkers of oxidative stress in plasma with cardiovascular effects. Heliyon 6 2020;e05487.
18. Bibi Z, Saeed S and Bano S. Metabolic and Behavioral Effects of Nicotine in Swim Stressed Mice. J Pharm Nutr Sciences 2011;1:54-60.
19. Muscat JE, Harris RE, Haley NJ, Wynder EL. Cigarette smoking and plasma cholesterol. Am Heart J. 1991;121(1 Pt 1):141-7.
20. Suleyman H, Gumustekin K, Taysi S, Keles S, Oztasan N, Aktas O, et al. Beneficial effects of Hippophae rhamnoides L. on nicotine induced oxidative stress in rat blood compared with vitamin E. Biol Pharm Bull 2002;25(9):1133-6.
21. Helen A, Krishnakumar K, Vijayammal PL, Augusti KT. Antioxidant effect of onion oil (Allium cepa. Linn) on the damages induced by nicotine in rats as compared to alpha-tocopherol. Toxicol Lett 2000;116(1-2):61-8.
22. Jain A, Flora SJ. Dose related effects of nicotine on oxidative injury in young, adult and old rats. J Environ Biol 2012;33(2):233-8.
23. Qiao D, Seidler F, Slotkin T. Oxidative mechanisms contributing to the developmental neurotoxicity of nicotine and chlorpyrifos. Toxicol Appl Pharmacol 2005;206:17–26.
24. Guan ZZ, Yu WF, Nordberg A. Dual effects of nicotine on oxidative stress and neuroprotection in PC12 cells. Neurochem Int 2003;43(3):243-9.

Original Article

Association Between Vitamin D, Calcium, Alkaline Phosphatase and Lipid Profile in Male and Female Subjects

Farhan Jaleel[1], Shabana Saeed[1], Sara Altamash[5], Waqar Hussain[2], Al-Farah Rehmat Ullah[3] and Muhammad Athar Khan[4]

ABSTRACT

Objective: To determine the association between vitamin D, Calcium, alkaline phosphatase and lipid profile in male and female subjects.

Study Design: Cross-Sectional Study

Place and Duration of Study: This study was conducted at the Darul-Sehat Hospital Karachi's outpatient department from July 2018 to January 2019 for a period of seven months.

Materials and Methods: A total of 100 male and female individuals between the ages of 40 and 60 were chosen. Vitamin D, lipid profile, alkaline phosphatase, and calcium levels were all tested in the individuals' blood. The participants were divided into two groups: those who had adequate vitamin D levels and those who were deficient in vitamin D.

Results: Total cholesterol and TGs were found to be higher in both male and female participants. Female subjects had lower LDL cholesterol, whereas male subjects had considerably higher LDL cholesterol. Serum HDL cholesterol, on the other hand, was exclusively elevated in female individuals while remaining unaltered in male respondents. Only female individuals had considerably higher serum calcium levels. Both male and female individuals had significantly higher serum alkaline phosphatase levels.

Conclusion: Despite the fact that there is a negative correlation between 25 (OH) D levels and lipid profile in both male and female participants, serum vitamin D has been reported as a putative cardio-protective vitamin in female subjects via boosting HDL-C. Alkaline phosphatase levels were higher in both genders.

Key Words: Vitamin D, Calcium, Alkaline Phosphatase, Lipid Profile

Citation of article: Jaleel F, Saeed S, Altamash S, Hussain W, Ullah AR, Khan MA. Association Between Vitamin D, Calcium, Alkaline Phosphatase and Lipid Profile in Male and Female Subjects. Med Forum 2021;32(10):141-145.

INTRODUCTION

Health, development and maintenance of bone require adequate amounts of vitamin D. Vitamin D deficiency has been linked to the development of osteoporosis as a result of secondary hyperparathyroidism, which causes calcium to be mobilized out of bones, increasing the risk of fall-related fractures.[1]

Vitamin D deficiency is also associated with lack of sun exposure in humans.

[1.] Department of Biochemistry / Medicine[2] / Pathology[3] / Community Medicine[4], Liaquat College of Medicine & Dentistry, Karachi.

[5.] Department of Orthodontics, Altamash Institute of Dental Medicine, Karachi.

Correspondence: Dr. Muhammad Athar Khan, Professor of Community Medicine, Liaquat College of Medicine & Dentistry, Karachi.
Contact No: 03232135932
Email: matharm@yahoo.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

Vitamin D-fortified foods and naturally occurring foods are usually insufficient to meet a child's or adult's vitamin D requirements. [2] Inadequate vitamin D levels have also been related to a higher risk of cancer, autoimmune disease, diabetes, hypertension, and infectious disease.[3, 4] Many factors contribute to vitamin D insufficiency, including changes in lifestyle such as the use of sunscreen, the adoption of covered clothes according to cultural standards, obesity, and the global environment.[5]

Skin exposure to sunshine is the primary source of vitamin D in humans. After absorbing sunlight, 7-dehydrocholesterol is converted to pro-vitamin D in the skin, which is then hydroxylated by hydroxylases in the liver and kidney into 25(OH) D and 1, 25-dihydroxyvitamin D3 (an active form). Vitamin D's primary role is to regulate calcium and bone metabolism. An integrated hormonal system that regulates calcium movement from the gut, kidneys, and bones regulates serum calcium levels. Calcium metabolism is facilitated by the parathyroid hormone PTH and the PTH receptor (PTHR), 1, 25 (OH) 2D and vitamin D receptor (VDR), calcitonin, ionised serum calcium, and the calcium-sensitive receptor (CaRare).[6] Other roles include modulating immunological

function, anti-inflammatory activity, regulating the rennin-angiotensin system, and decreasing insulin resistance.[7] Vitamin D insufficiency may play a role in the onset of endocrine-metabolic disorder.[8] Vitamin D insufficiency is thought to be linked to cardiovascular health issues. In patients with cardiovascular disease, vitamin D insufficiency has been related to an increased risk of death.[9] The relationship between vitamin D status and blood lipid levels may differ between men and women. Within each gender, more females than males were vitamin D deficient.[10]

The objective of present study was to determine the association between Vitamin D, Calcium, Alkaline Phosphatase and Lipid Profile in male and female patient attending outpatient department of Darul-Sehat Hospital Karachi.

MATERIALS AND METHODS

From July 2018 to January 2019, a cross-sectional study was conducted at Darul-Sehat Hospital in Karachi, Pakistan, in the outpatient department (OPD). A total of 200 healthy people, 100 males and 100 females, between the ages of 40 and 60, were chosen. They were divided into two groups: one with low vitamin D levels and the other with normal vitamin D levels. Participants with hyperlipidemia, a family history of hyperlipidemia, diabetes, chronic metabolic disorders such chronic renal failure and chronic liver failure, morbid obesity (BMI > 30), cigarette smokers, and those using vitamin D supplements or statin medication were all excluded from the study. Fasting blood samples were taken and maintained for estimate after receiving written consent and a medical history. Kit technique (Randox®, Private Ltd) was used to calculate serum cholesterol, triglycerides, HDL-C, LDL-C, calcium, and alkaline phosphatase. ELISA was used to determine vitamin D levels (Enzyme linked Immunosorbant Assay).

The ethical committees of Darul Sehat Hospital and Liaquat College of Medicine and Dentistry Karachi gave their clearance. SPSS version 24 was used for the statistical analysis (IBM corp, USA). The Student's t-test was used to determine the relationship between serum vitamin D, lipid profile, calcium, and alkaline phosphatase. Significant was defined as a p-value of less than 0.05.

RESULTS

The relationship between vitamin D and lipid profile in male participants is shown in Table I. Between participants with low vitamin D levels and those with normal vitamin D levels, there was a significant difference in vitamin D levels ($P<0.05$). Total and HDL cholesterol levels were not significantly different between the two groups, however LDL cholesterol levels in vitamin D deficient groups were significantly higher ($P<0.05$) than in vitamin D normal groups. There was a significant difference ($P<0.01$) in triglyceride levels between the two groups, with the vitamin D deficient group having greater levels than the vitamin D normal group.

The relationship between vitamin D and lipid profile in female participants is shown in Table I. Between participants with low vitamin D levels and those with normal vitamin D levels, there was a significant difference in vitamin D levels ($P<0.05$). The vitamin D deficient group had considerably higher total cholesterol when total cholesterol was compared between the two groups ($P<0.01$). When compared to the normal vitamin D group, LDL-cholesterol was considerably higher in the vitamin D deficient group ($P<0.01$). When the HDL-cholesterol levels of the two groups were examined, there was no significant difference. There was a significant difference ($P<0.01$) in triglyceride levels between the two groups, with the vitamin D deficient group having greater levels than the vitamin D normal group.

Table No.1: Effects of Vitamin D on Lipid Profile in Male & Female

Laboratory Profile	25 (OH) D <20 ng/ml (n=50)	25 (OH) D ≥20 ng/ml (n=50)	p-value
	Mean (SD)	Mean (SD)	
MALES			
VITAMIN D (ng/ml)	15.6 ± 2.3	32.0 ± 3.0	0.05
TC (mg/ml)	170.6 ± 2.5	172.0 ± 2.6	N.S
LDL-C (mg/ml)	153.0 ± 3.5	113 ± 3.9	0.01
HDL-C (mg/ml)	36.0 ± 5.0	39.6 ± 4.1	N.S
TG (mg/ml)	257.0 ± 4.5	168.5 ± 4.3	0.01
FEMALES			
VITAMIN D (ng/ml)	15.5 ± 1.3	30.0 ± 1.5	< 0.01
TC (mg/ml)	251.2 ± 4.1	180.2 ± 3.6	< 0.01
LDL-C (mg/ml)	197.5 ± 4.3	143.7 ± 5.1	< 0.05
HDL-C (mg/ml)	42.4 ± 4.0	40.3 ± 5.1	N.S
TG (mg/ml)	214.0 ± 4.1	148.5 ± 5.0	< 0.01

The effects of vitamin D on calcium in male participants are shown in Figure 1. The results demonstrate that in the normal vitamin D group, calcium levels were higher but within normal ranges, whereas in the vitamin D deficient group, calcium levels were lower. The effects of vitamin D on calcium in female participants are shown in Figure 2. It reveals that in the normal vitamin D group, calcium levels were higher but within normal ranges, whereas in the vitamin D deficient group, calcium levels were lower. The effects of vitamin D on Alkaline Phosphatase in male individuals are shown in Figure 1. When comparing the

vitamin D deficiency group to the vitamin D normal group, alkaline phosphatase was greater in the vitamin D deficient group. The effects of vitamin D on Alkaline Phosphatase in female participants are depicted in Figure II. When comparing the vitamin D deficient group to the vitamin D normal group, alkaline phosphatase was found to be greater.

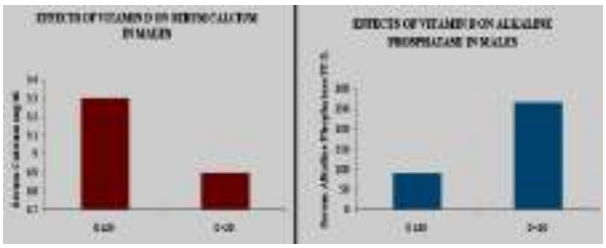


Figure No.1 Effects of Vitamin D on Calcium & Alkaline Phosphatase in Male Subjects

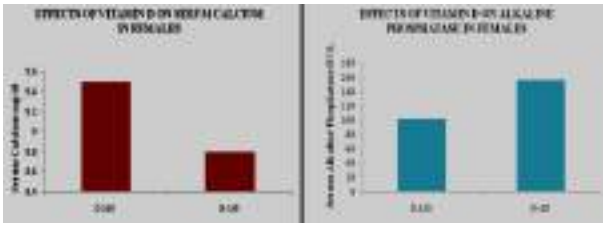


Figure No.2: Effects of Vitamin D on Calcium & Alkaline Phosphatase in Female Subjects

DISCUSSION

Hyperlipidemia has been associated to an increase in mortality and morbidity, leading to cardiovascular disease; regulating lipid levels with vitamin D replacement would be an intriguing area to follow. Vitamin D deficiency can be caused by a variety of factors in our society, including a high-fiber diet that inhibits fat and fat-soluble vitamin absorption, a low intake of fish, which is a good source of vitamin D, and limited sun exposure due to a variety of factors, including living in a high-rise building with no exposure to sunlight, wearing a burka, dark skin with high melanin, which reduces the skin's ability to produce vitamin D, and diseases which limits absorption of vitamin D and many other factors.

In our research, we discovered a link between vitamin D and serum lipid levels in both male and female participants. Vitamin D deficiency has been linked to elevated lipid levels, which are a risk factor for cardiovascular disease. Vitamin D deprivation raised total cholesterol, triglycerides, and LDL-C in both male and female individuals, but did not affect serum HDL-C in either group.

Vitamin D insufficiency has been linked to elevated lipid levels in numerous studies. [11, 12] Vitamin D has both direct and indirect effects on lipid profile adjustment, according to Wang et al, and the effect of vitamin D on decreasing blood triglyceride levels could be related to a regulatory mechanism that stimulates lipoprotein lipase activity in adiposity. [13] As lipoproteins amass in the arterial wall, platelets and monocytes anchor to the intima layer. Monocytes that have been internalized form macrophages, which eventually become foam cells. The lipids are then deposited intracellularly and in the ECM, causing the characteristic atherosclerotic plaque to develop. [14] Vitamin D controls triglyceride metabolism by promoting the production of VLDL cholesterol receptors in some cell types. [15] Hypertriglyceridemia is linked to low vitamin D levels, according to other studies. [16,17] Another study found that greater calcium uptake by the intestines, which is caused by higher vitamin D levels in the blood, lowers triglyceride levels in the blood. Calcium deficiency inhibits triglyceride production and release in the liver. [18] TG levels can be reduced by lowering PTH levels. [19] Due to the fact that both cholesterol and vitamin D share a same mechanism for production, a defective LDL-receptor reduces cholesterol uptake, which lowers vitamin D levels. [20] A 14-year longitudinal study showed a correlation between Vitamin D and lipid levels, as well as a link between low levels of vitamin D and TGs, which can contribute to high death rates. [21] Vitamin D levels were linked to insulin resistance, metabolic syndrome, hypertriglyceridemia, obesity, and hypertension in a study that looked at the link between vitamin D levels, metabolic syndrome, and subclinical atherosclerosis. High vitamin D levels were found to lower the risk of metabolic syndrome, while low vitamin D levels were linked to insulin resistance, metabolic syndrome, hypertriglyceridemia, obesity, and hypertension. [22]

The connection between calcium intake, circulating calcium levels, hormones, and bone condition is regulated by homeostatic mechanisms, with parathyroid hormone (PTH) and vitamin D being the most important contributors.[23,24] Alkaline is a term used to describe a substance that is alkaline in nature. Phosphatase levels were higher in both genders, possibly as a result of high PTH levels. When vitamin D levels are low, PTH levels rise, and when vitamin D levels are high, PTH levels fall. Increased PTH causes an increase in TGs due to sluggish lipolytic activity, which removes them from the peripheral; this is how vitamin D impacts PTH levels, which influences blood TG levels. [25]

The study's cross-sectional methodology and the inability to determine causation from the discovered associations were other drawbacks. To fully comprehend the relationship between vitamin D and blood lipid profiles, large randomized controlled trials are required.

CONCLUSION

Although there is a negative link between 25 (OH) D levels and lipid profile in both male and female

participants, serum vitamin D has been described as a putative cardio-protective vitamin by raising HDL-C in female subjects. Both genders had higher amounts of alkaline phosphatase.

Author's Contribution:

Concept & Design of Study:	Shabana Saeed, Farhan Jaleel, Sara Altamash
Drafting:	Waqar Hussain, Al-Farah Rehmat Ullah
Data Analysis:	Muhammad Athar Khan, Al-Farah Rehmat Ullah
Revisiting Critically:	Shabana Saeed, Farhan Jaleel, Waqar Hussain
Final Approval of version:	Shabana Saeed, Farhan Jaleel, Sara Altamash

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Simonelli C, Weiss TW, Morancey J, Swanson L, Chen YT. Prevalence of vitamin D inadequacy in a minimal trauma fracture population, Current Medical Research and Opinion 2005;21(7):1069-1074.
2. Chen TC, Chimeh F, Lu Z, et al. Factors that influence the cutaneous synthesis and dietary sources of vitamin D. Arch Biochem Biophysics 2007;460: 21-37.
3. Grant WB. An estimate of premature cancer mortality in the U.S due to inadequate doses of solar ultraviolet-B radiation. Cancer 2002;94: 1867-75.
4. Jeffrey L. Anderson, Heidi T. May, Benjamin D. Horne, Tami L. Bair, Nathaniel L. Hall, John F. Carlquist, Et al. Relation of vitamin D deficiency to cardiovascular risk factors, disease status and incident events in a general healthcare population. Am J Cardiol 2010;106(7):963-968.
5. Fatima H, Nazli H, Fatima N, Faiza J. Vitamin D deficiency in healthy female medical students of a public sector hospital. Pak J Med Res 2013; 52(1):12–15.
6. Vahe C, Benomar K, Espiard S, Coppin L, Jannin A, Odou M, et al. Diseases associated with calcium-sensing receptor. Orphanet J Rare Dis 2017;12:1–9.
7. Delvin EE, Lambert M, Levy E, O'Loughlin J, Mark S, Gray-Donald K, et al. Vitamin D Status Is Modestly Associated with Glycemia and Indicators of Lipid Metabolism in French-Canadian Children and Adolescents. J Nutr 2010;140(5):987–991.
8. Gokosmanoglu F, Onmez A, Ergenç H. The relationship between Vitamin D deficiency and polycystic ovary syndrome. Afr Health Sci 2020;20:1880–1886.
9. Iqbal AM, Dahl AR, Lteif A, Kumar S, Vitamin D. Deficiency: a potential modifiable risk factor for cardiovascular disease in children with severe obesity. Children (Basel, Switzerland) 2017;4(9).
10. Khan H, Ansar MA, Waheed U, Farooq N. Prevalence of Vitamin D deficiency in General population of Islamabad, Pakistan. Ann Pak Inst Med Sci 2013; 9 (1): 45-7.
11. Monlezun DJ, Camargo CA, Mullen JT, Quraishi SA. Vitamin D Status and the Risk of Anemia in Community Dwelling Adults: Results from the National Health and Nutrition Examination Survey 2001–2006. Medicine 2015;94(50):799.
12. Karhapää J, Pihlajamäki I, Pörsti G. Diverse associations of 25- hydroxyvitamin D and 1,25-dihydroxy-vitamin D with dyslipidaemias. J Int Med 2010;268(6):604–610.
13. Wang JH, Keisala T, Solakivi T, Minasyan A, Kalueff AV, Tuohimaa P. Serum cholesterol and expression of ApoAI, LXR [beta] and SREBP2 in vitamin D receptor knock-out mice. J Steroid Biochem 2009;113(3–5):222–226.
14. Kim DH, Mez CA, Clarke H, Kim JS, Hickne RC. Vitamin D and Endothelial Function. Nutr 2020; 12:575.
15. Kohno M, Takahashi S, Oida K. 1α25-dihydroxyvitamin D3 induces very low density lipoprotein receptor mRNA expression in HL-60 cells in association with monocytic differentiation. Atherosclerosis1997;133(1):45-9.
16. Hajas A, Sandor J, Csathy L, Csipo I, Barath S, Paragh G, et al. Vitamin D insufficiency in a large MCTD population. Autoimmun Rev 2011;10: 317-24.
17. Cigolini M, Iagulli MP, Miconi V, Galiotto M, Lombardi S, Targher G. Serum 25-hydroxyvitamin D3 concentrations and prevalence of cardiovascular disease among type 2 diabetic patients. Diabetes Care 2006;29(3):722–724.
18. Asma MA, Naser AA, Current Evidence on Vitamin D Deficiency and Metabolic Syndrome in Obese Children: What Does the Evidence from Saudi Arabia Tell Us? Children (Basel) 2018;5(1):11.
19. Choi HS, Kim KA, Lim CY. Low serum vitamin D is associated with high risk of diabetes in Korean adults. J Nutr 2011;141:1524–1528.
20. García-Bailo B, Da Costa LA, Arora P, Karmali M, El-Sohemy A, Badawi A. Plasma vitamin D and biomarkers of cardiometabolic disease risk in adult Canadians, 2007-2009. Prev Chronic Dis 2013;10:E91.

21. Jorde R, Figenschau Y, Hutchinson M, Emaus N, Grimnes G. High serum 25-hydroxyvitamin D concentrations are associated with a favorable serum lipid profile. Eur J Clin Nutr 2010;64: 1457-64.
22. Pacifico L, Anania C, Osborn JF, Ferraro F, Bonci E, Olivero E, et al. Low 25(OH)D3 levels are associated with total adiposity, metabolic syndrome, and hypertension in Caucasian children and adolescents. Eur J Endocrinol 2011;165: 603-11.
23. Reid IR, Horne AM, Mihov B, Stewart A, Garratt E, Wong S, et al. Fracture prevention with zoledronate in older women with osteopenia. N Engl J Med 2018;379:2407–2416.
24. Shaker JL, Deftos L. Calcium and Phosphate Homeostasis. [Updated 2018 Jan 19]. In: Feingold KR, Anawalt B, Boyce A, et al. editors. Endotext [Internet]. South Dartmouth (MA): MDText.com Inc;2000. Available from: https://www.ncbi.nlm.nih.gov/books/NBK279023.
25. Song SJ, Si S, Liu J, Chen X, Zhou L, Jia G, et al. Vitamin D Status in Chinese pregnant women and their newborns in Beijing and their relationships to birth size. Public Health Nutr 2013;16(4):687-92.

Original Article

Bolton's Ratio in Class I, II and III Malocclusion Patients

Bolton's Tooth Size Discrepancy in Skeletal and Dental Class I, II and III Malocclusion Patients, Seeking Orthodontic Treatment at Liaquat University Hospital Jamshoro/ Hyderabad

Tariq Aziz[1], Abdul Jabbar[2], Syed Rizwan Shah[3], Abdul Bari Memon[4], Ramesh Lal[2] and Maryam Mushtaq[5]

ABSTRACT

Objective: To evaluate Bolton's tooth size discrepancy in skeletal and dental Class I, II and III malocclusion.
Study Design: Analytic study
Place and Duration of Study: This study was conducted at the Department of Orthodontics, Institute of dentistry, LUMHS Jamshoro/Hyderabad from 01-07-2019 to 31-12-2019.
Materials and Methods: This study consisted of 73 patients. The patients were grouped into three classes of malocclusions based on Angle's molar classification on study cast and Steiner's ANB angle on lateral cephalometric radiograph. The Bolton analysis was performed on study cast. The researcher took all the measurements with the help of digital calipers, from right first molar to left first molar in both upper and lower arches. The data were analyzed by SPSS version 23.0 (Armonk, NY: IBM Corp.). Analysis of variance (ANOVA) was applied to statistically compare the overall and anterior ratios among the different malocclusions. To assess gender dimorphism independent student t-test was performed and level of significance was set at p- value < 0.05.
Results: Out of 73 patients included in this study 22 were female (30.13%) and 51 male (69.86%); with female to male ratio of 1:2.3. The mean age was 21±2.41 years. Of 73 patients, 14 (19.17%) were of Class I, 46 (63.01) Class II and 13 (17.8%) were of Class III patients. A mean Overall Bolton ratio of 92.30 ±2.93 and a mean anterior Bolton ratio of 79.17 ±5.19 was obtained for the complete sample. The one-way analysis of variance revealed insignificant relationship with p – value of 0.186 and 0.572 for overall ratio and anterior ratio respectively in different malocclusion groups. Regarding gender dimorphism, Independent sample t-test showed no significant relationship with P-value of 0.483 and 0.426 for overall ratio and anterior ratio respectively.
Conclusion: This study's result revealed no statistically significant difference between overall Bolton's ratio and anterior ratio in all malocclusion groups. Though higher anterior ratio was observed in Class I and III than the Bolton's standard values. Also, statistically insignificant relationship was observed between gender &Bolton's ratio.
Key Words: Tooth Size Discrepancy, Bolton ratio, Malocclusion

Citation of article: Aziz T, Jabbar A, Shah SR, Memon A, Lal R, Mushtaq M. Bolton's Tooth Size Discrepancy in Skeletal and Dental Class I, II and III Malocclusion Patients, Seeking Orthodontic Treatment at Liaquat University Hospital Jamshoro/Hyderabad. Med Forum 2021;32(10):146-150.

INTRODUCTION

[1.] Muhammad Dental College, Mirpurkhas.
[2.] Department of Orthodontics, Institute of Dentistry, Liaquat University of Medical and Health Sciences, Jamshoro.
[3.] Department of Orthodontics, Women Medical and Dental College, Abbottabad.
[4.] Bibi Aseefa Dental College @ SMBBMU Larkana Sindh.
[5.] Department of Orthodontics, CIMS, Multan.

Correspondence: Dr. Abdul Jabbar, Associate Professor of Orthodontics, Institute of Dentistry, LUMHS, Jamshoro.
Contact No: 0333-2608489
Email: a_jabbar_lumhs@hotmail.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

Orthodontic treatment comprises of different stages which has their own particular requirements and peculiar complications. Challenges and problems are encountered throughout the orthodontic treatment and especially the finishing stage. An excellent orthodontic finishing is essential to achieve a desired and optimum occlusion[1]. In time diagnosis of tooth-size imbalances prior to commencement of orthodontic treatment will result in minimum problems during finishing stages[2]. The ideal end result of perfect overjet, overbite and intermaxillary occlusion can be achieved by the early detection of intermaxillary tooth size discrepancy[3]. The definition of Tooth Size Discrepancy (TSD) is the asynchronous size of particular tooth or group of teeth as compared to the teeth in the same arch or opposing arch[4]. In order for maxillary teeth to align properly with the mandibular teeth, for esthetics, occlusal stability

and functional harmony there must be a definite proportionality of tooth size[5]. The exact location of tooth size discrepancy in a particular segment of arch can be detected by assessing the Bolton's anterior ratio. During orthodontic treatment the choice for extraction of particular tooth can be made by assessing Bolton's size ratio[6]. The mathematical formula developed by Bolton[1] after studying 55 cases with perfect occlusion, which defined the anterior Bolton index (ABI) of 77.2±1.65%. However, this index gives us a rough estimate of tooth sizes of different races and ethnicities and not the exact discrepancy.[3,7-12].

Jury is still out on whether tooth size discrepancy is gender related or not. Proponents of this hypothesis had observed statistically significant differences between tooth sizes of males and females[13,14] while the opponents didn't find any difference[15-17] like literature review of Othman and Harradine[18].According to estimate, 5% of general population has Significant Tooth size discrepancy[6]. There is scares data available in Pakistan regarding tooth size discrepancies among different malocclusions groups. Hence this study is designed to collect the data from local population to determine the incidence of tooth size discrepancy among different types of skeletal and dental malocclusion.

MATERIALS AND METHODS

This study was carried out at Department of Orthodontics, Institute of dentistry, LUMHS Jamshoro/ Hyderabad after approval from ethical review committee. Nonprobability consecutive sampling technique was employed. The Included samples consisted of Pretreatment lateral cephalometric radiograph and study cast from both male and female patients (age range 12-25 years). The inclusion criterion was; Good quality study cast, fully erupted permanent teeth except third molars, No inter-proximal or occlusal surface abrasion on teeth, absence of inter-proximal caries, restoration, as well as crown and bridge and absence of dental malformations or extra teeth.

The sample size of 73 patients was divided into three groups based on Angles Classification of Malocclusion and ANB angle. Class I malocclusion was diagnosed on Class I molar relationship and ANB angle between 0-4 degree. Class II Malocclusion with Class II molar relationship and ANB angle > than 4 degrees. Class III malocclusion was diagnosed based on class III molar relationship accompanied by ANB angle < 0 degree.

All the study casts were thoroughly examined. The mesio-distal width of each tooth was measured till permanent first molar in both arches. Second and third molars were excluded. The values obtained were used to calculate overall and anterior Bolton's ratio using the following formulas. The overall and anterior ratios were calculated by the following formula:

$$\frac{\text{Sum of lower 12 teeth}}{\text{Sum of upper 12 teeth}} \times 100 = \text{Overall Ratio}$$

$$\frac{\text{Sum of lower 6 teeth}}{\text{Sum of upper 6 teeth}} \times 100 = \text{Anterior ratio}$$

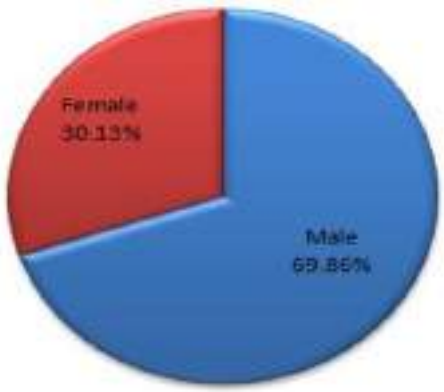
The data were analyzed by SPSS version 23.0 (Armonk, NY: IBM Corp.). To assess the normality of data Kolmogrov-smirnov test was applied. The test result showed normal distribution of the data hence parametric tests were used. Analysis of variance (ANOVA) was applied to statistically compare the overall and anterior ratios among the different malocclusions. To assess gender dimorphism independent student t-test was performed and level of significance was set at p- value < 0.05.

RESULTS

The study results are based on the analysis of 73 patients. Out of 73 patients, 22 were females (30.13%) and 51 were males (69.86%). Female to male ratio of 1:2.3 as shown in Figure No: 1, the patient's age ranges between 12 to 25 years. The mean age was 21±2.41 years**.**

Based on Angles Classification and cephalometric analysis, out of 73 patients, 14 (19.17%) were of Class I, 46 (63.01) Class II and 13 (17.8%) were of Class III patients. Detailed descriptive statistics of variable is shown in Table No: 1. A mean Overall Bolton ratio of 92.30 ±2.93 and a mean anterior Bolton's ratio of 79.17 ±5.19 was obtained for the complete sample. The mean Bolton's ratios for the different malocclusion groups are shown in Table No: 1. The one way analysis of variance was performed to determine the relationship among different malocclusion and Bolton ratio. The test results revealed insignificant relationship with p – value of 0.186 and 0.572 for overall ratio and anterior ratio respectively.

Independent sample t-test was applied to determine association between the Bolton ratio and gender. The test result shows there is no significant relationship between Bolton's ratio and gender with P-value = 0.483 and 0.426 for overall ratio and anterior ratio respectively.



N=73, Male: 51, Female: 22

Figure No. 1: Gender Distribution of Study Participants

Table No:1 Relationship between different Malocclusion and Bolton Ratio

Types of Malocclusion	N	Overall Ratio	Anterior Ratio
	73	92.30	79.17
Class I	14		
Mean		92.7	79.6
Std. Deviation		±2.97	±3.52
Class II	46		
Mean		91.43	78.15
Std. Deviation		±3.10	±4.81
Class III	13		
Mean		92.79	79.78
Std. Deviation		±3.4	±3.89
P-Value	0.186		0.572
F- Value	2.10		0.874

(One-way Analysis of Variance - ANOVA Significant level = > 0.05)

Table No.2: Relationship between Overall and Anterior Bolton Ratio and Gender

Bolton Ratio	Gender	N	Mean	Std. Deviation	F-Value	P-Value
Overall Ratio	Male	51	91.78	3.42	0.271	0.483
	Female	22	91.93	3.81		
Anterior Ratio	Male	51	78.93	2.79	0.719	0.426
	Female	22	78.26	3.16		

DISCUSSION

The presence of disproportionate tooth material in upper or lower arch can disturb the occlusal harmony. Bolton's ratio, which is the seventh key of occlusion, helps in analyzing the proportionality of upper and lower teeth. This analysis helps in proper diagnosis, and treatment of a case into a harmony that will result into structural and functional stability of maxillary and mandibular arch.

This study was designed to evaluate Bolton ratio in Class I, II and III malocclusions, in the Pakistani population. This study recruited relatively smaller sample size owing to restricting the selection upon a younger age group, in order to minimize the possibility of confounding factors like attrition, proximal restoration and caries in older age. The results of this study revealed that overall and anterior Bolton's ratio is statistically insignificant in Class I, II and Class III malocclusion which is in agreement to most of the studies done by the other authors. Though higher anterior ratio was observed in Class I and III than the Bolton's standard values.

Khateeb and Abu Alhaija[19] conducted a study on 140 orthodontics models of school children of Jordanian origin between the age of 13-15 years and found no statistically significant difference in Boltons ratios in different malocclusions. In another study, Crossby and Alexander found no correlation between malocclusion classification according to Angle and Bolton's Ratio in 109 pretreatment study models of orthodontic patients[12]. In contrast to our results, a study conducted by Ta et al, in 2001 in southern Chinese children, found significant difference between anterior Bolton ratio in Class III and Bolton's norms for anterior ratio. Significant difference was observed between Class II and Bolton's norms and between Class II and Class III cases in overall ratio[10].

Hashim in 2002 studied the difference in Bolton's ratio between different malocclusion and find no association[20]. In another study conducted by Laino et al on sample of 94 patients found no relationship between Bolton's discrepancies in different malocclusion groups[5].

In 2003 Araujo and Souki conducted a study to evaluate relationship between different malocclusion group and Bolton's ratio. There results were not in agreement with the results of the present study. They establish significantly higher anterior ratio in class III as compared to Class I and II malocclusion groups[2]. In another study performed in 2005 by Afzal et al calculated Bolton's ratio in different malocclusion groups and results showed insignificant relationship. Statistically higher ratios were observed in class III than Class I and Class II malocclusion groups. These findings are comparable to the results of present study[21].

Mujahid et al, in 2017 compared the mean anterior tooth size discrepancy in Class I and Class II malocclusion patients and find insignificant difference between two groups of malocclusions[22].

Batool et al, conducted a study to find tooth size discrepancy in different malocclusion group and selected patients based on ANB angle. They found that tooth size discrepancy in mandibular anterior segment in skeletal Class II group was higher that partially contradicts the results of present study[23].

This current study revealed that, the overall and anterior ratio (92.30 and 79.17 respectively) were slightly higher than the Bolton's original norms in our population. The results are in agreement with the study conducted by Oktay and Ulukaya in 2010 who calculated the Bolton's ratio in normal occlusion with different malocclusion groups in Turkish population. The results showed that overall and anterior ratios of Turkish population were larger in comparison to the original values of Bolton[24]. Another study conducted by V Mollabashi, M Karim Soltani et al, in Iranian population demonstrated the higher total Bolton and anterior ratio than the Boltons original norms[25].

With regard to gender, the present study found no statistically significant relationship between overall ratio and anterior ratio with p -value 0.483 and 0.426 respectively, which is in agreement with most of the studies conducted by other others. A study by Nourallah et al and Bernabe et al, found insignificant difference in tooth size discrepancy between male and female patients[26]. Also, Basaran et al studied gender

dimorphism and tooth size discrepancy in Turkish population, which failed to find any association between these two variables[27]. A study by Muhammad Tayyab et al, conducted on 90 Pakistani patients in 2014, demonstrated no sex predilection for overall ratio and anterior ratio. However, there are numerous studies that contradicts with current study in term of gender dimorphism and Bolton discrepancy.

A study conducted by Fattahi et al found that male patients had higher overall and anterior ratio than female patients[28]. Similar results were also found in a study conducted by Uysal et al, who found tooth size discrepancy and gender dimorphism[3]. Also Lavelle observed sexual dimorphism in Bolton's ratio which is not in agreement with the results of current study[14].

CONCLUSION

Following conclusion was deduced based on the results of this study,

There was no statistically significant difference between Overall Bolton's ratio and anterior Bolton's ratio in all three classes of malocclusion. Although higher Anterior Bolton's ratio was seen in Class I and III compared to Bolton's standard norms.

Though there was no statistically significant relationship between Gender and Bolton's Overall and anterior ratio, yet the male dentition showed tendency for slightly larger mesio-distal size than female counterparts.

Author's Contribution:

Concept & Design of Study:	Abdul Jabbar
Drafting:	Tariq Aziz, Syed Rizwan Shah
Data Analysis:	Abdul Bari Memon, Ramesh Lal, Maryam Mushtaq
Revisiting Critically:	Abdul Jabbar, Tariq Aziz
Final Approval of version:	Abdul Jabbar

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Bolton WA. Disharmony in Tooth Size and its Relation to the Analysis and Treatment of Malocclusion. Angle Orthod 1958; 28(3): 113-30.
2. Araujo E, Souki M. Bolton anterior tooth size discrepancies among different malocclusion groups. Angle Orthod 2003;73(3):307-13.
3. Uysal T, Sari Z. Intermaxillary tooth size discrepancy and mesiodistal crown dimensions for a Turkish population. Am J Orthod Dentofacial Orthop 2005;128(2): 226-30.
4. https://www.elsevier.com/books/mosbys-medical-dictionary/mosby/978-0-323-08541-0.
5. Laino A, Quraemba G, Pudano S, Stanzoine S. Prevalence of tooth size discrepancy among different malocclusion groups. J Orthod 2003;4: 37-44.
6. Bolton WA. The clinical application of a tooth-size analysis. Am J Orthod 1962;48(7):504-29.
7. Fields HW. Orthodontic-restorative treatment for relative mandibular anterior excess tooth-size problems. Am J Orthod 1981;79(2):176-83.
8. Profitt WR, Fields HW, Sanier DM. Contemporary Orthodontics. 5th ed. Elsevier;2012.p.181-5.
9. Lew K, Keng S. Anterior crown dimensions and relationship in an ethnic Chinese population with normal occlusions. Aust Orthod J 1991;12(2):105.
10. Ta TA, Ling JY, Hägg U. Tooth-size discrepancies among different occlusion groups of southern Chinese children. Am J Orthod Dentofacial Orthop 2001;120(5):556-8.
11. Santoro M, Ayoub ME, Arthur Pardi V, Cangialosi TJ. Mesiodistal crown dimensions and tooth size discrepancy of the permanent dentition of Dominican Americans. Angle Orthod 2000; 70(4):303-7.
12. Crosby DR, Alexander CG. The occurrence of tooth size discrepancies among different malocclusion groups. Am J Orthod Dentofacial Orthop 1989;95(6):457-61.
13. Smith SS, Buschang PH, Watanabe E. Interarch tooth size relationships of 3 populations: 'Does Bolton's analysis apply? Am J Orthod Dentofacial Orthop 2000;117:169-74.
14. Lavelle CL. Maxillary and mandibular tooth size in different racial groups and in different occlusal categories. Am J Orthod 1972;61:29-37.
15. Uysal T, Sari Z, Basciftci FA, Memili B. Intermaxillary tooth size discrepancy and malocclusion: is there a relation? Angle Orthod 2005;75:208-13.
16. Al-Tamimi T, Hashim HA. Bolton tooth-size ratio revisited. World J Orthod 2005;6:289-95.
17. Akyalcin S, Dogan S, Dincer B, Ertan Erdinc AM, Oncag G. Bolton tooth size discrepancies in skeletal class I individuals presenting with different dental Angle classifications. Angle Orthod 2006;76:637-43.
18. Othman SA, Harradine N. Tooth size discrepancy and Bolton's ratio: a literature review. J Orthod 2006;1:45-51.
19. Al-Khateeb SN, Abu-Alhaija ESJ. Tooth size discrepancies and arch parameters among different malocclusions in a Jordanian sample. Angle Orthod 2006;76:459–65.
20. Hashim HA. Bolton tooth size ratio among different malocclusion groups: A pilot study. J Pak Dent Assoc 2002;11:81–5.
21. Afzal A, Ahmed I, Vohra F, Uzair M. Bolton tooth size discrepancies among different malocclusion

groups. ANN Abbasi Shaheed Hosp Karachi Med Dent Coll 2005;10:670–5.
22. Mujahid R, Ahsan T, Anwar M, Farrukh M, Majeed O, Mirza D. Frequency of tooth size discrepancy with Class I& II dental malocclusion groups in patients seen at BUMDC dental OPD. Pak Oral Dent J 2017;31:37.
23. Iffat B, Asad A, Rizvi SAL, Abbas I. Evaluation of tooth size discrepancy in different malocclusion groups. J Ayub Med Coll Abbottabad 2008; 20(4):51-4.
24. Oktay H, Ulukaya E. Intermaxillary tooth size discrepancies among different malocclusion groups. Eur J Orthod 2010;32:307–12.
25. Mollabashi V, Soltani MK, Moslemian N, Akhlaghian M, Akbarzadeh M, Samavat H, et al. Comparison of Bolton ratio in normal occlusion and different malocclusion groups in Iranian population. Inter Orthod 2019;17: 143–150.
26. Nourallaha AW, Spliethb CH, Schwahnc C, Khurdajid M. Standardizing Interarch Tooth-Size Harmony in a Syrian population. Angle orthodontic 2005;75:996-9.
27. Basaran G, Selek M, Hamami O, Akkus Z. Intermaxillary Bolton tooth size discrepancies among different malocclusion groups. Angle Orthod 2006;76:26-30.
28. Fattahi HR, Pakshir HR, Hedayati Z. Comparison of tooth size discrepancies among different malocclusion groups. Eur J Orthod 2006;28:491–5.

Original Article

Safety and Efficacy of Minimally Invasive Percutaneous Nephrolithotomy for Kidney Stones in Infants in Pakistan

Tariq Ahmad[1], Nasrum Minallah[2] and Fazal e Manan[2]

ABSTRACT

Objective: To assess the safety and effectiveness of minimally invasive percutaneous nephrolithotomy in infants of age less than 12 months in Pakistan.

Study Design: Analytic study

Place and Duration of Study: This study was conducted at the Pediatric Urology Department at Institute of Kidney Diseases Peshawar from March 2020 to March 2021.

Materials and Methods: Children under the age of 12 months having renal stone of size ≥ 1cm in greatest dimension on CT-KUB were enrolled in this study. Patients with positive urine cultures, elevated serum creatinine, horse shoe kidneys, ectopic kidneys and bleeding diathesis were omitted from this study. All patients underwent mini-PCNL under general anesthesia in prone position.

Results: A total of 33 patients with mean age 9.3 ± 2.05 months were included in this study. The mean stone size, operative time, hospital stay and drop in hemoglobin (Hb) were 11.50 ± 1.37 mm, 52.12 ± 8.23 mins, 2.36 ± 0.74 days and 1.65 ± 0.89 g/dl respectively. We attained stone free status in 84.85% of the patients. Postoperative complications developed in 21.21% of the patients. Only 15.15% patients required retreatment.

Conclusion: We concluded that for renal stones, in the infantile stage group, mini-PCNL is safe and effective treatment for renal stones in infants.

