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Editorial

Diabetes – A Serious Threat for Public Health

Mohsin Masud Jan

Editor

Diabetes is the 8th leading cause of death globally, a number that has been rising rapidly in low- and middle-income countries according WHO. In 2019, an estimated 1.5 million deaths were directly caused by the disease. Another 2.2 million deaths were attributable to high blood glucose. One in five people above 65 years of age has diabetes. And almost 232 million people with diabetes are undiagnosed.

The International Diabetes Federation (IDF) publication, Diabetes Atlas 9th Edition, reports that the prevalence of diabetes in Pakistan has reached 17.1 per cent. In 2019, more than 19 million adults in Pakistan were estimated to be living with diabetes, putting them at risk of life-threatening complications. Diabetes kills approximately 90,000 people annually in Pakistan. Studies reveal that Pakistan ranks 7th among the top 10 countries with the highest number of people living with diabetes.

The rising number of diabetic patients is a threat to healthcare systems worldwide.

Diabetes is one of the fastest growing public health concerns worldwide. The prevalence of diabetes and lack of access to proper care increase the risk of the chronic disease turning into a public health crisis of considerable magnitude. Several factors are responsible for the increasing number of diabetic patients globally. These range from genetic disposition to lifestyle issues and the age factor.

The number of diabetics is projected to rise to 693 million by 2045 from 451 million in 2017 worldwide. It is also estimated that nearly 49.7 per cent of people living with Type-II diabetes remain undiagnosed. In patients with Type-II diabetes, the average life expectancy decreases by around ten years. Millions of people with diabetes around the world do not have access to diabetes care. Patients with the disease require constant care and support to manage their condition and avoid complications. Undiagnosed or poorly managed diabetes can result in avoidable blindness, kidney failure, heart attack, stroke and lower limb amputation, having long-standing medical and non-medical costs for patients, caregivers, families and communities.

There are three main types of diabetes; Type I can develop at any age but occurs most frequently in children and adolescents. Type II diabetes is more common in adults and accounts for around 90 per cent of all diabetes cases. In such a situation, the body does not make good use of the insulin that it produces. This requires oral drugs and/or insulin to keep their blood glucose levels under control. Gestational diabetes, the third type, that causes high blood glucose levels in the body during pregnancy is associated with birth-related stress.

High blood glucose leads to damage of the nerves, mainly the peripheral nervous system leading to neuropathy. This damages blood vessels that supply the kidneys circulation leading to kidney damage. This can lead to the accumulation of wastes in the blood. High blood sugars can also damage blood vessels in the eyes, causing cataracts and glaucoma. Diabetes can cause blockage of the blood vessels, increasing the risk of stroke and heart attack. Due to damage in the nerves of peripheral nervous system, foot ulcers or gangrenes can occur. These wounds heal slowly and sometimes may lead to amputation or loss of limb. Diabetes may gradually lead to cognitive impairment or memory loss in the patients.

Symptoms vary based on the type of diabetes. The general symptoms include weight loss, increased thirst, excessive hunger, increased urination, especially at night, visual disturbances, extreme fatigue, weakness, headache, drowsiness, numbness in hands and feet, slow and improper healing of cuts or bruises and dry mouth. Some of the risk factors are age, family history and diseases of the pancreas.

People with diabetes are at increased risk of severe disease if they contract the Covid-19. For this reason, the WHO and its partners continue to respond to the pandemic threat. Like everyone, people with diabetes must continue to be encouraged to diligently observe personal protective measures such as physical distancing, hand washing and mask wearing. The WHO suggests that a healthy diet, regular physical activity, maintaining a normal body weight and avoiding tobacco use are ways to prevent or delay the onset of Type 2 diabetes.

Simple lifestyle measures have been shown to prevent or delay the onset of Type II diabetes and related complications. Early diagnosis can be accomplished through relatively inexpensive testing. In addition, self-care such as proper foot hygiene, wearing appropriate footwear, seeking professional care for sore management, and regular examinations by health professionals are essential to avoid a serious threat.

Diabetes is a serious threat to global healthcare systems. The increasing number of patients in Pakistan should be a wake-up call. We must do more to prevent Type II diabetes through early diagnosis and ensure that every diabetic person has affordable and uninterrupted access to the care they need.

World Diabetes Day has been observed every year on November 14, since 1991, when the International Diabetes Foundation and the World Health Organisation first decided to raise awareness about the impact of the disease as well as promote the role of the family and community in the management, care, prevention and treatment of diabetes.

Original Article

Prevalence of Halitosis Among Students of Chandka Medical College, Larkana

Abdul Mateen[1], Abdul Qadir[1], Nabila Shaikh[1], Muhammad Wajahat Ghafoor[2], Qaiser Masud Sheikh[3] and Ahsan Malik[3]

ABSTRACT

Objective: To assess prevalence and knowledge about halitosis among MBBS students at Chandka Medical College Larkana, Sindh, Pakistan.

Study Design: Quantitative / descriptive / cross-sectional study

Place and Duration of Study: This study was conducted at the Chandka Medical College Larkana, Sindh, Pakistan from March 2020 to May 2020 for a period of 3 months.

Materials and Methods: A questionnaire based study was carried out on a total of 700 3rd, 4th, final year students of MBBS. Inferential statistical tests (Chi-square, pearson) were administered using IBM SPSS v22.

Results: 42.38% respondents having prevalence of malodor. Among those who had prevalence of bad breath, approximately half (56.33%) were self-aware of their bad breath. Among 335 respondents, 80.59% were aware that they should visit a dentist whereas majority were unaware of the medical term for bad breath i.e. meaning of Halitosis (65.67%, n=220). More than half of the respondents (61.79%) identified teeth & gum disease as the main cause of bad breath. The majority students reported using mouth washes and brushing their teeth twice a day.

Conclusion: The prevalence of halitosis among the students of Chandka Medical College was found to be 42.38 %.

Key Words: Halitosis, Oral Hygiene, Awareness, Medical Students

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INTRODUCTION

Halitosis is an offensive smell expelled out from oral cavity regardless of the root cause.(1) Halitosis, oral malodor, and bad breath can be used interchangeably.(2) It is multifactorial and involves extra oral and intraoral causes.(3) It occurs due to the putrefactive activities of gram negative anaerobic bacteria commonly in the dorso-posterior part of the tongue(4). Oral cavity related problems such as tongue coating, periodontal diseases(5), xerostomia(6), dentures(7), mucosal lesions(8) are more common causes of halitosis whereas extra-oral causes like disorders of the respiratory tract(9), gastrointestinal tract(10), endocrinological disturbances(11) and side effects of certain medications also contribute to halitosis(12). Smoking habits, behavior towards the oral hygiene habits plays important role towards its production in oral cavity(13).

Halitosis is a universal medico-social problem(14). Majority of the individuals face social embarrassment, phobias, depressions that may have a deleterious effect on an individual's self-esteem(15). Halitosis is an important issue for young people, and that a large part of the young population sees tongue cleaning as a part of oral hygiene and intraoral change as cause of halitosis(16). It is a common oral health problem around the globe(17). The prevalence of halitosis was indicated by various studies such as 42% in Lahore Pakistan(18) 7.14% in students of university of Kathmandu, Nepal(19) 22% in France(20) , 41.1% in China(14) , 44.6% in India(21), 59.9 % in Saudi Arabia (22) and in my study 57.2% in attitude and practice towards halitosis among medical students of Chandka Medical College Larkana, Sindh, Pakistan.

MATERIALS AND METHODS

The study is a quantitative, descriptive, cross-sectional design. Sampling strategy used was nonprobability convenience sampling. Required sample size was calculated using NCSS(23) calculator and required sample size was 295. Ethical review was obtained from Institutional Review Committee of Shaheed Mohtarma Benazir Bhutto Medical University, Larkana. Participating students were explained the objectives of

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the study and written informed consent was obtained from each respondent.

The questionnaire for data collection is based on a standard tool which was developed for halitosis prevalence at the Halitosis Clinic of University of Basel, Switzerland[24]. Additional items used in the questionnaire for data collection were harvested from previous studies conducted for finding prevalence of halitosis[17]. The tool was reviewed for face and content validity by subject and linguistic experts, while Cronbach alpha (r=0.81) demonstrated reliability.

The survey was administered in March 2020. A total of 335 students of MBBS responded through the filled questionaires; respondents were studying in 3rd, 4th and 5th year at Chandka Medical College Larkana, Sindh, Pakistan.

Resulting data was transcribed manually and analyzed using IBM Statistical Package for Social Sciences (SPSS) version 22.0, Minitab software, Microsoft excel for descriptive (frequency, percentage, mean, median, standard deviation) and inferential statistics (chi-square and Pearson correlation coefficient.

RESULTS

Responses were obtained from three hundred and thirty-five participants. Table 1 elucidates the socio-demographic characteristics of the respondents; mean age was 22.95(± 1.21).

Table No.1: Socio-demographic characteristics of the respondents

Variables	Frequency	Percentage
Age in years		
>23	159	47.5 %
≤23	176	52.5 %
GENDER		
MALE	190	56.7 %
FEMALE	145	43.3 %

Table 2 shows the medical history of the respondents related to halitosis; among them almost 32.72% had medical history. 41.7% (n=140) had health issues related to the oral cavity. A minority of the respondents (13.43%, n=45) reported a habit of smoking.

Table 3 illustrates 42.38% respondents having prevalence of malodor (n=142). Among those who had prevalence of bad breath, approximately half (56.33%, n=80) were self-aware of their bad breath, whereas 43.66% (n=62) responded that somebody else noticed their breath having bad odor. Those suffering from the condition for more than a year were 38.73% (n=55), while majority noticed bad breath less than one year ago (61.26%, n=87). Among 335 respondents, 80.59% (n=270) were aware that they should visit a dentist whereas majority were unaware of the medical term for bad breath i.e. meaning of Halitosis (65.67%, n=220). More than half of the respondents (61.79%, n=207) identified teeth & gum disease as the main cause of bad breath.

Table No.2: Medical history of the respondents related to halitosis

Variables	Frequency	Percentage
Gastrointestinal Disease		
Yes	37	11.04%
No	298	88.95%
Lungs Disease		
Yes	12	0.35%
No	323	96.41%
Sinusitis		
Yes	27	0.80%
No	308	91.94%
Nasal Problems		
Yes	23	6.86%
No	312	93.13%
Liver Disease		
Yes	06	0.18%
No	329	98.2%
Diabetes Mellitus		
Yes	05	0.15%
No	330	98.5%
Smoking Habits		
Yes	45	13.43%
No	290	86.56%
Oral Cavity (Cavities, Gums Problems)		
Yes	140	41.7%
No	195	58.2%

Table No.3: Respondents having prevalence of malodor

Question Statements	Answer Frequency	Percentage
Have you problem of bad breath?		
Yes	142	42.38%
No	193	82.98%
Who noticed bad breath from your mouth? (n-57)		
Myself	80	56.33%
Other person	62	43.66%
How long before you noticed it?		
<1 year	87	61.26%
>1 year	55	38.73%
To which professional you prefer to visit for bad breath problem?		
Dentist	270	80.59%
Gastroenterologist	25	7.46%
ENT Specialist	12	3.58%
Physician	23	6.86%
Do you Know the term Halitosis?		
Yes	105	31.34%
No	220	65.67%
Which factor you think is the cause of bad breath?		
Bad odour food onion, garlic etc.		
Yes	159	47.46%
Teeth or gum problem		
Yes	207	61.79%
Gastric problem		
Yes	189	56.41%
Nasal or pulmonary problem		
Yes	120	35.82%

Table No.4: Oral hygiene habits of respondents

Statement	Response	Frequency	% age
Do you practice interdental flossing?	Yes	34	10.1
	No	301	89.9
Do you use mouth wash?	Yes	120	35.7
	No	215	64.3
Do you brush your teeth twice a day?	Yes	295	88.1
	No	40	11.9

Table 4 illustrates the self-reported oral hygiene habits of respondents. The majority students reported brushing their teeth twice a day (88.1%, n=295) but did not practice interdental flossing (89.9%, n=301). Approximately only one third students reported using mouthwash for oral hygiene (35.7%, n=120).

DISCUSSION

This study was conducted to assess prevalence and knowledge about halitosis among MBBS students. A similar study was conducted at Sharif Medical & Dental College, Lahore, Pakistan[18]. In this study, when asked from the participants, 42% of the respondents stated 'bad breath' as a 'foul' which is comparable to studies done in India (43%). Various studies conducted in different parts of the world reported vastly different findings (75.1%) in a study done in Lahore(25) , 25.8% in Saudi Arabia, japan (44.9%), Nigeria (75%, Rwanda (23.1%)[21, 26,27, 28].

In our study most of the students responded that dentists are the first professionals to treat halitosis which corresponds to the study done by RT Firmino [29]. Students further responded that consultation with Gastroenterologist might be helpful[30]. Some of the socio-demographic characteristics also effects the prevalence and attitude towards the preventive measures against the halitosis like 50% elderly reported with halitosis in study of M Zellmer[31] and in the study of SP Mehta[32] about 43% youngsters reported with halitosis. These findings were found to be consistent with a study done by Kim et al[33] in Korea in which published that age and gender were significantly associated with halitosis but residence area was not a significant influencing variables for it. While a contradictory finding was reported by Alshehri in Saudi Arabia which showed none of the socio-demographic characteristics (age, sex, and marital status) were associated with halitosis[34,35,36]. Therefore, it can be said that difference of living standard, knowledge and communities has great impact on prevalence of halitosis in a society.

One of the studies reported smoking as a cause, is influencing prevalence of halitosis among undergraduate medical students[37]. This finding correlates with the study of R.D Cannon[38]. In study of Kermanshah High School Students[38] around one third participants do tooth brushing twice a day while almost the same proportion had the habit of using mouth wash and dental floss. A study done in Lebanon revealed nearly two third of dentist had insufficient knowledge about management of halitosis[20]. In survey done at Junior College and Dental College Students in Navi Mumbai (64%) did tooth brushing twice a day, (60%) used mouth wash and the resultant prevalence of malodour was 21%[32]. This finding went along with a study of Sabina Herman[8], a survey done in China[14] 26.3% participants had tongue cleaning habits. Similarly, other surveys reported different finding regarding tongue cleaning as in Saudi Arabia (13%), India (10%)[21,26]. Thus from the studies above it can be concluded that good oral hygiene habits like tooth brushing, using dental floss and mouth wash can mask the actual prevalence of halitosis.

This may be probably due to social stigma linked with bad breath[39]. The total score of knowledge, attitude and practice regarding halitosis was strongly positive correlated with each other which is statistically highly significant at $p<0.001$.

CONCLUSION

The prevalence of halitosis among the students of Chandka Medical College was found to be 42.38%. Most of the Medical students were not mindful of etiological factors for malodour and about its available options for treatment. Hence it is suggested to impart fundamentals of dentistry to medical students, which will be of assistance in long term to ascertain a need for interdisciplinary approach for management of bad breath resulting in prevention of needless treatments opted. No correlation to systemic/oral diseases or demographic factors was established.

Author's Contribution:

Concept & Design of Study:	Abdul Mateen
Drafting:	Abdul Qadir, Nabila Shaikh, Muhammad Wajahat Ghafoor
Data Analysis:	Qaiser Masud Sheikh, Ahsan Malik
Revisiting Critically:	Abdul Mateen, Abdul Qadir
Final Approval of version:	Abdul Mateen

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Original Article

Co-Incidence of Centric Relation and Maximum Intercuspation in Relation to Canine Guided, Group Guided Occlusion and Gender

Shazia Kiran[1], Kashif Aslam[1], H.R. Sukhia[4], Saad ud Din Siddiqui[2] and Syed Kashif Abrar[3]

ABSTRACT

Objective: The aim of this study is to evaluate the coincidence of centric relation (CR) and maximum intercuspation position (MIP) in relation to canine guided, group guided occlusion and gender.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Dow Dental College and Sir Syed College of Medical Sciences (dental section) for Girl, Karachi in November 2019 till February 2020.

Materials and Methods: Ninety-three subjects were selected according to the selection criteria by purposive sampling technique. Visual observation with articulating paper and subjective perception were the means to detect centric relation (CR) and maximum intercuspation position (MIP) coincidence in relation to canine guided, group guided occlusion and gender. Data was analysed by software SPSS 16. Pearson chi square was used to figure out the association of coincidence of centric relation and maximum intercuspation in relation to canine guided, group guided occlusion and gender.

Results: Group guided occlusion was more prevalent. Centric relation not coinciding with maximum intercuspation was also higher. However, no statistically significant association was found between centric relation and maximum intercuspation coincidence with canine guided, group guided occlusion and gender ($p>0.05$)

Conclusion: Coincidence of centric relation and maximum intercuspation is independent of canine guided, group guided occlusion and gender

Key Words: centric relation, maximum intercuspation, canine guided occlusion, group guided occlusion and gender

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INTRODUCTION

Dental occlusion plays a pivot role for providing efficient treatment in all the disciplines of dentistry. Occlusion refers to the setup of teeth in opposing dental arches and the way they come in contact. It may be static or dynamic. Static occlusion occurs when the maxillary and mandibular teeth are in maximum intercuspation. This intercuspal position is also known as centric occlusion, habitual centric or habitual occlusion.

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Dynamic occlusion comprises of lateral and protrusive mandibular movements occurring during speech, chewing and deglutition[2].

Regarding dynamic occlusion, three different types of occlusions can be found during latrotrusive mandibular movements.

1. Balanced occlusion
2. Canine guided occlusion
3. Group guided occlusion

Balanced occlusion is the simultaneous contact of opposing teeth on right and left sides in lateral excursions, a concept used for complete denture occlusion for denture stability[1]. Canine guided occlusion in which only maxillary and mandibular canines comes in contact on working side (right or left) during lateral excursions. Group guided occlusion also termed as "unilateral balanced occlusion" or "group function" in which multiple teeth contact on working side (right or left) during lateral excursion.

Centric relation (CR) is a musculoskeletal position with condyles in their most antero superior position in glenoid fossa. It is a reproducible position and anatomically determined. Centric occlusion (CO) which

can also be a maximum intercuspation position (MIP) is dentally determined position.

Ideally functional occlusion should have features like CR coinciding with MIP and canine guided occlusion, so the question arises that whether there is an association between these features. Therefore, the objective of this study is to evaluate the association of CR and MIP coincidence in relation to canine guided, group guided occlusion and gender.

MATERIALS AND METHODS

This study was conducted in Dow Dental College and Sir Syed College of Medical Sciences (dental section) for Girl, Karachi in November 2019 till February 2020. Ninety-three subjects were examined during this study from both the genders with a mean age of 22.22 years. Visual examination was done under dental chair light. Mouth mirror was used to retract the cheeks. The examination was done by two operators to ensure inter operator reliability and validity.

To observe the type of occlusion in lateral excursions (canine guided and group guided), subjects were asked to sit in an upright position on dental unit with Frankfort horizontal plane almost parallel to the floor. Articulating paper of 80 micron (Coltene, Germany) was placed between opposing teeth during lateral excursions. Articulating spots during lateral excursions were observed for both working sides (right and left) to determine the type of occlusion.

To observe the CR and MIP coincidence, bimanual manipulation method was used. Patient was kept in an almost supine position on the dental chair with operator at the back of the chair and lower jaw was passively manipulated. Patient was then asked to close the mandible and note the first tooth contact. If all the teeth contact simultaneously with maximum intercuspation at the first tooth contact, CR was regarded coincident with MIP and vice versa. Data analysis was done by using SPSS 16. Chi square test was used to analyse the association of CR and MIP coincidence in relation to canine guided, group guided occlusion and gender.

Inclusion Criteria:

1. At least 28 permanent teeth present.
2. Patients, attendants, students, doctors and staff.
3. No TMJ disorder.
4. No attrition.

Exclusion Criteria:

1. Subjects undergoing orthodontic treatment.
2. Subjects with fixed or removable prosthesis.
3. Carious teeth involving cusps.
4. Subjects with a history of craniofacial trauma.
5. Non cooperative subjects.
6. Presence of bilateral balanced occlusion.
7. Discrepancy in presence of same occlusion i.e. canine guided or group guided on both sides

RESULTS

This study included 93 subjects from 13-50 years of age. Mean age was 22.22 years. 10 (10.3%) were males and 83 (83.7%) individuals were females (Table 1).

Out of 93 subjects, (10 males and 83 females) only 6 males and 34 females (total 40) had coincidence present and the in the rest it was absent (Table 2).

Coincidence of CR and MIP was independent in relation to gender. Chi-square ($p>0.05$)

Out of 93 subjects 9, (males and females) had canine guided occlusion in which 6 had coincidence of CR and MIP and in remaining 3 it was absent. 84 (males and females) had group guided occlusion. CR and MIP coincidence was present in 37 and in remaining 47 it was absent. In total 43 had coincidence of CR and MIP and in the remaining 50 it was absent (Table 3).

Coincidence of CR and MIP was independent in relation to canine guided and group guided occlusion. Chi-square ($p>0.05$).

Table No.1: Frequency distribution of gender

Gender	Frequency	Percentage
Male	10	10.3%
Female	83	83.7%
Total	93	100.0%

Table No.2: CR and MIP in relation to gender

Gender	CR and MIP coincidence (present)	CR and MIP coincidence (absent)
Male	6	4
Female	34	49
Total	40	53

Table No.3: CR and MIP in relation to canine guided and group guided occlusion

Type of occlusion	CR and MIP coincidence (present)	CR and MIP Coincidence (absent)
Canine guided	6	3
Group guided	37	47
Total	43	50

DISCUSSION

Occlusion plays an important role in all the disciplines of dental sciences since it influences the dentition, periodontium as well as temporomandibular joint. Favourable occlusion allows these structures to perform their physiological functions smoothly whereas unhealthy occlusion can cause muscular and temporomandibular diseases. Therefore, both static and dynamic components of occlusion contribute towards the maintenance of stomathognathic system.

Numerous studies have been conducted to evaluate the prevalence of occlusal patterns during mandibular lateral excursions but at different mandibular positions. This accounts for vast variation among the results.

Many studies recorded the occlusal contacts in canines' edge to edge position. This position is mainly used for incising food and during para functional habits. Since it is more preferable to have a normal chewing pattern rather than specifically moving the mandible to specific dimensions in a lateral direction, therefore in this study lateral contact patterns were recorded in a normal chewing fashion**Error! Bookmark not defined.**.

Different techniques have been provided in literature to obtain centric relation position. These can be operator guided and patient guided. Operator guided methods has shown some promising results but without consensus that which type of operator guided method is best. Bimanual manipulation (a type of operator guided method) used in this study to make the candidate close in centric relation is one of the recommended method in published studies**Error! Bookmark not defined.**.

Different studies[Error! Bookmark not defined.] have used different materials to observe occlusal contacts. Articulating paper used in this study produces more occlusal contacts than the other material also shown in the study of Saad et al**Error! Bookmark not defined.**. One could argue on the thickness of the articulating paper used in this study because earlier studies have shown to recommend the thickness of less than 21 micron of occlusal registration strips. As per authors' search there is no consensus on material and thickness of occlusal registration strip to be used and also as per ease of availability 80 micron was used.

Gupta et al conducted a study to find out occlusal contact patterns during lateral excursion. Results showed that around 81% of the contact patterns were group function/guided with shim stock and 93% when articulating paper was used[6] which is in accordance to our study. Study by Asawaworarit et al also showed prevalence of group guided occlusion in Thai people. However these findings are against the finding of Aslam et al**Error! Bookmark not defined.**.

Various researches have been performed to elaborate centric occlusion and maximum intercuspation discrepancy among different population samples and their association with TMJ dysfunction[Error! Bookmark not defined.]. A research including 40 subjects was conducted between 2014 and 2015 in Romania. Results revealed 85% of the subjects had vertical while 87.5% had horizontal CR-MI discrepancy for both condyles[8].

In this study centric relation and maximum intercuspation was not coinciding in most of the individuals which is in accordance to other studies. In this study no association was found between centric relation and maximum intercuspation coincidence with gender which is in accordance to the study of Koc et al.

However, as per authors' search, none of the studies could be found where there is, an association of centric relation and maximum intercuspation coincidence with canine guided and group guided occlusion is observed so a direct comparison cannot be made.

CONCLUSION

Coincidence of centric relation and maximum intercuspation is independent of canine guided, group guided occlusion and gender.

Author's Contribution:

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Data Analysis:	Saad ud din Siddiqui, Syed Kashif Abrar
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Original Article

Effect of Ambient Temperature and Prolonged Storage on Prothrombin Time and Activated Partial Thromboplastin Time During Summers in Pakistan

Nada Sikander[1], Unaiza Qamar[2], Javeria Aijaz[3], Rafeeda Maab[4], Zahid Latif[5] and Muhammad Asif Naveed[6]

ABSTRACT

Objective: The current study was carried out to determine the effect of sample storage duration on PT and aPTT, when samples are stored at ambient temperatures during summers in Lahore, Pakistan.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Hematology department of King Edward Medical University in June 2021.

Materials and Methods: Eighty blood samples collected in 3.8% sodium citrate vial and PT and aPTT was performed manually at 0, 4, 8, 12 and 24 hours. First test was performed immediately after sample collection (0 hours) which was taken as reference. Paired sample t-test was used for comparison of PT and APTT at 4, 8, 12 and 24 hours with the value at 0 hours while a mean percentage difference of more than 10% from the baseline value was taken as clinically significant.

Results: Initially PT results did not show any clinically significant change until 24 hours and aPTT till 8 hours.

Conclusion: Samples for PT testing give acceptable results up to 8 hours post collection, and for aPTT testing up to 4 hours, when stored at ambient temperatures during summer seasons.

Key Words: Prothrombin time, Activated partial thromboplastin time, ambient temperature

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INTRODUCTION

Prothrombin time (PT) and activated partial thromboplastin time (aPTT) are among the most frequently ordered screening tests in the clinical laboratory.

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These screening tests are used in the evaluation of a wide variety of clinical conditions, either for diagnostic or monitoring purposes of anticoagulant therapy.

They form the basis of many special coagulation tests such as factor assays, and in some locations clot-based specialized assays (e.g., protein C [PC] and protein S [PS] activity assays, activated PC resistance [APCR]).[1]

The reference range for prothrombin time is usually around 10-13 seconds.[2] Prothrombin time can be prolonged as a result of deficiencies in vitamin K, warfarin therapy, malabsorption, liver disease, factor deficiency (II,VII,IX,X), disseminated intravascular coagulation and presence of antiphospholipid antibody syndrome.[3]

The reference range of aPTT is between 25- 39 seconds. Prolonged APTT may indicate use of heparin (or contamination of the sample with heparin), antiphospholipid antibody especially lupus anticoagulant, and coagulation factor deficiency (VIII, IX or XI).[4]

There are numerous preanalytical variables associated with coagulation testing that may impact the diagnostic accuracy of a test result. These variables are categorized into: patient selection (use of anticoagulants, liver disease, bleeding disorder), specimen collection (poor venipuncture, inadequate anticoagulant [ratio of 1:9 is not maintained], collection

in wrong tube, improper fill volume), specimen transport (old sample, improper temperature during transport, inappropriate handling of specimens) specimen processing and storage (inappropriate centrifuge speed and time, stored at warmer than recommended temperature, prolonged storage), others (volume expanders [e.g. crystalloids], antibiotics [lipoglycopeptides], autoimmune disorders, hematin, systemic fibrinolytic drugs) . Therefore, it is integral for each lab technologist and clinician to assess and consider the impact of these variables when interpreting coagulation test data. [1]

According to Clinical and Laboratory Standards Institute (CLSI) H21-A5 specimens should be analyzed within 24-h for PT and 4-h for APTT if stored at room temperature (25ºC).Therefore, the potential impact of pre-analytic factors such as storage temperature and time need to be taken into account when reporting PT and aPTT results.[5] In Pakistan, due to unavailability of temperature moderating systems in most centers, recent expansion in outreach laboratories, and suboptimal adherence to established guidelines, it has been observed that these requirements are often not met with. In summer (April to September), the average temperature in most cities in Pakistan ranges from 30-32ºC, and can even rise up to 45ºC. The current study was carried out to determine the effect of sample storage duration on PT and aPTT, when samples are stored at ambient temperature in summer. All published studies thus far have analyzed time-dependent changes in PT and aPTT by storing samples either at room temperature (20-24ºC), or lower (4ºC, -20ºC, -70ºC). Therefore, the current study is the first one documenting time-dependent changes in PT and aPTT when samples are kept at the prevailing temperature in summer in tropical and sub-tropical countries like Pakistan. Documentation of changes in PT and aPTT occurring as a result of delays in testing will, in turn, assist laboratories in Pakistan and other countries with similar summer climates to determine the course of action to be taken in individual cases – to accept or reject the sample, and the nature of comments, if any, to be included with the results.

MATERIALS AND METHODS

The study was conducted at King Edward medical University, Lahore in June 2021. It was a cross-sectional study. The study population consisted of 80 asymptomatic adults requiring routine blood investigation. Patients with liver disease, bleeding or thrombotic disorders, pregnancy or anticoagulant therapy were excluded. After obtaining approval from the institutional Ethical Committee, 80 blood samples sent to the laboratory for analysis of PT and aPTT were included in the study. Relevant data were recorded on the pre-designed proformas. PT and aPTT values at the specified time intervals were recorded.

Blood collected from the cephalic vein was transferred, within 20 seconds, into tubes containing 3.8% sodium citrate, and immediately centrifuged. Plasma from each sample was divided into five aliquots to assess PT and aPTT at the specified time intervals. The first aliquot was analyzed immediately after collection i.e. at 0 hour (reference sample), the second at 4 hours, the third at 8 hours, the fourth at 12 hours and the fifth at 24 hours. The samples were kept at ambient temperature throughout before analysis, recorded to be varying between 34ºC and 38ºC, all the times during the study period. Temperature was maintained by placing the samples in incubator to simulate the ambient temperature (daytime) so that fluctuation in temperature would not confound the results. Samples with clotting times of more 180 seconds were, however, excluded as these values depicted disease state (part of exclusion criteria) or improper sampling hampering the results. Each sample was tested in duplicate; the result being taken to be the mean of the two values.

The procedure for prothrombin time consisted of placing 100 µL of citrated plasma in a test tube preheated to 37ºC and subsequently adding 200 µL of tissue factor (PT reagent) in the test tube. Upon the addition of the reagent, a stopwatch was started and the time taken for the sample to clot was measured. The time, expressed in seconds, from the plasma-reagent mixing to a visually detected clot formation was defined as the PT.

The procedure for activated partial thromboplastin time consisted of placing 100 µL of citrated plasma and 100 µL of aPTT reagent (preheated to 37ºC) in a test tube preheated to 37ºC, followed by incubation for 3 min at 37ºC. After incubation, 100 µL of calcium chloride (preheated to 37ºC) was added to the test tube. Upon the addition of calcium chloride, a stopwatch was started and the clotting time was measured. The time, expressed in seconds, from this addition to a visually detected clot formation was defined as aPTT.

Statistical Analysis:

The normal value of PT was taken as 11-16 seconds, a value more than 16 seconds being considered deranged. The normal value for APTT was taken to be 28-40 seconds, while a value more than 40 seconds was taken as deranged. Data was recorded and analyzed in Statistical Package for Social Sciences (SPSS) Program version 23.0. PT and aPTT at different time intervals were expressed as mean ± SD. Paired samples t-test was used to determine the statistical significance of the differences between the initial values at 0 hour (reference value) and the successive ones. P-values of less than 0.05 were considered statistically significant. Clinically significant difference was calculated as the mean percentage change: (PT/aPTT z hr – PT/aPTT 0 hr)/PT/aPTT z hr × 100%. A mean percentage change of more than 10% was taken as clinically significant.

RESULTS

When compared with 0 hour, PT values at 4, 8, 12 and 24 hours showed mean percentage changes of 1.95%, 3.80%, 6.21%, and 8.97% respectively, but never crossed 10% cut off limit. When normal values were analyzed separately, the 10% cutoff was not crossed. (Table 1).

When aPTT values were analyzed, the mean percentage changes at 4, 8, 12 and 24 hours were 3.89%, 4.85%, 25.40 % and 40.40% respectively. The change hence was clinically significant after 8 hours. aPTT results analyzed separately for normal values that showed mean percentage changes less than 10% up to 8. (Table 2).

Table No.1: Comparison of normal values

	Mean ± SD	Percent Change	p-value
0 Hour	11.93±1.2		
4 Hour	12.24±2.4	1.38	<0.5
8 Hour	13.53±2.7	2.67	<0.05
12 Hour	14.20±2.6	5.50	<0.001
24 Hour	15.81±2.4	7.81	<0.001

Table 1: Mean ± SD of PT values, percent change from the value at 0 hour, and p-values of the differences at specified time intervals from the value at 0 hour.

Table No.2: Differences

	Mean ± SD	Percent Change	p-value
0 Hour	31.95±3.6		
4 Hour	33.95±2.4	2.98	<0.1
8 Hour	35.29±2.1	4.50	<0.01
12 Hour	45.184±2.3	24.45	<0.001
24 Hour	55.35±2.1	38.30	<0.001

Table 2: Mean ± SD of aPTT values, percent change from the value at 0 hour, and p-values of the differences at specified time intervals from the value at 0 hour.

DISCUSSION

The study was aimed at determining the effect of delays in testing on the validity of PT and aPTT results, when samples are stored at summer temperatures (34ºC-38ºC), commonly witnessed in tropical and sub-tropical countries like Pakistan. Samples for PT and aPTT are mostly drawn in wards or collection centres, and later transferred to laboratories. Plasma clotting factors have limited half-lives, and due to delays in testing as a result of sample transfers, PT and aPTT test results might be rendered unreliable.[5] According to BCSH guidelines, only a limited time frame (4 hours) at optimal temperatures (20-24ºC) is all that can be allowed for the performance of these tests reliably.[6] This, unfortunately, is not the case in most situations in Pakistan; due both to delays in testing, and storage of samples at sub-optimal temperatures.

The results of the current study suggest that PT tests do not affect clinical interpretation till 24 hours even when they are kept at a temperature as high as 38ºC. This, however, holds true only for samples in which PT falls within the normal range at 0 hour. For aPTT tests that are normal at 0 hour, valid results may be obtained uptil 8 hours, after which a marked deviation in results is seen which may be attributed to loss of labile factors.. The current study was carried out at temperatures ranging from 34ºC-38ºC. No published study analysing changes in PT and aPTT over time has been carried out at such high temperatures. All previous studies have been conducted either at room temperature (20ºC - 24ºC), or lower (4ºC, -20ºC, -70ºC). [7, 8]

According to a study conducted by Sajjad A Geelani et al[9], analyzing samples stored at 2-8ºC and at RT (room temperature), PT results remained reliable for upto 24 hours at RT and at 2-8ºC. APTT remained reliable upto 4 hours when tested at RT and at 2-8ºC A study conducted by Osta Manish et al[7] in India analysed PT and aPTT at RT (18-25 ºC) which revealed no clinically significant changes in PT for upto 24 hours and upto 4 hours for aPTT. According to a study conducted by Toulon P et al[10] PT/INR, and aPTT, can be reliably evaluated in tubes stored unspun at room temperature for up to 8 hours after blood collection. However some older studies conducted by Zhao et al[8] and Yao et al[11] demonstrated that storage time interval upto 24 hrs for PT and 8hrs for APTT at RT is acceptable. Similar studies have been done in early 2000 which revealed variable results. There results were analysed for the sake of comparison with our findings. M.A. Awad et al[12], analyzed samples stored at 4ºC and at 24ºC. He concluded that if samples are kept at 4ºC, results do not change clinical interpretation till 24 hours, but if kept at 24ºC then the results are valid only uptil 6 hours. The study conducted by GL Salvaign et al[13] concluded that whatever the temperature conditions, results for PT and APTT are valid only uptil 6 hours. The study conducted by Matthes B, Fischer R and Peetz D[14] reported that both PT and APTT can be reliably be tested uptil 8 hours post-collection. The storage temperature in this study is, however, not mentioned. According to another similar study conducted by Rao LV, Okorodudu AO, Petersen JR, Elghetany MT[15] either plasma or whole blood samples can be accepted for PT testing up to 24 hours post-collection and for aPTT testing up to 8 hours only, when transported at room temperature (20ºC -24ºC). Saghir S et al[16] concluded that when samples are stored at 24ºC, PT can only be performed till 4 hours and aPTT till 2 hours.

The wide variation in reported results may be attributed to the divergent preanalytical and analytical variables under which the studies were carried out, the most important of which is the storage temperature. Moreover, some studies have used statistical

significance of differences with initial values as an index of validity of results, while others have used the clinical significance for this index.

In the present study, we have reported both the mean percentage changes from initial values, as well as the statistical significance of the differences from the initial values. In our opinion, however, for all practical purposes, the mean percentage change from intial values can more reliably determine sample validity. The present study showed that though differences from initial values became statistically significant early on in the course of the study, clinically significant differences became apparent later on.

Therefore, PT can be reliably reported till 24 hours post-collection, and aPTT till 8 hours, even if samples are kept at a temperature of up to 38^{o}C. In situations where a reanalysis of samples is required, and the initial values are known, PT can be reliably reported even until 24 hours post-collection if the value obtained at 0 hour is known to be within normal limits. On the other hand, aPTT results remain valid until 8 hour if the initial results are within normal limits.

Ideally, PT and aPTT tests should be performed soon after sample collection, and it is desirable that we achieve complete adherence to established guidelines for sample storage. The present study demonstrates, however, that higher temperatures do not appreciably reduce the recommended time frames for testing of PT and aPTT. We would therefore recommend other comparative studies, carried out in similar conditions, validating or refuting the present one. This would enable laboratories to determine validity of samples that have been kept under less stringent conditions, especially in hot tropical and sub-tropical climates like those found in Pakistan.

CONCLUSION

Samples for PT testing give acceptable results up to 8 hours post collection, and for aPTT testing up to 4 hours, when stored at ambient temperatures during summer seasons.

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Original Article

Role of Transferrin Receptor Protein in Cancer Treatment

Quratulain Maqsood[1], Esha Ameen[2], Aleena Sumrin[1] and Hina Saleem[1]

ABSTRACT

Objective: This article aims to show the association of the transferrin receptors with cancer and take it as the target in cancer therapy.

Study Design: Prospective Experimental research study

Place and Duration of Study: This study was conducted at the Center for Applied Molecular Biology (CAMB) Punjab University Pakistan, from January 2021 till August 2021 for a period of 08 months.

Materials and Methods: Using the CellTiter 96 AQueous Assay (Promega), we determined the 50% growth inhibition values for the substances. Membrane proteins solubilized and separated on SDS PAGE, dyed, and digested in-gel using conventional methods. HPLC was used to identify the proteins. cDNA was generated using the Retroscript cDNA synthesis kit (Ambion). Time-delayed fluorescence was measured using a Wallac Victor plate reader (PerkinElmer) after each well was incubated with Europium-Streptavidin.

Results: Tumor cell apoptosis is triggered by GA binding to TfR. The results of these studies suggest that GA can be used for targeting the TfR in cancer therapy.

Conclusion: Targeting the TfR has been shown to be effective in the treatment of cancers but has shown some cytotoxic effects as well. The wide use of the TfR in the treatment of cancers has helped target specific receptors against cancer cells. In the future, it is expected that targeting TfR for cancer therapy can be improved to overcome the side effects of this therapy and highly target-specific drugs will be produced.

Key Words: Transferrin, Receptor 1, Cancer, Ferric, antibody, Expression

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INTRODUCTION

Ferric (iron) is an important biological element. It plays an important role in metabolism and other physiological processes. It has a function in every type of cell because it is related to heme formation and other proteins that have their role in the transportation of oxygen. With its role in oxygen transportation, it is found in all cells for energy production[1]. It acts as a cofactor in DNA replication. It is also the part of enzymes that play a role in repair and synthesis processes. While energy generation, iron produces oxygen free radicals in the cells[2]. These free radicals increase the oxidative stress in the cell and lead to the damage of DNA, lipids, and proteins.

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The high concentration of iron in the body can cause the formation of tumors and many other problems. Therefore, the proper maintenance of iron concentration in the body is necessary to avoid these kinds of complications. Likewise, the low concentration of iron can cause the death of the tumor cells[3].

Iron cannot be transported simultaneously in the cell; it needs another molecule for its transfer called 'transferrin'. It binds to the ferric iron and transports it to various parts of the body. It is a plasma glycoprotein present in the serum, milk, and melanin pigment[4]. Its function is to transfer iron within the body, mark inflammations, fight against foreign particles by helping the body's innate immune response and identify malignancies. The transferrin molecules also need a carrier protein called 'transferrin receptors[5]. These are the transmembrane glycoproteins. Various studies have clearly shown the role of the transferrin receptors in cancer therapy. A few methods are known to use transferrin in the treatment and diagnosis of cancer, one of them uses transferrin receptor 1 (TfR1). It targets intracellular iron reserves. It is based on the TfR1 mediated cytotoxic drug conjugates[6].

TfR1 is a type II transmembrane glycoprotein that binds to the transferrin molecule bound with ferric ions[7]. The binding of TfR1 with transferrin-iron (Tf-Fe) generates a clathrin-mediated endocytosis response. This process decreases the pH of the cell to 5.5 leading

to the release of the ferric ion[8]. This TfR1 is a recyclable molecule. The tumor cells have a high level of TfR1 and it helps in iron uptake. The clinical evidence has shown that there is a high level of TfR1 in cancer patients the antibody treatment against the TfR1 induced tumor is being studied as a cancer therapy because of the remarkable affinity of TfR1 towards the antibodies[9]. Therefore, TfR1 is considered the anticancer/antitumor agent for various types of cancers.

MATERIALS AND METHODS

Apoptosis Assays. Cellular viability assessment with propidium iodide, DAPI labeling, and cell cycle analysis. Caspase induction was performed. Using the CellTiter 96 AQueous Assay (Promega), we determined the 50% growth inhibition values for the substances.

Identification of GA Target. Membrane proteins solubilized and separated on SDS PAGE, dyed, and digested in-gel using conventional methods. HPLC was used to identify the proteins.

GA Target identification.

Conventional methods were used to solubilize, separate, dye, and digest membrane proteins. Identification of the proteins was conducted using HPLC.

cDNA synthesis, siRNA transfections, and real-time PCR: Ambion, Austin, Texas, chemically produced siRNA oligos for human transferrin receptors and caspase 8. Caspase-8 siRNA had a target sequence of 5 AAG GAA AGT TGG ACA TCC TGA 3 and TfR siRNA had a sequence of 5 AAC TTC AAG GTT TCT GCC AGC 3. Furthermore, Ambion provided human cyclophilin-control siRNA oligos and negative scrambled control siRNAs. In order to synthesize cDNA and run quantitative PCR assays, standard procedures were followed. cDNA was generated using the Retroscript cDNA synthesis kit (Ambion). In the Quantitect kit with normal settings and Sybrgreen inclusion, we performed quantitative PCR on the Light Cycler.

Assays for binding: The cells were then treated with 1 M tritium-GA with or without 20 M unlabeled GA at 37°C. A liquid scintillation counter was employed to measure bound tritium-GA at the pertinent time points. The TfR-coated wells were first treated with GAbiotin, followed by washing, and then incubated with nontagged analogs or binding washing buffer as a control. Time-delayed fluorescence was measured using a Wallac Victor plate reader (PerkinElmer) after each well was incubated with Europium-Streptavidin.

RESULTS

TfR Identified as the Molecular Target: A cell-surface target was activated by GA to induce apoptosis. Some GA derivatives were initially shown to be capable of withstanding bulky group changes while still inducing apoptosis. To better understand the target, we designed a biotin-conjugated GA that could be attached to fluorescein microspheres, streptavidin microspheres, or agarose conjugates. The binding of tritium-GA to Jurkat cells treated at 37 °C and 4 °C is saturable and temperature-dependent, which is inhibited by cold unlabeled GA. We used inactive-GA as a competition for determining the specificity of the bound protein. According to these results, GA mediates apoptosis through a cell surface receptor.

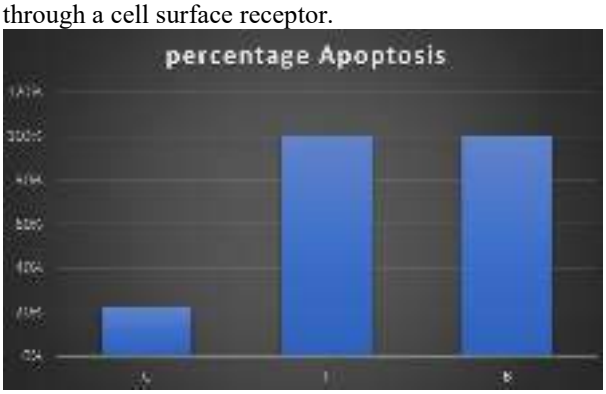

Figure No.1: The percentage of apoptosis when GA binds to receptor on the cell surface

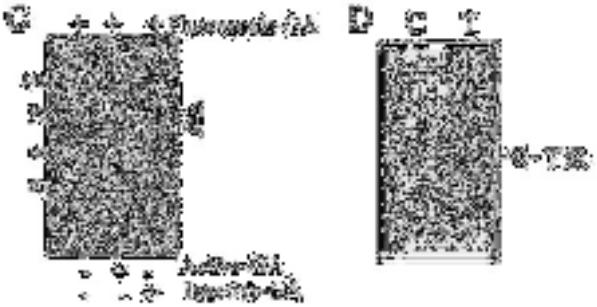

Figure No.2: Immunoblotting with anti-TfR antibody allowed detection of immunoprecipitated lysate

The downregulation of TfR affects cell apoptosis induced by GA: GA-induced apoptosis is more likely to occur in tumour cells that overexpress TfR (T47D and 293T). Proliferation rates did not vary with GA sensitivity, but TfRs expression was correlated with GA-induced apoptosis.GA-induced apoptosis is more likely to occur in tumour cells that overexpress TfR (T47D and 293T). A significant correlation was found between TfRs expression and GA-induced apoptosis, but no correlation was found between proliferation rates and GA sensitivity. Furthermore, we used paclitaxel, a recognized cytotoxic drug, to show that down-regulating TFR was not associated with reduced apoptosis. This indicates that cells lacking Tfr may not be resistant to every apoptotic trigger.

Mechanism of TfR-induced apoptosis: The apoptotic pathway is strongly activated by GA. The activation of caspase-8 by GA is similar to the activation of caspase-8 by anti-Fas. When certain regulatory molecules in this pathway are down-regulated, GA-induced cell death is delayed rather than inhibited. ADD loss has little to no

effect on GA-mediated apoptosis, based on these results.

Table No.1: Show the activity in apoptosis induction assay

Compound	Competition IC50 in TR binding assay, M	Fold caspase-3 activation	EC50
GA	5.1	19	535
Methyl-GA	4.6	23	325
Inactive-GA	>35	1.4	ND
unsaturated backbone	13.7	2	4160
saturated backbone	>33	1	ND

DISCUSSION

Brain Tumor: The regulation of the function of glioma cells (tumor of glial cells) and its progression in the brain cells is dependent on the TfR1 expression. It is observed that the level of TfR1 increases in brain cancer. Recent studies have shown that the TfR1 can be used in the prediction of glioblastoma prognosis and identification of targets to produce drugs[10].

Breast Cancer: Breast cancer is considered the most common and devastating cancer in females all over the world. The progression of this cancer also requires more uptake of iron. It can be identified by increased expression of TfR1. It helps in the identification of the biomarkers of cancer and its treatment at the early stages[11].

Colon Cancer: The level of transmembrane glycoprotein TfR1 is related to the rate of division of the tumor cells. Its expression is increased in the cancer cells; therefore, it is used as the target in cancer treatment [12].

Liver Cancer: Iron is considered a developmental factor for hepatocellular carcinoma (HCC) patients who also have hereditary hemochromatosis (HH). It is discovered that the wild type of HH is a complex of TfR with a mutation at two proteins, Cys 282 Tyr and His 63 Asp. It increases the binding strength of the TfR and Tf[13]. It eventually increases the uptake of iron and causes the rapid proliferation of HCC. The expression of the TfR gene increases with the increase in the stage of cancer. It was suggested that in HCC tissues, the level of miR-152 is decreased and TfR gene expression is increased. It is because of the downregulation of the miR-152 that mediates the post-transcriptional modification. Therefore, this process can be used in the treatment and diagnosis of HCC[14].

Ovarian Cancer: TfR level has a very vital role in ovarian cancer. It was proved that the metabolism of iron is interrupted during ovarian cancer by changing the targets. The level of TfR1 expression is raised in the tumor cells. This can be used in the diagnosis of cancer[15].

Prostate Cancer: The experimental studies have shown that the level of the serum transferrin receptors in males increases during this cancer. But the increasing stage of cancer does not affect the level of TfR1 expression. This raised expression of TfR1 is used as a biomarker for the diagnosis of this cancer[16].

Lung Cancer: It was suggested that the level of TfR1 increases in lung cancer along with the increase in the alpha-globin level. A receptor called the epidermal growth factor receptor controls the iron metabolism by binding to TfR1 and transporting it again to the cells of the lungs. This is a very important phenomenon in the proliferation of cancer and can be used in the therapy of lung cancer[17].

Leukemia (Blood Cancer): This is related to TfR1 in such a way that TfR1 is a carrier protein for iron transport and iron transport and metabolism is very high in the leukaemia's. The level of TfR1 is very high in blood cancer. Of the two types of leukaemia, T-cell leukaemia and B-cell leukaemia, the expression of the TfR1 is higher in the former[18]. The TfR1 causes an increase in the proliferation of the blood cells. The increase in the number of cells can increase the level of haemoglobin in the patients. Therefore, TfR1 can be used as a target for the treatment of leukaemia[19].

Cancer Therapy by TfR1: According to studies related to TfR1, curcumin can used be used as an effective drug in chemotherapy. It regulated the level of TfR1 and the iron regulatory proteins (IRP)[20]. It resuscitates the body's natural apoptosis phenomenon. The antibody therapy is used in it. The anti-transferrin receptor antibodies are designed against the transferrin receptors for the therapy of cancer. These are the monoclonal antibodies that inhibit the uncontrolled division of cells in T-cell leukaemia.

CONCLUSION

Cancer is a very deadly disease. It is caused by many reasons like mutations. The increase in TfR level is a very important cause of the progression of cancer. Targeting the increased level of TfR can be proved effective in cancer therapy. It is used in the diagnosis of cancer as well as in drug production and suggestion. Mainly, reviving apoptosis by inhibiting iron uptake is the key process to treat cancer. The drugs are being designed by taking all these points under consideration. The tumor-specific target therapy is considered the most promising way of treating cancer. Therefore, target-specific drugs should be produced. All these steps are taken to curb this fatal disease. To conclude, these therapies are being used worldwide and cancer is no more an untreatable malady.