Key Words: Infants, Pediatrics, Percutaneous, mini-PCNL, Urolithiasis

Citation of article: Ahmad T, Minallah N, Manan F. Safety and Efficacy of Minimally Invasive Percutaneous Nephrolithotomy for Kidney Stones in Infants in Pakistan. Med Forum 2021;32(10):151-154.

INTRODUCTION

The prevalence of pediatric urolithiasis in comparison to adult population is low but is steadily increasing[1]. The clinical presentation of renal stones in infants is variable because of their incapability to communicate. The main presentations are but not limited to fever, oliguria, hematuria, listlessness or crying and poor appetite[2]. Minimally invasive options for renal stones in infants include extracorporeal shockwave lithotripsy (ESWL), flexible ureteroscopy (URS) and percutaneous nephrolithotomy (PCNL). ESWL is the preferred technique to manage renal stones <2 cm diameter. However, ESWL in infants is performed under general anesthesia (GA) and requires repetitive sessions[3]. Furthermore, residual stones after ESWL may lead to recurrence. Pediatric URS has excellent stone free rate (SFR) with minimal intra or post-operative complications[4]. Flexible URS, however, requires LASER, which is not available in our part of the world. Besides, the procedure requires instruments that are disposable and costly, making it difficult to afford. Therefore to treat infantile nephrolithiasis mini-PCNL is suggested. This procedure does not need disposable instruments and can safely be done with pneumatic lithoclast[5]. Nonetheless, PCNL is associated with several complications and requires a steep learning curve especially in infants[6].

This research study was carried out in the Pediatric Urology Department, Institute of Kidney Diseases (IKD) Peshawar to assess the safety and effectiveness of minimally invasive percutaneous nephrolithotomy in infants of age less than 12 months.

[1.] Department of Pediatric Urology / Urology and Renal Transplant[2], Institute of Kidney Diseases, Phase IV, Hayatabad, Peshawar, Khyber Pakhtunkhwa.

Correspondence: Dr. Nasrum Minallah, Department of Urology and Renal Transplant Institute of Kidney Diseases, Phase IV, Hayatabad, Peshawar, Khyber Pakhtunkhwa.
Contact No: 03339161193
Email: drnasrumminallah@gmail.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

MATERIALS AND METHODS

This study was conducted in the Pediatric Urology Department, Institute of Kidney Diseases Peshawar from March 2020 to March 2021. Approval was obtained from the hospital ethical committee. All children included in this study were of ≤ 12 months age and diagnosed with renal stone ≥ 1cm in size in greatest dimension on CT KUB. Patients with positive urine culture, raised serum creatinine, horse shoe kidneys,

ectopic kidneys and bleeding diathesis were omitted from this study. An informed written consent was taken from the parents of all infants. All children underwent mini-PCNL with 10 Fr pediatric scope under GA in prone position. Renal access was obtained by single supracostal puncture and secured with 12 Fr or 14 Fr Amplatz sheath. Tubeless-PCNL was defined as insertion of DJS only without placing a nephrostomy tube whereas totally tubeless-PCNL was defined as inserting neither DJS nor nephrostomy tube. Plain CT-KUB was performed at one month post-operatively to look for any residual fragments in the ureter or kidney. The patients with no residual fragments at one month after the procedure were categorized as stone free and procedure was labelled as successful. SPSS version 26 was used to analyse the data. Mean±SD were computed for quantitative variables whereas percentages and frequency were also computed for categorical variables.

RESULTS

A total of 33 patients, 21 male (63.64 %) and 12 female (36.36 %) were included in this study. The overall mean age and stone size were 9.3±2.05 months and 11.50±1.37mm respectively. 17(51.52 %) of the patients had stones in the right kidney whereas 16(48.48%) had renal stones in the left. Renal pelvis was the only location of all 33 stone (100%). 25(75.76%) of the patients had Grade 0 hydronephrosis (HDN) and 8(24.24%) had Grade 1 HDN (Table-1). The mean operative time and hospital stay were 52.12±8.23 mins and 2.36±0.74 days respectively. 12(36.36%) patients had totally tubeless-PCNL and 21 (63.64%) required insertion of double J stent (DJS). The mean hemoglobin (Hb) drop observed was 1.65±0.89 g/d1. Overall, stone clearance was attained in 28/33(84.85%) patients. None of the patient had any major intra-operative complication. Patients having post-operative problems were 7(21.21%), including fever in 4(12.12%), transient haematuria in 1(3.03%) and haematuria requiring blood transfusion in 2 (6.06%) of the patients. 5(15.15%) patients required retreatment, including ESWL in 1(3.03%) and URS in 4(12.12%) patients. Stone analysis showed that 25(75.76%) patients had CaOx.CaP stones, 6(18.18%) patients had cystine stones and 2(6.06%) patients had uric acid stones (Table-2).

Table No.1: Patients and Stone Characteristics

Characteristic	Result
n	**33**
Gender	
Male	21(63.64 %)
Female	12(36.36 %)
Age (months)	9.3±2.05
Stone-Size (mm)	11.50±1.37
Stone Laterality	
Right	17(51.52 %)
Left	16(48.48%)

Table No. 2: Perioperative and Postoperative characteristics of patients

Characteristic	Result
n	**33**
Operative Time (minutes)	52.12±8.23
Hospital Stay (days)	2.36±0.74
Exit Strategy	
Totally-Tubeless	12(36.36%)
Tubeless	21(63.64%)
Drop in Haemoglobin (g/dl)	1.65±0.89
Stone Free Rate	28(84.85%)
Re-treatment Rate	5(15.15%)
ESWL	1(3.03%)
URS	4(12.12%)
Complications	7(21.21%)
Intraoperative Complications	None
Postoperative Complications	
Clavien Grade I	
Postop Fever	4(12.12%)
Transient Hematuria	1(3.03%)
Clavien Grade II	
Hematuria & Blood Transfusion	2 (6.06%)
Clavien Grade III	-
Clavien Grade IV	-
Stone Composition	
CaOx.CaP	25(75.76%)
Uric acid	2(6.06%)
Cystine	6(18.18%)
Struvite	-
Unknown	-

DISCUSSION

The procedure for infant's urinary tract stones is quite complicated. This is because of many factors such as anatomic abnormalities, the relatively smaller kidney, and developing parenchyma[7]. Consequently, the chance of stone recurrence in infants is more than that of in adults. It is critical to offer minimally invasive procedures in the pediatric age group. The less invasive approaches that are currently available for renal stones in pediatric patients include ESWL, PCNL, and flexible URS alone, or in combination[8]. ESWL is the recommended approach for paediatric renal stones. However, in addition to kidney damage, it may result in high retreatment rates due to residual stones[9].

Some studies show that RIRS could be a promising procedure while treating renal stones in infants[10]. However, in such cases the pelvicalyceal anatomy and narrow diameter of ureter may cause complications. These include ureteral injury, avulsion, perforation, ureteral stricture and pyelonephritis[11]. Since anesthesia is a prerequisite for all of the less invasive procedures in infants, thus a procedure should be selected which gives high success rate as monotherapy in infants. PCNL has become the preferable treatment option in children who require surgery for the kidney stone

disease. In addition, PCNL is recommended for those with a large stone burden, cysteine stones and residual fragments in case of ESWL failure[8]. However, percutaneous treatment of renal stones in infant remains a difficult task for urologist. Many studies have suggested the effectiveness as well as the safety of PCNL in preschool children (less than three years), On the other hand few studies have reported the efficacy and safety of this procedure for patients less than 12 months of age[12,13]. The PCNL procedure in children has been reported to have stone clearance rates of 80 to 100%[14].

In our view, the 80 % of stone clearance rate for PCNL as monotherapy in infants is acceptable. In this study, the stone clearance rate obtained was 84.85 %. This rate is higher than that reported by Dağgülli and Baydilli et al, which was 80% and 80.6% respectively[3,15]. Our stone clearance rate is comparable to Dede et al, which was 83.3 %[7]. In contrast, Jones et al, reported 97.1 % stone free rate, much higher than our study's observation[16]. To the best of our knowledge, this is, so far, the largest study which investigates the efficacy and safety of mini PCNL in infants under 12 months of age. Therefore, 84.85 % stone clearance rate with mini-PCNL monotherapy in infants is a successful procedure.

Renal access can be obtained through any of the upper, middle or lower calices, each having good efficacy to clear the stones[17,18,19]. In our study, supracostal puncture through upper pole by bull's eye technique was performed in all patients. The author has good experience with this puncture technique.

The mean operative time in the current study was 52.12 $\pm$ 8.23 minutes which is shorter than that reported by Pelit et al and Nadeem et al[12,13]. Our operative time is comparable to Dede et al[7]. We report, in our study, a mean hospital stay of 2.36 $\pm$ 0.74 days which is comparable to that reported by Dede et al.[7] and better than that reported by Pelit et al.[12] Tubeless or totally tubeless-PCNL method is associated with short hospital stay and reduced requirement for analgesia[20]. We did totally tubeless-PCNL in 12(36.36%) and tubeless-PCNL in 21(63.64%) patients. In the current study auxiliary procedures were needed in 5(15.15%) patients including ESWL in 1(3.03%) patient for residual renal stones and URS in 4 (12.12%) patients for migrated stone fragments into the ureter. Patients were stone free after performing these procedures under GA. Our re-treatment rate is comparable to that reported by Pelit et al.[12], however it is higher in comparison to that reported by Nadeem et al.[13]

In this study no major intra-operative complication was observed. 7 (21.21 %) of the patients developed minor post-operative complications (Clavien grade I and II). 4 (12.12%) patients developed post-operative fever who responded well to broad spectrum intravenous antibiotics. 3 (9.09 %) patients had postoperatively hematuria, two (6.06%) needed blood transfusion. Hematuria settled spontaneously without the need for angioembolization. The mean hemoglobin drop was 1.65 ± 0.89 mg/dL. Jones et al. stated a complication rate of 12.5 % for mini-PCNL, all Clavien grade I. Their complication rate is better than our study[14].

Bleeding is very critical factor because it affects both a patient's mortality and stone clearance rate. Keeping in mind small sized kidneys and compact collecting system in infants, we used 12 Fr and 14 Fr access sheath in order to minimize bleeding and renal trauma. Tracts of smaller size are not only effective in treating renal stones but also have the advantages of less blood loss, short hospital stay, reduced use of postoperative analgesia as well as overall reduced complication rates in comparison to standard PCNL[21]. Hence in children under age of 12 months during PCNL procedure small sized tracts and pediatric instruments should be used.

The PCNL procedure may result in hypothermia which in turn is due to the duration of anesthesia and the use of irrigation fluids during surgery[22]. However we did not encounter any such event in the current study. The reason was that during the perioperative periods, the room temperature was well adjusted and irrigation fluids were wormed to body temperature. The high pressure within pelvicalyceal system can result in extravasation of urine into the perirenal space or the abdominal cavity causing urinary ascites. During the course of this study, none of the patient reported this complication.

Even it has been more than forty years to the story of its development, PCNL still remains a bit difficult procedure to learn. It is an effective procedure for kidney stone removal. Nevertheless the complication rate is higher than other endoscopic procedures that are being followed for managing stones particularly in less experienced hands. In order to sustain it as a safe and effective procedure for the patients there is a strong need to improve the training for PCNL. For the procedure to be successful, urologists need to perform a handful of PCNLs to gain the required expertise and skills.

The limitations of our study may include small sample size and recruitment of patients from single institute. Another limitation is the need of GA for auxiliary procedure in this group of population.

CONCLUSION

Mini PCNL is a safe and effective treatment for managing renal stones in infants. It leads to higher stone clearance rates, lesser complications and shorter hospital stays.

Author's Contribution:

Concept & Design of Study:	Tariq Ahmad
Drafting:	Nasrum Minallah, Fazal e Manan

Data Analysis:	Nasrum Minallah, Fazal e Manan
Revisiting Critically:	Tariq Ahmad, Nasrum Minallah
Final Approval of version:	Tariq Ahmad

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Scoffone CM, Cracco CM. Pediatric calculi: cause, prevention and medical management. Curr Opin Urol 2018;28(5):428-432.
2. Li J, Xiao J, Han T, Tian Y, Wang W, Du Y. Flexible ureteroscopic lithotripsy for the treatment of upper urinary tract calculi in infants. Exp Biol Med (Maywood) 2017;242(2):153-159.
3. Dağgülli M, Sancaktutar AA, Dede O, Utanğaç MM, Bodakçi MN, Penbegül N, et al. Minimally invasive percutaneous nephrolithotomy: an effective treatment for kidney stones in infants under 1 year of age. a single-center experience. Urolithiasis 2015;43(6):507-12.
4. Jones P, Rob S, Griffin S, Somani BK. Outcomes of ureteroscopy (URS) for stone disease in the paediatric population: results of over 100 URS procedures from a UK tertiary centre. World J Urol 2020;38(1):213-218.
5. Kallidonis P, Tsaturyan A, Lattarulo M, Liatsikos E. Minimally invasive percutaneous nephrolithotomy (PCNL): techniques and outcomes. Turk J Urol 2020;46(Supp. 1):S58-S63.
6. Chaurasia A. Percutaneous nephrolithotomy: challenges for a novice urologist. Minim Invasive Surg 2020;5053714.
7. Dede O, Sancaktutar AA, Baş O, Dağgüllu M, Utangaç M, Penbegul N et al. Micro-percutaneous nephrolithotomy in infants: a single-center experience. Urolithiasis 2016;44(2):173-7.
8. Tekgül S, Stein R, Bogaert G, Nijman RJM, Quaedackers J, 't Hoen L, et al. European association of urology and european society for paediatric urology guidelines on paediatric urinary stone disease. Eur Urol Focus 2021:S2405-4569(21)00158-9.
9. Alsagheer G, Abdel-Kader MS, Hasan AM, Mahmoud O, Mohamed O, Fathi A, et al. Extracorporeal shock wave lithotripsy (ESWL) monotherapy in children: predictors of successful outcome. J Pediatr Urol 2017;13(5):515.e1-515.e5.
10. Chandramohan V, Siddalingaswamy PM, Ramakrishna P, Soundarya G, Manas B, Hemnath A. Retrograde intrarenal surgery for renal stones in children <5 years of age. Ind J Urol 2021;37(1): 48-53.
11. Baş O, Tuygun C, Dede O, Sarı S, Çakıcı MÇ, Öztürk U, et al. Factors affecting complication rates of retrograde flexible ureterorenoscopy: analysis of 1571 procedures-a single-center experience. World J Urol 2017;35(5):819-826.
12. Pelit ES, Kati B, Çanakci C, Sağir S, Çiftçi H. Outcomes of miniaturized percutaneous nephrolithotomy in infants: single centre experience. Int Braz J Urol 2017;43(5):932-938.
13. Iqbal N, Hasan A, Siddiqui FS, Iftikhar F, Siddiqui FS, Ilyas SM, et al. Outcome of percutaneous nephrolithotomy in preschool and school-age children-single center experience. J Ayub Med Coll Abbottabad 2019;31(3):391-396.
14. Jones P, Bennett G, Aboumarzouk OM, Griffin S, Somani BK. Role of minimally invasive percutaneous nephrolithotomy techniques-micro and ultra-mini pcnl (<15f) in the pediatric population: a systematic review. J Endourol 2017;31(9):816-824.
15. Baydilli N, Tosun H, Akınsal EC, Gölbaşı A, Yel S, Demirci D. Effectiveness and complications of mini-percutaneous nephrolithotomy in children: one center experience with 232 kidney units. Turk J Urol 2019;46(1):69-75.
16. Jones P, Mishra D, Agrawal M, Griffin S, Somani BK. Outcomes of ureteroscopy *vs* mini-percutaneous nephrolithotomy for pediatric upper urinary tract calculi: comparative nonrandomized outcomes from two tertiary endourology referral centers. J Endourol 2020;34(7):735-738
17. Khadgi S, El-Nahas AR, Darrad M, Al-Terki A. Safety and efficacy of a single middle calyx access (MCA) in mini-PCNL. Urolithiasis 2020;48(6): 541-546.
18. Blum KA, Parkhomenko E, Thai J, Tran T, Gupta M. A contemporary lower pole approach for complete staghorn calculi: outcomes and efficacy. World J Urol 2018;36(9):1461-1467.
19. Sahan A, Cubuk A, Ozkaptan O, Ertaş K, Canakci C, Eryildirim B, et al. Safety of upper pole puncture in percutaneous nephrolithotomy with the guidance of ultrasonography versus fluoroscopy: a comparative study. Urol Int 2020;104(9-10): 769-774.
20. Gupta S, Maurya AK, Pal DK. Observational prospective study for surgical outcome and anesthetic feasibility of tubeless and totally tubeless supine PCNL: a single centre initial experience. Turk J Urol 2018;45(2):146-149.
21. Heinze A, Gozen AS, Rassweiler J. Tract sizes in percutaneous nephrolithotomy: does miniaturization improve outcome? Curr Opin Urol 2019;29(2):118-123.
22. Hosseini SR, Mohseni MG, Aghamir SMK, Rezaei H. Effect of irrigation solution temperature on complication of percutaneous nephrolithotomy: a randomized clinical trial. Urol J 2019;16(6): 525-529.

Original Article

Evaluation of Progesterone Efficacy in Women with Threatened Miscarriage in Kohat

Beenish Samreen Hamid[1], Tajwar Sultana[2], M Irfan ul Akbar Yousufzai[3], Fouzia Qadir[5], Rana Tauqir Ullah Khan[4] and Muhammad Shereen[5]

ABSTRACT

Objective: The objective of this study to evaluate efficacy of progesterone in women with threatened miscarriage in Kohat.

Study Design: Case-Control study

Place and Duration of Study: This study was conducted at the Obstetrics and Gynecology KMU-IMS Kohat and Department of Pharmacology Muhammad College of Medicine's Peshawar from February 2020 to January 2021 for a period of 11 months.

Materials and Methods: Patients in the Test Group (Oral progesterone) ranging in age from 30.54 to 10.48 year. Patients in the Control Group (no progesterone) ranged in age from 30.55 to 10.38 years old. All of the women were given a thorough medical history and examination. Women were divided into two groups at random: test and control. The absence of vaginal bleeding was used to measure efficacy.

Results: A total of 210 women (105 in each group) were examined in this trial, with patients in the Test Group (Oral progesterone) ranging in age from 30.54 to 10.48 year. Patients in the Test Group (no progesterone) ranged in age from 30.55 to 10.38 years. Because Control Group (Oral progesterone) was effective in 91 (95.55 %) patients and Control groups resulted in 5 (5.25%) patients, Efficacy was measured in terms of absence of vaginal bleeding.

Conclusion: Oral progesterone was found to be more efficacious than placebo in reducing threatening miscarriages in the first trimester. Our findings suggest that progesterone medications are helpful in preventing miscarriage in women who are at risk of miscarriage.

Key Words: Oral progesterone, threatened miscarriage

Citation of article: Hamid BS, Sultana T, Yousufzai MIA, Qadir F, Khan RT, Shereen M. Evaluation of Progesterone Efficacy in Women with Threatened Miscarriage in Kohat. Med Forum 2021;32(10):155-158.

INTRODUCTION

In most of the pregnancy cases at least 15%–20%, Miscarriage problem faced by women. In pregnant women, it is a major problem which should be treated at time otherwise caused major cynically issues.[1] the fetus remains also visible and it is present inside the uterine cavity and the cervix of uterine cavity remains closed. In threatened miscarriage, vaginal bleeding is occurred with and without stomach pain. It means that bleeding and pain are major and main symptoms of threatened miscarriage.

[1.] Department of Obstet and Gynaecol, KMU-IMS Kohat.
[2.] Department of Pharmacology / Physiology[3] / Community Medicine[4], Muhammad College of Medicine, Peshawar.
[5.] Department of Biochemistry, Northwest School of Medicine Peshawar.

Correspondence: Dr. Asnad, Associate Professor of Biochemistry, MBBS Medical College, Mirpur AJ&K.
Contact No: 0332-3698204
Email: drasnadkhan@gmail.com

Received: June, 2021
Accepted: July, 2021
Printed: October, 2021

Major reason of miscarriage in women is due to their families and their psychological effect and impact. It is necessary that for the treatment of miscarriage to remove psychological effect and impact.[2] Deferent Physiological result showed that progesterone has multi-function in pregnancy from peri-implantation to the delivery of fetus in which (endometrium transformation, semi allogenic fetus from the mother's immune system man and control of uterine contractions etc.)[3] On the result of different research studies, for the miscarriage treatment, progesterone is used as medicine from long time and efficacy of progesterone is best as compare to other drugs.[4] in other clinical trials for impending abortion, the result for efficacy of progesterone treatment is varied. Controversial findings were found in threatening abortions during treatment of patients by doctor. Progesterone is a fundamental hormone from fertilized ovum to implantation it is also caused secretary changes in the uterine lining for conception and preservation of pregnancy in women.[5] Progesterone has great effect on controlling the mother's immunological response, for prevention the embryo from redetection, in mother uterine cavity.[6] Those women who are at risk of miscarriage, for maintaining pregnancy, progesterone has physiological significance for their treatment of

miscarriage .Different studies results of pregnancies (13–40%) showed that in first trimester, vaginal blood bleeding is stated loss.[8] The aim of this research to evaluate efficacy of progesterone in women with threatened miscarriage in Kohat.

MATERIALS AND METHODS

The research was carried out at the KMU-IMS Kohat Department of Obstetrics and Gynecology and the Muhammad College of Medicine's Pharmacology Department in Peshawar. The study lasted one year, from February 2020 to January 2021. Case-control research was used in this study. A total of 210 women (105 in each group) were examined in this trial, with patients in the Test Group (Oral progesterone) ranging in age from 30.54 to 10.48 year. Patients in the Control Group (no progesterone) ranged in age from 30.55 to 10.38 years old. All of the women were given a thorough medical history and examination. Women were divided into two groups at random: test and control. The absence of vaginal bleeding was used to measure efficacy. All information like age, address POG and efficacy were recorded on pre designed Performa. Data was analyzed using SPSS IBM 21.0. Quantitative variables like age was described as mean ± SD. Women who had experienced trauma during pregnancy or who had a history of bleeding issues were excluded. Following ethical permission from the hospital. The research included all women who met the eligibility requirements through the OPD or ER. All of the women were given a thorough medical history and examination. The women were divided into two groups at random using a lottery system. Oral progesterone was given to women in Group A. (10mg twice daily).

RESULTS

Table No.1: Participants Characteristics

	Test Progesterone Oral (n=105)	**Control (n=105)**
Age (years)	30.51±10.48	30.55±10.38
Education Basic Secondary University	 B-50% S-25% U-25%	 B-50% S-31% U-19%
Body Weight (Kg)	68.1±11.4	98.4±11.5
BMI (Kg/m2)	24.3±2.6	24.4±2.7

B: Basic, S: Secondary, U: University

A total of 210 women (105 in each group) were examined in this trial, with patients in the Test Group (Oral progesterone) ranging in age from 30.54 to 10.48 year. Patients in the Test Group (no progesterone) ranged in age from 30.55 to 10.38 years. Because Control Group (Oral progesterone) was effective in 91 (95.55 %) patients and Control groups resulted in 5 (5.25%) patients, Efficacy was measured in terms of absence of vaginal bleeding and pregnancy continuing beyond 2 weeks of gestation.

Table No.2: Efficacy of oral progesterone in threatened miscarriage women

Oral progesterone (n=105)	**No progesterone Control (n=105)**
Efficacy	
91 (95.55%)	05 (5.25%)

DISCUSSION

This prospective case-control study, in which examines vaginal bleeding in the first trimester and changes in in pregnant women. There is some impact of (mode of conception, Culture on maternal, maternal weight, gestational age, smoking status and parity) on blood aneuploidy screening indicators. [9-14]

The research was carried out at the KMU-IMS Kohat Department of Obstetrics and Gynecology and the Muhammad College of Medicine's Pharmacology Department in Peshawar. The study lasted one year, from February 2020 to January 2021. Case-control research was used in this study. A total of 210 women (105 in each group) were examined in this trial, with patients in the Test Group (Oral progesterone) ranging in age from 30.54 to 10.48 year. Patients in the Control Group (no progesterone) ranged in age from 30.55 to 10.38 years old. All of the women were given a thorough medical history and examination. Women were divided into two groups at random: test and control. The absence of vaginal bleeding was used to measure efficacy. In most of the pregnancy cases at least 15%–20%, Miscarriage problem faced by women. In pregnant women, it is a major problem which should be treated at time otherwise caused major cynically issues. The fetus remains also visible and it is present inside the uterine cavity and the cervix of uterine cavity remains closed. In threatened miscarriage, vaginal bleeding is occurred with and without stomach pain. It means that bleeding and pain are major and main symptoms of threatened miscarriage. Major reason of miscarriage in women is due to their families and their psychological effect and impact. It is necessary that for the treatment of miscarriage to remove psychological effect and impact. There are some studies indicate there no effect and it is said that maternal-fetal barrier is disturbed by early vaginal bleeding and it also enhance b-hCG transfer rate in maternal circulation.[15] There are some mixed result exist related progesterone in threatened miscarriage.[16,17] In our study, there is significant reduced vaginal bleeding in threatened miscarriage women. A total of 210 women (105 in each group) were examined in this trial, with patients in the Test Group (Oral progesterone) ranging in age from 30.54 to

10.48 year. Patients in the Test Group (no progesterone) ranged in age from 30.55 to 10.38 years. Because Control Group (Oral progesterone) was effective in 91 (95.55 %) patients and Control groups resulted in 5 (5.25%) patients, Efficacy was measured in terms of absence of vaginal bleeding and pregnancy continuing beyond 2 weeks of gestation.

Deferent Physiological result showed that progesterone has multi-function in pregnancy from peri-implantation to the delivery of fetus in which (endometrium transformation, semi allogenic fetus from the mother's immune system man and control of uterine contractions etc.) On the result of different research studies, for the miscarriage treatment, progesterone is used as medicine from long time and efficacy of progesterone is best as compare to other drugs. in other clinical trials for impending abortion, the result for efficacy of progesterone treatment is varied. Controversial findings were found in threatening abortions during treatment of patients by doctor. Progesterone is a fundamental hormone from fertilized ovum to implantation it is also caused secretary changes in the uterine lining for conception and preservation of pregnancy in women. Progesterone's physiological has effects dose-dependent in relaxation of smooth muscle of placenta .[18]

dose-dependent relaxation of placental vascular smooth muscle and the umbilical vein is one of progesterone's physiological effects.[18] Irregular fetal blood stream is observed in some study while taking progesterone tablets.[19,20] Progesterone has great effect on controlling the mother's immunological response, for prevention the embryo from redetection, in mother uterine cavity. Those women who are at risk of miscarriage, for maintaining pregnancy, progesterone has physiological significance for their treatment of miscarriage. Different studies result of pregnancies (13–40%) showed that in first trimester, vaginal blood bleeding is stated loss.

CONCLUSION

Oral progesterone was found to be more efficacious than placebo in reducing threatening miscarriages in the first trimester. Our findings suggest that progesterone medications are helpful in preventing miscarriage in women who are at risk of miscarriage.

Author's Contribution:

Concept & Design of Study:	Beenish Samreen Hamid
Drafting:	Tajwar Sultana, M Irfan ul Akbar Yousufzai
Data Analysis:	Fouzia Qadir, Rana Tauqir Ullah Khan, Muhammad Shereen
Revisiting Critically:	Beenish Samreen Hamid, Tajwar Sultana
Final Approval of version:	Beenish Samreen Hamid

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Health NCCFW. Ectopic pregnancy and miscarriage: Diagnosisand initial management in early pregnancy of ectopic pregnancy and miscarriage. RCOG 2012;1(4): 21–28.
2. Yassaee F, Shekarriz-Foumani R, Afsari S, Fallahian M. The effect of progesterone suppositories on threatened abortion: A randomized clinical trial. J Reprod Infertil 2014;15:147–151.
3. Schindler AE. Present and future aspects of dydrogesterone in prevention or treatment of pregnancy disorders: An outlook. Horm Mol Biol Clin Invest 2016;27:49–53.
4. Pandian RU. Dydrogesterone in threatened miscarriage: A Malaysian experience. Maturitas 2009;65:S47–S50.
5. Cunningham FG. Physiology of pregnancy. In: Cunningham FG, editor. Williams obstetrics. 21st ed. New York (NY): McGraw-Hill; 2001.
6. Meis PJ, Connors N. Progesterone treatment to preventpre- term birth. Clin Obstet Gynecol 2004;47: 784–795.
7. Palagiano A, Bulletti C, Pace MC, et al. Effects of vaginal progesterone on pain and uterine contractility in patients with threatened abortion before twelve weeks of pregnancy. Ann N Y Acad Sci 2004;1034(1):200–210.
8. Sotiriadis A, Papatheodorou S, Makrydimas G. Threatened miscarriage: evaluation and management. BMJ 2004;329(7458):152–155.
9. Spencer K, Ong CY, Liao AW, et al. The influence of ethnic origin on first trimester biochemical markers of chromosomal abnormalities. Prenat Diagn 2000c;20(6):491–494.
10. Spencer K, Bindra R, Nicolaides KH. Maternal weight correction of maternal serum PAPP-A and free betah CG MoM when screening for trisomy 21 in the first trimester of pregnancy. Prenat Diagn 2003a;23(10): 851–855.
11. Spencer K, Ong CY, Liao AW, et al. The influence of parity and gravidity on first trimester markers of chromosomalabnormality. Prenat Diagn 2000; 20(10):792–794.
12. Spencer K, Bindra R, Cacho AM, et al. The impact of correcting for smoking status when screening for chromosomal anomalies using maternal serum biochemistry and fetal nuchal translucency thickness in the first trimester of pregnancy. Prenat Diagn 2004; 24(3):169–171.
13. Liao AW, Heath V, Kametas N, et al. First trimester screening for trisomy 21 in singleton pregnanciesachieved by assisted reproduction. Hum Reprod 2001;16(7):1501–1504.

14. Kagan KO, Wright D, Spencer K, et al. First trimester screening for trisomy 21 by free beta-humanchorionic gonadotropin and pregnancy associated plasma protein- A: impact of maternal and pregnancy characteristics. Ultrasound Obstet Gynecol 2008;31:493–502.
15. Spencer K, Spencer CE, Stamatopoulou A. Early vaginal bleeding has no impact on markers used in first trimester aneuploidy screening. Prenat Diagn 2010; 30:547–550.
16. Cuckle H, Van Oudgaarden ED, Mason G, et al. Taking account of vaginal bleeding in screening for Down syndrome. Br J Obstet Gynaecol 1994; 101(11):948–953.
17. Heinig J, Steinhard J, Schmitz R. Does vaginal bleeding influence first-trimester markers for Down syndrome? Prenat Diagn 2007;27:312–316.
18. Omar HA, Ramirez R, Gibson M. Properties of a progesterone- induced relaxation in human placental arteries and veins. J Clin Endocrinol Metab 1995; 80(2):370–373.
19. Giorlandino C, Cignini P, Padula F, et al. Effects of exogenous progesterone on fetal nuchal translucency: an observational prospective study. Am J Obstet Gynecol 2015;212(3):335.e1–335.e7.
20. Özlü T, Güngör AÇ, Dönmez ME, Duran B. Use of progestogens in pregnant and infertile patients. Archives of Gynecol Obstet 2012;286(2):495.

Original Article

Influence of Celecoxib on Serum Urea Alongwith Favorable Effects of Lycopene on Albino Rats; An Investigational Study

Sadia Sundus[1], Ashok Kumar[3], Ata-ur-Rehman[5], Neelam Mallick[2], Muhammad Imran[2] and Ali Nawaz Bijarani[4]

ABSTRACT

Objective: To evaluate the influence of celecoxib on serum urea along with enhancement by lycopene.
Study Design: Investigational Study
Place and Duration of Study: This study was conducted at the Animal House of BMSI, JPMC, Karachi from May, 4th May 2016 to 3rd June 2016.
Materials and Methods: Physically fit forty adult male Albino rats of 200-220gm and 90-120 days old were taken for this study and distributed into 4 groups, control group was chosen as Group1A, In Group 1B Celecoxib was given 50 mg/kg orally, In Group 1C Celecoxib was given 50 mg/kg with lycopene50 mg/kg orally and In Group 1D lycopene was given 50 mg/kg orally for 30 days. At accomplishment of study, animals were sacrifice and tissues were preserved for staining.
Results: In Group 1B serum urea was markedly raised, however serum level were amended in Group 1c which were given celecoxib with lycopene.
Conclusion: This study reveals that lycopene amended the serum deviations of Group 1B.
Key Words: Celebrex, nephroprotective, chemoprotective, PGE

Citation of article: Sundus S, Kumar A, Ata-ur-Rehman, Mallick N, Imran M, Bijarani AN. Influence of Celecoxib on Serum Urea Alongwith Favorable Effects of Lycopene on Albino Rats; An Investigational Study. Med Forum 2021;32(10):159-161.

INTRODUCTION

NSAIDs epitomize utmost common medications used globally. NSAIDs has anti-inflammatory, analgesic and antipyretic properties by subdual synthesis of prostaglandin (PG), through preventing the cyclooxygenase enzyme.[1,2] COX-2 inhibitor like Celecoxib, probably decreases GI adversative outcomes, but it had a possibility of cardiovascular and renal side effects, because in kidney PGE2 shows an important role in hemodynamics and metabolism of fluid.[3-6] It augmented the autophagy and antioxidant indicators.[7]

1. Department of Anatomy / Pharmacy[2], Iqra University, Karachi.
3. Department of Anatomy / Pharmacology[4], Shaheed Mohtrmma Benazir Bhutto Medical College, Lyari.
5. Department of Pharmacology, Hamdard College of Medicine & Dentistry, Karachi.

Correspondence: Dr. Sadia Sundus, Associate Professor of Anatomy, Iqra University, Karachi.
Contact No: 0300-2850489
Email: usadsun_dr@yahoo.com

Received: April, 2021
Accepted: July, 2021
Printed: October, 2021

Prolonged usage of COX-2 inhibitors aggravate the raise in BP. COX-2 is the stimulator of PGE2 which is liable for conservation of renal function and arachidonic acid production and plays an inflammatory role. PGE2 raises progression, intrusiveness and metastasis of a malignant tumor, while prevents apoptosis and angiogenesis. Celebrex is a discriminatory COX-2 inhibitor so that it abrogate the PGE2 production and act as a tumor marker.[8,9]
Lycopene is the utmost copious and actual singlet-oxygen quencher and member of fat-soluble pigments as well as natural tomato carotenoids, which act prophylactically against proteins, lipids and DNA oxidation by scavenging free radicals due to its double bonds by direct in vivo reaction and neutralization. It is existent in red fruits and vegetables.[10-12] Instantaneous usage of antioxidant compounds can intrude in chemotherapy and malignancy management.[13] It reveals significant nephroprotective and chemoprotective properties.[14,15] It is present in LDL and VLDL of human plasma due to lipophilic nature, so shows itself as an anti- carcinogenic agent and should use after chemotherapy.[16-19] Lycopene has numerous properties like anti-inflammatory, antioxidant, anti-fibrotic and anti-apoptotic agent.[20-22]
In the intervening period, we didn't notice investigational study about influence of celecoxib on serum urea along with favorable effects of lycopene on albino rats therefore this opportunity is taken to initiate

this experimental work and compare the consequences with prior studies.

MATERIALS AND METHODS

A 30 days research work was accomplished on forty adult male albino rats indiscriminately allocated into four sets and were kept in pellet of BMSI animal house for seven days under observation. Three sets were administer Celebrex through gavage and one set was administer lycopene only. Assessment of serum BUN was carried by kit.

I: Control
II: Celebrex 50 mg/kg gavage. (Diseased group)
III: Celebrex with lycopene 50 mg/kg gavage.
IV: Lycopene 50 mg/kg gavage.

Throughout the entire research time animals were intensely observed for dissimilarity in their overall wellbeing. Blood serum samples were taken by direct cardiac puncture for the analyses of BUN renal function test by automated analyzer. To detect the serum urea levels, blood samples were processed in the DUHS laboratory Karachi Pakistan; where samples were centrifuged to separate the serum. Urea nitrogen levels were determined by spectrophotometric technique on Architect c 7D75 analyzer. Urea nitrogen estimation was performed Total Lab. Automation (TLA). The Kit used was Cat No. 7D75-21 and 7D75-31 reagent kits for serum Urea nitrogen SPSS version 20 were used for evaluation.

RESULTS

I: set I animals were remained in their best of wellbeing their dietary habits and response to Stimuli were adequate till the end of research. The mean value of serum urea level was 19.9±0.15. (Table-1, Figure1)

Table No.1: Mean Value of Serum Urea (Mg/Dl) in Various Sets of Albino Rats

Sets	Treatment given	Serum enzyme level urea
I (n=10)	ND	19.9±0.15
II (n=10)	Celebrex	51.60±0.49
III(n=10)	Celebrex + Lycopene	20.09±0.16

***Mean±SEM**

Numerical investigation of the variance in the mean serum level of urea among sets of Albino rats.

Numerical investigation	P-value
II vs. I	P<0.001****
III vs. I	P>0.05*
III vs. II	P<0.001****

Key:Non-significant* Significant**
Moderately significant* Highly significant******

II: Set II animals were perceived ill, lazy and inactive. Their diet became lessen and response was slothful. The mean value of serum urea in set II was 51.60±0.49. A very substantial raise (P<0.001) was detected in the mean value of serum urea level of set II, as compare to set I. (Table-1, Figure1)

III: Set III animals looked comparatively thriving, active as compare to II. Their food intake were habitual. The mean value of serum urea in set III was 20.09±0.16. A slight raise (P>0.05) was detected in mean value of urea level of set III, as compare to set I, while a very substantial decline (P<0.001) in the mean value of serum urea level was detected in set III, when it was compared with set II.(Table-1, Figure1)

IV: The results of set IV were similar to set I.

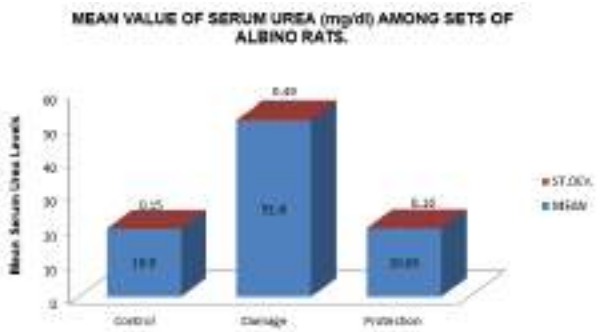


Figure No.1: Mean Value of Serum Urea (Mg/Dl) Among Sets of Albino Rats

DISCUSSION

NSAIDs epitomize the commonest prescribed and extremely efficient drug used internationally, in various diseases due to its anti- inflammatory, antipyretic, and palliative propertie[s.1,2] Celebrex is the key members of the selective COXII enzyme inhibitor group and helps in decreasing postoperative throbbing discomfort just like morphine, pethidine, and NSAIDs.[6]

Lycopene is the most effective antioxidant, which belongs to carotenoids family. It is present in red fruits, vegetables and tomato-rich products. It reduces the hazard of microbes, so it acts prophylactically as antioxidative agent, antiapoptotic agent, radical scavenging, and chelating agents.[10,12,15]

Set II animals exhibited a very substantial raise in the serum urea. Analogous effects were also expounded by.[1,5]

In set III animals a very substantial decline in the serum urea level was detected. Analogous effects were also expounded by.[10,19]

CONCLUSION

Experimentation determined that set II animals had raised serum levels of urea while III animals showed reduction in serum levels of urea as compared to II. So our interpretation from this study is that don't use celecoxib routinely and if required avoid using it without lycopene, in order to reduce its disadvantages.

Author's Contribution:
Concept & Design of Study: Sadia Sundus
Drafting: Ashok Kumar,

	Ata-ur-Reman
Data Analysis:	Neelam Mallick, Muhammad Imran, Ali Nawaz Bijarani
Revisiting Critically:	Ashok Kumar, Sadia Sundus
Final Approval of version:	Sadia Sundus

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Sivaraj R, Umarani S. Diclofenac-induced biochemical changes in nephrotoxicity among male Albino rats. Int J Basic Clin Pharmacol 2018; 7:640-3.
2. Cooper DL, Murrell DE, Conder CM, Palau VE, Campbell GE, Lynch SP, et al. Exacerbation of Celecoxib-Induced Renal Injury by Concomitant Administration of Misoprostol in Rats. PLoS ONE 2014;9(2):e89087.
3. Shin S. Safety of celecoxib versus traditional nonsteroidal anti-inflammatory drugs in older patients with arthritis. J Pain Res 2018;11:3211–3219.
4. Huang H, Luo M, Liang H, Pan J, Yang W, Zeng L, et al. Pain Medicine 2020;1–12.
5. Harirforoosh S, West KO, Murrell DE, Denham JW, Panus PC, Hanley GA. Assessment of celecoxib poly(lactic-co-glycolic) acid nano-formulation on drug pharmacodynamics and pharmacokinetics in rats. European Review for Medical and Pharmacological Sciences 2016;20: 4818-4829.
6. Vahabi S, Karimi A, Beiranvand S, Moradkhani M, Hassanvand K. Comparison of the Effect of Different Dosages of Celecoxib on Reducing Pain after Cystocele and Rectocele Repair Surgery. Open Anesthesia J 2020;11:30-34.
7. Okamoto K, Saito Y, Narumi K, Furugen A, KenIseki, Kobayashi M. Comparison of the nephroprotective effects of non-steroidal anti-inflammatory drugs on cisplatin-induced nephrotoxicity in vitro and in vivo. Eur J Pharmacol 2020;884:173339.
8. Luo L, Liang Y, Ding X, Ma X, Zhang G, Sun L. Significance of cyclooxygenase-2, prostaglandin E2 and CD133 levels in sunitinib-resistant renal cell carcinoma. Metrics 2019;1442-1450.
9. Al-Saffar FJ. Effect on renal histology and renal metabolizing enzymes and oxidative stress biomarkers in rats administered zerumbone against experimental osteoarthritis. Asian J Cell Biol 2015; 10 (3): 66-79.
10. Bayomy NA, Elbakary RH, Ibrahim MAA, Eman Abdelaziz Z. Effect of Lycopene and Rosmarinic Acid on Gentamicin Induced Renal Cortical Oxidative Stress, Apoptosis, and Autophagy in Adult Male Albino Rat. Anatomical Record 2017; 300:1137–1149.
11. Mohamed A, Dina S, Shaer F. Lycopene protects against renal cortical damage induced by nandrolone decanoate in adult male rats. Annals of Anatomy Anatomischer Anzeiger 2019;7(224): 142-152.
12. Rasheed HA, Al-Naimi MS, Hussien NR, Al-Harchan NA, Al-Kuraishy HM, Al-Gareeb AI. New insight into the effect of lycopene on the oxidative stress in acute kidney injury. Int J Crit Illn Inj Sci 2020;10(1):11–16.
13. Mahmoodnia L, Mohammadi K, Masumi R. Ameliorative effect of lycopene effect on cisplatin-induced nephropathy in patients. J Nephropathol 2017;6(3):144-149.
14. Lin J, Xia J, Zhao HS, Hou R, Talukder M, Lei Yu, et al**.** Lycopene Triggers Nrf2–AMPK Cross Talk to Alleviate Atrazine-Induced Nephrotoxicity in Mice. J Agric Food Chem 2018;66(46): 12385–12394.
15. Yu K, Zhang J, Cao Z, Qiang Ji, Han Y, Song M, et al. Lycopene attenuates AFB_1-induced renal injury with the activation of the Nrf2 antioxidant signaling pathway in mice. Food & Function 2018;(12):122-126.
16. Ibrahim SS, Said AM. Effect of Lycopene In Amelioration Of Testicular And Renal Toxicity Induced By Boldenone Undecylenate In Male Albino Rats. Int J Med Biomed Studies 2019;3(3): 58-66.
17. Patil AA, Doijad R, Koparde A. Renoprotective effect of Lycopene on Renal Functional and Histopathological changes in Gentamycin Induced Nephrotoxicity in Rats. Research J Pharm Tech 2020;13(7): 3237-3240.
18. JunXiaa, JiaLina, Xue-NanLia, CongZhanga, NanLiab, Zheng-Hai, et al. Atrazine-induced environmental nephrosis was mitigated by lycopene via modulating nuclear xenobiotic receptors-mediated response. J Nutritional Biochemis 2018;1(51):80-90.
19. Elkarim DG. Presumptive Ameliorative Effect of Lycopene on Lead-induced Nephrotoxicity in Males Wistar Rats. J Advanced Veterinary Res 2019;9(3): 91-96.
20. Yi Zhao, Mu-Zi Li, Yue Shen, Jia Lin, Hao-Ran Wan, et al. Lycopene Prevents DEHP-Induced Leydig Cell Damage with the Nrf2 Antioxidant Signaling Pathway in Mice. J Agric Food Chem 2020;68(7):2031–2040.
21. Santoso HS, Lestari S, Prayogo L, Kamsinah, Rochmatino. Renoprotective Effects of Lycopene in Tomato Extracts on Rat Exposed to Cadmium. Earth and Environmental Sci 2020;593-597.
22. Hussein SA, Azab M, Ahmed TE, Amin A, Abu Eldahab MMM. Cytoprotective, anti-apoptotic and anti-inflammatory effects of lycopene against mercuric chloride-induced hepatorenal injury in rats: Involvement of TNF-α/ NF-κβ/ and p53 signaling pathways. Benha Veterinary Med J 2019; 37(2):14-22.

Original Article

Impact of COVID-19 on Peripheral Nervous System Disorders

Amena Batool[1], Qurat-ul-Ain[2], Muhammad Waseem Akhtar[1], Sadaf Waris[2], Misbah Waris[1] and Fareed Ahmed Qureshi[1]

ABSTRACT

Objective: The objective of this study was to determine the frequency of peripheral nervous system disorders among COVID-19 survivors.

Study Design: Cross-sectional Survey

Place and Duration of Study: This study was conducted at the Department of Rehabilitation and Allied Health Sciences, Riphah International University Lahore Campus from December, 2020 to June, 2021 for a period of 06 months.

Materials and Methods: 144 patients recovered from Covid–19 through non probability convenience sampling were recruited for study. Patients were assessed for pain, smell, taste, balance and two-point discrimination and the ability to identify familiar objects. The data was collected according to the responses after patients approved to provide information. Data was coded in SPSS data sheet which was later analyzed for statistical frequencies and percentages.

Results: Mean age of patients was reported to be 34.5 ± 6.9 years. The mean score patients marked on the VAS scale for their pain was reported to be 4.96 with a standard deviation of 1.77. 42.4% of the 144 patients had complaints of symptoms associated to peripheral nerve involvements thus making a prevalence of 42.4%. Out of 144 patients in total, 39 i.e. 27.1% reported to have a total loss of smell i.e. Anosmia, 42 patients i.e. 29.2% sensed the smell accurately, 45 i.e. 31.3% had a reduced sense of smell whereas 18 patients i.e. 12.5% had an increased sensitivity to the different smells they were asked to sense. 47 patients i.e. 32.6% had ageusia i.e. a total loss of taste they were offered. 36 i.e. 25% had normal taste and accurately comprehended the different flavors they were offered, 41i.e. 28.5% had reduced taste sense i.e. hypoeusia and responded that they could taste but the intensity was lesser than normal.

Conclusion: Majority of the patients had peripheral nerve symptoms, a loss of smell, taste and impaired balance after recovery.

Key Words: COVID-19, Peripheral nerve disorders

Citation of article: Batool A, Qurat-ul-Ain, Akhtar MW, Waris S, Waris M, Qureshi FA. Impact of COVID-19 on Peripheral Nervous System Disorders. Med Forum 2021;32(10):162-166.

INTRODUCTION

With the outbreak of SARS-CoV-2 in China and ultimately around the globe, it leads to many medical, economic and social problems. In Pakistan, it leads to 3 waves at 3 different times. The government imported the vaccinations and had controlled it to a great extent now. But many of the people i.e. around 38% of the population hadcontracted Coronavirus since its outbreak in Pakistan [(1)]. Many of elder ages could not fight and combat the pathologies it caused and ultimately expired due to different respiratory complications it caused[(2)].

[1.] Department of Rehabilitation and Allied Health Sciences, Riphah International University Lahore campus.
[2.] Akhter Saeed Medical College, Lahore

Correspondence: Misbah Waris, Senior Lecturer, Riphah International University Lahore Campus
Contact No: 03008834613
Email: misbah.waris@riphah.edu.pk

Received: July, 2021
Accepted: August, 2021
Printed: October, 2021

Others had to combat the systemiccomplications caused by it[(3)]. Other than systemic and respiratory complications, SARS-CoV-2 is also known to produce neurological complications in patients after surviving from it. It was a general observation that people who contracted SARS- CoV-2 and survived from it, usually complained of vestibular symptoms, a generalfatigue in body, myalgia pain in upper and lower limbs especially and numbness inhands and feet [(4)]. This observation led us to conduct this research in order to document the prevalence of neurological symptoms in patients who have survived. Many neurological manifestations have already been documented as a result of Covid-19. These include encephalitis, encephalopathy, meningitis, steroid responsive encephalopathy etc. [(5)]. Few studies have also reported patients having symptoms of hyposmia or complete absence of smell for more than 2 months after being positive for Covid-19 [(6)]. Others had opthalmoparesis, facial muscles weakness and fatigue, symmetrical neuropathy i.e. bilateral pain and numbness in most of the time of day or night, critical illness myopathy, myositis, myalgias and Guillain Barre Syndrome as well. Few patients reported symptoms of rhabdomyolysis as well secondary to Covid 19 [(7)]. The

mechanism of peripheral nervous system involvement is still unclear but few analysts have thought it to be immune mediated. GBS is from long considered to be an immune mediated disease of peripheral nerve sheath or the Schwann cells of nerve [8]. This may be because of the resemblance which the glycoproteins on surface of virus and glycoconjugates of human nervous tissue with each other. The antibodies as a result of this complex starts acting against the glycoconjugates of nerve tissue of humans [9].

Some studies have also reported that Covid-19 also leads to multiple cranial neuropathies along with all other peripheral complications [10]. They have been reported in about 73% of the total cases infected. Some observational studies have also reported that patients often present with frequent complains of headache, nausea, myalgia, hyposmia, vomiting and dizziness. Others have also reported impaired levels of consciousness in patients of Covid-19[11]. Other possibly of the virus entering into the cerebral circulation is the hematogenous spread of the virus from systemic circulation [12]. Other experiments have also revealed that coronavirus compromises the central and peripheral nervous system as well as the respiratory drive through targeting the neurons located in cardiorespiratory centers [13]. Some animal studies have also reported that the virus affects the brainstem and brain in both patients as well as experimental animals[14]. An experiment following intranasal virus inoculation into the mice revealed that SARS CoV2 enters the central nervous system through the first cranial nerve i.e. olfactory nerve. The viruses were later detected in the central nervous system and not in the pulmonary tissues. Thus suggesting the direct transfer of virus through olfactory nerves [15]. Another possible explanation of this viral load in brain and brainstem after contracting infection is by the direct connection of vagus nerve to ambiguous and solitary nuclei which lie in the brain stem, thus indicating the spread of infection from respiratory tract to the central nervous system [16]. Olfactory nerve is the nerve most specific and the only one which provided us a sense of smell and because this nerve gets affected due to viral infections, the smell of smell too gets affected i.e. either the individuals smells more intense than normal, or lesser than normal [17]. Affected individuals lose their sense of smell completely during the active phases of viral infection [18]. The sense of taste is provided by two cranial nerves. The anterior 1/3rd is supplied by facial nerve whereas the posterior 2/3rd of the tongue is supplied by glossopharyngeal nerve. The nerve sensations are tested by alternativelytesting the taste buds with sugar and salt flavor and asking the respondent to inform about the taste with closed eyes. Patients of Covid-19 complain of altered balance until 3 months of being negative for SARS-CoV-2, reasons of which are yet unclear. In order to assess the patients for balance and their vestibular function,patients were asked to perform Fukuda step test and the angular deviation from the starting point were recorded [19]. The purpose of the current study was to find out effects on sensory changes in peripheral nervous system due to COVID-19.

MATERIALS AND METHODS

The study design was cross-sectional survey. Data was collected from the community of Lahore, Faisalabad, Sialkot, Rawalpindi and Islamabad. The study duration was six months after approval of synopsis i.e. December 2020 to June 2021. Study was conducted on patients who have been positive for Covid – 19 and have recovered from it. Patients were recruited through Non-probability convenient sampling technique. The sample size computed was 144. The online sample calculator was used to calculate the sample. Patients with SARS Cov-2 PCR positive reports from a reliable laboratory i.e. Shaukat Khanum Laboratory and Chughtai Labs, both males and females, age ranging from 18 to 60 were included. Patients with any respiratory complication prior to being positive for Covid-19, Diabetes mellitus, hypersensitive, allergic and with any neurological disorder before being positive for Covid-19 were excluded. Outcome measures were pain, smell, taste, balance- Labyrinthine function, stereognosis, and Two-point discrimination. VAS, NPRS, olfactory nerve test, Facial & Glossopharyngeal Nerve Test, Fukuda Test and Paper clip test for two-point discrimination were used as data collection tool. Patients were recruited according to the inclusion criteria and were asked for their consent after informing them the objective of this study. Patients who consented were included in the study. The research questionnaire including two sections was administered by the researcher herself. The first section of questionnaire included questions about their age, gender, marital status, co-morbidities and duration passed after they had their SARS Cov-2 test negative. Second session included the assessment based on pain score on VAS and NPRS for pain scale, olfactory nerve test for smell along with facial and glossopharyngeal Nerve test for taste. Other complaints of patients were also recorded.

RESULTS

Table No.1: Age of patients

N	Mean	Standard Deviation
144	34.51 years	6.889

Mean age of the patients was reported to be 34.51 ± 6.89 years.

Out of 144 patients, 84 i.e. 58.3% were females and 60 i.e. 41.7% were males. 55 i.e. 38.9% had hypertension, 78 i.e. 54.17% had no other medical problem whereas11 i.e. 7.64% reported to have renal problems (4), cardiac

problems (6) and psoriasis (1).28 i.e. 19.4% were unmarried and 116 i.e. 80.6% were married.

Table No.2: Demographics of patients

Sr. No.	Demographical Variable	Frequency (Percent)
1.	Gender of patients	Females – 84 (58.3%) Males – 60 (41.7%)
2.	Co-morbidities of patients	Hypertension – 55 (38.9%) None – 78 (54.17%) Others – 11 (7.64%)
3.	Marital status of patients	Unmarried – 28 (19.4%) Married – 116 (80.6%)

Table No.3: Duration passed after being negative for COVID -19

	Duration passed after being negative for Covid-19	Frequency (Percent)
1.	1-2 months	41 (28.5%)
2.	2-4 months	42 (29.2%)
3.	4-6 months	35 (24.3%)
4.	More than 6 months	26 (18.1%)

Out of 144 patients included in the study, 41 i.e. 28.5% had their SARS Cov 2 positive 1-2 months earlier and 42 i.e. 29.2% had 2-4 months back. 35 i.e. 24.3% had been positive 4-6 month back and 26 had been negative from more than 6 months' back.

Table No.4: Two-point discrimination interpretation

Interpretation	Frequency	Percent
Normal	131	91.0%
Fair	7	4.9%
Poor	6	4.2%
Protective	0	0.00%
Anesthesia	0	0.00%

Amongst 144 patients who were tested for their two-point discrimination, 131 i.e. 91.0% responded accurately i.e. they pointed to both the points touched at 2 mm to 5 mm, 7 i.e. 4.9% responded when both points were touched at a distance of 6 – 10 mm, 6 patients i.e. 4.2% responded with a distance of 11 mm to 15 mm. None of the patients fell into the protective and anesthetic category.

Table No.5: Interpretation of Fukuda Step Test for Balance

Interpretation of Fukuda step test	Frequency	Percent
Abnormal deviation to intact side	9	6.3%
Abnormal deviation to affected side	0	0.00%
Normal	135	93.8%

Patients under study were asked to perform Fukuda step test. The test was once demonstrated by the research administrator and was later asked to follow the instruction. Deviations of the patients were reported and thus, 135 i.e. 93.8% reported to have normal balance i.e. vestibular function whereas 9 patients i.e. 6.3% showed abnormal deviation and thus involvement of the vestibular system was reported.

DISCUSSION

The results of this study has shown that many of the patients who have had survived Covid-19 and came out negative for SARS CoV-2 showed features of peripheral neuropathy. Most of them had sensations of tingling and numbness in their distal extremities along with pain in their muscles of upper and lower limb. This resulted in higher scores of patients at LANSS scale. This showed that peripheral neuropathy had a higher prevalence of development after Covid 19. The results of this study were found to be consistent with a study from Mazya et al, the results of which showed that several neurological issues and complications arise because of the prone positioning among patients of Covid 19. The positioning recommended to treat ventilation perfusion matching and enhance drainage of secretions lead to increased intracranial pressure, median, radial as well as sciatic nerve injury. Brachial plexus damage was also reported among patients of Covid – 19.[20]

The same results were also observed by a study of Malik et al who studied 83 hospitalized patients and concluded the presence of nerve injuries in 14.5% of total patients. They also concluded that amongst these patients only one patient did not have a history of prone lying. 76.2 % of these had peripheral nerve injuries in the upper limb, ulnar nerve being the most common followed by radial nerve. Most commonly injured nerve from the lower limb was reported to be sciatic nerve. These findings were related to the finding of EMG studies of the same patients. According to the EMG findings, the patients had nerve injuries of Axonotmesis stage of injury.[21]

Zhang Y et al in their study concluded that Covid 19 leads to multiple cranial nerve involvement amongst which olfactory nerve is the most common one. Anosmia i.e. complete absence of the sense of smell was found to be present in about 73% of those infected with Covid 19. This study was a case study of a 35-year-old Covid 19 patient having right paralysis along with olfactory disturbance and an almost loss of sense of taste on same side of tongue while the sense of sweeter was preserved. The patient had complete loss of smell as he could not sense the smell of coffee and shampoo. The involvement of nerves started within 5 days of respiratory symptoms and it got resolve d in duration of more than 6 weeks [22].

Munro et al concluded in a self-reporting survey that patients recovered from Covid-19 had auditory

complications as well. They followed 138 adult individuals who experienced severe complications of Covid-19 and documented their symptoms 8 weeks after they were discharged from hospital. 13.2% of the total patients reported to have tinnitus and hearing difficulties after they had recovered from Covid-19. This study did not study the effects of Covid-19 on hearing due to which the results remain uncertain and the hearing tests should also have been conducted.

The results were found to be different from a study of Mao et al in which they concluded that the patients had problem identifying familiar objects when placed at palms of their hand and two-pint discrimination. Nerve pain was also found in these patients. Moreover, few patients amongst these had complaints of skeletal muscle injury which was ensured by the reports of Creatine Kinase elevation[23]. Our results did not show much disturbances in two-point discrimination. The patients were also able to identify keys, coin, paper clip and pen cap was placed on their palms. However, pain was found to be around 4-5 on the scale of VAS and NPRS[24].

CONCLUSION

Survivors of Covid – 19 have a higher rate of smell and taste abnormalities even after having negative results for their SARS CoV-2 PCR. Moreover, peripheral neuropathy was also observed considerably among these patients. These positive finding suggest a significant involvement of peripheral nervous system due to the viral invasion. This gives us an impression that Coronavirus influences both the central as well as peripheral nervous system.

Author's Contribution:

Concept & Design of Study:	Amena Batool
Drafting:	Qurat-ul-ain, Muhammad Waseem Akhtar,
Data Analysis:	Sadaf Waris
Revisiting Critically:	Misbah Waris
Final Approval of version:	Fareed Ahmed Qureshi

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Landi F, Barillaro C, Bellieni A, Brandi V, Carfì A, D'Angelo M, et al. The new challenge of geriatrics: saving frail older people from the SARS-COV-2 pandemic infection. J Nutrition, Health & Aging 2020;24(5):466-70.
2. Kim G, Wang M, Pan H, H. Davidson G, Roxby AC, Neukirch J, et al. A health system response to COVID-19 in long-term care and post-acute care: a three-phase approach. J Am Geriatr Society 2020;68(6):1155-61.
3. Lan L, Xu D, Ye G, Xia C, Wang S, Li Y, et al. Positive RT-PCR test results in patients recovered from COVID-19. JAMA 2020;323(15):1502-3.
4. Ahmed I. COVID-19–does exercise prescription and maximal oxygen uptake (VO2 max) have a role in risk-stratifying patients? Clin Med 2020;20(3):282.
5. Gautier J-F, Ravussin Y. A new symptom of COVID-19: loss of taste and smell. Obesity (Silver Spring). 2020;28(5):848.
6. Daniel J. Education and the COVID-19 pandemic. Prospects 2020;49(1):91-6.
7. Sedaghat Z, Karimi N. Guillain Barre syndrome associated with COVID-19 infection: a case report. J Clin Neurosci 2020;76:233-5.
8. Asadi-Pooya AA, Simani L. Central nervous system manifestations of COVID-19: a systematic review. J Neurological Sci 2020;116832.
9. Shereen MA, Khan S, Kazmi A, Bashir N, Siddique R. COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. J Advanced Res 2020;24:91-8.
10. Nersesjan V, Amiri M, Lebech A-M, Roed C, Mens H, Russell L, et al. Central and peripheral nervous system complications of COVID-19: a prospective tertiary center cohort with 3-month follow-up. J Neurol 2021;1-19.
11. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet 2020;395(10229): 1033-4.
12. Santoro L, Ferraro PM, Flex A, Nesci A, De Matteis G, Di Giorgio A, et al. New semiquantitative ultrasonographic score for peripheral arterial disease assessment and its association with cardiovascular risk factors. Hypertension Research 2016;39(12):868-73.
13. Wu C, Chen X, Cai Y, Zhou X, Xu S, Huang H, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Internal Med 2020;180(7):934-43.
14. Maggi S. Special issue nutrition and musculoskeletal health. Aging Clin Exp Res 2019;31(6):741.
15. Ilie PC, Stefanescu S, Smith L. The role of vitamin D in the prevention of coronavirus disease 2019 infection and mortality. Aging Clinical Exp Res 2020;32(7):1195-8.
16. Barazzoni R, Bischoff SC, Breda J, Wickramasinghe K, Krznaric Z, Nitzan D, et al. ESPEN expert statements and practical guidance for nutritional management of individuals with

SARS-CoV-2 infection. Elsevier;2020.
17. Butowt R, Meunier N, Bryche B, von Bartheld CS. The olfactory nerve is not a likely route to brain infection in COVID-19: a critical review of data from humans and animal models. Acta Neuropathologica 2021;1-14.
18. Mathew D. Loss of Smell in COVID-19 Patients: Lessons and Opportunities. Frontiers in Human Neurosci 2020;14.
19. Hjelmesæth J, Skaare D. Loss of smell or taste as the only symptom of COVID-19. Tidsskrift for Den norske legeforening 2020.
20. Golestani-Eraghi M, Mahmoodpoor A. Early application of prone position for management of Covid-19 patients. J Clin Anesthesia 2020;66:109917.
21. Chapman KM, Berger MJ, Doherty C, Anastakis DJ, Baltzer HL, Boyd KU, et al. Recommendations for Patients with Complex Nerve Injuries during the COVID-19 Pandemic. Canadian J Neurological Sci 2021;48(1):50-5.
22. Septyaningtrias DE, Susilowati R. Neurological involvement of COVID-19: from neuroinvasion and neuroimmune crosstalk to long-term consequences. Reviews in the Neurosciences 2021.
23. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan. JAMA Cardiol.
24. Ali AM, Kunugi H. Skeletal muscle damage in COVID-19: a call for action. Medicina 2021;57(4):372.
25. El-Tallawy SN, Nalamasu R, Pergolizzi JV, Gharibo C. Pain management during the COVID-19 pandemic. Pain and Therapy 2020;1-14.

Original Article

Assessment of the Level of Stress among Dental Students During Covid-19 in Teaching Hospital of Sialkot, Pakistan

Sana Zafar[1], Danish Javed[2], Hira Shafique[3], Muhammad Muddassar[4], Shakeel Ahmad[2] and Muhammad Osman Masood[5]

ABSTRACT

Objective: The check the level of stress due to COVID-19 in dental students.
Study Design: Descriptive cross-sectional study
Place and Duration of Study: This study was conducted at the Department of Oral Biology, Islam Dental College, Sialkot for a period of 06 months from June to November 2020.
Materials and Methods: The sample size has calculated with the help of Rao software. The total number of samples were 319 and recruited based on purposive sampling method. The data had analyzed descriptively.
Results: Out of 319 students, 123 were male and 196 of female. The average age of the students are 21.7 years. Maximum number of responders were having severe stress i.e. 186. Four different doubts were asked from the students. Out of 319 responders, 281 were replied no in response of "will you feel comfortable after COVID-19 pandemic" and 38 said yes. Five different questions were asked from the students i.e. Handwashing, using sanitizers, surgical masks, avoid social gathering and hand shaking. 271 replied yes in response of "Handwashing" and 48 said no. While the level of stress was also measured among the responses. 162 students who had severe stress were categorized in yes response, 62 students who had moderate level of stress were categorized in yes response and 47 students who had mild level of stress were categorized in yes response.
Conclusion: The present study explored the levels of stress among the dental students. The finding of the study indicated that the student in a teaching hospital needs the appropriate counselling and professional knowledge regarding the pandemic to deal with the current scenario of COVID-19.

Key Words: Stress, COVID-19, Dental, Pakistan

Citation of article: Zafar S, Javed D, Shafique H, Muddassar M, Ahmad S, Masood MO. Assessment of the Level of Stress among Dental Students During Covid-19 in Teaching Hospital of Sialkot, Pakistan. Med Forum 2021;32(10):167-171.

INTRODUCTION

The world health organization (WHO) defined the pandemic is a spread of any disease or infection in a certain community, or worldwide. [1]
The pandemic infections and a disease travel the across the globe hence appears to be prevailed internationally.[2]

[1.] Department of Oral Biology /.Oral Pathology[2] / Community Dentistry[3] / Oral Medicine[4] / Operative Maxillofacial Surgery[5] / Orthodontics[6], Islam dental college, Sialkot.

Correspondence: Dr. Danish Javed, Associate Professor and HOD, Islam Dental College, Sialkot
Contact No: 0333-444-3232
Email: danish_javaid@hotmail.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

The COVID-19 is a newly discovered infection of corona viruses, which started in late 2019, from city of china named Wuhan.
Later on, in the year 2020 the disease was declared as a "public health emergency" of the international concern[3]. The Crisis caused by COVID-19 were multiple during the year 2020, and it showed the multiple factors effecting the mental health of people.
The most common term during that phase was Depression due to the scenario and stress of getting effected. Plomecka et al, addressed the psychological symptoms associated with the pandemic among the students are responsible people of family.
The earliest spot of stress due to COVID-19 was China, Although the situation was getting worse among every part of the world. The focused was made on health care workers, children and elder patients during the epidemic. The students and general population are the most vulnerable group with surprised levels of stress during the quarantine period.[4]

The pandemic of COVID-19 effected almost every concern of life, closing the public places, roads, and markets hence the educational system. The education system of entire world transferred to virtual learning [5] The Medical students of Universities perceived being stressful due to tough schedule and competent professional life [6]. The previous studies show that the outbreak of a certain disease effects the mental health of wellbeing. There are many factors involves in developing the stress, but the pandemic related stress is predominant among students [7]. The psychological stress during the pandemic has been studied by many researchers, which showed a positive response against pandemic situation [8]. Many studies shown that stress may have negative impact on the cognitive functioning and learning of medical students. [9-10] The outbreak of COVID-19 had significant psychological stress on the students [11] Many studies in the past found that he stresses and anxiety are more prevalent among other mental disorders with more burden of illness [12]. The crisis of COVID-19 pandemic has intense the situation with multiple risks like exposure to the infection, the limitation to access the educational institutes, unable to access the medical practice and complicated virtual learning has great impact on the student's mental health [13] As the highlighted facts above assessed in different countries, and data available on the mental stress level of dental students it is an urgent need to assess the stress and associated factors. The current study aims to assess the levels of stress among the dental students during COVID-19, in a teaching hospital of Sialkot and Abbottabad, Pakistan.

MATERIALS AND METHODS

A descriptive cross-sectional study was conducted in the Department of Oral Biology at Islam dental college Sialkot, Pakistan for a period of 06 months from June to November 2020. The sample size has calculated with the help of Rao software. The total number of samples were 319 and recruited the help of purposive sampling method. Before starting the study, consent were taken from the student voluntarily without any financial benefits and conflict of interest. Dental students from first year to final year had enrolled in the study. The response was collected with the help of different sources i.e. physically taken the data from the students and online google form. There are various sections of the questionnaire such as Demographic, dental health during COVID-19, problems face in study during COVID-19 and anxiety/stress related questions. In questionnaire, 5-point Likert scale was also used to assess the responses. The questionnaire had run in 20 participants for validation. Based on the responses, the modifications took place in the questionnaire. The data had analyzed descriptively with the help of statistical software.

RESULTS

Table 01 described the demographic information of enrolled dental students. Out of 319 students, 123 were male and 196 of female. The students are of various classes from first year to fourth year and house job interns. Maximum number of students were from fourth year i.e. 89 followed by third year i.e. 63 and house job interns are 62. The average age of the students are 21.7 years.

Table No.1: Demographic Information of enrolled students

S.No	Gender	Frequency (N=319)	%age
1	Male	123	38.56
2	Female	196	61.44
Year of Students			
3	First year	47	14.73
4	Second Year	58	18.18
5	Third Year	63	19.75
6	Fourth Year	89	27.89
7	House Job Students	62	19.43

Table: 02 described the sources of COVID-19 information by the dental students. Out of 319 students, maximum was getting information from television source i.e. 132 followed by university officials i.e. 84. While 68 students were getting information from their friend and 35 from newspaper. Further the information was also categorized based on four levels i.e. Excellent, Good, Fair and Poor. Maximum number of students were categorized the getting information as excellent i.e. 139 while 69 were categorized as poor information.

Table No.2: Source of COVID-19 Information by the Dental students

S. No	Sources	Frequency	Percentage
1	TV	132	41.38
2	Newspaper	35	10.98
3	University	84	26.33
4	Friends	68	21.32
Categorization of Source of Information			
5	Excellent	139	43.57
6	Good	68	21.31
7	Fair	43	13.47
8	Poor	69	21.63

Table No.3: Level of Stress during COVID-19

S/No	Level	Frequency	Percentage
1	Severe	186	58.30
2	Moderate	78	24.45
3	Mild	55	17.24

Level of stress were also assessed in below table no 03. The stress are divided into three different categories i.e. severe, moderate and mild. Maximum number of

responders were having severe stress i.e. 186 followed by moderate level i.e. 78 and 55 were of mild stress.

Table number 04 explained the individual doubts of dental students regarding their profession in relation of level of stress. Four different doubts were asked from the students. Out of 319 responders, 281 replied no in response of "will you feel comfortable after COVID-19 pandemic" and 38 said yes. While the level of stress was also measured among the responses. 186 students who had severe stress were categorized in no response, 60 students who had moderate level of stress were categorized in no response and 35 students who had mild level of stress were categorized in no response. The details of other doubts were mentioned in below mentioned table.

Table No.4: **Individual doubts concerning the dental profession and its association with stress level**

Doubts	Response	Levels of Stress		
		Severe (N=186)	Moderate (N=78)	Mild (N=55)
Will you feel comfortable after COVID-19 pandemic	Yes=38	0	18	20
	No=281	186	60	35
Will you perform job efficiently after COVID-19 pandemic	Yes=67	10	17	37
	No=252	176	61	18
Can you think for change the profession	Yes=115	65	42	8
	No=204	121	36	47
Will you prefer to postponed the clinical rotations during COVID-19	Yes=279	169	62	48
	No=40	17	16	7

Table number 05 explained the comparative relation of stress with personal hygiene during COVID-19. Five different questions were asked from the students i.e. Handwashing, using sanitizers, surgical masks, avoid social gathering and hand shaking. Out of 319 responders, 271 replied yes in response of "Handwashing" and 48 said no. While the level of stress was also measured among the responses. 162 students who had severe stress were categorized in yes response, 62 students who had moderate level of stress were categorized in yes response and 47 students who had mild level of stress were categorized in yes response. The details of other questions were mentioned in below mentioned table.

Table No.5: **Comparative relation of stress with Personal hygiene during COVID-19**

Personal Hygiene	Response	Levels of Stress		
		Severe (N=186)	Moderate (N=78)	Mild (N=55)
Handwashing	Yes=271	162	62	47
	No=48	24	16	8
Using of Sanitizers	Yes=259	165	58	36
	No=60	21	20	19
Surgical Masks using	Yes=217	152	53	12
	No=102	34	25	43
Avoiding Social Distancing	Yes=185	136	32	17
	No=134	50	46	38
Avoid Hand Shaking	Yes=163	126	28	9
	No=156	60	50	46

DISCUSSION

Stress is sum of mental and emotional tension of a person that has many consequences and response to community. The medical students are the easiest target of emotional stress and physical tiredness, especially females as addressed in a study. [14] The students form fourth professional year were more 27.8% responsive against the stress whereas the least majority of response were collected from the first-year students from the teaching hospital, the students on their house job were approached to assess the stress, hence 19.4% response were collected from them [15] The students were approach to collect the information obtained about the COVID-19, the vast majority 41.3% of students obtained information from the television, as the media plays the important role in delivering the information [16] To assess the stress and its levels the stress was divided into three different categories Maximum number of responders were having severe stress i.e., 186 followed by moderate level i.e., 78 and 55 had mild stress similarly found in a study conducted. The reason behind developing the stress among the students can be physiological strains and hectic schedule, hence during the COVID-19 pandemic the restriction and limited resources during the quarantine period played the vital role similarly showed in a study [17] Many researchers tried to assess the factors hence the proven factors in studies showed that the virtual learning system and complex situation due to COVID-19 has scared the dental student. Presently the situation a developing country like Pakistan, the unavailability of medicines and appropriate vaccines for infected people is the scenario of a big concern, Sanders et al addressed the similar issues that the restriction and limited movement to the institutes has a role to develop the stress in all age groups [18]. The students were also approach to assess the stress regarding their profession. Out of all

responders, the 281 students addressed the uncomfortable situation after COVID-19 pandemic and 186 students had severe stress were categorized in no response, 60 students who had moderate level of stress were categorized in no response and 35 students who had mild level of stress were categorized in no response in accordance to our study [19] The comparative relation of stress with personal hygiene during COVID-19 was the important issue address in researches[20] The regular practices of Handwashing, using sanitizers, surgical masks, avoid social gathering and hand shaking were the main precautionary measure advised to every citizen and the most frequently practiced precaution was "Handwashing. Among those responses the 162 students who had severe stress were categorized for positive response regarding the handwashing, 62 students who had moderate level of stress were categorized in yes response and 47 students who had mild level of stress were categorized in yes response [21-22] The results of the study showed that stress was prevalent among the dental students during the pandemic period due to fear of getting infected, and anxiety levels and emotional stress were among those students with less knowledge and inability to access the appropriate health care system.

CONCLUSION

The present study explored the stress the levels of stress and anxiety among the dental students. The finding of the study indicated that the student in a teaching hospital needs the appropriate counselling and professional knowledge regarding the pandemic to deal with the current scenario of COVID-19. It is the emergent time to focus on the appropriate guidance and delivering the enough knowledge to the students and health care professionals as main Participants of the society.

Author's Contribution:

Concept & Design of Study:	Sana Zafar
Drafting:	Danish Javed, Kamal Khan Hoti
Data Analysis:	Shakeel Ahmad Muhammad Osman Masood
Revisiting Critically:	Imran Saleem Qureshi
Final Approval of version:	Muhammad Mudassar

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. AlAteeq DA, Aljhani S, AlEesa D. Perceived stress among students in virtual classrooms during the COVID-19 outbreak in KSA. J Taibah University Medical Sci 2020;15(5):398-403.
2. Rehman U, Shahnawaz MG, Khan NH, Kharshiing KD, Khursheed M, Gupta K, Uniyal R. Depression, anxiety and stress among Indians in times of Covid-19 lockdown. Community Mental Health J 2020;1-7.
3. Ellis WE, Dumas TM, Forbes LM. Physically isolated but socially connected: Psychological adjustment and stress among adolescents during the initial COVID-19 crisis. Canadian Journal of Behavioural Science/Revue canadienne des sciences du comportement 2020;52(3):177.
4. Husky MM, Kovess-Masfety V, Swendsen JD. Stress and anxiety among university students in France during Covid-19 mandatory confinement. Comprehensive Psychiatr 2020;102:152191.
5. Wang X, Hegde S, Son C, Keller B, Smith A, Sasangohar F. Investigating mental health of US college students during the COVID-19 pandemic: cross-sectional survey study. J Medical Internet Research 2020;22(9):e22817.
6. Schiff M, Zasiekina L, Pat-Horenczyk R, Benbenishty R. COVID-related functional difficulties and concerns among university students during COVID-19 pandemic: A binational perspective. J Community Health 2020;1-9.
7. Son C, Hegde S, Smith A, Wang X, Sasangohar F. Effects of COVID-19 on college students' mental health in the United States: Interview survey study. J Medical Internet Res 2020;22(9): e21279.
8. Nakhostin-Ansari A, Sherafati A, Aghajani F, Khonji MS, Aghajani R, Shahmansouri N. Depression and anxiety among Iranian Medical Students during COVID-19 pandemic. Iranian J Psychiatr 2020;15(3):228.
9. Liu X, Liu J, Zhong X. Psychological state of college students during COVID-19 epidemic 2020. Available at SSRN 3552814.
10. Thawabieh AM, Qaisy LM. Assessing stress among university students. Am Int J Contemporary Res 2012;2(2):110-116.
11. Średniawa A, Drwiła D, Krotos A, Wojtaś D, Kostecka N, Tomasik T. Insomnia and the level of stress among students in Krakow, Poland. Trends Psychiatr Psychotherap (AHEAD) 2019.
12. Ofoegbu F, Nwadiani M. Level of Perceived Stress Among Lectures in Nigerian Universities. J Instructional Psychol 2006;33(1):5-20.
13. Yusoff MSB, Rahim AFA, Yaacob MJ. Prevalence and sources of stress among Universiti Sains Malaysia medical students. Malaysian J Med Sci: MJMS 2010;17(1):30.
14. Cao W, Fang Z, Hou G, Han M, Xu X, Dong J, et al. The psychological impact of the COVID-19 epidemic on college students in China. Psychiatry Research 2020.

15. Chetterje P. Gaps in India's preparedness for COVID-19 control. Lancet Infectious Diseases 2020; 20(5):544.
16. Cheng V, Wong S, Chuang V, So S, Chen J, Sridhar S, et al. The role of community-wide wearing of face mask for control of coronavirus disease 2019 (COVID-19) epidemic due to SARS-CoV-2. J Infection 2020.
17. Currie C, Molcho M, Boyce W, Holstein B, Torsheim T, Richter M. Researching health inequalities in adolescents: The development of the Health Behaviour in School-Aged Children (HBSC) Family Affluence Scale. Social Science Med 2008;66(6):1429–1436.
18. Sanders J, Monogue M, Jodlowski T, Cutrell J. Pharmacologic treatments for Coronavirus Disease 2019 (COVID-19). JAMA 2020.
19. Dandekar A, Ghai R. Migration and reverse migration in the age of COVID-19. Economic & Political Weekly 2020;55(19):28–31.
20. Goyal K, Chauhan P, Chhikara K, Gupta P, Singh M. Fear of COVID 2019: First suicidal case in India! Asian J Psychiatr 2020;49:101989.
21. Hall R, Hall R, Chapman M. The 1995 Kikwit Ebola outbreak: Lessons hospitals and physicians can apply to future viral epidemics. General Hospital Psychiatr 2008;30(5):446–452.
22. Leung G, Lam T, Ho L, Ho S, Chan B, Wong I, et al. The impact of community psychological responses on outbreak control for severe acute respiratory syndrome in Hong Kong. J Epidemiol Community Health 2003;57(11):857–863.

Original Article

Phenotypic Presentation of Oculopharyngeal Muscular Dystrophy

Oculopharyngeal Muscular Dystrophy

Fahim Ahmed Soomro[1], Sajjad Jalbani[1], Mukhtiar Lakho[1], Ghafoor Magsi[1], Vijia Kumar Gemnani[2] and Sarmad Jamal Siddiqui[2]

ABSTRACT

Objective: The purpose of this paper is to present OPMD in Pakistan.
Study Design: Analytic study
Place and Duration of Study: This study was conducted at the Qamber Shahdadkot, recruited through Neurology department CMCH SMBBU Larkana from July 2019 to June 2020 for a period of one and a half year.
Materials and Methods: In a patient manifesting signs of OPMD, we arranged a camp to screen family members and close relatives for characteristic findings of OPMD. The analysis become made on scientific grounds. Demographic characteristics and clinical features were noted in structured proforma. Data analysis was done using SPSS.
Results: A total of 40 patients were diagnosed with OPMD. The mean age of patients was 27.75±14.27. The demographic presentation is shown in table-1. The mean age of patients when they had first symptoms was 18.85±10.12. 24 (60%) were male and 16 (40%) were female patients. First symptom was ptosis in 29 (72.5%) and dysphagia in 11 (27.5%) patients. Ptosis as the first symptom was seen in 18(62.1%) males and 11(37.9%) females. Dysphagia was the first symptom in 6(54.5%) males and 5(45.5%) female patients with p=.728. Ptosis was the most common symptoms present in 39(97.5%) patients. Ptosis was seen in all female patients included in our study while it was absent in only 1 male patient at the time of presentation with p=1.000. Dysphagia was the second most common symptom found in 32(80%) followed by proximal weakness found in 22(55%) and ophthalmoplegia found in 19(47.5%). Dysphagia was present in 21(65.6%) males and 11(34.4%) female patients with p=.229. Ophthalmoplegia was seen in 11(57.9%) males and 8(42.1%) females with p=0.769. Proximal myopathy was seen in 13(59.1%) males and 9(40.9%) female patients with p=.897. All patients had a positive family history of OPMD.
Conclusion: OPMD in our population has an earlier onset, which may be as early as the first few years of life. The disease is more severe. Common in the male population and about half of the patients present with proximal limb weakness and ophthalmoplegia besides ptosis and dysphagia.
Key Words: Phenotypic, Oculopharyngeal, Muscular, Dystrophy

Citation of article: Soomro FA, Jalbani S, Lakho M, Magsi G, Gemnani VK, Siddiqui SJ. Phenotypic Presentation of Oculopharyngeal Muscular Dystrophy. Med Forum 2021;32(10):172-175.

INTRODUCTION

The muscular dystrophies are an inherited group of progressive myopathic problems attributable to defects in many genes needed for normal muscle functions. Oculopharyngeal muscular dystrophy (OPMD) is a rare myopathy that is characterized by involving of ocular and pharyngeal muscle, lead to ptosis and dysphagia.[1, 2]

[1.] Department of Neurology / Community Medicine[2], CMCH (SMBBMU) Larkana.

Correspondence: Dr. .Vijia Kumar Gemnani, Associate Professor of Community Medicine, CMC (SMBBMU), Larkana.
Contact No: 0335-3135679
Email: gemnanivijay11@mail.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

First described in 1915 by Taylor, when a progressive cranial neuropathy was attributed to it.[3] Inheritance in an autosomal dominant manner and primary as myopathy was demonstrated by Victor in 1962.[1]The muscle histology reveals abnormal variability in fiber size., an increment in endomysial fibrosis, and cytoplasmic basophilic rimmed vacuoles like those found in incorporation body myositis.[4] Commonly OPMD present with ptosis, dysarthria, and dysphagia. It can likewise be related with proximal and distal limit weakness. Usually onset occurs in middle age. The diagnosis was at first based on clinical features, muscle histology, and positive family history.

Repeat expansion of trinucleotide (stable) at the N-terminus of a poly(A) binding protein gene (PABP2) chromosome 14 was notified by Brais and partners.[5] Autosomal recessive inheritance has been reported with alleles that have 11 repeats,[5-7] as has at least one case of probable autosomal dominant inheritance.[8]

Even though OPMD has globally distribution, highest prevalence seemed in French-Canadian Kindred. So in this scenario, we highlighted the clinical aspects of OPMD from Pakistan.

MATERIALS AND METHODS

Subjects were from a village of district Qamber Shahdadkot, recruited through Neurology department CMCH SMBBU Larkana. Study was carried out during the period of July 2019 to June 2020. We arranged a camp in the village of an indexed patient and family members were screened for presence and absence of abnormalities related to occulopharyngeal muscular dystrophy. A total of 16 to 20 families were screened related to the index patient. Details of the patients were noted confidentially. Ethical approval was obtained from the ethical review committee of the CMCH SMBBMU Larkana.

The diagnosis was made on clinical grounds. Demographic characteristics and clinical features were noted in structured proforma. Data analysis was done using SPSS 16 version.

RESULTS

A total of 40 patients were diagnosed with OPMD. The mean age of patients was 27.75±14.27. The demographic presentation is shown in table-1. The mean age of patients when they had first symptoms was 18.85±10.12. 24 (60%) were male and 16 (40%) were female patients. First symptom was ptosis in 29 (72.5%) and dysphagia in 11 (27.5%) patients. Ptosis as the first symptom was seen in 18(62.1%) males and 11(37.9%) females. Dysphagia was the first symptom in 6(54.5%) males and 5(45.5%) female patients with p=.728. Ptosis was the most common symptoms present in 39(97.5%) patients.