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Author's Contribution:

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Drafting:	Esha Ameen, Aleena Sumrin
Data Analysis:	Aleena Sumrin, Hina Saleem
Revisiting Critically:	Quratulain Maqsood, Esha Ameen
Final Approval of version:	Quratulain Maqsood

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

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Original Article

Association of Proton Pump Inhibitors with Hepatic Encephalopathy among Patients with Liver Cirrhosis

Syed Yasir Hussain Gilani[1], Rizwan Ali Khan[1], Saima Bibi[2], Farrukh Addil[2], Sidratul Muntaha[3] and Asif Mehmmod[4]

ABSTRACT

Objective: To find an association between PPIs and increased risk of hepatic encephalopathy in cirrhosis.
Study Design: Case-Control study
Place and Duration of Study: This study was conducted at the conducted in the department of Medicine and gastroenterology, Ayub Teaching Hospital; Abbottabad from August 2019 to June 2020 for a period of 10 months.
Materials and Methods: All patients with liver cirrhosis and hepatic encephalopathy presenting to the department of medicine and gastroenterology were included through a non-probability consecutive sampling.
Results: A total of 166 patients with liver cirrhosis were enrolled in the study including 93 (56.0%) male and 73 (44.0%) female patients. The mean age of the patients was 59.00±9.789 years. A total of103(62.0%) patients were found PPIs users and 63(38.0%) were found PPI nonusers. Patients using PPIs were 4 times more likely to develop Hepatic Encephalopathy as compared to those patients of liver cirrhosis who were not using PPIs (OR= 4.276, CI= 2.172-8.420).
Conclusion: Patients with liver cirrhosis who are using proton pump inhibitors are more likely to develop hepatic encephalopathy when compared to the control group.
Key Words: Proton Pump Inhibitors, Hepatic Encephalopathy, Liver Cirrhosis

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INTRODUCTION

Liver cirrhosis has emerged as a major cause of morbidity and mortality and affected about 2.8 million people worldwide and resulted in 1.3 million deaths in 2015.[1] In the developing countries, liver cirrhosis and its complications are a major health problem. Hepatic encephalopathy, a major complication of cirrhosis, has an estimated prevalence of 22–74% in USA.[2] Prevalence of hepatic encephalopathy in Pakistan is 63.4%.[3] Infection and upper gastrointestinal bleeding are major precipitating factors for hepatic encephalopathy. About 30% of patients with cirrhosis die due to hepatic encephalopathy.[4]
One year survival rate is 36% after onset of hepatic encephlopathy.[5]

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Proton pump inhibitors (PPIs) are widely used (78.3%) in cirrhosis to prevent bleeding associated with portal hypertension.[6] PPIs, by reducing acid secretion, can increase the risk of gastrointestinal infections by raising pH of stomach and making it more prone to colonization by various pathogenic bacteria.[7] PPIs may increase absorption of gut-derived nitrogenous substances because of its effect on retarding gastrointestinal motility, delaying gastric emptying rate and decreasing gastric mucus viscosity. Increased ammonia-producing enteric bacteria in patients is shown to be a risk factor for hepatic encephalopathy.[8]
In past, many trials have been conducted under different circumstances concerning the association of PPIs with hepatic encephalopathy in patients with liver cirrhosis. The available data is conflicting. In a case–control study by Tsai CF,[9] approximately 38% of cirrhotic patients with HE and 21% of patients without HE were taking defined PPIs. They concluded that PPI's are associated with increased hepatic encephalopathy (adjusted odds ratio was 1.738) while in a study by Dam G,[10] cumulative risk HE was 31% for those who used PPIs at baseline versus 25% for those who did not and the adjusted odds ratio was 1.36 ($p>0.05$).[11] The results of these two studies had shown variable results with Tsai CF establishing that using PPI is associated with higher risk for hepatic encephalopathy, where Dam G, et al concluded that there exist no association

with hepatic encephalopathy among patients with liver cirrhosis.

Liver cirrhosis is becoming an epidemic in Pakistan due to high prevalence of hepatitis B and C in our community i.e. 7.6%.[12] On the other hand, proton pump inhibitors are also frequently used in such patients. So, the relationship between PPI use and hepatic encephalopathy should be well-defined. Because cirrhosis, hepatic encephalopathy and widespread use of PPI are widely prevalent in our population, there is a dire need for assessing causal relationship if any. This study was conducted to find an association between use of PPIs and increased risk of hepatic encephalopathy in cirrhotic patients. There is a paucity of data in our region so the present study was designed with an aim to generate evidence so as to provide guidance to healthcare practitioners for careful prescription of PPI's in patients with liver cirrhosis.

MATERIALS AND METHODS

This case control study was conducted in the department of medicine and gastroenterology of a tertiary care hospital over a period of one year (1st August 2019 to 31st July 2020). Sample size was calculated by using the WHO software for sample size calculation taking confidence Level of 95% with Exposure Rates in Cases (use of PPI) = 38%[9] and Exposure Rates in controls (use of PPI) = 21%[9] and Relative Precision of 5%. A total of 166 patients with liver cirrhosis were included through a non- probability consecutive sampling after the approval of research and ethical committee of the institute. Informed consent was obtained and demographic profile (age, gender and contact) was noted. The patients with HE in liver cirrhosis were labeled as cases(n=83), and patients without HE in liver cirrhosis were labeled as controls(n=83). All the patients were evaluated for detection as PPI user (yes or no) as per operational definition in both groups. Data was entered on a structured proforma.

Cases were defined as patients of either sex between 30-70 years of age presenting with hepatic encephalopathy and admitted for the last 6 days, while controls were of the same characteristics with liver cirrhosis but without encephalopathy. Patients with HAV, HDV, HIV and CMV along with hepatocellular carcinoma, history of gastrointestinal bleeding or psychiatric illness were excluded from both case and controls.

The data was entered and analyzed in SPSS version 20.0. Mean and standard deviation was calculated for quantitative variables like age. Frequencies and percentages were calculated for categorical variables like gender and age groups. Odds ratio was calculated to measure association between proton pump inhibitors and hepatic encephalopathy among cirrhotic patients and calculating 95% confidence interval for ORs.

RESULTS

A total of 166 patients were enrolled into this study and were equally divided into cases and controls as per definition. Out of 166 patients, 93 (56.0%) were male and 73 (44.0%) were female. Mean age of the participants was 59.00±9.789 years. Patients were further divided into two age groups. A total of 136(81.9%) patients were found in age group of 51 to 70 years and 30(18.1%) were in age group of 30 to 50 years. Out of the total study population, 103(62.0%) were PPIs users and 63(38.0%) were PPI nonusers (Table 1). Patients were stratified on the basis of PPI usage. In the age group 30 to 50 years, 19(11.4%) were using PPI while 11(6.6%) were not. While in the age group 51 to 70 years, 84(50.6%) were PPI users and 52(31.3%) were nonusers. Among the male participants, 58(34.9%) were PPIs users and 35(21.1%) were nonusers while among females, 45(27.1%) were PPIs users and 28(16.9%) were nonusers (Table 2). The data analysis revealed that male patients with liver cirrhosis using PPIs were 1.09 times more likely to develop Hepatic Encephalopathy than female (OR= 1.09, CI= 0.37-3.18) (table 3). The association of hepatic encephalopathy in cirrhotic patients was assessed with respect to proton pump inhibitors usage. Among cases, 65(39.2%) patients were PPIs users and 18(10.8%) were non users while in controls 38(22.9%) patients were PPIs users and 45(27.1%) were non users. The patients with liver cirrhosis using PPIs were more than 4 times likely to develop Hepatic Encephalopathy as compared to those patients of liver cirrhosis who were not using PPIs (OR= 4.276, CI= 2.172-8.420) (Table 4).

Table No.1: Patient characteristics (n=166)

Mean age in years	59.00±9.789	
Mean age in years (Male)	60.80±8.350	
Mean age in years (Female)	56.71±11.001	
Gender	No. of Patients	Percentage
Male	93	56%
Female	73	44%
Total	166	100%
Age Groups		
30 to 50 years	30	18.1%
51 to 70 years	136	81.9%
Total	166	100%
PPI Usage		
PPI Users	103	62%
PPI nonusers	63	38%
Total	166	100%

Table No.2: Age group and gender wise distribution in relation to PPI Usage

Age group	PPI users	PPI Nonusers	Total
30 to 50 years	19 (11.4%)	11 (6.6%)	30 (18.1%)
51 to 70 years	84 (50.6%)	52 (31.3%)	136 (81.9%)
Total	103 (62.0%)	63(38.0%)	166(100%)
Gender			
Male	58 34.9%	35 (21.1%)	93 (56%)
Female	45 27.1%	28 (16.9%)	73 (44%)
Total	103(62%)	63 (38%)	166 (100%

Table No.3: Association of gender to PPI usage in patients with hepatic encephalopathy in Cirrhosis

Gender	Hepatic encephalopathy with liver cirrhosis		Total	Odds ratio	CI
	PPI User	PPI Non user			
Male	41	11	52	1.09	0.37-3.18
	49.39%	13.25%	62.6%		
Female	24	7	31		
	28.9%	8.4%	37.3%		
Total	65	18	83		
	78.31%	21.68%	100.0%		

Table No.4: Association of Hepatic encephalopathy to PPI usage in patients with cirrhosis

Liver Cirrhosis	PPIs		Total	Odds ratio	CI
	user	Nonuser			
HE among liver cirrhosis	65	18	83	4.276	2.172-8.420
	39.2%	10.8%	50.0%		
Without HE among liver cirrhosis	38	45	83		
	22.9%	27.1%	50.0%		
Total	103	63	166		
	62.0%	38.0%	100.0%		

DISCUSSION

Liver cirrhosis and its complications like hepatic encephalopathy have emerged as a major cause of morbidity and mortality worldwide. Studies have reported that PPIs use is positively associated with increased incidence of hepatic encephalopathy in patients with liver cirrhosis thus, potentially complicating the management of liver cirrhosis.

Our study showed a slight preponderance of male patients (56% males vs 44% females). The frequency of PPI users was higher than nonusers. Similar results are reported in literature while assessing hepatic encephalopathy in cirrhotic patients in PPIs users and nonusers in the study conducted by Tsai CF, et al.[9] In our study, the stratification by age showed that the majority of patients were in age group of 51-70 years. Of these, nearly half of the patients were PPI users 30 In another study, almost same results were reported regarding PPIs users and nonusers having cirrhosis with hepatic encephalopathy in the study conducted by Tapper EB et al. [12]

Our study demonstrated slightly higher number of male patients with hepatic encephalopathy using PPI (OR=1.09). In another study by Dam G et al, almost similar results have been reported[10]. Our study showed that a significantly higher number of patients with liver cirrhosis who were using PPI developed hepatic encephalopathy (OR=4.276). Similar results are reported in literature by Zhu et al where Proton Pump Inhibitor use in cirrhotics was significantly higher in patients with hepatic encephalopathy[13]. 128 In another study by Lin et al the PPI usage was higher in patients having hepatic encephalopathy with liver cirrhosis[14]. A meta-analysis encompassing nine studies reported a 2.08 fold greater chances of development of hepatic encephalopathy among PPI users[15]. Another study from Italy reported the association of PPI usage with development of hepatic encephalopathy and consequent decreased survival in patients with liver cirrhosis[16].

CONCLUSION

The patients with Liver cirrhosis who are taking PPIs are at an increased risk of developing Hepatic encephalopathy. Hence, proton pump inhibitors should be prescribed to patients with liver cirrhosis with great caution. This study has its own limitations as it was a single- center based study of a small sample size in our specific population, therefore the results cannot be generalized on general population.

Author's Contribution:

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Original Article

The Presentation and Surgical Management of Diabetic Foot

Surgical Management of Diabetic Foot

Gul Sher Khan[1], Muhammad Amir[4], Asif Mehmood[1], Alam Zeb[2] and Anwar Shah[3]

ABSTRACT

Objective: To highlight the presentation and management of diabetic foot disease.
Study Design: A retrospective study
Place and Duration of Study: This study was conducted at the Surgical Department of Khalifa Gul Nawaz Teaching Hospital (KGNTH) Bannu from June 2017 to July 2019 for a period of 02 years.
Materials and Methods: A total of 320 patients with diabetic foot ulcer with infection were included in this study.
Results: Out of these 320 patients, males were 208 (65%) and females 112 (40%). The average age was 53.5 years (30-75 yrs). Majority of the patients (90%) had type II diabetes mellitus (DM). 109 patients (34%) had suffered from DM for <10 years and 211 (66%) had been diagnosed for >10 years. In this study 272 patients (85%) were on oral hypoglycemic drug with diet control and the remaining 48 (15%) were on insulin. History of trauma preceding the infection was positive in 20% (64) patients. Previous history of ulcer and infection was positive in 45% (144) patients. Positive culture for polymicrobial infections was found in 90% (288) of patients. Staph aureus was the most common isolate along with strepto cocci, pseudomonas and anaerobes and fungi.
Conclusion: Diabetic foot infective disorder is a common cause of morbidity and mortality among patients with diabetes throughout the world and is a leading cause of non-traumatic lower limb amputation. A multidisciplinary team approach concentrating upon a tight glysaemic control, education on foot care, a suitable foot wear, control of infection and early surgical intervention is needed to decrease the morbidity and mortality of diabetic foot disease. Due to polymicrobial infection and antibiotic resistance, early surgical intervention must be provided.
Key Words: diabetic foot infections, diabetic foot ulcer, diabetic neuropathy, diabetic microangiopathy and amputation

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INTRODUCTION

Diabetic foot disease is a rising health problem worldwide and the most frequent cause for hospital admission [1, 2]. The incidence of diabetic foot disease is increasing [3]. Diabetic foot disease is a dangerous and disabling complication of diabetes and the number one cause for non-traumatic lower limb amputation [4]. 15-25% of patients of diabetes are likely to develop diabetic foot disease during their lifetime [2]. Some 40-70% of the non-traumatic amputations of the lower limb are because of diabetes mellitus [5].

Peripheral neuropathy and microangiopathy are the two important causes for diabetic foot ulceration and infection.

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Managing patients with diabetic foot ulcer and infection is a multidisciplinary team approach needing; [1] patient stability by controlling blood sugar, renal and cardiac functions and infection (by physician) and [2] early recognition of the lesion and prompt initiation of an appropriate antibiotic, aggressive surgical debridement of the dead and necrotic tissue and bone, tight control of blood sugar, correction of arterial insufficiency and delayed reconstruction to achieve limb salvage (by surgeon) [6, 7, 8] .

The risk factors for the development of diabetic foot disease are; gender (male), period of diabetes for more than 10 years, old age of the patient, high body mass index and other co-morbid conditions such as retinopathy, peripheral neuropathy and vasculopathy, high glycated hemoglobin level foot deformity, raised planter pressure, infection and inappropriate foot self- care[9,10]. Regular foot examination, patient education, simple hygiene practices, provision of appropriate foot wear, prompt treatment of minor foot injuries decrease diabetic foot infections and their recurrence by 50% and exclude the need for major amputation in non-ischemic lower limb [11].

MATERIALS AND METHODS

The medical record of 320 consecutive patients admitted to Khalifa Gul Nawaz Teaching Hospital

surgical ward with diabetic foot disease from June 2017- July 2019 were reviewed retrospectively. Patient demography e.g. age, sex, occupation, education level, socioeconomic state and co-morbid condition were collected. Clinical features e.g. the type and duration of diabetes, the treatment received, the specific site of diabetic foot infection, past history of ulcer, amputation and Wagner's grades were reviewed. The past history of any type of surgical procedure performed and the outcome, the length of hospital stay was recorded. Routine tests for diabetes mellitus e.g. blood sugar, glycated haemoglobin (HbA1C) (an indicator for glycemic control), swab for c/s from the depth of wound, urine analysis, blood urea and serum creatinin, ECG, echo and chest X-ray were reviewed. The results of lower limb arteriography, the doppler studies and the assessment of pedal pulses were also reviewed.

HbA1C $\leq$7% good control of diabetes.

Hb1AC 7-10% fair control.

Hb1AC $\geq$ 10% poor control of diabetes.

Statistical Data: The data collected were analyzed using SPSS computer software 22. The data were expressed in the form of proportions and frequency for categorical variables. Means and standard deviation were used for continuous variable. Student`s t test and chi square tests were used for differences between qualitative variable. Significance was defined as P value < 0.05.

Various Surgical Procedures Adapted

Type of operation	Frequency	Percentage
Debridement	192	60%
Lower limb amputation;		
Toes/Rye`s amputation	30	9.4%
Below knee amputation	20	6.25%
Above knee amputation	10	3%
Incision and Drainage	42	13%
Skin grafting	6	1.8%
Sequesterctomy	4	1.25%

RESULTS

A total of 320 patients (all having diabetic foot disease) were included in the study, males were > females. The mean age was 54 years (range 30-75 years). Most of the patients (95%) had type II diabetes mellitus (DM), the mean duration was 8 yrs since diagnosis of DM. In this study 109 patients (34%) had suffered from DM for <10 years and 211 (66%) had suffered for >10 years. 272 patients (85%) were on oral hypoglycaemic agents and 48 patients (15%) on insulin, both the group were having poor diabetic control. HbA1C assay indicated that 198 patients (62%) had >7 HbA1C (poor diabetic control). 144 patients (45%) had previous history of ulceration and infection. Only 64 patients (20%) were febrile on presentation and leucocytosis was present in 80 patients (25%).

The fore foot was commonly affected in 53% of cases. Neuropathic foot with infection was more common (52%) than ischemic foot (35%). Wagner's grades II & III were most common (62.5% and 14% respectively). Debridement and incision and drainage (for cellulitis and abscess) were the most common surgical procedures performed (65.5% & 14% respectively).

Table No.1: Wagner's Grades for the Wounds of Diabetic Foot Disease Patients

Grade	Frequency	Percentage
Grade I	35	11.1%
Grade II	200	62.5%
Grade III	45	14%
Grade IV	25	7.8%
Grade V	15	4.6%

Post-operative complication rate was 26.8 %. Surgical site infection was the most common one. Bacterial culture showed polymicrobial series. Staph aureus was the most common isolate, also were streph cocci, pseudomonas, E coli, anaerobes and fungi. The organism showed a high resistance to the commonly used antibiotics, however they were susceptible to lenzolids, vancomycine, clindamycine, imepenems and meropenmes.

There were 20 deaths with a mortality rate of 6.25 %. Mortality was associated with post-operative complications and Wagner's grades $\geq$ 4 ($p = 0.011$). Causes of death were; sepsis in 10 cases, diabetic coma in 4 cases, myocardial infarction in 3 cases and renal failure in 3 cases. The mean hospital stay was 14-21 days and the mortality rate was 6.25%.

Table No.2: Site Specific Incidence of Infection in Diabetic Foot

Site	Frequency	%age
Fore foot	170	53%
Mid foot	44	13.7%
Hind foot	42	13.5%
Whole foot (with ascending infections in some cases)	64	20%

DISCUSSION

The prevalence of diabetic foot disease in diabetic population is 4-10% and it is more frequent in older patients [12, 13, 14]. Some 15-20% patients with diabetes mellitus will develop diabetic foot during their life time. The prevalence of diabetic foot disease is variable worldwide, it was 2-6% in USA, 4.6% in Kenya, 20% in Netherland, 11-19% in Nigeria and 20.4% in Iran, due to the regional variation in the prevalence of DM. The high prevalence of diabetic foot disease in the developing countries is due to illiteracy, poor socioeconomic status, bare foot walking, inadequate control of diabetes and lack of self-care.

From this study it became clear that males were affected more than the females, the mean age of presentation was 54 years and the mean duration of DM was 8 years which are comparable with other studies [15,

[16]. It was also clear that those patients with poor glycemic control, illiterate, with poor socioeconomic conditions were the usual sufferer from diabetic foot infection and amputations. Past history of diabetic foot ulceration and amputation are the known risk factors for subsequent lower limb amputation. The combination of neuropathy and trauma from repetitive pressure during walking result in ulcer formation which resist to heal (Neuropathic/ Trophic ulcer).

In our study the recurrence rate of diabetic foot infection was 45% (144) which is similar to other studies [17].

Diabetic Foot Status (Regarding Vasculature and Sensation)

Type of diabetic foot	Frequency	%age
Neuropathic foot	166	52%
Ischemic foot	112	35%
Neuroischemic foot	42	13%

Wagner's grades II & III (for the severity and depth of diabetic foot wounds and which are widely used by surgeons) were more common (62.5% & 14% respectively) which is comparable to the other study.

Almost all diabetic foot ulcers are septic (infected) at the time of first assessment [18,19]. The least invasive infection is the cellulitis followed by an abscess. Ulceration arising from peripheral neuropathy, peripheral arterial disease and trauma are highly susceptible to secondary infection and gangrene.

Diabetic foot disease is a preventable and curable complication of DM. The rate of lower limb amputation in our studies was 18.75% which comes near to the other studies [16,20]. The mortality rate was 6.25% which is comparable to some other studies [21, 22, 20].

Surgical procedure was performed mainly to limit the spread of infection and gangrene through repeated debridement's and amputation. Minor trauma leading to major synergistic foot infection was the common story [23,24]. Patients were followed for the next one year. Diabetic control was mandatory.

Surgical Procedures Complications

Complications	Frequency	%age
Surgical site infection	25	7.8%
Revision amputation	8	2.5%
Stump gangrene	15	4.7%
Wound dehiscence	20	6.2%
Phantom pain	8	2.5%
Wound haematoma	10	3%

The mortality rate in our study is 6.25% and the mortality rates from western Sudan was 7.4%, 6.7% in a study conducted by Omdurman and 13.7% in Tanzania.

CONCLUSION

Diabetic foot infective disorder constitutes a major cause of morbidity and mortality worldwide and is leading cause of non-traumatic lower limb amputation. A multidisciplinary team approach, targeting a good glycemic control, education on foot care, appropriate foot wear, control of infection (through antibiotic) and early surgical intervention are required to reduce the morbidity and mortality associated with diabetic foot disease. Due to polymicrobial infection and the antibiotic resistance, surgical intervention must be provided.

Author's Contribution:

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Original Article

Green Tea Offers More Nephroprotection than Cinnamon against Bisphenol an Induced Tubular Damage in Rat Kidney: A Histological Quantitative Approach

Huma Beenish[1], Hira Cheema[1], Ayesha Yasser[1], Tooba Khurshid[2], Maleeha Bano[3] and Tayyaba Qurashi[1]

ABSTRACT

Objective: To compare protective efficacy of cinnamon extract and green tea against Bisphenol A induced histological changes in rat kidney.

Study Design: Randomized control trial study

Place and Duration of Study: This study was conducted at the Department of Anatomy, Islamic International Medical College, and National Institute of Health, Islamabad from September 2016 to September 2017.

Materials and Methods: Sixty adult male Sprague Dawley rats were divided into four groups with 15 rats in each group. Control group A rats were given distilled water for 30 days subcutaneously. Experimental group B rats were administered Bisphenol A at a dose of 30mg/kg/day subcutaneously for 30 days. Experimental group C rats were given cinnamon at a dose of 200mg/kg/day orally along with subcutaneous Bisphenol A injection. Experimental group D rats were given green tea orally along with subcutaneous Bisphenol A injections. After dissection right kidneys of all rats were examined for histological changes.

Results: The histological parameters of rat kidneys were observed under light microscope. These included height of epithelium of PCT, luminal diameter of PCT, height of epithelium of DCT and luminal diameter of DCT. Worsening of these parameters from control group was maximally seen in group B. However, both groups C and D caused improvement in all measured histological parameters but group D displayed more nephroprotection than group C.

Conclusion: The oxidative stress caused by Bisphenol A has adversely affected kidneys and green tea was found to be more beneficial in ameliorating nephrotoxic effects of Bisphenol A than cinnamon.

Key Words: Bisphenol A, Cinnamon extract, Green tea, Rat kidney, Histology

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INTRODUCTION

Kidney is the most vital component of urinary system which removes metabolic wastes of human body and conserves fluids and electrolytes.[1] Different disease processes affect histology and function of nephron which lead to renal diseases like glomerulosclerosis and tubulointerstitial fibrosis.[2].

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Acute renal diseases then progress to chronic kidney disease. The consequences related with chronic kidney disease (CKD) include loss of nephron resulting in end stage renal disease leading to early mortality.[3]

Chronic kidney disease also results from environmental toxins which cause oxidative stress to the renal tubular cells leading to cell death.[4] Bisphenol A (BPA) is one of them. BPA is a plasticizer, a polymer of polycarbonated plastics and epoxy resins.[5] Research shows BPA was greater than 2.2 million metric tonnes has since 2011. BPA is used in formation of food containers, drinking bottles, toys, inner lining of metal cans and water supply pipes.[6]

Numerous studies relate prevalence of BPA in human tissues and body fluids such as urine, serum, plasma, saliva and breast milk. Human exposure to BPA occurs mainly through food and drinking water.[7] BPA can be hydrolyzed under high temperature and acidic or basic conditions to leak into food and drink containers. BPA causes its effects in animal models at doses in range of human exposures.[8]

Natural plant derived antioxidants have been used extensively as compared to synthetic antioxidants due to safety, health benefits and consumer suitability.[9] Herbs are increasingly being investigated as adjunct therapies for CKD. Cinnamomum cassia is a common species of cinnamon widely distributed in Asia. Many studies have indicated antioxidative role of cinnamon against kidney damage caused by various toxins and diabetes.[10] A study on beneficial effects of cinnamon showed that a dose of 0.5g/kg can be used safely for medicinal purpose.[11]

In addition to cinnamon, green tea (Camellia sinensis) also protects kidneys due to its antioxidative potential. It possesses anti-inflammatory and anticarcinogenic properties as well. It is also protective against renal injury.[12] This study was planned to compare the modulatory effect of cinnamon and green tea consumption on daily basis to counteract the nephrotoxic changes caused by BPA.

MATERIALS AND METHODS

Research was carried out on sixty adult male rats of Sprague Dawley breed. They were selected by simple random sampling mechanism with balloting method. Their weight was approximately 250 to 300 grams. Animals were distinguished into four groups such that each group had 15 rats. Control group rats were given 1ml of refined water subcutaneously for 30 days. In group B rats were given 30mg/kg/day BPA, subcutaneously. Group C rats were given 200mg/kg/ day cinnamon aqueous extract via gavage tube 2 hours before daily subcutaneous injection of BPA. Group D rats were given 200mg/kg/day green tea aqueous extract via gavage tube 2 hours before daily subcutaneous injection of BPA. Animals were dissected after 30 days. Kidneys were stripped from disciple structures and were immediately placed in containers. Quantitative parameters measured by using image J software which were height of epithelium of PCT luminal diameter of PCT, height of epithelium of DCT, luminal diameter of DCT.

RESULTS

Group-wise distribution of Mean Height of Epithelium and mean Luminal Diameter in PCT.

Mean of height of epithelium in PCT of group B was found to be significantly less than group A (p=0.00). Both group C and D showed increase in this parameter but it was significantly increased in group D as compared to group C (p=0.000). Mean of luminal diameter in PCT of group B was significantly increased as compared to group A (p=0.00). This diameter was found to be decreased in both group C and D but group D showed significant decrease in this parameter as compared to group C. (p=0.000)

Table No.1: Group-wise distribution of Mean Height of Epithelium and mean Luminal Diameter in PCT

	Height of Epithelium in PCT in µm				Luminal Diameter in PCT in µm			
Groups	A	B	C	D	A	B	C	D
Mean	81.204	24.968	32.109	60.114	121.493	140.695	119.399	100.622
SEM	1.233	.781	.625	2.227	4.788	2.356	2.214	1.505
***P* value**	0.000*				0.000*			

**p<0.05*

Table No.2: Showing multiple comparison of the mean Height of Epithelium in PCT and mean luminal diameter in PCT

	Height of Epithelium		Luminal Diameter	
Groups	**Mean Difference**	**P value**	**Mean Difference**	**P value**
A vs B	56.236	0.000*	19.202	0.000*
A vs C	49.096	0.000*	2.093	0.960
A vs D	21.090	0.000*	20.871	0.000*
B vs C	7.141	0.003*	21.295	0.000*
B vs D	35.147	0.000*	40.073	0.000*
C vs D	28.006	0.000*	18.778	0.000*

*p<0.05

Table No.3: Group-wise distribution of Mean Height of Epithelium and mean Luminal Diameter in DCT

	Height of Epithelium in DCT in µm				Luminal Diameter in DCT in µm			
Groups	A	B	C	D	A	B	C	D
Mean	66.325	20.696	32.024	38.597	134.747	139.293	137.615	116.691
SEM	5.476	1.056	6.125	1.2033	3.566	2.792	4.444	5.941
P value	0.000*				0.002*			

*p<0.05

Group-wise distribution of Mean Height of Epithelium and mean Luminal Diameter in DCT.

Mean of height of epithelium in DCT of group B was found to be significantly less than group A (p=0.00). Both group C and D showed increase in this parameter. Mean difference between group C and D was 6.57 (p=0.685) which was statistically insignificant. Mean of luminal diameter in DCT of group B was significantly increased as compared to group A (p=0.00). This diameter was found to be decreased in both group C and D but group D showed significant decrease in this parameter as compared to group C. (p=0.000). (Table1).

Table No.4: Showing multiple comparison of the mean Height of Epithelium in DCT and mean luminal diameter in DCT.

	Height of Epithelium		Luminal Diameter	
Groups	**Mean Difference**	**P value**	**Mean Difference**	**P value**
A vs B	45.629	0.000*	4.546	0.881
A vs C	34.302	0.000*	2.868	0.966
A vs D	27.728	0.000*	18.056	0.024*
B vs C	11.327	0.234	1.678	0.993
B vs D	17.901	0.019*	22.602	0.003*
C vs D	-6.574	0.685	20.924	0.007*

DISCUSSION

Comparison of protective effect of cinnamon and green tea by measuring height of epithelium and luminal diameter of PCT indicated greater nephroprotection offered by green tea in measured histological parameters. Decrease in height of epithelium in group B was ameliorated both in group C and D but comparison of both showed that green tea increased epithelial height more than cinnamon.

Increase in luminal diameter was caused by BPA in group B. This parameter showed decreased both in group C and D but group D significantly improved this parameter as compared to C. Hence all the observed parameter of PCT indicate that green tea is more nephroprotective than cinnamon against BPA damage.

In present study the histomorphological alterations in group B might be due to vulnerability of the enzymatic systems of tubular membranes to toxins.[10] BPA was the chief event accountable for necrosis of renal tubules. Ahmed noticed similar changes in histology of PCT.[14] The alterations in PCT are in line with those described by Daniela-saveta.[15]

The study done by Morgan displayed amelioration of renal parameters of PCT in group C thus reflected shielding effect of cinnamon against BRA toxicity. Cinnamon leads in reduction of luminal obstruction and cloudy swelling of PCT.[15] Gehad E .Elshopakey in his publication inferred that cinnamon aqueous extract reduced the oxidative stress in kidneys initiated by diclofenac sodium and oxytetracycline.[16] All the above stated studies supported our results in group C which depicted substantial amelioration in PCT histology when compared with group B. In this study green tea upgraded PCT histology more than cinnamon.

Although ameliorative properties of green tea on histologicalmorphological changes due to BPA nephrotoxicity have not been studied but Sardana utilized green tea against nephrotoxicity caused by administration of gentamycin. The catechins inhibited degenerative changes of renal tubules in rat kidney owing to its antioxidative effects.[17] Wala Ahmad inferred in his study that green tea improved oxidative stress related tubular histological changes plus epithelial detachment and cast formation caused by bisphenol A.[18]

Beneficial properties of green tea on PCT were reflected by conclusions of Zhou who noticed same degeneration of PCT, while discovering the protective effect of EGCG (green tea polyphenol (−)-epigallocatechin-3-gallate) on obstructive nephropathy. The electron microscopy revealed that administration of EGCG in nephropathy exhibited intact basement membrane of PCT.[19] Ai Peng reflected that the EGCG ameliorated the tubular damage initiated by immune mediated glomerulonephritis.[20]According to Elzoghby green improved degeneration of epithelial cells of tubules caused by organophosphorus insecticide.[21]

The proximal tubular necrosis of cyclosporine treated rats was ameliorated by green tea as stated by Ryn.[22]

Height of epithelium in DCT showed significant decrease in this study, while luminal diameter showed significant increase in group B as compared to group A. Decrease in height of epithelium was ameliorated significantly both in group C and D. The increase in luminal diameter of DCT caused by BPA was found to be decreased both in group C and D.

Present findings of cellular debris in lumen of DCT and dilatation of DCT lumen in group B are supported by publication of Ahmed who described cellular debris in dilated lumen of DCT in BPA treated rats.[24] Study conducted by Fathy also supported the tubular degeneration with epithelial cells and hyaline casts in tubular lumen in fish kidney exposed to BPA.[25] Diminution of ATP causing oxidative stress leads to the necrosis of epithelium of DCT.[26] Tomza in 2018 reported that pre and postnatal exposure to 50µg/kg body weight of BPA shows enlarged cells lining renal tubules and decreased lumen space.[27]

Muhammad showed ameliorative effect of cinnamon on tubular degenerative changes caused by diabetes, thus supported the improved parameters in group C. Mnati proved that cinnamon is protective against prioxicam induced altered kidney morphology.[28] Amelioration of histomorphological parameters of DCT by use of green tea and cinnamon was due to their antioxidative properties.

CONCLUSION

Co-administration of cinnamon and green tea with BPA reduced the histological damage in proximal and distal convoluted tubules of nephrons in rats. Green tea is more effective than cinnamon to combat oxidative stress induced nephrotoxicity caused by BPA.

Recommendations: In present study we found that BPA causes nephrotoxic effects in rat kidney. Effects of BPA on human kidney should be explored with reference to its accumulation and excretion by human body. Green tea and cinnamon can be co administered against BPA nephrotoxicity to observe whether their nephroprotective effect is additive or not.

Author's Contribution:

Concept & Design of Study:	Huma Beenish
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Data Analysis:	Tooba Khurshid, Maleeha Bano, Tayyaba Qurashi
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Original Article

Frequency of Accelerated Idioventricular Rhythm in Patients with Acute ST Elevation Myocardial Infarction Receiving Thrombolytic Therapy

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ABSTRACT

Objective: To determine the frequency of accelerated idioventricular rhythm in patients with acute ST elevation myocardial infarction receiving thrombolytic therapy.

Study Design: Descriptive study

Place and Duration of Study: This study was conducted at the Cardiology Department District Head Quarter Teaching Hospital (DHQ-TH) Bannu from February 2020 to August 2020.

Materials and Methods: A Total 372 patient of ST Segment elevated myocardial infraction (STEMI) aged 25 to 75 years of both gender were enrolled following written informed consent. Streptokinase was used as thrombolytic therapy and accelerated idioventricular rhythm (AIVR) was noted.

Results: In our study total 372 patients were enrolled with the mean age of 53.8±11.9 years. There were 53.2% males and 46.8% females. The most frequent risk factor was Hypertension in 83.9% patients, followed by Diabetes Mellitus 65.6%. Accelerated Idioventricular rhythm was present in 45.2% patients.

Conclusion: We observed that AIVR is a common reperfusion arrhythmia after thrombolysis with streptokinase

Key Words: Myocardial infraction, reperfusion, ventricular arrhythemia

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INTRODUCTION

Myocardial infarction (MI) is the permanent loss of cardiac muscles caused by prolonged and an inadequate delivery of oxygen to the heart muscles.[1] It is caused by an imbalance in blood oxygen demand and supply owing to a variety of reasons, including plaque deposition and the formation of immovable thrombus in the coronary arteries that provide blood to the myocardium.[2]

In 2015, 15.9 million persons worldwide experienced a myocardial infarction, with more than 3 million having ST segment elevation and nearly 4 million having non-ST segment elevation MI.[3,4] Severe chest discomfort extending to the lower jaw and shoulder is a frequent sign of MI. Preexisting coronary artery disease (CAD)[6], high blood pressure, diabetes, smoking, poor nutrition, and lack of exercise[7] are all risk factors for MI. If the underlying reason is thrombus development in the coronary arteries, thrombolytic medicines are prescribed, which are administered intravenously to activate the fibrinolytic system in the blood, allowing plaques to be broken and blood flow to myocardial tissues to be restored.[8,9] Streptokinase, reteplase, alteplase, and tenecteplase are the most frequent thrombolytics utilized in acute ST segment raised MI (STEMI).[10] These medications are prescribed for individuals who have recently developed a STEMI and must be administered within 12 hours of the onset of symptoms in order to provide the most benefit to the patient.[11]

Resolution of ST segment elevation, reduction in chest discomfort, and the emergence of specific arrhythmias, particularly accelerated idioventricular rhythm, have all been proven to be valuable non-invasive markers for detecting coronary reperfusion in Acute MI.[12-15] Following fibrinolytic treatment, the AVIR is the most prevalent kind of arrhythmia, in the setting of STEMI.[16] Accelerated idioventricular rhythm, defined as a ventricular ectopic rhythm with more than 3 consecutive beats and a rate between 50 and 120 bpm,[17-18] is frequently observed during the reperfusion

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phase of acute myocardial infarction (AMI), and has therefore been proposed as a specific non-invasive marker for successful coronary artery reperfusion in the prethrombolytic and thrombolytic era.[19-20]

Acute intervention in the presence of reperfusion has not been demonstrated to enhance clinical outcomes, and coronary angiography should be postponed in instances when noninvasive reperfusion signs are of sufficient predictive value.[21-22] Emergency PTCA, on the other hand, is likely to be beneficial if coronary blood flow has not been restored. In Contrast if coronary blood flow has not been restored, emergency PTCA is likely to be helpful.[23]

MATERIALS AND METHODS

Descriptive study conducted at the Cardiology department DHQ teaching hospital Bannu from 21st February 2020 to 20th August 2020.

Sample Size: Sample size is 372 patients, using 41% frequency of accelerated idioventricular rhythm in acute myocardial infarction receiving thrombolytic therapy, 95% confidence interval and 5% margin of error on WHO sample size calculator.[17]

Sampling Technique: Non probability consecutive sampling

Sample Selection:

Inclusion criteria:

- Patients who presenting with chest pain within 12 hours' duration and ECG show ST segment elevation of more than 2 mm in chest leads or more than 1 mm elevation in limbs leads.
- Either gender.
- Age 25 years to 75 years.

Exclusion criteria:

- Those having contraindications to thrombolytic (Contraindications: CVA, active bleeding, suspected case of aortic dissection, malignant intracranial malignancy, head trauma)
- Previous myocardial infarction
    - Left bundle branch block.

Data Collection Procedure: This study was being carried out after the approval of the hospital Research Ethical Committee in the department of cardiology DHQ-TH Bannu. The purpose and benefit of study was explained to patients and written inform consent was taken. Patients who fulfilled inclusion criteria were subjected to detail history and examination. Patients were monitored continually for 24 hours during and after infusion of thrombolytic (streptokinase) and appearance of accelerated idioventricular rhythm was noted. A twelve leads ECG was recorded by Fukuda Me C110 machine at standard paper speed of 25mm/second with 0.1 mm voltage representation standardization showing idioventicular rhythm. All information like age, gender, duration of disease, diabetes, hypertension and accelerated idioventricular rhythm was recorded using structured proforma.

Data Analysis: Data was analyzed using statistical package for social sciences version 16. Frequencies and percentages are calculated for categorical variables like gender, diabetes, and hypertension. Mean and standard deviation is calculated for numerical variables like age, duration of disease, accelerated idioventricular rhythm. Accelerated idioventricular rhythm is stratified among age, gender, diabetes, hypertension, and duration of disease in order to see effect modifiers. Post stratification chi square test is applied keeping p value < 0.05 as significant. Results are presented in tables and charts.

RESULTS

In our study total 372 patients were enrolled with mean age of 53.8±11.9 years (28-75). There were 53.2% (n, 198) males and 46.8% (n, 174) female patients Table 1. Hypertension and Diabetes was present in 83.9% (n, 312) and 65.6% (n, 244) patients, respectively.

Frequency of accelerated Idioventricular rhythm was present in 45.2% (n, 168) patients as shown in Table 1.

Table No.1. Baseline characteristics and Frequencies

Sr. No	Variable	Freq-uency	%age
1.	Male	198	53.2%
2.	Female	174	46.8%
3.	Hypertensive	312	83.9%
4.	Normotensive	60	16.1%
5.	Diabetes	244	65.6%
6.	Non Diabetic	128	34.4%
7.	Idioventricular Rhythm Present	168	45.2%
8.	Idioventricular Rhythm Absent	204	54.8%

Table No.2: Data stratification for age groups

			AIR		Total
			Yes	No	
Age group	25-50 years	Count	75	66	141
		% within Age group	53.2%	46.8%	100.0%
	51-75 years	Count	93	138	231
		% within Age group	40.3%	59.7%	100.0%
Total		Count	168	204	372
		% within Age group	45.2%	54.8%	100.0%
p-value: 0.015 significant					

Age (p-value 0.015) and gender (p-value< 0.001), duration of MI (p-value 0.029) was significantly affecting the presence of AIR in the study subjects Table 2, 3 and 4.

Hypertension (p-value 0.978) and DM (p-value 0.255) was insignificantly associated with accelerated Idioventricular rhythm.

Table No.3: Data stratification for gender

			AIR		Total
			Yes	No	
Gender	Male	Count	48	150	198
		% within Gender	24.2%	75.8%	100.0%
	Female	Count	120	54	174
		% within Gender	69.0%	31.0%	100.0%
Total		Count	168	204	372
		% within Gender	45.2%	54.8%	100.0%
p-value <0.001 significant					

Table No.4: Data stratification for duration of MI

			AIR		Total
			Yes	No	
Duration of MI	2-4 hours	Count	27	15	42
		% within Duration of MI	64.3%	35.7%	100.0%
	4-6 hours	Count	39	45	84
		% within Duration of MI	46.4%	53.6%	100.0%
	6-8 hours	Count	48	79	127
		% within Duration of MI	37.8%	62.2%	100.0%
	10-12 hours	Count	54	65	119
		% within Duration of MI	45.4%	54.6%	100.0%
Total		Count	168	204	372
		% within Duration of MI	45.2%	54.8%	100.0%
p-value: 0.029 significant					

Table No.5: Data stratification for diabetes

			AIR		Total
			Yes	No	
DM	Yes	Count	105	139	244
		% within Diabetes	43.0%	57.0%	100.0%
	No	Count	63	65	128
		% within Diabetes	49.2%	50.8%	100.0%
Total		Count	168	204	372
		% within Diabetes	45.2%	54.8%	100.0%
p-value: 0.255 not significant					

Table No.6: Data stratification for hypertension

			AIR		Total
			Yes	No	
HTN	Present	Count	141	171	312
		% within HTN	45.2%	54.8%	100.0%
	Absent	Count	27	33	60
		% within HTN	45.0%	55.0%	100.0%
Total		Count	168	204	372
		% within Hypertension	45.2%	54.8%	100.0%
p-value: 0.978 not significant					

DISCUSSION

We observed in the present study that majority of patients with Acute STEMI were elderly.

A total 372 patients were enrolled with mean age of 53.8±11.9 years. This is in consistent with previous research[24] that that onset of this disease is mostly common in the older age. The predominant gender was male (53.2% males and 46.8% females) suffering acute STEMI. The most frequent risk factor observed was HTN and DM (83.9% and 65.6%, respectively) in our study. Khan S has reported even more male (Male:Female, 1:1.9) with Acute Myocardial infarction and Hypertension and Diabetes was the most frequent risk factor in the older age acute STEMI group patients in local population.[25] Khan A et al also confirmed almost similar results with mean age of 59 ± 10.8, (68% male) and hypertension (n, 52), Smoking (n, 48) and diabetes (44) were the most frequent risk factor in elderly patients group.[17]

Frequency of AVIR in post thrombolytic patients with acute STEMI was observed in 45.2% (n, 168) in the present study. Khan et al reported AVIR 51% patients develop AIVR after thrombolytic therapy. Gressin et al[20] studied arrhythmias of ventricular origin during thrombolytic therapy administered for acute myocardial infarction using twenty-four-hour Holter monitoring in patients treated with streptokinase Ventricular arrhythmias were present in all patients. Tolerance was good (1 cardioversion for ventricular fibrillation). The incidence of AVIR was 90% with patent artery and 82% with non-patent artery. This frequency is almost double than our result which can be attributed to use of sophisticated holter monitoring as compared to random ECG monitoring done in our study. Wehren et al[26] found that AVIR was documented in 51% patients after thrombolytic therapy. These results are close to our results but it was done with small sample size of 110 patients.

In recent a study by Tatli et al[27] the incidence of AIVR in successfully thrombolysed patients was 73%. These all studies validate results of my study so my study can be used as reference study for taking AIVR as marker of reperfusion after thrombolytic therapy in the local population.

AIVR occurring in the first 6h were found significantly higher in patients with arterial patency and these arrhythmias were defined as non-invasive indicators of early coronary reperfusion.[28]

CONCLUSION

To conclude, our study demonstrated the results that AIVR is the frequently recorded arrhythmia of

reperfusion during and or post thrombolysis with Streptokinase.

Author's Contribution:

Concept & Design of Study:	Noshed Khan
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Data Analysis:	Muhammad Niaz Khan, Sadullah Shah, Raza Muhammad
Revisiting Critically:	Noshed Khan, Samiullah Khan
Final Approval of version:	Noshed Khan

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

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Original Article

Frequency of Myalgia in Patients Using Statin Therapy in Patients with Obstructive Coronary Artery Diseases

Abdul Waris[1], Samiullah Khan[2], Muhammad Niaz Khan[3], Muhammad Kashif Iltaf[4], Raza Muhammad[5] and Sadullah Shah[6]

ABSTRACT

Objective: To determine the frequency of myalgia in patients using statin therapy for obstructive coronary artery diseases (CAD) presenting at Bannu Interventional Cardiac Center Bannu, Pakistan.

Study Design: Descriptive Study

Place and Duration of Study: This study was conducted at the Bannu Interventional Cardiac Center (BICC) Bannu, Pakistan, June 2020 to May, 2021.

Materials and Methods: Patients with Obstructive CAD, were recruited during the study period, following ethical approval and informed written consent, while stricltly following inclusion and exclusion Criteria. Demographic and clinical characteristics of the patients were recorded on predesign research proforma.

Results: A total of 267 using statin therapy for obstructive coronary artery diseases (CAD) were enrolled in this study. Mean age was 44.65 ± (8.87) (SD) years, ranging from 18-70 years. BMI was 27.21 ± (5.41) most of the patients were found overweight. Out of total n=267 Cases 165[62%] were male and 102 [38%] were female. Intensity of stain were categorized in to three categories, most of the 48[18%] patients were belonging to low intensity, 100[37.5%] were moderate intensity and most of them were belong to 119[44.6%] had high intensity. Frequency of myalgia was found to be 35[13%].

Conclusion: In our study the frequency of myalgia in patients using statin therapy for obstructive CAD was found to be only in 35[13%].

Key Words: Coronary artery diseases, Myalgia, Creatine kinase low-density lipoprotein cholesterol, non-high density lipoprotein, Statin

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INTRODUCTION

Statin therapy is generally well tolerated and very effective in the prevention and treatment of cardiovascular disease, regardless of cholesterol levels; however, it can be associated with various adverse events.

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Patients frequently discontinue statin therapy without medical advice because of perceived side effects especially statin-associated muscle symptoms. These symptoms most often consist of myalgia unaccompanied by significant creatine kinase (CK) elevations. Less often, myositis (elevated CK >10 times the upper limit of normal) or rhabdomyolysis (CK level >10,000 IU/L or accompanied by significant elevation in creatinine level) develops.

Despite Statins are generally safe and well tolerated, but not all patients are able to use a statin. Statin intolerance is most frequently attributed to muscle-related adverse symptoms.

However, statins are considered underutilized in patients for whom they are indicated and are frequently discontinued. Unfortunately, statin non-adherence correlates highly with risk for acute CV events, increasing the risk for recurrent MI and CHD.

Myalgia refers to patients with symptoms of muscle aches in the absence of an elevated CK, whereas myositis is the presence of symptoms with a CK elevation. Statins have long been associated with muscle-related toxicity, including myalgia myopathy

and myositis the last two of which involve significant CK elevations.

Muscle pain (myalgia) and weakness is experienced by up to 10% of patients taking statins. However, myalgia is commonly experienced by all people at some stage in their life, regardless of statin use.

Routine laboratory monitoring for statin-associated adverse effects is not recommended in asymptomatic patients. Statin discontinuation rates remain high, even among patients with CAD (over 50% after 1 year).[4, 6, 12]

A study conducted by Parker et al. reported myalgia in 9.4% of the patients using high intensity statin therapy

Since there is no information on the frequency of myalgia in patients using high intensity statin therapy for CAD under everyday conditions, the goal of the study were to develop a method to report myalgia in patients using high intensity statin.

MATERIALS AND METHODS

This descriptive Study was carried out at BICC, Bannu, Pakistan, from 1st June 2020 to 31st May, 2021, following ethicath approval from the ethical and research committee and informed written consent from the indvidual patient.

Sample size: Taking the frequency of Myalgia as 9.4% in patients using statin therapy[15], confidence interval at 95% and margin of error at 3.5% and putting this information in WHO sample size calculator version 2.0 the calculated sample size is 267.

Sample Technique: Non-probability consecutive sampling technique were used.

Objective: To determine the frequency of myalgia in patients using statin therapy for obstructive CAD presenting at BICC, Bannu.

Inclusion Criteria:

Patient of age between 18 to 70 years, either gender, on Statin therapy and diagnosed with obstructive CAD as per operational definition

Exclusion Criteria: Patients with prior history of Myalgia, CKD or baseline CK exceeded 10 times the ULN – (normal range; 22 to 198 U/L).

LFTs exceeded 3 times the ULN– (normal range; AST 8 to 48 U/L).

Operational Definitions: Obstructive CAD: It was defined as ≥70% stenosis in one or more of the major coronary arteries or ≥50% stenosis in left main (LM) coronary artery on coronary angiography at presentation.

Statin Therapy: Patient receiving any dosage of the Atorvastatin or Rosuvastatin for at least two months.

Intensity of Statin Therapy: Were classified as follow;

Low Intensity: simvastatin 10 mg/day, Pravastatin 10-20mg or pitavastatin 1 mg/day.