Table No.1: Demographic presentation of OPMD

Characteristics		MEAN ± SD
Age (Mean ± SD)		27.75±14.27
Age of First symptom		18.85±10.12
Characteristics		Number (percentages)
Gender	Male	24(60%)
	Female	16(40%)
First Symptom		
	Ptosis	29(72.5%)
	Dysphagia	11(27.5%)
Symptoms	Ptosis	39(97.5%)
	Dysphagia	32(80%)
Ophthalmoplegia	Proximal weakness	22(55%)
	Family History	40(100%)

Ptosis was seen in all female patients included in our study while it was absent in only 1 male patient at the time of presentation with p=1.000. Dysphagia was second most common symptom found in 32(80%) followed by proximal weakness found in 22(55%) and ophthalmoplegia found in 19(47.5%). Dysphagia was present in 21(65.6%) males and 11(34.4%) female patients with p=.229. Ophthalmoplegia was seen in 11(57.9%) males and 8(42.1%) females with p=0.769. Proximal myopathy was seen in 13(59.1%) males and 9(40.9%) female patients with p=.897. All patients had positive family history of OPMD.

DISCUSSION

We identified 40 cases of OPMD belonging to different families from district Qamber Shahdadkot. All families were interlinked to each other with inter-marriages within families. Until recently, the OPMD diagnosis was made on common clinical findings, positive family history, and demonstration of characteristic inclusions in muscle biopsy. However, diagnosis can be confirmed by molecular genetic analysis. Since its first report in 1915 it has been reported in many countries and there are as many as 300 published papers on OPMD. Until the 1980s OPMD was more considered a disorder of racially white western people. However, there are reported cases from Japan, Israel, and Siberia.[9-11] Very few papers have been reported from Asia including China, India, and Taiwan, probably due to underdiagnosis. The majority of patients in our study have an earlier onset of symptoms, before the age of 45 years, pointing to dominant OPMD with severe disease in individuals' homozygote for OPMD.[12-14] Yu-Yi Chien in his paper on OPMD reported 3 cases of OPMD in a Chinese immigrant family where 1 patient was a 67-year-old male, the second patient was a 46-year-old female, although she had prolonged symptoms she was diagnosed after her father was diagnosed with OPMD and the third patient was a 38-year-old female.[15]Blumen SC et al. in their paper on OPMD reported all 5 patients with late-onset disease.[16] Mirabella M et al. in their study in the Italian population reported onset as early as 30 years of age.[17] In our study mean age of the first symptom was 18.85±10.12. Age at the time of the first symptom in our study was seen as early as 2 years of life. A similar pattern of illness was seen by Fukuhara N et al. They found 2 cases of OPMD; case 1 had onset of symptoms at the age of 23 years and case 2, son of case 1 had onset of symptoms at the age of 2 years.[9] Hill ME et al. in UK population-based study found age at the onset ranging from 17 to 70 years of age.[18] Contrary to that Kuo HC et al. in Taiwanese study reported age at the onset ranging from 35 to 50 years.[19]24(60%) of patients in this study were male and 16(40%) were female, in contrast to the UK population-based study by Hill ME et al. where 61% of individuals included in the study were female.[18]Similar percentages consistent with our study were seen by Kuo HC et al. in Taiwanese study where 60% of patients were male and 40% were female patients.[19] Muller T et al. in German paper on 16

OPMD patients found 10(62%) female and 6 (38%) male patients.[20] the First symptom was ptosis present in 29(72.5%) of patients in this study, a finding consistent with Hill ME et al. where two-thirds of patients noted ptosis as the first symptom at the onset of disease.[18] Fukuhara N et al. in their study found ptosis as the initial symptom in case 1 and muscle weakness as presenting symptom in case 2.[9] Contrary to that Kuo HC et al. in their Taiwanese study reported dysphagia as the initial symptom in two-thirds of patients.[19] Muller T et al. reported all 16 patients included in their study presented with ptosis as an initial symptom.[20] Same findings were seen by Mirabella M et al. in their Italian study, whereof 16 patients included in study 15 presented with ptosis as an initial symptom.[17] Finally Blumen SC et al. in their OPMD study on Bulgarian Jewish patients reported 3 had severe ptosis at the time of presentation and 2 had h/o blepharoplasty at the time of diagnosis.[16] Ophthalmoplegia was seen in 19(47.5%) patients in this study, a finding not consistent with that seen by Muller T et al, were only 5(31%) of 16 patients had ophthalmoplegia.[20] Contrary to that Kuo et al. found 6(60%) of 10 patients in their study had ophthalmoplegia with a frequency higher than we found in our study.[19] While Hill ME et al. found half of their patients had ophthalmoplegia, a finding consistent with our study.[18] Proximal myopathy was present in 22(55%) patients in our study, a finding not consistent with findings by Kuo HC et al. where only one of ten patients had proximal weakness and Hill ME et al. where 3 of 31 patients presented with limb weakness.[18, 19] Our findings remained consistent with a study published by Muller T et al. where 9(56%) of 16 patients had proximal muscle weakness.[20] 5(31%) of 16 patients from the Mirabella M et al. study reported proximal weakness, a finding not consistent with our study.[17] Proximal upper limb weakness was seen in all 5 patients and 3 of 5 patients involving proximal lower limb in Bulgarian Jewish patients study, a finding not consistent with our study.[16]

The main limitations of this study were that due to lack of resources we diagnosed patients only on clinical grounds and positive family history. Neither we could perform a muscle biopsy to look for characteristic pathological findings nor we could perform molecular genetic analysis for mutations.

In summary OPMD in our population has an earlier onset, which may be as early as the first few years of life. The disease is more severe. Common in the male population and about half of the patients present with proximal limb weakness and ophthalmoplegia besides ptosis and dysphagia.

CONCLUSION

OPMD in our population has an earlier onset, which may be as early as the first few years of life. The disease is more severe. Common in the male population and about half of the patients present with proximal limb weakness and ophthalmoplegia besides ptosis and dysphagia.

Author's Contribution:

Concept & Design of Study:	Fahim Ahmed Soomro
Drafting:	Sajjad Jalbani, Mukhtiar Lakho
Data Analysis:	Ghafoor Magsi, Vijia Kumar Gemnani, Sarmad Jamal Siddiqui
Revisiting Critically:	Fahim Ahmed Soomro, Sajjad Jalbani, Mukhtiar Lakho
Final Approval of version:	Fahim Ahmed Soomro

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Victor M, Hayes R, Adams RD. Oculopharyngeal muscular dystrophy. A familial disease of late life characterized by dysphagia and progressive ptosis of the eyelids. N Engl J Med 1962;267:1267-72.
2. Trollet C, Boulinguiez A, Roth F, Stojkovic T, Butler-Browne G, Evangelista T, et al. Oculopharyngeal Muscular Dystrophy. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, et al, editors. GeneReviews ®. Seattle (WA): University of Washington, Seattle Copyright © 1993-2020, University of Washington, Seattle. Gene Reviews is a registered trademark of the University of Washington, Seattle. All rights reserved;1993.
3. Taylor EW. Progressive vagus-glossopharyngeal paralysis with ptosis. A contribution to the group of family, diseases. J Nervous Mental Disease 1915;42(3):129-39.
4. Coquet M, Vital C, Julien J. Presence of inclusion body myositis-like filaments in oculopharyngeal muscular dystrophy. Ultrastructural study of 10 cases. Neuropathol Applied Neurobiol 1990;16(5):393-400.
5. Brais B, Bouchard JP, Xie YG, Rochefort DL, Chrétien N, Tomé FM, et al. Short GCG expansions in the PABP2 gene cause oculopharyngeal muscular dystrophy. Nature Genetics 1998;18(2):164-7.
6. Raz V, Butler-Browne G, van Engelen B, Brais B. 191st ENMC international workshop: recent advances in oculopharyngeal muscular dystrophy research: from bench to bedside 8-10 June 2012, Naarden, The Netherlands. Neuromuscular disorders: NMD 2013;23(6):516-23.
7. Hebbar S, Webberley MJ, Lunt P, Robinson DO. Siblings with recessive oculopharyngeal muscular dystrophy. Neuromuscular disorders: NMD 2007; 17(3):254-7.

8. Richard P, Trollet C, Gidaro T, Demay L, Brochier G, Malfatti E, et al. PABPN1 (GCN)11 as a Dominant Allele in Oculopharyngeal Muscular Dystrophy-Consequences in Clinical Diagnosis and Genetic Counselling. J Neuromuscular Diseases 2015;2(2):175-80.
9. Fukuhara N, Kumamoto T, Tsubaki T, Mayuzumi T, Nitta H. Oculopharyngeal muscular dystrophy and distal myopathy. The intrafamilial difference in the onset and distribution of muscular involvement. Acta Neurologica Scandinavica 1982;65(5): 458-67.
10. Tamir G, Hauben D. [Oculopharyngeal muscular dystrophy]. Harefuah 1990;118(11):634-6.
11. Puzyrev VP, Maximova NP. Hereditary diseases among Yakuts. Russian J Genetics 2008; 44(10):1141-7.
12. Brais B BJ, Xie YG, et al. A more severe form of oculopharyngeal muscular dystrophy is documented in a genetically proven homozygous patient. Neurol 1995;45:293P.
13. Blumen SC, Sadeh M, Korczyn AD, Rouche A, Nisipeanu P, Asherov A, et al. Intranuclear inclusions in oculopharyngeal muscular dystrophy among Bukhara Jews. Neurol 1996;46(5):1324-8.
14. Bouchard JP, Gagné F, Tomé FM, Brunet D. Nuclear inclusions in oculopharyngeal muscular dystrophy in Quebec. Canadian J Neurological Sciences Le J Canadien des Sciences Neurologiques 1989;16(4):446-50.
15. Chien YY. Oculopharyngeal muscular dystrophy -- an under-diagnosed disease in China? Report a China-born Chinese with PABPN1 mutation and epidemiology review of the literature. J Formosan Medical Association = Taiwan Yi Zhi 2012; 111(7):397-402.
16. Blumen SC, Kesler A, Dabby R, Shalev S, Khayat M, Almog Y, et al. Oculopharyngeal muscular dystrophy among Bulgarian Jews: a new cluster? The Israel Med Assoc J: IMAJ 2013;15(12): 748-52.
17. Mirabella M, Silvestri G, de Rosa G, Di Giovanni S, Di Muzio A, Uncini A, et al. GCG genetic expansions in Italian patients with oculopharyngeal muscular dystrophy. Neurol 2000;54(3):608-14.
18. Hill ME, Creed GA, McMullan TF, Tyers AG, Hilton-Jones D, Robinson DO, et al. Oculopharyngeal muscular dystrophy: phenotypic and genotypic studies in a UK population. Brain: A J Neurol 2001;124(Pt 3):522-6.
19. Kuo HC, Chen CM, Lee-Chen GJ, Hu FJ, Chu CC, Liou CW, et al. Study of a Taiwanese family with oculopharyngeal muscular dystrophy. J Neurological Sciences 2009;278(1-2):21-4.
20. Müller T, Schröder R, Zierz S. GCG repeats and phenotype in oculopharyngeal muscular dystrophy. Muscle Nerve 2001;24(1):120-2.

Original Article

Lateral Anal Sphincterotomy for Chronic Anal Fissures- A Comparison of Outcomes and Complications under Local Anaesthesia Versus Spinal Anaesthesia

Sumta Khan, Farhan Zaheer, Shafaq Naseer, Usama Iqbal Khatri, Rizwan Khan, Qamaruddin Baloch

ABSTRACT

Objective: To compare the mean pain scores at 6 hours and 24 hours after lateral internal sphincterotomy under local anesthesia versus spinal anesthesia.

Study Design: A double-blind prospective randomized controlled trial study

Place and Duration of Study: This study was conducted at the conducted at surgical unit 2, Civil Hospital Karachi, Pakistan from June, 2018 to December, 2018 for a period of six months.

Materials and Methods: A total of 60 patients were selected by non-probability consecutive sampling, aged 18-65 years of either gender with complaint of chronic anal fissure lasting 3 months, underwent lateral internal sphincterotomy. They were randomized into 30 patients who received local anesthesia and 30 patients who received spinal anesthesia by closed envelop method. Mean pain score was measured as the primary outcome at 6 hours and 24 hours after the procedure.

Results: There was no statistically significant difference found in mean pain score at 6 hours and 24 hours after the LIS in both groups. Mean pain score at 6 hours was 5.40 (±1.886) and 5.40 (±2.568) respectively (p-value=0.102) while at 24 hours mean pain score was 1.77 (±1.278) and 2.37(±1.159) respectively (p-value=0.859). Moreover, the patients who had local anesthesia were met withlow risk of anesthesia, short hospital stay and early return to home.

Conclusion: Lateral internal sphincterotomy can be safely performed under local anesthesia with minimum risk of complications.

Key Words: Chronic anal fissure, Bupivacaine, Local anesthetic, Lateral internal sphincterotom

Citation of article: Khan S, Zaheer F, Naseer S, Khatri UI, Khan R, Baloch Q. Lateral Anal Sphincterotomy for Chronic Anal Fissures- A Comparison of Outcomes and Complications Under Local Anaesthesia Versus Spinal Anaesthesia. Med Forum 2021;32(10):176-179.

INTRODUCTION

Fissure in Ano is described as a linear breach or ulcer in the anoderm which usually remains distal to the dentate line. Even though the definite cause of anal fissure is still unknown[1], it is one of the most common anorectal diseases associated with pain in the anal region.[2,3] and bleeding during defecation; thereby, leading to the clinical diagnosis of the disease.[4] It is often associated with increased resting anal sphincter tone and decreased blood supply[5] and is classified into acute and chronic fissures.

Department of Surgery, Civil Hospital, Dow University Of Health Sciences, Karachi.

Correspondence: Dr. Farhan Zaheer, Associate Professor of Surgery, Surgical Unit-6, Civil Hospital, Dow University Of Health Sciences, Karachi.
Contact No: 03002108924
Email: farhan.zaheer@duhs.edu.pk

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

Acute anal fissures resolve within four weeks while, chronic anal fissure usually persists beyond four weeks with a non-healing indurated edge and prominent internal sphincter fibers at the base of the fissure.

The treatment modalities commonly include non-operative and operative techniques, however, both work in a similar manner, that is, by reducing the anal sphincter tone and improve blood supply.[6] Although majority of non-operative techniques include topical application of lignocaine gel, nitrates or calcium channel blockers, sitz baths, high fiber diet, and stool softeners [6,7,] Lateral internal sphincterotomy (LIS) is considered the gold standard surgical treatment for chronic anal fissures.[8] is also preferred in the cases of, complicated, and acute anal fissures refractory to non-operative treatment.[9] The overall procedure of the LIS surgical technique involves dividing the lower fibers of internal sphinchter to relieve muscle spasm subsequently, improving blood supply accompanied by incontinence, the persistence of fissure, and recurrence like complications.[10]

LIS may be performed under local anesthesia or spinal anesthesia. Generally, LIS is routinely performed under spinal anesthesia which provides good intra- operative

and immediate post-operative pain relief, however it carries risks of complications like hypotension, urinary retention, spinal headache, spinal hematoma, meningitis, prolonged hospitalization, and immobilization.[11,12] The effectiveness of local anesthesia in terms of patient's cost, decreased morbidity, and short hospital stay[13,14,15] is highlighted by Romero AS, Siddique T, and Kulkarni in their separate studies. Furthermore, an in study by Kashani SMTit was observed that LIS performed under local anesthesia was associated with less postoperative pain (mean pain score 1.90 ± 1.07) as compared to that performed under spinal anesthesia (mean pain score 3.77 ± 1.25) at 6 hours.[16] Moreover, lateral sphincterotomy performed under Local anesthesia has advantage of shorter duration of surgery.[17]

This study was designed to compare postoperative pain scores at 6 and 24h hours in patients undergoing LIS under local anesthesia with spinal anesthesia, consequently, assessing the efficiency of local anesthesia in this particular procedure. This would contribute in increasing the frequency of future LIS performed under local anesthesia, which would not only enhance and expedite hospital services delivery by catering more patients on operation theater lists but would substantially play an important role in saving the patients from the complications associated with spinal anesthesia.

MATERIALS AND METHODS

A double-blinded prospective randomized controlled trial was conducted from 25th June' 18 to 25th December' 18 at surgical unit 2, Civil Hospital Karachi, Pakistan. A total of 60 patients were selected by non-probability consecutive sampling, aged 18-65 years of either gender with a complaint of chronic anal fissure lasting 3 months or more diagnosed clinically by history and examination at OPD. Patients with clinical evidence of Anal stenosis, Incontinence, Perianal abscess, Hemorrhoids, Fistula-in-ano, and known biopsy-proven Intestinal Tuberculosis, Crohn's disease, and Anorectal carcinoma were excluded from the study. After ethical and Institutional Reviewer Board (IRB) approval, informed consent was taken from all the participants, who were then randomly allocated in two groups of thirty patients by closed envelop method. Group A was given local anesthesia (10ml of 2% lignocaine with 10ml of 0.5% bupivacaine) around the anal verge while group B was operated in spinal anesthesia (0.5% hyperbaric bupivacaine in the intrathecal space).

Thereafter, LIS and all other relevant procedures were conducted by specialized consultant general surgeons, working in the civil hospital for 5 years. In order to control the risk of bias, an on-duty general surgery resident, unaware of the type of anesthesia used (local or spinal), collected the data regarding post-operative pain scores (using visual analog scale) at 6 hours and 24 hours through a manual Performa (attached).

RESULTS

With the sample size remaining consistent throughout the study, a total of 60 patients, who fulfilled the inclusion criteria, were identified from 25 June'18 to 25 December'18. The ages of the included patients were between 18 and 61 years with an overall mean age (± SD) of 35.50 (±10.679) years. The mean age in group A (± SD) was 34.77 (± 10.325) years, whereas in group B (± SD) was 36.23 (± 11.150) years with no significant difference between the two groups (p-value = 0.647) (Table 1). Furthermore, the study consisted of 19 (31.7%) male and 41 (68.3%) female patients. Group A consisted of 11 male and 19 female patients, while group B constituted eight male and 22 female patients (Table 1). The mean pain scores after two hours of LIS were then compared between both groups by applying the t-test.

According to the visual analog scale (measured 0-10 cm), pain scores at 6 hours and 24 hours after LIS for chronic anal fissure were recorded by the on-duty resident. As a result, at 6 hours mean pain scores (±) were [group A 5.40 (± 1.886) versus group B 5.40 (± 2.568)], while at 24 hours mean pain scores (±) were [group A 1.77 (± 1.278) versus group B 2.37 (± 1.159] (Table 2). In addition to this, as per the calculation of independent t-tests, no significant differences were observed between the mean pain scores of the two groups at 6 hours (p-value = 0.102) and 24 hours (p-value = 0.859) (Table 2).

Table No.1: Characteristics of Patients

Variable	GROUP	
	Group A (local anesthesia) (n=30)	Group B (spinal anesthesia) (n=30)
Age Group (years)		
≤ 35	14(46.66%)	13(43.33%)
> 35	16(53.33%)	17(56.66%)
Gender		
Male	11(36.66%)	8(26.66%)
Female	19(63.33%)	22(73.33%)

Table No.2: Pain Score at 6 and 24 Hours Lateral Internal Sphincterotomy

Group	N	Mean pain scores	Std. Deviation	p-value
At 6 Hours				
Group A (local anesthesia)	30	5.40	1.886	0.102
Group B (spinal anesthesia)	30	5.40	2.568	
At 24 Hours				
Group A (local anesthesia)	30	1.77	1.278	0.859
Group B (spinal anesthesia)	30	2.37	1.159	

DISCUSSION

Despite the recent advances in non-operative treatment modalities, lateral internal sphincterotomy still remains the primary surgical treatment option for chronic anal fissure mainly because it guarantees rapid healing and decreased recurrence rates.[18] LIS is generally performed under general anesthesia, spinal anesthesia, and local anesthesia. In a multi-centre randomized controlled trial, Brown CJ et al. found lateral internal sphincterotomy as the most suitable procedure for the treatment of chronic anal fissure[19]. In this procedure anterior fibers of internal anal sphincter are divided either with sharp dissection or diathermy. Conventionally this procedure was performed under spinal anesthesia which was widely accepted by patients in terms of intra operative and immediate post-operative pain relief, then again this type of anesthesia carries risk of complications like urinary retention, headache, hypotension etc.[15] However , recent studies are in favor of favour local anesthesia due to its safe and cost-effective nature accompanied by early recovery and decreased morbidity of patients.[20] As observed by Antonio Arroyo in his study, local anesthesia substantially benefited patients in terms of less morbidity, less hospital expenses, early resumption of daily routine, thereby, leading to greater patient's satisfaction.[21] In another study, local anesthesia was again found as the fruitful treatment for patients undergoing LIS for chronic anal fissure.[22]

Furthermore, Nessar, et al. reported postoperative pain as the most common cause of discomfort and inconvenience to the patient after LIS (n=9,20.9%) in his study. Similarly in our study experienced pain was the most frequent post-operative complication observed in our study. In our study no statisticticaly significant differences were observed in the mean pain scores at 6 hours and 24 hours of both groups (spinal versus local anesthesia), which were 5.40 ±1.886 vs 5.40 ±2.568 (p-value= 0.102) and 1.77 ±1.278 vs 2.37 ±1.159 (p-value= 0.859) respectively. The results of this research trial were in line with the study of Manoharan R, et al (2017), where no statistically significant difference was observed between the pain scores of the two groups with spinal and local anesthesia in the immediate post-operative period (p=0.097)[18]. Thus the efficacy of local anesthesia was found similar to spinal anesthesia in terms of pain relief in the postoperative period. Kashani et al also reported significantly less pain at 6 hours after LIS in the LA local anesthesia group as compared to the spinal anesthesia group (1.90 ± 1.07 vs. 3.77 ± 1.25)[16]. In addition to pain, bleeding was also noted.in two patients at second post-operative day reported the complaint of bleeding in OPD, which was, however, mild and stopped spontaneously. Urinary retention was also observed in three patients who underwent the procedure in spinal anesthesia.

Literature suggests that individuals from all age groups are equally prone to the anal fissures, however, chronic anal fissure is more frequent in the younger age group.[23, 24] Correspondingly in this study of 60 patients, the mean age group was 35.5 years, the youngest subject being 18 years and the oldest 61 years. Further more it is reported by Isbister et al that chronic anal fissure is more common in males with a ratio of 1.3:1[25]. On the contrary, our study demonstrates an increased number of females having the disease (2.1:1) compared to males. Nonetheless, when data was stratified for age and gender, no difference was found in mean pain scores between the groups for age, whereas the mean pain score in the female gender was prominen.

CONCLUSION

In this study, we did not found any significant differences between mean pain scores in patients undergoing LIS in local anesthesia versus spinal anesthesia. our results suggest that local anesthesia may routinely be used as a day case procedure to avoid possible complications that are associated with spinal anesthesia.

Author's Contribution:

Concept & Design of Study:	Sumta Khan
Drafting:	Farhan Zaheer, Shafaq Naseer
Data Analysis:	Usama Iqbal Khatri, Rizwan Khan, Qamaruddin Balcoh
Revisiting Critically:	Sumta Khan, Farhan Zaheer
Final Approval of version:	Sumta Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Beaty JS, Shashidharan M. Anal Fissure. Clin Colon Rectal Surg 2016;29(1):30-7.
2. Peker K, Yilmaz I, Demiryilmaz I, Inal A, Işik A. The effect of lateral internal sphincterotomy on resting anal sphincter pressures. Turk J Med Sci 2014;44(4):691-5.
3. Golfam F, Golfam P, Khalaj A, Mortaz SS. The effect of topical nifedipine in treatment of chronic anal fissure. Acta Med Iran 2010;48(5): 295-9.
4. Adamová Z, Slováček R, Bár T, Sankot J, Vlček P. Anal fissure. Cas Lek Cesk 2015;154(1):11-3.
5. Esfahani MN, Madani G, Madhkhan S. A novel method of anal fissure laser surgery: a pilot study. Lasers Med Sci 2015;30(6):1711-7.
6. Giridhar CM, Babu P, Rao KS. A Comparative Study of Lateral Sphincterotomy and 2% Diltiazem Gel Local Application in the Treatment of

Chronic Fissure in ano. J Clin Diagn Res 2014;8(10):NC01-2.
7. Fox A, Tietze PH, Ramakrishnan K. Anorectal conditions: anal fissure and anorectal fistula. FP Essent 2014;419:20-7.
8. Madalinski MH. Identifying the best therapy for chronic anal fissure. World J Gastrointest Pharmacol Ther 2011;2(2):9-16.
9. Higuero T. Update on the management of anal fissure. J Visc Surg 2015;152(2 Suppl):S37-43.
10. Kang WH, Lim CH, Choi DH, Shin HK, Lee YC, Jeong SK, et al. Comparison of skin incisions used for open lateral internal sphincterotomies--radial versus circumferential incisions: a retrospective cohort study. Int J Surg 2014;12(11):1141-5.
11. Toyonaga T, Matsushima M, Sogawa N, Jiang SF, Matsumura N, Shimojima Y, et al. Post-operative urinary retention after surgery for benign anorectal disease: potential risk factors and strategy for prevention. Int J Colorectal Dis 2006;21(7): 676-82.
12. Talpur AA, Memon GN, Memon N, Jamali AH, Ghumro AA. Comparison between treatment of benign perianal diseases under local anaesthesia and regional or general anaesthesia. Med Channel 2007;13(4):22-4.
13. Romero AS, Sebastián AA, Vicente FP, Paz PS, Polo FC, Gómez AT, et al. Open lateral internal anal sphincterotomy under local anesthesia as the gold standard in the treatment of chronic anal fissures. A prospective clinical and manometric study. Rev Esp Enferm Dig 2004;96(12):856- 63.
14. Siddique T, Khan SA, Rehman M, Islam HR, Ahmad W. Lateral internal sphincterotomy for chronic anal fissure under local anesthesia as a day case surgery. Ann King Edward Med Uni 2003;9(1):52-4.
15. Kulkarni SV, Agarwal P, Nagraj K. To compare the outcome of minor anorectal surgeries under local anesthesia versus spinal anesthesia. Ind J Surg 2014;76(5):343-9.
16. Kashani SMT, Ali MH, Marzie L, Ali ZS. Lateral internal sphincterotomy under local anesthesia (randomized clinical trial). Eur Surg 2006; 38(5):364-367.
17. Sarkar S, Kapur N. Lateral internal sphincterotomy under local and spinal anaesthesia for chronic anal fissure: A randomised control trial. Hellenic J Surg 2016;88(6):398–401.
18. Manoharan R, Jacob T, Benjamin S, et al. Lateral Anal Sphincterotomy for Chronic Anal Fissures- A Comparison of Outcomes and Complications under Local Anaesthesia Versus Spinal Anaesthesia J Clin Diagn Res 2017; 11(1):PC08–PC12.
19. Brown CJ1, Dubreuil D, Santoro L, Liu M, O'Connor BI, McLeod RS. Lateral internal sphincterotomy is superior to topical nitroglycerin for healing chronic anal fissure and does not compromise long-term fecal continence: six-year follow-up of a multicenter, randomized, controlled trial. Dis Colon Rectum 2007;50(4):442-8.
20. Gudityte J, Marchertiene I, Pavalkis D. Anesthesia forambulatory anorectal surgery. Medicina (Kaunas) 2004;409:101–111.
21. Arroyo A, Pérez F, Serrano P, Candela F, Calpena R. Open versus closed lateral sphincterotomy performed as an outpatient procedure under local anesthesia for chronic anal fissure: prospective randomized study of clinical and manometric longterm results. J Am Coll Surg 2004;199: 361– 367.
22. Liratzopoulos N, Efremidou EI, Papageorgiou MS, Kouklakis G, Moschos J, Manolas KJ, et al. Lateral subcutaneous internal sphincterotomy in the treatment of chronic anal fissure: our experience. J Gastrointestine Liver Dis 2006;15(2):143–47.
23. Lund JN, Scholefield JH. Aetiology and treatment of anal fissure. Br J Surg 1996;83:1335–44.
24. Isbister WH, Prasad J: Fissure in ano. Aust N Z J Surg 1995;65:107-08.

Original Article

Single Dose of IV Tranexamic Acid Preoperatively Reduces the Incidence of Post-Operative Scrotal Edema Following Lichtenstein Hernioplasty. A Randomized Prospective Cohort Analysis

Farhan Zaheer[1], Qamaruddin Baloch[1], Sidra Abbas[2], Shafaq Naseer[1], Osama Muhammad[1] and Ayesha Anees[1]

ABSTRACT

Objective: to determine the single Dose of IV Tranexamic acid perioperatively reduces the incidence of post-operative scrotal oedema following Lichtenstein hernioplasty.

Study Design: A randomized prospective analysis

Place and Duration of Study: This study was conducted at the Civil Hospital Karachi, Pakistan from June, 2019 to December, 2020 for a period of six months.

Materials and Methods: All patients operated for inguinal hernia repair on elective basis at Surgical Unit of a tertiary care hospital was done after taking the approval from the hospital ethics committee. 40 patients in each group. All the patients aged between 18 and 65 years who underwent elective repair of inguinal hernia were a part of this study. Patients who were excluded from the study were the ones classified as ASA class III or IV by anaesthesiologist, patients with chronic end-organ diseases including CLD, CKD, CHF, history of intracranial haemorrhage, connective tissue disease or hypoalbuminemia, Patients with a history of convulsions, patients previously on anticoagulants and antiaggregant and patients having hypersensitivity to tranexamic acid.

Results: A total of 80 patients undergoing inguinal hernia repair were divided into 2 groups. The mean age for the control group was 39.33 ± 11.72, while for the intervention group was 41.53 ± 11.76 [$p<0.05$]. The most common complication apart from scrotal edema was urinary retention in both the groups. [27.5% in control vs 10% in TXA group], the rate of complications was more significant in control group [$p=0.02$]. The mean operating time for the intervention group was significantly reduced in the intervention group [68.25 ± 22.60 min vs 85.62 ± 31.78 min, $p=0.006$]. Edema resolved in 1.57 ± 1.44 days in intervention group while it took 4.85 ± 3.20 days for edema to resolve in the control group $p<0.001$. The patients who received TXA returned to work earlier than the ones without administration [$p<0.001$] along with a significantly reduced rate of complication [$p<0.001$].

Conclusion: A single dose of intravenous tranexamic acid 1gm can be safely administered to reduce scrotal edema following Lichtenstein hernioplasty with no demonstrable side effects.

Key Words: Lichtenstein hernioplasty; Tranexamic Acid; Scrotal edema; SERG score

Citation of article: Zaheer F, Baloch Q, Abbas S, Naseer S, Muhammad O, Anees A. Single Dose of IV Tranexamic Acid Preoperatively reduces the Incidence of Post-Operative Scrotal Edema Following Lichtenstein Hernioplasty. A Randomized Prospective Cohort Analysis. Med Forum 2021;32(10):180-184.

INTRODUCTION

[1.] Department of Surgery, Civil Hospital, Dow University of Health Sciences, Karachi.
[2.] Department of Surgery, Baqai Medical University, Karachi.

Correspondence: Dr. Farhan Zaheer, Associate Professor of Surgery, Civil Hospital, Dow University of Health Sciences, Karachi.
Contact No: 03002108924
Email: farhan.zaheer@duhs.edu.pk

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

Around the globe, millions of people undergo hernia surgery annually[1]. Lichtenstein hernioplasty is considered a gold standard approach for inguinal hernia repair. Though a very safe and effective procedure, one of the troublesome postoperative problems is the development of scrotal swelling which includes seroma as well as hematoma. Despite being a benign complication, it's very irritating to the patients with an incidence rate approaching 1.4 to 12% [2,3].

Different approaches have been devised to avoid this problem. The use of intramuscular hydrocortisone has been shown to reduce the immediate post-operative scrotal edema after an inguinal varicocelectomy [4]. Scrotal compressions have been widely used to avoid scrotal edema after inguinal hernia surgeries [5]. However, the use of per-operative intravenous [IV]

Tranexamic acid [TXA] has not been explored in this regard. Tranexamic acid being an anti-fibrinolytic agent has been used on various occasions both intra and postoperatively. Zaman et al reported a single dose of IV TXA can result in less postoperative nasal bleed following a septoplasty [7]. Similarly, Goldstein et al showed that intravenous tranexamic acid can result in decreased bleeding in end prosthesis knee and hip surgeries [8]. Its role in the management of coagulopathy of trauma showed in the CRASH trial has proven revolutionary [9].

The prime focus of our study was to assess the role of IV TXA, given intraoperatively at doses of 10mg/kg [up to 1000mg] in preventing the development of immediate [1st postoperative day] and latent [within 7-8 operative days] scrotal edema.

MATERIALS AND METHODS

A randomized prospective analysis was conducted from June 2019 to December, 2020 at Civil Hospital Karachi, Pakistan. All patients operated for inguinal hernia repair on elective basis at Surgical Unit of a tertiary care hospital was done after taking the approval from the hospital ethics committee. 40 patients in each group. The participation in the study was voluntary and all the patients enrolled in the study were thoroughly briefed about the study methodology**.** Informed consent was then obtained from every participant in the native language 'Urdu'. Each participant was administered prophylactic antibiotics at the time of incision, as per the protocol.

All the patients aged between 18 and 65 years who underwent elective repair of inguinal hernia were a part of this study. Patients who were excluded from the study were the ones classified as ASA class III or IV by anesthesiologist, patients with chronic end-organ diseases including CLD, CKD, CHF, history of intracranial hemorrhage, connective tissue disease or hypoalbuminemia, Patients with a history of convulsions, patients previously on anticoagulants and antiaggregant and patients having hypersensitivity to tranexamic acid.

The factors examined included age, comorbidities, complications other than scrotal edema, scrotal edema on 2nd and 7th postoperative day, and duration of edema. The quantification and grade of scrotal edema was measured using scrotal edema Rating Grade [SERG] score as a statistically significant difference in SERG score among the two groups implies increased prevalence/ incidence of scrotal edema in group with increased SERG score as compare to the group with lower SERG score. It is calculated by asking the patient to be in standing position and measuring the widest scrotal circumference using a numbered tape. The SERG score was measured preoperatively, on 2nd post-op, and 7th post-op day for every patient. The score ranged from 0 to 3 as follows:

0 = no edema = the pre-operative scrotal circumference
1 = mild edema = < 2 folds increase in the widest scrotal circumference
2 = moderate edema = 2 - 3 folds increase in the widest scrotal circumference
3 = severe edema = > 3 folds increase in the widest scrotal circumference.

RESULTS

A total of 80 patients undergoing inguinal hernia repair met the inclusion criterion and were selected for analysis. The patients were divided into 2 groups. After matching for age, co-morbidities, and BMI, both the groups contain 40 patients.

Table No.1: Comparison of Demographics and Co-morbidities in two groups

	TXA given (n=40)	**TXA not given (n=40)**
Demographics		
Mean Age	41.53 SD 11.76	39.33 SD 11.72
Gender	Man	Man
Co-morbidities		
Chronic Kidney Disease (CKD)	1	2
Diabetes Miletus (DM)	3	5
Chronic Liver Disease (CLD)	0	0
Hypertension (HTN)	5	6
Ischemic Heart Disease (IHD)	2	5
DM + CKD	1	0
DM + CLD	0	1
DM + HTN	2	2
HTN + IHD	1	0
IHD + DM + HTN	0	1
None	25	18

Table No.2: Rate of complications in two groups

Complication	**TXA given (n=40)**	**TXA not given (n=40)**
Ileus	0	3
Urinary Retention (UR)	3	9
Wound Infections	2	5
Post-Operative Pain	1	3
Ileus + UR	1	0
Wound Infection + UR	0	1
Thrombotic complication	0	0

The mean age for the control group was 39.33 ± 11.72, while for the intervention group was 41.53 ± 11.76 [p<0.05]. Hypertension [Htn] was the most common abnormality found amongst the two groups [22.5% in the control group vs 20.5% in the intervention group]. However, no statistically significant difference was found among the co-morbidities of the two groups [p=0.60], See Table 1. The most common complication apart from scrotal edema was urinary retention in both the groups. [27.5% in control vs 10% in TXA group], the rate of complications was more significant in control group [p=0.02]. See Table 2 for further detail.

Table 3 shows the multivariate logistic regression analysis for pre-op and post-operative characteristics among the 2 groups. The mean operating time for the intervention group was significantly reduced in the intervention group [68.25 ± 22.60 min vs 85.62 ± 31.78 min, p=0.006]. There was a remarkable difference in the SERG score at 2nd postoperative day among the two categories [0.62 + 0.92 vs 1.45 ± 1.01, p=0.005], showing a distinguishable reduction in edema in the patients receiving TXA per-operatively. However, no statistically significant difference in SERG score at 7th operative day was found [0.10± 0.30 vs 0.27 ± 0.55, p=0.09]. Edema resolved in 1.57 ± 1.44 days in intervention group while it took 4.85 ± 3.20 days for edema to resolve in the control group p<0.001. The patients who received TXA returned to work earlier than the ones without administration [p<0.001] along with a significantly reduced rate of complication [p<0.001]. See Table 3 for further details.

Table No.3: Multivariate logistic regression among the two groups for per-operative and post-operative factors

	TXA group	No TXA group	OR	p-value
Duration of Surgery, (min, mean± SD)	68.25 ± 22.60	85.62 ± 31.78	0.977[0.961-0.994]	0.009
SERG at 2nd Post op Day, (mean ± SD)	0.62 + 0.92	1.45 ± 1.01	0.429[0.262-0.703]	0.001
SERG at 7th Post op Day, (mean ± SD)	0.10± 0.30	0.27 ± 0.55	0.381[0.121-0.197]	0.09
Duration of Edema Resolvement, (days, mean ± SD)	1.57 ± 1.44	4.85 ± 3.20	0.690[0.577-0.824]	<0.001
Days of Return to work, (days, mean ± SD)	4.32 ± 1.84	6.67 ± 2.53	0.590[0.452-0.770]	<0.001
Incidence of complications other than scrotal edema (n)	33	18	0.174[0.062-0.484]	<0.001

DISCUSSION

Post-operative scrotal edema is one of the most significant complications diagnosed post inguinal hernioplasty. The pathogenesis behind its development involves multiple factors. One of the widely acknowledged mechanisms is that damage to the tissue causes the release of inflammatory mediators [Ca, nitric oxide, VEGF, EGF, and PDGF] which cause the contraction of endothelial cells and increase the permeation between capillaries and interstitial fluid. Iatrogenic trauma to the tissue is further augmented by poor tissue handling causing damage to the capillary membrane which in turn leads to extravasation of fluid from vessels into interstitial space [6]. TXA being an anti-fibrinolytic agent has proven to be a useful adjunct to reduce this edema. TXA reversibly binds to plasminogen and blocks its conversion to plasmin which in turn halts the fibrin degradation which is an essential step in blood leaking out from the capillaries[10]. Furthermore, the role of TXA as an anti-inflammatory has also been described as it has been shown to decrease the levels of interleukins and acute phase reactants which are essential factors in inflammatory cascades following surgeries [11].

In our study, we reported a decreased incidence of postoperative scrotal edema following IV administration of 1gm TXA during the procedure as compared to the control group. The literature regarding the use of TXA in inguinal hernia surgery is very limited. However, its use in different operative procedures to reduce post-operative edema/seroma is not unpopular. Orteli D et:al reported a decreased rate of post-op seroma following TXA administration in patients with breast cancer undergoing mastectomy or lumpectomy with axillary clearance [12]. Similar results were demonstrated after topical TXA application following reduction mammoplasty [13]. An extensive meta-analysis concerning nasal operative procedures such as septoplasty and rhinoplasty, also demonstrated the efficacy of intravenous TXA in reducing the post-operative eyelid edema, a complication of such procedures [14]. Sara et al also described the decreased incidence of post-op complication eyelid edema, following rhinoplasty when intravenous TXA was used intraoperatively [15].

Our study also reports that there was a significant reduction in intraoperative time in patients in whom TXA was administered. Also, the hospital length of stay in the TXA group was found out to be significantly less

than the control group. These findings are concordant with Goobie et al who also demonstrated that TXA use reduces the intraoperative bleeding in adolescent scoliosis surgery leading to a decrease in hospital stay hence an earlier return to work[16]. Goyal et al also concluded that the use of intraarticular TXA can reduce the length of hospital stay in patients undergoing total knee arthroplasty [17].

Considering the rate of complications between the two groups, the TXA group revealed a decreased incidence than the control group. This differs from Zhou et al who showed no significant difference in complications after inter-trochanteric fracture surgeries between TXA and placebo group [18]. TXA administration is considered a risk factor for venous thromboembolic events [19]. We reported no incidence of such an event similar to findings described by Nishida et al [20]. However, we relied on the demonstration of symptoms to diagnose this complication and didn't perform any radiological investigation which can be considered a limitation of our study

Henceforth, the benefits offered by TXA far outshine the risks associated with its use. Very few side effects have been reported when TXA is given in a single dose of 500 mg to 1gm. The patient in this study stated no adverse reaction that is known to be associated with TXA use [21]. Considering the benefits, the TXA group in our study was superior in all aspects of a surgical procedure be it decreased duration of surgery, decreased incidence of postoperative scrotal edema, earlier return to work, and reduced complication rate. This completely shifts the equilibrium in favour of TXA. However, more extensive trials are recommended to enhance the precision and validity which is limited by the limited sample size of our study.

CONCLUSION

A single dose of intravenous tranexamic acid 1gm can be safely administered to reduce scrotal edema following Lichtenstein hernioplasty with no demonstrable side effects, but with additional benefits of the decreased duration of operative procedures, earlier return to normal life and reduced complication rate. However, more extensive prospective clinical trials are required to increase the validation regarding its use.

Author's Contribution:

Concept & Design of Study:	Farhan Zaheer
Drafting:	Qamaruddin Baloch, Sidra Abbas
Data Analysis:	Shafaq Naseer, Osama Muhammad, Ayesha Anees
Revisiting Critically:	Farhan Zaheer, Qamaruddin Baloch
Final Approval of version:	Farhan Zaheer

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Simons MP, Smietanski M, Bonjer HJ et al. International guidelines for groin hernia management. Hernia. 2018; 22[1]:1-165.
2. Chen PH, Chiang HC, Chen YL, Lin J, Wang BF, Yan MY, et al. Initial experience with application of single layer modified Kugel mesh for inguinal hernia repair: Case series of 72 consecutive patients. Asian journal of surgery. 2017 Mar 1;40(2):152-7..
3. Samaali I, Zenaidi HH, Dougaz W, Khalfallah M, Jarraya H, Nouira R, Bouasker I, Dziri C. Treatment of inguinal hernia by lichtenstein technique: an open prospective study. La Tunisie medicale. 2016 Dec 1;94(12):872-5.
4. Elhanbly S, Youssef T, Elkholy A, Abdel-Gawad M, Mostafa T. Hydrocortisone relieves the immediate post-operative scrotal edema after inguinal varicocelectomy: A prospective clinical trial. J Advanced Research 2017;8(4):445-7.
5. Wilms MC, Hellmold P. Avoiding scrotal haematoma after repair of extensive scrotal hernias by postoperative scrotal compression through scrotal suspension by scrotal-abdominal skin suture. Tropical Doctor 2012;42(2): 86-7.
6. Duan CY, Zhang J, Wu HL, Li T, Liu LM. Regulatory mechanisms, prophylaxis and treatment of vascular leakage following severe trauma and shock. Military Medical Res 2017;4(1):1-1.
7. Zaman SU, Zakir I, Faraz Q, Akhtar S, Nawaz A, Adeel M. Effect of single-dose intravenous tranexamic acid on postoperative nasal bleed in septoplasty. Eur Annals Otorhinolaryngol, Head Neck Dis 2019;136(6):435-8.
8. Goldstein M, Feldmann C, Wulf H, Wiesmann T. Tranexamic acid prophylaxis in hip and knee joint replacement. Deutsches Ärzteblatt Int 2017;114(48):824-6.
9. Ackery A, Rizoli S. Tranexamic acid for trauma-related hemorrhage. CMAJ 2014;186(15):E587-9.
10. McCormack PL. Tranexamic acid. Drugs 2012;72(5):585-617.
11. Jimenez JJ, Iribarren JL, Lorente L, Rodriguez JM, Hernandez D, Nassar I, et al. Tranexamic acid attenuates inflammatory response in cardiopulmonary bypass surgery through blockade of fibrinolysis: a case control study followed by a randomized double-blind controlled trial. Critical Care 2007;11(6):1-9.
12. Oertli D, Laffer U, Haberthuer F, Kreuter U, Harder F. Perioperative and postoperative tranexamic acid reduces the local wound

complication rate after surgery for breast cancer. J Br Surg 1994;81(6):856-9.
13. Ausen K, Fossmark R, Spigset O, Pleym H. Randomized clinical trial of topical tranexamic acid after reduction mammoplasty. J Br Surg 2015;102(11):1348-53.
14. Ping WD, Zhao QM, Sun HF, Lu HS, Li F. Role of tranexamic acid in nasal surgery: A systemic review and meta-analysis of randomized control trial. Medicine 2019;98(16).
15. de Vasconcellos SJ, do Nascimento-Júnior EM, de Aguiar Menezes MV, Mendes ML, de Souza Dantas R, Martins-Filho PR. Preoperative tranexamic acid for treatment of bleeding, edema, and ecchymosis in patients undergoing rhinoplasty: a systematic review and meta-analysis. JAMA Otolaryngol–Head Neck Surg 2018;144(9):816-23.
16. Goobie SM, Zurakowski D, Glotzbecker MP, McCann ME, Hedequist D, Brustowicz RM, et al. Tranexamic acid is efficacious at decreasing the rate of blood loss in adolescent scoliosis surgery: a randomized placebo-controlled trial. JBJS 2018;100(23):2024-32.
17. Goyal N, Chen DB, Harris IA, Rowden N, Kirsh G, MacDessi SJ. Clinical and financial benefits of intra-articular tranexamic acid in total knee arthroplasty. J Orthopaedic Surg 2016;24(1):3-6.
18. Zhou XD, Zhang Y, Jiang LF, Zhang JJ, Zhou D, Wu LD, et al. Efficacy and Safety of Tranexamic Acid in Intertrochanteric Fractures: A Single-Blind Randomized Controlled Trial. Orthopaedic Surg 2019;11(4):635-42.
19. Johnston LR, Rodriguez CJ, Elster EA, Bradley MJ. Evaluation of military use of tranexamic acid and associated thromboembolic events. JAMA Surg 2018;153(2):169-75.
20. Nishida T, Kinoshita T, Yamakawa K. Tranexamic acid and trauma-induced coagulopathy. J Intensive Care 2017;5(1):1-7.
21. Whalen K, Finkel R, Panavelil TA. Lippincott's illustrated reviews: Pharmacology. Philadelphia, PA: Wolters Kluwer; 2015.

Original Article

Comparative Effects of Postural Correction VS Myofascial Release Among E-Sports Players with Neck Pain and Disability

Haris Bin Tariq[1], Muzna Munir[2], Ammar Hameed[3], Zainab Hassan[2], Naveed Anwar[2] and Kehkshan Khalid[2]

ABSTRACT

Objective: To assess the comparative effects of posture correction vs myofascial release in e-sports players with neck pain and disability.

Study Design: A randomized controlled trial study

Place and Duration of Study: This study was conducted at the Kanaan Physiotherapy & Spine Clinic, Lahore from June 2020 till November 2020.

Materials and Methods: This trial was conducted on 50 e-sports players. Participants were selected through non-probability convenient sampling. Participants who fulfilled the inclusion/exclusion criteria were identified by an assessor and were enrolled for particular study. Informed written consent was taken by the participants and were randomly allocated to two groups. The study was single blinded. The assessor was unaware of the treatment given to both groups. Group A received the myofascial release treatment using Hawk Grips IASTM and Group B received posture correction exercises. The total no. of sessions was 12 and duration of treatment was 4 weeks (3 sessions per week).

Results: The mean age of participants was 19.28 $\pm$ 2.157 years. Non-parametric tests were performed as the data was not normally distributed. Within group comparison was done by using Wilcoxon signed rank test and it showed significant results in both groups, *p*-value 0.000 for both neck pain and neck disability. Between groups comparison was made by using Mann-Whitney U Test and it showed no significant changes in neck pain and neck disability, *p*-value 0.832 & 0.465 respectively.

Conclusion: It is concluded that the comparison between the myofascial release treatment and posture correction exercise program is insignificant however, significant improvements in neck pain and disability are seen within the participants of both groups.

Key Words: Neck Pain, Neck Disability, E-sports Players, Myofascial release technique, Posture correction

Citation of article: Tariq H, Munir M, Hameed A, Hassan Z, Anwar N, Khalid K. Comparative Effects of Postural Correction VS Myofascial Release Among E-Sports Players with Neck Pain and Disability. Med Forum 2021;32(10):185-189.

INTRODUCTION

Non-specific neck pain is known as pain in the lateral and posterior part of the neck mainly between the spinous process of the first thoracic vertebra and the superior nuchal line with no characteristics of chief structural disease and no or slight to main meddling with actions performed in daily life also without the presence of neurological signs and symptoms of precise pathologies; such as: tumor, traumatic sprain and fracture, inflammatory or infectious cervical spondylolysis, etc.[1] overall it shows around 25% of all outpatient visits to physiotherapy[2] with an occurrence of 12 to 70% between overall population[1], in comparison men are less expected to be affected than women.[3] In terms of research conclusions, Neck pain is often labelled as a "poor cousin" of the lower back pain even after its incidence and socioeconomic values. Due to its multifactorial etiology, it is rarely diagnosed and termed as nonspecific neck pain.[4]

There has been a consistent rise in the incidence of musculoskeletal disorders among the e-sports professionals and gamers as the growing number of players in this industry.[5] One of the key factors responsible for this situation is prolonged sitting during the gaming activities. Also, the poor postures adapted

[1.] Department of Physiotherapy, KKT Orthopedic and Spine Centre.
[2.] Riphah International University, Lahore.
[3.] Department of Physiotherapy, Chughtai Labs

Correspondence: Naveed Anwar, Assistant Professor, Riphah International University, Lahore.
Contact No: 03218616029
Email: Naveed.anwer@riphah.edu.pk

Received: March, 2021
Accepted: August, 2021
Printed: October, 2021

during the gaming activities would make the neck pain worst.

Many health problems including psychosomatic symptoms and musculoskeletal disorders happening in the early adulthood might persists later and merge into lifestyle and psychosocial factors.[6] The most leisure activity performed by adolescents majorly includes online gaming. In recent times, gamers have preference for multiplayer online role playing games (MMORPGs)[7], frequently related to negative consequences. A new health risk factor is identified as frequent computer-related activities[8] related to psychosomatic and physical complaints.[9,10] Adverse significances due to online gaming are described by one third of gamers. In specific, extreme gaming (more than five hours per day) in adolescence seems to rise these risks. Extreme gamers and those facing difficulties due to gaming have decreased life fulfilment scores and higher levels of undesirable indications such as depression and anxiety. [11]

Posture correction exercises have been described as one of the most efficient approach for reinstating function. To enhance muscle action between force mixtures, the designated workout should highlight not only muscle power but also on providing proper ratio of muscle activity in relation to each other. Likewise, by means of the outcomes of electromyography readings could be obliging.(12) Individuals having cervical complaints are shown to have improved axial and scapular muscle activation while having lower engagement of the inferior trapezius and serratus anterior. Treatment plan including different exercises was identified as the best approved by studies among the individuals throughout their intervention span.(13)

Myofascial release (MFR) is extensively utilized to overcome pain related with musculoskeletal injuries, and its sequences of healing effects are exploited by soothing muscles at the injury as much as possible. Moreover, MFR is usually the physical therapy of select to fuel blood flow for patients with neck pain.(14) It also aids to encourage extreme relaxation of stressed tissues, is extensively used in primarily adjusting discomfort from musculoskeletal injuries like myofascial trigger points and myo-fibrosis and make the most of a healing effect by comforting muscles of associated lesions.(15)

In this study we aim to provide the best treatment options to e-sports players with neck disability and to guide some of the treatments which they can perform quite easily by themselves so that they can get rid of those myofascial pains and can participate in their tournaments with least muscle and postural impairments.

MATERIALS AND METHODS

A randomized controlled trial was conducted on 50 e-sports players. Participants were selected through non-probability convenient sampling. Sample size was calculated as following:

$$\mathbf{n = \frac{Z^2_{1-\alpha/2} P(1-P)}{d^2}}$$

A sample size of 46 was calculated from epitools. Attrition rate of 10% was supposed so the final Sample size came out to be 50, 25 patients in each group.

Sample Selection: Participants who fulfilled the inclusion/exclusion criteria were identified by an assessor and were enrolled for particular study. Participants were selected through specific inclusion criteria which was male e-sports player between 15 to 30 years of age having neck pain and disability symptoms. Participants having any cervical fracture, recent surgery, any inflammatory diseases, neuropathies, psychological disorders or any vascular disorder were excluded from the study.

Data collection procedure: Informed written consent was taken by the participants. The study was single blinded. The assessor was hired for data collection and baseline data was collected before assigning the participants into two groups. In this way, assessor was unaware of the treatment given to both groups. Data was collected by administering questionnaire. After collecting the baseline data, participants fulfilling the inclusion criteria were randomly allocated into two groups (group A and B) by using a fish bowl method. Group A received IASTM treatment given by certified Hawk grip IASTM practitioner while Group B was treated with postural corrective exercises. The total number of sessions was 12 and duration of treatment was 4 weeks (3 sessions per week). Follow-up reading was taken after 4 weeks of intervention.

Intervention: Group A: Group A received myofascial release treatment. This treatment was given by using an instrument called Hawk Grips IASTM designed for releasing the myofascial knots and tissue resistance. This IASTM treatment was given by certified level 2 Hawk Grip IASTM practitioner. Prior to the treatment thermotherapy was given using hot pack for 10 minutes. After that instrumental assisted myofascial treatment was given for 15 minutes. After the end of the session, participants were advised to perform active cervical range of motion in all planes (flexion, extension, lateral rotation, lateral flexion) 3 times. Then, neck isometrics were performed with 3 repetitions (10 second hold). Treatment was given for 8 weeks (Three sessions per week on alternative days)

Group B: Group B received postural correction program. Prior to this program, thermotherapy was given using hot pack for 10 minutes. After that, patient performed active cervical range of motion in all planes (flexion, extension, lateral rotation, lateral flexion) 3 times. Then, neck isometrics was performed with 3 repetitions (10 seconds hold). Then, postural correction program was started. In this program, different methods were used. Mirror therapy was used in which

participants were asked to maintain their body in a correct posture by visualizing their selves in the mirror. After that, participants were asked to stand straight by the wall and they were asked to hold their neck and flatten their shoulder for 30 seconds. This was performed 3 times. After that, stretches of the anterior chest muscles (pectoralis major and minor) were given in sitting position. Stretches were given 3 times (30 seconds hold). Treatment was given for 8 weeks (Three sessions per week on alternative days)

Statistical Analysis: Data was analyzed on SPSS Version 21.0 (Statistical Package of Social Sciences) Software. Normality assessed by Shapiro Wilk Test. Standard deviation and mean of quantitative variables were measured. Pre and Post-tests values were measured after 4 weeks of treatment by using non parametric tests (Mann Whitney U test and Wilcoxon signed ranked test) according to the given data.

RESULTS

During the trial, patients were selected randomly and allocated into two groups. The mean age of participants was 19.28 ± 2.157 years. Non-parametric tests were performed as the data was not normally distributed. Within group comparison was done by using Wilcoxon signed rank test and it showed significant results in both groups, *p*-value 0.000 for both neck pain and neck disability. Between groups comparison was made by using Mann-Whitney U Test and it showed no significant changes in neck pain and neck disability, *p*-value 0.832 & 0.465 respectively.

Table No.1: shows the descriptive statistics of Age (n=50)

Study Group		N	Mean+ Std. Deviation	P-value
Group A (IASTM)	Age of Participants	25	18.96±2.010	0.151
Group B (Postural Correction)	Age of Participants	25	19.60±2.291	0.065

Table No.2: Shows within group comparison in which Pre & Post mean ± S.D score of NPRS & NDI among Group A (IASTM) and Group B (Posture Correction) were mentioned.

Study variables	Groups	Pre-treatment Mean ± SD	Post-treatment Mean ± SD	Mean Difference	*P* value
NPRS	A	3.44±1.121	1.56±1.083	1.88	0.000
	B	3.12±1.092	1.64±1.150	1.48	
NDI	A	15.58±5.173	12.76±4.755	2.82	0.000
	B	16.68±3.881	11.68±3.288	5.00	

*** (P < 0.000); there is a significant difference within all groups.

Table No.3: Shows between group comparison in which Pre & Post mean ± S.D score of NPRS & NDI among Group A (IASTM) and Group B (Posture Correction) were mentioned.

Study variables	Groups	Pre-treatment Mean ± SD	Post-treatment Mean ± SD	Mean Ranks Pre-treatment	Mean Ranks Post-treatment	*P* value
NPRS	A	3.44±1.121	1.56±1.083	27.56	25.08	0.832
	B	3.12±1.092	1.64±1.150	23.44	25.92	
NDI	A	15.58±5.173	12.76±4.755	23.70	27.00	0.465
	B	16.68±3.881	11.68±3.288	27.30	24.00	

DISCUSSION

The present study analysed the comparison of the efficacy of myofascial release and posture correction program. In this study, within group results showed that there were significant improvements in neck pain and disability while there was no difference in the efficacy of both treatments when between group comparison was made.

Cho S. et al. explained that Active trigger points (ATrP) may be triggered by acute factors such as muscle sprains, or gradually by chronic overloads such as faulty posture. ATrP induces myofascial pain syndrome, which can cause reduced joint range, muscle weakness, and sleep ailments. Their results presented that the treatment of MFR efficiently decreases ATrP in the suboccipital muscle region, which can lead to the improvement of neck function and sleep quality.[16] The findings of this study corelated with the above research as there was significant improvement within myofascial release group, however targeted population in this study was e-sports players.

Arshadi et al. elaborated that eight-week corrective exercise are effective in diminishing activity of sternocleidomastoid and upper trapezius muscles, upper trapezius/serratus anterior and upper trapezius/lower trapezius ratio, increasing activity of serratus anterior and lower trapezius. With respect to concluding large effect size it can be quantified corrective exercise (stretching, strengthening, and stabilization exercises) is

a harmless and low-cost means to improve the muscles of the upper quadrant. Corrective exercises can be recommended as a fruitful treatment to restore and preserve balanced muscle activity in individuals with upper cross syndrome.[17] The above-mentioned study showed similar results to this study as posture correction group showed significant improvements in pain reduction. However, target population was not same in both researches as this research aimed to find the effects of corrective exercises in e-sports players.

Toprak Celenay et al. the goal of the study was to look into and evaluate the quick benefits of interventions including balance exercises with manual treatment, rather than balance exercises solely on mobility, discomfort, range of motion and standards of living in subjects with mechanical neck pain. At four weeks, the investigation presented the particular results, when compared to balance exercises individually, stabilization exercises along with manual treatment reduced impairment, severity of pain at night, neck rotation mobility and life quality. Pressure pain threshold improved solely in stabilization exercises and manual techniques group. Improved extension and lateral flexion mobility as well as reduced pain in resting position and severity of pain in activity were not easily comparable in stabilization exercises and manual therapy group in comparison to the stabilization exercises individually in subjects with chronic mechanical neck pain.[18] The above-mentioned study conflicted with this study as posture correction exercises showed significant improvements in their neck pain and disability without any manual therapy technique. There was a difference of target population as well so changes in results may be due to the difference in target population. This study also showed no statistically significant difference in the efficacy of posture correction group and myofascial release group.

Falla, D. et al.[19] investigated the acute effects of precise exercise for individuals with chronic neck pain. In addition to evaluating the efficacy on pain and supposed disability, the study assessed the effect on the specificity of neck muscle control. The results illustrate that an 8-week specific exercise programme is efficient for improving the directional specificity of neck muscle movement and dropping pain in the immediate term. Future studies were related to assess whether this type of exercise has further helped such as a decrease in neck pain reappearance in the long run. The findings of the above-mentioned study also coincided with the results of this study as posture correction group also showed significant improvements in alleviating neck pain and disability. However, the program designed in this study was for 4 weeks only as compared to 8-week program mentioned in above study.

CONCLUSION

It is concluded that the comparison between the myofascial release treatment and posture correction exercise program is insignificant however, significant improvements in neck pain and disability are seen within the participants of both groups.

Limitations:

- Study was only single blinded.
- Long term follow up reading was not recorded.
- Other confounding factors like poor sleep and nutrition were not investigated.

Recommendations: Further studies should be conducted on participants with all age groups, with different musculoskeletal disorders such as upper cross syndrome, cervicalgia and cervical spondylosis. Studies should be conducted on a larger scale to gather more information.

Author's Contribution:

Concept & Design of Study:	Haris Bin Tariq
Drafting:	Muzna Munir, Ammar Hameed
Data Analysis:	Zainab Hassan, Naveed Anwar, Kehkshan Khalid
Revisiting Critically:	Haris Bin Tariq, Muzna Munir
Final Approval of version:	Haris Bin Tariq

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Lau HMC, Chiu TTW, Lam T-H. The effectiveness of thoracic manipulation on patients with chronic mechanical neck pain–a randomized controlled trial. Manual therapy 2011;16(2):141-7.
2. Vincent K, Maigne J-Y, Fischhoff C, Lanlo O, Dagenais S. Systematic review of manual therapies for nonspecific neck pain. Joint Bone Spine 2013;80(5):508-15.
3. Madson TJ, Cieslak KR, Gay RE. Joint mobilization vs massage for chronic mechanical neck pain: a pilot study to assess recruitment strategies and estimate outcome measure variability. J Manipulative Physiological Therapeutics 2010;33(9):644-51.
4. Nagrale AV, Glynn P, Joshi A, Ramteke G. The efficacy of an integrated neuromuscular inhibition technique on upper trapezius trigger points in subjects with non-specific neck pain: a randomized controlled trial. J Manual Manipulative Therapy 2010;18(1):37-43.
5. Martín Luján CE. Ergonomics and videogames: Habits, diseases and health perception of gamers 2016.
6. Prins Y, Crous L, Louw Q. A systematic review of posture and psychosocial factors as contributors to

upper quadrant musculoskeletal pain in children and adolescents. Physiotherapy Theory Practice 2008;24(4):221-42.
7. Jackson LA, Von Eye A, Fitzgerald HE, Witt EA, Zhao Y. Internet use, videogame playing and cell phone use as predictors of children's body mass index (BMI), body weight, academic performance, and social and overall self-esteem. Computers in Human Behavior 2011;27(1):599-604.
8. Rehbein F, Psych G, Kleimann M, Mediasci G, Mößle T. Prevalence and risk factors of video game dependency in adolescence: results of a German nationwide survey. Cyberpsychology, Behavior, and Social Networking 2010;13(3): 269-77.
9. Hakala PT, Saarni LA, Punamäki RL, Wallenius MA, Nygård CH, Rimpelä AH. Musculoskeletal symptoms and computer use among Finnish adolescents-pain intensity and inconvenience to everyday life: a cross-sectional study. BMC Musculoskeletal Disorders 2012;13(1):1-7.
10. King DL, Delfabbro PH. Internet gaming disorder treatment: a review of definitions of diagnosis and treatment outcome. J Clin Psychol 2014; 70(10):942-55.
11. Mentzoni RA, Brunborg GS, Molde H, Myrseth H, Skouverøe KJM, Hetland J, et al. Problematic video game use: estimated prevalence and associations with mental and physical health. Cyberpsychology, behavior, and Social Networking 2011;14(10):591-6.
12. Armijo-Olivo S. A new paradigm shift in musculoskeletal rehabilitation: why we should exercise the brain? Brazilian J Physical Therapy 2018;22(2):95.
13. Yesil H, Hepguler S, Dundar U, Taravati S, Isleten B. Does the use of electrotherapies increase the effectiveness of neck stabilization exercises for improving pain, disability, mood, and quality of life in chronic neck pain? A randomized, controlled, single-blind study. Spine 2018;43(20): E1174-E83.
14. Park YK, Hyun SW, Seo HK. The effectiveness of joint mobilization and myofascial release on the neck. J Korean Academy Orthopedic Manual Physical Therapy 2009;15(2):69-79.
15. Kim J, Kim S, Shim J, Kim H, Moon S, Lee N, et al. Effects of McKenzie exercise, Kinesio taping, and myofascial release on the forward head posture. Journal of physical therapy science. 2018;30(8):1103-7.
16. 17.Cho S. Effects of Myofascial Release and Posture Correction Exercise on the Neck Movement and the Quality of Sleep in Patients with Chronic Tension-Type Headaches. J Int Academy Physical Therapy Research 2019;10(4):1897-902.
17. Arshadi R, Ghasemi GA, Samadi H. Effects of an 8-week selective corrective exercises program on electromyography activity of scapular and neck muscles in persons with upper crossed syndrome: Randomized controlled trial. Physical Therapy Sport 2019;37:113-9.
18. Toprak Çelenay Ş, Akbayrak T, Özer Kaya D. A Comparison of the Effects of Stabilization Exercises Plus Manual Therapy to Those of Stabilization Exercises Alone in Patients With Nonspecific Mechanical Neck Pain: A Randomized Clinical Trial 2016.
19. Falla D, Lindstrøm R, Rechter L, Boudreau S, Petzke F. Effectiveness of an 8 week exercise programme on pain and specificity of neck muscle activity in patients with chronic neck pain: A randomized controlled study. Eur J Pain 2013;17(10):1517-28.

Original Article

Comparison of Post-Operative Astigmatism Followed by Extracapsular Cataract Extraction (ECCE) Surgical Procedure Demographically

Post-Operative Astigmatism Followed by ECCE

Aiman Khan Panezai, Imran Bazai, Mahtab Mengal, Afzal Mandokhel, Chakar Tajwidi and Manzor Ahmed Khan

ABSTRACT

Objective: To compare post-operative astigmatism demographically between continuous and interrupted sutures in patients undergoing ECCE surgery.
Study Design: Longitudinal study
Place and Duration of Study: This study was a multicenter study conducted from March 2019 to September 2020.
Materials and Methods: 314 patients meeting the inclusion criteria were selected for the study and divided into two groups. In both the groups ECCE surgery was to be performed. Group A was to receive Limbal interrupted sutures, while group B Limbal continuous sutures. Astigmatism was recorded through keratometry and final outcomes were evaluated after 6 weeks. Data was analyzed using SPSS. Two groups were compared using Chi-square test, with level of significance being P-value ≤0.05.
Results: 314 patients fulfilling the inclusion criteria were included in this study. The mean ± standard deviation age of study population was 60.55± 6.612 years. No significant difference was seen between the group of continuous and interrupted sutures in terms of astigmatism (P=0.32), but the patients undergoing continuous suturing technique had more astigmatism. Astigmatism was found to be significant for males (P=0.018) and age less than 50 years (P ≤0.00).
Conclusion: There is no difference in the amount of Post-operative astigmatism between continuous and interrupted suture technique, male gender and age group less than 50 is more predisposed to astigmatism after ECCE
Key Words: Astigmatism, ECCE, Surgical Procedure

Citation of article: Panezai AK, Bazai I, Mengal M, Mandokhel A, Tajwidi C, Khan MA. Comparison of Post-Operative Astigmatism Followed by Extracapsular Cataract Extraction (ECCE) Surgical Procedure Demographically. Med Forum 2021;32(10):190-192.

INTRODUCTION

The formation of an opacity on the lens is termed as a cataract. Cataract can be either unilateral or bilateral, congenital or acquired[1]. It is regarded as the leading cause of blindness globally, with a survey in 2017 suggesting that cataract was regarded as the predominant reason for blindness (57%)[2]. The blindness caused by cataract is one of the greatest public health dillema in the 21st century[3]. If efforts are not increased to prevent the development of avoidable blindness worldwide there is a chance that by the year 2020, 76 million people will be affected by blindness globally[4].

Helpers Eye Hospital Quetta.

Correspondence: Dr. Aiman Khan Panezai, Assistant Professor, Helpers Eye Hospital, Quetta.
Contact No: 0333-7801918
Email: panezai2000@yahoo.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

Thus far, other than preventing cataract, the only way to treat cataract is by performing cataract surgery. The two most common types of surgeries for cataracts are Phacoemulsification and extracapsular cataract extraction (ECCE)[5]. In both of these surgical methods the aim is to create a wound that is penetrating on the sclera or the cornea which can then act as a weak point against the increased ocular pressure that arises through a blunt ocular injury. ECCE involves a scleral incision of 9-13mm. ECCE still remains the most preferred and cost-effective surgical method in developing countries in which economical barriers play a part in the decision making of the diseased burden patients. Furthermore, surgeons are trained more efficiently by their predecessors in this method in such countries. Although ECCE shows good prognosis, it has its drawbacks owing to large corneal incisions as well as a greater amounts of astigmatism in the short-term and a longer time-frame to achieve rehabilitation of visual function post-surgically[6-7]. Patients may also need to return back for suture removal to achieve the best visual acuity after surgery. In Pakistan Cataract accounts for more than half of the total blindness and cataract surgery is the

most common ocular surgery performed in this region. In regards to this we decided to conduct a study to assess the demographic data of the incidence of astigmatism between patients who have undergone ECCE using continuous suture, and those with interrupted suture technique.

MATERIALS AND METHODS

The study was conducted a multicenter study was conducted from March 2019 to September 2020, after gaining ethical approval from the institutional review board. 314 patients were selected through the calculation formula of two proportions. All patients diagnosed with mature cataract on slit lamp examination aged 45-70 years were selected. Patients that met our inclusion criteria were then selected for this study. The patients inducted into our study were informed about their involvement in this clinical study and a written informed consent was also taken. A proper history was taken of each and every patient being admitted who complained of decreased vision and blurring. A slit lamp examination was conducted to confirm the presence of mature cataract and exclude and other disorders. Through a draw method, patients were then divided into two groups. In both the groups ECCE surgery was performed by an experienced surgeon who had also previously done cataract surgeries. In Group A Limbal interrupted sutures were given and in group B Limbal continuous sutures were given. In both groups Nylon Sutures was used. Under Aspetic measures, the surgically treated eyes were padded in both groups. On the next day dressings were under strict aseptic conditions. Astigmastism was then recorded by Keratometry and noted. The final outcomes were then recorded 6 weeks post-operatively. Data was analyzed using SPSS version 20.0. data was presented through frequency and percentages. Two groups were compared for post-operative astigmatism by applying chi square test. Effect modifiers which included age and gender were controlled through stratification, chi square test was applied with the level of significance being kept at P-value $\leq$0.05 level of significance.

RESULTS

Table No.1: Shows the mean ± standard deviation age of study population, which was 60.55±6.612 years

Table No.2: Shows the frequency of Astigmatism between the two groups

Table No.3: Shows the stratification according to Gender

Table No.4: Stratification according to Age

Table No.1: Analysis of age of study population

	Minimum	Maximum	Mean	Std. Deviation
Age	45	70	60.55	6.612

Table No.2: Frequency of Astigmatism

		Astigmatism		Total
		Yes	No	
Type of technique	Continuous	69	88	157
	Interrupted	52	105	157
Total		121	193	314

P=0.32

Table No.3: Stratification according to gender

Gender			Astigmatism		Total
			Yes	No	
Male	Type of technique	Continuous	37	59	96
		Interrupted	22	72	94
	Total		59	131	190
Female	Type of technique	Continuous	32	29	61
		Interrupted	30	33	63
	Total		62	62	124

Significant for males P=0.018

Table No.4: Stratification according to age

Age			Astigmatism		Total
			Yes	No	
Less than 50	Type of technique	Continuous	31	2	33
		Interrupted	23	35	58
	Total		54	37	91
50 and above	Type of technique	Continuous	38	86	124
		Interrupted	29	70	99
		Total	67	156	223

For age < 50 years p <0.000

For age 50 year and above, p=0.472

DISCUSSION

To achieve optimal surgical results, it is crucial that there is a reduction in Surgically induced Astigmatism and correction of any residual astigmatism 8. Astigmatism also depends upon the size and site of incision, along with the presence of any pre-operative astigmatism[9]. The aim of our study was to see demographically if continuous or interrupted suturing technique have any effect on the post-operative astigmatism (POA). Although the amount of POA was found to be more in the continuous suture group (n=69), statistically this was found to be insignificant (p=0.32). However, there are other studies that have stated that astigmatic errors are more in interrupted suturing then in continuous suturing[10]. Raout et al (2021) also investigated in his study the influence of suturing technique and found that there is no significant different in visual or refractive outcome between continuous and interrupted suturing techniques[11]. The finding of astigmatism was also seen as significant in the male gender population as compared to the female gender. This finding is similar to another finding conducted by Ninn-Pederson et al (1996) which showed men had developed more astigmatism then women. Mimouni et al (2019) in his study also showed that male population will tend to have more preoperative astigmatism than female and that male gender also

likely to have retreatment surgery for refractive correction[13]. On the contrary, Pontikos et al (2019) determined the frequency and distribution of corneal astigmatism, his results showed an association of astigmatism with females[13]. Age is also an important factor when considering the amount of POA astigmatism. A statistically significant finding was seen in age less than 50 years ($p<0.00$). All of the following suturing was performed using Nylon. Nylon can induce with the rule (WTR) astigmatism in the meridian of incisions, this can help to explain the tendency of Limbal incisions in ECCE towards WTR astigmatism[14-16]. Future studies can be done to compare the effect of different suture materials after ECCE.

CONCLUSION

There is no difference in the amount of Post-operative astigmatism between continuous and interrupted suture technique, male gender and age group less than 50 is more predisposed to astigmatism after ECCE.

Author's Contribution:

Concept & Design of Study:	Aiman Khan Panezai
Drafting:	Imran Bazai, Mahtab Mengal
Data Analysis:	Afzal Mandokhel, Chakar Tajwidi, Manzor Ahmed Khan
Revisiting Critically:	Aiman Khan Panezai, Imran Bazai
Final Approval of version:	Aiman Khan Panezai

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Aslam K, Sufyan M, Ansari A, Khalid I, Nafees K. Frequency of cataract in diabetic verses non-diabetic patients. Pak J Ophthalmol 2019;35(1).
2. Open Access Research Prevalence and causes of visual... [Internet].[cited 2018Oct14]. Available from:https://bmjopen.bmj.com/content/bmjopen/8/3/e018894.full.pdf
3. Tabin G, Chen M, Espandar L. Cataract surgery for the developing world. Current opinion in ophthalmol 2008;19(1):55-9.
4. Frick KD, Foster A. The magnitude and cost of global blindness: an increasing problem that can be alleviated. Am J Ophthalmol 2003;135:471–476.
5. Pershing S, Kumar A. Phacoemulsification versus extracapsular cataract extraction: where do we stand? Current opinion in ophthalmol 2011;22(1): 37-42.
6. de Silva SR, Riaz Y, Evans JR. Phacoemulsification with posterior chamber intraocular lens versus extracapsular cataract extraction (ECCE) with posterior chamber intraocular lens for age-related cataract. Cochrane Database of Systematic Reviews 2014(1).
7. Abo El Maaty GM, Elmoddather M, Elkareem AMG, Yousef HS. A Comparative Study Between Manual Small Incision Cataract Surgery, Planned Extracapsular Cataract Extraction and Phacoemulsification In Mature Cataract Cases. J Am Sci 2014;10(10):122-126.
8. Rainer G, Menapace R, Vass C, Annen D, Findl O, Schmetterer K. Corneal shape changes after temporal and superolateral 3.0 mm clear corneal incisions. J Cataract Refractive Surg 1999;25(8): 1121-6.
9. Habib A, Khan MS, Ishaq M. Effect of using version image guided system on surgically induced astigmatism (SIA) in patients undergoing cataract surgery. PAFMJ 2018;68(6):1533-37.
10. Kim SJ, Wee WR, Lee JH, Kim MK. The effect of different suturing techniques on astigmatism after penetrating keratoplasty. J Korean Medical Sci 2008;23(6):1015-9.
11. Raouf A, Hasan SM, Othman MM, El-Hefney Atta EM, Mostafa A. Impact of Different Suturing Techniques on Visual Outcomes in Penetrating Keratoplasty. Egyptian J Ophthalmol (Mansoura Ophthalmic Center) 2021;1(3):161-7.
12. Mimouni M, Kaiserman I, Spierer R, Spierer O, Rabina G, Varssano D, et al. Factors Predicting the Need for Re-treatment After Laser Refractive Surgery in Patients With High Astigmatism: A Large Database Analysis. J Refractive Surg 2021; 37(6):366-71.
13. Pontikos N, Chua S, Foster PJ, Tuft SJ, Day AC, UK Biobank Eye and Vision Consortium. Frequency and distribution of corneal astigmatism and keratometry features in adult life: Methodology and findings of the UK Biobank study. PloS One 2019;14(9):e0218144.
14. Kiambo WKD. Comparative study of ECCE and ICCE in Kinshasa, Zaire. Bull-Soc-Belge-Ophth 1993; 249: 81-7.
15. Yaycioglu AR, Gozum N, Gucukoglu A. Pseudoaccommodation with IOLs implanted in the bag. J Refract Surg 2002;18(3):193.
16. Pandey SK, Werner L, Apple DJ. Capsular Dye Enhanced Cataract Surgery, Recent Advances in Ophthalmology. 1st ed. Delhi: Lordson Publishers; 2002.p.11-29.

Original Article

Barriers to Patients Participation in Cardiac Rehabilitation

Mahtab Ahmed Mukhtar Patafi[1], Ayesha Bashir[1], Muhammad Kaleem[2], Hafiz Muhammad Wassam[3] and Muhammad Iqbal[4]

ABSTRACT

Objective: To identify the barriers faced by patients to participate; both attendees and non-attendees, in cardiac rehabilitation.

Study Design: A cross-sectional study

Place and Duration of Study: This study was conducted at Different Hospitals providing Cardiology and Cardiac Surgery services in Karachi from June 2019 to June 2020.

Materials and Methods: The total duration of the study was 6 months and Modified Cardiac Rehabilitation Barrier Scale (CRBS) questionnaire was used.

Results: About 100 participants took part in the study, out of which 63% where male and 37% where female. The mean age of the participants was 57.2900; age 88 being maximum and age 35 being minimum. It was seen that majority of the adults were illiterate and almost 50% being unemployed. Additionally, it highlights that distance, cost, transportation, family responsibilities and patient referral system was the major barrier for the respondents not attending or missing few sessions of cardiac rehabilitation program. Subsequently, not major but, time constraints, energy to continue and work responsibilities were also a barrier.

Conclusion: It has been concluded from the study that non-attendees show more barriers to cardiac rehabilitation as compared to attendees. It is expected in the future that the scale of developing cardiac rehabilitation centers and its performance will be increased, and efforts will be made to overcome the major barriers.

Key Words: Cardiac Rehabilitation, Barriers, Patients

Citation of article: Patafi MAM, Bashir A, Kaleem M, Wassam HM, Iqbal M. Barriers to Patients Participation in Cardiac Rehabilitation. Med Forum 2021;32(10):193-197.

INTRODUCTION

The diseases related to cardiac system are considered to be the first leading causative reason of death worldwide or over globe. Hence, least possible treatment measures and protocols are present or if they are available then it is beyond the reach of people. The term Cardiac Rehabilitation (CR) is a structured program of exercise and education, which not only helps in subsiding problems related to cardiac diseases but also helps in reducing other related co-morbidities. It helps the patient to return to optimal fitness and functioning following cardiac event. [1,2]

[1.] Cardiac Center, Quaid e Azam Medical College Bahawalpur.
[2.] Department of Physiotherapy, Bahwal Victoria Hospital, Bahawalpur.
[3.] Department of Physiotherapy, National College of Physiotherapy, Bahawalpur.

Correspondence: Mahtab Ahmed Mukhtar Patafi, Physiotherapist, Cardiac Center, Quaid e Azam Medical College Bahawalpur.
Contact No: 03017766019
Email: mahtab.patafi1@gmail.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

A variety of national entities have described cardiac rehabilitation with their own perspectives, which encompasses "Cardiac rehabilitation is a secondary preventive, long term and comprehensive approach which involves the process from patients evaluation to discharge planning; involving exercise prescription, counseling, education and knowledge, and cardiac risk factors.[3]

Cardiac rehabilitation is tailored to each cardiac patient according to his requirements. Although nearly all cardiac patients can benefit from rehabilitation but it is important that patients do not follow their own exercise program and only follow the program prescribed. Rehabilitation involves patient's education regarding the cardiac symptoms and issues, stress management and modification, nutrition and diet consultation and modification of lifestyle. On the other hand, patient should fully understand the significance of motivation and rehabilitation. [4]

It is considered that cardiac events are a major threat to patient's life physically as well as psychologically. If a person has had gone through Heart Failure (HF), Coronary Artery Bypass Graft Surgery (CABG), Myocardial Infarction (MI), Valve Repair or Percutaneous Coronary Artery Intervention than they have fear of having any of the condition again due to which they are psychologically disturbed. The fear takes the patient into anxiety and isolation and if these fear becomes dominant than counseling is a necessity.

In today's world counseling have profound beneficial effects on patient's health and life style, and rehabilitation not only treats cardiac issues but also treats fears and puts it to rest. [5]

In 2001 by the Institute of Medicine, which is in United States, serious demands were raised because of safety failures and suboptimal benefits from the physical therapy practice. As a result, the health care system was redesigned and the main domains of quality were covered in it. These main domains which are necessary for quality appraisal are: safety, effectiveness, patient-centeredness, timeliness, efficiency, and equity. [5, 6]

Cardiac rehabilitation was prescribed for those who suffered or had heart failure. But with time elapse the inductions have changed. Among the heart failure group, only stable class II and II group who don't have complex arrhythmias can go for exercise trainings protocols. Cardiac rehabilitation is prescribed to heart transplant patients as well. [6,7]

Currently, it is seen that acute cardiac care and rehabilitation has already decreased the mortality rate so much that exercise training program, isolated interference, might not be able to cause any further change in the mortality and morbidity rate. Consequently, now for cardiac rehabilitation the outcome measure is to improve quality of life (QOL). Services of cardiac rehabilitation are safe and effective interventions and these services are potential for contemporary treatment of patients with multiple cardiac issues or problems.

MATERIALS AND METHODS

Study Design: Descriptive cross sectional study.

Setting: The study was conducted in cardiac hospitals/ institutes; private and government, at Karachi

Sample Size: Sample size of 100 patients were selected for the study by convenient non-probability sampling technique.

Inclusion Criteria: Following criteria was considered to be necessary to the inclusion of the subjects:

- Patients with cardiac issues; inpatients and outpatients.
- Patients prescribed for cardiac rehabilitation but were not attending.
- Patients prescribed for cardiac rehabilitation but were not regular.

Exclusion criteria:

- Patients who did not have/ had cardiac issues and age less than 18 years. And with any visual, cognitive or serious mental conditions were excluded from the study.

Data collection tool: Modified Cardiac Rehabilitation Barrier Scale (CRBS) questionnaire was used in this study.

Data collection method: Data was collected from the participants by face to face interview. Consent form was also given to ensure participants voluntary participation.

Data analysis Procedure: Data was analyzed by using the software Statistical Packages of Social Sciences (SPSS) version 21.0. Descriptive statistical methods such as mean, median and frequency were used for analysis.

RESULTS

The sample for this study comprised of 100 participants who consented to participate in the study and completed the Cardiac Rehabilitation Barrier Scale (CRBS). The mean age of the study was 57.2900, for which minimum age of the respondent was 35 years and maximum age of the respondent was 88 years. (Fig. 1).

The quantitative data for the exceeding barriers in percentages is detailed as followed: 85% agreed and 15% disagreed to it; 82% agreed that and 18% disagreed to it; 86% agreed that I was unable to go to the CR program, or if I went to the program I missed few of the sessions for the reason: of transportation problems and 14% disagreed to it; 52% agreed that I was unable to go to the CR program, or if I went to the program I missed few of the sessions for the reason: travel (e.g., holidays, business, and cottage), 30% disagreed and remaining 18% neither agreed nor disagreed; 83% agreed that I was unable to go to the CR program, or if I went to the program I missed few of the sessions for the reason: I don't have any idea about CR program (example; my physician or health care provider did not tell me regarding it), 16% disagreed and only 1% neither agreed or disagreed; 81% agreed that I was unable to go to the CR program, my physician or health care provider didn't felt that it was needed and 19% disagreed; and 53% agreed that I was unable to go to the CR program, or if I went to the program I missed few of the sessions for the reason: of family responsibilities (e.g., care giving), 35% disagreed and 12% neither agreed nor disagreed (Table I; respectively for distance, cost, transportation, travel, didn't know about cardiac rehabilitation, doctor did not feel it was necessary and family responsibility).