Moderate Intensity: Atorvastatin 10-20mg/day or Rosuvastatin: 5-10 mg/day

High Intensity: Atorvastatin 40-80mg/day or Rosuvastatin: 20-40mg/day[15]

Study Outcome: Myalgia:

were labelled "Yes" if patient met the study definition for "myalgia" if all of the following occurred[15]:

Reported new or increased muscle pain, cramps, or aching not associated with exercise

Symptoms persisted for at least 2 weeks

Symptoms resolved within 2 weeks of stopping the statin therapy.

Symptoms reoccurred within 4 weeks of restarting the statin therapy.

Effect Modifiers:

HTN and DM were labeled as "Yes" if patient has documented history of HTN or DM and on its medication for at least 6 months otherwisewere labeled as "No"

Smoking: were labeled as "Yes" if patient currently or has history of smoking 10 or more cigarettes per day for at least 5 years or 5 or more cigarettes per day for at least 10 years otherwise were labeled as "No"

Family history of CAD: were labeled as "Yes" if the patient has family history of CAD in first degree relatives, male less than 55 years of age or female less than 65 years of age, otherwise were labeled as "No".

Obesity: were labelled as "Yes" if the patient has BMI > 27.5 kg/m 2,

otherwise were labelled as "No". Kilograms BMI were calculated by using formula;

$$\text{BMI} = \frac{\textit{Weight in kilograms}\ kg}{\textit{Height in metters}^2}\frac{}{m^2}$$

Data Collection: All patients presenting with Obstructive CAD at BICC, Bannu and on Statin therapy were enrolled, following strict inclusion and exclusion criteria. A comprehensive history and physical examination were performed. Demographic and clinical characteristics of the patients were recorded at the time of presentation. Type and dosage of statin were recorded. Myalgia were recorded after two months of statin therapy for all the patients. All the collected data were recorded on predesigned proforma.

Data Analysis: Data were entered and analysis using SPSS version-16 (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp). Shapiro-Wilk test were applied to check the hypothesis of normality for age (years), weight (kg), height (cm), and BMI (kg/m2) of the patients and were expressed using appropriate descriptive statistics such as mean ± SD, maximum and minimum. Frequency and percentages were calculated for categorical variables such as gender, age group, obesity, smoking status, DM, family history, hypertension, intensity of statin, and Myalgia. Effect modifiers like age groups, gender, obesity, smoking status, diabetic mellitus, and family history of CAD,

hypertension, and intensity of statin were controlled through stratification. Post stratification appropriate chi-square test or fisher exact test were applied. Two sided p-value of ~ 0.05 were taken as criteria of statistical significance. For the graphical presentation of data, bar graphs and pi-charts were used.

RESULTS

A total of 267 patients using statin therapy for obstructive CAD were enrolled in this study. Mean age was 44.65 ± (8.87) years, [18-70], average height and weight was found to be 165.91 ± (5.41) & 27.21 ± (5.41), BMI was 27.21 ± (5.41) most of the patients were found overweight. (Table-1)

Out of total n=267 Cases 165[62%] were male and 102[38%] were female. The maximum number of cases 116(43.4%) were between 51-70 years of age (Chart-1)

Intensity of statin therapy categories showed that, the lowest frequecy of 48 [18%] patients were belonging to low intensity, 100[37.5%] were moderate intensity and most of them were belong to 119[44.6%] had severe intensity. (Chart-2)

Almost half of the patients in our study were obese 138[51.7%]. Pertinent Family histor of CAD was present in 36[13%] as compared to 231 [87%] those having no family history (Table 02).

The most common presented risk factor was hypertension 136 [50.9%] followed by DM which was 128[48%] and smoking in 61 [22.58%] cases. (Table 02)

Frequency of myalgia in patients using statin therapy for obstructive CAD was found to be only in 35[13%]. (Chart-3)

Table No.1: Descriptive Statistics in patients using statin therapy for obstructive CAD (n=267)

Descriptive	Mean ± SD	Range [Max -Min]
Age in years	44.65 ± (8.87)	[70 - 18]
Weight kg	74.5 ± (0.09)	[110 - 55]
Height cm	165.91 ± (5.41)	[180 - 150]
BMI Kg/m2	27.21 ± (5.41)	[43.85 - 18.17]

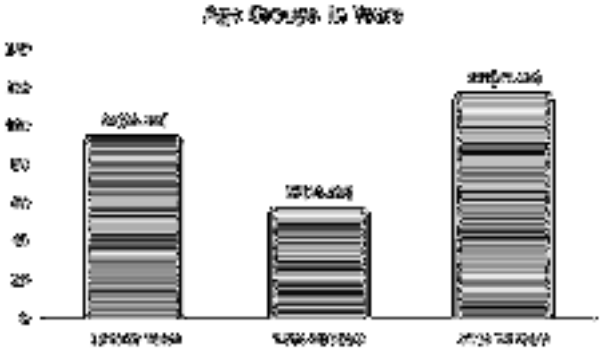

Figure No.1: Classification of age groups

Comparison of frequency of myalgia with intensity of statin were found statistically significant and observed that most of the myalgia patients had belong to high intensity and moderate intensity as compared to low intensity (P-value<0.001 *) (Table-3).

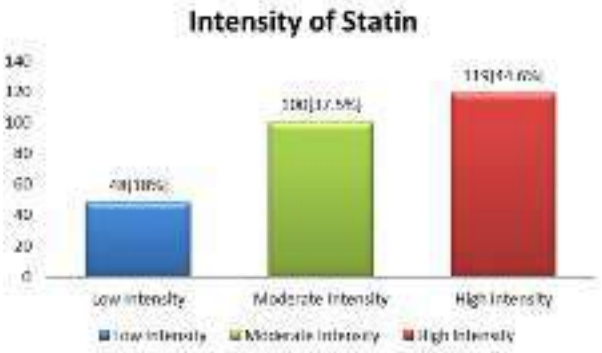

Figure No.2: Classification of intensity of stain

Table No.2: Frequencies of Risk Factor for Obstructive CAD

S.No	Risk Factor	Yes	No
1.	HTN	136 [50.9%]	131 [49.1%]
2.	DM	91[34.1%]	176[65.9%]
3.	Smking	61[22.8%]	206[77.2%]
4.	Obesity	138[51.7%]	129[48.3%]
5.	Family History	36[13%]	231 [87%]

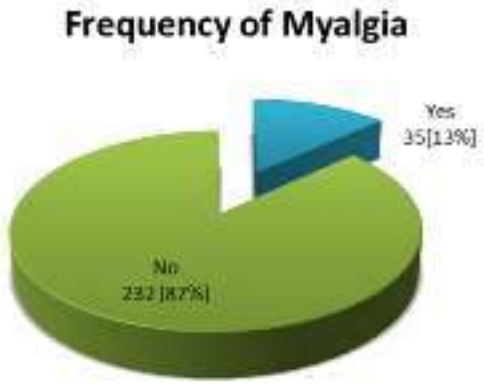

Figure No.3: Frequency of myalgia in patients using statin therapy for obstructive CAD

Table No.3: Comparison of frequency of myalgia in patients using statin therapy for obstructive CAD with intensity of statin (n=267)

Intensity of Statin	Myalgia			P-value
	Yes [n=35]	No [n=232]	Total [n=267]	
Low Intensity	1 [2.9%]	47 [20.3%]	48 [18%]	<0.001*
Moderate Intensity	8 [22.9%]	92 [39.7%]	100 [37.5%]	
High Intensity	26 [74.3%]	93 [40.1%]	119 [44.6%]	
Total	35 [100%]	232 [100%]	267 [100%]	

Comparisons of myalgia among demographics and confounding variables, indicate that, patients who had

documented history of diabetes mellitus and hypertension were found statistically associated with presence of myalgia (pvalue=0.007* & <0.001*), and those patient who do not obese, were found significant with myalgia (P-value=0.01 0*). (Table-4).

Table No.4: Comparison of myalgia in patients using statin therapy for obstructive CAD (n=267)

	Myalgia			
	Yes	No	Total	P-value
	[n=35]	[n=232]	[n=267]	
Gender				
Male	17 [6.4%]	148 [55.4%]	165 [61.8%]	0.084
Female	18 [6.7%]	84 [3 1.5%]	102 [38.2%]	
Total	35 [13.11%]	232 [86.89%]	267 [100%]	
Obesity				
Yes	3 [1.1%]	68 [25.5%]	71 [26.59%]	0.010*
No	32 [12%]	164 [61.4 %]	196 [73.41%]	
Total	35 [13.11%]	232 [86.89%]	267 [100%]	
Family History of CAD				
Yes	3 [1.12%]	33 12.36%]	36 [13.48%]	0.361
No	32 [11.99%]	226 [84.6%]	231 [86.52%]	
Total	35 [13.11%]	232 [86.89%]	267 [100%]	
Diabetes Mellitus [DM]				
Yes	19 [7.12%]	72 [26.97%]	91 [34.08%]	0.007*
No	16 [5.99%]	160 [74.53%]	176 [64.92%]	
Total	35 [13.11%]	232 [86.89%]	267 [100%]	
Hypertension [HTN]				
Yes	29 [10.86%]	107 [40.07%]	136 [50.94%]	<0.001*
No	6 [2.25%]	125 [46.82%]	131 [49.06%]	
Total	35 [13.11%]	232 [86.89%]	267 [100%]	
Smoking Status				
Yes	10 [3.75%]	51 [19.10%]	61 [22.85%]	0.387
No	25 [9.36%]	181 [67.79%]	206 [77.15%]	
Total	35 [13.11%]	232 [86.89%]	267 [100%]	
Age Groups				
18 to 35 Years	16 [5.99%]	78 [29.21%]	94 [35.21%]	0.354
36 to 50 Years	7 [2.62%]	50 [18.73%]	57 [21.35%]	
51 to 70 Years	12 [4.49%]	104 [38.95%]	116 [43.45%]	
Total	35 [13.11%]	232 [86.89%]	267 [100%]	

DISCUSSION

The mean age of our patients was quite young 44.65 ± (8.87) years, in contrast to western nation where this is the disease of elderly population. Male were more predominant (62%) as compared to female in the present study. This is in consistent with other studies from the region. Khan S has reported even more male (Male:Female, 1:1.9) with Acute Myocardial infarction. Almost half of the patients with obstuctive CAD in our study were obese 138[51.7%]. Anne B et al reported that 84% of their patient were obese or overweight.

In our study the frequency of myalgia in patients using statin therapy for obstructive CAD was only 35[13%] which is most similar study conducted by Parker et al.[15] reported myalgia in 9.4% of the patients using high intensity statin therapy. Many studies reported the incidence rate of myalgia during statin therapy has varied from 1% to 25%. Hansen et al grouped patients with a number of statin-induced muscle disorders together. A study by El~Salem, K., et al. (201 1) has demonstrated a higher prevalence of myalgia muscle symptoms was reported (21%) among patients using statins, as compared with most other report in the literature has been reported same prevalence of myalgia respectively.

Most previous estimates of adverse muscle reactions of statins were derived from clinical trials originally designed to test their efficacy and case reports and case series. Another study done by Sadeeqa, S., et al. (201 8) prevalence of statin induced myopathy was 51%in local population. She also reported more prevalent myalgia in age range 40-50, with females 57% and males 47%. Statin's-associated muscle symptoms cover a broader range of clinical presentations, usually with normal or minimally elevated CK levels, with a prevalence of 7–29% in registries and observational studies (Stores et al., 201 5)[13].

According the associations this study indicates that, patients who had documented history of diabetes mellitus and hypertension were found statistically associated with presence of myalgia (p-value=0.007* & <0.001*), and those patient who do not obese, were found significant with myalgia (P-value=0.010*). These results should prompt additional studies examining muscular performance with long-term statin treatment in both healthy patients and those with confirmed statin-associated myalgia.

CONCLUSION

In our study the frequency of myalgia in patients using statin therapy for obstructive CAD was found to be only in 35[13%].

Author's Contribution:

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Data Analysis:	Muhammad kashif Iltaf, Raza Muhammad, Sadullah Shah
Revisiting Critically:	Abdul Waris, Samiullah Khan
Final Approval of version:	Abdul Waris

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

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Original Article

To Find Out the Association of Vitamin D with Cardiometabolic Syndrome

To Explore the Link Between Vitamin D and Cardiometabolic Syndrome

Najma Fida[1], Asma Mehmood[2], Maham Khalid[1], Bazilina Majid[3], Afshan Gul[1] and Syed Shahmeer Raza[1]

ABSTRACT

Objective: To explore the link between vitamin D levels and the risk of developing cardiometabolic syndrome.
Study Design: Cross sectional study
Place and Duration of Study: This study was conducted at the Dept. of Medicine at Hayatabad Medical Complex Peshawar. Duration: December 2019 to April 2020.
Materials and Methods: Subjects were recruited according to the inclusion criteria. Patients were divided into two cohorts; Patients with Cardiometabolic Syndrome (CMS Group) and a Non Cardiometabolic Syndrome group (Control group). Blood for Vitamin D Levels was taken and analysed at the Hospital Lab. Blood Pressure readings in mm Hg via Yamasu mercury sphygmomanometer. Height, Weight and Waist Circumference were also noted. Data was analysed using SPSS 26.0.
Results: Mean and Standard Deviations (SD) for the levels of vitamin D (ng/mL) recorded as 31.77 ± 6.18 for control group and 21.91 ± 8.15 for CMS Group.
Conclusion: Our study found a positive link between lower vitamin D levels and an increased risk for developing Cardiometabolic Syndrome**.**
Key Words: Vitamin D; Vitamin D Deficiency; Cardiometabolic Syndrome

Citation of article: Fida N, Mehmood A, Khalid M, Majid B, Gul A, Raza SS. To Find Out the Association of Vitamin D with Cardiometabolic Syndrome. Med Forum 2021;32(11):43-45.

INTRODUCTION

Vitamin D plays a vital role in optimal functioning of many body tissues and organs; including amongst other the cardiovascular system. [1] Over the last two decades cardiometabolic syndrome (CMS) have seen a drastic rise in incidence, making it a major cause of disease and death. [2,3,4]

A wide range of cardiometabolic conditions are caused due to the presence of Metabolic Syndrome. This is characterized by the presence of various pathological conditions i.e., Obesity, dyslipidemias, hypertension, raised triglycerides, and deranged blood glucose. [5-8]

Vitamin D (fat-soluble steroid pro-hormone) is produced in the body as cholecalciferol (D3). When sunlight is exposed to the skin it is activated.[9] This form (vitamin D) is then transported to the liver for hydroxylation to produce 25-hydroxyvitamin D. It is next converted in the Kidney to the biologically potent form 1,25 hydroxyvitamin D. [10,11]

Vitamin D has a role in the extra skeletal properties including cardiovascular functions, nervous functions and immunity amongst others related to calcium and phosphate balance of the body. [12] Keeping this in sense growing evidence of scientific works investigating the physio-pathological mechanisms behind development of cardiometabolic disorders has revealed that lower levels of vitamin D play a key role in the development of CMS. [13,14]

It is therefore of utmost importance to determine if vitamin D levels are linked with cardiometabolic syndrome. There have been many interventional studies that recorded and examined the effect of vitamin D levels to cardiometabolic syndrome.

There have been many interventional studies that recorded and examined the effect of vitamin D levels to cardiometabolic syndrome. Still, many systemic reviews, meta-analysis and level I evidence studies are going on to understand the medical condition. It is therefore adamant to explore and find out the association and correlation of vitamin D levels in cardiometabolic syndrome patients.

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MATERIALS AND METHODS

This study was performed in the Dept. of Medicine at Hayatabad Medical Complex in Peshawar from Dec 2019 to April 2020. Inclusion criteria included patients older than age 20, of both sexes. diagnosed cardiometabolic syndrome (diagnosis made by consultant keeping both clinical and haematological values of the variables in account). Exclusion criteria included patients with kidney disease, secondary hypertension, thyroid, liver or parathyroid related medical conditions. These were excluded.

Subjects were recruited according to the inclusion criteria. Subjects were divided into two cohorts; Patients with Cardiometabolic Syndrome (Group I N=40) and a Non Cardiometabolic Syndrome group (Control group N=40). Blood for Vitamin D Levels was taken and analysed at the Hospital Lab via Cobas 6000 E 501 analyzer. 8.2 ng/ml was kept as the cut off for vitamin d deficiency. Blood Pressure readings in mm Hg via Yamasu mercury sphygmomanometer. Height, Weight and Waist Circumference were also noted. Written informed, voluntary consent was obtained. The Institutional Review and Ethics Board approved the study. Bias will be controlled by following strict inclusion criteria for patient selection, diagnosis of new cardiometabolic syndrome patients with measurable operational definitions and using same methods and parameters for cardiometabolic syndrome and vitamin D levels. All the data were collected on a research proforma for this study's protocol. Data was analysed on SPSS 26.0. (Armonk, NY: IBM Corp.).

RESULTS

Mean and standard deviations for age were recorded as 37.5 ± 10.1 for the Control Group while 29.5 ± 10.1 for the CMS Group. Mean and Standard Deviations (SD) for the levels of vitamin D (ng/mL) recorded as 31.77 ± 6.18 for control group and 21.91 ± 8.15 for CMS Group with a mean difference of 12.59 ng/mL.

Figure. 1 shows the levels the vitamin D for both groups; Cardiometabolic Syndrome Group and a second group that included healthy individuals as the control group (C)

CMS=Cardiometabolic Syndrome Group, C=Control Group (Healthy individuals)

Table No. 1: Shows vitamin D levels, Age and Weight both groups; Cardiometabolic Syndrome Group and a second group that included healthy individuals as the control group (C).

	Control (N=40)	CMS (N=40)	Mean difference	p-value
Vitamin D (ng/mL)	34.5 ± 10.1	21.91 ± 8.15	12.59	0.015
Age (years)	37.5 ± 10.1	29.5 ± 10.1	(+)8.00	0.000
Weight (kg)	92.09 ± 5.46	74.36 ± 3.41	(+)17.73	0.000

DISCUSSION

The current study sought to elucidate whether Vitamin D plasma levels are linked to the risk of developing CMS. It is therefore of utmost importance to determine if vitamin D levels are linked with CMS or not. There have been many interventional studies that recorded and examined the effect of vitamin D levels to CMS.

A study showed that lower levels of vitamin D are inversely linked to CMS. [15] It was also observed in a similar study that the ratio of CMS was found to be higher in patients with low vitamin D levels in comparison to patients with normal vitamin d levels. [16] Likewise in our study the Vitamin D Levels showed a mean difference of 12.59 ng/mL between CSM Group and the Control Group. (p=0.015).

Another study found out that low levels of vitamin D are linked with increased risk for CMS. Around 2/3rd of the obese or overweight patients (CMS) were deficient of vitamin D vs when the levels were compared to healthy individuals. [18] This study was carried out on more than 6000 adults. It reported that lower vitamin d levels were linked with not only an increased risk of CMS but also a higher waist circumference, deranged triglyceride levels, deranged blood glucose (fasting) and increased insulin resistance (followed up at 5 years). [18]

We observed in our study that lower levels of vitamin D were found in the CMS Group. The CMS Group showed lower than normal levels of vitamin D (Mean) on average. The mean difference to the Control group was 12.59 ng/mL. (Fig. 1 and Table. 1).

CONCLUSION

Our study found out that relation exists between lower vitamin D levels and increased risk of developing CMS. Vitamin D has a protective role. Systemic reviews, meta-analysis and level I evidence studies are required for not only to understand the medical condition but also establish a possible link and to further help us understand the pathophysiology governing this risk of developing CMS with the variation in the vitamin D levels.

Author's Contribution:

Concept & Design of Study:	Najma Fida
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Original Article

Effects of Nicotine Treatment on Viability of Inflamed Reconstituted Model of Oral Mucosa

Muhammad Nauman Sheikh[1], Sajid Hanif[2], Muhammad Atif[2], Muhammad Sibghat Ullah Khan[3], Humera Akhlaq[2] and Mohid Abrar Lone[2]

ABSTRACT

Objective: The objective of this assignment is to evaluate the effects of nicotine for over a span of 5 minutes and more than 24 hours on an inflamed stratified epithelial layer.

Study Design: Observational research

Place and Duration of Study: This study was conducted at the Department of Oral Pathology at Bart's and the London Queen Mary School of Medicine and Dentistry at Queen Mary, University of London from July 2018 to July 2019 for a period of one year.

Materials and Methods: The effects of nicotine on an in vitro Viability of Inflamed Reconstituted Model of Oral Mucosa are the subject of this study. Skin Ethic Laboratories, Nice, France, produced and supplied the reconstituted human epithelial model used in this study. The MTT test was used to determine the effect of different nicotine treatments on tissue viability.

Results: The effect of nicotine on the viability of inflamed stratified epithelium layer viability after 5 minutes and 24 hours with working solutions (10M, 100M, 1mM, and 10mM) on inflamed oral mucosa was determined to be insignificant.

Conclusion: This study found that all nicotine concentrations applied after 5 minutes and 24 hours had no effect on the viability of inflamed tissue.

Key Words: Tobacco, Nicotine, Oral mucosa, viability

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INTRODUCTION

Tobacco smoke is a main cause of early death globally[1,2]. Tobacco smoking causes more deaths worldwide than other diseases like TB, HIV and malaria together [3,4]. Tobacco smoking is responsible for around 6 million deaths per year in the world[5]. Tobacco smoking in countries such as west Europe, Australia, North America and the developing countries is increasing[6]. People use a wide variety of smoke tobacco products include cigars, cigarettes, bidis, kreteks, sticks, and snuff [7]. Use of all kinds of tobacco products lead to developing cancer in humans [8].

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Tobacco smoking is also responsible for serious conditions such as cardiovascular disease, COPD, stroke, pneumonia, aortic aneurysm and ischemic heart diseases [9]. Nicotine is a key component of tobacco [10]. The amount of nicotine consumed by individuals who use tobacco varies and it is well know that cigarette smoking has a direct link to nicotine addiction [11]. Tobacco smoking side effects are linked to time duration as well as a dose – response relationship to heavy smoking [6].

Tobacco smoking is a very popular habit and is associated with the development of cancers in humans[8]. The incidence of oral cancer is correlated to the use of tobacco products[12]. Oral cancer is considered as the 6th commonest cancer mostly affecting the male population of the world with a poor prognosis[13]. The higher incidence of cardiovascular morbidity and mortality is due to active and passive (environmental) cigarette smoking [14].

Active Tobacco smoking significantly increases the risk of RCC compared with passive smoking [15].

Low birth weight, ectopic pregnancy, spontaneous abortion and limb reduction defects are risks associated with smoking in pregnancy[9]. According to WHO, the greatest risk ever found to world's health is tobacco use causing several congenital defects in children[16]. Precancerous lesions such as leukoplakia,

erythroplakia, and smokeless tobacco keratosis, as well as cancerous lesions such as squamous cell carcinoma of the tongue, floor of mouth, lip, gingiva, and verrucous carcinomas of the buccal mucosa, gingiva, and alveolar ridge, are all linked to tobacco use [17]. Tooth stains, abrasions, smoker's melanosis, acute necrotizing ulcerative gingivitis, burns, keratotic patches, nicotinic stomatitis, peri-implantitis, and diseases such as increased plaque deposition, calculus depositions, gingival recession, and alveolar bone loss are all linked to tobacco use [18].

Nicotine concentration in oral snuff and pipe tobacco is equivalent to that in cigarette tobacco, however nicotine concentration in cigar and chewing tobacco is half that of cigarette tobacco [19].

The average tobacco rod contains 10 to 14 mg of nicotine. During smoking, 1 to 1.5 mg of nicotine is absorbed systemically on average.

Because of pH effects, buccal absorption of nicotine is reduced even when flue-cured tobacco smoke is held in the mouth [20]. Smoke from air cured tobacco used in pipes, cigars, and certain European cigarettes, which is the major tobacco, is more alkaline (pH6.5 or higher), contains significant unionised nicotine, and is easily absorbed in the mouth [21].

Nicotine enables smokers to operate more efficiently and with more concentration , by making them calm under stressful situation, as it is a type of psychomotor stimulant [11].

MATERIALS AND METHODS

The objective of this assignment is to evaluate the effects of nicotine for over a span of 5 minutes and more than 24 hours on an inflamed stratified epithelial layer. A modified MTT assay will be used to assess the tissue viability. In this study, The model utilised was a reconstructed human epithelium which was a model of three-dimensional tissue culturing and was TR146 altered oral keratinocytes (TR146) originating from a buccal cancer were cultured.This model SkinEthic Laboratories, Nice, France, produced and provided the product [22]. The model cultures were transported on agar and then rearranged into fresh 24 well culture plates (Costar, UK), each well containing 500l maintenance medium, and incubated for 2 hours in a humified environment at 37oC in 5% CO2. For all tests, each of the 24 cultures was moved to a fresh medium housed in a new 24 well plate. To make nicotine working solutions (10µM, 100µM, 1mM, and 10mM), a 2.5M stock solution was utilised. (Sigma, United Kingdom).

A phosphate buffered saline was used to dilute the working solutions. TNF-α solutions at (1000u/ml) was also prepared immediately before use. All solutions were discarded after each experiment under experimental conditions, the percentage of cells that did not survive were quantified by designed viability assays. In current study, modified MTT assay was used. A modified MTT assay The activity of mitochondrial dehydrogenase in the cells is measured. was used to assess the viability of exposed cultures. A colour reaction is produced by the MTT assay which allows a measure of the cell activity. A pale-yellow substrate got transformed into an insoluble dark blue formazan product when living MTT (3-(4, 5-dimethyl-thiazol-2-yl)-2, 5-diphenyltetrazolium bromide) was used to incubate the cells. A densitometry was used to measure the amount of formazan uptake.

Once the treatment period ended, a 300µl MTT (0.5mg/ml in PBS) solution contained in a new 24 well plate was used for the transfer of the cultures. Aluminum foil was used to wrap the plates and then, in a humidified atmosphere at 37°C in 5% CO2, incubated for 60 minutes. After incubation, 750l of isopropyl alcohol was sprayed to the epithelium's surface to transfer the cultures to a fresh 24-well plate containing 750l isopropyl alcohol each well.

To prevent evaporation, the plates were sealed with Parafilm®, and incubated at 37°C for 2 hours for extraction of formazan. All the surface solution which remained was preserved in the well, when insert was removed. To equilibrate the colour density the plate was agitated and all the cultures expended were discarded.

Three 200l aliquots were transferred from each well to a 96-well plate (Costar UK), and the optical density was determined using a Titertek Multiskan Plus plate reader (OD). The absobance at 570 nm was used to measure epithelial viability.

RESULTS

5 Minute Nicotine Treatment on Inflamed Mucosa: There is no significant effect of nicotine on TNF-α stimulated stratified epithelial layer viability after 5 minutes at 10µM (108.38 ± 23.51 %), 100µM (94.13 ± 15.31 %), 1mM (121.86 ± 12.79 %) and 10mM (107.79 ± 6.26 %) as compared to the PBS control concentrations (100 ± 14.35 %), (Table 1 and Figure 1).

Table No.1: MTT findings on TNF-stimulated tissue after 5 minutes of nicotine administration

Treatment	Mean viability %	Standard deviation	n
10µM	108.38	23.51	3
100µM	94.13	15.31	3
1mM	121.86	12.79	3
10mM	107.79	6.26	3
PBS	100	14.35	3

Nicotine Treatment on Inflamed Mucosa for 24 Hours: There is no significant effect of nicotine on the inflamed stratified epithelial layer viability after 24 hours at 10µM (117.46 ± 9.29 %), 100µM (118.48 ± 10.21 %), 1mM (102.69 ±12.93 %) and 10mM (122.03

± 15.31 %) as compared to the PBS control concentrations (100 ± 24.60 %), (Table 2 and Fig 2).

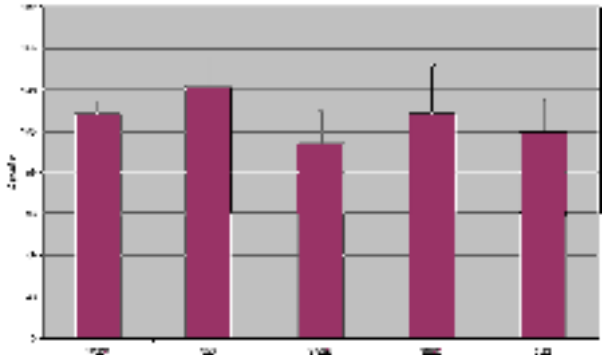

Figure No.1: Effects of a 5-minute nicotine administration on inflamed tissue viability

Table No.2: MTT findings on inflamed tissue following a 24-hour nicotine administration

Treatment	Mean viability %	Standard deviation	n
10µM	117.46	9.29	3
100µM	118.48	10.21	3
1mM	102.69	12.93	3
10mM	122.03	15.31	3
PBS	100	24.60	3

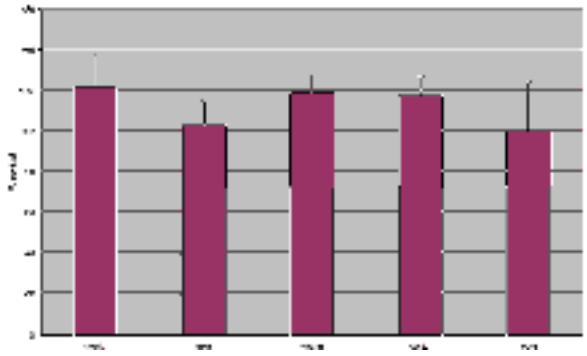

Figure No.2: Effects of a 24-hour nicotine administration on inflamed tissue viability

DISCUSSION

The purpose of this study is to see how nicotine affects a reconstituted oral mucosa that has been injured and activated by TNF. The epithelial model allows researchers to investigate the effects of nicotine on epithelial layers without the presence of mesenchyme. Stratified cultures were treated for 5 minutes and 24 hours, respectively.

The results indicated that there was no impact on viability after 5 minutes and 24 hours of the cells with the nicotine treatment of TNF-α stimulated reconstituted oral mucosa.

However, the viability studies suggest that there are only subtle changes in the membrane integrity from the nicotine, and most importantly there are no significant changes in the epithelium appearance. Surprisingly, nicotine has been shown to alter viability.

In a previous *in vivo* study by Anderson and Warfving, it was revealed that nicotine exerts its biological effect on the oral mucosa and resulted in changes in the appearance of the epithelium [(23)]. A similar study by Kwon *et al* found there was no effect of nicotine At concentrations of 10uM and 100uM, the viability of the cells was reduced dose-dependently with mucosal epithelial thickness.on reconstituted oral mucosa however it did reduce the viability of cells in the epidermal keratinocyte at a 100µM concentration [(24)].

A study by Alpar *et al* revealed that nicotine with higher doses (10.5-15.5mM) had a direct relationship in initiating changes in morphological appearance of the cells which were irreversible [(25)]. The findings of Squier and Johnson also stated that when on oral mucosa 0.2M nicotine was topically applied, after 2 hours it induced acantholysis and nuclear shrinkage within the epithelium [(26)].

The limitations of the findings in this study could be due to several factors such as the permeabilizing effect of nicotine on the mucosa. In addition, the tissue culture models used in this study were *in vitro* whereas many of the studies looked at tissue culture models *in vivo*. Therefore, it could suggest that the results obtained, with nicotine at the range of concentrations used, cannot be used to quantify the amount of mitochondrial disruption.

CONCLUSION

The viability of the inflamed oral mucosa was unaffected by nicotine concentrations ranging from 10µM to 10mM.

Author's Contribution:

Concept & Design of Study:	Muhammad Nauman Sheikh
Drafting:	Sajid Hanif, Muhammad Atif
Data Analysis:	Muhammad Sibghat Ullah Khan, Humera Akhlaq, Mohid Abrar Lone
Revisiting Critically:	Muhammad Nauman Sheikh, Sajid Hanif
Final Approval of version:	Muhammad Nauman Sheikh

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Original Article

Practice of Self-Medication among Medical and Non-Medical Undergraduate Level University Students in District Abbottabad

Self-Medication among Medical and Non-Medical Students

Zainab Nazneen[1], Arooj Batool[1], Afsheen Siddiqi[2] and Sobia Ali[1]

ABSTRACT

Objective: To determine the practice of self-medication and its associated factors among the medical and non-medical undergraduate level university students in Abbottabad.

Study Design: Comparative cross sectional study

Place and Duration of Study: This study was conducted at the Department of Community Medicine, Ayub Medical College, Abbottabad for a period of 10 months from Nov 20, 2018 to Aug 31, 2019.

Materials and Methods: It was carried out on 400 undergraduate students with 200 medical and 200 non-medical students. Data was gathered on a structured questionnaire and analysis was conducted both for descriptive and inferential statistics by SPSS version 20. Chi square test of association was employed to determine the association between self-medication and the independent variables. p value of ≤0.05 was considered significant.

Results: Out of 400 students participating in the research, self-medication practice was found in total 326(81.5%) students with 46% among medical and 35.5% among non-medical students. Relative frequency of self-medication out of 200 medical undergraduates was 184(92%) while out of 200 non-medical students it was 142(71%) with statistically significant association (p<0.001). Self-medication was also found to be associated significantly with gender and reasons for practicing self-medication (p < 0.001). Most frequently used group of medicines for self-medication was analgesics 127 (63.5%) and the most usual symptom was pain 75(37.5%).

Conclusion: Self-medication is more frequent among medical undergraduate students. It was found to be associated with gender and multiple reasons for practicing self-medication.

Key Words: Self-Medication, Medical Students, Analysis

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INTRODUCTION

Self-medication is administration by a person of certain traditional and recent medicines for treatment purposes without consulting a registered medical practitioner prior to intake of such medicines.[1]Presently, the practice of self-medication is increasing worldwide especially by the young adults in the developing nations.[2-4] It is quite common practice among the university students more specifically in the medical students.[5,6] Prevalence ranges between 78.1% to 96.8% among university students worldwide.[1,5,6] In various main cities of Pakistan it ranges between 76-99%.[7-9] In Abbottabad a research conducted on self-medication in non-medical undergraduates reports prevalence of 95.5%.[10] Inappropriate use of over the counter medicines can result in serious implications like drug abuse and drug addiction, delayed diagnosis of diseases and drug resistance.[5,11,12] It is also associated with higher odds of suicide attempts.[13]

The reasons of self-medication among students include considering illnesses to be minor, to save time, intake of medicines based on past experience and confident about knowledge regarding medicines.[14]Most of the studies on the students report headache to be the most usually occurring symptom for self-medication and after that common cold, flu and temperature.[14,15] The medicines used more frequently for the purpose of self-medication were analgesics or painkillers, common antibiotics, antipyretics, antiallergics and anxiolytics.[1,5,14,15] The literature regarding self-medication among the educated youth in Pakistan is inadequate and only a few researches have been conducted at the national level. To the best of our knowledge no regional data on comparison of self-medication between medical and non-medical

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university students is available. Therefore this study was conducted to determine self-medication and its associated factors amid medical and non-medical undergraduates. The results of this study will be helpful to build baseline data at the regional level especially in Abbottabad. It will also raise awareness among students regarding self-medication and help the policy makers to take steps to improve our health system.

MATERIALS AND METHODS

This comparative cross sectional study was carried out in Ayub Medical College and COMSATS University Abbottabad Campus for duration of ten months from Nov 20, 2018 to Aug 31, 2019 after taking permission from the Ethical review board and Head of COMSATS University. The sample comprised of total 400 undergraduate university students with 200 medical and 200 non-medical students. The Sample size was calculated by means of WHO software for sample size calculation with 95% CI, precision of 0.05 and taking prevalence of self-medication practice equal to 80.4%.[15,16] The calculated sample size was 385 but we rounded off the figure to 400 students after excluding 57 students i.e 22(4.8%) medical and 35(7.6%) non-medical students who refused to give data. The students were selected by convenience sampling technique and approached in the courtyards and classrooms. Data was collected on a non-validated self-devised structured questionnaire from Pakistani national students but those students who did not give their informed consent were excluded.

Descriptive and inferential statistical analysis of the data was done by SPSS version 20. Frequencies and percentages were calculated for the demographic variables (age groups, gender) and other research variables including category of students, self-medication habit, type of medicine used for this purpose, type of symptom for which medicines were self-administered and its reasons. Chi square test of association was employed to determine the association of demographic and research variables with self-medication and p value below and equal to 0.05 was considered as statistically significant.

RESULTS

The number of students participating in this research in total was 400. Out of these 200 were medical and 200 were non-medical undergraduates. Out of these 221(55.2%) students were male and 179(44.8%) were females. Regarding age, 230(57.5%) students were below 20 years of age while 170(42.5%) were 20 years or above. Out of all 400 students participating in the study, Self-administration of medicines was present in total 326(81.5%) students with 46% in medical and 35.5% in non-medical. Out of 326 students practicing self-medication, 184(56.4%) were medical students and 142(43.6%) were non-medical undergraduates.

The most usual symptom for which students self-medicated was pain in any part of the body 143(35.7%) followed by flu 70(17.5%), fever 56(14%), diarrhea 21(5.25%), allergy 20(5%), weakness 8(2%) and other symptoms 8(2%). Other symptoms included dyspepsia and sore throat. The most habitual group of drugs used for self-medication were the pain relievers 240(60%) followed by antibiotics 32(8%), multivitamins 23(5.75%), antihistamines 8(2%), antidepressants 8(2%), other allopathic 8(2%) and homeopathic medicines 7(1.75%).

The relative frequency of self-medication out of 200 medical undergraduates was 184(92%) while among 200 non-medical students it was 142(71%). The association of self-medication practice with category of students exhibited statistical significance (p=<0.001) as illustrated in Table 1.

The self-administration of drugs was also significantly associated with gender of the undergraduates. The female students were found to be practicing it more as compared to the other students. However self-medication was not found to be associated with age of the students. Frequencies, percentages and p values can be seen in Table 2.

The most common reason associated with self-medication among the students was found to be lack of resources like shortage of time and money with a significant association (p=<0.001). The frequencies of reasons other than lack of resources associated with self-medication are shown in Table 3.

Table No.1: Self-medication in undergraduate students

Category of students	Self-medication		Total	P value
	Yes	No		
Medical	184	16	200	
	92.0%	8.0%	100.0%	<0.001*
Non-Medical	142	58	200	
	71.0%	29.0%	100.0%	
Total	326	74	400	
	81.5%	18.5%	100.0%	

(*): significant association

Table No.2: Association of demographic variables with self-medication

Variables	Categories	Self-medication		P value
		Yes	No	
Gender	Male	157	64	<0.001*
	Female	169	10	
Total		326	74	400
Age groups	<20years	192	38	0.23
	≥20years	134	36	
Total		326	74	400

(*): significant association

The self-administration of drugs was also significantly associated with gender of the undergraduates. The female students were found to be practicing it more as compared to the other students. However self-medication was not found to be associated with age of the students. Frequencies, percentages and p values can be seen in Table 2.

The most common reason associated with self-medication among the students was found to be lack of resources like shortage of time and money with a significant association (p=<0.001). The frequencies of reasons other than lack of resources associated with self-medication are shown in Table 3.

Table No.3: Association of Reasons with self-medication

Reasons	Self-medication		Total	P value
	Yes	No		
lack of resources	87	0	87	<0.001*
flaws in health care delivery	77	0	77	
mild illness	35	0	35	
drugs accessibility	71	0	71	
Other reasons**	56	0	56	
Not applicable	0	74	74	
Total	326	74	400	

*significant association

**Other reasons: prescribing medicines on the basis of own past experience, advised by a friend/relative, thought of having enough knowledge about drugs, lack of awareness about hazards of self-medication and casual attitude regarding safety of medicines.

DISCUSSION

This research was conducted to determine the patterns of self-medication practice among the medical and non-medical university level undergraduates. Our results indicate that this practice is comparable between the two groups and more common among the female medical students. Self-medication is usually done by the students to relieve their pain using analgesics.

Overall frequency of self-medication was 81.5% in this research which is quite big and needs to be considered. A similar study carried out by Mumtaz Y also reports it to be 80.4% among university students[15]which is quite near to 84.8% in general community in Karachi[17]. A study conducted in Baghdad shows the frequency of self-medication in the university undergraduates to be much higher than our results i.e. 92.4%.[18] The reason for differences in frequency of self-medication could be as a result of differences in medical knowledge and awareness about self-medication and sample size variations.

In our research, Self-administration of drugs was more frequently associated among medical students (46%) as compared to non-medical students (35.5%). The reason may be that medical undergraduates have more understanding and approach to the drugs in contrast to the non-medical ones. However their knowledge is still inadequate at the undergraduate level and makes them prone to the hazards of self-medication as it increases the chances of drug abuse and drug addiction.[5, 11] Furthermore, the early diagnosis of the diseases is delayed due to masked signs and symptoms of diseases as a result of self-medication. Similarly resistance to drugs also increases.[12] It is also associated with higher odds of suicide attempts.[13]

These results are consistent with the results of a study in Saudi Arabia (96%) and the other in Rawalpindi (95.3%) which also report higher frequency in medical students[5,14] and among female students[14]. However some studies report insignificant difference amid medical and non-medical undergraduates[19] which may also be due to the same level of confidence and knowledge about self-medication in both the groups.

Pain in any part of the body was the most usually occurring symptom associated with self-medication among the undergraduates. Analgesics were used more among both the groups followed by medicines for the treatment of flu and high temperature in the present research. Mushtaq M et al and Afridi MI also found body pains especially headache (20% & 32.7% respectively) to be the most common symptom for practicing self-medication.[19,17] Pain killers were also found to be used more for self-medication as in study of Bareera et al in Rawalpindi.[14]

Reasons associated with self-intake of drugs in this research were lack of resources (shortage of time and money), flaws in health care delivery (difficult access to the health facilities due to overburdened hospitals, unfriendly attitude of the health care workers), minor illness (considering the ailment as minor), drugs accessibility (easy access to the various over-the-counter drugs from pharmacies) and other reasons (prescribing medicines due to one's own past experience, advised by a friend/relative, thinking knowledge regarding medicines being adequate, lack of awareness about hazards of self-medication and casual attitude regarding safety of medicines). Reasons were found to be different in different regions but ill-natured attitude of the health staff, lack of transport and time were also found to be most common factors in Esan et al study.[1] Other reasons in different studies were like considering illness as minor[15], self-awareness regarding self-medication, availability of over the counter medicines[5].

This study has certain limitations which require to be highlighted. First of all, the results of this study cannot

be applied to the whole community as the sample consisted of subjects from subgroup of the population i.e. students only selected from specific universities and a limited geographic area. Secondly it covers only the acute conditions and association of self-medication with diseases of longer duration could not be evaluated. Another limitation is that not all the demographic variables were studied and convenience sampling technique was employed for sample selection.

CONCLUSION

Self-medication is a common among both medical as well as non-medical university students but more frequent among medical students. It was found to be associated with gender and multiple reasons for practicing self-medication.

The study will be beneficial to the students to raise awareness regarding self-medication and its associated factors. It will also help the policy makers to take steps to improve our health system.

It is recommended that students should be health educated and awareness should be created about the self-administration of drugs and its associated risks especially among the medical students who know more about different diseases and their treatment. Health care delivery system should be improved and flaws should be rectified. Proper Legislation should be made and implemented regarding active sale of over the counter drugs and pharmacies should be supervised. Further research involving better study designs should be carried out as this attitude is becoming more prevalent in our society so measures should be taken for its prevention.

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Original Article

Outcome of Autogenous Bone Marrow Injection in Tibial Fractures with Signs of Delayed Union

Shahid Rahman[1], Aman ul Haq[2], Inayat ur Rehman[1], Israr Ahmed[1], Muhammad Bilal[1] and Kifayat Ullah[1]

ABSTRACT

Objective: To determine the outcome of autogenous bone marrow injection in tibial fractures with signs of delayed union in terms of clinical and radiological evidence of union.

Study Design: Descriptive randomized prospective study

Place and Duration of Study: This study was conducted at the Department of Orthopedic Surgery, LRH, Peshawar for a period of 6 months from January, 2020 to July, 2020.

Materials and Methods: Patients admitted with delayed union of tibial shaft fractures were included in the study. Under local anesthesia, bone marrow is aspirated from the anterior iliac crest using a special bone marrow aspiration needle into heparinized syringes to avoid clotting of the aspirate. The bone marrow is aspirated from multiple sites to minimize dilution of the aspirate with blood. Under fluoroscopy control, the aspirate is injected percutaneously into and around the fracture site.

Results: Total 38 patients include with delayed union of tibial fractures. 32 (84.2%) males & 06 (15.8%) females. In 22 (57.9%) patients mid-shaft of tibia was involved followed by distal tibia in 9(23.7%) patients and proximal tibia was involved in 7(18.4%) patients. 25(65.8%) patients were smokers while 13(34.21%) patients were nonsmokers. In 22 (57.5%) patients right side of limb was involved while in 16 (42.5%) left side of limb was involved. In 18 (47.5%) patients there is only 1 follow up followed by 2 follow ups in 11(28.9%) and 3 follow ups in 9(23.7%) patients. In 30 patients (78.94%), union was established after 3 months of follow-up and at the end of six months follow-up in 6(15.78%) patients. In delayed union of tibial fractures, the union rate was 94.73%.

Conclusion: Percutaneous autogenous bone marrow injection is a slightly invasive, safe, & inexpensive treatment option for tibial delayed unions and should be considered when the retained hardware seems to be intact & stable.

Key Words: Delayed union, Bone marrow, long bones, fracture healing, tibial shaft fractures

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INTRODUCTION

Delayed union is one of the most common complication in fracture healing which an orthopedic surgeon faces quite commonly. [(1)] Delayed union is defined as failure to reach bony union by 6 months or an un-united fracture that continues to show progress towards healing but taking time longer than expected. The delayed union is not always non-union but it can lead to one.[(2)]

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The most frequently involved bone is tibia. Both systemic & local factors are responsible for delayed union especially inadequate reduction, improper immobilization, distraction, loss of blood supply secondary to open fractures, infection and drugs intake etc.[(3)]

There are various methods available for the treatment of delayed union, each with a different level of invasiveness & outcome.[(4)] Low-intensity ultrasound or electromagnetic stimulation are two non-invasive approaches. Invasive method includes the use of bone morphogenic protein, stem cell therapy, open bone grafting, bone substitutes and finally Ilizarov, which is a versatile method of distraction osteogenesis. [(3)]

Open grafting of bone is related with risk of complications like infection, formation of hematoma & nerve injury etc.[(5)] The idea of percutaneous bone marrow injection was established to overcome the problems associated with traditional autogenous open bone grafting. [(6)]

Mesenchymal stem cells, also known as marrow stromal cells, are found in adult bone marrow. MSCs can differentiate into osteocytes, osteoblasts, adipocytes

& chondrocytes which are connective tissue cells. MSCs' ability to develop into bone-producing cells has sparked an interest in their clinical application in orthopaedic injuries to improve fracture repair & to treat bone abnormalities.[7] The marrow is taken from iliac crest by needle and then using a percutaneous approach, injected at the fracture site under the guidance of an image intensifier. [8]

Bone marrow is logically the transplant of choice since it is the only tissue that includes both inducible and determined osteoprogenitor cells.[9] Union has been achieved in 75% - 90% of reported tibial delayed union case series treated with bone marrow aspirate. [8]

Bone marrow injection promotes healing and it has many distinct advantages over the standard operative grafting. First, the complications at the donor and recipient sites are significantly diminished. Second, it can be performed in cases that are not fit for open bone grafting because of the poor condition of skin. Third, it can be repeated easily. Fourth, it utilizes the most osteogenic cells of a bone graft. Fifth, it can be performed under local anesthesia & avoids the risks of general and spinal anesthesia and can be used for patients with contraindication for general and spinal anesthesia. Sixth, it can be performed on an outpatient basis and decreases hospital stay. Seventh, it is cost effective.[9]

As our hospital is a very busy trauma Centre and receiving a large number of patients on daily basis, the procedure will be performed on patients as outpatient procedure. The procedure is suitable for high risk patients who are otherwise unfit for spinal and general anesthesia and for patients who are not willing for 2nd major procedure.

MATERIALS AND METHODS

This descriptive randomized prospective study was conducted from 16 Jan to 15 July 2020 in Orthopedic B Ward, Lady Reading Hospital Peshawar. It was done with the permission of the institutional review board. The minimum sample size was 651 calculated by WHO calculator, keeping the confidence interval 95%, standard deviation 1.96, the margin of error 0.012 and the expected prevalence/proportion of delayed union of tibia is 2.5%.[8] Due to rare cases of tibial delayed union previously operated with tibia plating, we can only include 38 patients in my study in the duration of 06 months.

All patients with delayed union of tibial fractures previously operated with tibial plating and also presented with 18-60 years with ASA1 and ASA2 status were included from the study. Patients with pathological fractures, malnourished patients (having lymphocyte count less than 10%) and infected fractures were excluded.

Patients history and examination were obtained. All surgeries conducted by single experienced orthopedic surgeon, CPSP fellow having minimum of five years of experience. Once the surgery is completed, standard post-operative protocols will be maintained. All patients were followed up for the next 4-6 weeks to detect clinical and radiological union.

Data was entered in SPSS 23. Age was presented as mean & standard deviation. Categorical data like gender, indication of surgery, smoking, post-surgery alignment and efficacy presented as frequency and percentages. Efficacy was compared by applying chi square test at ≤ 0.05 level. Test were applied on post stratification of age, gender, smoking and post-surgery alignment in which p Value less than 0.05 was considered as significant.

RESULTS

Total 38 patients were enrolled. There were 32 (84.2%) males & 06 (15.8%) female. The average age was 41.26 ± 10.87. The majority of the patients were between the ages of 31 and 40, 17 (44.73%) followed by 41-50 years 08 (21.05%). Table: 1. In 22 (57.9%) patients mid-shaft of tibia was involved followed by distal tibia in 9(23.7%) patients and proximal tibia was involved in 7(18.4%) patients. 25(65.8%) patients were smoker while 13(34.21%) patients were nonsmokers. Post-surgery alignment was good in 23(60.5%) while poor in 15(39.5) patient. Table: 2.

Table No. 1: Age & Parity Distribution

		Frequency (%)
Age	**Mean± SD**	41.26±10.87
	18-30 years	6(15.7%)
	31-40 years	17(44.73%)
	40-50 years	8(21.05%)
	51-60 years	7(18.42%)
Gender	**Male**	32(33%)
	Female	6(67%)

Table No.2: Frequency of Habits, fractures site, post-surgery alignment wise

		Frequency (%)
Habits	Smoker	25(65.8%)
	Non-smokers	13(34.21%)
Fracture site wise	Proximal	7(18.4%)
	Midshaft	22(57.9%)
	Distal	9(23.7%)
Alignment	Good alignment	23(60.5%)
	Poor alignment	15(39.5%)

Time to intervene after injury (duration in months) was 7 months in 15(39.5%) patients, 6 months in 13(34.2%) patients, 8 months in 9(23.7%) patients while 9 months in only 1(2.6%) patient. 27(71.1%) patients were given 2 injections while 11(28.9%) patients were given only 1 injection. In 18 (47.5%) patients there is only 1 follow up followed by 2 follow ups in 11(28.9%) and 3 follow ups in 9(23.7%) patient. Table:3

Table No.3: Distribution of duration of months, no of injection and follow ups

		Frequency(%)
Duration in months	**6**	13(34.2%)
	7	15(39.5%)
	8	9(23.7%)
	9	1(2.6%)
No. of injection	**One**	11(28.9%)
	Two	27(71.1%)
No. of follow ups	**One**	18(47.4%)
	Two	11(28.9%)
	Three	9(23.7%)

Table No.4: Frequency Attitude aboutThree IUCD as EC

		Frequency(%)
Limb Side	Right	22(57.9%)
	Left	16(42.1%)
Fracture union wise	Healed Fractures	36(94.7%)
	Non-union	2(5.27%)
Effectiveness (clinical/radiological/ both)	Clinical	3(7.9%)
	Radiological	7(18.4%)
	Both	28(73.7%)
Indication of surgery wise	Delayed union	36(94.7%)
	Non-union with implant failure	2(5.27%)

Table No.5: Stratification of effectiveness with respect to age, Gender, smoking status and indication of surgery

		Effectiveness		P value
		Yes	No	
Age	18-30 years	5	1	0.69
	31-40 years	15	2	
	40-50 years	7	1	
	51-60 years	5	2	
Gender	Male	29	3	0.78
	Female	5	1	
Smoking status	Smokers	17	8	0.57
	Non-smokers	11	2	
Indication of surgery	Delayed union	33	3	0.59
	Non-union with implant failure	2	0	

In 22 (57.5%) patients right side of limb was involved while in 16 (42.5%) left side of limb was involved. Post intervention effectiveness was clinically and radiologically in 28(73.7%) patients followed by only radiologically in 7(18.4%) patients while only clinically in 3(7.9%) patients. In 30 patients (78.94%), union was established after 3 months of follow-up and at the end of six months follow-up in 6(15.78%) patients, only two people (5.26%) were unable to form a union at the end of the six-month follow-up period. Other procedure, also open bones grafting or revisions surgery, was required for these patients. In delayed union of tibial fractures, the union rate was 94.73%. Table: 4.

DISCUSSION

There is no universally accepted definition of delayed union of a fracture. It is known that every given type of fracture tends to unite within a certain time period. Delayed union is defined as failure to reach bony union by 6 months or an un-united fracture that continues to show progress towards healing but taking time longer than expected.[10, 11] Bone marrow injection promotes healing more rapidly and effectively compared with standard operative grafting. It has many distinct advantages over the standard
operative grafting.

- First, the complications at the donor and recipient sites are significantly diminished.
- Second, it can be performed in cases that are not fit for open bone grafting because of the poor condition of the skin.
- Third, it can be repeated easily.
- Fourth, it utilizes the most osteogenic cells of a bone graft and does not introduce devitalized tissue (dead bone) and this could be used in children without damaging the growth plate.
- Sixth, it can be performed under local anesthesia and avoids the risks of general anesthesia or can be used for patients with contraindication for general anesthesia.
- Seventh, it can be used for certain clinical situations that would not be strong enough indications for open bone grafting, such as delayed union or fractures prone to delay union.
- Eighth, it is safe.
- Ninth, it is practical and time saving, as it can be performed on an outpatient basis and decreases hospital stay.
- Tenth, it is cost effective

However, bone marrow injection has some disadvantages; these include the lack of providing immediate mechanical stability as well as the risk of dilution with peripheral blood.[12]

In our study the mean age of the patients was 41.26 years. This was close to the studies by Nazar M et al[3]

and Akram M et al[7] 38 years while in Elsatter TA et al(9) the mean age was 37.66 years.

In our study we had 38 patients with male-to-female ratio was 5.4:1. This was close the study by Elsatter TA et al[9] which is 4:1 and by Nazar M et al[3] which was 1.5:1. In our study we have 25 smokers and 13 nonsmoker's patient which was close to the study Smoking was associated with an increased rate of non-union and delayed union as well as an increase in time to union in fractures of the tibial shaft.[13] Smoking is an important modifiable factor associated with delayed healing of fracture. Bones of smokers take longer to unite following tibia fractures or established delayed union.[13, 14]

In our study midshaft of tibia was in 22 cases while in the study by kaseem et al[15] the distal tibia was involved in maximum cases. Post-surgery alignment was good in 23 patients and poor in 15 patients who develop delayed union. It was close to the study by Nazar M et al[3] where post-surgery alignment was good in 30 patients and poor in 12 patients.

In our study two injections were given to 27 patients while one injection was given to 11 patients while in study by Elsatter TA et al[9, 16] three injection were given to 11 patients, four injection were given to 7 patients and two injection were given to 2 patients.

In this study there was one follow-up in 18 patients, two follow-ups in 11 patients and three follow-ups in 9 patients. While in the study by Elsatter TA et al and Akram M et al there were two follow ups in maximum patients. Right side of limb was involved in 22 patients and left side in 16 patients. It was close to the study by Akram M et al [7] and Nazar M et al [3]where the right to left ratio was 3:2.

Effectiveness (fracture healing) of Bone marrow injection was seen both clinically and radiologically while in study by kaseem et al [15] effectiveness was assessed only radiologically and in study by Elsatter TA et al [9] effectiveness was assessed only clinically. Union rate was 94.73% in delayed union of tibial fracture.it is close to the study by Nazar M et al [3] and Akram M et al [7] where the union rate was 92%.

CONCLUSION

Bone marrow aspirate is a big source of osteoinductive factors create by resident cells like endothelial cells, MSCs, osteoblasts, platelets & macrophages. It's essentially an auto-graft without bone matrix, and clinical evidence of its healing capacity is growing. In more nearly 90% of patients, cutaneous BMA injections for delayed unions resulting in lengthy bone bridging. At the end, we showed that protracted bone healing with autogenous BMA was equally effective as ABG therapy in achieving delayed union.

The conclusion of the study, percutaneous autologous bone marrow injection is slightly invasive, safe & cost-effective treatment option for tibial delayed unions & should be explored when the retained hardware appears to be intact & stable

Smoking is a significant modifiable factor linked to fracture healing delays. Smokers; bones take longer to fuse, after tibia fractures or established delayed union. [13,14].

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Original Article

To Elucidate the Decrement of Testicular Weights After Oral Doses of Lithium Carbonate in Albino Rats

Tazeen Kohari[1], Meshaal Azhar[2], Faryal Azhar[2] and Usama Faruqui[3]

ABSTRACT

Objective: To find out the effects of Lithium carbonate on the testes weights in Control group and the treated group with Lithium carbonate of albino rats.
Study Design: Experimental study
Place and Duration of Study: This study was conducted at the Department of Anatomy, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi, from 30th June till July 2013.
Materials and Methods: Forty male adult albino rats of three months of age were chosen for this study and distributed into two equal groups A, B. They were, treated for six weeks .Group A served as control received laboratory oral diet, group B received lithium Caronate orally in flour pellets at a dose of 34 mg/kg body weight. For six weeks. At the end of treatment testes weights were recorded in both groups.
Results: The rodents were weighed on digital weighing balance at the start and end of the study. The body weights were recorded and compared. The Body weight of Albino rats of group A were highly significantly increased as compared to Group B. The mean values of weights of testes were highly significantly decreased in B, when comparing with group-A. The values of weights of testes in groups A were highly significantly increased when compared with group B. These findings showed that Lithium induced testicular toxicity due to reduction in testes weights.
Conclusion: One of the many harmful adverse effects of lithium is its reduction of testicular weights in albino rats.

Key Words: Elucidate, Decrement, Testes. Reproductive toxicity

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INTRODUCTION

The male glands testis is present one on each side in the scrotum[1] and in humans testicular weights[2] vary from 10 to 25 grams each. The organ of male fertility that is testis in adult rats weights around 1000 milligrams each[3]. Lithium caronate[4] has an impact on manic disorders, its long standing use it causes damage to spermatogenic cells, such as reduced number of primary and secondary spermatocytes which leads to decreased testicular weight.[5] Ghajari G, Nabiuni M, Amini[6] E, (2021) in study found that Lithium causes induces oxidative stress through lipid peroxidation which causes germ cells apoptosis and decrease in sperm count leading to decrease in testicular weights.

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The soft alkali metal causes degeneration of heart and testis due to increased lipid peroxidation[7] and decrease in glutathione reductase leading to increased oxidative stress, which causes increase in sperm death all leading to decreased testicular weight.
The favourable mood stabilizer Lithium is prescribed for a manic episode in bipolar disorder as well as maintenance therapy of bipolar disorder [8] but its deleterious effects on male reproductive organs has been documented by researchers, one such study showed a marked decrease in spermatozoa and spermatids in seminiferous tubules, Epididymis, due to which there is marked reduction in male genital organ weights[9]
We carried out this research as there is scanty knowledge and documentation of the adverse effects of Lithium carbonate at a dose of 34 mg/kg on testis for a period of six weeks.

MATERIALS AND METHODS

According to the experimental designing, forty male adult Albino rats of 90 days of age were chosen from the Animal House of Basic Medical Science Institute, Jinnah Postgraduate Medical Centre, and Karachi .The rodents were observed for seven days prior to the commencement of the study. The rats were kept in the cages of Animal House under natural environment, water and food supplied ad libitum

The animals were divided into two groups of twenty albino rats in each groups:
Group A: served as control, on Lab diet.
Group B: received Lithium carbonate 34mg[10]/kg/day
Group A received its respective designed lab diet and Group B ingested LI2CO3 according to the period of treatment, which was 6 week. Laboratory diet was fresh green vegetables and flour pellets
Group B received Tablet Lithium carbonate at a dose of 34 mg/kg/day. The dose of lithium was calculated according to body weight of each animal. The tablet was crushed into powder form weighed at a dose of 34 /mg/kg on departmental weighing balance mixed in flour pellets and was only given at fixed time of 10 am daily for six weeks daily.
At the start and end of treatment rats were weighed in both groups and the weight was documented Testis were weighed at the end of treatment after sacrifice of the animals. At the end of treatment the animals were sacrificed under ether anesthesia. A midline abdominal incision extending up to the skin of scrotum was made the testes were identified and removed and then placed on dissection tray to study the morphology .The testes were dried weighed on Sartorius balance.
Testicular weight was calculated by the given formula[11]

The weight of the testes =

$$\frac{\text{Mean weight of testes (mg)}}{\text{Final Weight of the animal (mg)}} \times 100$$

Testes weights were calculated for each group. Significant (P) value was calculated with the help of student's t-test. The highly significance level was considered as $p < 0.001$. All the calculations were done utilizing, SPSS 15.

RESULTS

The rodents were weighed on digital weighing balance at the start and end of the study. The body weights were recorded and compared .The Body weight of Albino rats of group A were highly significantly increased as compared to Group B.
The mean values of weights of testes were highly significantly decreased in B, when comparing with group-A. The values of weights of testes in groups A were highly significantly increased when compared with group B as shown in Table-2. These findings showed that Lithium induced testicular toxicity due to reduction in testes weights.

Table No.1: Mean* Body Weights (gms) of Albino Rats in Different Groups at Variable Time interval

Groups	Treatment Received	Body Weights (Gm.)		P-value
		Mean Initial Weight	Mean Final Weight	A vs. B
A (n=20)	Control Group A	238.88 ±2.12	381.60±2.27	P<.001

B (n=20)	Lithium Group B	302.46±0.48	212 .28±5.10	

Table No.2: Mean* Weights (mg) of Testes of Albino Rats in Different Groups at Variable Time interval

Groups	Treatment Received	Duration of Treatment		P-value
		Final Weight		A vs B
A (n=20)	Control Group A	1302 ±2.51	P<.001	P<.001
		F	----	
B (n=20)	Lithium Group B	1126.68±0.55		
		----	----	

DISCUSSION

Heavy metal mixture[12] has been found to increase DNA fragmentation and sperm apoptosis resulting in decreased testicular weight .The same is in accordance with our study this may be due to the fact that Lithium blocks adenosine triphosphate (ATP) production leading to decreased motility of sperms which justifies infertility .[13]
Similar results were observed by T. Iqbal [14] et al, they in their research had reported that other metals like cadmium causes cellular infiltration, tissue degeneration leading to increase in the distance of spermatozoa in tubules this causes a decrease in testicular weight .This study is in agreement with our findings
Similar results of male infertility due to reduction in testicular weights were observed by Semet [15] (et al) they in their study reported the adverse effects of antipsychotic drugs like spermatogenesis impairment and their observations are in agreement with the results of our research. This may be due to the reason that Lithium causes increased release of reactive oxidant[16] species which leads to increased DNA fragmentation[17] which plays a pivotal role in sperm death and reproductive toxicity[18]

CONCLUSION

This study concluded that lithium reduce the testes weights in albino rats, which is more pronounced with increase time period. It is suggested that, ingestion of Antipsychotic and mood stabilizers drugs may lead to reproductive toxicity and the clinicians along with our population should be made aware of the adverse effects of popular drugs like lithium carbonate.

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Original Article

Assessment of Knowledge, Attitude and Practices of the General Public in Combating COVID-19

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ABSTRACT

Objective: To know knowledge, attitude and practices of the general public in combating Covid-19.
Study Design: Prospective study.
Place and Duration of Study: This study was conducted at the at two tertiary care hospitals of Khyber Pakhtunkhwa i.e. Lady Reading hospital Peshawar, and Mardan Medical Complex Mardan from 1st January 2021 to 30 June 2021.
Materials and Methods: A pre-validated online questionnaire was distributed among the general population. Adequate knowledge was assigned as a score of > 4 (range: 0–8) and good perception as a score of > 3 (range: 0–5). Chi-square test was used to determine the significance of difference in knowledge and perception of COVID-19 with socio-demographic characteristics. Logistic regression analysis was run to identify factors associated with adequate knowledge and perception. $P < 0.05$ was considered as significant.
Results: A large no of participants had appropriate knowledge of Covid 19 disease (98.9%). Regarding attitudes of people COVID-19 is a treatable disease, agreed 28.5% disagreed. 9.1%. Neutral 25.8%, strongly agreed 31.5% and strongly disagreed 3.4%. COVID-19 can be avoided by washing hands and wearing facemasks Agreed 26.8%, disagreed 1.7%. Neutral 4.9%, strongly agreed 64.5% and strongly disagreed 0.4. Regarding practices, I avoid unnecessary going out of my home Missing 2.3%, always 64.3%. never 1.1%. Often 22.0%rarely .23% and sometimes 8.0%.
Conclusion: Albeit the surge of COVID-19 cases in Pakistan, the participants demonstrated an overall adequate knowledge and good perception towards COVID-19.

Key Words: Covid-19, Knowledge, Attitude, Practice.

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INTRODUCTION

Since the emergence of COVID-19, a number of casualties have occurred throughout the world. COVID-19 pandemic documented in China, world has changed immensely. With its advent the health professionals and systems got failed. The exact treatment of COVID is not known and we are still experimenting. COVID-19 affects different people in different ways. Most patients have mild to moderate disease and recover without hospitalization. Most common symptoms are fever, dry cough and tiredness. Less common symptoms are body aches, sore throat, diarrhoea, headache, loss of taste.[1]

The dreadful thing about Covid-19 is that when severe, it leads to serious complications like pneumonia, ARDS, Acute liver and kidney injury, sepsis, DIC, DVT, chronic fatigue and death[2]. We have colleagues who are testing COVID positive and getting ill. We are losing doctors all over the country. Each one of us while working is potentially exposed to a deadly pathogen with no cure. Pakistan reported its first case of Covid-19 on February 26,2020 when a young man from Karachi tested positive after returning from Iran – one of the worst-hit countries by the virus. This Covid-19 – affected 85,264 people in the country, claimed 1,770 lives, while 30,128 individuals recovered from the respiratory illness. A total of 615,511 tests had been conducted in these 100 days across the country. Until now, 31,104 cases of the Covid-19 pandemic have been reported in Punjab, 32,910 in Sindh, 11,373 in Khyber-Pakhtunkhwa, 5,224 in Baluchistan, 824 in Gilgit-Baltistan, 3,544 in Islamabad and 285 in Azad Jammu and Kashmir.[3]

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The route of infection is determined by the site of infection. It is usually by respiratory droplets and secretions and indirectly through contaminated inanimate surfaces. Oro faecal and direct contact transmission has also been reported[4].

The approximated incubation period for SARS CoV2 is 1- 14 days based upon epidemiological data[5]. The virus is less lethal but more contagious than SARS –CoV and MERS–COV. The main worrisome thing is the continuous careless attitude of the public and not observing precautions. Vaccine can reduce the severity of disease. Unfortunately, many people are reluctant to get vaccinated. The result is that there is no bed empty in almost all the hospitals of the country and having seen our neighbouring country India, where patients are dying on the streets is very horrifying. It's time to wake up , wear masks, maintain social distance, stay at home and restrict going to markets and get Vaccinated. The best defence against this disease is by taking all these precautions. We are putting our and our loved one's lives in danger if we are ignoring these precautions.[6]

A variant called B.1.351, which first appeared in South Africa, may have the ability to re-infect people who have recovered from previous attack of coronavirus. It might also be somewhat resistant to some of the coronavirus vaccines in development. Still, other vaccines currently being tested appear to offer protection from severe disease in people infected with B.1.351.

The main rationale of the study was that people of Khyber Puktunkwa (KP) were in continuous denial about the disease and we want to assess their knowledge, practices and attitudes towards it keeping in mind the magnitude of the problem.

MATERIALS AND METHODS

This prospective Study was done at Lady Reading Hospital Peshawar and Mardan Medical Complex from 1st January 2021 to 30 June 2021. The sample size was 473 and technique being non probability convenient sampling. Patients of COVID 19 diagnosed by positive PCR were included. We excluded Patients with chest infections other than COVID-19. Our research was approved by the hospital ethical board. The rationale of the study was explained to the participants who met the inclusion criteria. Obtaining an informed consent, a validated questionnaire was used for recording the responses of participants.

The questionnaire consisted of 4 parts. The first part contained questions related to the demographic information of the participants such as gender, age, education and occupation. To investigate the knowledge of participants 28 questions were asked in 2nd part with 3 options: "yes, No and don't know". Total score was 88. 70% knowledge was considered as good.

Attitude section comprised of 14 questions, assessing attitude of people towards treatment, infection control and information regarding COVID -19. Response of each question was recorded on 5 point Likert scale as follows: strongly agree, agree, undecided, disagree and strongly disagree. Total score ranges from 1 to 75. Total score ranges from 5 to 75. Score above 75% will be considered as good.

Practice section has 17 questions assessing the practices of people towards COVID-19. Each response was recorder on a 5 point Likert scale as follow: always, often, sometimes, rarely and never. Total score ranges from 1-85. Response above 75% was considered as good.

The required information and demographic variables like age, gender was provided in proforma.

After data collection, analysis was done using SPSS version 25. Mean and Standard deviation was applicable to quantitative data. Frequency was applied for categorical data. Chi square was applied taking p value less than 0.05 as significant.

RESULTS

A large no of participants had appropriate knowledge of Covid 19 disease. Have you heard about the new disease COVID-19, with 98.9% saying yes., Fever is a symptom of COVID-19 with 96.19%., This disease was found more dangerous in old individuals 94.71%. Different age groups according to disease vulnerability are ,0-10 Years= 10(2.1%), 11-20 years= 2(0.4%), 21-30 years=1(0.2%), 31-40 years=11(2.3%), >40 years=445(94.1%), Missing response=4(0.8%).

Regarding attitudes of people, COVID-19 is a treatable disease, agreed 28.5% disagreed. 9.1%. Neutral 25.8%, strongly agreed 31.5% and strongly disagreed 3.4%. COVID-19 can be avoided by washing hands and wearing facemasks Agreed 26.8%, disagreed 1.7%. Neutral 4.9%, strongly agreed 64.5% and strongly disagreed 0.4 %.

Regarding practices, I avoid unnecessary going out of my home Missing ,2.3%, always 64.3%. never 1.1%. Often 22.0%rarely .23% and sometimes 8.0%.

Table No.1: Practices

In order to prevent contracting and spreading COVID-19		Missing		Always		Never		Often	
Sn	**Questions**	**n**	**%**	**n**	**%**	**N**	**%**	**n**	
1	I avoid unnecessary going out of my home	11	2.3	304	64.3	5	1.1	104	2
2	I avoid consuming outdoor food	16	3.4	261	55.2	8	1.7	122	2
3	I avoid hugging, handshaking and kissing	12	2.5	217	45.9	12	2.5	129	2

4	I avoid public transportation				17	3.6	228	48.2	10	2.1	116	2
5	I practice social distancing at work				13	2.7	275	58.1	8	1.7	57	1
6	I frequently wash my hands				11	2.3	334	70.6	1	0.2	95	2
7	I pay more attention on my hygiene than usual				12	2.5	286	60.5	6	1.3	94	1
8	I use disinfectant and solution to clean items in frequent contact				15	3.2	155	32.8	166	35.1	80	1
9	I use facemask				16	3.4	356	75.3	9	1.9	63	1
10	I Avoid touching my eyes, nose, and mouth with unwashed hands				16	3.4	281	59.4	13	2.7	94	1
11	I Cover my mouth and nose when i cough or sneeze				13	2.7	373	78.9	11	2.3	46	9
12	I Avoid going to the doctor with issues that could be postponed				16	3.4	277	58.6	23	4.9	91	1
13	Bought drugs that I heard that are good for treating COVID-19				14	3.0	101	21.4	222	46.9	48	1
14	Asked family members or friends not to visit me				18	3.8	132	27.9	91	19.2	79	1

Age (Years)	32.93±13.41 (13-80)	
	Frequency	**Percent**
Gender		
Male/Female	219/254	46.3/53.7
Education		
Illiterate	4	0.85
Primary	74	15.64
Secondary	66	13.95
Middle	31	6.55
Higher Secondary	48	10.15
Bachelors	170	35.94
Masters	42	8.88
Other	38	8.03

Table No.2: Attitude

S.No.	**Questions**	**Missing**		**Agree**		**Disagree**		**Neutral**		**Strongly Agree**		**Strongly Disagree**	
		n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**N**	**%**
1	It is my opinion that early detection of COVID-19 can improve treatment	7	1.5	129	27.3	32	6.8	46	9.7	217	45.9	42	8.9
2	COVID-19 is a very much preventable disease	9	1.9	141	29.8	26	5.5	59	12.5	227	48.0	11	2.3
3	COVID-19 can be avoided by washing hands and wearing facemasks	8	1.7	127	26.8	8	1.7	23	4.9	305	64.5	2	0.4
4	COVID-19 is a treatable disease	8	1.7	135	28.5	43	9.1	122	25.8	149	31.5	16	3.4
5	COVID-19 results in death in all cases	8	1.7	80	16.9	137	29.0	75	15.9	48	10.1	125	26.4
6	COVID-19 can be transmitted from pets	8	1.7	72	15.2	111	23.5	159	33.6	44	9.3	79	16.7
7	Authorities should quarantine COVID-19 should be separately detention	11	2.3	151	31.9	13	2.7	60	12.7	234	49.5	4	0.8
8	Awareness regarding COVID-19 in society is sufficient	8	1.7	112	23.7	103	21.8	64	13.5	165	34.9	21	4.4
9	Travel restrictions is helping prevent disease	8	1.7	146	30.9	11	2.3	50	10.6	254	53.7	4	0.8
10	Closure of educational institutes is a good step	8	1.7	116	24.5	29	6.1	45	9.5	267	56.4	8	1.7
11	Closure of mosques is a good step	8	1.7	104	22.0	53	11.2	73	15.4	202	42.7	33	7.0
12	Drastic increase in disease, burden authorities should	9	1.9	124	26.2	35	7.4	55	11.6	242	51.2	8	1.7

	be ready to lock down city and quarantine												
13	More tests for coronavirus infection should be carried out in the population	8	1.7	103	21.8	29	6.1	69	14.6	226	47.8	38	8.0
14	Anyone moving in public areas should be required to wear a face mask	10	2.1	68	14.4	12	2.5	20	4.2	327	69.1	36	7.6

Table No.3: Attitude

S.No.	Questions	Missing		Agree		Disagree		Neutral
		n	%	n	%	n	%	n
1	It is my opinion that early detection of COVID-19 can improve treatment	7	1.5	129	27.3	32	6.8	46
2	COVID-19 is a very much preventable disease	9	1.9	141	29.8	26	5.5	59
3	COVID-19 can be avoided by washing hands and wearing facemasks	8	1.7	127	26.8	8	1.7	23
4	COVID-19 is a treatable disease	8	1.7	135	28.5	43	9.1	122
5	COVID-19 results in death in all cases	8	1.7	80	16.9	137	29.0	75
6	COVID-19 can be transmitted from pets	8	1.7	72	15.2	111	23.5	159
7	Authorities should quarantine COVID-19 should be separately detention	11	2.3	151	31.9	13	2.7	60
8	Awareness regarding COVID-19 in society is sufficient	8	1.7	112	23.7	103	21.8	64
9	Travel restrictions is helping prevent disease	8	1.7	146	30.9	11	2.3	50
10	Closure of educational institutes is a good step	8	1.7	116	24.5	29	6.1	45
11	Closure of mosques is a good step	8	1.7	104	22.0	53	11.2	73
12	Drastic increase in disease, burden authorities should be ready to lock down city and quarantine	9	1.9	124	26.2	35	7.4	55
13	More tests for coronavirus infection should be carried out in the population	8	1.7	103	21.8	29	6.1	69
14	Anyone moving in public areas should be required to wear a face mask	10	2.1	68	14.4	12	2.5	20

DISCUSSION

Epidemics are usually very dangerous, and there are multiple difficulties for the affected population. Lack of knowledge and denial make it enormously difficult to curb the disease. Pakistan with fragile health system and substandard emergency preparedness mechanisms struggles to combat the corona virus. The number of recorded cases has grown exponentially, especially after the lockdown imposed in March 2020 was eased in May 2020 due to poor economic conditions; with a daily rise of approximately 1000 cases per million population. Punjab and southern Sindh provinces which make up 75% of the total cases in Pakistan, have slightly over only 14,000 beds for COVID-19 patients at state-run and private hospitals, causing most of the patients with milder symptoms to be managed at home instead. Moreover, the total number of functional ventilators are low unable to combat the large no of cases. As a result, in an attempt to reform the health sector, Pakistan has inaugurated its first ever local production of ventilators, with an average manufacturing capacity of 250–300 units per month.[7] Fever is a symptom of COVID-19 with 96.19%., This disease is more dangerous in old individuals 94.71% which is higher than that in previous studies from Pakistan.

The overall adequate knowledge of COVID-19 reported in our survey was very high. For example, disease i.e. have you heard about the new disease COVID-19 (CORONA) with 98.9% saying yes. This is parallel to a survey conducted in Tanzania where 84.4% had good knowledge. Such figures aren't astonishing as government have taken a lot of constructive steps by educating the public through television programmes, mobile phones, seminars and spreading pamphlets. Additionally, about 80% of the study population had a minimum education level of bachelor's which may account for their high level of knowledge; this is further confirmed by the significant association of education level with adequate knowledge-similar to a study conducted in China. It is interesting to note that the mean knowledge score for this sample was about 82% (6.59/8) which was quite comparable to the more developed parts of the world such as the United States and China with around 80 and 90% mean scores respectively. In particular, the knowledge regarding symptoms of COVID-19 was good where about 93% were well-aware and around 79% knew that there is only supportive treatment available for the virus; both these findings were in accordance with a study from Jordan. On the other hand, only 70.5% of the sample agreed that the virus spreads through air droplets and contact, whereas a similar study from Egypt showed a

wholesome 95% of the population to be aware of the same.[8] About 14% of the sample believed that wearing medical masks does not protect against infection, which is noteworthy, as a report on health care workers reported about 17% to believe the same. On the other hand, where almost 80% from this study agreed that wearing a mask offers protection, only 35% from a study in Egypt had parallel views. These positive findings explain how the seriousness of the disease has been highlighted by multiple media and health platforms during the pandemic, successfully reaching the masses in the country. A study on health care workers from Uganda reported a poor attitude towards COVID-19. However, a study among Malaysian, Chinese and Vietnamese citizens showed positive attitudes towards overcoming the COVID-19 crisis.

Despite much less faith in the government of Pakistan, 67.3% were optimistic that COVID-19 would be successfully controlled; though this was relatively low as compared to that in China and Malaysia. The government of Pakistan has taken several actions to limit the dispersion of the virus. Some important measures include suspension of incoming flights, closure of educational institutions and commencement of online learning.[9] However, despite these extensive preventative measures, 36.8% of the participants showed just a 'neutral' attitude regarding the competency of the government of Pakistan in controlling the pandemic. This wasn't surprising as lockdown restrictions were eased; educational institutions and markets were opened. Additionally, the aggressive media and the constant protests by political and religious leaders towards the government's shortfall in controlling the pandemic played an important role in orchestrating the pessimism among citizens.[10-11]

This study has some constraints. First, since the methodology is derived from a cross-sectional design. Hence, causal inferences may not be established.

CONCLUSION

The participants demonstrated adequate Knowledge and good perception towards Covid-19.[11] There is a need to follow the preventive protocols and dissemination of correct information through conducting educational interventions that target safe health practice and provide appropriate information on this infection. This has already brought great results in our country to combat the disease.

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Original Article

Subtle Changes by Bio-Aerosol, Addiction & Height on Routine Spirometry in Workers of New Subzi Mandi, Karachi

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ABSTRACT

Objective: Comparison of Spirometric changes in workers of New Subzi Mandi Karachi with control. It was also consisting on Air sampling for detection of Microorganisms in subzi mandi & control area.

Study Design: Case control study

Place and Duration of Study: This study was conducted at the new Subzi Mandi Karachi & control area, more than 5 kms from Subzi mandi from August 2019 till Jan 2020 for a period of five months.

Materials and Methods: 100 controls of similar age & socioeconomic strata were included. Known COPD & asthma & cardiovascular disease were excluded. Chi square and independent t-test was applied. Four different media used to collect ambient organisms, allowed to proliferate on kits & detected in microbiology lab.

Results: Bacteria & fungi detected by us were more concentrated in Subzi mandi. From 245 individuals 145 cases while 100 controls. Smokeless tobacco abusers were found significant association in cases. Height was again found more in cases. The mean of spirometric parameters provided clues of present article & only Predicted FVC% has significant association between groups.

Conclusion: Bio-aerosol & smokeless tobacco abuse causes subtle changes on modern routine spirometry. Clue found subtle because workers were tall & had optimum BMI. Spirometric results of controls were far behind from ideal value of adult male because they had significantly raised association of smoking.

Key Words: Spirometry, Forced Vital capacity (FVC), chronic obstructive pulmonary disease(COPD), Bio aerosols

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INTRODUCTION

New Subzi mandi Karachi is a whole sale vegetable & fruit market & is overcrowded. Major source of Bio aerosol & association with pulmonary dysfunction [1]. Spore-forming bacteria (especially gram-positive) after being aerosolized are possible of surviving in the atmosphere for long periods of time. On the other hand, even gram-negative bacteria are able to survive in the atmosphere for about 390 minutes; these organisms can multiply in bio aerosols[2]. According to WHO occupational lung diseases will be 3rd most common cause of death in near future & any big city can be contaminated [3].

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Due to decaying of vegetable waste, waterlogging, animal garbage, poor sanitary condition and mud, high amounts of organic waste are produced in and around the vegetable markets. Poor storage facilities and resources of dumping waste cause faeco-oral route leading to poorer hygienic conditions which further aggravate the problems [4]. A survey report that agricultural & vegetable market workers are prone to asthma even without risk of smoking & fungi are more virulent due to smaller size [5].

The effect of bio aerosols in vegetable market further lead to constriction of the bronchioles, fibrosis and permanent airway wall thickening [6]. Other attributions causing mild to moderate restrictive changes are mawa and gutka (smokeless tobacco). These may be involved in oxidative damage. For that reason, it is important for assessment of spirometry as much as possible [7]. Endotoxins in organic dust have been associated with deranged PFTs [8].

Workers of vegetable markets are observed to encounter frequent bouts of allergic rhinitis & hypersensitivity pneumonitis [9]. Inhalation of bio aerosols in air can either be through oral route i.e. mouth or through the nasal route, i.e. nose. Chances of inhalation depend upon aerodynamic diameter and

particle's dimension, rate of breathing and movement of air around body [10]. Spirometry is the most common tool used for respiratory problems [11].

MATERIALS AND METHODS

Statistical formula applied while calculating sample size.

Micro biological tests for detection of K Pneumonae. From Indol test we confirmed that it is Enterobacteraecae. Vp (Vogous Proscure test) found negative means that it is some other species of Klabsiella. Then from Citrate test & MR (Methyl red) test we detect K Pneumonae.

Inclusion Criteria

- Male manual workers ranging in-between 18-60 years,
- 100 individuals in control group with similar age and socio-economic status working & living minimum five kilometers away from vegetable market,

Exclusion Criteria

- Females,
- Individuals with established lung (Asthma & COAD) & cardiovascular disease.

Method of Air Sampling: A total of 3 samples were taken from Subzi Mandi approximately 5 meters away from shops so that no shop or particular shop is specified while three samples from control area were taken (environment of less bio-aerosol concentration, i.e. ghazi goth). Samples were taken 2 meters above the ground for matching inspired air. For fungal growth, Sabourads dextrose agar (SDA) medium was used while for bacterial growth, blood, Nutrient & Mac-Conkeys agar media was used. Incubation was done through chocolate agar medium. Exposure time to air was 30 minutes.

Data Collection Procedure: After ethical approval and informed consent from cases and controls. Data collected, it consisted of cases & control history of occupation, respiratory symptoms and other medical history. For spirometry, electronic digital portable spirometer was used to measure 3 routine parameters. These were forced expiratory volume in 1st second (FEV1%), forced vital capacity (FVC%) and FEV1/FVC% calculated.

Data Analysis: For analysis of data, SPSS version 23.0 was used. Qualitative data was represented as frequency and percentages while quantitative data was presented as mean and standard deviation. To test for association in-between cases and controls, Pearson Chi-square test [12] was applied on qualitative data whilst on quantitative data, independent sample t-test [13] was applied. All test was applied keeping p-value of <0.05 as statistically significant.

RESULTS

Table No.1: Coagulase Negative Gamma Hemolytic Staphlococci (Staph Epidermidis & Staph Hemolyticus**)**

Sample Code	*C1,2 & 3	*VM1,2 & 3
*Cfu/m^2	500	1200
Hemolysis on blood agar	γ hemolytic +ive	γ hemolytic +ive
Coagulase test result	Coagulase -ve	Coagulase -ve

*C1, 2 & 3 are 3 are samples from 3 sites of control area, Ghazi Goth,
*VM1, 2 & 3 are sample from 3 sites of Subzi mandi,
*cfu/m^2 = Colony forming unit per meter square

Table No.2: Total bacterial load (Staphlococci, Streptococci & Pseudomonas sp:**)**

Sample Code	C1,2 & 3	VM1,2 & 3
(Cfu/m^2)	500	1200

Nutrient agar used which allows the growth of even non-fastidious organisms.

Table No.3: Fungus Aspergillus niger

Sample Code	C1,2 & 3	VM1,2 & 3
Asp.niger	01 Large spreaded black mold colony	03,01 & 01 small spreaded black mold colony

Table No.4: Klebsiella Pneumonie

Sample Code	C1,2 & 3	VM1,2 & 3
K.peumoneae cfu/m^2	01,03 & 05 respectively	06,04 & 00 respectively

All of above found more in concentration in Subzi mandi than in control area.

Table No.5: Age & Anthropometry in cases and controls included in the study (n=245)

Parameters	Cases	Controls	p-value
Age (Years)	31.9 ± 11.3	33.2 ± 14.3	0.43
Weight (Kg)	67.1 ± 15.0	64.5 ± 14.1	0.17
Height (cm)	164.8 ± 6.4	161.6 ± 6.1	<0.001
BMI (Kg/m^2)	25.0 ± 5.0	25.2 ± 5.2	0.82

Note significant association in height

Table No.6: History of Smokeless tobacco abuse in cases and controls

History of addiction	Cases	Control	p-value
Naswar	54 (78.3%)	17 (65.4%)	<0.001
Gutka	10 (14.5%)	4 (15.4%)	
Mawa	5 (7.2%)	-	
Pan	-	5 (19.2%)	

Note significant association

Control group was indulged more in Smoking. I took history of "Pack years" (No: of packets of 20 Cigarettes per day x no: of years since smoking). In controls 53.77 ± 6.14 while in cases 36.68 ±3.42, p-value <0.001 i.e, significantly raised. Mean of 1st 2 parameters of spirometry of control, FEV_1 = Mild derangement & Predicted FVC% = low (Table 8) as regard ideal value of adult male is concerned & far behind the cut off value that denies obstructive pattern.

Table No.7: Mean comparison of Routine Spiro metric Parameters between Cases and Controls

Parameters	Cases (n=145)	Controls (n=100)	p-value
Predicted FEV1 (%)	76.5 ± 35.4	75 ± 25.8	0.73
Predicted FVC (%)	122.4 ± 74.7	90 ± 36.1	<0.001
Predicted FEV1/FVC %)	80.6 ± 41.7	74.2 ± 39.1	0.22

Table No.8: Interpretation of Routine Spirometry (Based on ATS/ERS Criteria). **Interpretation of means of spirometry of cases**

PATTERNS	
Obstructive (Limitation of expiratory airflow)	Restrictive (Decrease lung volumes)
FEV_1 (Decrease)	FEV_1 (Decrease)
FVC (Normal or Decrease) Above 135% denies the pattern	FVC (Decrease) Above 135% denies the pattern
FEV_1/FVC (Decrease)	FEV_1/FVC (Normal to Increase)
SEVERITY	
Criteria of Mild Obstruction	% Predicted Values of Routine Spirometry
Normal FEV_1 and FVC	80 - 120
MILD FEV_1 (Obstruction or restriction)	70 - 79
NORMAL FEV_1/FVC	70 (According to age group of present study)
FEV_1/FVC	Decrease in obstruction and Increase in restriction (Fibrosis)

DISCUSSION

We plan to record changes of routine spirometric parameters purely due to pathognomies of Subzi Mandi hence tried to keep similar mean of age, BMI & weight (Table 5) duration of working since years & hours of daily working were similar i.e, non-significant association (p-value > 0.05) between cases & control.

While taking history, I saw that frequency of respiratory complaints are related to period since working in Subzi mandi. i.e, cough, sneeze & sputum expectoration.

The bacteria and fungi detected in our study again usually cause **obstructive changes.**

FEV_1 % again in mild derangement (Table 7 and 8). This means there is air flow resistance/limitation in mid & small air ways. **FVC%** although slightly above normal limit (Table 7 & 8) but again far behind the cut-off value of clue towards initial obstructive changes. **Ratio of above 2 parameters** is moderately raised (Table 7 & 8). It is affected by age which in present study is upto 60. After exclusion of diseases it is a sign of fibrosis, chronic exposure to bio aerosol can cause fibrosis. More important is smokeless tobacco abuse (Table 6).

In our study there found significant difference (p-value < 0.05) in abusers of smokeless tobacco (Gutka, mawa, paan and naswar) found more in workers of subzi mandi than control (Table 6). The third parameter, Ratio of first 2 parameters i.e, Mean of Predicted FEV_1/FVC% is moderately elevated (Table 7 & 8) means a clue towards fibrosis, restrictive pattern. This factor causes local fibrosis in mouth first than spirometry.

The case group found taller i.e. having more body surface area than control i.e. significant difference (p<0.05) in height (Table 5). This factor most probably can affect result i.e. otherwise there will be significant association in FEV_1% and FEV_1/FVC% between cases and control and will match the previous Indian study [8]. It is established fact that spirometric parameters depend on body surface area. Calculation of value of **Height** that can affect spirometric parameters is very much bias. At last it is reported that increase in height of +1% can affect Predicted % values of spirometry from 0.9% - 40%.

Hence we discuss 2 primary/major factors that affect our result of spirometry (p-value) i.e, Smoking of controls (described in results) & Height of cases (discussed above in last para). There are 2 other secondary factors that can upset the values of parameters of spirometry i.e, **Physical activity** & obesity. The manual workers must have handle weight of few kgs: many times in a day which can affect the status of their respiratory muscles (more strong) [14], although I excluded professional loaders while doing spirometry. 2nd is **Optimum BMI.** Only 16% of workers were found obese. Hence we can't able to receive clear cut association in p-values of remaining 2 parameters i.e, 1st & 3rd. Or in other words effect of bio-aerosol on spirometry is masked by these factors.

There is another 3rd reason i.e. chronic effect of organic dust affects the spirometric parameters more in childhood. The effect is limited in adults [15]. In our study adolescent up to 18 were excluded.

Why other 2 parameters are not showing significant association, as already mentioned in result that control group was indulge more in smoking & clue is present in mean of all 3 parameters but this is not the subject of present article so I would not like to discuss here. Otherwise there will be significant association in FEV_1 & Ratio of both parameters as present in FVC%.
FVC is known to be most important Spiro metric parameter.

CONCLUSION

Hence present article gives following conclusions:-

1. Bio aerosol (Bacteria & Fungi identified in our study) are related to obstructive changes in air ways (clue provided by mild decrease in mean of FEV_1 of workers),
2. Abuse of smokeless tobacco is related to fibrosis, restrictive pattern on modern routine spirometry (clue provided by moderate elevation in Predicted FEV_1/FVC% of workers).
3. As we know case control study based on clear-cut association of p-value & I am talking about mean of spirometric parameters hence I used terminology of "subtle effect" in title. There are 2 primary & 2 secondary factors that affect spirometric parameters i.e,

A) Height of cases (Para 5 of Discussion),
B) Smoking in control (Describe in results),
C) For 2 minor factors see Para 6 of Discussion

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Author's Contribution:

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

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Original Article

Evaluation of the Color Distribution of Natural Teeth by Age in Saudi Sub-Population Using an Intraoral Spectrophotometer

Natural Teeth Colour Distribution By Different Age Groups

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ABSTRACT

Objective: To evaluate the natural teeth shades distribution by different age groups and gender in a Saudi sub-population using a Spectrophotometer.

Study Design: Descriptive Cross-sectional Study

Place and Duration of Study: This study was conducted at the Qassim University dental clinics, Saudi Arabia from September 2020 to April 2021 for a period of 08 months.

Materials and Methods: Total of 180 participants with healthy Maxillary anterior teeth were recruited and were divided into 3 different age groups young (16-30), middle (31-49) and elderly (50-70). Color distribution of maxillary central incisors was evaluated using intra oral spectrophotometer. Data was collected and was analyzed using SPSS version 23. Chi square test and ANOVA two-way analysis of variance tests were applied to identify the influence of age and gender on each color variable, respectively.

Results: Chi-square test was used to compare gender with tooth shades and results showed that males have whiter teeth than females (P=0.016). Comparison of age of individual to tooth shades was done and results showed that with age, the shade of teeth becomes darker (P=0.027) and older individuals have darker teeth than younger ones.

Conclusion: The present study revealed that both the age and gender resulted in statistically significant difference with teeth shades. It was evident that males have whiter tooth shades than females and older people have darker tooth shades than younger individuals.

Key Words: Age, Color, Gender, Spectrophotometer, Tooth, Saudi Arabia

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INTRODUCTION

The knowledge and understanding of the shade distribution of natural teeth among different age groups is of a significant importance not only to facilitate the color selection for the dentist, but also to avoid color mismatch [1-3]. Color is not something physical rather it is a sensation[3].

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Tooth color determination can be attributed to complex physical and optical phenomena which take place when light interacts with dental tissues[4-7]. Combination of the light reflected from the enamel surface and the light scattered and reflected from both enamel and dentin results in the color of the natural tooth[1-4,8-10]. Dentin of tooth contains organic components which absorbs light in range of ultraviolet and visible spectrum. Light transmission through tooth can be affected by dentin thickness and enamel translucency[2,8].

Color can be described in terms of three dimensions of hue, value and chroma according to Munsell [1], Hue is the quality by which we distinguish one color from another. It is also called the basic color. Value is the relative lightening or darkness of a color and chroma is defined as the saturation of hue [2,11-16]. Keeping in view the previous studies, we came to know that hue of natural teeth lies in the range of yellow red to yellow[1,10-14]. Various factors affect tooth color among which age, gender and ethnicity are considered to be most important ones to affect the color distribution of central incisors. As the individuals age the color of teeth also change[1-3,17-19]. With aging, teeth become yellowish, reddish and darker due to formation of

secondary dentin, pigmentation in dentin, and enamel wear. Previous studies have reported that females have lighter and less saturated anterior teeth than men while in some studies no difference has been found between male and female tooth color[1-3,13].

The most frequently used method of shade taking is subjective in which tooth color is matched using shade tabs from a color guide but now it can also be measured objectively using electronic devices like spectrophotometer [1,2,4]. Various dental shade matching devices are being used which are far more reliable than visual assessment. Choosing the right color can be easily achieved by using an intraoral device called spectrophotometer (VITA Easyshade), which is an optical instrument for measuring the intensity of light relative to wavelength[4]. Spectrophotometer measures the amount of visible spectrum light reflected from an object and converts it into various tooth shade values. Studies have shown that it is much more accurate than visual tooth color assessment[4,5-7]. Pecho et al. noted that spectrophotometers provide reliable assistance in shade matching when it is used in combination with visual color assessment[1].

Main aim of esthetic dentistry is to create a refreshing pretty smile with ideal tooth color and arrangement in harmony with surrounding structures. Knowledge of tooth color distributions and the factors that influence these colors is greatly essential for esthetic restorations[13,20-23]. The aim of this study is to know and assess the color distribution in different ages in the Saudi population using intra oral spectrophotometer according to VITA Easy shade system in order to minimize the color mismatch between the restoration and the natural tooth and to facilitate the color selection for the dentist.

MATERIALS AND METHODS

An ethical approval was obtained from institutional ethical review board at Qassim University (Ref no: EA/m-2019-3023) prior to initiation of data collection. A descriptive cross sectional study was performed to assess the color distribution of maxillary central incisors in Saudi population from September 2020 to April 2021. Informed consent was taken from the Saudi students studying at college of dentistry, Qassim University and individuals coming to visit dental clinics of Qassim University. Individuals with healthy maxillary anterior teeth with no oral and systemic diseases were included in the study while subjects with missing, badly decayed, restored and crowned anterior teeth were excluded from the study. Individuals with history of smoking or tooth bleaching and who disagreed to participate in the study were also excluded. Total (N) of 180 Saudi subjects were recruited for this study. The participants were recruited through convenience sampling technique. These individuals were divided into three age groups young (16-30), middle age (31-49) and elderly (50-70). In each group color distribution of maxillary central incisors were evaluated as a representative of natural tooth color via spectrophotometer (VITA Easy shade)[1,4,15]. After testing the device for reliability and performance, the subjects were asked to brush their teeth for two minutes. In addition, the tip of device was covered with infection control shield to avoid cross infection. Finally, the color was measured placing probe tip perpendicular on the tooth surface.

Data was analyzed using SPSS version 25. Mean and comparison between each age group were calculated. Chi square test was used to compare the teeth shades of participants for statistical significance. ANOVA test was used to compare the shades of the three age groups.

RESULTS

The current sample obtained was 180 (N) participants, 93 (51.6%) Saudi males and 87 (48.3%) Saudi females with healthy maxillary anterior teeth aged from 16-70 years. The percentage of young age group (16-30) was higher (38.3%) when compared with the middle age group (36.1%) and elderly group (25.6%) (Table-1). The frequency and percentages of different shade groups is shown in Table-2.

Table No.1: Distribution of participants according to age groups

Age Groups	Frequency (Percentage)
16-30	69 (38.3%)
31-49	65 (36.1%)
50-70	46 (25.6%)
Total	180 (100%)

Table No.2: Distribution of different shade groups

Shade Group	Frequency (Percentage)
A1	13 (7.2%)
A2	22 (12.2%)
A3	33 (18.3%)
B1	18 (10.0%)
B2	26 (14.4%)
B3	24 (13.3%)
C1	19 (10.6%)
C2	12 (6.7%)
C3	13 (7.2%)
Total	180 (100%)

The age group-wise comparison of frequency of different tooth shades revealed that in younger age group (N=69), B3 (11) shade was most common. Alternatively, in the middle age group (N=46), A3 (14) shade was found to be most. On the other hand, old age group (N=46) had A3 shade (14) as the common color (Table-3). The application of Anova test found statistically significant differences (P-value = 0.027) in teeth shades between age groups suggesting that with increasing age the shades become darker.

Table No.3: Distribution of different tooth shades based on age groups

		Tooth Shade									
		A1	**A2**	**A3**	**B1**	**B2**	**B3**	**C1**	**C2**	**C3**	**Total**
Age Group	**16-30**	5	9	5	8	8	11	9	5	9	69
	31-49	8	11	14	6	11	5	4	4	2	65
	50-70	0	2	14	4	7	8	6	3	2	46
Total		13	22	33	18	26	24	19	12	13	180

The gender-wise comparison of different shade groups exhibited significant difference between male and female individuals (p-value=0.016) with the male participants having lighter tooth shades as compared to females (Table-4).

Table 4: Distribution of different tooth shades based on gender

		Tooth Shade									
		A1	**A2**	**A3**	**B1**	**B2**	**B3**	**C1**	**C2**	**C3**	**Total**
Gender	**Male**	11	16	15	9	9	9	13	4	7	93
	Female	2	6	18	9	17	15	6	8	6	87
Total		13	22	33	18	26	24	19	12	13	180

DISCUSSION

According to the results of this study, there were significant age and gender differences ($p<0.05$) in tooth shades of central incisors in Saudi population. The prime objective of esthetic dentistry is to create a beautiful pleasing smile with well aligned, adequately proportioned teeth in harmony with surrounding gingiva and facial symmetry[2,9,13]. Various factors including age, gender ethnic groups, skin color and gingival color influence the differences and changes in tooth color. Limited scientific knowledge exists regarding these factors[1,17,18]. This knowledge is significant for dentists regarding tooth shade selection for restorations and dental prosthesis[17,20]. In our study we have used spectrophotometer to determine tooth shades. Paul et al[4] and Bahannan et al[5] showed in their studies that spectrophotometer was far more superior in shade selection than visual methods.