41% agreed that I was unable to go to the CR program, or if I went to the program I missed few of the sessions for the reason: of time constraints (example; too busy, inconvenient class time), 39% disagreed and 20% neither agreed nor disagreed, and 42% agreed that I was unable to go to the CR program, or if I went to the program I missed few of the sessions for the reason.

And, when the respondents were interviewed about whether they find exercise tiring and painful or if they feel that they don't have energy to continue program then 47% disagreed, 33% agreed and 20% neither agreed nor disagreed and 48% disagreed that I was unable to go to the CR program, or if I went to the program I missed few of the sessions for the reason: I

do not have enough energy, 34% agreed and 18% neither agreed nor disagreed.

Furthermore, 71% disagreed that I was unable to go to the CR program, or if I went to the program I missed few of the sessions for the reason: I did not want CR, 18% neither agreed nor disagreed and 11% agreed, 74% disagreed that I was unable to go to the CR program, or if I went to the program I missed few of the sessions for the reason.

Compatibly it is seen that 68% disagreed that I was unable to go to the CR program, or if I went to the program I missed few of the sessions for the reason: most of the people with heart related conditions do not go, and they are absolutely well, 21% neither agreed nor disagreed and remaining 11% agreed and 64% disagreed that I was unable to go to the CR program, or if I went to the program I missed few of the sessions for the reason: I am capable of managing my own heart related conditions, 27 neither agreed nor disagreed and 9% agreed.

Moreover, when the participants were questioned about taking care of health alone or in group then 64% neither agreed nor disagreed that I was unable to go to the CR program, 33% disagreed and only 3% agreed. Also, 65% neither agreed nor disagreed, 31% disagreed and only 4% agreed, and 66% neither agreed nor disagreed that I was unable to go to the CR program, or if I went to the program I missed few of the sessions for the reason. (Table I).

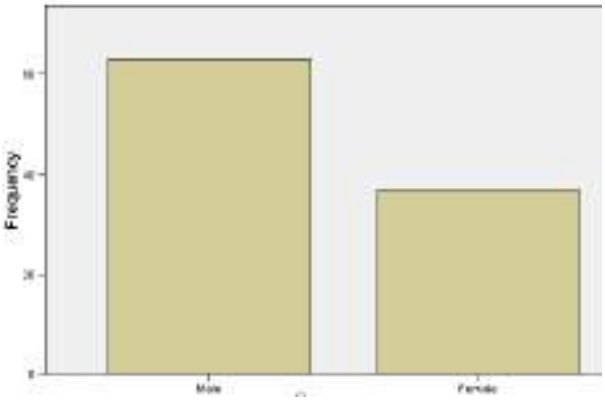


Figure No.1: Gender of participants

Table No.1: Barriers Faced by patients towards participation in cardiac rehabilitation

S #	Barriers	Strongly Disagree (Frequency)	Disagree (Frequency)	Neither Agree or Disagree (Frequency)	Agree (Frequency)	Strongly Agree (Frequency)
	I was unable to go to the CR program, or if I went to the program I missed few of the sessions for the reason of:					
1	Distance (e.g., not located in your area, too far to travel)	14	1	0	1	84
2	Cost (example; parking, gas)	16	2	0	2	80
3	Transportation problems (example; access to car, public transportation)	14	0	0	1	85
4	Family responsibilities (e.g., care giving)	35	0	12	4	49
5	I don't have any idea about CR program (example; my physician or health care provider did not tell me regarding it)	16	0	1	1	82
6	I did not want CR (example; heart problem treated, feel well, not severe)	71	0	18	1	10
7	I am exercising in my community, or at home	74	0	21	0	5
8	Severe weather	75	0	21	0	4
9	I find exercise tiring or painful	46	1	20	2	31
10	Travel (e.g., holidays, business, cottage)	30	0	18	5	47
11	Time constraints (example; too busy, inconvenient class	38	1	20	4	37

	time)					
12	Work responsibilities	40	0	18	2	40
13	I do not have enough energy	48	0	18	2	32
14	Additional health related issues restrict me from going; like kidney stones or dialysis, knee osteoarthritis, common flue or fever	72	0	19	2	7
15	I am too old	68	3	9	3	17

DISCUSSION

Cardiac Rehabilitation is a broad spectrum for the management of cardiovascular diseases and cardiac issues; whether recurring or may occur once. CR is significantly related to reduce mortality and morbidity rate and hence it is grossly practiced around the globe.

April 2007, an article was published by the name of barriers to participation in cardiac rehabilitation. In this article it was resulted that rural persons feel that lack of resources perceived distance is the major barrier.[8]

Many of the participants in this study said that they were never referred for cardiac rehabilitation program or their physician or health care provider didn't felt that it was needed. As depicted earlier as well that 83% agreed that I was unable to go to the CR program, 16% disagreed and only 1% neither agreed nor disagreed, and 81% agreed that I was unable to go to the CR program, or if I went to the program I missed few of the sessions for the reason, and 19% disagreed. Hence, in year 2016, "Assessing Physician Barriers to Cardiac Rehabilitation Referral Rates in a Tertiary Teaching Centre" article was published. This survey has concluded that there are physician barriers; which include staff and medicine residents. [10]

In year 2008, resulted that barriers were seen for both patients and health care professionals. It was concluded that health care professionals should take measures including making changes in health policies, increasing referral ratio and enhancing CR program with respective to women needs and preferences [11,12].

It is seen one of the studies published in year 2013, mounting a questionnaire to recognize apparent obstacles to put into practice the Dutch physical therapy chronic obstructive disease, clinical practice principle, article was published. Whereas, this study shows that the quantitative data for the exceeding barriers, related to financial problems in percentage, is detailed as followed 82% agreed that I was unable to go to the CR program and 18% disagreed to it.

A study concluded that those who did not attended cardiac rehabilitation reported have more barriers as compared to those who attended it. It is expected that stipulation of CR will rise and developmental schemes would be in a proper way which subsides the major obstacles[13]. It is observed that attendance rate has been low in participating for cardiac rehabilitation. Out of all 84% said no they are currently not attending the CR program and reaming 14% said that they were attending CR program. And, when the respondents were asked about that did they ever attend the cardiac rehabilitation program, 96% of them said they never attend the CR program earlier in their life but only 4% said that they had previously attended the CR program as well.

CONCLUSION

It has been concluded from the study that there are numerous barriers at the level of health care system, patients, society and environment that prevent patients to participate in the program of cardiac rehabilitation. Many of the participants found distance, cost, travel, and transportation and family responsibilities as their major barrier.

Author's Contribution:

Concept & Design of Study:	Mahtab Ahmed Mukhtar Patafi
Drafting:	Ayesha Bashir, Muhammad Kaleem
Data Analysis:	Hafiz Muhammad Wassam, Muhammad Iqbal
Revisiting Critically:	Mahtab Ahmed Mukhtar Patafi, Ayesha Bashir
Final Approval of version:	Mahtab Ahmed Mukhtar Patafi

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. verywell.com/four-phases-of-cardiac-rehabilitation-2696089accessed on April 25, 2016.
2. Dalal HM, et al. Cardiac rehabilitation. BMJ 2015;351.
3. Barry L. Zaret, Cardiac Rehabilitation Chap # 28.
4. Rebecca Chloe Echeverri. Barriers to Participation in Cardiac Rehabilitation: A Rural Perspective, 2007.
5. Andrew Duncan MD, Natarajan MK, Schwalm JD. Assessing Physician Barriers to Cardiac Rehabilitation Referral Rates in a Tertiary Teaching Centre, Canadian J General Internal Med 2016;11(1):14-18.

6. cscr.org/what-is-cardiac-rehab accessed on April 27, 2016.
7. Emedicine.medscape.com/article/319683-overview accessed on April 25, 2016.
8. De MeloGhisi, et al. Barriers to cardiac rehabilitation use in Canada versus Brazil 2013;33:173-179.
9. Parkosech, et al. Cardiac rehabilitation barriers and opportunities among young women with cardiovascular disease 2008;16:36-52.
10. Mair V, et al. Evaluating compliance to a cardiac rehabilitation program in a private general hospital, Study carried out at Hospital Israelita Albert Einstein, São Paulo, SP. Brazil 2013;11(3):278-84.
11. De Angelis C, et al. Exploring the barriers and enablers to attendance at rural cardiac rehabilitation programs 2008;16:137-142.
12. Mak YMW, Chan WK, Yue CSS. Barriers to participation in a phase II cardiac rehabilitation program, Hong Kong Med J 200;11(6):472-75.
13. De Vos C, et al. participating or not in a cardiac rehabilitation programme: factors influencing a patient's decision 2013;20(2):341-8.

Original Article

Visual Loss Due to Retinal Disorders: A study on 1496 Cases

Attaullah Shah Bukhari[1], Imran Ali Pirzado[2], Sarmad Jamal Siddiqui[3], Shahid Jamal Siddiqui[1], Suhail Ahmed Shah[4] and Arif Rabbani[5]

ABSTRACT

Objective: The aim of this hospital based study is to ascertain the frequency of various retinopathies in the upper Sindh.

Study Design: quasi experimental study

Place and Duration of Study: This study was conducted at the CMC and KMC for duration of January, 2016 to January, 2021 for a period of 5 years.

Materials and Methods: Patients with retinal disorders were selected as they came to the OPD for checkup or were referred to from other centers. A complete history and ocular examination along with biochemical test and radiological investigations were thoroughly carried out at the institution with strict protocols being followed at every step. Data was collected accordingly and analyzed using SPSS. All the data was quantitative and hence represented as frequency and percentage.

Results: A total of 1496 patients were included in the study that were diagnosed with retinal disorders, 963 (64.37%) Male and 533 (35.62%) Female aged between 3-92 years. 625 (41.77%) Patients had diabetic retinopathy in which 234 had Non-Proliferative Diabetic Retinopathy, 216 had Proliferative Diabetic Retinopathy, and 387 had clinically significant macular Edema. Retinal Vein occlusion was found in 116 (7.75%) of the patients in which 73 had Central Retinal Vein Occlusion, 34 Branch Retinal Vein Occlusion, and 9 had Hemiretinal Vein Occlusion. Central Serous Chorioretinopathy was seen in 102 (6.81%) of patients aged 17-55 years. Retinal Vasculitis was seen in 70 (4.67%) patients aged 16-60 years.

Conclusion: Diabetic Retinopathy was amongst the most prevalent retinal vein disorder. Others in high frequency included retinal vein occlusion, Central Serous Chorioretinopathy, and Retinal Vasculitis.

Key Words: Retinal Disorders, Diabetic Retinopathy, Retinal Vein Occlusion, Chorioretinopathy

Citation of article: Bukhari AS, Pirzado IA, Siddiqui SJ, Siddiqui SJ, Shah SA, Rabbani A. Visual Loss Due to Retinal Disorders: A study on 1496 cases. Med Forum 2021;32(10):198-201.

INTRODUCTION

The retina is a component of the eyes that is 0.5mm in thickness and lies at the back of the eye. The retina is the part of the eye that produces sight as it contains the necessary sensory nerve fibers which can transmit light into electrical signals that are then conveyed to the brain by the optic nerve (CN II). More than 60 types of distant neurons are inhabited by the retina, each playing a specific role in the processing and development of visual images [1]. Unfortunately, visual impairment is a very damning issue in the world. Visual impairment and visual loss can occur through many reason, one of these reasons is retinal diseases. It is unfortunate that in developing countries prevention measures are inadequate for retinal disorders. The reason is due to the fact that retinal disorders are considered to be an uncommon cause in the developing nations[2]. In Pakistan even the leading cause of blindness is not said to be from retinal disorders, but it is because of cataract. In a national survey on blindness in Pakistan conducted in 2004-05 stated that 53% cataract related blindness existed [3]. Previously a greater chunk of proportion was taken up by cataract as the leading cause of visual impairment and blindness globally with WHO stating that 51% of 285 million people visually impaired globally were due to cataracts[4-5]. Advancement in surgical correction, treatment, and prevention of cataract has reduced its prevalence, however, the prevalence rate and burden of disease has however increased for retinal disorders globally. Retinal diseases are on the horizon, especially in diabetic individuals. In Pakistan, when the second national disease survey for prevalence of blindness was conducted in 2004-05 posterior segment diseases were said to be responsible

[1.] Department of Ophthalmology, Khairpur Medical College Khairpur Mir's.
[2.] Department of Ophthalmology / Community Medicine[3], SMBBU Larkana.
[4.] Al-Ibrahim Eye Hospital, Isra Postgraduate Institute of Ophthalmology, Malir Karachi.
[5.] Department of Ophthalmology, PUMHS Nawabshah.

Correspondence: Dr. Attaullah Shah Bukhari, Associate Professor of Ophthalmology, Khairpur Medical College Khairpur Mir's
Contact No: 03052011900
Email: drattaullahbukhari@yahoo.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

for 9.5% of total blindness, as compared to 5.4% in the first national survey that took place in 1990 6. Furthermore, retinal disorders prevalence found in population based surveys in Iran and India showed a prevalence of 8.56% and 12.7% 7-8. There are many retinal diseases and their prevalence is different in different demographic. Our aim is to deduce the frequency of various retinopathies among patients that presented to the retinal clinic of Khairpur Medical College.

MATERIALS AND METHODS

A longitudinal study was conducted on patients coming to the Outpatient department (OPD) or being referred to from other centers at CMC and KMC for duration of 1st January 2016 to 1st January 2021. The study was approved from the institutional review board for ethical approval after which it was then conducted. All patients that had retinal findings were selected for the study and further evaluated and investigated. Before the inclusion of the patients in this study, informed consent were taken regarding their participation in the study and were also assured that they can easily leave the study if they choose to do so without the risk of any hindrance in their future treatment. A proper history of the duration of the disease, any other comorbidities, family history, and past treatment related to the disease was taken by a well-qualified ophthalmologist. A complete ocular examination consisting of visual acuity, slit lamp examination, gonioscopy, fundus examination, and applanation tonometry was carried out. Furthermore, additional biochemical laboratory tests were also conducted which included CBC, ESR, peripheral blood smear, RBS, LHbA1c, Lipid profile, serum calcium levels, VDRL, FTA-ABS, ANA, RA Factor, ACE, and Montaux Test. Radiological examination included a chest radiograph along with a radiograph of the sacroiliac joint also being done. Ultrasound and Fundus Fluorescein Angiography was also conducted where required. Data was recorded and analyzed using SPSS version 20.0. All the data was quantitative and represented in frequency and percentage.

RESULTS

A total of 1496 patients that consented to be part of the study and attended the retina clinic were included in the study. Out of the 1496 that attended 963 (64.37%) were male and 533 (35.62%) were female. The age of the patients ranged from 3-92 years.

Table 1: Shows the number of patients with Diabetic Retinopathy. Advanced Diabetic Eye Diseases were found in 113 eyes.

Table 2: Shows the number of patients with Retinal Vein Occlusion.

Table 3: Shows the number of patients with Macular Hole degeneration due to hypertensive changes and myopic changes

Table 4: Shows the number of patients with Retinal artery occlusion.

Table No.1: Shows the number of patients with Diabetic Retinopathy

Diabetic Retinopathy	Aged: 20-75 years
No. Of Patients	625 (41.77%0)
Male	376
Female	249
No. Of Eyes	950
Non-proliferative Diabetic Retinopathy (NPDR)	234
Proliferative Diabetic Retinopathy (PDR)	216
Clinically Significant Macular Edema (CSMO)	387

Table No.2: Shows the number of patients with Retinal Vein Occlusion

Retinal Vein occlusion	
No of Patients: 116 (7.75%0 Aged 18-80 years)	
Male: 67	Female: 49
Central Retinal Vein Occlusion	
No of Patients: 73	
Male: 44	Female:29
Branch Retinal Vein Occlusion	
No of Patients: 34	
Male: 16	Female: 18
Hemiretinal Vein Occlusion	
No of Patients: 9	
Male: 7	Female: 2

Table No.3: Shows the number of patients with Macular Hole degeneration due to hypertensive changes and myopic changes

Macular Hole	
No of Patients	15 aged 22-65 years
Male: 4	Female: 11
Hypertensive Retinopathy	
No of Patients	9 aged 12-66 years
Male: 7	Female: 2
Myopic Degeneration	
No of Patients	9 aged 15-50 years
Male: 5	Female: 4

Table No.4: Shows the number of patients with Retinal artery occlusion

Retinal Artery Occlusion	
No of Patients	8 (0.53%) Aged 20-60 years
Male: 5	Female: 3
Central Retinal Artery Occlusion	
Male: 4	Female: NIL
Branch Retinal Artery Occlusion	
Male: 3	Female: 1

Central serous Chorioretinopathy (CSCR) was found in 102(6.81%) patients between the age of 17-55 years in 113 eyes, 88 were male patients whereas 14 were

female patients. 69 (4.61%) patients showed macular degeneration aged 50-90 years in 137 eyes, 40 were male and 29 were female. Retinal Vasculitis was seen in 70 (4.67%) of patients aged 16-60 years in 115 eyes among which were 68 male and 8 female. Retinitis pigmentosa was seen 53 (3.54%) patients aged 3-70 years.

DISCUSSION

Visual loss is a common issue faced globally, with enormous amounts being invested into public health care and treatment to improve vision and quality of life. However, visual loss still remains high. The estimated global prevalence of retinal disorders is said to be 1 in 3000 individuals 9. Retinal disorders are also inherited with retinitis pigmentosa being the most frequent phenotype among retinal disorders with every 1 in 4000 individuals being affected due to it 10. Our study also saw 3.54% of patients having retinitis pigmentosa. Retinal disorders are not well defined in Pakistan in terms of frequency however, autosomal retinitis pigmentosa is said to be the most prevalent 11. The consanguinity of marriages is said to be a high factor leading to the development of autosomal disorders and this is also true for the country of Pakistan in which 60% marriages are consanguineous 12. Diabetic Retinopathy was the most prevalent retinal disorder in our study with 625 (41.77%0 individuals suffering from it. Diabetic retinopathy is also the most common cause of blindness in the United States among adults13. Due to modern day diabetic management and timely intervention with glucocorticoids, laser photocoagulation, and anti-vascular endothelial (VEGT) agents vision threatening diabetic retinopathy can be controlled and can significantly reduce loss of vision 14-16. Retinal vein occlusion was seen in 116 (7.75%) patients, which is another cause of visual impairment. Retinal vein occlusion is the second most common disorder after diabetic retinopathy 17. Previous studies showed a poor prognosis of vision without treatment, however, with the development of VEGT inhibitors a new page has turned in the management of retinal vein occlusion 18-20. CSCR was the third most common retinal vein disorder identified in our study with a frequency of 6.81%. The exact pathology of the disease still remains unclear, although ischemia to the choroid and choroidal vascular hyper permeability being implicated as the cause of the disease which can ultimately result in serous macular detachment 21-22. CSCR is more prevalent in Asian population as compared to other demographics such as white and black races 23. Islam et al (2016) identified risk factors in CSCR to be stress, psychiatric illnesses, hypertension, peptic ulcer diseases, use of steroids and other medications 24. Retinal Vasculitis was the fourth most prevalent disorder in our study. A number of causes are linked to retinal Vasculitis including autoimmune diseases and infectious diseases 25. Our study didn't identify the particular cause of retinal Vasculitis, future studies can be modified to do so.

CONCLUSION

Diabetic Retinopathy is more frequently seen retinal disorder more commonly in male individuals. Non-Proliferative diabetic Retinopathy is more common. The second common frequent disorder is retinal vein occlusion. CSCR is the third common frequently seen disorder. Retinal Vasculitis is the fourth common frequently seen retinal disorder.

Author's Contribution:

Concept & Design of Study:	Attaullah Shah Bukhari
Drafting:	Imran Ali Pirzado, Sarmad Jamal Siddiqui
Data Analysis:	Shahid Jamal Siddiqui, Suhail Ahmed Shah, Arif Rabbani
Revisiting Critically:	Attaullah Shah Bukhari, Imran Ali Pirzado
Final Approval of version:	Attaullah Shah Bukhari

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Masland RH. The neuronal organization of the retina. Neuron 2012;76(2):266-80.
2. Yorston D, Jalali S. Retinal detachment in developing countries. Eye 2002;16:353–8.
3. Aslam K, Sufyan M, Ansari A, Khalid I, Nafees K. Frequency of cataract in diabetic verses non-diabetic patients. Pak J Ophthalmol 2019;35(1).
4. Wang W, Yan W, Fotis K, Prasad NM, Lansingh VC, Taylor HR, et al. Cataract surgical rate and socioeconomics: a global study. Investigative Ophthalmol Visual Sci 2016;57(14):5872-81.
5. Pascolini D, Mariotti SP. Global estimates of visual impairment: 2010. Bri J Ophthalmol 2012;96(5):614-8.
6. Mumtaz SN, Fahim MF, Arslan M, Shaikh SA, Kazi U, Memon MS. Prevalence of diabetic retinopathy in Pakistan; A systematic review. Pak J Med Sci 2018;34(2):493.
7. Hatef E, Fotouhi A, Hashemi H, et al. Prevalence of retinal diseases and their pattern in Tehran: the Tehran eye study. Retina 2008; 28:755-62.
8. Dandona L, Dandona R, Srinivas M, et al. Blindness in the India State of Andrapradesh. Invest Ophthalmol Vis Sci 2001;42:908-16.
9. Robson AG, Michaelides M, Saihan Z, Bird AC, Webster AR, Moore AT, et al. Functional characteristics of patients with retinal dystrophy that manifest abnormal parafoveal annuli of high

density fundus autofluorescence; a review and update. Documenta ophthalmologica 2008;116(2): 79-89.
10. Ayuso C, Millan JM. Retinitis pigmentosa and allied conditions today: a paradigm of translational research. Genome Medicine 2010;2(5):1-1.
11. Bittles AH. Endogamy, consanguinity and community disease profiles. Public Health Genomics 2005;8(1):17-20.
12. Bittles AH. Consanguinity and its relevance to clinical genetics. Clinical Genetics 2001;60(2): 89-98.
13. DCCT/EDIC Research Group. Frequency of evidence-based screening for retinopathy in type 1 diabetes. New Engl J Med 2017;376(16):1507-16.
14. Nathan DM. Complications Trial/Epidemiology of Diabetes I, Complications Research G. Effect of intensive diabetes therapy on the progression of diabetic retinopathy in patients with type 1 diabetes: 18 years of follow-up in the DCCT/EDIC. Diabetes 2015;64:631-42.
15. Wang JK, Huang TL, Su PY, Chang PY. An updated review of long-term outcomes from randomized controlled trials in approved pharmaceuticals for diabetic macular edema. Eye Sci 2015;30(4):176-83.
16. Gardner TW, Antonetti DA, Barber AJ, LaNoue KF, Levison SW, Penn State Retina Research Group. Diabetic retinopathy: more than meets the eye. Survey Ophthalmol 2002;47:S253-62.
17. Feroz L, Uzair N, Shamim M, Mehmood SA. Optical Coherence Tomography Angiography in Retinal Vein Occlusion: Correlation between Foveal Avascular Zone Area and Visual Acuity. Pak J Ophthalmol 2021;37(3).
18. Hayreh SS, Podhajsky PA, Zimmerman MB. Natural history of visual outcome in central retinal vein occlusion. Ophthalmol 2011;118(1):119-33.
19. Boyer D, Heier J, Brown DM, Clark WL, Vitti R, Berliner AJ, et al. Vascular endothelial growth factor Trap-Eye for macular edema secondary to central retinal vein occlusion: six-month results of the phase 3 copernicus study. Ophthalmol 2012;119(5):1024-32.
20. Brown DM, Campochiaro PA, Singh RP, Li Z, Gray S, Saroj N, et al. Cruise Investigators. Ranibizumab for macular edema following central retinal vein occlusion: six-month primary end point results of a phase III study. Ophthalmol 2010;117(6):1124-33.
21. Liew G, Quin G, Gillies M, Fraser-Bell S. Central serous chorioretinopathy: A review of epidemiology and pathophysiology. Clin Experiment Ophthalmol 2013;41:201-14.
22. Shahin MM. Angiographic characteristics of central serous chorioretinopathy in an Egyptian population. Int J Ophthalmol 2013;6:342-5.
23. Liegl R, Ulbig MW. Central Serous Chorioretino-pathy. Ophthalmologica 2014;232:65-76.
24. Islam QU, Hanif MK, Tareen S. Frequency of systemic risk factors in central serous chorioretinopathy. J Coll Physicians Surg Pak 2016; 26(8):692-5.
25. Rosenbaum JT, Sibley CH, Lin P. Retinal vasculitis. Current opinion in Rheumatol 2016; 28(3):228.

Original Article

Preventive Role of Antioxidants in Phenytoin Induced Toxicity of Rat Testes: A Microscopic Analysis

Khalique-ur-Rehman[1], Khalid Shehzad[2], Syed Muhammad Masood Ali[3], Sonia Khan[3], Sarah Sughra[5] and Raja Faisal[4]

ABSTRACT

Objective: To analyze the preventive role of Virgin Coconut Oil (VCO) and Corn Oil (CO) in the testes of rats upon administration of Phenytoin.

Study Design: Analytic study

Place and Duration of Study: This study was conducted at the Al-Tibri Medical College, Karachi from November 2020 to March 2021.

Materials and Methods: 32 male albino rats were acquired by random sampling technique and divided into 4 interventional groups. Group 1 was given Normal Saline Only, Group 2 was given Phenytoin only, Group 3 was given VCO + Phenytoin, and Group 4 was given VO + Phenytoin. The diet, water intake, and light exposure were well regulated and the subjects were then euthanized on the 4th, 5th, and 6th week of the study to assess the germinal layer thickness on the microscope. The testes were removed from the subjects, and tissue samples were acquired and placed on the microscope accordingly and the germinal layer thickness and morphology was assessed at 400x magnification.

Results: Our results showed a significant decrease in the germinal layer thickness in the phenytoin group 2, owing to the generation of oxidative stresses. In the VCO group, a significant improvement was seen compared with the phenytoin group as the germinal layer thickness was restored in this group. Unfortunately, CO wasn't able to restore the germinal layer thickness and the microscopic findings of the CO group were similar to the phenytoin group. VCO due to its antioxidant potential because of the presence of polyunsaturated fatty acids helps in restoring the germinal layer thickness in the presence of phenytoin.

Conclusion: VCO is a potent antioxidant and can mitigate the toxicity of phenytoin on testes

Key Words: Virgin Coconut Oil, Germinal Layer, Phenytoin, Coconut Oil

Citation of article: Rehman K, Shehzad K, Ali SMM, Khan S, Sughra S, Faisal R. Preventive Role of Antioxidants in Phenytoin Induced Toxicity of Rat Testes: A Microscopic Analysis. Med Forum 2021;32(10):202-205.

INTRODUCTION

Epilepsy is a very devastating neurological disorder that significantly impacts the quality of life of the individual facing it as well as the family members that are associated with the patient[1].

[1.] Chandka Medical College, Shaheed Benazir Butto Medical University, Larkana.
[2.] Department of Anatomy, Liaquat College of Medicine and Dentistry, Karachi.
[3.] Department of Pharmacology / Anatomy[4], Isra University Karachi Campus
[5.] Sir Syed College of Medical Sciences for Girls, Karachi Clifton.

Correspondence: Dr. Sonia Khan, Department of Pharmacology, Al-Tibri Medical College, Isra University Karachi Campus
Contact No: 0312-2218880
Email: drsonia.azeem@gmail.com

Received: June, 2021
Accepted: July, 2021
Printed: October, 2021

Apart from the constant seizures that can spontaneously arise in the patients, they also have to suffer the adverse effects of many anti-epileptic drugs as well[2]. One of the most promising, and well-known drugs used in the field of medicine for Epilepsy is Phenytoin, which is an established drug for treating acute repetitive seizures as well as Status Epilepticus[3]. Although it is the most widely used anti-epileptic drug available on the market, it needs to be monitored due to it possessing a narrow therapeutic range[4]. Side effects of Phenytoin include gingival hyperplasia, dermatological reactions such as toxic-epidermal necrolysis and Steven-Johnson Syndrome, Cardiovascular effects, and Respiratory problems[5-7]. Furthermore, studies have also indicated that phenytoin is said to have a negative effect on the male reproductive system[8]. Phenytoin can cause a significant decrease in the sperm count, active sperm motility, viable sperm number, and increase the number of abnormal sperms[9]. The factor that has been identified to cause toxicity in the male reproductive system is the development of oxidative stress. It occurs due to the state of imbalance between free radical production and

antioxidant, thereby damaging the cells responsible for sperm formation and ultimately having an effect on the male reproductive system[10]. If the antioxidant level in the body is restore to counteract the free radical generation and the subsequent oxidative stress, the toxic potential of the phenytoin drug on the male testes can be successfully neutralized. Many antioxidants such as β-carotene, Vitamin C, and E all provide major protective against the free radicals that generate oxidative stresses in the body by reducing reactive oxygen species[11]. Virgin Coconut Oil (VCO) and Corn Oil (CO) are some more examples of antioxidant agents that have seen promising results in reducing oxidative stress[12-14]. As the use of phenytoin is massive among reproducing male, we decided to conduct a study to determine the role of antioxidant oils in phenytoin induced toxicity on testes in rats.

MATERIALS AND METHODS

This experimental study was conducted after approval from the institutional review board at Al-Tibri Medical College and Hospital, Karachi from November 2020 to March 2021. For this study we randomly selected 32 male albino rats that weight 15-250 grams. The animals were randomly divided into 4 treatment groups in which we carried out the following interventions

Group 1:

The control group of our study was to receive an intra-peritoneal injection of 1unit Normal Saline with a normal diet

Group 2:

Received only 10/mg/kg/body weight of Phenytoin through an intra-peritoneal injection once daily.

Group 3:

Received both 10mg/kg/body weight of Phenytoin plus 6.7ml of Virgin Coconut Oil once daily.

Group 4:

Received both 10mg/kg/body weight of Phenytoin plus 2.5ml Corn Oil once daily.

The diet and water intake was well regulated along with the duration of light. The subjects were monitored thoroughly with samples being acquired on the 4th, 5th, and 6th week of the study by euthanizing the rats under anesthesia and then incising the subjects and removing both the testes for microscopic analysis. The tissues were carefully removed from the tests and preserved in 10% formalin. The tissues were then processed for slide preparation and staining using H&E staining technique. The germinal layer thickness was assessed under the microscope to see how its thickness and appearance will be affected in all of the mentioned groups. The magnification was fixed at 400x.

RESULTS

Figure 1: Photomicrographs of the seminiferous tubules using H&E staining and representing the germinal layer thickness on the 4th week among Different Groups

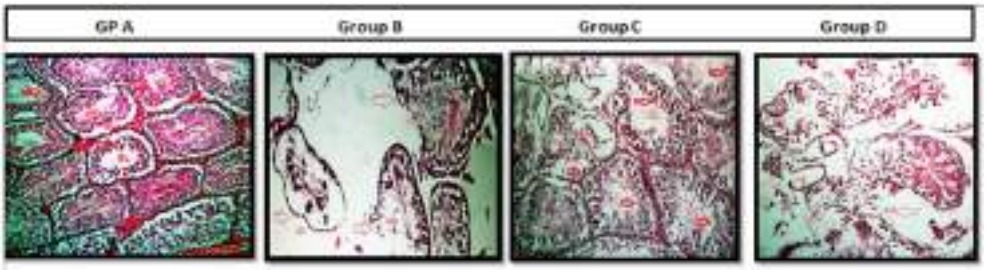


Figure 1: Photomicrographs of the seminiferous tubules using H&E staining and representing the germinal layer thickness on the 4th week among Different Groups. Magnification 400x, GL: Germinal Layer. In group B significant reduction in numbers of seminiferous tubules with marked thinning of Germinal epithelium. In Group C the virgin coconut oil significantly restore the germinal tissue of the testes. In Corn oil treated group the non-significant reduction of germinal epithelium, as compare to group B.

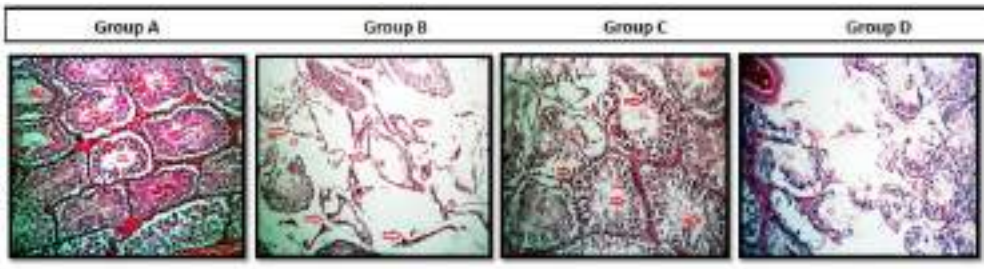


Figure 2: Photomicrographs of the seminiferous tubules using H&E staining and representing the germinal layer thickness on the 5th week among Different Groups. Magnification 400x, GL: Germinal Layer. In group B significant reduction in numbers of seminiferous tubules with marked thinning of Germinal epithelium. In Group C the virgin coconut oil significantly restore the germinal tissue of the testes. In Corn oil treated group the significant reduction of germinal epithelium, as compare to group B minimum restoration of germinal layer.

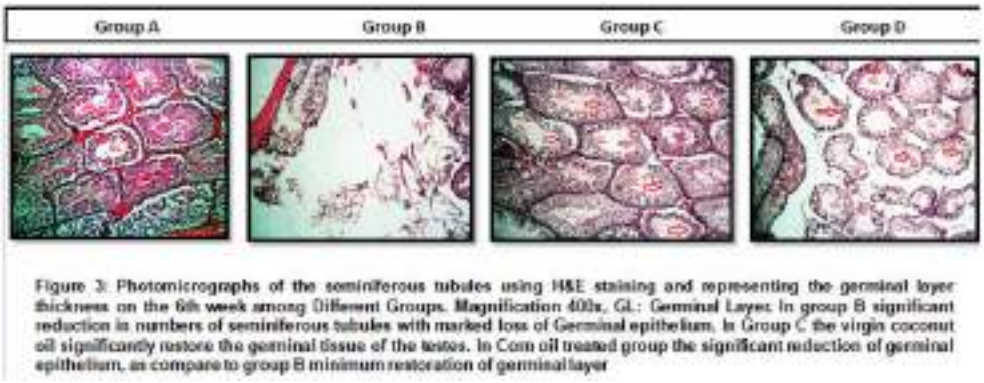


Figure 3: Photomicrographs of the seminiferous tubules using H&E staining and representing the germinal layer thickness on the 6th week among Different Groups. Magnification 400x. GL: Germinal Layer. In group B significant reduction in numbers of seminiferous tubules with marked loss of Germinal epithelium. In Group C the virgin coconut oil significantly restore the germinal tissue of the testes. In Corn oil treated group the significant reduction of germinal epithelium, as compare to group B minimum restoration of germinal layer

Figure 2: Photomicrographs of the seminiferous tubules using H&E staining and representing the germinal layer thickness on the 5th week among Different Groups.

Figure 3: Photomicrographs of the seminiferous tubules using H&E staining and representing the germinal layer thickness on the 6th week among Different Groups.

DISCUSSION

Apart from Phenytoin, other anti-epileptic drugs such as sodium valproate, topiramate, carbamazepine, gabapentin, and levetiracetam all lead to some sort of testicular toxicity[15-18]. Therefore, it is critical to find agents that can limit the amount of toxicity these drugs can do. We studied the histological features of all our interventional groups. The microscopic findings revealed that phenytoin causes a reduction in the germinal layer thickness thus proving to create disastrous consequences on the reproductive organs. However, upon the administration of the interventional agents which were VCO and CO, we did see favorable results with the VCO+ Phenytoin group in preventing a reducing in the germinal layer thickness. CO however failed to show significantly sound results as the histological findings of germinal layer thickness were fairly similar to the group in which only phenytoin was administered. In another study Ogendengbe et al (2016) induced testicular toxicity using anti-retroviral therapy and showed that significant decrease in the seminiferous tubular architecture, as well as a decline in the epithelial height, a finding which mirrors our study. Furthermore, in accordance with our study it was also found in the same study that intervention using VCO along with phenytoin also did lead to a decrease in the seminiferous tubular diameter, but other morphometric and histological parameters were in resemblance to the control group or VCO group[19]. VCO is highly rich in polyunsaturated fatty acids that have a potent inhibitory effect on lipid peroxidation. This is what may have led to a much better histological architecture in the group administered with VCO. VCO showed its antioxidant characteristics in another similar study to ours in which comparison was done with Groundnut oil and Copra oil[20]. There have been other antioxidant agents that have further cemented the potential to treat toxicity caused by phenytoin in tests. Olatunde et al (2015) compared the antioxidant role of Kolaviron and Vitamin E in phenytoin induced hepatic and testicular dysfunction in Wistar rats, his results showed a significant reduction in the seminal epithelium thickness along with a decrease in the diameter of seminiferous tubules, a finding similar to our study. Furthermore, the antioxidant status of the liver and testes were restored to normal levels in rats that were treated with Kolaviron and Vitamin E, a finding that matches our results with the administration of VCO [21]. Dosumu et al (2010) also showed that VCO also has a therapeutic potential in limiting the oxidative stress in the testes by improving the antioxidant stress by reducing the malondialdehyde (MDA) and allowing the lipid profile status to attain near normal levels once again[22].

CONCLUSION

We can safely say that the antioxidant potential of Virgin coconut oil is vital in maintaining and restoring the germinal thickness of testes induced with phenytoin.

Author's Contribution:

Concept & Design of Study:	Khalique-ur-Rehman
Drafting:	Khalid Shehzad, Syed Muhammad Masood Ali
Data Analysis:	Sonia Khan, Sarah Sughra, Raja Faisal
Revisiting Critically:	Khalique-ur-Rehman, Khalid Shehzad
Final Approval of version:	Khalique-ur-Rehman

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Taylor RS, Sander JW, Taylor RJ, Baker GA. Predictors of health-related quality of life and costs in adults with epilepsy: a systematic review. Epilepsia 2011;52(12):2168-80.
2. Wong IC, Lhatoo SD. Adverse reactions to new anticonvulsant drugs. Drug Safety 2000;23(1): 35-56.

3. Guldiken B, Rémi J, Noachtar S. Cardiovascular adverse effects of phenytoin. J Neurol 2016;263 (5):861-70.
4. Sharma B, Handa R, Prakash S, Nagpal K, Gupta P. Phenytoin toxicity presenting as encephalopathy with fatal outcome: A case report. J Neurol Res 2014;3(6):184-6.
5. Gunturu LN. Case report on phenytoin-induced iatrogenic gingival hyperplasia. Asian J Pharm Clin Res 2020;13(10):1-2.
6. Voora L, Shastry CS, Bhandari R, Sukeerthi D, Rawal KB, Chand S. Phenytoin-induced erythroderma. J Young Pharmacists 2019;11(3): 320.
7. Kheir F, Daroca P, Lasky J. Phenytoin-Associated Granulomatous Pulmonary Vasculitis. Am J Therapeutics 2016;23(1):e311-4.
8. Olutunde PF, Emmanuel OS, Moyosore SA, Olusola AA, Olutoyin OO, Ebenezer AA, et al. Chronic use of phenytoin reversibly suppresses fertility in male Sprague-Dawley rats. Scientific Research and Essays 2010;5(9):999-1004.
9. Kadhem WM, Majhwol EM. Effect some of antiepileptic drugs (AEDs) on some male reproductive parameters in white rats. Eur Asian J Bio Sci 2020;14(1).
10. Agarwal A, Durairajanayagam D, Halabi J, Peng J, Vazquez-Levin M. Proteomics, oxidative stress and male infertility. Reproductive Biomedicine Online 2014;29(1):32-58.
11. Biswas SK. Does the interdependence between oxidative stress and inflammation explain the antioxidant paradox? Oxidative Medicine Cellular Longevity 2016.
12. Ghani NA, Channip AA, Chok Hwee Hwa P, Ja'afar F, Yasin HM, Usman A. Physicochemical properties, antioxidant capacities, and metal contents of virgin coconut oil produced by wet and dry processes. Food Sci Nutr 2018;6(5):1298-306.
13. Yeap SK, Beh BK, Ali NM, Yusof HM, Ho WY, Koh SP, et al. Antistress and antioxidant effects of virgin coconut oil in vivo. Experimental Therapeutic Med 2015;9(1):39-42.
14. Kim JY, Kim MJ, Yi B, Oh S, Lee J. Effects of relative humidity on the antioxidant properties of α-tocopherol in stripped corn oil. Food Chem 2015;167:191-6.
15. Bairy L, Paul V, Rao Y. Reproductive toxicity of sodium valproate in male rats. Ind J Pharmacol 2010;42(2):90.
16. El Makawy AI, Ibrahim FM, Mabrouk DM, Ahmed KA, Ramadan MF. Effect of antiepileptic drug (Topiramate) and cold pressed ginger oil on testicular genes expression, sexual hormones and histopathological alterations in mice. Biomedicine Pharmacotherapy 2019;110:409-19.
17. Iamsaard S, Sukhorum W, Arun S, Phunchago N, Uabundit N, Boonruangsri P, et al. Valproic acid induces histologic changes and decreases androgen receptor levels of testis and epididymis in rats. Int J Reproductive BioMed 2017;15(4):217.
18. Baysal M, Ilgin S, Kilic G, Kilic V, Ucarcan S, Atli O. Reproductive toxicity after levetiracetam administration in male rats: Evidence for role of hormonal status and oxidative stress. PLoS One 2017;12(4):e0175990.
19. Ogedengbe OO, Jegede AI, Onanuga IO, Offor U, Naidu EC, Peter AI, et al. Coconut oil extract mitigates testicular injury following adjuvant treatment with antiretroviral drugs. Toxicological Res 2016;32(4):317-25.
20. Nevin KG, Rajamohan T. Virgin coconut oil supplemented diet increases the antioxidant status in rats. Food Chem 2006;99(2):260-6.
21. Owoeye O, Adedara IA, Adeyemo OA, Bakare OS, Egun C, Farombi EO. Modulatory role of kolaviron in phenytoin-induced hepatic and testicular dysfunctions in Wistar rats. J Dietary Supplements 2015;12(1):105-17.
22. Dosumu OO, Akinola OB, Akang EN. Alcohol-induced testicular oxidative stress and cholesterol homeostasis in rats–The therapeutic potential of virgin coconut oil. Middle East Fertility Society J 2012;17(2):122-8.

Original Article

Effects of Sensory Motor Training On Balance and Proprioception among Post-Menopausal Obese Women

Sehar Shabir[1], Binash Afzal[1], Tehreem Mukhtar[1], Ghazal Awais Butt[1], Sumera Abdul Hameed[1] and Arshad Nawaz Malik[2]

ABSTRACT

Objective: To determine the impact of sensory motor training on balance and proprioception among postmenopausal obese women.