Influence of gender on tooth shade has been previously studied and results have shown that in some studies there has been no difference between genders[6-8]. Alternatively, the researchers reported that females have whiter teeth than men[2,9,10,11]. Conversely, in current study male population has been found to have lighter tooth shades than women. A lot of factors can be responsible for this change like ethnicity, oral hygiene habits and dietary habits.

It has been reported that with age the central incisors get darker, yellowish and reddish in color. Eiffler and colleagues[12] found no significant difference in tooth color among two age groups of 50 years and 70 years. However significant color changes with aging were found in several previous studies[13-15,19]. Likewise, findings of the present study showed that in Saudi population teeth get darker in shade with aging. These changes in tooth color with aging may be associated with secondary dentine deposition, oral hygiene habits, use of certain medications, environmental factors and systemic diseases[8,9].

Our study gives us vital information regarding tooth color changes with age and gender in Saudi population. Color is much more than something physical, it is a sensation[3]. Dentists play a vital role in providing esthetic smiles. Shade matching is a very crucial and sensitive step in providing esthetic restorations and dental prosthesis. Dentists can use this vital information of tooth color shade selection while choosing the most accurate shade before providing esthetic restorations and dental prosthesis[14].

Our study has several limitations like the sample size was less and it can be increased to make the study more accurate and results more promising. In order to identify the most significant modulator of dental color change in aging, we need longitudinal researches to analyze the effect of environmental factors, dietary habits and personal habits on tooth shade as they can be responsible for changes in tooth color due to aging and gender difference[1,3].

CONCLUSION

In conclusion, the present study showed that both, the age and gender resulted in significant difference in teeth shades ($p<0.05$). As for the relation between the teeth shades and gender, it shows that the males have whiter shades when compared to females. As for the age groups, it shows that the older the age the darker the tooth shade.

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

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Original Article

Prevalence of Carpal Tunnel Syndrome in Third Trimester of Pregnancy

Sameena Pari[1], Mehwish Niaz[2], Laraib Khan[3], Rida Aziz[4] and Aneela Aslam[5]

ABSTRACT

Objective: To find out the prevalence of carpal tunnel syndrome in women during the third trimester of pregnancy.
Study Design: Cross-sectional survey research study
Place and Duration of Study: This study was conducted at the conducted at the Department of Physiotherapy, CMH, Lahore from Oct 2020 to March 2021.
Materials and Methods: Three hundred and twenty-two pregnant women in the third trimester had participated in this study taken from both private and government hospitals, aged between 18 to 40 years, women with a history of multigravida and prim gravida were included. Data was shown in the form of frequencies and percentages. A cross-sectional survey was used for research. A validated questionnaire (Boston Carpal Tunnel Syndrome questionnaire) was used as a tool for data collection.
Results: 29.11% of women were reported with carpal tunnel syndrome in their third trimester of pregnancy.
Conclusion: The severity of hand or wrist pain at night, frequency of pain in hand or wrist at night, numbness and tingling sensation in hand.
Key Words: Carpal tunnel syndrome (CTS), Median neuropathy, Third trimester, Entrapment, Boston carpal tunnel questionnaire

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INTRODUCTION

Carpal tunnel syndrome (CTS) is symptomatic neuropathy caused by compression of the median nerve at the level of the wrist. It's characterized by discomfort, numbness, and tingling sensation in the hand, which progresses to decreasing muscle strength and sensory loss. The symptoms might be confined in the hand, or they might radiate upto the elbow. Patients frequently report waking up in the middle of the night and shaking their hands for relief. This is known as the flick sign, and it is 93% sensitive and 96% specific for CTS.[1] The canal on the volar side of the wrist is known as the carpal tunnel. The Piriformis bones, a hook of Hamate on the medial side, and Scaphoid and Hamate on the lateral side are the bones that bind it. Flexor Retinaculum connective tissue surrounds these bones and forms a tunnel. Carpal tunnel syndrome is caused by entrapment of the median nerve at two levels: either at the narrow section of the hook of Hamate or by wrist flexion at the proximal border of the carpal tunnel, either owing to tunnel narrowing or swelling of the palmer's tendons.[2]

Carpal Tunnel Syndrome is usually attributed to hereditary factors or idiopathic. The nocturnal rise in carpel pressure in idiopathic carpal tunnel syndrome could be linked with many mechanisms, like shifting of lymphatic drainage of the upper limb in the supine position, a lack of muscle pump mechanism that assist significantly in the outflow of interstitial fluid in the carpal tunnel, a placing of the wrist in bending position, enhancing intra-canalicular pressure, also later night spike in BP and decrease cortisol hormone.[3] Thyroid dysfunction and diabetes mellitus, menopause, sedentary lifestyle, pregnancy, and inflammatory arthritis of the wrist joint are all secondary disorders that reduce the tunnel's space.[4] And also many diseases mimic the characteristics of carpal tunnel syndrome, but they do not include the median nerve, so medical practitioners narrow down the real finding.[5]

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Pregnancy is divided into three trimesters. The most prevalent problem of the last trimester is carpal tunnel syndrome (CTS) with unknown cause. As typically pregnancy lasts between 37 and 42 weeks, during which time the body undergoes various changes to support the developing fetus. The median nerve may be compressed due to a variety of changes connected to pregnancy. Many hormone levels, including angiotensin, rennin, and progesterone, rise in response to physiological changes, resulting in fluid retention, weight gain, fetal growth, and edema. Weight gain during pregnancy may raise the risk of carpal tunnel syndrome, but a more well-known cause is widespread edema, which causes local swelling. Carpal tunnel syndrome is more likely in pregnant women with preeclampsia.[6]

Clinically significant examination finding for the assessment is Phalenmaneuver, flick sign, and median nerve compression test.[1] Boston carpal tunnel questionnaire is a standardized score to predict the severity of Carpal tunnel syndrome (CTS). Usually for secondary conditions imaging is recommended for the affirmation of carpal tunnel syndrome. It is investigated based on symptoms presentation in the clinical setting and affirmed by Electromyogram (EMG) and ultrasonography criteria are very reliable.[7] Along with that median nerve or tunnel, swelling is more accurate for diagnosis through ultrasonography.[8]

Treatment of CTS is surgical and nonsurgical both depending upon the severity of symptoms. Its management must start with the appearance of symptoms.[9] Carpal tunnel syndrome symptoms that normally show during the third trimester may manage and resolve after pregnancy non-operatively.[10]

Meems et al. conducted a cohort study in 2015 to determine the frequency, severity, and edema of pregnancy-related CTS syndrome symptoms in gravida. In the Netherlands, he took a sample of 693 pregnant women. He utilized the Boston carpal tunnel questionnaire to measure Carpal Tunnel Syndrome indications in all trimesters. Edema and sleep difficulties were recorded at several points throughout the pregnancy. To measure depression, he used the Edinburg depression scale. Symptoms of carpal tunnel syndrome were reported in 219 women. The Boston Carpal Tunnel Questionnaire was quite raised after 32 weeks. Only a few women have severe symptoms, although it was observed that pregnant women with Carpal Tunnel Syndrome have higher fluid retention than those who do not have CTS symptoms. The presence of Carpal Tunnel Syndrome has nothing to do with sleep issues.[11]

Descriptive cross-sectional research on pregnant women was undertaken by Khosrawiet al.[12] To diagnose carpal tunnel syndrome, he employed ultrasound imaging, the Boston Carpal Tunnel Questionnaire (BCTQ), and the functional status scale. A total of 100 patients, ranging in age from 17 to 41 years, were studied. CTS affected 19 percent of the population, with bilateral CTS accounting for 47% of the total, and severe CTS accounting for 26.3%. Clinical indications had a sensitivity and specificity of 52% and 23% respectively, when compared to electrodiagnostic results. Pregnancy without indications of CTS before conception was the only criterion for inclusion. Women who had trauma or fracture were excluded.[12]

Syed Rehan Iftikhar Bukhari et al conducted an observation and cross-sectional study. He used Boston Carpal Tunnel Questionnaire, Ultrasonic imaging, functional status scale to confirm the diagnosis. A total of 300 patients ages ranged from 20 – 40 years were included in the research. And among them, 103 patients showed all the symptoms and signs positive and having a prevalence of 34.3%. Out of 300 patients, 103(34%) patients had CTS, and 193 (64%) cases did not show any CTS symptoms.[13]

Yazdanpanahet al[14] had conducted a cross-sectional analytical study. He used ultrasonic imaging, Boston Carpal Tunnel syndrome, Functional status scale to confirm the diagnosis. Total 2656 non-pregnant women and 1508 pregnant women and having the prevalence of pregnant and non-pregnant 3.4% and 2.3 % respectively. 51 pregnant women had CTS. 59% had mild,18.8% had moderate and 21% had severe CTS. Women suffered from paresthesia (88%) and in the physical exams were Tinel's signs (58.9%) and Phalen's test (50.9%).

MATERIALS AND METHODS

This cross-sectional survey research was conducted in different hospitals within six months, from Oct 2020 to March 2021 and comprised 322 patients. Pregnant women with no prior history of carpal tunnel syndrome, Age between 18 to 40 years, women with history of multigravida and primigravida were included. Exclusion criteria involves women who have cervical radiculopathy and osteoarthritis, women who have fracture of wrist or any trauma that leads to chronic pain in arm, age <18 and >40 years. Data was analyzed by using SPSSV-22.

RESULTS

Prevalence of carpal tunnel syndrome in pregnant women during third trimester was 29.11%. Women with severity of hand and wrist pain at night was 45.3%, 31.4% had hand or wrist pain during daytime and 38.8% women feels numbness or tingling sensation in hand. 54.7% participants were normal, 27.6% had slight,12.1% had medium 2.8% had severe, 2.8% had very serious pain in wrist or hand at night (Table 1).

72% were normal, 16.1% had 1-2times/day, 7.4% had 3-5times/day, 3.1% had more than 5 times, 1.2% had continued wrist or hand pain during day time (Fig. 1).

61.2% were normal, 22.7% had slight, 11.8% had medium, 3.7% had severe, .6% had very serious numbness or tingling at night (Table 2).

Table No.1: Severity of hand or wrist pain at night (n=322)

Variable	No.	%
Normal	176	54.7
Slight	89	27.6
Medium	39	12.1
Severe	9	2.8
Very serious	9	2.8

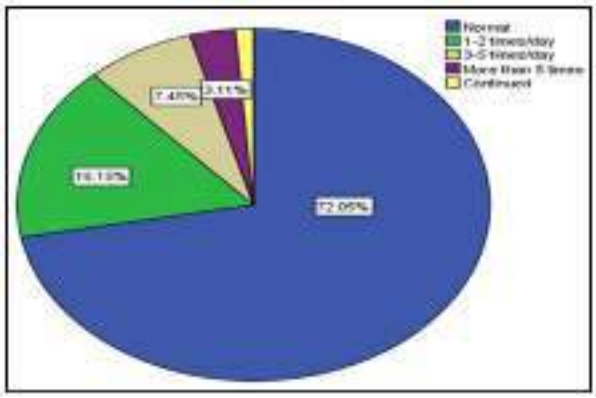

Figure No.1: Frequency of hand or wrist pain during daytime

Table 2: Numbness or tingling at night (n=322)

Variable	No.	%
Normal	197	61.2
Slight	73	22.7
Medium	38	11.8
Severe	12	3.7
Very serious	2	0.6

DISCUSSION

The study focused on the "prevalence of Carpal Tunnel Syndrome in the Third Trimester of pregnancy" in Lahore. This topic has a great importance as there is high prevalence of Carpal Tunnel Syndrome during pregnancy especially in the third trimester, by finding the prevalence, we will be able to educate the women about its symptoms and get it diagnosed and treated as early as possible. The results of this study reflected that women in their third trimester of pregnancy had the highest risk of developing Carpal Tunnel Syndrome. Most of the studies till 2019, different were discussed by different authors separately, in their respective studies. But this study considered all major and most significant variables, which are related to each other. Also these variables are greatly associated with the prevalence of Carpal Tunnel Syndrome in pregnant women in their third trimester.

Guan.[15] used the Boston Questionnaire to measure the severity of the symptoms and functional status. He took the sample of 482 pregnant women, results of the study showed prevalence of 23.03%, whereas in our study, we took the sample of 322 pregnant women, result showed prevalence of 29.11%.[15]

A study conducted by Bukhari[13], they used the Boston Questionnaire. He took 300 pregnant women ranging from 20 to 40 years, out of them 103 pregnant women showed positive results of Carpal Tunnel Syndrome and had a prevalence of 39 34.3%. While in our study, we took 322 pregnant women, results showed 29.11% prevalence of Carpal Tunnel Syndrome.[13].

CONCLUSION

Prevalence of Carpal Tunnel Syndrome in different trimesters of pregnancy in Pakistan and educate them to avoid this syndrome to convert into a more severe and debilitating condition by using proper techniques and preventive measures.

Author's Contribution:

Concept & Design of Study:	Sameena Pari
Drafting:	Mehwish Niaz
Data Analysis:	Laraib Khan, Rida Aziz, Aneela Aslam
Revisiting Critically:	Sameena Pari, Ayesha Siddiqa
Final Approval of version:	Sameena Pari

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

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Original Article

Impact of COVID-19 on Teaching and Learning in Medical Institutions of Sialkot

Sajid Hussain, Iqra Ishaq, Aqsa Ishaq

ABSTRACT

Objective: To find out the impact of COVID-19 on teaching and learning in medial institutes of Sialkot and to indentify the need of communication skills, decision making, problem solving and improving learning assessment outcomes in students.

Study Design: Prospective cohort study

Place and Duration of Study: This study was conducted at the medical institutes of Sialkot from January 2021 to August, 2021 for a period of 08 months.

Materials and Methods: Total 50 professionals of various designations from professors to Senior Registrar of 03 medical institutions namely Khawaja Muhammad Safdar Medical College Sialkot, Islam Medical college Sialkot, Sialkot Medical College were including in the study.

Results:

Conclusion: The impact of COVID-19 on teaching and learning process affects globally, nationally and regionally. The results are to be determined in order to find out barrier in teaching and learning process. The study issues can be resolved by experienced quality instructors, student interest, effective curriculum design and uninterrupted online tutorials.

Key Words: Impact, COVID-19, Challenges, Online, Approaches

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INTRODUCTION

COVID-19 Pandemic has become one of the major health problems throughout this world which was first identified in Whohan china in December, 2019. On 11 March 2020 the WHO declared COVID-19 a pandemic, later on, it went across the whole world and has affected all age group with poor outcomes in particularly those patients who are with Co-morbiditties.[1,2,3] This COVID-19 Pandemic has affected the cultural economic sectors of worldwide countries and at the same time it has affected the teaching and learning process throughout the world. [4] There was a sense of fear among the parents and for which all over schools and colleges were closed and later on it has affected many teachers due to which a lot of intellectual and educational damage has occurred in the college, schools and universities face to face. [5,6] The students and teachers relation stopped and the spiritual relation was converted into an electronic format through internet and other modes of electronic formats. There is a big gap which needs to be bridged up to compare the situation before and after the pandemic in regard to learning and teaching process. The students were not able to work in contact with the patients and thereby they were not able to find out progress of these patients. The clinical skills and at the same time their mode of evaluation. [7-9] Had affected the objective of our study is to find out the impact of COVID-19 Pandemic on teaching and learning process with prospective to teachers. The teachers are in a better position to describe the impact of mode of information transfer, clinical skills and communication skills, decision making, problems solving and criteria.

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MATERIALS AND METHODS

This study has been conducted in Medical colleges where 10 years teaching experience professionals were interviewed from January 2021 to 31st August, 2021. The convenience purpose sampling was carried out.

Exclusion Criteria: - All those teachers with less than 10 years experience was excluded from study. The questionnaire was handed over to teachers after taking proper consent from them.

RESULTS

Most of the subjects (96%) confirmed about the challenges faced during COVID-19 agreed on acceptance of challenges. (As shown in figure no. 1).

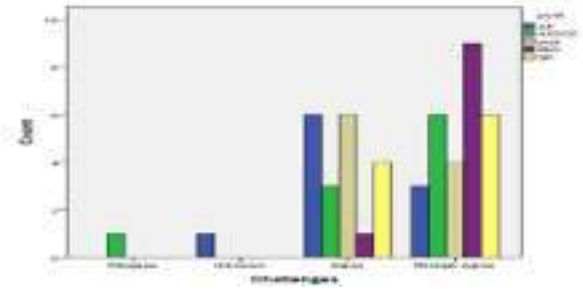

Figure No.1: Graph / Bar (Grouped)=Count by 02 by Post

While 26% of the subjects disagreed on achievement of the learning outcomes as framed in curriculum while 22%. They were in the opinion that they have achieved the learning outcomes. (As shown in figure no. 2).

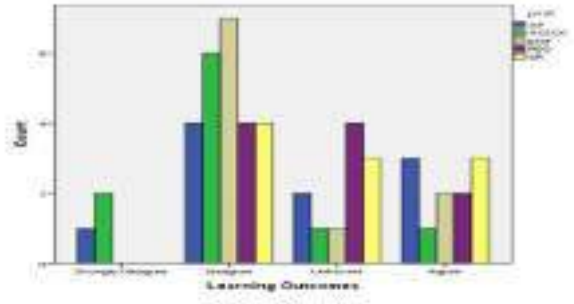

Figure No.2: Learning Outcomes

Similarly, as regard the students academic performance is concerned 80% disagreed regarding the achievement of the improvement in academic performance (As shown in figure no. 3).

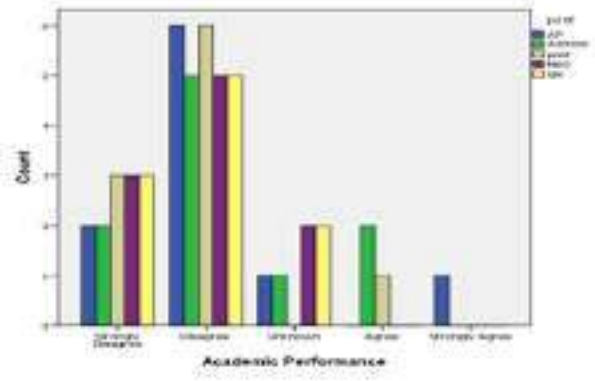

Figure No.3: Academic Performance

When the comparison was done on campus and on the education leading to improvement in their performance revealed 82% of the professionals they were in the opinion that there was no improvement in performance as compared on campus education. (As shown in figure No. 4).

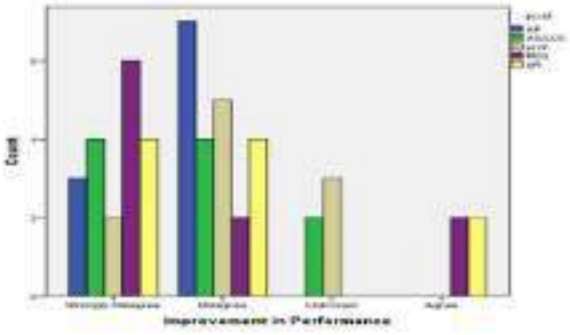

Figure No.4: Improvement in performance

On the need assessment of the new approaches 92% of the participants they agreed to have new approaches (as shown in figure no. 5) as compare to other previous methods used during this COVID-19.

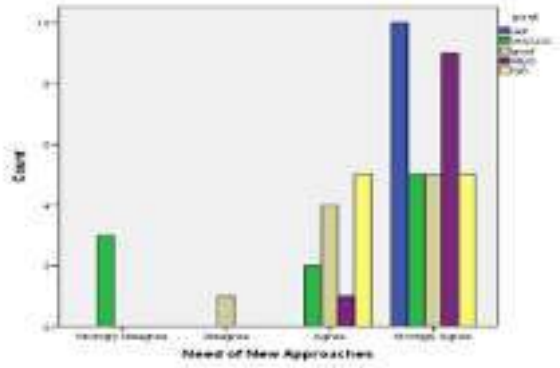

Figure No.5: Need of new approaches

DISCUSSION

When the whole world was facing crisis of pandemic, it was realized that there is need of in depth studies to find out the impact of crises of COVID-19 outbreak.

In our study which was conducted between January, 2021to 31st August, 2021. We tried to find out that how COVID-19 pandemic affected the teaching and learning process in this aspect to students from on sight to online teaching methodologies.

Many academic social, emotional, financial and other challenges were faced by students as predicted in our study. Adapting a new way of teaching, uncertainty, stress are unforeseen challenges. Our study is consistent with survey which was carried out by Martih AJ and ET-all in Australia[10] The face to face encounter of students teachers was withheld and the institute has to modify the curriculum design in order to get the learning objectives in line for which the administration has to hire experienced staff for delivering those curriculum to the students. This study of curriculum design has been highlighted by Jenkins 2015 to get satisfaction from students and our study is consistent

with study carried out by Jenkin. Lectures organized their contents and learning outcomes according to their mode of transmission on the students as occurred during this pandemic and our study is also consistent with our study carried out by Khan Alberto [11] where they have carried out a National survey of medical students in Philippine at time of COVID-19[12] and similarly our study was also incongruent to Sub-Saharen Africa [13] and in odd line survey carried education in other parts of world. From academic performance, we were concerned to find out availability of home infrastructure, students expertise in computer network and both. These issues were raised in the study which was carried out by comcarian at all [14] and also in North America, Europe with students, they were not having any excess to printers connectivity problem as seen in study of Tormay [15].

There was no improvement, whatsoever in student academic performance due to loss of.

CONCLUSION

There is intense need to find out impact of COVID-19 on teaching and learning process. Globally, nationally, and regionally as there are devastating effects of this of this pandemic with unsolved mysterious paradox and negative effects on quality educational outcomes in this distant electronic format learning. There are needs to address these issues through experienced quality instructor, student, interest, proper and timely feedback, effective curriculum design and uninterrupted online learning process.

Author's Contribution:

Concept & Design of Study:	Sajid Hussain
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Data Analysis:	Aqsa Ishaq
Revisiting Critically:	Sajid Hussain, Iqra Ishaq
Final Approval of version:	Sajid Hussain

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

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Original Article

Association between Anemia and Periodontitis- A Case Control Study

Muhammad Jamil[1], Hussam[1], Muhammad Ifham Khan Jadoon[2], Muhammad Naveed Khan[1], Zuhra Anwar[1] and Mashal Riaz[3]

ABSTRACT

Objective: The purpose of this study was to compare frequency of anemia and blood indices in patients with and without chronic periodontitis.

Study Design: Case control study

Place and Duration of Study: This study was conducted at the department of periodontology Khyber college of Dentistry Peshawar Pakistan from January 2020 to October 2020 from a period of 10 months.

Materials and Methods: This case control study was done on 100 participants (50 cases and 50 controls). The inclusion criteria were Pakistani nationals, both genders, age range from 30 to 60 years, having more 16 teeth in the mouth and systemically healthy subjects. The participants were categorized into two groups; cases and controls. Cases were those who had periodontitis while controls were healthy subjects. The collected data were age, gender, presence of chronic periodontitis, and blood parameters. Data analysis was done in STATA 14. Chi-square test and Independent t test was used to compare categorical and continuous variables between cases and controls respectively.

Results: The mean age was 42.51±10.314 years. The males were 54(54%) and females were 46(46%). There was positive and statistically significant association between anemia and chronic periodontitis (P=0.009). Among cases the frequency of anemia was higher (n=14, 28%) than control (n=4, 8%). All the blood parameters had lesser mean values in cases than controls statistically (P<0.05).

Conclusion: There is statistically significant and positive association between anemia and chronic periodontitis. The blood parameters are low in patients with chronic periodontitis than healthy subjects.

Key Words: Anemia, chronic periodontitis, Hemoglobin, blood indices, periodontal pocket

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INTRODUCTION

The term periodontitis is used for chronic inflammation of tooth supporting structure and loss of attachment apparatus leading to either increased sulcus depth or root exposure.(1) The common pathogens involved in chronic periodontitis are gram-negative anaerobic bacteria. Although periodontitis is localized infection but it have enormous systemic effects on human beings.(2, 3)

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The epithelium presents in periodontal sulcus play the role of protective barrier and inhibits the entrance of bacteria and other sort of irritants to the circulatory system.(4) The adverse interaction between host and pathogen in the presence of periodontitis results in ulceration of junctional epithelium.(5) This ulcerated epithelium provides a portal for bacterial entrance into blood resulting in bacteremia. Bacteremia has direct relation with severity of periodontitis.(6) In turn the host response culminates in the activation of tumor necrosis factor-α, interleukin-6 and C-reactive proteins. These activated mediators depress the process of erythropoietin production and ultimately lead to anemia.(1) Chronic anemia is most common type of anemia and has association with many diseases.(7),(8)

In literature many studies have been reported on association of anemia and chronic periodontitis. No association was found between anemia and periodontitis by Gayatri et al.(9) On other hand two other studies reported significant association between anemia and chronic periodontitis.(10, 11)

In recent times interest have been raised regarding the two-way relationships of anemia and chronic periodontitis. There is conflict in studies already done on association of chronic periodontitis and anemia.

There is lack of literature on our local population. This case control study will to help to determine whether real positive association exists between these two conditions in our patients or not.

This study was aimed to compare frequency of anemia and blood indices in patients with and without chronic periodontitis.

MATERIALS AND METHODS

This case control study was conducted at department of Periodontology, Khyber College of Dentistry Peshawar from January 2020 to October 2020 on 100 participants (50 cases and 50 controls). The sampling technique was non-probability consecutive. Verbal informed consent was taken from all participants after detailed explanation about the study.

The inclusion criteria were Pakistani nationals (on basis of NIC), both genders, age ranging from 30 to 60 years, having more than 16 teeth in the mouth and systemically healthy subjects. Participants having hypertension, diabetes, malignancy or any sort of chronic pathology except for chronic periodontitis were excluded from this study.

The included participants were categorized into two groups; group I contain cases and group II had controls. Cases were those participants who had chronic periodontitis while controls were healthy subjects with no sign of gingivitis or periodontitis. Chronic periodontitis was labeled as positive when the loss of attachment of tooth or teeth manifested as increased pocket depth (>3mm) or gingival recession.

The collected data were age, gender, presence of chronic periodontitis, and blood parameters. Venous blood was obtained from each participant in pathology laboratory of Khyber College of Dentistry by specialized nurse. The recorded blood parameters were hemoglobin (Hb), red blood cell count, mean corpuscular hemoglobin (MCH) mean corpuscular volume (MCV), MCH concentration (MCHC) by automated hematologic analyzer machine. Anemia was labeled as positive as per WHO definition <12.0 g/dL in women and <13.0 g/dL in men.

The data analysis was done in STATA 14. Continuous variables were computed as mean and SD while frequencies were calculated for categorical. Chi-square test was applied for association of anemia between cases and controls. Independent t test was used to compare continuous variables (blood parameter) between cases and controls. P≤0.05 was significant level.

RESULTS

The mean age of the study was 42.51±10.314 years with range from 20 to 58 years. The males were 54(54%) and females were 46(46%). The most common age group was 41 to 50 years (n=35, 35%) followed by 51 to 60 years (n=26, 26%). The details are given in Fig 1.

There was positive and statistically significant association between anemia and chronic periodontitis in overall sample (P=0.009) and in both males (P=0.043) and females (P=0.045). For overall sample among cases (chronic periodontitis) the frequency of anemia was higher (n=14, 28%) than controls (n=4, 8%). Similar results were found for both males and females. The details are given in table 1.

There was no statistically significant difference in age between cases and controls (P=0.321). All the blood parameters had lesser mean values in cases than controls statistically (P<0.05). The mean hemoglobin was 13.26±0.77 g/dl in cases and 13.76±0.77 g/dl in controls and the difference was statistically significant (P=0.002). Rest of detail is shown in table 2.

DISCUSSION

This case control study was conducted to determine the association of anemia and chronic periodontitis. Our findings showed that there was positive and statistically significant association between anemia and chronic periodontitis in overall sample (P=0.009) and in both males (P=0.043) and females (P=0.045).

Anemia is quantitative or qualitative reduction in number of red blood cells. In quantitate the actual numbers of RBCs are reduced while in qualitative the hemoglobin level is reduced.[12] Blood indices like mean corpuscular volume, mean corpuscular hemoglobin (MCH), and MCH concentration are used to further classify anemia.[13]

The real pathogenesis of chronic periodontitis in the causation of anemia is not clear. The chronic periodontitis is though localized infection of the periodontium but it has systemic effects. During periodontitis sulcular epithelial barrier breakdown and bacteria from oral cavity enter the blood stream results in bacteremia. The bacteria released interleukin-1, tumor necrosis factor, and C-reactive protein. These mediators in turn suppress erythropoiesis and cause anemia.[1]

In literature two way relationships between anemia and chronic periodontitis have been reported. One school thought is that anemia is the cause of chronic periodontitis[14] while other have reverse concept.[10]

Our study showed positive association between anemia and chronic periodontitis. Diversity exist in literature, few studies showed no association between anemia and chronic periodontitis [9] while most of the studies revealed positive association between these two conditions. [10, 11, 15]

Our findings showed that all blood indices like RBC count, mean corpuscular volume, mean corpuscular hemoglobin (MCH), and MCH concentration were low in participants with periodontitis than healthy subjects. Parihar et al.[15] conducted a case control study on

Indian population on 80 patients (40 were cases and 40 were controls) on association of anemia and chronic periodontitis. Their results showed that all these blood indices were low in cases than control statistically. These results are in consistent with our study.

CONCLUSION

There is statistically significant and positive associations exist between anemia and chronic periodontitis. The blood parameters are low in patients with chronic periodontitis than healthy subjects.

Author's Contribution:

Concept & Design of Study:	Muhammad Jamil
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Comparison between Efficacy of Triphasic CT and FDG-PET in the Follow-Up Evaluation of Hepatocellular Carcinoma

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ABSTRACT

Objective: To analyze the efficacy of FDG PET as compared to triphasic CT in diagnosing the residing or reoccurred tumor lesions of HCC following TACE therapy.

Study Design: A cross-sectional study

Place and Duration of Study: This study was conducted at the department of radiology and oncology department of Nishtar Medical University & Hospital Multan from April 2020 to April 2021 for a period of 01 year.

Materials and Methods: After passing through the inclusion and exclusion criteria, 35 patients diagnosed with hepatocellular carcinoma and undergoing TACE were evaluated for residing or reoccurred tumor lesions through FDG-PET and triphasic-CT. Image analysis for each imaging modality was done by following a standard protocol. Imaging, clinical, and laboratory findings were used as a reference for validating the accuracy of the data. SPSS was used for statistical analysis.

Results: Analysis of reference data demonstrated proved 23 (65.7%) true positive cases. Whereas FDG-PET had shown positivity in 26 (74.2%) and triphasic-CT had positivity in 27 (77.1%) patients. FDG-PET has a sensitivity of 100%, specificity of 65.7%, a positive predictive value of 88.4%, and a negative predictive value of 100%. Whereas, triphasic-CT has a sensitivity of 80.5%, specificity of 65.2%, a positive predictive value of 85.1%, and a negative predictive value of 66.6%.

Conclusion: The study found better accuracy of FDG-PET in detecting residing or reoccurred HCC tumor lesions than triphasic CT.

Key Words: Triphasic-CT, FDG PET, hepatocellular carcinoma, TACE

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INTRODUCTION

Hepatocellular carcinoma (HCC) is one of the most reported primary malignancies of the liver. It is ranks fifth among the most common malignancies and the third most frequent cause of tumor-related death [(1)]. However, the recent decades have witnessed a sudden rise in the incidence of HCC which is majorly related to the increased frequency of disorders that pose a risk of hepatic cirrhosis like alcohol abuse, obesity, and viral hepatitis [(2)].

Surgical interventions such as liver transplants and hepatic resection are deemed as the most effective treatment strategy. However, patients presenting with inoperable HCC are managed through conventional treatment schemes[(3)]. Among these schemes, Transarterial chemoembolization (TACE) is a reliable non-surgical approach that involves the blockage of blood supply to the tumor through injecting chemotherapeutic agents to the tumorous area [(4)]. It is found that around 15-55% partially respond to TACE management and therefore regular assessment of the therapy is compulsory to decide the future treatment plan [(5)].

In this regard, in recent years, Positron emission tomography (PET) with 18F-2-fluoro-2-deoxyglucose (18F-FDG) has increasingly being utilized for initial staging and assessing the treatment response in multiple malignancies. 18F-FDG PET monitors the glucose metabolic activity of cancers and provides a critical assessment that is usually not provided by conventional imaging technologies [(6, 7)].

However, 18F-FDG PET has still not completely replaced the Computed tomography (CT) scan in most of the setups in Pakistan. This study, therefore, is designed to analyze the efficacy of FDG PET as compared to triphasic CT in diagnosing the residing or reoccurred tumor lesions of HCC following TACE therapy. The study will help to adopt better imaging modalities for the management of HCC.

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MATERIALS AND METHODS

A cross-sectional study was conducted from 30th April 2020 to 30th April 2021 at the department of radiology and oncology department of Nishtar Medical University & Hospital Multan. The Patients aged between 35 to 60 years, having clinically proved HCC and managed by TACE were included in the study. Whereas, the patients who had a history of allergic reactions to contrast material, who had never undergone a locoregional treatment for HCC, or were on treatment protocol other than TACE were excluded from the study. Patients were informed of the study objectives and their consent was sought. The study was approved by the ethical committee of the hospital.

All patients were guided to maintain a low-carbohydrate and a high protein diet for at least 24 hrs. before the scan whereas fasting state was asked to maintain 6 hrs. before the scan. The diabetic patients, however, were allowed to take early breakfast with their anti-diabetic medicine. This was done to achieve recommended glucose levels before the scan. i.e. ≤150 mg/dl. Similarly, physical activity was guided to be kept minimal a day before the study, and water intake was kept high to keep the bladder full before the scan. Patients were kept in a warm environment to avoid fat uptake and beta-blockers were also administered to those where keeping in a particular environment was not adequate. The muscular activity was restricted before the scanning such that patients were not allowed to talk. Lastly, metal objects accompanying patients were removed to avoid their interference in the results. PET and triphasic CT scans were done for all patients to evaluate the occurrence of newly developed focal lesions and assess the management of old ones.

Negative oral contrast was administered to all patients 1 hour before the examination. Then, the radioactive tracer, 18F-FDG, was administered with a dose of .1-.4 mCi/kg. For one hour patients were kept in a dark hot environment and were restricted to talk or take any physical movement. In both examination types, scans were taken from the skull base to the mid-thigh. Both imaging protocols were preceded by low-dose CT without contrast. Afterward, FDG PET [8] and contrast-enhanced triphasic CT [9] was performed according to recommended protocols. Following the examination, the patients were advised to avoid contact with infants, pregnant women, and high-risk individuals and to drink plenty of water to pass out the tracers.

The image analyses were conducted by two independent consultant radiologists who were kept blinded to study objectives. However, they were informed of the patient's history of TACE management, including management routine and focal lesion characteristics. For analysis of FDG-PET scans, axial, coronal, and sagittal reconstructed images were first visually analyzed. The standard cutoff value was based on uptake by normal hepatic parenchyma which ranged from 2.4 to 4.5 standardized uptake value (SUV). So pathology was attributed to any area with FDG greater than these values. Maximum standardized value (SUVmax) represented FDG uptake quantitatively. Similarly, the CT sagittal, coronal, and axial reconstructed images were first visually analyzed. Then characteristics of focal lesions such as size, site, contrast enhancement, unilobar or bilobar lipiodol retention, and pattern of contrast in three phases. CT scans were also looked for new lesions.

Patients were then followed up clinically, through serum level measurement of Alfa-fetoprotein, and radiologically through various imaging technologies such as MRI, ultrasonography, or PET/CT. This was done to confirm the accuracy of our analyzed techniques.

SPSS (version 18) was used for the statistical analysis of the data. We utilized the follow-up data (imaging, laboratory, and clinical) as a reference for determining the accuracy of CECT as compared to FDG/PET in detecting recurrence or development of any new lesion. In this regard, specificity, sensitivity, negative predictive value, and positive predictive value were calculated.

RESULTS

A total of 35 patients, 30 males (85.7%) and 5 females (14.2%) and aged from 35 to 60 were enrolled in the study. The reference data collected through clinical, laboratory, and imaging analysis demonstrated new focal lesions development or tumor recurrence in 23 patients at TACE-managed HCC. The maximum diameter of an individual HCC lesion was 6.5cm while those residing in multiple forms ranged from 4.1cm to 7.5 cm. All lesions were unipolar.

PET examination showed enhanced pathological uptake of tracer in 26 (74.2%) patients at the TACE bed while 9 (25.7%) patients had no pathological uptake. Whereas, triphasic-CT examination demonstrated typical pathological images of contrast enhancement at the HCC site in 17 (48.5%) patients. The pathological pattern depicted arterial phase wash in and wash out in both delayed and portal phases. 8 (22.8%) patients had atypical contrast enhancement either faint or marginal arterial enhancement presenting with no washout whereas 8 (22.8%) patients had no enhancement at all. Among these 14 patients, 5 were positive for pathological uptake of FDG in PET scans (Table I).

Comparison with the reference data showed PET gave accurate positive results in 23 patients, true negative results in 9 patients, false-positive results in 3 patients while no false-negative result. Whereas, CECT reported accurate positive results in 23 patients, true-negative in 8 patients, false-negative in 4 patients, and false-positive results in 4 patients. Table 2 shows a comparison of reference data with the findings of

CCET and PET for the detection of local residue or recurrence of HCC.

By analyzing the data, we could calculate the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of the two analyzed modalities, CECT, and PET. FDG-PET has a sensitivity of 100%, specificity of 65.7%, PPV of 88.4%, and NPV of 100%. Whereas, triphasic-CT has a sensitivity of 80.5%, specificity of 65.2%, PPV of 85.1%, and NPV of 66.6% (Table 3).

Table No.1: Imaging features of lesions under management

Imaging modality	Managed lesion criteria	Patients count	age (%)
FDG PET	Enhanced tracer uptake	26	74.2%
	No uptake	9	25.7%
Triphasic CT	Contrast enhancement	17	48.5%
	Atypical contrast enhancement	8	22.8%
	No contrast enhancement	8	22.8%

Table No.2: Comparison of findings of PET and CECT with true reference cases

	Positive cases	age (%)	Negative case	age (%)
Accurately diagnosed Reference cases	23	65.7%	12	34.2%
PET	26	74.2%	9	25.7%
CECT	27	77.1%	8	22.8%

Table No.3: Comparison of statistical analysis of PET and CECT hepatic tumorous lesions under TACE management

Imaging modality	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
CECT	80.5%	65.2%	85.1%	66.6%	77.3%
PET	100%	65.7%	88.4%	100%	92%

DISCUSSION

Imaging technology has a critical role in managing HCC, and response to any adopted treatment strategy is mostly assessed and monitored radiologically [10]. Usually, the recommended therapies aim to reduce the tumor vascularization, enhance the necrotic area, and often produce cavities in large tumors [11]. To analyze these changes following any locoregional intervention procedure imaging modalities like dynamic MRI, CECT, and ultrasound are utilized. However, the deposition of lipiodol in patients under TACE management hinders efficient evaluation through imaging [12].

In HCC patients under TACE management, contrast-enhanced triphasic CT examination provides significant details regarding tumor vascularity and its size which may influence the viability or recurrence of the tumor. However, the existence of hyperdense lipiodol and their masking effect of intra-le tumor tissues mainly limits the diagnostic capacity of CT [13]. FDG-PET evaluates glucose metabolism of the cancers that are managed by TACE, the frequent therapeutic strategy in oncology. It also gives the advantage of investigating the entire body so that intra- and extra-hepatic tissue examination can be made which is critical in planning for hepatic transplantation [14]. Several studies have been conducted to evaluate the role of PET in assessing the locoregional treatment of HCC. This study aimed to compare the potency of FDG-PET against triphasic-CT in evaluating the local tumor recurrence and new lesion formation of hepatic tumor following TACE.

The results demonstrated that the triphasic-CT had a specificity of 65.2%, a sensitivity of 80.5%, PPV of 85.1%, an NPV of 66.6%, and accuracy of 77.3%. However, PET had specificity and sensitivity of 65.7% and 100%, respectively. Moreover, PPV and NPV were 88.4% and 100%, respectively. Contrastingly, Jinpeng et al, who studied recurrence of HCC in 29 patients who underwent TACE, reported that sensitivity of CECT was 63.8% and that of PET was 95.4% [11]. Similarly, Song et al, also reported dominance of FDG-PET, performed in conjunction with CT, over CECT in the detection of HCC following TACE [15]. Azab et al evaluated patients undergoing local therapy including TACE and radiofrequency for HCC. The authors reported higher sensitivity and specificity of FDG-PET/CT when compared with contrast CT, regardless of tumor vascularity [16]. Similarly, Wenhui et al proved the diagnostic value of 18F-FDG PET/CT in diagnosing viable HCC. Also, it was concluded that the accuracy of PET is directly related to the grade of the tumor i.e. low-grade tumors are better evaluated.

The study was limited in terms of smaller sample size and lesser study period. Moreover, the study depended upon follow-up data for determining the accuracy of data which might have produce bias in the results. The bias could have been removed by referring to histopathological findings.

CONCLUSION

The study found better accuracy of FDG-PET in detecting residing or reoccurred HCC tumor lesions than triphasic CT.

Author's Contribution:

Concept & Design of Study:	Soban Shahid
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Risk Factors and Prognosis of Acute Kidney Injury in Pre-Eclampsia

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ABSTRACT

Objective: To explore the risk factors and clinical outcomes in women with preeclampsia who developed AKI.
Study Design: A prospective observation study
Place and Duration of Study: This study was conducted at the gynecology department of Bakhtawar Amin Trust Teaching Hospital Multan from June 2020 to June 2021.
Materials and Methods: The study was conducted on pregnant women admitted to the hospital with pre-eclampsia. Women with maximum creatinine ≥90 µmol/L during admission were assessed for pre-pregnancy serial creatinine level. Kidney Disease Improving Global Outcomes criteria were adopted to evaluate the renal injury and its recovery. Predetermined risk factors, maternal and neonatal outcomes were contrasted between AKI stages.
Results: Among the total of 50 women with pre-eclampsia, 13 (26%) women qualified for the AKI KDIGO criteria. Of these, 7 (14%) had AKI stage 1, 4 (8%) had stage 2, and 2 (4%) had stage 3. Women with AKI (Stages 1-3) had a significantly higher incidence of stroke (risk ratio (RR), 15.5; 95% CI, 1.5- 157.7; p=0.012), eclampsia (RR, 1.6; 95% CI, 1.1-2.5; P=0.003) and were likely to die more (RR, 3.9; 95% CI, 1.2-12.3; P=0.002) than the woman who didn't develop AKI. Similarly, women with AKI were more prone to experience a stillbirth (RR, 1.9; 95% CI, 1.6-2.6; P<0.01) and neonatal death (RR, 2.3; 95% CI, 2.2-2.5; p=0.001). Hypertensive disorder in a previous pregnancy was the strongest predictor of the development and severity of AKI. It was found that the recovery rate reduced with an increase in the severity of the disease.
Conclusion: Conclusively, AKI was found to be a common complication in women with pre-eclampsia and resulted in considerable maternal and neonatal mortality. The failure to acquire absolute recovery of the affected population requires serious consideration of risk factors.

Key Words: AKI, pre-eclampsia, renal outcomes, pregnancy

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INTRODUCTION

Globally, the prevalence of pregnancy-associated acute kidney injury (AKI) has declined over the last few decades due to betterment in reproductive health care [1]. However, it remains a major factor behind dialysis initiation in low developing states [2,3], including Pakistan, and contributes to increasing rates of neonatal and maternal morbidity and mortality[2,4]. The situation is majorly due to the scarce understanding of contributing risk factors that limits the utilization of available resources. Additionally, the majority of studies published on this subject have contradicted due to reliance on diverse AKI definitions and only a few document incidence as per Kidney Disease Improving Global Outcomes (KDIGO) criteria [3].

Regardless of pregnancy, AKI is a strong risk factor for chronic kidney disease (CKD) [5,6] and the literature suggests a higher incidence of CKD in low-income states. The incidence of CKD in women of reproductive age is twice in low-income states as that of high-income states (9% vs 5.9%, respectively) [7], but the association between pregnancy-associated AKI and consequent CKI is largely unknown in developing states.

Across the world, hypertensive disorders during pregnancy are majorly recognized as the cause of pregnancy-associated AKI [4,2,8,9]. However, to the best of our knowledge, no study in Pakistan has yet investigated the association between the two conditions. Therefore, this study was designed to explore the risk factors and clinical outcomes in women with preeclampsia who developed AKI.

MATERIALS AND METHODS

A prospective observational study was conducted at the gynecology department of Bakhtawar Amin Trust Teaching Hospital Multan for 1 year between 5th June

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2020 to 5th June 2021. All women diagnosed with preeclampsia were consecutively enrolled according to a predetermined sample size of 50, calculated considering 95% confidence interval and 80% power of the study. Written consent was acquired from all enrolled women and ethical approval was sought from the ethical committee of the hospital. At admission, age, parity, body mass index (BMI), systolic blood pressure (SBP) and diastolic blood pressure (DBP), serum creatinine levels, and results of urine analysis through dipstick were recorded. Women with serum creatinine ≥90 µmol/L were asked to provide serial pre-pregnancy creatinine reports and were also evaluated for hematological and other biochemical indicators. Women who failed to provide previous medical data were excluded from the study.

Following potential risk factors for AKI were assessed: BMI, maternal age, parity, gravidity, various comorbidities, including anemia (Hb <9g/dL), chronic hypertension, and HIV, and history of former pregnancy with the hypertensive disorder. The KDIGO creatinine criteria were used to classify AKI stages and to determine kidney recovery at the day of discharge and during follow-up in all women with maximum creatinine ≥90 µmol/L while admitted for pre-eclampsia. Baseline creatinine was referred to lowest creatinine level <90 µmol/L before pregnancy whereas, if no such pre-pregnancy creatinine value is found, the lowest creatinine level at pregnancy was considered baseline creatinine. Maximum creatinine referred to highest creatinine value ≥90 µmol/L while admitted in the hospital. Discharge and follow-up creatinine was characterized as single minimum creatinine at the day of discharge and during follow-up after discharge, respectively. Maximum to baseline creatinine ratios were calculated according to KDIGO staging criteria. Ratios higher than 1.5, 2, and 3 denoted 1, 2, and 3 stages, respectively. Creatinine levels were evaluated during the first 48 hrs. After admission to assess minimum and maximum values. Minimum creatinine at discharge or follow-up to baseline ratios <1.5 determined recoveries at discharge and follow-up.

SPSS (version 17) was used for statistical analysis. Logistic regression analysis determined the relationship between baseline data and clinical conditions and the incidence & severity of AKI. Outcome data were categorized as: no AKI, max creatinine ≥90 µmol/L but not satisfying AKI criteria, AKI stage 1, AKI stage 2, AKI stage 3. Kruskal-Wallis test was used for simple comparisons between study groups.

RESULTS

A total of 50 women with pre-eclampsia were enrolled in the study. Among them, 16 (32%) women reported a maximum creatinine level ≥90 µmol/L during admission. Further, of these 16 women, Serial changes in creatinine level of 13 (26%) women qualified the AKI KDIGO criteria. Of these, 7 (14%) had AKI stage 1, 4 (8%) had stage 2, and 2 (4%) had stage 3. In these 13 women, urea, creatinine, and white blood cells were found to be raised whereas hemoglobin levels were reduced. Among 2 women with AKI stage 3, 1 (50%) required dialysis for a median duration of 5 days (range 2-6).

Table 1 presents the demographics and admission characteristics of patients whereas maternal and neonatal outcomes are described in Table II. Women with AKI (Stages 1-3) had a significantly higher incidence of stroke (risk ratio (RR), 15.5; 95% CI, 1.5-157.7; p=0.012), eclampsia (RR, 1.6; 95% CI, 1.1-2.5; P=0.003) and were likely to die more (RR, 3.9; 95% CI, 1.2-12.3; P=0.002) than the woman who didn't develop AKI. There were 2 (2%) maternal deaths in the AKI group and no statistical difference was found between 3 sub-groups based on AKI stages. However, the incidence rate of stroke and eclampsia were significantly different between the groups. Similarly, women with AKI were more prone to experience a stillbirth (RR, 1.9; 95% CI, 1.6-2.6; P<0.01) and neonatal death (RR, 2.3; 95% CI, 2.2-2.5; p=0.001). The incidence rate of stillbirth and neonatal death increased with the severity of AKI; however, no significant difference was found between these sub-groups.

Individual and step-wise logistic regression of predicted risk factors indicated that age, gravidity, parity, chronic hypertension, the hypertensive disorder in a previous pregnancy, admission SBP, and DBP at maximum SBP significantly played role in the incidence and severity of AKI (Table 3).

Table IV presents the recovery rate among women with AKI. It was found that the recovery rate reduced with an increase in the severity of the disease.

Table No.1: Demographics and admission characteristics of participants

Variable	No AKI		AKI		
	Max Cr <90 (n=37)	Max Cr ≥90 but AKI criteria reached (n=3)	Stage 1 (n=7)	Stage 2(n=4)	Stage 3(n=2)
Baseline creatinine umol/L, mean (SD)	-	-	72 (21)	60 (40)	58 (32)
Time at which creatinine was measured					
Prepregnancy			2 (1.9)	3 (4.5)	1 (1.6)
During admission			86 (80.4)	45 (67.2)	52 (82.5)

Following discharge			1 (0.9)		
Maternal demographics					
Age (years), mean (SD)	26.3 (5.2)	25.1 (6.5)	27.3 (5.8)	27.1 (5.5)	26.9 (5.8)
Body mass index (kg/m^2), mean (SD)	29.5 (6.9)	26.3 (5.9)	30.4 (6.9)	29.4 (5.8)	27.6 (6.2)
Primiparous, n (%)	14 (37.8%)	2 (66.6%)	2 (28%)	1(30.5%)	1 (50%)
Admission characteristics					
Admission SBP (mmHg), mean (SD)	143 (18)	145 (16)	149 (19)	151 (23)	159 (29)
Admission DBP (mmHg), mean (SD)	94 (15)	94 (13)	97 (20)	103 (17)	106 (22)
Admission urine dipstick, n (%)*					
1+	9 (13%)	-	1 (14.2%)	-	
2+	12 (32%)	2 (66.6%)	2 (28.5%)	1 (25%)	1 (50%)
3+	10 (27%)	1 (33.3%)	4 (57.1%)	2 (50%)	1 (50%)
Negative	6 (16.2%)	-	-	1 (25%)	

*= statistical significance between groups ($p<0.05$)

Table No.2: Maternal and neonatal outcome of study groups

Variable	No AKI		AKI		
	Max Cr <90 (n=37)	Max Cr ≥90 but AKI criteria reached (n=3)	Stage 1 (n=7)	Stage 2(n=4)	Stage 3(n=2)
Maximum SBP* (mmHg), mean (SD)	169 (15.5)	171 (16)	177 (17)	180 (20)	185 (23)
Maximum DBP* (mmHg), mean (SD)	99 (15)	103 (17)	110 (17)	112 (19)	112 (22)
Mode of delivery					
Caesarean section	27 (72.9%)	2 (66.6%)	5 (71.4%)	3 (75%)	2 (100%)
Vaginal delivery	10 (27%)	1 (33.3%)	2 (28.5%)	-	-
Eclampsia*	3 (11.1%)	-	-	1 (25%)	1 (50%)
Stroke*	1 (2.7%)	-	1 (14.2%)	-	-
Maternal death*	1 (2.7%)		1 (14.2%)	-	1 (50%)
ICU admission*	10 (27%)	1 (33.3%)	3 (42.8%)	2 (50%)	2 (100%)
Neonatal outcomes (n=54), n (%)					
No. Of babies	37	4	7	4	3
Still birth*	5 (13.5)	-	3 (42.8%)	2 (50%)	1 (50%)
Neonatal death*	2 (5.4)	1 (33.3%)	1 (14.2%)	-	1 (50%)

*= statistical significance between groups ($p<0.05$)

Table No.3: Logistic regression of predicted risk factors of development and severity of AKI

Risk factors	Odd ratio	95% CI	Z-score	P-value
Anemia	1.21	0.45–2.99	0.38	0.71
HIV	1.30	0.61–2.23	0.76	0.42
Primiparous	.70	0.43–1.16	-1.37	0.23
Parity (ascending)	1.23	1.00–1.48	2.12	0.02
Gravidity (ascending)	1.20	1.02–1.39	2.23	0.03
Chronic hypertension	1.90	1.12–3.43	2.47	0.013

Hypertensive disorder in a previous pregnancy	2.0	1.22–3.54	2.81	0.004
BMI	0.90	0.78–1.14	-0.81	0.32
Age	1.01	1.04–1.11	2.75	0.007
Admission SBP	0.94	.98– .99	-2.12	0.02
DBP at maximum SBP	1.01	1.0–1.04	2.41	0.012

DISCUSSION

The study found out that 26% of women with pre-eclampsia developed pregnancy-associated AKI according to KIDGO standard. Moreover, stillbirths, stroke, maternal death, and eclampsia were raised in women with AKI than their counterpart. It was unique to find out the significant impact of hypertensive complication in previous pregnancy on the development and severity of AKI. 84% of patients recovered fully after the completion of follow-up.

The significant association of AKI with stillbirths and maternal deaths reported in this study is in alliance with the description given in a related meta-analysis [3]. However, it is challenging to compare the incidence reported in different studies due to the adoption of various pregnancy-associated AKI[4,10]. Only a few previous related studies followed KIDGO AKI criteria[7]. In similar studies, less than 20% of AKI experiencing cases suffered maternal death while the need for dialysis ranged from 0-54.6% [11, 12, 13] with absolute renal recovery in 69.4% [4], 89.4%[2], and 84.6% [13] cases. Another study reported that 1.25% of cases were dependent on dialysis [4]. These contradicting outcomes are majorly due to variable definitions of AKI and different etiologies. The high incidence of eclampsia in our study complies with a South African study[14]. Given this high eclampsia rate, a higher cesarean section was expected since most of the women experienced preterm pre-eclampsia that is mostly linked with placental dysfunction that commonly hinders birth through vaginal route [15].

The literature considers cardiovascular diseases, diabetes mellitus, hypertension, renal insufficiency, and high gestational age as likely risk factors for the development of AKI in non-pregnant cases[16,17]. However, it seems to be scare when it comes to risk factors of pregnancy-related AKI. Our study found a significant association of history of hypertension in a previous pregnancy was significantly associated with AKI development and this risk factor remained independent of other risk factors. It has recently been proposed that individuals having reduced renal reserve are more prone to develop AKI as they can't respond to protein loading[18]. Subsequently, it is predicted that hypertensive disorder in previous pregnancy likely reduces renal reserve and thus the capacity to deal with psychological changes of the subsequent pregnancy. Moreover, it is found that pre-eclampsia incidence increases by 4 fold in women with a former pregnancy with AKI despite the recovery. Thus, non-apparent sub-clinical renal disease likely influence the incidence of pre-eclampsia and AKI.

Our study found out that 15.3% of women failed to recover fully after the follow-up period which is higher than reported in the previous study (9.5%) [12]. This might be due to the difference in the severity of the disease and the follow-up scheme. The recovery rate of non-pregnant women is found to be lower than that of pregnant probably due to any protective effect of pregnancy[19].

CONCLUSION

Conclusively, AKI was found to be a common complication in women with pre-eclampsia and resulted in considerable maternal and neonatal mortality. The failure to acquire absolute recovery of the affected population requires serious consideration of risk factors.

Author's Contribution:

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Original Article

Frequency of Left Main Coronary Artery Stenosis with ST-Segment Elevation in Lead aVR in Patients of Acute Coronary Syndrome

Left Main Coronary Artery Stenosis with ST-Segment Elevation

Azhar Shahzad[1], Syed Naseem Bukhari[1], Ali Bin Saeed[1], Tariq Mehmood Khan[1], Nauman Ali[2] and Muhammad Zubair Zaffar[1]

ABSTRACT

Objective: To determine the frequency of STEL-aVR with left main coronary artery (LMCA) stenosis among patients with Acute Coronary Syndrome (ACS).

Study Design: A 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 May 2020 to May 2021.

Materials and Methods: Patients from both genders within the age bracket of 35-75 years, diagnosed with Acute Coronary syndrome and having AT elevation≥ 0.5mm on aVR lead were included in the study. All the participants were then under coronary angiography to diagnose left main coronary artery (LCMA) stenosis. SPSS (version 18) was used for statistical analysis.

Results: A total of 220 patients were enrolled. Out of them, 188 (85.4%) were positive for the LCMA stenosis. Moreover, 140 (63.6%) were male that indicated male dominance. The majority 170 (77.2%) were aged above 55 years. However, no significant association was found between age and gender and LMCA stenosis. STEMI was the most frequent disorder (47.7%), so the maximum positivity rate of stenosis was found in patients with STEMI.

Conclusion: ST-elevation-aVR is an effective tool for the diagnosis of left main coronary artery stenosis in patients suffering from the acute coronary syndrome.

Key Words: Acute coronary syndrome, left main coronary artery stenosis, electrocardiography (ECG), STEL>aVR, cardiac disorders.

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INTRODUCTION

Coronary artery disease (CAD) is one of the major causes of mortality in the United States [(1)] and across the world. Acute coronary syndrome (ACS) is categorized into three types: acute ST-elevation myocardial infarction (STEMI), acute non-ST elevation myocardial infarction (NSTEMI), and unstable angina (UA). In cardiac disease patients, especially with ACS, accurate and timely diagnosis of significant left main coronary artery disease is very important [(1, 2)].

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A Left Main Stem (LMS) stenosis is defined as a lesion when its size grows significantly larger to an extent that mostly 50% of the vessel is occupied. About 4-6% and 30% of all the patients undergoing coronary angiography[(3)] and Coronary Artery Bypass Grafting (CABG), respectively, demonstrates LMS stenosis[(4,5)]. In 70% of cases, LMS is associated with multi-vessel coronary artery disease (MVCAD) [(6, 7)]. The affected obstructed vessel can compromise up to 75% of blood flow to the left ventricle if left unprotected by a patent bypass graft in the Left Circumflex artery or the Left Anterior Descending (LAD) artery or through collateral flow. Such unprotected patients are at high risk of experiencing severe cardiovascular events. Before the practice of revascularization with CABG as standard care, patients with ACS had a poor prognosis with only a 37% of survival rate [(8)]. CABG has significantly improved the clinical outcomes and fatality rate related to cardiovascular diseases [(9)].

In one of the previous studies, patients within the LMS group were distinguished from those in the LAD group with the electrocardiogram finding of ST-Segment elevation-aVR≥V1[(10)]. Based on these results, we have designed this study to evaluate the frequency of STEL-

aVR with left main coronary artery stenosis among patients with ACS. Patients with comorbidity of these two clinical features will then undergo coronary angiography. Accessing the diagnostic value of lead aVR for LMCA stenosis will underscore the diagnostic ability of ECG for this disorder.

MATERIALS AND METHODS

A cross-sectional study was conducted from 11th May 2020 to 11th May 2021at the department of Cardiology in Ch.Pervaiz Elahi Institute of Cardiology Multan. A sample size of 220 patients was calculated for the study by considering 6% prevalence of LMCA stenosis with STEL-aVR in ASC, 3% margin of error, and 95% confidence interval. Patients aged between 35 to 75 years, diagnosed with ACS and presenting STEL-aVR>0.5mm were included in the study. Whereas, patients with chronic kidney disease; those with severe anemia; those with dextrocardia; those who had the experience of circulatory shock or any other major complication during angioplasty; those with left ventricular ejection fraction (LVEF)<20%, and patients with the history of coronary artery bypass graft (CABG). After passing through the inclusion and exclusion criteria, 220 patients visiting the cardiology department were consecutively enrolled. Participants of the study were informed of the research objectives and their consent was sought. The study was approved by the ethical committee of the Hospital. Initially, baseline data included demographics and clinical history of all participants was collected. The possible effect of confounding variables such as gender and age was controlled by stratification. All the patients then coronary angiography-a gold standard for diagnosis of coronary artery disease.

SPSS (version 18) was used for the statistical analysis of the data. Categorical data were presented as frequency and percentage. Whereas, continuous data were presented as mean with standard deviation. Data were stratified for gender and age. The significance of the data was assessed through Pearson's chi-square test. A p-value less than 0.05 was considered statistically significant.

RESULTS

A total of 220 with ACS and STEL-aVR were consecutively enrolled. Coronary angiography demonstrated LCA stenosis in 175 (79.5%) patients who presented with STEL-aVR lead of ECG. Among the participants, 140 (63.6%) were male and 80 (36.3%) were female, indicating male dominance among the patients with ACS. The majority of patients 170 (77.2%) were aged between 55 years. 105 (47.7%) had STEMI, 86 (39%) had NSTEMI, and 29 (13.1%) had unstable angina. (Table I). 100 (95.2%) with STEMI, 72 (83.7%) with NSTEMI, and 16 (55.1%) with UA were positive for LMCA stenosis.

Table No.1: Data stratification of the participants

		Frequency	age (%)
Gender	Male	140	63.6%
	Female	80	36.3%
Left main coronary artery stenosis	Yes	175	79.5%
	No	45	20.5
Age	>35-55	50	22.7%
	>55	170	77.2%
Diagnosis	STEMI	105	47.7%
	NSTEMI	86	39%
	UA	29	13.1%
Total		220	100

Table No.2: Frequency of Left Main Coronary Artery Stenosis among patients with ACS

Provisional Diagnosis		Left main coronary artery stenosis		Total
		Yes	No	
STEMI	Count	100	5	105
	age (%)	95.2%	4.76%	100%
NSTEMI	Count	72	14	86
	age (%)	83.7%	16.2%	100%
UA	Count	16	13	29
	age (%)	55.1%	44.8%	100%
Total	Count	188	32	220
	age (%)	85.4%	14.5%	100%

Table No.3: Gender and Left Main Coronary Artery Stenosis

Gender		Left Main Coronary Artery Stenosis		Total
		Yes	No	
Male	Count	125	15	140
	Percentage	89.2%	10.7%%	
Female	Count	63	17	80
	Percentage	78.7%	21.2%	100%
Total	Count	188	32	220
	Percentage	85.4%	14.5%	100%

Table No.4: Age and Left Main Coronary Artery Stenosis

Age brackets	Left Main Coronary Artery Stenosis		Total
	Yes	No	
>35-55	35	15	50
Percentage	70%	30%	100%
>55	153	17	170
Percentage	90%	10%	100%
Total	188	32	100%
Chi-square	0.13	1	0.63

	Value	Df	p-value
Chi-square	0.72	1	0.49

Table 3 presents the correlation of gender with LCA stenosis. 125 (89.2%) patients of the total male population and 63 (78.7%) of female patients were positive for LCA stenosis. However, no significant association is found between gender and LCA stenosis ($p>0.05$). Similarly, no significant association was found between age and LMCA stenosis ($p=0.63$) (Table 4).

DISCUSSION

Left coronary artery diseases like stenosis in patients with ACS require a timely diagnosis for better management and reduction of associated mortality rate. ECG is the most frequently used bedside tool for the rapid diagnosis of ACS in emergency cases. However, diagnosis of LMCA stenosis in ACS is majorly associated with the ST-elevation in lead aVR which then suggests the need for urgent and aggressive interventions. Moreover, the indication of lead avR is also considered a major factor in initial management choices and greatly influences mortality and morbidity rate. Thus its ability to correctly diagnose LMCA stenosis is very significant in the good prognosis of the disease.

This study has assessed the significance of association between LMAC stenosis and STEL≥0.5 mm in lead aVR in patients with ACS. Out of the total of 220 patients, 188 (85.4%) were positive for LMCA. This result shows that a significant number of patients with STEL in lead aVR were positive for LMCA stenosis which demonstrates earlier as a strong predictor of the analyzed disease in the patients. This finding complies with the earlier studies conducted by Kosuge et al [(11)] and Barrabes et al [(12)] who declared ST-elevation –aVR as the strongest predictor of the existence of stenosis in the left coronary artery.

The study also stratified the findings according to gender distribution and age but no significant association was found between these factors and the diagnosis of the LMCA stenosis. These findings go hand in hand with the results of Rostoff et al [(13)], Hengrussamee et al [(14)], and Yamaj et al [(15)].

The study is limited in terms of consecutive enrollment of patients instead of randomization which might produce bias in the results. Moreover, it has produced the outcome data. Therefore, further studies should be conducted to report the clinical implications of early diagnoses of LMCA stenosis through ECG including its influence on mortality rate.

CONCLUSION

ST-elevation-aVR is an effective tool for the diagnosis of left main coronary artery stenosis in patients with the acute coronary syndrome.

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Data Analysis:	Tariq Mehmood Khan, Nauman Ali, Muhammad Zubair Zaffar
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Comparison of Spectrum of Complications of Hemodialysis in Pre and Post Transplanted Renal Failure Patients

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ABSTRACT

Objective: To compare complications of hemodialysis in pre and post transplanted renal failure patients; to determine the prevalence of observed complications; to evaluate underlying comorbid illness between two groups.
Study Design: A cross-sectional study observational study
Place and Duration of Study: This study was conducted at the department of Nephrology in Nishtar Medical University & Hospital Multan from July 2020 to December 2020 for a period of six months.
Materials and Methods: 100 patients with confirmed renal failure and on hemodialysis treatment were included in the study. Among them, 50 never had a transplant while other half were on dialyses after graft rejection. Patients were observed during hemodialysis and symptomatic complications were recorded. In addition, medical history of participants was obtained to evaluate underlying comorbidities. SPSS 25.0 was used for statistical evaluation. One way analyses of variance (ANOVA) and student's t-test were used to compare two study groups.
Results: A total of 100 patients of renal failure underwent conventional HD. Patients from Bothe the groups showed no significant difference in basic characteristics. However, significant difference ($p>0.05$) was found between frequency of acute complication between two groups. Similarly, higher incidences of variable comorbidities is found among graft rejected renal failure patients.
Conclusion: Hemodialysis act as the major life saving maintenance treatment among renal failure patients. However, multiple complications are associated with this therapeutic approach. Given the findings, it is suggested to modify dialysis procedures to mask the effects of underlying comorbidities during dialysis especially for the graft rejected renal failure patients.

Key Words: Renal failure, Chronic Kidney disease, Hemodialysis, Graft Rejection, Acute Complications

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INTRODUCTION

Chronic kidney disease (CKD) or Rena failure is described as atypical functionality or morphological appearance for more than 3 months [(1)]. Annually, around 8% to 16% of individual worldwide are diagnosed of chronic kidney disease. The affected individual mostly belong to developed or under developing countries[(2)].

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Mostly, diabetes or hypertension serve as significant underlying disorders but pathology can be contributed to infection, glomerulonephritis, environment generated factor, including herbal remedies, air pollution and pesticides, or genetic alterations[(2)]. The diagnostic criteria of CKD is decline of glomerulus filtration rate (GFR) by less than 60ml/min/ /1.73m^2; secretion of at least 30mg of albumin in 24hrs, or persistence of other sign of kidney damage such as hematuria for more than 3 months [(3)]. Facts state that, in the USA every year 1ml/min/1,73m^2 GFR decline on average among the population and 50% of them are at risk to suffer from chronic renal damage in their life time [(4, 5)].

The CKD patients often prefer to undergo transplantation as it provides superior survival and quality life style; however, low supply of donor kidney remains a limiting factor and graft survival rate is around 15 years. After this survival time, most of transplanted kidneys lose their functionality [(6, 7)]. Apart from this haemodialysis is only life-saving treatment approach that is under operation from last 35 years [(8)]. Haemodialysis is recommended to begin when creatinine clearance rate of symptomatic individual becomes15ml/min and 10ml/min in diabetic and non-

diabetic patients and 3 dialysis per week are required to maintain urea clearance rate of 20ml/min in 70kg individual [9]. Although, data suggest that one in 75,000 treated individuals are at mortality risk due to technical errors; yet, several acute complications are reported during treatment which decline the quality of life of treated individuals [8].

Several studies have been evaluating the incidence of various complications of haemodialysis yet no study so far has compared the complications between first term renal failure patients and those who lost their kidney functionality after the transplant, termed as second term renal failure patients. The following study aimed to compare severity and occurrence of complications in pre and post-transplant renal failure patients. Moreover, evaluation of underlying comorbid illness between two study groups is also the matter of interest of the study.

MATERIALS AND METHODS

A cross-sectional observational study was conducted in Nishtar Medical University & Hospital, Multan for the period of six months from 7th July 2020 to 7th December 2020. Both male and female patients who were diagnosed of end stage renal disease and sustaining on regular haemodialysis were enrolled in the study. Initially, complete clinical history of participants was obtained to determine the presence of any comorbidity. The participants were divided into two groups based on their transplant history: First group comprised of renal failure patients who had yet not undergone kidney transplantation while the second group consisted of patients who were on hemodialysis for second time after their transplanted went into failure again. A complete Performa was prepared to record the hemodialysis complications for each patient which was to be filled by on-duty doctor or technician during each hemodialysis session for the period of six months. Every patient was evaluated for body weight, blood pressure, respiratory rate, pulse, and temperature before the start of dialysis session and then after every 45 minutes during the session. Studied complication included muscular cramps, vomiting, hypotension, abnormal pulse rate, chest pain, restless leg and sugar level alterations. Patients with acute renal failure and acute on chronic renal failure were excluded from the study.

Statistical Analyses: Collected data was analysed through SPSS version 25.0. Results were reported as mean, standard error of mean (SE), and frequency of complications. The difference between continuous and categorical variables were compared for statistical significance between two groups through student's t-test and one-way ANOVA.

RESULTS

During the study period, a total of 1000 hemodialysis (HD) sessions were observed for 100 patients, 50 first term and 50 second term renal failure patients with a mean of 5.5 sessions per patients. The participants included 78 male and 22 female patients with the mean age of 39.8 ± 15.2 years and 47.5 ± 7 years of first term and second term renal failure respectively. Similarly, no significant difference was found between duration of disease and ultrafiltration rate between two groups. The patients showed association between their underlying comorbidities and the acute complications they suffered during HD sessions. It was found that except of obesity significant difference was found between incidences of comorbidities.

Table No.1: Comparative Analyses of Comorbidities between Two Studied Groups (n=100)

	First term renal failure	2nd term renal failure	P-Value
Characteristics			
Age (SE)	39.8 (15.2)	47.5(7)	0.77
Duration of Dialysis	3.9	4.7	0.87
Ultrafiltration rate	8.7ml/kg/hr	10.2ml/kg /hr	0.63
Comorbidities			
Obesity	39%	43%	0.61
Myocardial infarction	3%	8%	0.50
Congestive heart failure	8%	13%	0.43
Diabetes	20%	35.4%	0.002
Diabetes with serious complications	9.1%	22%	0.001
Hepatitis B/C	33.2%	45%	0.05
Liver disease	33.2%	45%	0.05
Hypertension	54%	87%	0.0001

Table No.2: Comparison of Acute Complications of Hemodialysis between Two Studied Groups (n=100)

Acute Complications (%age)	First term renal failure	2nd term renal failure	P-Value
Hypotension	7.2%	13%	0.43
Muscular cramps	10%	22%	0.001
Vomiting	3.2%	3.7%	0.67
Abnormal Pulse rate	20.9%	31.4%	0.03
Restless Leg	4.3%	7.1%	0.002
Sugar Level Alteration	12.3%	35.2%	0.001

It was analyzed that difference in occurrence of severe diabetes (p=0.002), hypertension (p=0.0001), liver disease including hepatitis B/C (0.05), and cardiac disorders reached the significance threshold (Table I).

Among the observed acute complications, it was found that occurrence of complications was magnified in second term renal failure patients as compared to First term renal failure patients to significant level. We observed that majority of second term renal failure patients were repeatedly suffering from the observed complication in their regular HD sessions and the intensity of complication was also greater than first term renal failure patients (Table 2).

DISCUSSION

Around 8 to 16% of individuals around the world are suffering from chronic renal failure and are sustaining on haemodialysis to maintain the quality of life. Moreover owing to immunogenic reaction against the graft, mostly maximum survival time of allograft is restricted to 15 years (10) after which patients return to haemodialysis. We have conducted this study to ascertain the difference in complications of HD between first term renal failure patients and second term renal failure patients.

In the study it has been found that significant difference exists between the incidences of complications between two groups. It was observed that evaluated complications were found in both groups but the frequency of occurrence multiplied in second term renal failure patients. The most contrasting difference occurred in hypotensive and sugar level variability episodes between two study group. These results are found to be consistent with previous studies results.

In a study conducted by Yoowannakul et al., 57.7% of patients suffered from fall in systolic blood pressure [11]. The authors observed that fall in blood pressure was not only related to patient's hydration status before the start of HD session, but also to cardiac morphology. Similarly, ultrafiltration rate also influences the cardiac load. In our study, it can be predicted that second term renal failure patient were maintained on higher ultrafiltration rate and had greater underlying cardiac comorbidities which influenced their blood pressure levels. Kim et al., found out diabetic neuropathy as a significant cause of graft rejection [12]. Thus, in our study most of the graft rejected patients had severe diabetes and suffered from extreme sugar level variations during HD sessions. On comparison, first term renal failure patients had significantly moderate intensity of diabetes mellitus, so they showed lesser degree of sugar level alterations during HD session.

Similarly, significant difference was observed in pulse rate between the patients of two groups. Literature suggests that patients on chronic dialysis witness morphological and functional abnormalities of heart which intensify with age [13]. In our study, second term renal failure patients were of comparatively high age; therefore, cardiac abnormalities can be predicted among them. It is recommended to conduct cardiac diagnostic and imaging tests in graft rejected renal failure patients in future studies to validate our interpretation.

Besides, patients from both the groups also reported restless led syndrome disorder; however, the frequency was higher in graft rejected renal failure patients. Studies have confirmed that iron deficiency, uremia, and diabetes mellitus 2 are some of the secondary causes of this presentation [14]. Therefore, it is very likely that in given conditions the presentation of syndrome is magnified in second term renal failure patients. We have also reported the frequency of comorbidities among the patients from both the groups which in already reported in several studies [15,16]. However, no established study is made so far regarding differences between two types of renal failure patients. Thus, the current study can be used as guiding light for future research in this area.

CONCLUSION

Hemodialysis act as the major life saving maintenance treatment among renal failure patients. However, multiple complications are associated with this therapeutic approach. Given the findings, it is suggested to modify dialysis procedures to mask the effects of underlying comorbidities during dialysis especially for the graft rejected renal failure patients.

Author's Contribution:

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

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Original Article

Concurrent Chemo Radiation with Carboplatin and Paclitaxel versus Sequential Chemotherapy followed by Radiotherapy in Esophageal Cancer

Atique Anwer Khan, Ahmed Ijaz Masood and Muhammad Arshad

ABSTRACT

Objective: This study was conducted to compare the concurrent chemo radiation with Carboplatin and Paclitaxel and Sequential Chemotherapy followed by Radiotherapy in Esophageal Cancer patients.

Study Design: A randomized control study design

Place and Duration of Study: This study was conducted at the Oncology Department in Nishtar Medical University and Hospital Multan from Feb 2020 to Feb 2021 for a period of one year.

Materials and Methods: Total 60 participants, 30 in each treatment group were included in the study. The Patients aged between 22-75, confirmed cases of esophageal cancer were included in the study. The Patients with organ metastasis, complete obstruction, or tracheoesophageal fistula, and the ones who had lost more than 10% of their body weight or have any other primary cancer or had undergone any defined surgery were excluded from the study. Patients' baseline data related to family history, physical examination, and laboratory work-up were collected. The participants were randomly grouped into two groups Group A and Group B. Group A patients received concurrent chemo radiation therapy. Group B patients received 2 cycles of chemotherapy followed by radiotherapy the tumor response was then evaluated.

Results: Demographic variables of the patients show that the median age of the patients in Group A & B was 58 & 60 years respectively. Among Group A 24 (80%), 4 (13.3%), 1 (3.3%), 1 (3.3%) patients showed complete response, partial response, stable disease & progressive disease respectively. While among Group B patients 12 (40%) showed complete response, 7 (23.3%) showed partial response, 7 (23.3%) showed stable disease and 4 (13.3%) showed progressive disease. The resultant toxicity of treatment was assessed using RTOG scheme. More toxicity was assessed in group A participants who were treated with concurrent chemo radiation.

Conclusion: The study concluded that concurrent chemo radiation with Carboplatin and Paclitaxel provide comparatively better tumor response than sequential chemotherapy followed by Radiotherapy in Esophageal Cancer. However, besides efficacious tumor response, it is also associated with acute and delayed toxicity.

Key Words: Concurrent Chemo radiation, Esophageal cancer, Sequential chemotherapy, Radiotherapy

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INTRODUCTION

Esophageal cancer is characterized as a highly malignant cancer that carries a high potential for metastasis and local recurrence. Although diagnostic and therapeutic sciences have seen significant improvement, the malignancy is still fatal for a large number of patients[1].

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Sequential chemotherapy followed by radiotherapy is a well-established treatment protocol for non-surgery esophageal cancer patients, whereas the intake of 5-fluorouracil (5-FU) with cisplatin is the most followed chemotherapy regimen [2]. However, studies have concluded that 5-year survival rates have been as low as 26% following a definitive chemo radiation treatment. Therefore, less-toxic and more sensitive chemo-therapy regimens are highly needed [3].

Paclitaxel is an effective agent in esophageal malignancy since a response rate of around 32%, when delivered as a single-drug treatment, is seen among metastatic patients. Paclitaxel acts through inhibition of cells during the G2M phase of mitosis, a highly radiosensitive phase, having a 1.48 sensitizing enhancement ratio[4]. Paclitaxel in combination with carboplatin (TC) and concurrent radiotherapy has already been tested in patients with metastasized non-

small-cell lung cancer and the response rate was found to be between 71%-79% [5].

A study conducted phase 2 study of neoadjuvant chemo radiotherapy (nCRT) trial was based on weekly delivery of paclitaxel and carboplatin along with radiotherapy. The treatment regimen resulted in incomplete resection of the tumor with one millimeter of resection margins among the treated patients [6]. Moreover, variable toxicities such as esophagitis, neutropenia, and thrombocytopenia were reported. 96% of the patients had to undergo surgical resection at a later stage. Similarly, other studies have also concluded esophagitis as a major toxic side effect among the patient treated with concurrent radiotherapy regimens. In a study, 10-46% of the treated patients reported grade three or four esophagitis [7].

Therefore besides testing the efficacy of the combined delivery of paclitaxel and carboplatin, it is important to decide the timing of radiotherapy among patients with high-grade esophageal cancer [8]. This study is designed to compare the two chemo-radiotherapy regimens, sequential and concurrent, along with testing of paclitaxel and carboplatin as chemotherapeutic agents for such patients.

MATERIALS AND METHODS

A randomized control study design was used. The study was carried out for one year at the Oncology Department of Nishtar Medical Hospital and University Multan. Written approval was taken from the ethical review board before initiating the study.

Total 60 participants, 30 in each treatment group were included in the study. The Patients aged between 22-75 who were histologically or cytological confirmed cases of esophageal cancer with Eastern Cooperative Oncology Group (ECOG) score 0–2 and locally advanced cases with T2-4NxM0-1a or TxNxM1b were included in the study. The

Patients with organ metastasis, complete obstruction, or tracheoesophageal fistula, and the ones who had lost more than 10% of their body weight or have any other primary cancer or had undergone any defined surgery were excluded from the study. After getting informed consent from the patient's baseline data related to family history, physical examination, and laboratory work-up was collected. The participants were randomly grouped into two groups: concurrent (Group A) and sequential (Group B). In Group A, the patients received 50.4 Gy at 1.8 Gy per fraction for 5.5 weeks along with concurrent infused paclitaxel (50 mg m–2) and carboplatin (AUC=2). In Group B, patients received 2 cycles of chemotherapy, adopting a similar schedule, followed by radiotherapy fractionated in a similar way and at a similar dose. In both the set of patients, chemotherapy was preceded by 25-mg promethazine intramuscular injection at the half-hour, twenty-seven oral doses of dexamethasone (0.75 mg/tablet) at twelve and six hours before the treatment, and 300 mg of intravenous administration of half-hour before paclitaxel treatment. The tumor response was then evaluated.

Data analysis: The primary effect of tumor response was evaluated by following the "Response Evaluation Criteria in Solid Tumors (RECIST) guideline" (version 1.1). Radiation-associated toxicity was weekly assessed through the "Radiation Therapy Oncology Group (RTOG) radiation morbidity scheme". Acute and delayed toxicity was considered as an outcome of radiation therapy. SPSS (version 25) was used for data analysis. Fisher's exact probability test and chi-square test were used. P-value <0.05 was considered significant.

RESULTS

Among 60 participants, 30 were included in each group randomly. Group A was treated with concurrent chemo radiation and Group B was treated with sequential chemotherapy followed by radiotherapy. Demographic variables of the patients show that the median age of the patients in Group A & B was 58 & 60 years respectively. Group A was comprised of 18 (60%) males and 12 (40%) females while 17 (56.6%) males and 13 (43.3%) females were included in Group B. No significant difference was observed in ECOG status, Cancer stage, and dysphagia among both groups (Table I).

Laboratory and radiological findings were considered to assess tumor response in both groups by using RECIST criteria. Among Group A 24 (80%), 4 (13.3%), 1 (3.3%), 1 (3.3%) patients showed complete response, partial response, stable disease & progressive disease respectively. While among Group B patients 12 (40%) showed complete response, 7 (23.3%) showed partial response, 7 (23.3%) showed stable disease and 4 (13.3%) showed progressive disease (Table II). The p-value for difference in tumor response was statistically significant among both groups (<0.05).

The resultant toxicity of treatment was assessed using the RTOG scheme. The profile was prepared by considering a combination of Grade 0 & I and Grade II & III. Statistically, a significant difference was seen in terms of acute toxicity of Skin, GIT, Kidney, Lung, and resultant neutropenia among group A & B participants. More toxicity was assessed in group A participants who were treated with concurrent chemo radiation. On follow-up, relapse was reported in more patients from Group A however the difference among the number of relapses reported among the two groups was not significant (p>0.05).

DISCUSSION

Many research studies based on randomized clinical trials have revealed that sequential chemotherapy is a better treatment option in comparison to concurrent

chemo radiation [9]. In terms of prevalence, about 6% of gastrointestinal malignancies are Esophageal carcinoma [10]. More males than females are likely to get affected with esophageal cancer. The typical and most frequently seen symptom of this condition is Dysphagia [11]. We also report the presence of dysphagia in the current study group. The treatment for esophageal cancer is chosen based on the prognosis. Nonsurgical is more often selected for patients with bad prognosis for example the ones presenting with metastasized tumors. Chemo radiation is mostly the procedure of choice in patients with contraindication for chemotherapy [3]. Moreover, with advances, hyper-fractionated radiotherapy which offers better results is being used over conventional one [12].

One of the previous studies with the "ECOG EST-1282 trial" showed that combination (modality) therapy is more effective than only radiotherapy however that trial had an element of surgery in it. Besides this, no significant improvement was achieved in terms of survival rate [13]. In another study, the clinical trial was designed to compare concurrent chemo radiation with systemic chemotherapy. The results showed a better median survival rate in patients who received concurrent chemo radiation [14]. Likewise, in a study conducted by "The German Esophageal Cancer Study Group," a comparison was made "between preoperative chemo radiation followed by surgery versus chemo radiation alone". The follow-up of 10 years showed no significant difference in survival rate among the two groups [15]. Despite these results, it is important to explore different treatment modalities in combination and alone in order to assess both efficacy and toxicity [16]. Our study results indicate a significantly efficacious response rate towards patients treated with concurrent chemo radiation therapy showing complete response (effectively killing and reducing tumor cells) in 24 (80%). A longitudinal study was done at Department of Oncology of Jinnah Postgraduate Medical College. "A partial clinical response was acheived in majority of the patients following concurrent chemoradiation therapy (CCRT) (55.7%). However, 14 patients achieved complete response, 10 patients showed stable disease, 6 patients expired and only one patient showed disease progression with metastases" [17]. Studies also show that concurrent chemo radiation therapy also reduces symptoms of dysphagia in patients with esophageal cancer. However concurrent chemo radiation therapy is also linked with enhanced toxicity profile. Several studies have concluded that higher incidence of Grade 3 and Grade 4 toxicities are more associated with chemo radiation than radiotherapy only.

CONCLUSION

The study concluded that concurrent chemo radiation with Carboplatin and Paclitaxel provide comparatively better tumor response than sequential chemotherapy followed by Radiotherapy in Esophageal Cancer. However, besides efficacious tumor response, it is also associated with acute and delayed toxicity.

Author's Contribution:

Concept & Design of Study:	Atique Anwer Khan
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Original Article

Acute Coronary Syndrome with Serum with Serum Uric Acid

The Association of Risk Factors and Severity of Acute Coronary Syndrome with Serum Uric Acid Levels in Female Population Younger Than 45 Years

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ABSTRACT

Objective: The study aimed to evaluate Uric Acid levels in the female population younger than 45 years and to demonstrate if its levels are correlated with severity and risk factors of Coronary Artery disease in Acute Coronary Syndrome patients.

Study Design: A Cross-sectional analytical study

Place and Duration of Study: This study was conducted at the Cardiology ward of Ch.Pervaiz Elahi Institute of Cardiology Multan from July 2020 to Dec 2020 for a period of six months.

Materials and Methods: A total of 60 women aged less than 65 years old were included in the study following inclusion and exclusion criteria. Patients were evaluated for their family history and coronary artery risk factors such as hypertension, diabetes, dyslipidemia, family history, smoking, and body mass index. Blood samples were collected for evaluation of serum uric acid and two groups were formed: hyperuricemia and non-hyperuricemia. Coronary angiography was performed to determine the number of coronary arteries involved. Each risk factor and extent of severity of disease was compared for mean serum uric acid level between two groups. Statistical analysis was conducted on SPSS using version 23.

Results: Among analyzed 60 female patients, 31% had STEMI, 48% were diagnosed with NSTEMI, and 21% had unstable angina. 75% of patients were aged between 30-45 years. Among risk factors, hypertension (mean value=7.55± 1.72), diabetes (7.62±2.13), and dyslipidemia (7.77±1.78) were found to be significantly associated with hyperuricemia. Similarly, the higher number of involved coronary arteries was significantly related to higher uric acid levels (p=0.0001).

Conclusion: Shortly, serum UA is correlated with risk factors of coronary artery disease (CAD) like diabetes, hypertension, and dyslipidemia in the young female population. Similarly, it is a significant predictor of the severity of Coronary artery disease.

Key Words: Acute coronary syndrome, Coronary artery disease, Hyperuricemia, Female cardiac disease patients, Serum uric acid

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INTRODUCTION

Acute coronary syndromes (ACS) are one of the major causes of mortality and morbidity across the world [(1)].

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Though several types of research have already been conducted on risk assessment of ACS [(2)], many risk aspects remain poorly understood. Uric acid (UA) is produced as a result of purine catabolism in man and is a part of regular clinical testing. Although uric acid has been associated with cardiovascular diseases (CVD) for the last 130 years, its correlation with CVD as a risk factor is still under exploration. The association between raised uric acid and magnified mortality risk has already been explored in the general population with CVD [(3)], hypertension [(4)], coronary artery disease [(5)], and diabetes [(6)]. Elevated UA level in serum is a frequent finding in patients with hypertension, obesity, CVD, and diabetes.

Multiple epidemiological studies have demonstrated deranged Uric acid levels in patients with CVD to establish their relationship. However, in some studies, independent relations between the two diseases couldn't be found [(7)]. It is predicted that lack of independent

relation could be due to the likely association of UA with other risk factors of CVD such as obesity, decreased high-density lipoprotein cholesterol, hyperinsulinemia, hypertension, hypertriglyceridemia, and increased insulin resistance. Similarly, other clinical outcomes of atherosclerosis, including oxidative stress, endothelial dysfunction, and inflammation, have also been related to higher UA levels.

The young population specifically those less than 45 years is ignored when studies on risk factors and diagnosis of CVD are conducted. However, ascending trend of the incidence rate of CVD has also been demonstrated among the young population in some studies [8]. Pakistan has a high incidence rate of hyperuricemia, especially among the female segment. According to certain epidemiological studies, the reported prevalence rate is 30-39% [9]. The rationale of the present study is to evaluate hyperuricemia in the younger female population with coronary vessel disease in ACS so that UA could be established as a viable biomarker for risk analysis and severity assessment of CVD in the young population. Moreover, to our knowledge, no such study has been conducted to address this aspect, especially in the Pakistani setting. The study aimed to evaluate UA levels in the female population younger than 45 years and to demonstrate if its levels are correlated with severity and risk factors of CAD in ACS patients.

MATERIALS AND METHODS

A cross-sectional analytical study was conducted in the Department of Cardiology at Ch. Pervaiz Elahi Institute of Cardiology Multan, for the period of 6 months from 21st July 2020 to 21st Dec 2020. A total of 60 consecutive female patients who were under 45 years old, admitted with the diagnosis of ACS, which includes ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable Angina, and undergoing coronary angiography were included in the study. Whereas, those with renal disorders, gout, know malignancy, any inflammatory disorder, those on hyperuricemia medication, and those not undergoing coronary angiography were excluded from the study.

After acquiring informed consent from patients and approval from the ethical committee of the hospital, detailed physical examination, family history of the participants, and baseline laboratory analysis, including CBC, renal function tests, electrolytes, and cardiac enzyme level, was conducted. Blood samples were then collected on an empty stomach for the analysis of serum UA and the lipid profile. For lipid profile following levels were regarded as normal: total cholesterol less than 200 mg/dl, serum HDL-C less than 40mg/dl, serum LDL less than 100mg/dl, and serum triglyceride less than 150 mg/dl. Women were declared of having hyperuricemia if the serum levels were ≥6.0 mg/ dL in women. Based on serum UA level, patients were divided into two groups: hyperuricemia and non-hyperuricemia. The severity of CAD was characterized based on the number of coronary arteries: absent, 1 vessel, 2 vessels, and 3 vessels. The extent of stenosis was determined by comparing the reduction in luminal diameter with the closest normal segment. Besides patients were also assessed for established CAD risk factors: smoking, hypertension, diabetes mellitus, obesity (body mass index> 30kg/m^2).

Statistical Analysis: Statistical analysis was conducted on SPSS (version 23). Mean serum UA of the patients from two studied groups was compared for different risk factors of CAD and coronary angiographic results using the student's t-test. The statistical significance between two groups for different variables was found using the chi-square test. P-value less than 0.05 for any variable was considered statistically significant.

RESULTS

A total of 60 females complied with inclusion and exclusion criteria and were included in the study. Among the studied subjects, 31% had STEMI, 48% were diagnosed with NSTEMI, and 21% had unstable angina. Upon classifying patients in terms of their ages, it was found that only 10% of women were between 21-25 years, 15% were between25-30 years old, while 75% were between 30-45 years old (data not shown). In the study, 49% of females had hyperuricemia with a mean serum UA level (mg/dl) 7.10± 2.11. The association of serum UA was assessed with every CAD risk factor. The hypertensive patients had a mean serum UA level of 7.55± 1.72 whereas non-hypertensive had 6.1± 1.55 and this difference was found to be statistically significant. A significant association was also found between hyperuricemia and hypertension. Similarly, a significant difference was found in the mean serum UA level of diabetics (7.62±2.13) and that of non-diabetics (6.3±1.7). A significant difference was observed between the mean values of those who had dyslipidemia (7.77±1.78) than those had normal lipid profile (6.21±1.1). Furthermore, positive correlation was found between serum UA and triglycerides ($r = 0.687$, $p<0.001$) while UA was negatively correlated with low density lipoproteins ($r = .079$, $p>0.01$) (Table I). Thus, a significant association was interpreted between diabetic status and UA. However, no statistical difference was found between UA levels and family history ($p=0.72$), smoking (0.08), and BMI (0.67) (Table I). The patients with hyperuricemia had higher involvement of coronary vessels. Those with no coronary lesion were found to have mean serum UA level of 3.1mg/dl, while significantly different mean serum UA level of 5.53, 6.93, and 11.01 was found in those with involvement of 1, 2, and 3 vessels respectively. Hence, hyperuricemia was significantly associated with the severity of CVD (Table 2).

Table No.1: Association of Coronary Artery Risk Factors with Uric Acid Level of Patients (N=60)

Variables		Mean serum uric acid ±SD(mg/dl)	Hyper Uricemia (%)	Non-hyperuricemia (%)	P-value
Hyper Tension	Yes (N= 40)	7.55± 1.72	29/40 (72.5)	11/40 (27.5)	P=0.001
	No (N= 20)	6.1± 1.55	16/20 (80)	4/20 (20)	
Diabetes mellitus	Yes (N=25)	7.62±2.13	17/25 (68)	8/25 (22)	P=0.02
	No (N=35)	6.3±1.7	15/35 (42.8)	20/35 (57.1)	
Dyslipidemia	Yes (N=38)	7.77±1.78	29/35 (82.8)	6/35 (17.1)	P=0.005
	No (N=22)	6.21±1.1	5/22 (22.7)	17/22 (77.2)	
Family history	Yes (N=18)	7.26± 2.15	7/18 (38.8)	11/18 (61.1)	0.72
	No(N=42)	7.08 ± 1.64	20/42 (47.6)	22/42 (52.3)	
Smoking	Yes (N=8)	6.99±1.53	3/8 (37.5)	5/8 (62.5)	0.08
	No (N=52)	7.51± 2.322	23/52 (44.2)	29/52 (55.7)	
BMI<30kg/m2	Yes (N=15)	7.092 ± 1.54	8/15 (53.3)	7/15 (46.6)	0.67
	No (N=45)	7.341 ±2.44	22/45 (48.8)	23/45 (51.1)	

Table No.2: Comparison of Angiographic Findings between Two Study Groups (N=60)

Coronary angiographic findings	Mean SUA±SD (mg/dl)	Hyperuricemia (%)	Non-hyperuricemia (%)	P-value
0 vessel, n=1	3.1 ± 1.543	0/1 (0)	1/1(100)	P=0.001
1 vessel, n=15	5.53± 2.11	6/15 (40)	10/15 (60)	
2 vessel, n=35	6.93± 1.87	24/35 (68.5)	9/35 (31.5)	
3 vessel, n=9	11.01± 2.01	9/9 (100)	0 (0)	

DISCUSSION

The study aimed at targeting the female young population with ACS and tried to build a correlation between their serum Uric acid levels and risk factors and severity of the disease. Our study was conducted on 65 female patients diagnosed with ACS (including STEMI, NSTEMI, and unstable angina). The mean serum UA level of the patients was 7.10± 2.11 mg/dl. In recent times, studies have been conducted to assess the significance of UA as a biomarker in acute myocardial infarction (MI), but only a few have demonstrated its role in causing the severity of CAD and correlated it with ACS. Similarly, to the best of our knowledge, very few studies have specifically targeted the female population in this regard.

Our study has developed a significant relationship between high serum UA levels and the number of the coronary artery involved. In a study conducted by Sun et al, hyperuricemia was found to be an independent risk factor in the occurrence of CAD in more than 80% of the assessed women, when compared to men. However, the study didn't address the correlation with the severity of the disease[10]. In another Japanese study, both male and female patients with acute MI were assessed and correlation was analyzed between serum UA levels and Killip classification. The results found out high reports of short-term adverse effects in patients with hyperuricemia[11]. Similarly, Nadkar et al conducted a cross-sectional study and reported higher serum UA concentration in patients with acute MI [12].

In a study conducted by Culleton et al, serum UA was not only found to be significantly related to the incidence of CAD but a higher rate of adverse effects reported was reported in women than men, after age adjustment[7]. Zhang et al reported serum UA as a valuable predictor of CVDs in premenopausal women[13].

We also assessed the association of serum UA with different CAD risk factors. It was found that the majority of hypertensive were hyperuricemia and the relation was tending to be significant. Similar results were reported by Schmidt et al, who compared normotensive participants with hypertensive patients and found significantly higher serum UA in the later participants[14]. The Framingham Heart Study has established serum UA as an independent predictor of incidence and progression of hypertension. Similarly, hyperuricemia was found to be significantly correlated with diabetic status (p=0.002). Similar results were found in another cohort study where the majority of diabetic patients were having higher UA concentrations and were later involved in CVD-related morbidities [15]. Similar to the positive correlation between UA level and triglycerides found in our study, Desai et al, reported independent and linear relation between UA and TG and HDL [16]. Although the underlying mechanism between the association of two variables, it is predicted that the two metabolic disorders might have common genetic alteration.

Our study demonstrated the association of hyperuricemia with angiographic findings. We found higher involvement of coronary arteries in hyperuricemic patients (p=0.001). Similar results were found by Goodarzynejad et al who conducted a study on angiographically approved patients with atherosclerosis. It was shown that hyperuricemia might be linked with the severity of CAD (p=0.05). It is anticipated that higher serum UA leads to the formation of uric acid crystals and consequently atherosclerosis.

In compliance with our results, Tuttle and his colleagues found a linear correlation between the severity of CAD and serum Uric acid level in women when compared to men [17].

CONCLUSION

Shortly, serum Uric acid is correlated with risk factors of coronary artery disease (CAD) like diabetes, hypertension, and dyslipidemia in the young female population. Similarly, it is a significant predictor of the severity of CAD.

Author's Contribution:

Concept & Design of Study:	Kashif Ali Hashmi
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Data Analysis:	Amir Shahzad
Revisiting Critically:	Kashif Ali Hashmi, Tariq Mehmood Khan
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Effectiveness of Sequential Peeling as Mono-Therapy for Mild Acne Vulgaris

Sabah Ibad[1], Sumeera Zulfiqar[1] and Anum Sharif[2]

ABSTRACT

Objective: Glycolic acid and salicylic acid peels frequently used to treat acne vulgaris. However rarely the two agents are applied as a sequential peel to treat acne vulgaris. The objective of the present study was to reveal the effectiveness of sequential peeling as mono-therapy to treat mild acne vulgaris.

Study design: A randomized control clinical trial study.

Place and Duration of Study: This study was conducted at the Dermatology Department of Combined Military Hospital Multan from July, 2020 to Dec, 2020 for a period of six months.

Methodology: 60 Patients with only mild acne vulgaris who fulfilled inclusion criteria were included in the study. The patients were divided into 3 groups. Group 1 underwent sequential peeling with only 70% Glycolic acid. Group 2 was treated with 30% Salicylic acid. The group 3 received sequential peeling with the combination of glycolic acid and salicylic acid. Acne grading was done by performing lesion count before and after the treatment. Follow up was done to record any worst outcome of the procedure.

Results: 60 patients divided into 3 groups, 20 participants each were included in the study. The course of disease duration ranges from few months to 10 years. 12(60%), 15(75%) & 14(70%) patients in group 1, group 02 and group 3 had skin type III respectively. While 8(40%), 5(25%) and 6(30%) participants had skin type IV in successive groups accordingly. There was a considerable reduction in lesion count after treatment in all 3 groups ($p< 0.05$). Regarding patient's satisfaction, the difference between the 3 groups regarding lesion count before and after treatment was not significant. There was also no significant difference in disease duration between 3 groups. However, there was a significant difference regarding patients satisfaction following treatment among 3 groups with $P=0.001$ for group 03 which is significantly higher than group 01 and 02 both with ($P > 0.05$).

Conclusion: It was concluded that sequential peeling is an effective treatment to be used as a monotherapy against mild "acne vulgaris". Moreover, "Glycolic acid" and "salicylic acid" might give improved results while being used in combination.

Keywords: Acne vulgaris, Chemical peels, Glycolic acid, Salicylic acid

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INTRODUCTION

Acne vulgaris is a well-known chronic inflammatory multifactorial disorder[1]. It results in formation of pilosebaceous follicles[2]. It affects more than 85% of adults and persists frequently[3]. It is not a life-threatening condition but it is a major cause of physical and psychological stress [4]. It may be as well linked to post inflammatory hyperpigmentation and scarring [5].

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The understanding of pathophysiology provides main targets for treatment. The main elements involve in pathophysiology of Acne Vulgaris include follicular epidermal hyper proliferation, inflammation and increased sebum production by androgens[6]. In addition to this bacterial colonization of hair follicles being caused by Propionibacterium acnes can also be used as a potential target for developing treatment modalities[7]. Most frequent sites affected by acne vulgaris are face, chest and back. Severe inflammation & scarring that occurs as a consequence can lead to social stigma and impairs quality of life [8].