Study Design: Interventional randomized clinical trial

Place and Duration of Study: This study was conducted at the THQ hospital Faisalabad from September 2020 to March 2021 for a period of six months.

Materials and Methods: A convenient sample of 40 postmenopausal obese women with age range 45-65 years were included after obtained informed consent and randomly divided into two equal groups. Group A (n=20) was received sensory motor training along with conventional therapy while group B (n=20) was only given conventional therapy. The interval of training was 6 weeks. Both groups were assessed by using functional reach test (FRT), time up and go test (TUG) and one leg stance test (OLS) at baseline and 6th week (pre- and post-estimation of postural strength). Values were obtained after intervention analyzed for any change using SPSS 25.

Results: The results of this study found that SMT exhibited significant improvement in FRT score in Group A as compared with Group B at post-test, 11.35±1.34 vs 10.35±1.30 (p=0.022) respectively. TUG score significantly lower in Group A as compared with Group B, 9.00±1.52 vs 10.75±1.61 (p=0.001) respectively and proprioception OLS significantly increased with DO, 25.01±2.69 vs 22.46±2.27 (p=0.003), DC 6.54±.73 vs 5.99±.84 (p=0.034), OO 20.06±1.18 vs 17.61±1.28 (p=0.0001) respectively but non-significant increase in OLS with OC 3.49±.72 vs 3.09±.71 (p=0.089) respectively.

Conclusion: This study concluded that sensory motor training show improvement in balance as well as proprioception. Static and dynamic balance indicated more improvement in sensory motor training when compared with conventional training while proprioception demonstrated almost similar outcomes for the both groups.

Key Words: Menopause; Obesity; Postural balance; Proprioception; Sensory motor training

Citation of article: Shabir S, Afzal B, Mukhtar T, Butt GA, Abdul Hameed S, Malik AN. Effects of Sensory Motor Training On Balance and Proprioception among Post-Menopausal Obese Women. Med Forum 2021;32(10):206-210.

INTRODUCTION

The most frequently used definition of natural menopause is amenorrhea for 6 continuous months without hysterectomy.[1] Postmenopausal women may have postural changes, for instance, forward head, changed shoulders, extended kyphosis, diminished lumbar lordosis and flexed hips just as, knees.[2]

These progressions might be because of loss of flexibility in connective tissues, lessened capacity to neutralize gravitational powers and decrease of muscles strength just as, endurance.[3] All of these postural changes influence day by day living exercises, equilibrium and walk, henceforth; increase the high fall risk.[4] It is accepted that estrogen may avoid fractures by reducing bone loss, motivating postural balance, increasing well-being and minimizing sleep disturbances thus, decreasing the risk of falling.[5] Loss of estrogen during menopause may impair protective reflexes,[6] as well as increase bone resorption leading to faster bone loss which is a foremost risk factor for decline in postural balance and fracture.[7]

Menopause is also accompanied by reduction in resting metabolic rate, physical activities and energy expenditure leading to obesity[8]which is usually represented as an increase in fat mass and abdominal adipose tissue accumulation.[9] Obesity is linked with an infinite list of diseases such as diabetes, hypertension, chronic heart diseases, stroke, osteoarthritis and sleep apnea.[10]

Balance is a complex process in which the support of a position is controlled by postural changes in accordance with intentional movement and because of outside

[1.] Department of Physical Therapy / Rehabilitation Sciences[2], Riphah International University, Lahore.

Correspondence: Binash Afzal, Assistant Professor, Riphah International University, Lahore.
Contact No: 03350318699
Email: binash.afzal@riphah.edu.pk

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

bother.[11] Balance training and individualized muscle strength programs bring about wide scope of advantages. These incorporate less fair of falling, prevent moderate wounds, and improve muscle strength and postural balance just as, keep up actual work level.12 Balance is characterized as, the capacity to keep up the body's focal point of gravity (COG) over its base of help (BOS) .[13]

The proprioception is a nature of the somato sensibility that can be characterized as the view of body and segment position as for the space, or of each portion of the body as for the body itself. Proprioception is a complex sense contributing to muscle sense, joint stability, and postural equilibrium. This occurs through mechanoreceptors located in the muscles, ligaments, tendons, joint capsules, and skin. In this manner, proprioception has been characterized as a person's capacity to incorporate the sensory signals from different mechanoreceptors to consequently decide body position and developments in space.[14] Sensorimotor training (SMT) is a distinct type of proprioceptive and balance exercise that was planned for management of patients with chronic musculoskeletal problems (e.g., pain syndrome). The impression on which it relays that instead of focusing the isolated strength of a group of muscles around a joint. Sensorimotor training involves help of sensory data sources (proprioception and somatosensory sources of info, remedying muscle imbalance and guaranteeing right pattern at the degree of focal sensory system.[9]

The rationale of this study was to assess the effect of sensorimotor training in post-menopausal obese women to improve balance measures and proprioception, before and after training.

MATERIALS AND METHODS

An interventional randomized clinical trial (Registration number: Clinical Trials.gov Identifier: NCT04820738) was conducted at THQ Hospital Faisalabad, from September 2020 to March 2021. Ethical approval was gained from institutional review board (IRB) committee of Riphah International University Lahore campus as well as from the hospital. The sample size was calculated by WHO sample size with following parameters; the mean body mass index (BMI) in control group 24 kg/m^2 and in experimental group was 26 kg/m^2, confidence interval (CI) 95%, and power of test was 80%.[10] 40 postmenopausal women who met the inclusion criteria and entered the trial with non-probability consecutive sampling technique. Women between the age of 45-65 years with post-menopause obesity, BMI $\geq$ 30 kg/m^2 at assessment with independent in daily living activities (ADLs), self-ambulatory, and healthy women (having no known condition in which sensorimotor training would be contraindicated) were included in the study. Women having history of ankle sprain, uncontrolled diabetes mellitus, psychological and cognitive problems, women with severe visual impairment and retinopathy, women with other medical complications foot ulcers, orthopedic or other neurological impedance (e.g., neuropathy, major vascular problem, inability to walk independently with or without an assistive gadget), also Covid-19 positive findings on PCR were excluded from the study. The researcher thoroughly gone through the case history and detailed examination. Women were equally allocated (each group=22) in experimental (A) and controlled (B) groups via computerized method. Randomization sequence computer-generated numbers by a biostatistician and allocation was sealed in opaque envelopes to ensure concealment. The data was gathered on structured questionnaire, "Functional reach test (FRT)", "Time up and go test (TUG)" and "One leg stance test (OLS)" as subjective measure. Controlled group was given conventional treatment that includes dietary guidelines (cutoff fat foods, plenty drinking water, low sugar and salt in meal, eat fruits and vegetables, took calcium iron and fiber diet), walking treadmill for 15 mints, stairs climbing and balance exercises on gym ball. While the experimental group was given dietary guidelines, treadmill walking for 15 mints and the intensity of 50%–60% HRmax, where HR max=206.9−0.69 × age (years) included in warm up session, "sensorimotor training" included wall slide, core exercises (planks, leg raises, crunches, bridging), and balance exercises (single leg side lift, leg lift with dumble, balance on stability gym ball) on unstable surface for 15 minutes (3 sets of 10 rep) of exercises and gait training (different patterns of walking). Exercises included for cool down 5–10 min of profound breathing, abdominal breathing, and slight stretching for both groups.[15]The workout was directed thrice a week for 6 weeks. Data was collected at baseline (initial assessment), then at 6th week post treatment. Balance and proprioception were reassessed on FRT, TUG, and OLS.

By following CONSORT guidelines final analysis done with 40 patients, 20 in group A and 20 in group B. Data analysis was completed with SPSS version 25. The normality of the data was assessed by Shapiro-Wilk's test of normality and uniformity.

RESULTS

Table No.1: The Demographic data of both groups, n = 40

	Mean± S.D
Age (years)	50.27±3.17
Weight (kg)	82.57±8.64
Height (meter)	1.47±0.12
BMI (kg/m^2)	33.95±2.03

The total number of patients was 40 with 20 in each group. The mean age of participants was 50.27, weight

was 82.57kg and height 1.47 in meters. The average BMI was estimated to be 33.95 which fall under the category of obesity. The demographic characteristics of patients were studied (Table-1).

Shapiro Wilk test was applied as test to check the normality of data and found all the data was normally distributed as p value was >0.05.

Table No.2: Between group Comparison of FRT, TUG and OLS scores at baseline and at 6th week

Functional reach test (FRT)	Sensorimotor training	Conventional training	t*	p-value
	Mean±SD	Mean±SD		
At baseline week 0	7.65±1.26	9.00±1.68	-2.862	.007
End of treatment week 8	11.35±1.34	10.35±1.30	2.380	.022
Time up and go test (TUG)				
At baseline week 0	12.60±1.72	12.65±1.78	-.090	.929
End of treatment week 8	9.00±1.52	10.75±1.61	-3.523	.001
One leg stance (Dominant Leg Eyes Open) score				
At baseline week 0	16.56±2.46	18.24±2.62	-2.091	.043
End of treatment week 8	25.01±2.69	22.46±2.27	3.236	.003
One leg stance (Dominant Leg Eyes Closed) score				
At baseline week 0	5.63±.73	5.77±.77	-.617	.541
End of treatment week 8	6.54±.73	5.99±.84	2.199	.034
One leg stance (Other leg eyes open) score				
At baseline week 0	15.39±1.06	15.34±1.14	.141	.888
End of treatment week 8	20.06±1.18	17.61±1.28	6.270	.0001
One leg stance (Other leg eyes closed) score				
At baseline week 0	2.87±.67	2.99±.75	-.520	.606
End of treatment week 8	3.49±.72	3.09±.71	1.748	.089

*: Independent sample t test

DISCUSSION

The current study analyzed proprioceptive balance among sensorimotor training and conventional therapy in post-menopausal women. Sensorimotor training presented significantly increased in TUG, FRT and proprioception regardless of BMI, while One Leg Stance (Eyes Open and Eyes Close) in conventional therapy indicated essentially more modest changes when compared with sensorimotor training. The results of this study found that sensorimotor training group showed greater improvement in Functional Reach test score in participants of Group A after compared with participants of Group B. While TUG grade fundamentally reduced in Group A after in comparison with Group B and proprioception. Previous studies results showed at 6, 8 and 12 weeks of balance activities, and improvement in balance (TUG, FRT) and walk over a beam.[16,17] Richardson JK, et al.,[18] conducted a study and revealed that no improvement after 3 weeks of balance training. The majority of the participants of both groups (A & B) in present study had Time Up and Go test in the range of 9.00 and 10.75s respectively. TUG score ≤ 10s shows low fall risk, and ≥14s demonstrates high fall risk. Although through assessment of fall was not ended, the activities decreased the risk of fall in post-menopausal obese women.

In present study maximum participants of both groups had FRT estimation of 11.3 inches and 10.35 inches respectively at the end of treatment. FRT score of 6 or less illustrate a critical expanded higher fall risk. A score between 6-10 inches demonstrates a moderate fall risk, and a score more than 10 inches shows the generally low fall risk. The present study investigated static balance by assessing One Leg Stance with eyes open and eyes close state in the two legs, therefore balance and proprioception improvement significantly smaller changes. The results showed significantly increase in one leg stance (OLS) with eye open (EO) dominant leg eyes open and other leg eyes open (DO & OO) and eyes closed (EC) dominant leg eyes open (DO) yet non-significant increase in OLS, other leg eyes closed (OC) in post-menopausal obese women.

Lee K, et al.[19]similarly reports increase in OLS after balance training. OLS and FRT showed significant improvements in interventional group ($p < 0.05$) but not in the control group after balance training. Kruse RL, et al., [20] didn't locate any significant changes after intervention. Rojhani-Shirazi Z, et al., [21] study showed OLS with eyes open and close in the two different kinds of balance training. OLS (dominant and other leg) with EO and EC significantly improved in both treatment groups from pre to post-test ($p \leq 0.001$). However, in control group no significant changes found in OLS with closed and open eyes. Improved OLS with EO and EC found in both legs with two different types of balance training. Ahmed I, et al., [22] study on diabetic peripheral neuropathy patients, balance (static and dynamic) actions progressed with sensorimotor training following two months. Static balance shows more prominent improvement in the moderately elderly than more age group, whereas proprioception and dynamic balance

demonstrate comparable improved within the participants of both age groups.

Song CH, et al., [17] study claimed development in trunk proprioception following a month and a half of equilibrium training in postmenopausal women. In the exercise group functional reach test score significantly improved ($P < 0.01$). However, no significant difference was seen in the FRT score in control group. TUG time in the exercise group significantly decreased ($P < 0.01$). In the control group TUG score no significant difference was seen in pre- and post-testing**.**

CONCLUSION

This study concluded that exercise intervention sensorimotor training improved balance (static and dynamic) over and above proprioception actions. Static and dynamic balance indicated more prominent improvement in sensorimotor training group when contrasted with conventional therapy in post-menopausal obese women while proprioception demonstrated comparative outcomes for both treatment protocols.

Author's Contribution:

Concept & Design of Study:	Binash Afzal
Drafting:	Sehar Shabir, Tehreem Mukhtar
Data Analysis:	Ghazal Awais Butt, Sumera Abdul Hameed
Revisiting Critically:	Arshad Nawaz Malik
Final Approval of version:	Binash Afzal

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Roberts H, Hickey M. Managing the menopause: An update. Maturitas 2016;86(4):53-58.
2. Hita-Contreras F, Martínez-Amat A, Cruz-Diaz D, Perez-Lopez FR. Fall prevention in postmenopausal women: the role of Pilates exercise training. Climacteric 2016;19(3):229-233.
3. Ettinger B, Li DK, Klein R. Continuation of postmenopausal hormone replacement therapy: comparison of cyclic versus continuous combined schedules. Menopause 2018;25(11):1187-1190.
4. Tariq S, Delpech V, Anderson J. The impact of the menopause transition on the health and wellbeing of women living with HIV: a narrative review. Maturitas 2016;88(6):76-83.
5. Zhao R, Zhang M, Zhang Q. The effectiveness of combined exercise interventions for preventing postmenopausal bone loss: a systematic review and meta-analysis. J Orthop Sports Phys Ther 2017;47(4):241-251.
6. Manson JE, Kaunitz AM. Menopause management-getting clinical care back on track. N Engl J Med 2016;374(9):803-806.
7. Soares CN. Depression and Menopause: An Update on Current Knowledge and Clinical Management for this Critical Window. Med Clin North Am 2019;103(4):651-667.
8. Gaba A, Cuberek R, Svoboda Z, Chmelik F, Pelclova J, Lehnert M, et al. The effect of brisk walking on postural stability, bone mineral density, body weight and composition in women over 50 years with a sedentary occupation: a randomized controlled trial. BMC Women's Health 2016;16(1):1-10.
9. Kemmler W, Engelke K, von Stengel S. Long-Term Exercise and Bone Mineral Density Changes in Postmenopausal Women-Are There Periods of Reduced Effectiveness? J Bone Miner Res 2016;31(1):215-222.
10. Palmer MK, Toth PP. Trends in lipids, obesity, metabolic syndrome, and diabetes mellitus in the United States: An NHANES analysis (2003-2004 to 2013-2014). Obesity. 2019;27(2):309-314.
11. Avelar BP, de Almeida Costa JN, Safons MP, Dutra MT, Bottaro M, Gobbi S, et al. Balance Exercises Circuit improves muscle strength, balance, and functional performance in older women. Age 2016;38(1):14-24.
12. Moutzouri M, Gleeson N, Billis E, Panoutsopoulou I, Gliatis J. What is the effect of sensori-motor training on functional outcome and balance performance of patients' undergoing TKR? A systematic review. Physiotherapy 2016;102(2): 136-144.
13. Khodashenas E, Moradi H, Asadi Ghaleni M, Heydari E, Shams A, et al. The effect of selective training program on the static and dynamic balance of deaf children. Medi J Mashhad Uni Medi Sci 2017;60(1):383-391.
14. Han J, Waddington G, Adams R, Anson J, Liu Y. Assessing proprioception: a critical review of methods. J Sport Health Sci 2016;5(1):80-90.
15. Serrano-Guzman M, Aguilar-Ferrandiz ME, Valenza CM, Ocana-Peinado FM, Valenza-Demet G, Villaverde-Gutierrez C. Effectiveness of a flamenco and sevillanas program to enhance mobility, balance, physical activity, blood pressure, body mass, and quality of life in postmenopausal women living in the community in Spain: a randomized clinical trial. Menopause 2016;23(9):965-973.
16. Allet L, Armand S, De Bie RA, Golay A, Monnin D, Aminian K, et al. The gait and balance of patients with diabetes can be improved: a randomised controlled trial. Diabetologia 2010;53(3):458-466.

17. Song CH, Petrofsky JS, Lee SW, Lee KJ, Yim JE. Effects of an exercise program on balance and trunk proprioception in older adults with diabetic neuropathies. Diabetes Technol Ther 2011; 13(8):803-811.
18. Richardson JK, Sandman D, Vela S. A focused exercise regimen improves clinical measures of balance in patients with peripheral neuropathy. Arch Phys Med Rehabil 2001;82(2):205-209.
19. Lee K, Lee S, Song C. Whole-body vibration training improves balance, muscle strength and glycosylated hemoglobin in elderly patients with diabetic neuropathy. Tohoku J Exp Med 2013;231(4):305-314.
20. Kruse RL, LeMaster JW, Madsen RW. Fall and balance outcomes after an intervention to promote leg strength, balance, and walking in people with diabetic peripheral neuropathy:" feet first" randomized controlled trial. Phys Ther 2010;90(11):1568-1579.
21. Rojhani-Shirazi Z, Barzintaj F, Salimifard MR. Comparison the effects of two types of therapeutic exercises Frenkele vs. Swiss ball on the clinical balance measures in patients with type II diabetic neuropathy. Diabetes Metab Syndr 2017;11(3): 29-32.
22. Ahmad I, Noohu MM, Verma S, Singla D, Hussain ME. Effect of sensorimotor training on balance measures and proprioception among middle and older age adults with diabetic peripheral neuropathy. Gait Posture 2019;74(2):114-120.

Original Article

Correlation of Myofascial Trigger Points with Shoulder Pain and Function in Post-Stroke Patients with Painful Shoulder

Mahnoor Asif, Yasha Sajjad, Saima Riaz, Fizza Nasir and Humaira Azam

ABSTRACT

Objective: To find out the correlation of shoulder pain and disability with myofascial trigger points (MTrPs) in post stroke patients having shoulder pain.

Study Design: A cross-sectional survey was conducted with non-probability convenient sampling

Place and Duration of Study: This study was conducted at the Riphah Rehabilitation Center, Riphah International University, Lahore from January 2019 to June 2019.

Materials and Methods: Patients were recruited with six months or older stroke history and having post stroke shoulder pain. Upper Trapezius, Supraspinatus, Infraspinatus and Teres Minor muscles were targeted. MTrPs were diagnosed by using the palpation method described by Simons, and Travell. Shoulder disability was measured by using the DASH (Disability of Arm, Shoulder and Hand) score and pain was recorded through NPRS (Numeric Pain Rating Scale). Data analysis was done by IBM SPSS Statistics 21.

Results: Total 70 stroke patients participated. Males were 41.4%. Mean age was 55.53±14.98 years. MTrPs were moderately correlated with shoulder disability for supraspinatus, upper trapezius and infraspinatus (r= 0.53, r= 0.49 and r=0.54 respectively. All have p<0.001). Moderate correlation was found between MTrPs and pain for supraspinatus, upper trapezius and infraspinatus (r= 0.50, r= 0.47 and r= 0.47 & all have p<0.001 respectively).

Conclusion: MTrPs in the upper trapezius, supraspinatus and infraspinatus were moderately correlated with shoulder pain and disability in stroke patients.

Key Words: myofascial trigger points, post-stroke, shoulder disability, shoulder pain, stroke

Citation of article: Asif M, Sajjad Y, Riaz S, Nasir F, Azam H. Correlation of Myofascial Trigger Points with Shoulder Pain and Function in Post-Stroke Patients with Painful Shoulder. Med Forum 2021;32(10):211-214.

INTRODUCTION

Stroke is caused by a sudden loss of oxygen supply to brain cells resulting in the death of some brain cells. Globally stroke is the 2nd leading cause of death and third leading cause of disabilities[1]. Types of stroke are Ischemic Stroke (IS), Primary Intracerebral Hemorrhagic Stroke (ICH), and Subarachnoid Hemorrhage (SAH)[2]. 34% stroke cases are hemorrhagic in middle and low income countries and 84% of patients die within 3 years of diagnosis[3] . Hemiplegic shoulder pain (HSP) can be a chief issue in neurological patients[4]. Incidence of HSP is 16% to 84% [5]. The most important of these muscles are rotator cuff muscles: Supraspinatus, Infraspinatus, Teres Minor, and Subscapularis.

Riphah International University, Lahore.

Correspondence: Saima Riaz, Assistant Professor, Riphah College of Rehabilitation & Allied Health Sciences, Riphah International University, Lahore.
Contact No: 03334349520
Email: saima.riaz.rz@gmail.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

Studies have shown that there is a link between shoulder pain and activity limitation[6],[4]. Shoulder pain after stroke can be due to many reasons, and MTrPs are[7,8]. A myofascial trigger point is a localized hyperirritable spot[9] in a taut band of muscles[10].

According to one study, the Prevalence of trigger points is around 30% in patients with shoulder pain[11]. Another study in 2019 shows a high Prevalence of MTrPs in stroke patients. Functional damage occurs in about 40% of stroke patients[12]. HSP is a hindrance in the progression of rehabilitation program, it increases the duration of hospital stays, it increases the depression and decreases the activities of daily living and quality of life[13].

A study about prevalence and anatomical localization of referred muscle pain due to active MTrPs showed that the referred pain provoked from active MTrPs shared similar pain patterns as spontaneous tension headache in adults and children[14]. According to a systematic review in 2018, few studies have been conducted so far regarding the Prevalence of MTrPs. There are some studies about the Prevalence of stroke in different ages, but very few studies are present regarding the correlation of MTrPs with function and pain in patients presenting with stroke.[15] This study investigated the correlation of MTrPs with shoulder pain and function. This study aimed to help

physiotherapists to plan evidence-based treatment for shoulder disability and pain in post-stroke patients.

MATERIALS AND METHODS

It was a Cross-Sectional study and the data was collected from Riphah Rehabilitation Center, Lahore from January 2019 to June 2019. Chronic stroke patients with six months or older history of stroke were included. Both male and female stroke patients between the ages of 25 to 85 years who had hemiplegic shoulder pain for six months and more were included. Both ambulatory and non-ambulatory stroke patients participated in the study. To keep the spasticity factor at the same level for every patient, only those who had a score of ≤ 2 on the modified Ashworth scale were included in the study. Clinically unstable patients like comatose patients, diabetic patients, patients with sensory loss, cognitive impairments or with communication issues were excluded from the study.

The recruitment of participants was through the Non-Probability Convenient Sampling Technique based on predefined criteria through consensus of 3 researchers for recruitment of every subject that reduced any subjective judgment bias. The researchers conducted a detailed review of the participant's medical history and demographic data. Riphah Ethical Review Committee approved the study. All participants were asked for their written informed consent before they participated in the study.

The questionnaires were distributed as hand-outs in Riphah Rehabilitation Clinic. Data was collected in-person/ through representatives appointed in the selected clinic. Infraspinatus, supraspinatus, teres minor and upper trapezius were screened for MTrPs by doing perpendicular palpation to the fibres' direction. Once a trigger point was recognized, a compression test was done for 30 seconds for categorizing the trigger point into a latent or active trigger point.

The criteria recommended by Simons, Travell, and Simons [16] [17] were used to diagnose (MTrPs) considering four points criteria: (1) Presence of a taut band (TB) (2) Presence of a palpable nodule (PN) (3) Presence of a hypersensitive point (HP) (4) Presence of referred pain (RP). The level of pain was recorded using NPRS, Level of dysfunction of the shoulder was assessed using a standardized questionnaire named DASH score and demographic information including the age of the patient, gender, stroke type, hemiplegic side, and characteristics of shoulder pain. Analysis of data was done by using IBM SPSS Statistics 25. Spearman Correlation test was used for data analysis.

RESULTS

Total 70 stroke patients were recruited in the age range of 25 to 81 years with mean age =55.3 (Table 1).

Table No. 1: Clinical and demographics stats of Patients

Variable n(%)	
Male	29(41.4%)
Female	41(58.6%)
Age (years)	55.3(14.98%)
Ischemic Stroke	45(64.29%)
Hemorrhagic Stroke	25(35.71%)
Right Hemiplegic Side	36(51.4%)
Left Hemiplegic Side	34(48.6%)
DASH score	60.451(20.78%)
NPRS score	5.014(2.12%)

Dash: Disability of arm, shoulder and hand score;

NPRS: Numeric Pain Rating Score

Table 2 shows correlation between MTrPs and shoulder disability was strongly significant with r=0.72; the correlation between active MTrPs and shoulder disability was moderately significant with r=0.44; the correlation between latent MTrPs and shoulder was strongly significant with r=0.60. A strong correlation was there among MTrPs and pain with r =0.68; moreover, moderate correlations were observed in the cases of active MTrPs and latent MTrPs with pain. All were with p<0.001. When individually main muscles of the shoulder were observed, results showed a moderate correlation between MTrPs and shoulder disability for upper trapezius, supraspinatus and infraspinatus; whereas, no significant correlation was found among MTrPs found in teres minor muscle and shoulder disability. The correlation was moderate between MTrPs and shoulder pain for supraspinatus, upper trapezius and infraspinatus. Contrary to the above, no correlation was found between MTrPs in teres minor and pain. No MTrPs were found in 19 participants.

Table No.2: Muscle wise correlation of myofascial trigger points with Pain & Disability

Muscle wise MTrPs*	DASH* (r)	NPRS* (r)
Upper trapezius Myofascial Trigger Points	0.485[a]	0.469[a]
Supraspinatus Myofascial Trigger Points	0.528[a]	0.500[a]
Infraspinatus Myofascial Trigger Points	0.541[a]	0.473[a]
Teres Minor Myofascial Trigger Points	0.041[b]	0.068[b]
a= Significant correlation (p<0.05); b= not significant correlation (p>0.05). *Dash: Disability of arm, shoulder and hand score; NPRS: Numeric Pain Rating Score; r: correlation coefficient		

Table No.3: Muscle wise percentage of myofascial trigger points

Muscle	Active trigger points (percent) (TB+PN+HP +RP)	Latent Trigger points (percent) (TB+PN+ HP)	Total Trigger Points (percent) (active+la tent MTrPs)
Upper trapezius	27.14%	18.57%	45.71%
Supraspin atus	30.00%	11.43%	41.43%
Infraspinat us	8.57%	18.57%	27.14%
Teres Minor	2.86%	8.57%	11.43%
TB=taut band, PN= palpable nodule, HP=hypersensitive point, RP=referred pain.			

Table 4 shows that with the increasing total number of MTrPs, the correlation becomes strongly significant with with r=0.682 in case of pain and r=0.720 in case of disability & with p<0.01.

Table No.4: Correlation of number of Myofascial Trigger Points with Pain/Disability

Total MTrPs	NPRS (r)	Dash (r)
	0.682[a]	0.720[a]
a= significant correlation with p<0.05		
MTrPs: Myofascial Trigger Points; Dash: Disability of arm, shoulder and hand score; NPRS: Numeric Pain Rating Score; r= correlation coefficient		

DISCUSSION

The current study's primary findings showed a strongly significant correlation of MTrPs with shoulder disability and pain. These MTrPs should be examined and explicitly treated on a priority basis for better prognosis and speedy recovery in a population with hemiplegic shoulder pain because of correlation.

In 2019, J.H Villafane et al. found a moderate correlation of shoulder dysfunction with latent MTrPs in infraspinatus and active myofascial trigger points in supraspinatus [(18)]. In contrast to this study, the present study found that shoulder disability is moderately significant with myofascial trigger points found in supraspinatus and infraspinatus.

The mean Dash score of the current study was similar to that previous study conducted in 2019 by J.H Villanfane et al. (60.45 versus 73.9). This research found that MTrPs present in the upper trapezius are moderately correlated with shoulder disability, whereas that previous study by J.H Villafane et al. found no correlation. However, similar to this study, the present investigation found no correlation of teres minor MTrPs with shoulder pain and disability. Like the study conducted about the high presence of MTrPs in shoulder girdle in patients with shoulder pain by Bron et al. [(13)] , this study also found few active MTrPs in infraspinatus.

Another study conducted by Hidalgo-Lozano et al. about the Prevalence of MTrPs in unilateral shoulder impingement also found a similar finding with the current study that the highest percentage of active MTrPs exists in supraspinatus [(19)].

A study by Casteldo et al. about correlation of MTrPs with pain intensity in patients with whiplash injuries showed that the current pain intensity (visual analogue scale) of the patients was significantly correlated with the number of active MTrPs[(20)]. This study found the similar findings to the current investigation.

The current study and others indicate a dire need to resolve myofascial trigger points, specifically in supraspinatus, infraspinatus, and upper trapezius, to manage pain and disability of the shoulder, specifically in people with stroke who have already been living a low quality of life due to impaired shoulder functions.

CONCLUSION

In conclusion, MTrPs in the upper trapezius, supraspinatus and infraspinatus were moderately correlated with shoulder pain and dysfunction in stroke patients. Furthermore, MTrPs in teres minor showed no correlation with pain and disability.

Recommendations: Future researchers are suggested to conduct studies with different patient populations, sample sizes, muscle groups, and interventional studies focusing MTrPs concerning pain and disability.

Author's Contribution:

Concept & Design of Study:	Mahnoor Asif, Yasha Sajjad, Saima Riaz, Fizza Nasir, Humaira Azam
Drafting:	Mahnoor, Yasha, Humaira Azam
Data Analysis:	Saima Riaz
Revisiting Critically:	Saima Riaz
Final Approval of version:	Mahnoor Asif, Yasha Sajjad, Saima Riaz

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Johnson W, Onuma O, Owolabi M, Sachdev S. Stroke: a global response is needed. Bulletin of the World Health Organization 2016;94(9):634.
2. Krishnamurthi RV, Barker-Collo S, Parag V, Parmar P, Witt E, Jones A, et al. Stroke incidence by major pathological type and ischemic subtypes in the Auckland regional community stroke studies: changes between 2002 and 2011. Stroke 2018;49(1):3-10.

3. Owolabi MO, Arulogun O, Melikam S, Adeoye AM, Akarolo-Anthony S, Akinyemi R, et al. The burden of stroke in Africa: a glance at the present and a glimpse into the future. Cardiovascular J Afr 2015;26(2 H3Africa Suppl):S27.
4. Lindgren I, Jonsson AC, Norrving B, Lindgren A. Shoulder pain after stroke: a prospective population-based study. Stroke 2007;38(2):343-8.
5. Koog YH, Jin SS, Yoon K, Min BI. Interventions for hemiplegic shoulder pain: systematic review of randomised controlled trials. Disability Rehabilitation 2010;32(4):282-91.
6. Wanklyn P, Forster A, Young J. Hemiplegic shoulder pain (HSP): natural history and investigation of associated features. Disability Rehabilitation 1996;18(10):497-501.
7. Jones AK, Brown CA. Post-stroke shoulder pain: Nociceptive or neuropathic? Pain 2013;154(2):189.
8. Benlidayi IC, Basaran S. Hemiplegic shoulder pain: a common clinical consequence of stroke. Practical Neurol 2014;14(2):88-91.
9. Villafañe JH, Lopez-Royo MP, Herrero P, Valdes K, Cantero-Téllez R, Pedersini P, et al. Prevalence of myofascial trigger points in post-stroke patients with painful shoulders: a cross sectional study. PM&R 2019.
10. Gerwin RD. Diagnosis of myofascial pain syndrome. Physical Medicine and Rehabilitation Clinics 2014;25(2):341-55.
11. Skootsky SA, Jaeger B, Oye RK. Prevalence of myofascial pain in general internal medicine practice. Western J Med 1989;151(2):157.
12. Pillastrini P, Rocchi G, Deserri D, Foschi P, Mardegan M, Naldi MT, et al. Effectiveness of neuromuscular taping on painful hemiplegic shoulder: a randomised clinical trial. Disability and Rehabilitation 2016;38(16):1603-9.
13. Borboni A, Villafañe JH, Mullè C, Valdes K, Faglia R, Taveggia G, et al. Robot-assisted rehabilitation of hand paralysis after stroke reduces wrist edema and pain: a prospective clinical trial. J Manipulative Physiological Therapeutics 2017; 40(1):21-30.
14. Alonso-Blanco C, Fernández-De-Las-Peñas C, Fernández-Mayoralas DM, de-la-Llave-Rincón AI, Pareja JA, Svensson P. Prevalence and anatomical localization of muscle referred pain from active trigger points in head and neck musculature in adults and children with chronic tension-type headache. Pain Med 2011;12(10):1453-63.
15. George MG, Tong X, Kuklina EV, Labarthe DR. Trends in stroke hospitalizations and associated risk factors among children and young adults, 1995–2008. Annals Neurol 2011;70(5):713-21.
16. Simons DG, Travell JG, Simons LS. Myofascial pain and dysfunction: the trigger point manual, Vol 1, upper half of body. London, Lippincott Williams and Wilkins 1999.
17. Zuil-Escobar JC, Martínez-Cepa CB, Martín-Urrialde JA, Gómez-Conesa A. The prevalence of latent trigger points in lower limb muscles in asymptomatic subjects. PM&R 2016;8(11): 1055-64.
18. Villafañe JH, Lopez-Royo MP, Herrero P, Valdes K, Cantero-Téllez R, Pedersini P, et al. Prevalence of myofascial trigger points in poststroke patients with painful shoulders: A cross-sectional study. PM&R 2019;11(10):1077-82.
19. Hidalgo-Lozano A, Fernández-de-las-Peñas C, Díaz-Rodríguez L, González-Iglesias J, Palacios-Ceña D, Arroyo-Morales M. Changes in pain and pressure pain sensitivity after manual treatment of active trigger points in patients with unilateral shoulder impingement: a case series. J Bodywork Movement Therapies 2011;15(4):399-404.
20. Castaldo M, Ge HY, Chiarotto A, Villafane JH, Arendt-Nielsen L. Myofascial trigger points in patients with whiplash-associated disorders and mechanical neck pain. Pain Med 2014;15(5):842-9.

Original Article

Comparison of Static Cycle and Treadmill Training on Gait Parameters in the Children with Down Syndrome

Faisal Ghafoor[1], Zainab Hassan[2], Faseeh Zulqernain[1], Muhammad Sajjad Hassan[1], Hafiz Muhammad Waseem Javaid[3] and Sameen Saeed[4]

ABSTRACT

Objective: To compare the effects of Static Cycle and Treadmill Training on Gait Parameters in the Children with Down syndrome.

Study Design: Randomized Control trial study

Place and Duration of Study: This study was conducted at the Ali Children Clinic Shadman, Lahore from April 2020 to October 2020 for a period of six months.

Materials and Methods: Non-probability sampling technique was used to select a sample of 30 patients from Ali children clinic, Shadman Lahore. Patients randomly allocated into two groups. Group A was given conservative treatment along with static cycle and group B was given conservative treatment with Static cycle and treadmill training 2 days per week. The Pre and Post values of the gait parameters are taken by using the Wisconsin and Dynamic gait index as a tools. Gait can be corrected by using various exercise interventions. Data was analyzed by using SPSS version 25.

Results: Group B showed better outcomes. It has suggested that group B who received both treadmill and static cycle showed significant improvement in the gait parameters.

Conclusion: It was concluded that static cycling along with treadmill intervention showed significant improvement in terms of gait parameters in Down syndrome children.

Key Words: Static Cycle, Treadmill Training, Gait Parameters, Children, Down Syndrome

Citation of article: Ghafoor F, Hassan Z, Zulqernain F, Hassan MS, Javaid HMW, Saeed S. Comparison of Static Cycle and Treadmill Training on Gait Parameters in the Children with Down Syndrome. Med Forum 2021;32(10):215-219.

INTRODUCTION

Down syndrome is also called the trisomy 21; it is a genetical abnormality that is caused by the presence of all or part of a third copy of chromosome 21. Down syndrome disease affect the children the most effected part of the child is brain because the capacity of the brain to perceive and to respond appropriately will diminished in these child they have some defect in the cognitive function and certain limitation in communication and other social skills. Down syndrome is the chromosomal defect and it is develop in 1 out of 691 babies[1-3]. It is usually related to, delay in physical growth and mild to moderate intellectual disability and other associated characteristic. Down syndrome child are mostly affected by several infection and the prevalence of the infection rate is extremely high. Because poor immunity. The defense system of the body has poor power to fight against the foreign invading infection. To prevent from the recurrent attack of infection the immunization program is recommended by Pediatrician. In first year of the life down syndrome has 62 fold higher ration to develop the pneumonia[4]. In children with Down syndrome compromised function, physical growth delay, affected Lower limb strength, step length, stride length and improper weight shifting during walk are major problems, in down syndrome, Reduced strength in lower limb muscle contributes to the decline in velocity and walking pattern of Down syndrome child. These problems can be minimized by Applying Various Techniques that purely fall under the category of the neuromuscular physical therapy.[5] Moreover, children with Down syndrome also appear to exhibit delayed motor development due to hypotension, ligamentous

1. City Institute of Management and Emerging Sciences, Lahore.
2. Riphah International University, Lahore Campus.
3. Shalamar Institute of Health Sciences, Lahore.
4. Allama Iqbal Medical College, Lahore.

Correspondence: Zainab Hassan, Senior Lecturer, Riphah International University, Lahore Campus
Contact No: 0336-7936515
Email: zainab.hassan@riphah.edu.pk

Received: April, 2021
Accepted: July, 2021
Printed: October, 2021

weakness, Frequent history of fall due to poor postural control and balance problem has seen while performing task in the outside enviourment[6].Treadmill device helps to prevent the disuse atrophy in Down syndrome child. Treadmill help to increase the transmission of sensory information (pro-pioceptive sensation) to brain also increase the awareness of body posture and improvement in the balance. If we start the treadmill training in early life it will start helping the child to attain the alternating walking without any delay. Down syndrome child has a major issue of hypotonia and osteoporosis. These problems can be reduce by progressively increasing the speed of the treadmill and time of treadmill training.[7] In infant normal development will have a wider gait pattern in start of the life due to poor balance and joint control. Infant used to walk with wider Stride length or base and small step length. But with the passage of time the gait pattern and the stride width and step length and other parameter has changed. It is very difficult for these children to learn the new task and complete their milestones on time. Static cycle helps to improve the proprioceptive and kinesthetic sensation and this will increase the speed to complete the milestones like walking running sitting standing and weight shifting as well. Sound information about the Static cycling in child also shows many significant results. Some study proved its effect in development of gait parameter in child and increased the speed as well. Increase in lower limb strength will help the children to improve its ambulation.[8]

The gait is consisted of the two major phases the swing phase and the stance phase. The swing phase is further subdivided in the initial swing, pre swing, mid swing and terminal swing. The stance phase is subdivided into heel contact, foot flat, mid stance, heel off and toe off. The 60% of the gait walk is consisted of the stance phase and 40% of the overall gait cycle is consisted of swing phase. Normal gait helps an individual to perform its entire daily task, any issue in the gait will leads to the improper walk, frequent fall, improper weight shifting, slow speed.[9]

MATERIALS AND METHODS

i. Inclusion Criteria

- Children categorized at level I of the Gross Motor Function Classification System.
- Children with Down syndrome with Age group 5-13 years old children were included, Children with normal (BMI) (normal BMI 18.5-24.9)[10]

ii. Exclusion Criteria:

- Those children who could not followed appropriately the guidelines given through the therapist, i.e., that rejected to collaborate with the therapist (even after several attempts.

A. Data Collection Tool:

- **Dynamic Gait Analysis**

(Inter-rated reliability (0.96-0.96) and intra-rated reliability (0.68-0.83)[11]

- **Wisconsin Gait Scale for Child**

Inter-rated reliability (0.81-0.91) and intra-rated reliability (0.75-0.90)[12]

B. **Place and Duration of Study:**

This study was conducted at Ali children clinic Shadman Lahore from April 2020 to October 2020 for a period of six months.

C. Data Collection Procedure:

Firstly, consent was taken. Subjects willing to participate are divided into two groups.

Before the treatment of both groups, detailed gait analysis was assessed by a Wisconsin gait scale and dynamic gait index.

D. Intervention

Static cycle intervention in Group A

Group A received the specific conservative treatment and followed the protocol by receiving the Static cycle training around 10 minute. We had broken the whole treatment protocol in 3 different intervals, with time duration of 3, 3, 4 minute and rest interval was 2 minute in each interval.[13]

E. Treadmill training and Static cycle intervention in Group B

Group B received the conservative treatment along with static cycle also received the specific treatment and follows the protocol by receiving the treadmill training around 10 minute. We break the whole treatment protocol in 3 different intervals, with time duration of 3,3,4 minute and rest interval was around 2 minute in each interval Speed was Around 5-7km/h.[14]

F. Data Analysis Procedure:

Statistical analysis was performed to analyze the effect of the treatment applied to the subjects of both control and experimental groups. It was done by using the IBM SPSS Inc.25.0 version. For this, the data was incorporated in MS excels spreadsheet. Out of 30 subjects 15 were randomized into Group 1 and 15 are randomized into Group 2. All the 30 subjects complete the entire protocol as defined by 6 months of treatment. The outcomes of the study were gait parameters. Statistical tools paired t-test was performed for parameters in between groups and paired sample t-test for parameters within the group. Descriptive measures like mean, the standard deviation was reported along with the p-value.

RESULTS

The mean age of participants in experimental group was 8.11± 2.27 and mean age of conventional group 9.50± 1.78 of. Mean and standard deviation of BMI for experimental group was 19.14 ±0.43 and 19.29±0.45 for conventional group.

The outcomes were assessed by Wisconsin gait scale and dynamic gait index.

The mean and standard deviation of Wisconsin gait scale in pre value was 26.25± 6.75 and the post value of Wisconsin gait within group was 21.68±6.04. The mean difference between pre and post Wisconsin gait value were calculated 4.75±0.71. The P value between pre and post value with in group (<0.05) show significant difference. The mean and standard deviation of Dynamic gait scale in pre value was 11.16± 4.64 and the post value of Dynamic gait within group was 13.76±4.34. The mean difference between pre and post Dynamic gait value were calculated -2.6±0.3. The P value between pre and post value with in group (<0.05) show significant Difference. Between groups comparison was made by using T test and it showed no significant change has seen in both group. but some Gait parameters like Hip hiking, Step length, Stride width show significant difference.

Figure 1: Shows Histogram of Frequency of the mean Age of 8.80 both Group A and Group B. The standard deviation was 2.