The management of Acne Vulgaris depends upon the severity of the disease[9]. Mild cases are often treated with topical antibiotics, topical retinoid & benzoyl peroxide. In moderate acne oral antibiotics are prescribed in addition to topical ones [10]. Severe cases are dealt by using systemic approach with medications such as anti-androgens e.g. spironolactone & isotretinoin[11]. Alongside traditional therapies, combination therapy including adjuvant use of phototherapy, lasers and chemical peels are being

investigated in acne research [12]. The chemical peeling is a simple, economic, safe and non-invasive procedure. There are no reports suggesting systemic toxicity following peeling procedure [13]. The agent particularly involved in chemical peeling is salicylic acid (SA). SA is 2-hydroxybenzoic acid or orthohydroxybenzoic acid. It can be derived from willow bark, wintergreen leaves and sweet birch[13]. It functions by softening the stratum corneum, the consequent loosening of the intracellular matrix and corneocyte connections causes skin shedding[14]. It also decreases inflammatory lesions by causing inhibition of arachidonic acid cascade. In this way it effects most of the pathogenic mechanisms underlying acne vulgaris[15].

Another frequently used chemical peel is Glycolic acid (GA). Based on chemical composition "GA is a hydrophilic alpha hydroxyl acid (AHA) with desquamating properties capable of reducing cohesion and plugging of skin cells resulting in extrusion of inflammatory contents"[16]. The aim of the present study was to evaluate the efficacy of sequential peeling as a monotherapy to treat mild acne vulgaris.

MATERIALS AND METHODS

The randomized controlled clinical trial was comprised of 60 patients with mild acne vulgaris. The participants were recruited from the dermatology department of CMH Multan. The study was conducted after taking written approval from institutional Review Board and Ethical committee. Inclusion criteria were mild acne vulgaris with active lesions. The participant with history of no systemic or topical treatment and skin photo "types III and IV" were included in the study. The patients with severe acne vulgaris were excluded from the study. Other factors on the basis of which participants were excluded include pregnancy, breast feeding, steroid use, hormonal acne, allergic skin disorders, HSV and psoriasis.

Detailed history was taken from the selected participants. It included onset, duration, and any other dermal disorder. Participants were asked to provide details of any recent dermal procedure done including hair epilation & bleaching. The participants were examined dermatologically. The examination included site, type of acne lesion and total lesion count. Patients were randomly divided into 3 groups, 20 patients each. We used sequential peels one with GA only and SA only on two groups. The concentrations were reversed with SA 70% and GA 20% for the second group. The effects of both combinations were analyzed comparatively. Group 1 was treated with sequential peeling sessions with GA once every 2 weeks for 4 months. Group 2 was treated with SA once every 2 weeks for 4 months. While group 3 was treated with 70% GA for 3 minutes followed by 30% SA once every 2 weeks for 4 months. The participants' skin was cleaned with alcohol and acetone was used to degrease. All safety precautions were followed during whole procedure of sequential peeling. Participants were advised to apply topical antibiotic cream following the day of treatment and to apply sunscreen daily. Participants were also instructed to use non soap cleansers and to avoid rubbing or scratching the treated skin. Follow up was done to record any worse outcome for example skin infections, erythema, blisters or edema.

Statistical analysis: The statistical analysis of the data was done using SPSS. The data was analyzed and presented in terms of mean ± standard deviation and range. P-value <0.05 were considered statistically significant. "Chi-square test" or "Fisher's exact" test was used for comparing categorical data.

RESULTS

The study included 60 patients divided into 3 groups. Each group was consisting of 20 participants. The ages of patients were between 16 -31. The minimum & maximum course of disease duration ranges from few months to 10 years. 12(60%), 15(75%) & 14(70%) patients in group 1, group 02 and group 3 had skin type III respectively.

Table No.1: Demographic data and comparison between groups before and after treatment

Variables	Group 1 n=20	Group 2 n=20	Group 3 n=20
Age Median (range)	20(16- 31)	20(16-26)	18(18-24)
Mean ± SD	21.27 ± 3.41	20.67 ± 2.02	18.93 ±3.12
Duration (years) Median (range)	4.66 (0.35 – 8)	2.73 (1 – 6)	4.13 (1 -10)
Mean ± SD	3.94 ± 3.15	3.12 ± 2.13	4.91 ± 4.04
Skin Type III	12 (60%)	15 (75%)	14 (70%)
Skin Type IV	8 (40%)	5 (25%)	6 (30%)
Lesion count (Before) Median (range) Mean ± SD	16 (12 -40) 18.33 ± 8.65	18 (12 – 36) 19 ± 8.59	24 (10 – 42) 24.33 ± 12.45
Lesion count (After) Median (range) Mean ± SD	3 (2-7) 3.17 ± 2.21	02 (0-8) 2.19 ± 1.54	2 (0 -06) 1.91 ± 1.58
Patient satisfaction Before Range Median	1-3 2	1-3 2	1-3 2
After Range Median	3-4 4	3-4 4	3-4 4

While 8(40%), 5(25%) and 6(30%) participants had skin type IV in successive groups accordingly. There was a significant reduction in lesion count after treatment in all 3 groups ($p < 0.05$). The lesion count

before treatment was 16, 18 and 24 in group 1, group 02 and group 03 respectively. Following treatment, the lesion count gets reduced to 3,2 and 2 in group 1, 02 and 03 respectively. The patients' satisfaction rate was also increased following treatment. There was no statistically significant difference between the 3 groups regarding lesion count before and after treatment. There was also no significant difference in disease duration between 3 groups. The median of the disease duration for group 01, 02 and 03 was 4.66, 2.73 and 4.13 years respectively. However, there was a statistically significant difference regarding patients satisfaction following treatment among 3 groups with P=0.001 for group 03 which is significantly higher than group 01 and 02 both with (P > 0.05).

There was no adverse effect reported within 03 months following sequential peeling in any participant.

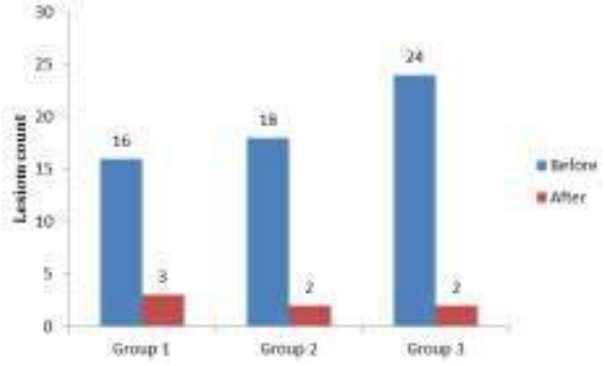

Figure No.1: Total lesion count in Group 1, Group 2 and Group 3 before and after treatment

DISCUSSION

Chemical peeling is a relatively economic and generally safe method for treatment [17]. It is used in treatment of some skin disorders where it refreshes and rejuvenates skin. The chemical peels are being used in routine clinical practice as a peel but less frequently used as a sequential peel [15]. Based on the penetrating ability or depth of action, Chemical peels are classified into superficial, medium, and deep peels [18]. The penetration of the peeling agent is correlated with clinical changes achieved. The greatest changes are achieved by peels at higher concentrations. However, the depth is also associated with the number of sessions [19].

In the present study, the efficacy of sequential peeling was evaluated against mild acne using glycolic acid and salicylic acid. There was significant improvement in lesion count of all 3 groups. The rate at which the lesion counts in group 1 and 2 get decreased was almost similar. The participants in these groups were treated with GA or SA alone. However, there was increased reduction in lesion count in group 3 where participants received combination of GA and SA for sequential peeling for the same treatment duration. Although there was no statistically significant difference among 3 groups but the improvement rate was high in group 3 participants. In addition to that the patient's satisfaction rate was significantly high in group 3 as compared to group 1 & 2.

There are several studies that provide evidence on the effectiveness of sequential peeling for treatment of acne vulgaris[20]. GA peels are available at concentrations ranging from 20% to 70%[21]. At increased concentration the intensity and penetrating ability of GA increases. According to the previous studies that utilizes GA at varying concentrations it was reported that GA is a potential agent for treatment of all types of acne. It induces rapid improvement and restores skin to normal [22]. Hereby the results obtained in study group 1 were significant in terms of reducing lesion count before and after treatment with the 70% GA as peeling agent. According to the initial studies that used only SA as sequential peel it was reported that SA was proven to be an efficient peeling agent for minimizing both inflammatory and non-inflammatory lesions [23]. SA is known for anti-inflammatory properties. Because of its lipophilic nature it can penetrate comedones and helps in preventing clogging of the pores [19]. 5 to 30% of the SA is considered to be safe for sequential peeling [24]. Most of the previous studies are based on mild acne that can be treated with topical retinoid, antibiotics or benzoyl peroxide-containing products if inflammatory lesions are present. As inflammation becomes more widespread or intense, topical retinoid and oral antibiotics make sense. Only few studies focus on use of sequential peel as a treatment for mild acne vulgaris[25]. Our study group 2 results are in accordance to the previous studies both in context of SA efficacy and treatment safety[1]. Most of the studies till date determined % efficacy of different peeling agents while using only one agent at a time. In other instances, comparative analysis was performed among different chemical peels. In this study we treated group 3 with combination of SA and GA while applying both peeling agents in suitable concentrations. We get statistically significant results as per patients satisfaction in the group treated with combination of GA & SA. Moreover, the lesion count also decreases considerably. This reveals that while using sequential peeling as a mono therapy for treatment of acne vulgaris, it might be a good idea to use peeling agents in combination.

CONCLUSION

It was concluded that sequential peeling is an effective treatment to be used as a mono-therapy against mild acne vulgaris. Moreover, Glycolic acid and salicylic acid might give improved results while being used in combination.

Author's Contribution:

Concept & Design of Study:	Sabah Ibad
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Data Analysis:	Anum Sharif
Revisiting Critically:	Sabah Ibad, Sumeera Zulfiqar
Final Approval of version:	Sabah Ibad

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

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Original Article

Evaluation of Association between Dyslipidemia and Smoking Routine of Smokers in Southern Punjab

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ABSTRACT

Objective: To establish the association between blood lipid levels and smoking and to develop the dose-dependent relationship between smoking habits and dyslipidemia.

Study design: An analytical cross-sectional study.

Place and duration of study: This study was conducted at the Cardiology Department of Ch. Pervaiz Elahi Institute of Cardiology Multan from May 2020 to October 2020 for a period of six months.

Methodology: A total of 150 participants were included in the study who were divided into three groups: smokers, non-smokers, and former smokers based on their responses to the self-designed questionnaire. Additionally, the participants were investigated about their economic situation and physical activity to predict confounding variables. The blood sample of all the participants was then collected and serum levels of high-density lipoprotein, low-density lipoprotein, cholesterol, and triglycerides were measured.

Results: Among the participants, 80 (53.3%) were currently smoking while the lifetime prevalence was 86.3%. Dyslipidemia was significantly greater in smokers (55.1%) than non-smokers (37%) or formal smokers (43%). The majority of smokers (42, 52.5%) were within the age bracket of 40-50 and largely belonged to the lower class (39, 48.7%) and reported moderate physical activity, in terms of MET (41, 51.25%). As for dose-response association, the significant association developed between no of cigarettes and blood High-density lipoprotein and triglycerides level in current smokers while in former smokers risk was high for high-density lipoprotein [OR, CI (1.85, 0.7-1.2)], low-density lipoprotein (1.47, 1.2-2.9), and cholesterol (1.22, 0.9-1.7).

Conclusion: It is concluded that smoking significantly disturbs the body level of lipids. Moreover, the smoking dose holds a variable relationship with the different components of the blood lipid profile.

Keywords: Dyslipidemia, smoking, cigarette, Cholesterol, high-density lipoproteins, low-density lipoproteins, triglycerides.

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INTRODUCTION

It is well-established that that dyslipidemia enhances the probability of occurrence of cardiovascular diseases (CVD) [(1)]. It is the underlying cause of more than half of fatalities in different regions [(2)]. Given the strong evidence of its effects on CVD, the intact metabolic pathway fats in the body are important [(3)]. Dysregulation in any component of the pathway leads to the development of long-lasting non-communicable diseases[(4)].

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The prevalence rate of dyslipidemia is generally associated with ethnicity, cultural, economic, and social components of society and their living style.

Undoubtedly, many risk factors of dyslipidemia have already been well-established. However, the studies predict that several are still unknown [(5)]. Due to this inadequate knowledge, no completely effective therapeutic plan could be introduced. Factors including body mass index, age, alcohol intake, and physical activity are usually considered as risk factors for dyslipidemia [(6)]. Similarly, smoking is also believed to be a potential agent for change in blood lipid levels. Although to date, no study could build a definite relationship between the two [(7)], some have predicted that cigarette smoking can affect the level of blood lipids through nicotine absorptions which alter the functioning and metabolism of body lipids [(8)]. It has been reported by some researchers that nicotine enhances total cholesterol, triglyceride, LDL cholesterol (LDL-C), and reduces HDL cholesterol (HDL-C) while others noted that it reduces total cholesterol, LDL-C, HDL-C, and multiplies the level of triglyceride [(9)].

In addition to the role of smoking in developing heart diseases and lung cancer, it is also believed as a causative agent of several non-communicable chronic health issues[10]. Moreover, several other health conditions are linked with tobacco intake because of its potential to disturb the immune system and physical condition of the smoker. However, no consensus could be built on the association between smoking and dyslipidemia [11,12]. Therefore, the study is conducted to establish an association between blood lipid levels and smoking among smokers in the southern part of Punjab.

MATERIALS AND METHODS

An analytical cross-sectional was conducted at the Cardiology Department of CPEIC Multan for six months from 3rd May 2020 to 3rd October 2020. A total of 200 patients, who visited the outdoor patient department (OPD), were initially shortlisted through random sampling technique. For the final selection of the participants of the study, patients were passed through the following inclusion criteria: those who were in the age bracket from 30-60 years; being the resident of the same area from at least past 1 year; and who willingly signed the informed consent to participate in the study. Whereas, to limit the influence of confounding variables, participants with high blood pressure, renal failure, diabetes, hepatitis, and dyslipidemia medication were excluded from the study.

For assessment of the smoking habits, the number and duration of smoking were considered. Based on smoking character, Participants were classified into three groups: non-smokers, former smokers, and smokers. The assessment of the smoking habit was based on self-reporting of the participants. Smokers were characterized as those who smoked minimum hundred cigarettes, and were currently smoking regularly; non-smokers were those who claimed to smoke less than the minimum criteria of 100 cigarettes, while the participants who reported to quit smoker and had a history of at least 100 cigarettes were classified as former smokers [12]. Similarly, socioeconomic status was assessed through the administration of a specially designed questionnaire, and the subjects were divided into the lower class, middle class, and upper class. Similarly, another questionnaire evaluated the physical activity status of the participants. Based on the responses and other associated variables, the metabolic equivalent of task (MET) of every activity was calculated. Physical activity status was categorized as low (23.5-37.5 MET-hours every week), moderate (37.7-45.0 MET-hours every week), and heavy (MET greater than 45 hours every week) [13]. After the initial assessments, participants' blood was collected in a fasting state according to the protocol. The serum was separated and the lipid profile was run on an automated analyzer. For the analysis of results, dyslipidemia was characterized as triglycerides (TG) greater than 200 mg/dL, total cholesterol ≥240, low-density lipoprotein (LDL) ≥160 mg/dL, and high-density lipoprotein (HDL) less than 40 mg/dL (14).

Statistical Analysis: The data was analyzed was using SPSS version 20.0. All the qualitative data were presented as a percentage. The association between smoking-dose and probability of abnormal lipid levels were presented through odd ratio (OR) within 95% confidence interval. For all the calculations, $p< 0.05$ was considered statistically significant.

RESULTS

A total of 160 were eligible for the study. Out of which, 100 (62.5%) were male while 60 (37.5%) were female. The majority of participants (76, 51.2%) were aged between 35 to 45 years whereas the majority of smokers (42, 52.5%) were within the age bracket of 40-50. Smokers largely belonged to the lower class (39, 48.7%) and reported moderate physical activity, in terms of MET (41, 51.25%). Additionally, dyslipidemia was significantly greater in smokers (55.1%) than non-smokers (37%) or formal smokers (43%) (Table I).

As for the dose-response association between dyslipidemia and no. of smoked cigarettes, current smokers had a significantly abnormal level of HDL and TG than non-smokers. However, the relation couldn't reach a significant level of total cholesterol and LDL. For instance, the risk of having abnormal HDL was 1.10 and 1.83 higher among those who smoke less than and more than 10 cigarettes, respectively, in contrast to those who don't smoke. However, the distinction couldn't be drawn between smokers and non-smokers in terms of total cholesterol and LDL. Whereas, a significant correlation was found between no cigarettes smoked and blood HDL, LDL, and total cholesterol when former smokers were compared with non-smokers. That is, those who smoked less than 10 cigarettes had 1.85, 1.45, and 1.22 times higher risk of developing abnormal HDL, LDL, and cholesterol, respectively (Table 2).

Table No.1: Baseline Characteristics of the Participants of the Study (N=150)

Variables	Total n=150 (n, %)	Smoker n=80 (n, %)	Former Smokers n=30, (n, %)	No Smokers n=50, (n, %)	p-Value
Gender					
Male	100 (66.6)	78 (97.5)	30 (100)	15 (30)	<0.001
Female	50 (33.3)	2 (2.5)	0 (0)	35 (70)	

Age Group					
30-40	76 (51.2)	23 (28.7)	2 (66.6)	12 (24)	0.04
40-50	48 (32)	42 (52.5)	10 (33.3)	21 (42)	
50-60	23 (15)	15 (18.7)	18 (60)	17 (34)	
Wealth index					
Lower class	70 (46.6)	39 (48.7)	18 (60)	18 (36.6)	0.69
Middle class	45 (30)	25 (31.2)	7 (23.3)	15 (30)	
Upper class	35 (23.3)	16 (20)	5 (16.6)	17 (34)	
Physical Activity (MET-hrs/week)					
Low	39 (26)	13 (16.25)	7(23.3)	5 (10)	0.004
Medium	77 (51)	41 (51.25)	15 (50)	25 (50)	
Heavy	33 (22)	26 (32.5)	8 (26.6)	20 (40)	
No. of Cigarettes/day					
1-10	-	75 (93.7)	-	48 (96)	0.07
>10	-	5 (6.25)	-	2 (4)	
Abnormal HDL					
Yes	106 (61)	46 (57)	14 (46)	21 (42)	P<0.05
No	44 (29)	35 (43)	16 (54)	29 (48)	
Abnormal LDL					
Yes	4 (2.5)	1 (1.25)	1 (3.33)	3 (3.75)	P<0.001
No	146 (97.5)	79 (99)	29 (97)	47 (94)	
Abnormal Cholesterol					
Yes	129 (85.25)	58 (73)	14 (48)	27 (53)	P<0.05
No	21 (14.05)	22 (27)	16 (52)	25 (45)	
Abnormal Triglyceride					
Yes	129 (85.2)	54 (67)	16 (52)	18 (37)	P<0.001
No	21 (14.8)	26 (33)	14 (48)	32 (63)	

Table No.2: Multiple Logistic Regression for Associating Smoking Habits with Dyslipidemia (N=150)

	Variables	HDL OR (95% CI)	LDL OR (95% CI)	TG OR(95% CI)	Cholesterol OR(95%CI)
Current Smokers (regarding non-smokers)					
-	**No. of cigarettes/ day**				
-	1-10	1.10(0.8-1.44)	0.70 (0.62-1.2)	1.54(1.23-2.3)	0.89(05-1.4)
-	>10	1.83 (1.32-2.2)	0.30 (0.5-1.2)	1.70(1.33-2.1)	0.07 (0.05-1.0)
Former Smokers (concerning non-smokers)					
-	No. of cigarettes/ day				
-	1-10	1.85 (0.7-1.2)	1.47 (1.2-2.9)	0.80(0.65-1.3)	1.22 (0.9-1.7)
-	>10	1.67 (1.06-2.3)	2.24 (1.8-2.5)	0.79(0.55-1.8)	1.30 (1.2-2.1)

DISCUSSION

Our study found out 58.4% prevalence rate of dyslipidemia which lies within the range established by previous studies, between 14% to 79% [15]. The purpose of the study was to explore the effect of smoking on blood lipid levels. Thus, the dyslipidemia patients with other comorbidities were excluded to remove the bias.

The prevalence of smoking found in our study is following the review conducted in 2015 [16]. Our study found 53% of smokers within the age bracket of 30-60, where 97.5% were men and around 2.5% were women. The investigation has established a significant relationship between levels of lipids in blood and smoking which was earlier on not proved by a closely related Chinese study [14], probably due to variable sex and age structure of the included population.

Some of the previous studies claimed that nicotine decreases HDL-C, LDL-C, and total cholesterol and elevates triglycerides in the body [17, 18] while others found that smoking multiplies triglyceride, LDL-C, and total cholesterol and reduces HDL-C level (19). These opposing results were also found after matching the potential confounders such as BMI, sex, and age (10). It can be interpreted that such contrast could be due to the relationship between blood lipid levels and other contributing agents such as the use of alcohol or any other intoxicant [10].

Analysis of the findings based on multiple logistic regression revealed that current smokers, smoking 10 cigarettes or more than that, are at higher risk of having

HDL-C abnormalities than non-smokers which in alliance with already established similar literature [20]. Additionally, similar to the findings of previous studies, total cholesterol, and LDC is reported to be higher among the former smokers, who used to smoke up to 10 cigarettes or more than that, in contrast to non-smokers[21].

The regression model also exhibited that the probability of having an abnormal level of LDL-C, total cholesterol, and HDL-C among the former smokers is associated with the number of smoked cigarettes. Thus the observed variations among both current and former smokers enhance with the increase in the amount of nicotine intake.

However, it was astonishing to find that with the rise in the number of cigarettes in former smokers, the risk of HDL-C abnormality decreases as compared to their non-smoker counterparts. It is assumed that it could be possibly due to the adoption of a healthy diet routine or better lifestyle which couldn't be reported in the study or could be exactly deduced from the evaluated factors. This interpretation, however, requires further analytical research and clinical trials.

This study is limited in some aspects as the participants self-reported about their smoking habits, which creates the risk of recall bias in the results. Similarly, the cross-sectional design of the study doesn't allow to explore the causalities due to the relationship between dyslipidemia and smoking.

CONCLUSION

It is concluded that smoking significantly disturbs the body level of lipids. Moreover, the smoking dose holds a variable relationship with different components of the blood lipid profile.

Author's Contribution:

Concept & Design of Study:	Sadia Iqbal
Drafting:	Muhammad Ramzan
Data Analysis:	Azhar Shahzad
Revisiting Critically:	Sadia Iqbal, Muhammad Ramzan
Final Approval of version:	Sadia Iqbal

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

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Original Article

Neuroimaging of Subdural Findings with Traumatic Brain Injury in Children

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ABSTRACT

Objective: To assess the frequency of findings (Neuroimaging and Neurological) in children with traumatic brain injury.

Study Design: A longitudinal study

Place and Duration of Study: This study was conducted at the Neurology & Radiology Department in Children Hospital & Institute of Child Health Multan from July 2020 to December 2020.

Materials and Methods: Children from 3 months to 7 years hospitalized for traumatic brain injury were included in the study. The CT/MRI scans of the participants were collected and reviewed by radiologists who were blind to the study. Neuroimaging findings like skull fracture, parenchymal involvement, extra axial collection, hygroma and soft tissue swelling were ruled out. Among neurological aspects seizures, hemiparesis and cranial nerve abnormality were reported if present. Based on medical records/history the children were grouped under the category of inflicted and non-inflicted traumatic brain injury.

Results: The neuroimaging findings were analyzed for both groups. "Inflicted Traumatic brain injury" group was quite young at the time of injury as compared to non-inflicted group ($p<0.001$). Subdural hematomas were ruled out in only 1 child among inflicted traumatic brain injury patients. However, 25% of the patients among non-inflicted traumatic brain injury group patients were diagnosed to have Epidural hematomas ($p<0.04$)" Parenchymal involvement, intracerebral hematomas" were present in 35% of the non-inflicted Traumatic brain injury group and 10% of the inflicted traumatic brain injury group ($p<0.04$). Cerebral atrophy was diagnosed on CT/MRI scan of 40% children among inflicted Traumatic brain injury ($p<0.004$). Shear injury on the contrary was only found associated with 20% of the non-inflicted Traumatic brain injury group ($p<0.04$). Subdural hygromas were visualized among 20% of children in inflicted Traumatic brain injury and only 5% in non-inflicted Traumatic brain injury.

Conclusion: A high frequency of subdural findings on neuroimaging is associated with inflicted traumatic injury in children.

Key Words: Neuroimaging, Neurological, Traumatic brain injury, Non-Traumatic brain injury, Hematomas

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INTRODUCTION

Traumatic brain injury (TBI) is one of the most common and potentially devastating neurologic disorders. It affects millions each year "resulting in over 50000 deaths and more than 70,000 patients suffer from permanent neurological deficits". Therefore, Traumatic brain injury (TBI) is a major public health problem[1].

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Inflicted TBI can be defined as non-penetrating or penetrating injury and it is an acquired brain injury. Non inflicted TBI causes damage to the brain by internal factors, such as a lack of oxygen, exposure to toxins, pressure from a tumor, etc. "TBI occurs in 12% of cases of physical child abuse". Among these, the majority of children are less than 2 years of age. According to an epidemiologic study of TBI, an assault was the cause of injury externally [2] It manifested "in 56% of the cases of serious brain injury in children less than 1 year of age". Although the assault was the cause of "only 5% of TBI in children ages 1 to 4 years, assault caused 90% of serious brain injury" [3].

TBI also accounts for a health care budget of up to 10% and also causes an estimated annual cost to society. TBI sequelae can significantly get altered by prompt proper management especially during the first 48 h following injury [4]. Neuroimaging techniques can indicate the presence and can rule out the extent of the injury. Based on the results, guidance on surgical planning can be obtained[5]. It can also be inferred from the

neuroimaging that either it is possible to use minimally invasive interventions as acute therapy to manage TBI [6]. Neuroimaging can also be reliable in the chronic therapy of TBI. It allows to identify chronic sequelae, determines prognosis, and also provides a guide for rehabilitation [7]. All head injuries do not require neuroimaging. Neuroimaging is expensive and can consume the scanner time unnecessarily. It is however difficult to define minor head injuries versus major head injuries [8]. Certain situations suggest major injury and require imaging such as in cases with reduced level or loss of consciousness for more than 5 minutes, seizures, failure of improvement in mental status, confusion, aggression, or penetrating skull injuries [9].

Biomechanical forces that are produced during injury are different in "inflicted & non inflicted TBI". Injuries impact arise from "contact and inertial forces". Contact forces are mostly associated with the head traumas that result in focal injuries to the brain [10]. For example, "lacerations, fractures, contusions, and epidural hematomas". Inertial forces on the other hand "acceleration – deceleration forces" causing more diffused injuries "such as concussion, subdural hematoma, and diffuse axonal injury". In young children, the "acceleration-deceleration forces" occur frequently in inflicted TBI as compared to non-inflicted TBI[11]. The different biomechanical forces yield characteristics inflicted and non-inflicted TBI [12]. In the current study, we did a comparative analysis of acute CT/MRI findings, physical findings along with initial developmental outcomes in children. The comparison was used to analyze whether inflicted TBI is associated with a higher rate of subdural findings on neuroimaging than non-inflicted TBI. Here by the current study was to characterize neuroimaging findings with traumatic brain injury in children.

MATERIALS AND METHODS

Physical findings were analyzed in 40 children between ages 3 months to 7 years at the time of injury. The developmental status was also evaluated of these children as they were admitted from 01 July 2020 to 01 December 2020 at Neurology & Radiology Department to the Neurology Department of Children Hospital & Institute of Child Health Multan. After being affected with either inflicted or non- inflicted TBI. It was a cross sectional study design. The inclusion criteria were comprised of intermediate to severe TBI with no known history of neurologic injury, no metabolic disorder, and gestation age of a minimum of 32 weeks. Patient with any metabolic disorder and pre mature birth on history were excluded from the study. All enrolled children underwent a proper physical examination by a pediatrician. After taking informed consent from parents the study was observed during the hospitalization. The study was conducted as per the ethical guidelines. "CT/MRI scans" of the patients were obtained at the hospital and were reviewed by a consultant radiologist. The radiologist was blind to the cause of injury. The scans done within one week of the injury were considered.

Medical records were taken into consideration to check out the presence of "ocular injury, bruises, fractures", or any neurological findings. The division of children among inflicted and the non-inflicted group was done based on the history including the type, severity, and pattern of injury.

Data Analysis: "Chi-square test" was applied to estimate the distribution of normal and abnormal CT/MRI and physical findings in "inflicted & non inflicted TBI groups". A P-value of <0.05 was considered significant**.**

RESULTS

Demographic and history variables for both groups showed the participants were from all three socioeconomic backgrounds. Among TBI groups, more male participants were present than females. Inflicted injuries occur mostly during infancy, in accordance to that "inflicted TBI group" was quite younger at the time of injury in comparison to "non-inflicted group" ($p<0.001$). Some associated complications are also indicated in Table I. The neuroimaging findings are categorized and depicted in Table II. Extra axial collections were found to be present in all children in "inflicted TBI" group and also in the "non-inflicted TBI" ($p<0.04$). Subdural hematomas were found more associated with inflicted TBI.

Table No.1: Neuroimaging Findings from Acute CT/MRI Scans

Neuroimaging Findings	Group "Inflicted TBI" (n=20)	Group "Non-inflicted TBI" (n=20)
Soft tissue swelling		
Present	12 (60%)	17 (85%)
Absent	8 (40%)	3 (15%)
Skull fracture		
Present	9 (45%)	16 ((80%)
Absent	11 (55%)	4 (20%)
Extraaxial collection		
Hematoma	15 (75%)	10 (50%)
Subdural	1 (5%)	5 (25%)
Epidural	5 (25%)	5 (25%)
Subarchnoid		
Hygroma		
Subdural	4 (20%)	1 (5%)
Parenchymal involvement	6 (30%)	7 (35%)
Edema/infarction	2 (10%)	7 (35%)
Hematoma	3 (15%)	2 (10%)
Diffuse swelling	8 (40%)	0
Atrophy	0	5 (25%)
Shear injury		

Table No.2: Neurological Findings in inflicted and Noninflicted TBI Groups

Neurological Findings	Group "Inflicted TBI" (n=20)	Group "Non-inflicted TBI" (n=20)
Seizure	14 (70%)	2 (10%)
Hemiparesis	6 (30%)	11 (55%)
Cranial nerve abnormality	8 (40%)	7 (35%)

Epidural hematomas were ruled out in only 1 child among inflicted TBI patients. However, 25% of the patients among non-inflicted TB group patients were diagnosed to have Epidural hematomas ($p<0.04$).

Subarachnoid hemorrhage was present in an equal ratio among inflicted and non-inflicted TBI groups. In the context of "parenchymal involvement, intracerebral hematomas" were seen in 35% of the "non-inflicted TBI group" and 10% of the inflicted TBI group ($p<0.04$). The edema/infarct was found to be distributed comparably across the groups. Cerebral atrophy was characterized as proof of preexisting brain injury. Cerebral atrophy was diagnosed on CT/MRI scan of 40% children among inflicted TBI ($p<0.004$). Shear injury on the contrary was only found associated with 20% of the non-inflicted TBI group ($p<0.04$). Subdural hygromas were visualized among 20% of children in inflicted TBI and only 5% in non-inflicted TBI. Skull fractures & soft tissue swelling was reported in a comparable ratio among both groups with no significant difference.

DISCUSSION

Traumatic brain injury (TBI) in children had a different pattern of results on neuroimaging and physical findings [13]. The study determined comparatively the presence of subdural & other findings on neuroimaging of two groups of children with TBI. Despite having no history of any brain injury there was a sign of cerebral atrophy in children with inflicted TBI. Subdural hematomas were more frequently visualized in children with inflicted TBI however, the children in the "non-inflicted'' group who were found to have subdural hematomas had a history of motor vehicle accidents rather than fall or crush injuries. Epidural hematomas and shear injuries were abundantly seen in non-inflicted TBI. In the context of intraparenchymal hemorrhages, it was analyzed that both groups are affected in the same way. The details of the physical examination of these patients showed poor neurobehavioral and motor outcomes. The presence of skull fractures and soft tissue damage goes in accordance with the "shaking-impact mechanism of injury" [14]. No association was found between skull fracture and soft tissue. Likewise, no link was found between parenchymal involvement and hemorrhage. The age difference between the two groups was compared. Although the inflicted injury is correlated with infancy, however, the age distribution of non-inflicted injury was found to be constant during infancy and pre-school years [15].

More longitudinal design studies are required to find details about neuropsychologic deficiencies in children with inflicted and non-inflicted TBI either injured during infancy and pre-school years [16]. Clinical evaluations in children can be sometimes misleading for example significant parenchymal injury can be ruled out in children "with spontaneous eye opening and spontaneous movements" [17]. Besides this, based on primitive motor patterns, the infants may also show the ability to withdraw from painful stimuli when applied to limbs. Furthermore, the consciousness levels could also be misleading to assess especially in infants [18]. Therefore, the neuroimaging findings play a vital role in providing a comprehensive insight into the severity of injury in infants. Most of the time children with inflicted TBI are difficult to diagnose because of the lack in the accuracy of the provided history. In such situations, physicians must be vigilant to find out the aspects of injury that can aid in precise diagnosis and detection of the underlying cause of injury [19]. Hereby in all these scenarios where the history being provided by guardians is unreliable and unrealistic the neuroimaging techniques play a particularly important role. The cases that more specifically need neuroimaging techniques are the ones without trace of external injury [9] These types of injuries are the shaking impact injuries that result in lethal consequences with no evidence of external injury [20]. Skeletal surveys can also add valuable information to aid in suspicions of "inflicted injury". Due to the poor developmental outcomes associated with traumatic brain injury in children with similar indices of the severity of trauma [15]. It is important to identify the cause (that can be abusive) followed by neuropsychologic assessment to initiate rehabilitation and family intervention. Neuroimaging also aids in proving clues for cases involving abused brain injury [21]. It is important to correlate neuroimaging findings with "neuropsychologic evaluations and rehabilitation services". Based on the diagnosis the follow-up should be done. The effects of early brain injury become more evident with time [22]. Sequential evaluations are required to determine the rate at which the children are developing new skills. In this way, it is possible to identify potentially deficient areas that require intervention, either it needs to ensure "referral for rehabilitation or to monitor & family environment" [23]. Much literature on the neuroimaging of subdural findings in TBI is based on secondary approach. A little primary research has been done in this area.

There are some limitations to the study in context of sample size. More extended study duration with increased number of cases can provide more insightful results.

CONCLUSION

A high frequency of subdural findings on neuroimaging is associated with inflicted traumatic injury in children.

Author's Contribution:

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

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Original Article

Frequency of Early Puerperal Complications after Vaginal Delivery

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ABSTRACT

Objective: To evaluate the frequency of early puerperal complications following vaginal delivery. To compare the frequency of early puerperal complications after home delivery and delivery at tertiary care hospital.

Study Design: A Descriptive Case Series study

Place and Duration of Study: This study was conducted at the Department of Obstetrics and Gynecology in Nishtar Medical University & Hospital Multan from Aug 2020 to July 2021 for a period of one-year.

Materials and Methods: A total of 331 women presented in emergency with PPH, history of home/institution delivery with parity 1-4 were included in the study. Patients with history of hypertension, diabetes, renal disease and pre-eclampsia were excluded. Detailed clinical assessment of the patient was done and variables like secondary PPH and severe anemia was recorded along with basic demographic information such as place (home/institutional) of vaginal delivery, age, gestational age, parity and BMI. Information was recorded on specially designed proforma.

Results: Participants of the study ranged from 20 to 35 years with mean age of 28.142±2.19 years, mean gestational age was 38.362±1.00 weeks and mean BMI was 26.561±1.45 Kg/m^2. 68% women delivered at home and 32% patients had institution delivery. Secondary PPH was seen in 9.4% patients. Severe Anemia was seen in 10.6% patients. Secondary PPH was seen in 11.1% patients with home delivery and 5.7% patients with institution delivery (p=0.112). Severe Anemia was seen in 13.3% patients with home delivery and 4.7% patients with institution delivery (p=0.017).

Conclusion: Our study showed that there were more early puerperal complications in patients with home delivery compared with delivery at tertiary care hospital.

Key Words: Home delivery, Delivery at tertiary care hospital, Puerperal complications

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INTRODUCTION

A large proportion of women are dying due to pregnancy-related complications and out of these about 98% of deaths are occurring in the developing countries[1]. In our country maternal mortality ratio is 276 per 100,000 live births[2]. In developing countries, about 16.5 pregnancy related complications and more than 100 acute complications are related to maternal deaths[3]. Data on maternal morbidity is mostly collected from record of deliveries occurring in hospitals or women's self-reports[4] but these deliveries conducted in hospital are not the true representative of the events in community.

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Various measures are being taken to improve estimation of morbidity through these household surveys[5] and data collected from interviews of individuals have little value in estimating the biomedical maternal morbidity[6]. Puerperal fever is difficult to determine by retrospective inquiries in areas where fevers are common[7]. In an International study, frequency of secondary PPH in vaginal deliveries that occurred at home was 9.6% that occurs at home and it was reported as approximately 6.6% in the vaginal delivery that occured at tertiary care hospitals and severe anemia was reported 11.6% versus 5.8%[8]. Secondary PPH was reported as 27.2% after vaginal delivery at home by Tuladhar H et al[10]. No such study has been done before in our general population because different population has different socioeconomic characteristics. Moreover, information on maternal morbidity at home could provide the evidence necessary for planning safe motherhood outreach activities in developing countries.

MATERIALS AND METHODS

Study was conducted in the Department of Obstetrics and Gynecology, Nishtar Hospital Multan from 1st Aug 2020 to 31st July 2021. It was a descriptive case series.

Non probability consecutive sampling was used. A total of 331 women aged 20-35 years presented in emergency with PPH with history of home/institution delivery were enrolled for this study after permission from ethical committee and research department. Informed consent was taken by researcher herself. Detailed clinical assessment of the patient was done and variables like secondary PPH and severe anemia was recorded along with basic demographic information such as place (home/institutional) of vaginal delivery, age, gestational age, parity and BMI. Information was recorded on specially designed pro forma. IBM-SPSS (version-20) was used for statistical analysis of the data. Qualitative variables like, age groups, parity, economic status, secondary PPH and severe anemia were presented as number and frequency. Mean ±SD was presented for quantitative variables like age, gestational age and BMI. Stratification was done with regard to age, economic status, parity, gestational age and BMI to see the effect of these variable on PPH and severe anemia. Chi square test was applied to compare secondary PPH and severe anemia in home and institutional delivery. P ≤0.05 for any variable was considered statistically significant.

RESULTS

Age range in this study was from 20 to 35 years with mean age of 28.142±2.19 years, mean gestational age was 38.362±1.00 weeks and mean BMI was 26.561±1.45 Kg/m^2.

Table No.1: Frequency and %age of patients according to age, parity, economic status and place of delivery n=331

Age Group	No of Patients	%age
20-27	111	33.5%
28-35	220	66.5%
Parity	**No of Patients**	**%age**
1-2	255	77%
3-4	76	23%
Economic Status	**No of Patients**	**%age**
Poor	89	26.9%
Middle	220	66.5%
Rich	22	6.6%
Place of Delivery	**No of Patients**	**%age**
Home	225	68%
Institution	106	32%

Majority of patients belongs to 28-35 age group (66.5%). 68% women delivered at home and 32% patients had institution delivery as shown in Table 1. Secondary PPH was seen in 9.4% patients and severe Anemia was seen in 10.6% patients as shown in Table 2. Secondary PPH was seen in 11.1% patients with home delivery and 5.7% patients with institution delivery (p=0.112) as shown in Table 3. Severe Anemia was seen in 13.3% patients with home delivery and 4.7% patients with institution delivery (p=0.017) as shown in Table 4.

Table No.2: Frequency and %age of patients according to Secondary PPH and severe anaemia n=331

Secondary PPH	No of Patients	%age
Yes	31	9.4%
No	300	90.6%
Severe Anemia	**No of Patients**	**%age**
Yes	35	10.6%
No	296	89.4%

Table No.3: Comparison of Secondary PPH according to Place of Delivery

Secondary PPH	n=225 Home Delivery	n=106 Institution Delivery	*P Value*
Yes	25 (11.1%)	6 (5.7%)	0.112
No	200 (88.9%)	100 (94.3%)	
Total	225 (100%)	106 (100%)	

Table No.4: Comparison of Severe Anemia according to Place of Delivery

Severe Anemia	n=225 Home Delivery	n=106 Institution Delivery	*P Value*
Yes	30 (13.3%)	5 (4.7%)	0.017
No	195 (86.7%)	101 (95.3%)	
Total	225 (100%)	106 (100%)	

DISCUSSION

Various controversies are exist regarding the place of birth and there are strong evidences both for and against home deliveries[9]. Various blogs and social media groups have potentiated the issue; some are in favor while others are against the risks of births at home. Safety of these births at home is dependent on many factors including availability of the support, experience of the midwives, community educational programs and availability of infrastructure[10].

The result of our study revealed mean age of patient as 28.142±2.19, the mean gestational age was 38.362±1.00 and mean BMI (Kg/m^2) of studied population was 26.561±1.45. In this study Secondary PPH was seen in 9.4% patients and Severe Anemia was seen in 10.6% patients while Secondary PPH was seen

in 11.1% patients with home delivery and 5.7% patients with institution delivery and severe Anemia was seen in 13.3% patients with home delivery and 4.7% patients with institution delivery. Frequency of secondary PPH after home delivery and delivery at tertiary care hospital as 9.6% and 6.6% respectively was reported by Iyengar K[8]. Similarly frequency of severe anemia was 11.6 in patients who delivered at home versus 5.8% in those who delivered at hospital[8]. Secondary PPH after vaginal delivery was recorded in 27.2% of cases in a study conducted by Tuladhar and his colleagues[11].

In Pakistan, home birth attendants faces many hurdles for transferring their clients and to access the hospital care[12]. Rate of transfer for the planned home birth women in the other areas was reported as 9.9% to 31.9 and it was reported even higher in the areas where well established maternity services were avaiable[13]. In planned home delivery group, difficulty or delay in the transfer due to long distance from hospitals was associated with adverse neonatal outcome in these cases[14].

Uniform guidelines on this issue and proper selection of these cases are considered as the important factors for safe home births and where these guidelines were strictly followed, outcomes were reported to be as good as that of hospital birth settings for the low risk cases[15]. Contrary to this an increase in both neonatal morbidity and mortality was reported where high risk cases were planned for home birth. In the properly selected low risk cases, there is a strong evidence that home birth is more cost effective than birth in hospitals[16].

CONCLUSION

The results of our study revealed that there were more early puerperal complications in patients with home delivery compared with delivery at tertiary care hospital.

Author's Contribution:

Concept & Design of Study:	Rida Iqbal
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Original Article

Acute IWMI with and without RVI

Comparison of In-hospital Acute Inferior Wall Myocardial Infarction Outcomes in Elderly Patients with and without the Right Ventricular Involvement

Gul Zaman Khan[1], Fahar Adnan[1], Syed Naseem Bukhari[1], Noor Dastagir[2], Tariq Mehmood Khan[1] and Urwah Imtiaz[3]

ABSTRACT

Objective: The major aim of the current study is to determine the in-hospital outcomes of acute inferior wall myocardial infarction (IWMI) in elderly patients with the presence and absence of right ventricular myocardial infarction (RVMI).

Study Design: A comparative cross-sectional study

Place and Duration of Study: This study was conducted at the department of Cardiology in Ch. Pervaiz Elahi Institute of Cardiology Multan from March 2020 to March 2021 for a period of one-year.

Materials and Methods: A cross-sectional study was designed using a sample size of 165 elderly patients with IWMI. The study was performed using a one-year patient's data from Chaudhary Pervaiz Elahi Institute of Cardiology, Multan. Both male and female IWMI patients with age's ≥60 years were considered for the study. Baseline data and risk factors were recorded for all patients after the informed consent. The older IWMI patients were categorized into two groups namely, the RVMI and non-RVMI groups respectively. In-hospital outcomes such as serious complications, cardiogenic shocks, complete AV blockage, ventricular tachycardia and in-hospital deaths were monitored.

Results: Out of total 165 IWMI patients, 80 (48%) patients had RVMI whereas, the remaining 85 (52%) were non-RVMI patients. Our results show that RVMI is an important determinant of the in-hospital outcomes such as serious complications (76%), shock (48%), cardiogenic shocks (36%), complete AV blockage (38%) and in-hospital death rates (53%) in the elderly IWMI patients.

Conclusion: Our study has shown that the RVI in older IWMI patients lead to frequent complications thus exacerbating and aggravating the in-hospital outcomes of acute IWMI due the increased risk of shocks, serious complications, cardiogenic shocks, complete AV blockage and in-hospital deaths.

Key Words: Acute Inferior wall myocardial infarction (IWMI), Right ventricular myocardial infarction (RVMI), in-hospital outcomes, coronary artery disease (CAD), acute coronary syndrome (ACS), cardiogenic shock (CS), anterior wall myocardial infarction (AWMI)

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INTRODUCTION

Regardless of the remarkable advancements achieved in the treatment and administration of coronary artery disease (CAD), it remains the major reason for the fatalities occurring globally [1,2]. Most prominently, the Acute coronary syndrome (ACS) is the severest demonstration of CAD resulting in high mortality rates thus, concerning around 5 to 8% of the patients within a six month duration of diagnosis [3]. ACS manifests a broader range of disease conditions related to the abrupt and reduced blood flow to the heart mainly due to the obstructions or narrowing of the coronary arteries [4, 5]. Unstable angina, cardiac arrest, electrical instability with cardiogenic shock (CS), non-ST elevation myocardial infarction and ST-Elevation myocardial infarction are the other clinical presentations associated with ACS [5, 6].

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Moreover, the interrupted blood supply causes the necrosis of myocytes thus leading to the acute ST elevation myocardial infarction (STEMI). Depending on the vessel supplying blood to a particular area, the STEMI can be concomitant to the lateral, posterior, inferior or anterior walls of left ventricle [6]. Generally, a destructive course has been indicated for the anterior wall myocardial infarction (AWMI). Whereas, an inferior wall myocardial infarction (IWMI) can also pose serious risks when occurring in concomitance with the right ventricle myocardial infarction (RVMI) [7]. The complications in the form of RVMIs are mainly evident subsequent to the STEMI [8]. Moreover, a greater association of RVMI with the higher morbidity and mortality rates at earlier stages has been reported frequently in literature [8-10].

Particularly, the acute inferior wall myocardial infarction (IWMI) constitutes about 40%-50% of the total myocardial infarctions that are acute in nature. The IWMIs display better prognosis (both short and long term) with mortality rate of ~ 2% to 9% in comparison to the AWMIs [11-14]. Approximately 20-50% of all acute IWMIs are reported to be complicated by the RVMI and a poor prognosis is observed for the acute IWMI when it is complicated by the RVMI [14, 15]. Various studies have reported different in-hospital outcomes of IWMIs either with the presence or absence of the RVMI [16-18]. Literature reports differences being observed in the documented in-hospital outcomes of patients of IWMI with and without RVMI. Therefore, the present study was designed for the elucidation of in-hospital outcomes of IWMI patients with the presence and absence of RVMI mainly in the elderly population of South Punjab. The study will aid the comparative analysis of the in-hospital outcomes in elderly patients. Herein, our study focuses on the older patients as they are amongst the subgroups of acute inferior myocardial infarction patients that are at a greater risk. Moreover, the RVMIs clinical implications in elderly patients have been studied to a limited extend previously.

MATERIALS AND METHODS

A comparative cross-sectional study with a sample size of 165 elderly patients with IWMI was conducted using one year from 2nd March 2020 to 2nd March 2021 patients data from the Chaudhary Pervaiz Elahi Institute of Cardiology, Multan. Both male and female IWMI patients with age's ≥60 years were considered for the study. Patients were excluded from the study sample on the basis of a CCU admission time greater than 48 hours, repolarization abnormalities in V3R or V4R, bundle-branch blockage and those with pacemaker cardiac rhythm. These criteria were used for final sample selection as the patients with the described conditions are not adequate or suitable for the assessment of size and function of the right ventricle. Additionally, patients with myocardial infarction, chronic obstructive pulmonary disease, renal failure and chronic liver disease histories were also omitted from the study sample.

The screening and analysis of IWMI was performed if a prolonged chest pain lasted above 30 minutes along with a ST segment elevation of about 0.1 mv or above in two or more electrocardiographic (ECG) inferior leads including II, III, and aVF leads. However, the presence of RVMI in patients was diagnosed at an ST-segment elevation of 0.1 mV or above in the precordial leads of the right side i.e. V3R or V4R leads. The baseline data was collected to analyze the in-hospital outcomes of IWMI patients after an informed consent. Gender, age, patient's body mass index (BMI) and cardiovascular risk factors including diabetes, hypertension, smoking, chest pain and dyslipemia were considered for each patient as shown in Table 1. The selected IWMI patients were divided into groups on the base of the absence or presence of a concomitant RVMI in accordance with the operational definition provided by the consultant cardiologist using the clinical history, physical examination and the ECG result.

Data Analysis: Data analysis was performed using the software SPSS 20.0. Median values were calculated for the selected continuous variables. For quantitative variables (i.e. age and BMI) mean and standard deviation values were calculated. For qualitative variables such as cardiovascular risk factors (i.e. hypertension, diabetes, cigarette smoking, dyslipemia and chest pain) frequency and percentages were calculated. Two tests including the $\chi 2$ test and Wilcoxon U test were used for the analyzing the significance of proportions and the comparison of means of the studied variables. The independent weightage of RVMI was evaluated using multiple logistic regression analysis. Two tailed probability values were used for the current study and a P-values ≤ 0.05 were considered to be statistically significant.

RESULTS

The mean values for the age and BMI of the patient sample (n=165) included in the study were 69.90±8.04 years and 25.01±3.36 kg/m^2 respectively. About 48% (n=80) patients with inferior wall acute myocardial infarction (IWMI) were diagnosed with RVMI and the remaining 52% (n=85) patients were characterized with the absence of the RVMI. No significant differences were observable in the baseline demographic and clinical presentations of patients from both groups i.e. RVMI and non-RVMI IWMI patients as shown in Table 1. The in-hospital outcomes of patients have shown that a greater number of IWMI patients displayed serious complications, both shock and cardiogenic shocks and complete AV blockage (Table 2). The implications of in-hospital outcomes for both RVMI and non-RVMI IWMI patients are presented in Table 2. However, the in-hospital fatality rates were

higher (53%) for IWMI patients with RVMI and lower (25%) for IWMI patients without RVMI. The results from the multiple logistic regression analysis reveal that the RVMI is an important independent predictor of in-hospital deaths in older IWMI patients.