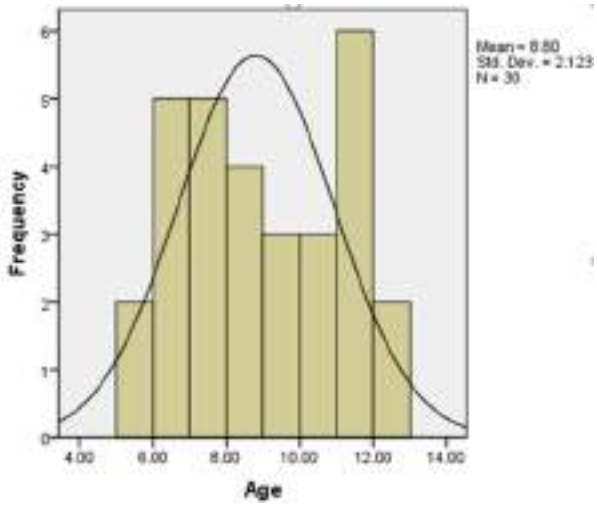


Figure No.1: Age

Figure 2: Shows Histogram of Frequency of Mean BMI 19.22 of both Group A and Group B Combine. The standard deviation was 0.437.

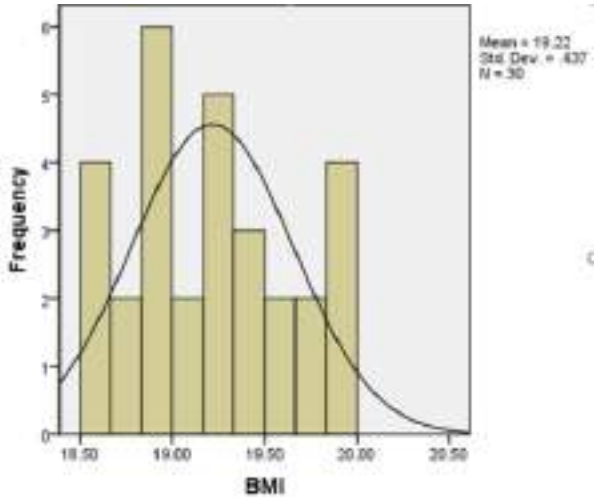


Figure No.2: BMI

Table 1: Shows the descriptive Means and standard deviation of Pre and post Dynamic gait index and pre and post Wisconsin gait scale Separately of Group A and B Overall.

Table No.1: Descriptive Means and standard deviation

	Overall	Treatment	
		Group A	Group B
Pre Wisconsin Gait	26.75 ± 6.62	26.47 ± 7.43	27.03 ± 5.95
Pre Dynamic Gait	10.80 ± 4.54	10.53 ± 5.01	11.07 ± 4.17
Post Wisconsin Gait	21.68 ± 6.06	23.45 ± 7.35	20.04 ± 4.18
Post Dynamic Gait	13.76 ± 4.34	12.33 ± 4.92	15.08 ± 3.40

Table 2: Shows within group comparison in which pre and post mean score of Dynamic and Wisconsin scale among group A and B> There is a significance difference.

Table No.2: Within Group Comparison

		Mean ± SD	P-value
Pair 1	Pre Wisconsin Gait	26.25 ± 6.76	0.001*
	Post Wisconsin Gait	21.68 ± 6.05	
Pair 2	Pre Dynamic Gait	11.16 ± 4.64	0.001*
	Post Dynamic Gait	13.76 ± 4.34	

Table:3 Shows the In between group comparison There was not a significance difference (p<0.05) between Post Wisconsin value of the both groups.

Table No.3: In between group comparison

	Wisconsin Gait scale	Conventional Group	Experimental Group	P value
Mean ± Standard Deviation	Pre Wisconsin	26.47±7.43	27.03±5.95	0.823
	Post Wisconsin	23.45±7.35	20.04±4.18	0.163
	Mean Difference	3.02±0.08	6.99±1.77	

Table:4 Shows the between group comparison There was not a significance difference (p<0.05) between Post dynamic value of the both groups.

Table No.4: The between group comparison

	Dynamic Gait	Conventional Group	Experimental Group	P value
Mean ± Standard Deviation	Pre Dynamic	10.53±5.01	11.07±4.16	0.754
	Post Dynamic	12.33±4.92	15.08±3.40	0.116
	Mean Difference	-1.8±0.09	-4.01±0.76	

DISCUSSION

There was no significant difference between the pretreatment values of two groups according to

Wisconsin gait and Dynamic gait (p value <0.05). Overall the post Wisconsin gait significantly improve in both groups but the P value while comparing the post value of group A and group B was not significant .also the Overall post dynamic gait improved in both groups but the P value had not been significant. This was coherent with the study of Gehan H El-Meniawy, et.al (2012) in which two different exercise interventions given to the groups.[15]

.It had observed that significant improvement had seen because the p value was significant (<0.05) while comparing the post value in the step length and hip hiking, stride width and walking speed of both groups A and B. This result of this study was coherent with the study of Amber Calhoun et al.[16]

The result of our study has showed a significant(<0.05) improvement in the motor development and speed of the walking off Down syndrome child after taking specific static and treadmill training. The values of result in post value of the step length between both groups show a significant improvement in the step length and walking speed. This improved the walking speed and more shift of stance phase toward swing this study is coherent with the study conducted by Matthew beers et al.[17]

The stretching exercises had given a better result in improving the control and flexibility in the body structure. This is coherent with the study of Goncalo V Mendoca et al. (2011) they proved that combined aerobic and resistance exercise increase the exercise capacity if patients with down syndrome.[18]

These findings were also coherent with the study of Christophe Maïano et al. which showed that exercise intervention improve balance and gait pattern in children and adolescents with Down syndrome.[19]

Group B patients was significantly(<0.05) improve as compare to that of patient in Group A, which showed that addition of treadmill training efficiently improve the Wisconsin gait as compare to the static cycling alone. It is coherent with the study of Dale A et al.[20]

CONCLUSION

Static cycles along with treadmill training were more effective and improving the gait parameters as compare to the static cycle alone. The results of our study show a significant improvement in the group B who received the both static cycle and treadmill training along with some conventional treatment protocol (stretching And Isotonic resistance training).

Limitation:

i. Due to pandemic the follow up visit should not have conducted as we have planned.
ii. The behavior of child is major stereotype to break during this treatment protocol.
iii. Wisconsin gait Tool has been used and it was too long having 14 different parameters and children were reluctant during the assessment time.

Recommendation:

i. To reduce the Error, future researchers should use a larger sample size.
ii. Future studies on gait metrics in Down syndrome children will use a sample size of less than ten children. Because as people get older, they have various aberrant synergies associated to gait. This will aid in the development and improvement of the results.
iii. Subsequent research should focus on using visual graphical aid to commence gait in children with severe gait issues.

Author's Contribution:

Concept & Design of Study:	Faisal Ghafoor
Drafting:	Zainab Hassan, Faseeh Zulqernain
Data Analysis:	Muhammad Sajjad Hassan, Hafiz Muhammad Waseem Javaid, Sameen Saeed
Revisiting Critically:	Faisal Ghafoor, Zainab Hassan
Final Approval of version:	Faisal Ghafoor

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Frank K, Esbensen AJ. Fine motor and self-care milestones for individuals with D own syndrome using a Retrospective C hart Review. J Intellectual Disability Research 2015;59(8):719-29.
2. Bull MJ. Health supervision for children with Down syndrome.
3. So S, Urbano R, Hodapp R. Hospitalizations of infants and young children with Down syndrome: evidence from inpatient person-records from a statewide administrative database. J Intellectual Disability Res 2007;51(12):1030-8.
4. Smith DS. Health care management of adults with Down syndrome. Am Family Physician 2001;64 (6):1031.
5. Pangalos C, Avramopoulos D, Blouin JL, Raoul O, DeBlois MC, Prieur M, et al. Understanding the mechanism (s) of mosaic trisomy 21 by using DNA polymorphism analysis. Am J Human Genetics 1994;54(3):473.
6. Palisano RJ, Walter SD, Russell DJ, Rosenbaum PL, Gémus M, Galuppi BE, Cunningham L. Gross motor function of children with Down syndrome: creation of motor growth curves. Archives of Physical Medicine Rehabilitation 2001;82(4): 494-500.
7. Tsimaras V, Giagazoglou P, Fotiadou E, Christoulas K, Angelopoulou N. Jog-walk training in cardiorespiratory fitness of adults with Down

syndrome. Perceptual and motor skills 2003;96 (3_suppl):1239-51.
8. Torfs CP, van den Berg BJ, Oechsli FW, Cummins S. Prenatal and perinatal factors in the etiology of cerebral palsy. J Pediatr 1990;116(4):615-9.
9. Xue D, Sayana A, Darke E, Shen K, Hsieh JT, Luo Z, et al. Vision-based gait analysis for senior care. arXiv Preprint arXiv:181200169. 2018.
10. Bax M, Goldstein M, Rosenbaum P, Leviton A, Paneth N. Proposed definition. Dev Med Child Neurol 2005;8:571-6.
11. Jonsdottir J, Cattaneo D. Reliability and validity of the dynamic gait index in persons with chronic stroke. Archives of Physical Medicine and Rehabilitation 2007;88(11):1410-5.
12. Yaliman A, Kesiktas N, Ozkaya M, Eskiyurt N, Erkan O, Yilmaz E. Evaluation of intrarater and interrater reliability of the Wisconsin Gait Scale with using the video-taped stroke patients in a Turkish sample. Neuro Rehabilitation 2014;34(2): 253-8.
13. Siebert KL, DeMuth SK, Knutson LM, Fowler EG. Stationary cycling and children with cerebral palsy: case reports for two participants. Physical & Occupational Therapy Pediatr 2010;30(2):125-38.
14. Holzapfel SD, Ringenbach SD, Mulvey GM, Sandoval-Menendez AM, Cook MR, Ganger RO, et al. Improvements in manual dexterity relate to improvements in cognitive planning after assisted cycling therapy (ACT) in adolescents with down syndrome. Research in developmental disabilities 2015;45:261-70.
15. Lloyd M, Burghardt A, Ulrich DA, Angulo-Barroso R. Physical activity and walking onset in infants with Down syndrome. Adapted Physical Activity Quarterly 2010;27(1):1-16
16. Calhoun SPT A, Halle SPT S, Looper P. Center-Based Treadmill Training for an Infant with Down Syndrome Not Yet Pulling to Stand 2020.
17. Beerse M, Henderson G, Liang H, Ajisafe T, Wu J. Variability of spatiotemporal gait parameters in children with and without Down syndrome during treadmill walking. Gait Posture 2019;68:207-12.
18. Mendonca GV, Pereira FD, Fernhall B. Effects of combined aerobic and resistance exercise training in adults with and without Down syndrome. Archives Physical Medicine Rehabilitation 2011; 92(1):37-45.
19. Maïano C, Hue O, Lepage G, Morin AJ, Tracey D, Moullec G. Do exercise interventions improve balance for children and adolescents with down syndrome? A systematic review. Physical Therapy 2019;99(5):507-18.
20. Ulrich DA, Lloyd MC, Tiernan CW, Looper JE, Angulo-Barroso RM. Effects of intensity of treadmill training on developmental outcomes and stepping in infants with Down syndrome: a randomized trial. Physical Therapy 2008; 88(1):114-2.

Original Article

Usage of Outcome Measuring Tools and Treatment Protocols of Bell's Palsy by Physical Therapists

Treatment Protocols of Bell's Palsy

Afreen Qadir, Tehreem Mukhtar, Qurat ul ain, Iqra Abdul Ghafoor, Saba Rafique and Hafiza Shabnum Noor

ABSTRACT

Objective: To evaluate usage of measuring tools and treatment protocols of Bell's palsy by physical therapists.
Study Design: Cross-sectional study
Place and Duration of Study: This study was conducted through online survey in many cities of Pakistan. Data was collected in 6 months from 15 January 2020 to 15 June 2020.
Materials and Methods: All the Physiotherapists who had minimum one-year experience in clinical practice were included in the study. Self-design questionnaire which was made by the pilot project run circulate online for the data collection. Recorded values were analyzed by SPSS 26.
Results: The research was conducted on 300 PTs, within which 55% were male and 45% were females. The mean of PT's age was 34 years and standard deviation was ±5.71. 181(51.7%) PTs were doing only clinical practice whereas remaining 119(39.67%) were doing academic along with clinical practice. 30.67% PTs were implementing Evidence-based Practice(EBP) daily while 21%, 38.3%, and 10% were implementing Once in a week, Twice in a week and Monthly respectively. 75% PT's patients show better recovery when they implement EBP on the treatment of Bell's palsy. Out of 300, 40(13.33%) PTs respond that the patients of Bell's palsy show recovery after implement EBP in two weeks, 80(26.67%), 128(42.67%), 52(17.3%) PT's patients show recovery in 4 weeks, 6 weeks and 8 weeks respectively. 39.3% therapists are using sunny brook facial grading system for the assessment and treatment of Bell's palsy. 15%, 11.67% and 34% are using House Brackman, Sydney and other facial nerve grading system respectively.
Conclusion: The study concluded that by the usage of standardized and valid measuring tools along with EBP implementation in the assessment and treatment, the patients of Bell's palsy show better prognosis.
Key Words: Bell's palsy, assessment, diagnosis, physiotherapy, knowledge, attitude, practice, physical therapists

Citation of article: Qadir A, Mukhtar T, Qurat ul ain, Abdul Ghafoor I, Rafique S, Noor HS. Usage of Outcome Measuring Tools and Treatment Protocols of Bell's Palsy by Physical Therapists. Med Forum 2021;32(10):220-223.

INTRODUCTION

Bell's palsy is an idiopathic weakness or paralysis of facial muscles.[1] It is very common in people especially with other medical conditions like hypertension, diabetes or other heart diseases.[2] One person in 70 people always suffer by the Bell's palsy in their lifetime. Cause of disease is idiopathic; therefore, people are more stressed about the disease. The researchers are still busy in finding the cause. Many researches indicate that the pregnant females are dispose to disease because of the accumulation of too much fluid.[3] After delivery the symptoms relieved automatically. Some conclude that the hypertensive patients are more prone to the disease. All the researches are proving different causes; therefore, the reason is not still proved scientifically. The symptoms are very problematic for the one who is suffering. The seventh cranial nerve of patient inflame or compressed.[4] Due to that reason, the one side of the face droop and patient is not able to make facial expressions.[5] The onset of Bell's palsy is very much problematic because it is effecting the facial appearance of patient and effect the facial expressions. [6] The onset of palsy is rapid. Initially, it represents as weakness and patient can be careless about it but later on it can cause the total paralysis of one side.[7] On the affected side, the smile and closing of eye will be more difficult. Patient may find eating and drinking as most difficult tasks.[8] The Bell's palsy is temporary in some cases and after few weeks, symptoms will be gone without any kind of progress in disease. It can be occurred at any age or any time. The people of age 16 to 60 years are more effected by the disease. Sir Charles Bells was the first anatomist who describe the bell's palsy.[9]

Department of Physical Therapy, Riphah International University, Lahore.

Correspondence: Tehreem Mukhtar, Assistant Professor, Riphah International University, Lahore.
Contact No: 03134715275
Email: tehreem.mukhtar@riphah.edu.pk

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

Bell's palsy is an idiopathic disease. It is still not clear why it is occurring but, in most cases, the herpes virus was involved.[10] This virus is also activated in cold sores. It is not known as main cause because many other patients who are suffering from bell palsy, the virus is not found in them. The doctors and researchers believe that many other health conditions such as diabetes, hypertension or heart diseases cause weakness which results in Bell's palsy due to the inflammation of facial nerve. The Etiology of Bell's palsy is still unknown; hence the treatment is difficult to design. [11] Although the cause is not known but by the use of sunny brook facial grading system, the facial nerve damage can be evaluated and treated.[12] The tool can measure the severity of paralysis easily and efficiently. The specificity of the scale is 0.85 and sensitivity is 0.9. The assessment of symmetry in resting state, voluntary movements level and synkinesis are composing to make a score. The scores are from 0-100 in which 0 is indicating complete paralysis and 100 is for normal functioning. The score below 70 is the indication in which the condition is not normal or there is no recovery. Hence, it is very suitable to use the tool for diagnosis and assessing patient present condition. [13, 14] There are few more assessment scales for Bell's palsy. In one study the scale divides in three grading categories. These are Gross, regional and specific scales. The proposed gross scale was Botman and Jongkees, May, and Peitersen scales. Janssen, Smith, Adour and Swanson, and Yanagihara has categorize in regional grading systems. Stennert has devised as a specific criteria scale.[15] The validity and reliability of all scales were good, only the Stennert and Yangaihara are not showing relatively good validity and reliability.[16] For the management of bell's palsy many physiotherapy treatments are considered.[17] For the recovery from Bell's palsy there are some physiotherapy treatments are recommended which will be helpful in the decreasing the inflammation of facial nerve and increase the blood circulation. In result, facial nerve relaxes and the symptoms will eliminate.[7] The physiotherapy treatments include facial exercises, massage, and electrical stimulation. These treatments work fast in acute cases as compare to chronic. The recovery time can be reduced by facial exercises in acute stage as compare to moderate or severe cases.[18] The aim of this study was to distinguish assessment and management in one study as well as the preferences of physiotherapists as well. In older studies, the researchers never find both things together by the experience of professional therapists in Pakistan. Additionally, the evaluation of KAPS were also going to implement on physical therapists for their considerations regarding assessment and management of Bell's palsy.

MATERIALS AND METHODS

The study design was descriptive/cross-sectional which was conducted through online survey in many cities of Pakistan. Data was collected with in duration of 6 months from 15 January 2020 to 15 June 2020.All the Physiotherapists who had minimum one-year experience in clinical practice either they are working in clinical or academic setup were included in the study. Physiotherapists who were not practicing were excluded. Undergraduates and internship physiotherapy students were also not included. Only those physiotherapists were including who are willingly agree to be a part of research sample. The physiotherapists data was confidential and only use for the research purpose. Self-design questionnaire which was made by the pilot project run. The tool was reviewed with 20 physiotherapists and finalize after adding all the suggestion and changes recommended by them. The questionnaires were circulated online to the PTs for the data collection. Recorded values were analyzed by SPSS 26. 350 Sample size was calculated by online Rao software.

RESULTS

The research was conducted on 300 PTs, within which 55% were male and 45% were females. The mean of PT's age was 34 years and standard deviation was ±5.71. 181(51.7%) PTs were doing only clinical practice whereas remaining 119(39.67%) were doing academic along with clinical practice. 30.67% PTs were implementing Evidence-based Practice daily while 21%, 38.3%, and 10% were implementing Once in a week, Twice in a week and Monthly respectively. 75% PT's patients show better recovery when they implement Evidence-based Practice on the treatment of Bell's palsy. Out of 300, 40(13.33%) PTs respond that the patients of Bell's palsy show recovery after implement EBP in two weeks, 80(26.67%), 128(42.67%), 52(17.3%) PT's patients show recovery in 4 weeks, 6 weeks and 8 weeks respectively. 39.3% therapists are using sunny brook facial grading system (SBFGS) for the assessment and treatment of Bell's palsy. 15%, 11.67% and 34% are using House Brackman (HB), Sydney and other facial nerve grading system respectively.

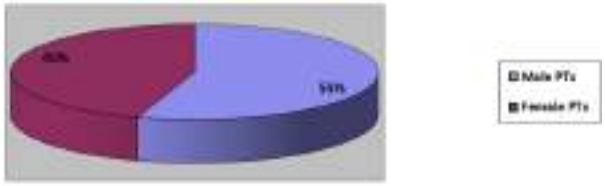


Figure No.1: Frequency of Physiotherpists according to gender

Table No.1: Demographics of PTs in frequency and percentages

Characteristics	Sub groups	Frequency& percentages
Age	Minimum	24
	Maximum	48
Gender	Male	165
	Female	135
Practice in years	Only clinical practice	181(60.33%)
	Academic with clinical practice	119(39.67)

Table No.1 shows the descriptive characteristics of the study

Table No.2: Frequency of PTs

	Frequency of PTs	Percent
Total participant PTs	300	100%
PTs in clinical practice	181	60.3%
PTs in both clinical and academic practice	119	39.67%

Table No.3: Assessment tool used for diagnosis of Bell's palsy

Assessment tools	Frequency	Percent
Sunny brook facial grading system	118	39.3%
House Brackman	45	15%
Sydney	35	11.67%
other facial nerve grading system	102	34%
Total	300	100%

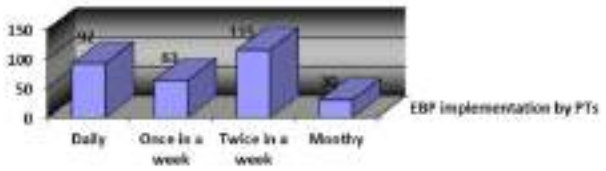
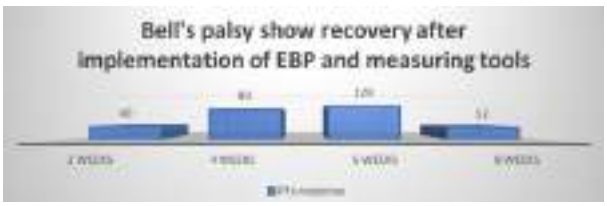


Figure No.2, 115(38.3%) PTs implementing EBP twice in a week



In **figure No.3**, **128(42.67%)** PTs responds that patients of Bell's palsy show recovery after implement EBP in 6 weeks.

Table 2 shows that 300 PTs were participating in the study within which 181 PTs were doing only clinical practice whereas 119 PTs were doing clinical practice as well as academics.

In table No.3, 118 PTs were using SBFGS which was 39.3% out of 300 PTs.

DISCUSSION

In 2020, Marotta N conducted a randomised control trial to evaluate the PTs preferences regarding the assessment and management of Bell's Palsy. In the study, different measurement tools were considered to see which one is better for assessment. By asking PTs, the comparison of all tools takes place. In the previous studies, it was found out that the correct assessment matters a lot in the better prognosis of pts.[19] In this study, it was concluded that the patients can get better treatment and show better prognosis if the tools are used for facial nerve assessment. This study found that the patients of bell's palsy show better prognosis after **6 weeks** of providing effective evidence-based treatment.In 2020, Coulson SE indicates that the SBFGS and house brackmann are the best tool for the assessment of bell's palsy.[20] In this study, the tools which is better for assessment of facial nerve is SBFGS. **39%** PTs are using this tool for the assessmnt and management of Bell's palsy patients.In 2020, Bylund N conducted a prospective cohort study, the researchers only found that the attitude of physiotherapists regarding implementing EBP in their practice is positive. But they didn't specify how many times they are applying EBP in their practice.[21] In 2020, this study describes that the knowledge, attitude, and practice of PTs towards the use of assessment and management of bells palsy. The study also assessed the 38% PTs implements EBP in practice twice in a week to evaluate their patients of Bells palsy. In 2017, Yahui HC conducted a survey in which he was comparing the usage of assesment tools to check the prognosis of bells palsy patients. But they never compared it with the attitude of PTs towards treatment along with the implementation of EBP.[22] This research was conducted to found the EBP implementation in the treatment of Bell's palsy patients and concludes that mostly PTs are applying EBP in their practice. The study also assessed the 38% PTs implements EBP in practice to evaluate patients of Bells palsy. The results were satisfactory but some PTs still need to take EBP implementation seriously as it is very much helpful in the better prognosis of pts.In 2017, Alshehri MA conducted a cross sectional study. He only found the implementation of EBP generally in clinical practice. They won't found it with the Bell's Palsy and also don't find anything about the recovery of patients after implementing EBP.[23] This research was conducted to found the EBP implementation in the treatment of Bell's palsy patients and concludes that mostly PTs are applying EBP in their practice especially while they are treating bell's palsy patients. 75% PTs found better

recovery in their pts of bells palsy after implementing EBP.

CONCLUSION

The study concluded that by the usage of standardized and valid measuring tools along with EBP implementation in the assessment and treatment, the patients of Bell's palsy show better prognosis.

Author's Contribution:

Concept & Design of Study:	Tehreem Mukhtar
Drafting:	Afreen Qadir, Saba Rafique
Data Analysis:	Iqra Abdul Ghafoor, Hafiza Shabnum Noor
Revisiting Critically:	Qurat ul Ain
Final Approval of version:	Tehreem Mukhtar

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Chen N, Zhou M, He L, Zhou D, Li N. Acupuncture for Bell's palsy. Cochrane Database of Systematic Reviews 2010(8).
2. Yanagihara N, Hyodo M. Association of diabetes mellitus and hypertension with Bell's palsy and Ramsay Hunt syndrome. Annals of Otology, Rhinology Laryngol 1988;97(6_suppl3):5-7.
3. Qadir A, Tanveer F, Arshad HS. Frequency and effects of bell's palsy in multigravida of 3rd trimester. Int J Rehabilitation Sci (IJRS) 2017;5(01):13-6.
4. Cayir S, Hizli O, Kayabasi S. Is C-reactive protein to albumin ratio an indicator of poor prognosis in Bell's palsy? Eur Archives Oto-Rhino-Laryngol 2020;277(1):115-9.
5. Huang W. Energy alterations and chakras energy deficiencies in the pathophysiology of bells palsy. J Neurol Experimental Neural Sci 2020.
6. Vakharia K, Vakharia K. Bell's palsy. Facial Plastic Surgery Clinics 2016;24(1):1-10.
7. George E, Richie MB, Glastonbury CM. Facial nerve palsy: Clinical Practice and Cognitive Errors. Am J Med 2020.
8. Majeed A, Festi Lova MV, Ahsan A. Clinical Manifestations of Bell's palsy: A Case Report.
9. Neil EE. 50 Years Ago in The Journal of Pediatrics: Comments on Current Literature: Bell's Palsy in Children. J Pediatr 2019;208:213.
10. Ordoñez G, Rivas V, Santos M, Mondragon M, Pineda B, Rodríguez K, et al. Herpes viruses in optic neuritis: Similar to Bell's palsy. Clin Neurol Neurosurg 2020;188:105588.
11. Zhang W, Xu L, Luo T, Wu F, Zhao B, Li X. The etiology of Bell's palsy: a review. J Neurol 2019:1-10.
12. Puls WC, Jarvis JC, Ruck A, Lehmann T, Guntinas-Lichius O, Volk GF. Surface electrical stimulation for facial paralysis is not harmful. Muscle Nerve 2020;61(3):347-53.
13. Berg T, Bylund N, Marsk E, Jonsson L, Kanerva M, Hultcrantz M, et al. The effect of prednisolone on sequelae in Bell's palsy. Archives Otolaryngol–Head Neck Surg 2012;138(5):445-9.
14. Abd Elfattah M, Eliwa EA, Abdelal IT, Ebaid AM. Role of Electroneurography as a Prognostic Indicator for Bell's Palsy Patients. Zagazig University Med J 2019.
15. Urban E, Volk GF, Geißler K, Thielker J, Dittberner A, Klingner C, et al. Prognostic factors for the outcome of Bells' palsy: a cohort register based study. Clin Otolaryngol 2020.
16. House JW. Facial nerve grading systems. Laryngoscope 1983;93(8):1056-69.
17. Javaherian M, Attarbashi MB, Bashardoust TS, Dabbaghipour N. Efficacy of low-level laser therapy on management of Bell's palsy: a systematic review. Lasers Med Sci 2020.
18. Somasundara D, Sullivan F. Management of Bell's palsy. Australian Prescriber 2017;40(3):94.
19. Marotta N, Demeco A, Inzitari MT, Caruso MG, Ammendolia A. Neuromuscular electrical stimulation and shortwave diathermy in unrecovered Bell palsy: A randomized controlled study. Medicine 2020;99(8).
20. Coulson SE, Croxson GR, Adams RD, O'Dwyer NJ. Reliability of the "Sydney,""Sunnybrook," and "House Brackmann" facial grading systems to assess voluntary movement and synkinesis after facial nerve paralysis. Otolaryngology-Head and Neck Surg 2005;132(4):543-9.
21. Yahui HC, Swaminathan N. Knowledge, attitudes, and barriers towards evidence-based practice among physiotherapists in Malaysia. Hong Kong Physiotherapy J 2017;37:10-8.
22. Bylund N, Hultcrantz M, Jonsson L, Marsk E. Quality of Life in Bell's Palsy: Correlation with Sunnybrook and House-Brackmann Over Time. Laryngoscope 2020.
23. Alshehri MA, Alalawi A, Alhasan H, Stokes E. Physiotherapists' behaviour, attitudes, awareness, knowledge and barriers in relation to evidence-based practice implementation in Saudi Arabia: a cross-sectional study. Int J Evidence-Based Healthcare 2017;15(3):127.

Original Article

Pre and Post Analysis of Stress Reduction Following Pilates Exercise among Undergraduate Students of Physical Therapy

Noman Ahmed[1], Nasir Mehmood[2] and Ghazala Noor Nizami[3]

ABSTRACT

Objective: Stress is a widespread issue with all students facing some level of stress. We conducted a study to assess if Pilates exercise can reduce stress among undergraduate students of Physical Therapy.

Study Design: Longitudinal study

Place and Duration of Study: This study was conducted at the Isra Institute of Rehabilitation Sciences and Karachi University from January 2019 to May 2020.

Materials and Methods: A Pilates expert was hired to do sessions of Pilates 3 times a week for six weeks. Pre and Post assessment of stress was carried out using the Perceived Stress Scale (PSS-14), a five-unit scale used to measure perceived stress. Data were then analyzed using SPSS Version 21.0 by applying paired t-test and setting the statistical significance at $P \leq 0.05$.

Results: A significant difference ($P \leq 0.05$) in perceived stress was shown before and after the students took part in Pilates exercise.

Conclusion: Pilates showed to be a reliable method in reducing stress among undergraduates of Physical Therapy. Pilates should be used more widely among different populations in reducing stress.

Key Words: Celebrex, nephroprotective, chemoprotective, PGE_2

Citation of article: Ahmed N, Mehmood N, Nizami GN. Pre and Post Analysis of Stress Reduction Following Pilates Exercise among Undergraduate Students of Physical Therapy. Med Forum 2021;32(10):224-227.

INTRODUCTION

Stress is a reality that all of us must have to face in our lives, in some way. The term stress was first applied in the science of Physics. Later on, its usage transitioned from being used in physics to behavioral sciences [(1)]. There is no agreed-upon definition of stress. However, McEwen states that "stress is a word used to describe experiences that are challenging emotionally and physiologically"[(2)]. Examples of stress include financial setbacks, health problems, personal and work-related issues, and stress on the person physically and psychologically [(3)]. Everyone experiences stress, and the same can be said for students [(4)]. Furthermore, most of the physical and emotional symptoms that students come across in their academic life include fatigue, headaches, depression, anxiety, and the inability to cope, all of which can be related to or exacerbated by the stress [(5)]. The good thing is that there are various ways to reduce stress among undergraduate students, including cognitive, mindfulness, and behavioral interventions [(6)]. Among the stress management techniques is what is called Pilates. Pilates was introduced by Joseph Pilates in the latter part of World War I, calling his method the "The Art of Contrology." [(7)]. The method of Pilates is a strong tool in the self-management of stress reaction. The six core principles of Pilates (relaxation, breath, concentration, guide imagery, heightened body awareness, and mindfulness), in a combination of strong curing skills, successfully help in coping and reducing harmful stress among people [(8,9)]. Considering how much widespread stress is among students of universities in Pakistan, a study was conducted among the undergraduate students of Physical Therapy to evaluate and Pilates can reduce stress.

[1.] Isra Institute of Rehabilitation Sciences, Isra University Karachi Campus
[2.] Taqwa Institute of Physiotherapy & Health Sciences
[3.] Jinnah College of Rehabilitation Sciences, Sohail University

Correspondence: Noman Ahmed, Assistant Professor Isra Institute of Rehabilitation Sciences, Isra University Karachi Campus
Contact No: 03332759899
Email: nomanissani@gmail.com

Received: May, 2021
Accepted: July, 2021
Printed: October, 2021

MATERIALS AND METHODS

An experimental longitudinal study was conducted at Isra Institute of Rehabilitation Science, Isra University, and Karachi Campus after the ethical board and research committee's approval. The study spanned for six months, during which 30 undergraduate students of Physical Therapy were selected from different Karachi colleges. The selection was made based on a simple random sampling technique. Only after consent was,

they selected for the study. A Pilate's expert was hired independently to carry out 3 Pilates exercise and training sessions a week for six weeks. The following exercises of Pilates were conducted in the study:

Warm-Up Exercises:

1. Squat
2. Spinal Cord Rotation
3. Side Bends
4. Roll Down
5. Breathing

Beginning of Pilates Class

1. The Hundred
2. Roll Up
3. Single-Leg Circles
4. Rolling Like a Ball Prep
5. Single-Leg Stretch
6. Double Leg Stretch
7. Spine Stretch
8. Open Leg Rocker Prep
9. Corkscrew Prep I
10. Swan Dive Prep I

Cool Down Exercise:

1. Hamstring Stretch
2. Side-Lying Quadriceps and Hip Flexor Stretch
3. Piriformis Stretch

Data was collected using the Perceived Stress Scale-14 (PSS-14) questionnaire. The questionnaire consisting of 14 questions was given to the selected students before the Pilates classes' commencement and after the classes were concluded. The PSS-14 will evaluate the degree of stress a person experiences during the past month. The PSS-14 scores each question from 0-4; 0-Never, 1-Almost Never, 2-Sometimes, 3-Fairly Often, 4-Very Often, with the scale being reverse for question 4,5,6,7,9,10, and 13. The PSS scores for low stress were 0-18, moderate stress 19-36, and 37-56 corresponded for High Stress (10). The data was then analyzed and evaluated using SPSS Version 21.0, with paired t-test being applied to the group. Statistical significance was set at ≤ 0.05.

RESULTS

Table 1 shows the gender-based distribution among the participants

Table 2 shows the response Frequency and percentage of the participants

Table 3 shows the frequency and percentage of stress level among the participants

Table 4 shows the level of significance on comparison of pre and post stress levels.

Table No.1: Gender of the participants

		Frequency	Percent (%))
Valid	**Male**	**12**	**40.0**
	Female	**18**	**60.0**
	Total	**30**	**100.0**

Table No.2: Shows the Frequency and percentage of the response of the participants

Questions	Pre- Pilates Exercise Perceived Stress					Post Pilates Exercise Perceived Stress				
	Frequency (Percentage)					Frequency (Percentage)				
	Never	Almost Never	Some times	Fairly Often	Very Often	Never	Almost Never	Some times	Fairly Often	Very Often
Have you been upset in the last month because of the unexpected things?	0 (0)	3 (10)	11 (36.6)	4 (13.3)	12 (40)	6 (20)	10 (33.3)	9 (30)	2 (6.7)	3 (10)
Have you felt in the last month that you failed to control important things?	0 (0)	4 (13)	12 (40)	7 (23.3)	7 (23.3)	5 (16.7)	10 (33.3)	11 (36.7)	4 (13.3)	0 (0)
Last month have you felt stressed and nervous?	0 (0)	1 (3.3)	14 (46.7)	7 (23.3)	8 (26.7)	4 (13.3)	12 (40)	10 (33.3)	4 (13.3)	0 (0)
Last month have you deal successfully with irritating life hassles?	2 (6.7)	15 (50)	9 (30)	4 (13.3)	0 (0)	2 (6.7)	7 (23.3)	18 (60)	3 (10)	0 (0)
During the last month have you felt that you were able to cope up the important changes happening in life effectively?	6 (20)	15 (50)	7 (23.3)	2 (6.7)	0 (0)	6 (20)	12 (40)	8 (26.7)	4 (13.3)	0(0)
During the Last month have you felt confident enough to solve the personal problems?	7 (23.3)	12 (40)	8 (26.7)	3 (10)	0 (0)	0 (0)	0 (0)	8 (26.7)	14 (46.7)	8 (26.7)
Have you felt during the last month that the things were going according to the way you want?	3 (10)	16 (53.3)	10 (33.3)	1 (3.3)	0 (0)	3 (10)	7 (23.3)	12 (40)	4 (13.3)	4 (13.3)
Last month have you found that you could not copeup with all things that you had to do?	4 (13.3)	3 (10)	15 (50)	4 (13.3)	4 (13.3)	5 (16.7)	16 (53.3)	8 (26.7)	1 (3.3)	0 (0)

During the last month have you been able to manage frustrations of your life?	4 (13.3)	10 (33.3)	15 (50)	1 (3.3)	0 (0)	1 (3.3)	1 (3.3)	4 (13.3)	19 (63.3)	5 (16.7)
During the last month have you felt that you were on top of things?	4 (13.3)	13 (43.3)	12 (40)	1 (3.3)	0 (0)	0 (0)	1 (3.3)	9 (30)	13 (43.3)	7 (23.3)
During the last month have you been annoyed because of the uncontrolled things?	0 (0)	5 (16.7)	15 (50)	7 (23.3)	3 (10)	5 (16.7)	16 (53.3)	7 (23.3)	2 (6.7)	0 (0)
Have you found during the last month that yourself you were thinking about things that you want to achieve?	0 (0)	1 (3.3)	15 (50)	9 (30)	5 (15.7)	5 (16.7)	11 (36.7)	10 (33.3)	4 (13.3)	0 (0)
Have you been able to control during the last month that way you want to spend time?	6 (20)	13 (43.3)	9 (30)	2 (6.7)	0 (0)	0 (0)	3 (10)	13 (43.3)	7 (23.3)	7 (23.3)
During the last month have you felt that you are unable to overcome the difficulties piling up so high?	0 (0)	1 (3.3)	17 (56.7)	9 (30)	3 (10)	3 (10)	16 (53.3)	7 (23.3)	2 (6.7)	2 (6.7)

Table 1: Pre stress level of Pilate exercises * Post stress of Pilate exercises Cross tabulation

		Post stress of Pilate exercises		Total
		Low level of stress	Moderate level of stress	Low level of stress
Pre stress level of Pilate exercises	Moderate level of stress	13	13	26
	High level of stress	2	2	4
Total		15	15	30

Table No.2: Paired Samples Statistics

		Mean	N	Std. Deviation	P-value
Pair 1	Pre Pilate exercises test	33.37	30	2.918	0.00517
	Post Pilate exercises test	18.4333	30	6.73480	

DISCUSSION

Stress is an issue that all students must face nowadays. Our study results showed that the majority of the students faced stress and had a high level of irritation, causing them to pursue different coping measures to deal with stress. Another study conducted by V.R. Zare et al.; that went onto assess depression, anxiety, and stress in school children found that stress was high among students regardless of their schooling in the public or private sector[11]. Our study showed that students were highly stressed out and were not able to tackle their life problems because of this reason. Another study similar to our study using the perceived stress scale showed that personal and academic sources of stress contributed to a high level of perceived stress among students[12]. Jacob et al. also hinted in his student conducted on physical therapy students that clinical practice is a much higher risk factor for students' stress than academic activities. This shows students of physical therapy also face different levels of stress, and their faculty staff must identify students who are dealing with stress.

A systematic review conducted showed that spending time in the outdoor environment, particularly those with greenery and open spaces, reduces stress, and ultimately improves health[13].

Similarly, we used Pilates to see if it had any effect on stress reduction among students of Physical therapy. Pilates help reduce the students' perceived stress, with significant difference ($P \leq 0.05$) among the students after the Pilates sessions had been concluded. This shows that Pilates is a useful technique in reducing stress among undergraduate students of physical therapy. Another study also showed that a 16-week Pilates-based training regime helped significantly improve the health and sleep quality of women[14]. This further shows that once people undergo Pilates exercise, they will have lower stress, better sleep, and overall improved health.

CONCLUSION

Pilates was shown to be an effective method in reducing perceived stress among the students of physical therapy. Students showed significant improvement in stress levels, coping, and dealing with problems in their life after taking part in Pilate's sessions. Students should participate in activities such as Pilates and more exercises to reduce the stress they face during their personal and academic life.

Author's Contribution:

Concept & Design of Study: Noman Ahmed
Drafting: Nasir Mehmood
Data Analysis: Ghazala Noor Nizami

Revisiting Critically:	Noman Ahmed, Nasir Mehmood
Final Approval of version:	Noman Ahmed

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Krohne HW. Stress and coping theories. Int Encyclopedia Social Behavioral Sci 2002;22:15163-70.
2. McEwen BS. Physiology and neurobiology of stress and adaptation: central role of the brain. Physiological Reviews 2007;87(3):873-904.
3. Kassymova K, Kosherbayeva N, Sangilbayev S, Schachl H. Stress management techniques for students. Int Conference Theory Practice Personality Formation in Modern Society (ICTPPFMS 2018) 2018 Sep. Atlantis Press.
4. Hussain I, Ahmed M, Ahmad S, Suleman Q, Khalid N. A Study to Investigate the Availability of Educational Facilities at the Secondary School Level in District Karak. Language Ind 2012;12(10).
5. Dusselier L, Dunn B, Wang Y, Shelley iI MC, Whalen DF. Personal, health, academic, and environmental predictors of stress for residence hall students. J Am Coll Health 2005;54(1):15-24.
6. Regehr C, Glancy D, Pitts A. Interventions to reduce stress in university students: A review and meta-analysis. J Affective Disorders 2013; 148(1):1-1.
7. Anderson BD, Spector A. Introduction to Pilates-based rehabilitation. Orthopaedic Physical Therapy. Clin North Am 2000;9(3):395-410.
8. Pilates JH. Return to Life Through Contrology. Incline Village, NV: Presentation Dynamics Inc 1945.
9. Clark M, Romani-Ruby C. Pilates Matwork for Fitness and Rehabilitation Professionals. Pittsburgh: Word Association Publishers 2003.
10. Shaikh S, Shaikh S, Shaikh S, Shaikh AA, Saleem SG. Prevalence of hair loss and stress as the cause; a cross-sectional study. International Journal of Advanced Research (2016), Volume 4, Issue 7, 327-333.
11. Zare VR, Ramesh B, Kokiwar P. Assessment of "depression, anxiety and stress" among students of schools at RHTC area catered by private medical college in South India. Int J Community Medicine Public Health 2018;5(7):3116-20.
12. Jacob T, Gummesson C, Nordmark E, El-Ansary D, Remedios L, Webb G. Perceived stress and sources of stress among physiotherapy students from 3 countries. J Physical Therapy Education 2012;26(3):57-65.
13. Akbaş E, Ünver B. A six-week pilates exercise protocol for improving physical and mental health-related parameters. Malaysian Journal of Movement, Health Exercise 2018;7(2):65-79.
14. Fleming KM, Herring MP. The effects of Pilates on mental health outcomes: A meta-analysis of controlled trials. Complementary Therapies Med 2018;37:80-95.