Table No.1: Baseline demographic data of Inferior wall myocardial infarction (IWMI) patients with and without RVMI

	RVMI	Non-RVMI	P
Sample size	(n=80)	(n=85)	
Age (years)	82 (60-85)	75(61-87)	0.07
Sex (Male/Female)	(48/32)	(53/32)	0.85
Hypertension n (%)	43 (54)	52 (61)	0.97
Diabetes mellitus n (%)	30 (38)	28 (33)	0.32
Cigarette smoking n (%)	28 (35)	27 (32)	0.19
Dyslipemia n (%)	20 (25)	25 (31)	0.70
Chest pain, n (%)	70 (88)	76(89)	0.99

Table No.2: The in-hospital outcomes for IWMI patients with and without RVMI (N=165)

Occurrence	RVMI	Non-RVMI	*P*
Sample size	(n=80)	(n=85)	
Serious complications n(%)	61 (76)	39 (45)	0.0001
Pulmonary congestion n(%)	20 (25)	29 (34)	0.73
Shock n(%)	38 (48)	11(13)	0.0001
Cardiogenic shock n(%)	29 (36)	9 (11)	0.0001
Complete AV blockage n(%)	30 (38)	15 (18)	0.0001
Ventricular tachycardia n(%)	15 (19)	8 (9)	0.046
Arrhythmias (Supraventricular) n(%)	20(25)	18 (21)	0.54
Death n(%)	42(53)	20 (25)	0.0001

DISCUSSION

It is reported that a destructive course has been indicated for the anterior wall myocardial infarction (AWMI), however, the inferior wall myocardial infarction (IWMI) can also pose serious risks when occurring in concomitance with the right ventricle myocardial infarction (RVMI) [7]. Thus, a greater association of RVMI with the higher morbidity and mortality rates at an earlier stage has been reported frequently in literature where, RVMI incidence is reported to be approximately 10-50% [8-10, 19, 20]. Previously, various IWMI subgroups with higher risks have been defined and it is also reported that older IWMI patients have worse outcomes in comparison to younger IWMI patients [11, 21, 22]. Moreover, the clinical implications of RVMI in older IWMI patients have been previously investigated on a limited scale.

Therefore, in the present study we assessed the effect of RVMI in older patients with IWMI and it is shown that a poor diagnosis is displayed by older IWMI patients with RVMI in comparison to the non-RVMI patients. Patients implicating significant RVMI might represent hypotension, shock or a higher incidence of in-hospital complications [23, 24].Our results also show that RVMI is a strong determinant of the in-hospital outcomes such as serious complications (76%), shock (48%), cardiogenic shocks (36%), complete AV blockage (38%) and in-hospital death rates (53%). Our results in terms of the studied variables are well in line with the study outcomes of Zehender et al and Bueno et al [10, 16].

Various studies without the consideration of age factor have reported the occurrence of cardiogenic shock to be within 8 to 49% [25-27]. However, taking in to consideration the age of patients, we report the incidence of the cardiogenic shock (36%) within the reported range. Moreover, a higher death rate is observable for elderly IWMI patients considered in the current study. Ali et al, reported incidence of ventricular tachycardia (VT) and mortality rate of about 30.30% and 21.6% respectively in IWMI patients with RVMI. However, in the current study a lower incidence of ventricular tachycardia (VT) (19%) and a higher mortality rate (53%) has been reported for older patients [28]. Moreover, similar to our study, poor outcomes in IWMI patients with RVMI are reported by Ali et al, in comparison to the non-RVMI patients [28]. Similar to our study, Zahender and coworkers have also reported higher death rates (31%) and a poor prognosis in IWMI patients with RVMI [10].

In conclusion it shown by the current study that RVMI in older IWMI patients leads to frequent complications thus exacerbating the in-hospital outcomes of acute IWMI due the increased risk of shocks, cardiogenic shock, serious complications, complete AV blockage and in-hospital deaths. Besides this the current study might display certain limitations since the study is observational in nature thus, it might lack some relevant functional and clinical information. Therefore, there is an extensive need to explore and understand the pathophysiological mechanisms of cardiogenic shocks in older IWMI patients with RVMI.

CONCLUSION

Our study has shown that the RVMI in older IWMI patients lead to frequent complications thus exacerbating and aggravating the in-hospital outcomes of acute IWMI due the increased risk of shocks, serious complications, cardiogenic shocks, complete AV blockage and in-hospital deaths.

Author's Contribution:

Concept & Design of Study:	Gul Zaman Khan
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Fulminant Hepatic Failure in Pregnancy and its Association with Viral Hepatitis E

Hepatic Failure in Pregnancy with Viral Hepatitis E

Fahmida Parveen Memon[1], Sakeena Ahmed Memon[1], Almas[2] and Shahla Afsheen[2]

ABSTRACT

Objective: To determine the frequency of fulminant hepatic failure in pregnancy and its association with viral hepatitis E.

Study Design: A retrospective study

Place and Duration of Study: This study was conducted at the Department of Obstetrics & Gynecology, Liaquat Medical University Hospital, Hyderabad, from April 2019 to April 2021 for a period of two years.

Materials and Methods: One hundred fulminant hepatic failure pregnant ladies were enrolled. Main variables of study were gestational age, duration of disease, IgM (positive/negative) for hepatitis E virus, maternal complications and mortality. Statistical package for social sciences version 23 was used for data analysis. Mean and standard deviation for numerical data like age and gestational age and frequency and percentages for categorical data like IgM (positive/negative).

Results: The mean age, gestational age of patients and duration of disease were 26.25±4.87 years, 31.16±3.82 weeks and 2.45±1.14 weeks respectively. Most of the patients had 3 or more weeks of disease. Number of patients n=61 (61.0%) were found to be IgM positive for the hepatitis E virus. Maternal mortality was noted as n=71 (71.0%) and live births were 41 (41.0%). No association was found between age, gestational age and duration of disease (P-value, 0.364, 0.107 and 0.956 respectively).

Conclusion: Hepatitis E infection during third trimester of pregnancy can leads to fulminant hepatic failure and associated with number of fetal and maternal complications. Special prevention plan is necessary along with awareness and public health facilities. Timely diagnosis especially IgM anti HEV is mandatory.

Key Words: Fulminant Hepatic Failure, Hepatitis E virus, Maternal complications, Pregnancy

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INTRODUCTION

ALF, acute liver failure is a rare clinical syndrome. It is described as abrupt and extensive hepatic necrosis in a healthy liver without any prior disease, which culminate in jaundice, hepatic encephalopathy and coagulopathy (INR>1.5)[1]. It can be sub-fulminant or fulminant hepatic failure (FHF); both are described by progression of hepatic encephalopathy following the emergence of critical liver disease.

The difference between Sub-fulminant and fulminant hepatic failure is characterized by the time of emergence of symptoms; in former it is between 8 weeks and 6 months of liver disease and in later within 8 weeks[2].

There is little chance of recovery in both cases but there is a hope of reversal and recovery towards normal health life. Hepatitis E virus (HEV) is a small quasi-enveloped, single-stranded RNA virus. Its incubation period is between two and nine weeks. Its transmission occurred through feco-oral route[3]. In parts of Asia, Africa, the Middle East and Central America this virus is believed to be of endemic scale, where sizeable outbreaks occur due to insufficient hygiene and water-borne diseases. HEV Genotype 1 is hyper-endemic in Asia and Africa, which causes the following conditions of sporadic acute hepatitis, acute or chronic hepatic failure and acute hepatic failure[4]. HEV Genotype 2, also causes same ailments, is found in Mexico and Nigeria. HEV Genotypes 3 and 4 are predominant in the developed nations[5].

Humans are thought to be primary reservoir of HEV genotype 1 and 2 and for HEV genotype 3 and 4 pigs are considered as primary reservoirs, therefore zoonotic transmission is a common occurrence[6]. While HEV genotypes 3 and 4 have not been found associated with severe liver disease but further research is required to validate this observation. Hepatitis E causes serious problems in pregnant women[7].

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FHF in pregnant women due to HEV is a severe condition with symptoms such a short pre-encephalopathy period; consumptive coagulopathy also known as disseminated intravascular coagulation and rapid development of cerebral edema[8]. Pregnant women with HEV related acute hepatitis have unfortunate maternal and fetal results. A study in India done and reported that 81% of cases of fulminant hepatic failure during pregnancy were due to hepatitis E virus[9,10].

The main aim of this investigation is to seek out independent validation of high rate of fulminant hepatic failure caused by Hepatitis E virus during pregnancy in our region and to estimate the related mortality and morbidity.

MATERIALS AND METHODS

Study was carried out at department of Obstetrics & Gynecology, Liaquat Medical University Hospital, Hyderabad, from April 2019 to April 2021 in two years duration. This was a retrospective Study. Ethical approval was taken from hospital ethical board. Informed written consent was obtained from patient after detailed information. Patients presented with FHF during antenatal period were enrolled in study. Pregnant women with age below forty years and 3 months gestational amenorrhea were included in the study. Hepatic failure presented as hepatic encephalopathy, jaundice and coagulopathy (INR below 1.5) were labeled as fulminant hepatic failure.

Complete physical examination was done in all patients and complete blood count, liver function test, urine complete examination, serum urea and creatinine, ultrasonography of abdomen and pelvis were done. Viral serology with IgM for hepatitis E virus was calculated. Patients with known cardiac disease, eclampsia, pre-eclampsia and chronic liver failure were excluded from the study. Antibiotic treatment (Ceftriaxone) was administered to all patients.

Patient's data was entered in SPSS version 23 for data analysis and mean ± SD was calculated for numerical variables like age, gestational and frequency and percentages were calculated for categorical data like hepatitis E. Test of significance were applied to see association among variables. P Value less than or equal to 0.05 was considered as significant.

RESULTS

One hundred three fulminant hepatic failure patients were included in this study. The mean age of the patients was 26.25±4.87years. Majority of the patients were between 26-35 years. The mean gestational age of the patients was 31.16±3.82 weeks. The mean duration of disease was 2.45±1.14 weeks. Most of the patients had 3 or more weeks of disease. n=61 (61.0%) patients were found to be IgM positive for the hepatitis E virus. (Table. I).

There was no association between IgM and age, gestational age and duration of disease. (Table. 2).

Table No.1: Demographic variables of the patients

Variable	N (%)
Age distribution (years)	
18-25	46 (46.0)
26-35	49 (49.0)
36-45	5 (5.0)
Gestational age (weeks)	
25-28	28 (28.0)
29-31	36 (36.0)
32-37	29 (29.0)
38-45	7 (7.0)
Duration of disease (weeks)	
1	22 (22.0)
2	35 (35.0)
3 or more	43 (43.0)
IgM	
Positive	61 (61.0)
Negative	39 (39.0)
Parity	
Primi	71 (71.0)
G2	19 (19.0)
G3 or more	10 (10.0)

Table No.2: Association of IgM with independent variables

Variable	Category	IgM		P-value
		Positive	Negative	
Age distribution (years)	18-25	31	15	0.364
	26-35	28	21	
	36-45	2	3	
Gestational age (weeks)	25-28	14	14	0.107
	29-31	23	13	
	32-37	17	12	
	38-45	7	0	
Duration of disease (weeks)	1	13	9	0.956
	2	22	13	
	3 or more	26	17	

Table No.3: Maternal mortality and other complications of the patients

Complication	N (%)
Second trimester	24 (24.0)
Third trimester	76 (76.0)
Hepatic encephalopathy	14 (14.0)
Gastrointestinal hemorrhage	12 (12.0)
Ascites	69 (69.0)
Renal failure	29 (29.0)
Coagulation defeat	41 (41.0)
ICU admission	17 (17.0)
Transfusion (blood/blood products)	38 (38.0)
Mortality	71 (71.0)

Maternal mortality was noted as n=71 (71.0%). Medical complications presented in table 3. There was n=26 (26.0%) IUD and spontaneous abortions. Still births were 26 (26.0%) and live births were 41 (41.0%). Fetal outcomes were shown in table. 4.

Table No.4: Fetal outcomes of the patients

Outcome	N (%)
IUD	26 (26.0)
Spontaneous abortions	2 (2.0)
Preterm babies	68 (79.1)
Still birth	26 (26.0)
Live birth	41 (41.0)
Neonatal death	71 (71.0)
Low birth weight	47 (54.7)
Meconium stained liquor	6 (7.0)
NICU admissions	27 (31.4)

DISCUSSION

During pregnancy complication may arise due to severe liver issues including hepatic failure. As some liver disorders are particular to pregnancy, AFLP (acute fatty liver of pregnancy) and HELLP syndrome are rare, whereas obstetric cholestasis and liver dysfunction associated with preeclampsia are common[11]. Some hepato-biliary disorders are cause of concern as they are more expected to occur during pregnancy and can cause serious damage, like gall stones and hepatic vein thrombosis and acute hepatitis E[12].

Hepatitis E virus is one of the major causes of fulminant hepatic failure in pregnant women. Its occurrence during pregnancy is sudden and severe; the results are often fatal. About 20% of pregnant women are infected with viral fulminant hepatitis; out of which 20% of women die during the third trimester of pregnancy[13]. Furthermore, it increases the risk of fetal complications and fetal death. At the moment there is no antiviral medicine or vaccine available for HEV, though some trials are undergoing for the development of vaccines[14].

In our research, out of n=100 pregnant women suffering from fulminant hepatic failure 61 (61%) were infected with HEV. This result agrees with the following studies conducted by Jaiswal et al[15] in India, Al-Mahtab et al[16] in Dhaka and Khuroo et al[13] where they found HEV to be in 57.5%, 56.52% and 61.8% of the FHF cases respectively.

However, Kumar A et al[17] recorded 81% of FHF cases due to HEV. This dissimilarity is perhaps due to the following factors; they included all jaundice patients during pregnancy and did not exclude patients with co morbid diseases. Moreover, their sample size was smaller in comparison. About 80% of our studied patients were 20 to 34 years of age group. This observation matches with Shrestha et al[18] from Nepal; their 76% of patients were in this age group. We observed 61% of women were between 29 to 42 gestational weeks. Yuel et al[19] in India observed similar pattern with 52% of women.

We observed maternal mortality due to HEV in 71% of the cases. Higher results regarding mortality in Bangladesh was 80% in hepatitis E patients associated with FHF reported by Mamun-Al-Mahtab et al[20]. It is probably due to the fact that we excluded the patients with chronic liver diseases or other comorbidities. Most of our patients were less than 35 years; Survivability chances decreases with advancement of age. Timely administration of broad spectrum antibiotics has been related to decrease in mortality rate of FHF patients[21].

A study was conducted by Brohi et al[22] and reported that fulminant hepatic failure and its association with pregnancy is a huge clinical issue that can be recovered with early diagnosis and treatment. We administered antibiotics of Ceftriaxone in all of our patients, which could have resulted in low mortality[23]. However, we cannot validate this conclusion since no parallel group of patients existed to which no antibiotics were administered.

It is imperative that HEV associated diseases should be taken seriously owing to its worldwide existence, an effective vaccine with long term immunity is immediately needed. This necessitates the responsiveness of public health scientists, academia and the health authorities. It is a need of hour to reduce the morbidity and mortality caused by HEV.

CONCLUSION

Hepatitis E infection during third trimester of pregnancy can leads to fulminant hepatic failure and associated with number of fetal and maternal complications. Special prevention plan is necessary along with awareness and public health facilities. Timely diagnosis especially IgM anti HEV is mandatory.

Recommendations: There is need for further studies on comparison of fetomaternal outcomes and women diagnosed with hepatitis E during pregnancy and its complications associated with liver injury. Conclusion of this study will be helpful in selection of more precise treatment plan of hepatitis E patients in acute phase of disease. Studies of this type are highly recommended in obstetrical research.

Author's Contribution:

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Data Analysis:	Almas, Shahla Afsheen
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Immediate Clinical Outcomes in Patients with Multi-Vessel Coronary Artery Disease and Left Ventricular Dysfunction following Off-Pump CABG

Multi-Vessel Coronary Artery Disease and Left Ventricular Dysfunction

Muhammad Yasir Khan, Shafqat Hussain, Muhammad Moeen, Iftikhar Paras, Muhammad Hamid Ch and Muhammad Kamran Khan

ABSTRACT

Objective: To determine the immediate clinical outcomes in patients with Multi-vessel coronary artery disease and left ventricular dysfunction following off-pump coronary artery bypass graft surgery.

Study Design: A Prospective observational study

Place and Duration of Study: This study was conducted at the department of Cardiac Surgery in Ch.Pervaiz Elahi Institute of Cardiology Multan from May 2019 to May 2021 for a period of two years.

Materials and Methods: Eighty-nine patients who were treated with OPCAB were included as study participants. The patients who intraoperatively underwent on-pump CABG were excluded from the study. Procedures were performed by "consultant cardiothoracic surgeons". The demographic variables of the patients were collected. Preoperative care was provided to the patient till the day of surgery. Proper technique of OPCABG was followed. The immediate clinical outcomes that included all the in-hospital outcomes till 30 days follow-up were recorded.

Results: The prospective observational study included 89 participants. Among these 89 patients, 54% (48) were male and 46% (41) were female. The mean age and standard deviation were 58±8.2 & 60±8.5 of the male and female groups respectively. History of the patients revealed that 60% (53) were hypertensive, 61% (68) had a previous history of myocardial infarction, 16% (14) had peripheral vascular disease, 63% (56) were known cases of diabetes. Moreover, 45% (41) has a deranged lipid profile, 16% (14) had chronic kidney disease while 5% (4) had severe LV dysfunction. The mean hospital stay in days was reported as 4 ± 2 days while the mean time spent on a ventilator was recorded as 9.2 ± 7.8 hrs. It was seen that factors like post-operative atrial fibrillation, severe left ventricular dysfunction, and end-stage renal failure contributed to mortality. Among Postoperative outcomes stroke & sternal infections were witnessed in 2.24% (2), atrial fibrillation in 13.4% (12), and re-exploration was done in 2.24% (2) of cases. Septicemia occurred in 8.9% (8), 16.8% (15) patients were readmitted following CABG. Total 5 deaths were reported.

Conclusion: In conclusion, off-pump CABG for patients with Multi-vessel coronary artery disease and left ventricular dysfunction had better in-hospital/immediate clinical outcomes with long-term survival rates.

Key Words: Left Ventricular dysfunction, Multi-vessel coronary artery disease, Off-pump CABG, Post-operative atrial fibrillation

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INTRODUCTION

Multivessel coronary artery disease (MVD) is more often associated with cardiovascular risks. Consequently, it also leads to a higher prevalence of left ventricular dysfunction as compared to single-vessel coronary artery disease [(1)]. Coronary artery bypass grafting (CABG) is a standard treatment regimen used to revascularize coronary artery in patients with Multi vessel coronary artery disease. In comparison to percutaneous coronary intervention (PCI), CABG has been proved to be more efficacious in treating left main disease, left ventricular dysfunction & multivessel disease [(2)].

Cardiopulmonary bypass & cardioplegic arrest are the usual ways by which patients underwent CABG. It has been estimated that with the use of cumulative approach 10% reduction has occurred in major adverse outcomes following CABG. It can be performed using a bypass machine or on a beating heart that is off-pump coronary

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artery bypass grafting (OPCAB) [3]. In the 1990s, with the use of cardiac stabilizers, a shift took place in the technical application of the procedure (without CPB). The studies based on comparative analysis revealed that OPCAB resulted in less postoperative morbidity & mortality than on-pump CABG [4]. If we take a look at associated complications "OPCAB patients had less transfusion requirement, less inotropic support, shorter ventilation time, lower stroke rate, lower incidence of acute kidney injury, and shorter intensive care unit stay" [5].

The reports based on the correlation of age with substantial advantages of OPCAB demonstrate a positive correlation. It means it is quite possible that generally, OPCAB results in excellent treatment outcomes however it has shown enhanced efficacy in high-risk & elderly individuals. Despite this, a significant decrease in CABG practice can be seen worldwide [6]. The most stated reasons include the technical difficulties along with the high probability of "incomplete vascularization, lower graft patency & reduced long term survival following OPCABG". In addition, comparatively fewer benefits of OPCABG have been acknowledged in patients with depressed left ventricular function [7].

Although these studies are mostly based on the study population from the west. There can be considerable differences following OPCABG in the Asian population [8]. Hereby we designed a study to analyze the clinical outcomes in patients with Multivessel coronary artery disease and left ventricular dysfunction following Off-Pump CABG.

MATERIALS AND METHODS

We designed a prospective observational study to analyze immediate clinical outcomes in patients following OPCABG. The study was carried out from 1st May 2019 to 1st May 2021 at department of Cardiac Surgery in Ch. Pervaiz Elahi institute of cardiology Multan. Eighty-nine patients who were treated with OPCAB were included as study participants. The patients who intraoperatively underwent on-pump CABG were excluded from the study. Procedures were performed by "consultant cardiothoracic surgeons".

Written approval was taken by the ethical review committee of the Hospital. The participants were informed of the details and purpose of the study and informed consent was taken into consideration. The demographic variables of the patients were collected. The variables included age, gender, and detailed history including complications. Preoperative care was provided to the patient till the day of surgery. Proper technique of OPCABG was followed. The immediate clinical outcomes that included all the in-hospital outcomes till 30 days follow-up were recorded.

The variables like age gender history and associated health conditions were expressed through mean and standard deviation. The early clinical outcomes were expressed with the help of n numbers and percentages. The Chi-square test was applied and p-value of <0.001 was considered significant. SPSS version 20.0 was used to do the Statistical analysis.

RESULTS

The prospective observational study included 89 participants. Among these 89 patients, 54% (48) were male and 46% (41) were female. The mean age and standard deviation were 58±8.2 & 60±8.5 of the male and female groups respectively. History of the patients revealed that 60% (53) were hypertensive, 61% (68) had a previous history of myocardial infarction, 16% (14) had peripheral vascular disease, 63% (56) were known cases of diabetes. Moreover, 45% (41) has a deranged lipid profile, 16% (14) had chronic kidney disease while 5% (4) had severe LV dysfunction. (Table I)

Table No.1: Demographic variables of the patients undergoing OPCABG

Variables	%/Mean/Standard deviation
Male	54% (48)
Female	46% (41)
Age	
Male	58 ± 8.2
Female	60 ± 8.5
Other complications (History)	
Hypertension	60% (53)
Myocardial infarction	61% (68)
Peripheral vascular disease	16% (14)
Diabetes mellitus	63% (56)
Dyslipidemia	46% (41)
Kidney disease (GFR < 60)	16% (14)
Severe LV dysfunction	5% (4)

Table No.2: Immediate clinical outcomes in patients who underwent OPCABG

Clinical outcomes	% (n)	P value
Hospital stay (in ICU)	4 ± 2 (days)	<0.001
Time spent on ventilator	9.2 ± 7.8 (hrs)	<0.001
Post-operative		
Stroke	2.24% (2)	<0.001
Dialysis	3.37% (3)	<0.001
Sternal infections	2.24% (2)	>0.001
Atrial fibrillation	13.4% (12)	>0.001
Re-exploration	2.24% (2)	>0.001
Septicemia	8.9% (8)	>0.001
Readmissions	16.8% (15)	>0.001
Deaths	5	>0.001

The mean hospital stay in days was reported as 4 ± 2 days while the mean time spent on a ventilator was

recorded as 9.2 ± 7.8 hrs. Immediate clinical outcomes are listed in (Table II). It was seen that factors like post-operative atrial fibrillation, severe left ventricular dysfunction, and end-stage renal failure contributed to mortality. Among Post-operative outcomes stroke & sternal infections were witnessed in 2.24% (2), atrial fibrillation in 13.4% (12), and re-exploration was done in 2.24% (2) of cases. Septicemia occurred in 8.9% (8), 16.8% (15) patients were readmitted following CABG. Total 5 deaths were reported.

DISCUSSION

The current study revealed that "severe LV dysfunction, post-operative atrial fibrillation & dialysis-dependent renal failure were the factors associated with mortality". Many previous studies also show the factors like emergency surgery, chronic kidney disease, post-operative atrial fibrillation, and severe left ventricular factors increase the chances of deaths in cardiac failure [9]. In the present study atrial fibrillation turns out to be a lethal factor. It was considered in the past that post-operative atrial fibrillation is a kind of benign arrhythmia and mostly a self-limiting condition [10]. However, the recent reports are in accordance with the results of our study as these studies regard post-operative atrial fibrillation as a cause of morbidity & mortality either in short or long term duration [11].

The pathophysiology behind this clinical outcome is the hemodynamic instability among patients with diastolic and systolic dysfunction leading towards low cardiac output ultimately enhancing the risk of mortality [12].

It is really important to assess the risk factors that contribute to mortality. The quality of the CABG performance, the role of the hospital, and the expertise of the surgeon can be evaluated by measuring the steps taken to minimize the risk associated [13]. The results obtained from the study reveal that there are considerable differences between the data published in western countries. For instance, the incidence of diabetes mellitus reported in studies from developed countries is lower than 63% (56) as reported in our study. Contrary to this comparatively higher incidence of post-operative atrial fibrillation has been reported in the west than the one seen in our study group [14].

Factors like age, race, and BMI are more likely to contribute to the occurrence of this phenomenon. More accurate detection of these incidence can be done by doing continuous monitoring through ECG instead of only monitoring the patients during their ICU stay [15]. Although factors like reexploration due to excessive bleeding, post-operative need for dialysis, septicemia have shown lower incidence but are still valuable to consider. Another significant outcome of cardiac surgery is stroke. It is directly related to morbidity, has a bad impact on lifestyle, and also increases the hospital stay and overall expenses [16]. Hereby we reported a 2.24% (2) stroke rate which is similar to the one reported in several studies. Age often correlates to stroke incidence.

Some studies have demonstrated that OPCABG can reduce the risk of stroke. Worst outcomes are also linked to the intra-operative conversion of surgery to on-pump CABG. Improvement is needed to reduce ventilator hours, readmitted cases, and to enhance the quality of life [17]. Several studies measure clinical outcomes of CABG only in the context of factors like morbidity & mortality however it should be considered a "multidimensional phenomenon" with long-term effects on survival, lifestyle, physical activity, and cognitive abilities [18].

CONCLUSION

In conclusion, off-pump CABG for patients with Multi-vessel coronary artery disease and left ventricular dysfunction had better in hospital/immediate clinical outcomes with long-term survival rates.

Author's Contribution:

Concept & Design of Study:	Muhammad Yasir Khan
Drafting:	Shafqat Hussain, Muhammad Moeen
Data Analysis:	Iftikhar Paras, Muhammad Hamid Ch, Muhammad Kamran Khan
Revisiting Critically:	Muhammad Yasir Khan, Shafqat Hussain
Final Approval of version:	Muhammad Yasir Khan

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

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Original Article

In Hospital Outcomes of Obese Patients with Multi-Vessel Coronary Artery Disease undergoing Off Pump Coronary Artery Bypass Graft Surgery

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ABSTRACT

Objective: To determine the outcomes of obese patients with multi vessel coronary artery disease undergoing Off Pump coronary artery bypass graft (CABG) surgery.

Study Design: A retrospective study

Place and Duration of Study: This study was conducted at the Cardiac Surgery department of Choudhary Pervaiz Elahi Institute of Cardiology (CPEIC) Multan from January 2021 to August 2021 for a period of 08 months.

Materials and Methods: All the patients that underwent OPCAB were grouped in two categories on basis of BMI, In A group patients were obese and in B group patients were non-obese. They were compared for the following variables: age, gender, weight, Heart association of New York Functional Class (NYHA), Angina Class of Canadian Cardiovascular Society (CCS), extent of coronary artery involved disease, Number of grafts and left ventricular ejection fraction (EF). Data in groups was compared by using ANOVA test in normally distributed variables and in not normally distributed variables Kruskal-Wallis test was applied. *P*-value of less than 0.05 was taken as significant.

Results: Majority of patients in our study were males. (87%, n=75) whereas only 11 % (n=9) patients were female. The mean age of patients in our study was 43.36±7.6 years. The most important finding of this study is that the rate morbidity and mortality was same in the patients that were labelled as obese and non-obese and underwent OPCAB. Regarding the post-operative course mean duration of inotrope usage was 11.17±2.29 hours and when the comparison was done among the two study groups a statistically significant was observed ($p<0.05$).

Conclusion: In obese patients off pump coronary artery bypass grafting is beneficial. These patients are already compromised due to the associated side effects of obesity and avoiding CPB may be beneficial for short term outcome of these patients.

Key Words: Obesity, Multi-vessel coronary artery disease, Off-pump CABG, Bypass circuit machine (CPB)

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INTRODUCTION

In case of coronary artery bypass grafting (CABG) is most frequently performed surgery in coronary heart disease. This surgery can be conducted either with the use of a bypass circuit machine (CPB) or on a beating heart that is known as off pump coronary artery bypass grafting (OPCAB).

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Literature is divided on the best approach among these two methods due to inconsistent results. The benefits that are expected theoretically for the off-pump CABG technique have not been validated by latest randomized clinical trials[1-2]. Some observational studies have concluded that off pump CABG has certain benefits in high-risk subgroups such as diabetics, low ejection fraction patients and obese patients[3-4]. Traditionally, the off-pump technique was favored to avoid the harmful side effects of using an extra corporeal circuit, the extra corporeal circuit activates the inflammatory response in the body as the blood comes in contact with it[5-6].

Coronary artery by-pass grafting is the most frequently done surgery in patients of coronary artery disease. This surgery can be conducted by off pump or on pump technique. The number of patients suffering from obesity is increasing day by day in both the developing and the developed countries[7-8]. Internationally, the incidence ofobesity has developedinto an epidemic. There more than a billion people that are termed as

overweight and obese patients are estimated at a staggering 300 million[9]. Conventionally, obesity is thought as a common risk factor for the patients that are undergoing CABG surgery. Risk of in hospital mortality and post-operative morbidity is increasing in patients with increased BMI or obese[10-11]. So this study is designed to report the in hospital results of off pump coronary artery by-pass grafting in patients that are obese because of it is cleared considered as risk factor for surgery. There is no current study conducted on the outcomes of off pump CABG in obese patients.

MATERIALS AND METHODS

This retrospective study was conducted at cardiac surgery department of CPE Institute of Cardiology Multan. The information of all the patients operated for Off Pump CABG between January 2021 to August 2021 by a single surgeon were retrospectively collected and analyzed from the cardiac surgery database. Due approval was taken from the Hospital ethical committee. The patients were grouped as A and B. In group A obese patient (BMI $\geq$ 30 kg/m^2) while Group B was made of patients who were not obese (BMI less than 30 kg/m^2). The patients with recent MI, congestive cardiac failure, emergency CABG, renal failure and redo cases were not included in the study.

The following variables were extracted from the data: age, gender, weight, Heart association of New York Functional Class (NYHA), Angina Class of Canadian Cardiovascular Society (CCS), extent of coronary artery involved disease, Number of grafts and left ventricular ejection fraction (EF). The main outcome measures for our study were hospital stay, in hospital mortality, ventilation time, ICU stay and period of inotropic support.

All the patients underwent median sternotomy. An activated clotting time of greater than 400s was achieved with full Heparin dose of 300U/kg. Internal Mammary artery of left side was harvested and anastomosed to left anterior descending artery. The rest of the vessels were bypassed using the vein grafts. Heparin was fully annulled with protamine after the procedure. Patients were shifted to a dedicated intensive care unit (ICU) for post-operative monitoring.

The data was managed and analyzed using SPSS version 26. Shapiro Wilkins test was used to assess the normality of data. All the continuous variables were shown as mean and standard deviation. The categorical variables were shown as frequencies and percentages. Data in groups was compared by using ANOVA test in normally distributed variables and in not normally distributed variables Kruskal-Wallis test was applied. *P*-value of less than 0.05 was taken as significant.

RESULTS

The results were analyzed using SPSS version 26, in the study time period a total of 86 patients fulfilled the inclusion criteria and were included in this study. Majority of patients in our study were males. (87%,n=75) whereas only 11 % (n=9) patients were female. Regarding the age of patients. The mean age of patients in our study was 43.36±7.6 years. Regarding symptoms of patient, majority had angina for a time period of 1-5 years (81.4%, n=65). Regarding CCS classification, 90% (n=78) had a CCS Class of III, whereas 8.1%(n=7) patients had CCS Class IV. The risk factors of the patients in our study are summarized in table 1.

Table No.1: Different risk factors of the patients

Diabetes	
On Insulin	25(29%)
On Oral hypoglycemic	11 (12.7%)
No diabetes	53 (62.6%)
Hypertension	
No hypertension	37(43%)
Controlled on Medication	49 (57%)
Smoking	
No smoking	29(33.7%)
Smoking >8 weeks	57(66.3%)
Hypercholesterolemia	
Yes	15(17.5%)
No	71(82.5%)
Unknown	2(2.32%)

Table No.2: The disease characteristics

Extent of significant CAD	
1 vessel Disease	7(8.13%)
2 vessel Disease	60(70%)
3 vessel Disease	19(22%)
Left Main disease	
>70%	19(22.1%)
51-70%	13(15.1%)
50%	6(7%)
No LMS	48(56%)

Table No.3: Pre-operative and post-operative details of patients

Pre-operative details	
	Mean ± SD
Hemoglobin(g/dl)	11.181±1.387
Creatinine (mg/dl)	0.63 ± 0.12
Post-operative details	
Inotropes Usage (hours)	11.17±2.29
ICU stay(hours)	34.74±15.012
Ventilation time (hours)	8.16±4.625
Total Chest Drainage (mls)	876.70±345.838
Total Hospital Stay(days)	7.45±2.94
In hospital Mortality	0(0%)

Regarding the status of coronary artery disease, the majority of patients in our study were having two vessel disease (80%, n=69). The disease characteristics are summarized in table 2 and the pre-operative and post-operative characteristics, are summarized in Table 3.

The patients in our study were divided into two groups based on the ejection fraction. In group A obese patient (BMI ≥ 30 kg/m^2) while Group B was made of patients who were not obese (BMI less than 30 kg/m^2). Shapiro Walkins test was used to test normality of data and since the variables were not normally distributed so Kruskal Wallis 1-way ANOVA test was used to compare the three groups. The results of the comparison are summarized in table 4.

DISCUSSION

The important finding in this study is that despite having a BMI greater than 30 in majority of patients, there was no in-hospital mortality in our study. Majority of patients in our study had two vessel diseases. (70%). This result may be due to the late presentation of patients to cardiac surgery services. Regarding the post-operative course. The mean duration of inotrope usage was 11.17±2.29 hours and when the comparison was done among the two study groups, it was found that the difference between the two groups was statistically significant, ($p<0.05$) the maximum duration of inotropes was in the study group that had the ejection fraction below 30%. This result can be explained by the fact the that these patients already have a compromised heart with reduced contractility and these patients need high inotropic support for an extended period of time so that they can undergo an uneventful recovery after off pump coronary artery bypass grafting. The other post-operative details like ventilation time, total chest drainage, total hospital stay was similar in all groups and there was no significant difference found between the groups.

The most important finding of this study is that the morbidity and mortality rates were same in the patients that were labelled as obese and non-obese and underwent OPCAB. These results are promising due the increasing incidence and prevalence of obesity and the medical conditions that are associated with increase weight. It is pertinent to know that a BMI greater than 30kg/m^2 is associated with excessive surgical risks[12]. This is in contradiction to the results that are obtained in our study, as in our study we had zero mortality. This result could only be explained due to the surgical technique used in this study i.e. OPCAB technique. Literature shows that the use of off pump CABG surgery in patients that are obese, decreases the in-hospital morbidity and mortality rates as paralleled with conventional surgery that involves CPB and cardioplegic arrest[13]. Furthermore, there is undeniable proof that the off pump technique causes a decreased levels of interleukins in the circulation. This has a very vital role because the levels of circulating interleukins have a role in neutrophil movement and thus have a role in myocardial injury.

Though increased BMI is considered to be a key risk factorin any surgery especially the CABG surgery, the results of our study show that obesity is not a risk factor when the patients undergoing off pump coronary bypass grafting are considered.This result is identical to the results that have been reported in previous studies[12, 14].

In contrast to this study, Prabhakar et al. concluded that in patients that have a BMI greater than 35kg/m^2, there is a substantial increase in the incidence of in hospital mortality. They also stated that the there is a small but significant increase in morality in moderately obese patients where there is 50% rise in mortality in patients that have a BMI greater than 40kg/m^2 [15, 16].

Our study showed no differences, among the two study groups in various variables like duration of mechanical ventilation, ICU stay. These results are comparable to other studies[17].

There are several limitations of this study. First and the foremost, this study is a retrospective study conducted at a single center with a small sample size and short follow up duration. This may have an impact on the generalizability of the findings. More studies are needed with a large sample size to determine the long-term effects of OPCAB in obese patients.

CONCLUSION

Off pump coronary artery bypass grafting in obese patients is beneficial. These patients are already compromised due to the associated side effects of obesity and avoiding CPB may be beneficial for short term outcome of these patients.

Author's Contribution:

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Original Article

Effects of Breathing Exercises on Breathing Pattern, Lung Capacities and Quality of Life in Asthmatic Patients: A Randomized Controlled Trial

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ABSTRACT

Objective: To access the effects of breathing exercises on dysfunctional breathing pattern and quality of life in the patients of asthma.

Study Design: Randomized Controlled Trial study

Place and Duration of Study: This study was conducted at the Kanaan Physiotherapy & Spine clinic for 5 months from June 2021 to October 2021.

Materials and Methods: Study included 20 participants with age ranges from 15 to 45 years. All the participants were divided into two groups. Participants were assessed pre and post treatment by using spirometry, 10-item breathing pattern observational questionnaire and asthma- related quality of life questionnaire (Mini AQLQ). Group A received papworth breathing technique and Group B received buteyko breathing technique.

Results: The age of the individuals included in this study has mean age 31.20 ± 6.371 ranging from 15 years to 45 years. The quality of life of asthma patients was accessed using mimi AQLQ questionnaire which gave non-significant results. The 10-item breathing pattern observational questionnaire gave significant results. Whereas, the effect of breathing techniques on lung capacities was non-significant as measured by spirometery.

Conclusion: The results of the breathing techniques used in this study named papworth and buteyko methods were accessed using mini asthma quality of life questionnaire, spirometry measurements and Breathing Pattern, 10- item Observational List. The study concludes that breathing techniques showed no significant changes in quality of life but breathing pattern of asthmatic patients can be improved using these techniques.

Key Words: Breathing retraining exercises, asthma, dysfunctional breathing, lung capacities of asthmatic patients, quality of life in asthma.

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INTRODUCTION

A chronic disease that involves the lung airways is defined as asthma. These airways also called the bronchial tubes, allow bilateral flow of air into and out of the lungs. Asthmatic patients have inflamed airways. When the person is exposed to various irritants and substances that trigger allergies (allergens) they become even more swollen and the surrounding muscles of the airways can tighten[1].

Acute asthmatic patients characteristically hyperventilate which is refelected by low PaCO2 levels. These levels effect the value of FEV1. McFadden and Lyons1 noted mean FEV1; 59 % reflects mild airway obstruction, mean FEV1; 35 % reflects severe airway obstruction and mean FEV1; 18% reflects severe airway obstruction. Hypercapnia occurs when FEV1 falls below 15 %. Hyperventilation in asthmatic patients is based on the measurements of PaCO2. But direct measurement of minute ventilation is very difficult to obtain in patients who have a severe attack because they can poorly tolerate mouthpieces and noseclips. However, according to evidence the patients experiencing an acute attack or patients with chronic history of asthma display an increased minute ventilation along with elevated respiratory center drive.[2-5]

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In addition to above mentioned symptoms, asthmatic patients display other abnormalities in breathing pattern such an increase in tidal volume or short period of inspiratory time, although the respiration frequency may be normal or increased.[6-8]

There are breathing techniques that deals with asthma. The aim of these exercises is to the correct the dysfunctional or irregular pattern of breathing. Dysfunctional breathing comprises multidimensional entity with three key dimensions being biochemical, biomechanical and psychophysiological. The objective is to explore these dimensions and their impact on asthmatic patients and to view how breathing therapy protocols effect these dimensions. It also determines if there is any evidence that suggests breathing therapy protocols and their optimization.[9]

Previous studies have shown the relation between asthma and dysfunctional breathing pattern. Dysfunctional breathing patterns may response to therapeutic exercises defined as breathing retraining; improvements have previously been reported in different clinical studies.[10,11] According to 2009 Physiotherapy Guidelines[12], breathing retraining results in the reduction of respiratory rate and/or tidal volume alongwith relaxation training, which helps in controlling the symptoms of asthmatic patients.

A patient having disoriented breathing pattern may go for compensation for lung filled with air and being over-inflated and elevated tidal volume (e.g., end of tidal volume over functional residual capacity FRC) to achieve the FRC. An increase in FEV1 of 12% or 200 ml explains the reversibility of the airflow obstruction. That's why the lung capacities will also be measured in this study.

Breathing retraining comprise of teaching the breathing techniques (route of breathing, speed of breathing, techniques of relaxation) to modify the patterns of breathing and to improve the efficiency of breathing[13]. It can reduce the symptoms and helps in the improvement of quality of life (QoL) of asthma people. It may also reduce medications[14] and recommended as an adjuvant treatment for adults with uncontrolled asthma despite taking the standard treatment protocols.[12]

The study aimed to guide physiotherapy breathing retraining exercises to the patients of asthma who have dysfunctional breathing symptoms. And the effect of these exercises will be determined over time. These breathing retraining exercises may provide an opportunity to improve the life of people treated for asthma in the community, and may also create awareness regarding physiotherapy services and its role in pulmonary rehabilitation.

MATERIALS AND METHODS

This study was a Randomized Controlled Trial. This study was conducted in Kanaan Physiotherapy & Spine clinic for 5 months from June 2021 to October 2021. This research included 20 participants with age ranges from 15 to 45 years. All the participants were divided into two groups. Participants were assessed pre and post treatment by using spirometry, 10-item breathing pattern observational questionnaire and asthma- related quality of life questionnaire (Mini AQLQ). The subjects were assigned in two groups A&B by lottery method.

Group A: After taking informed consent, papworth breathing technique is guided in a supervised session to the patient and is practiced in independent sessions five days per week for a period of 3 months.

Group B: After taking informed consent, buteyko breathing technique is guided in a supervised session to the patient and is practiced in independent sessions five days per week for a period of 3 months.

Study was completed in six months after synopsis approval. Asthma patients with age ranging between 15-45 years with receipt of at least one anti-asthma medication in the past 1 year and impaired quality of life due to asthma were included in the study. Whereas, asthmatic patients with pregnancy, any severe disease diagnosed by physician and who have participated in any other respiratory interventional research project were excluded. SPSS was used for statistical analysis. Qualitative variables were presented by using histogram for age and pie chart for gender. Whereas, quantitative variables were provided as mean standard deviation. After normality testing, Man-Whiteny test was used for non- parametric data and Shapiro-walk test was used to check the data normality according to which further statistical tests were applied. To access the results of change over time data was analyzed through pre and post independent T test. To access the results of difference between groups paired sample t test was used. All quantitative variables were provided as mean standard deviation. P-values less than 0.05 were considered significant.

RESULTS

Age: The individuals included in this study have mean age 31.20 ± 6.371 ranging from minimum 18 years to maximum 42 years with total 20 number of individuals.

Gender: The gender of individuals that participated in this study were 55.00% male and 45.00% female with total 20 number of individuals.

Table No.1: Pre and post treatment with mean different and p value

	Group A	Group B	Mean Diff	P value
Pre Treatment	57.67 ±11.47	58.67 ± 8.4	1.00	0.82
Post Treatment	60.56 ± 8.97	61 ± 8.46	-0.44	0.91
Mean Diff	-2.89	-2.33		
P value	0.16	0.45		

Mini AQLQ: Data across the group was determined using independent sampleT test, with pre-treatment p-value 0.82 and post-treatment p-value 0.9.Data within the group was determined using paired sample test, with group A having p-value of 0.16 and group B hng p-value 0.45 (Table 1).

FVC/FEV1: Data across the group was determined using independent sample T test, with pre-treatment p-value 0.95 and post-treatment p-value 0.98. Data within the group was determined using paired sample test, with group A having p-value of 0.45 and group B having p-value 0.43. (Table 2)

Table No.2: Group details with p values

	Group A	Group B	Mean Diff	P value
Pre Treatment	74.22 ± 10.18	74.10 ± 6.48	0.20	0.957
Post Treatment	76.55 ± 6.34	76.5 ± 6.41	0.05	0.985
Mean Diff	-2.33	-2.4		
P value	0.45	0.43		

Rhythmic Respiration: The pie charts shows significant changes in post-rhythmic respiration which has been increased to 80% from pre-treatment value which was 50%. Accordingly, the post-treatment value of patients with no rhythmic respiration has been reduced to 20% from pre-treatment value which was 50%.

Inspiration by Upper Thorax: The pie charts shows significant changes in post treatment inspiration by upper thorax. As 30% patients with no upper thoracic inspiration has been reduced to 10%, 30% patients with partly upper thoracic inspiration has been increased to 50%, whereas, 40% of patients with upper thoracic inspiration remained the same.

Nasal Inspiration: The pre-treatment percentage of patients with nasal inspiration has been increased to 80% which was previously 50%, patients with partly nasal breathing has been reduced to 20% from 40%, whereas, no patients were found with no nasal breathing after the treatment was induced.

Bodily Movement: The bodily movements were improved from 60 % to 70 % post treatment value. Accordingly, patient percentage with no bodily movement has been reduced to 30% which was previously 40%.

DISCUSSION

The age of the individuals included in this study have mean age 31.20 ± 6.371 ranging from 15 years to 45 years with total 20 number of individuals. While the gender of individuals that participated in this study were 55.00% male and 45.00% female with total 20 number of individuals.

The quality of life of asthmatic patients was accessed using mini AQLQ questionnaire. The questionnaire was filled before and after treatment sessions given. The results of the data across the group was determined using independent sample T test, with pre-treatment p-value 0.82 and post-treatment p-value 0.91. Same data within the group was determined using paired sample test, with group A having p-value of 0.16 and group B having p-value 0.45. Both gave non-significant results.

Another study explained that breathing training resulted in improvements in asthma-specific health status and other patient-centred measures but not in asthma pathophysiology. Such exercises may help patients whose quality of life is impaired by asthma, but they are unlikely to reduce the need for anti-inflammatory medication. Whereas, in current study patients reported improvement in their quality of life following the exercise regime. But no significant results were found by using the asthma related quality of life questionnaire. Added benefit of relaxation was achieved due to breathing pattern control.[14]

The spirometery measurements were used to access the FVC/FEV1 ratio to determine the effect of the techniques used in this study. Data was taken before and after the sessions. Data across the group was determined using independent sample T test, with pre-treatment p-value 0.95 and post-treatment p-value 0.98. Same data within the group was determined using paired sample test, with group A having p-value of 0.45 and group B having p-value 0.43. Both the results are not significant.

In 2018 von Bonin, D., Klein, S.D., Worker, J conducted a study which finds that speech guided breathing retraining significantly improves asthma control and quality of life in patients with asthma. Whether ATS may improve lung function remains to be shown. In our study patients included in the study shows no significant improvement in lung function test as accessed through spiromtery measurements.[15]

The breathing pattern observational questionnaire was used to access the effect of breathing techniques on the breathing pattern of asthmatic patients. According to the results, the breathing exercises used gave no significant improvement in breathing pattern.

Respiration frequency data across the group was determined using independent sample T test, with pre-treatment p-value 0.75 and post-treatment p-value 0.61. Same data within the group was determined using paired sample test, with group A having p-value of 1.0 and group B having p-value 0.70.

The pie charts shows significant changes in post-rhythmic respiration which has been increased to 80% from pre-treatment value which was 50%. Accordingly, the post-treatment value of patients with no rhythmic respiration has been reduced to 20% from pre-treatment value which was 50%.

The pie charts shows significant changes in post treatment inspiration by upper thorax. As 30% patients with no upper thoracic inspiration has been reduced to 10%, 30% patients with partly upper thoracic inspiration has been increased to 50%, whereas, 40% of patients with upper thoracic inspiration remained the same.

The pie chart shows changes in partly inspiration by diaphragm value which has been increased post treatment to 40% from pre-treatment value which was 30%, whereas, patients with inspiration by diaphragm have been reduced to 50% from pre-treatment value which was 60%. The percentage of patients which no diaphragmatic inspiration remained the same 10%.

The pre-treatment percentage of patients with nasal inspiration has been increased to 80% which was previously 50%, patients with partly nasal breathing has been reduced to 20% from 40%, whereas, no patients were found with no nasal breathing after the treatment was induced.

The bodily movements were improved from 60% to 70% post treatment value. Accordingly, patient percentage with no bodily movement has been reduced to 30% which was previously 40%.These results of breathing pattern questionnaire shows that prominent changes have been seen over a period of 3 weeks in the breathing pattern of asthma patients followed by breathing retraining exercises.

A study done in 2012 by O'Connor, Patnode et al concludes that behavioral approaches that include hyperventilation reduction techniques can improve asthma symptoms or reduce reliever medication use over 6 to 12 months in adults with poorly controlled asthma and have no known harmful effects. Evidence supporting yoga breathing is weaker and applicability to the United States is very low. Whereas, in this study we used two breathing techniques and compared them to find out the best possible exercise that could be used in case of asthma. Non significant results were analysed during their comparison. Although patient relaxation and reduction in symptoms was observed.[1]

CONCLUSION

The results of the breathing techniques used in this study named papworth and buteyko methods were accessed using mini asthma quality of life questionnaire, spirometry measurements gave non-significant results. Whereas, significant changes have been observed in breathing pattern after these methods were used to improve the breathing as accessed through Breathing Pattern, 10-item Observational List. Therefore, it concludes that these techniques showed no significant changes in quality of life but breathing pattern of asthmatic patients can be improved using these techniques.

Author's Contribution:

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Original Article

Knowledge, Interest and Perception of Academic Physiotherapists with Regard to Professional Ethics

Maria Sohail[1], Hafiza Sana Ashraf[1], Lubna Zafar[2], Anam Zafar[2], Maha Zaheer[2] and Naveed Anwar[3]

ABSTRACT

Objective: To determine the level of interest, perception and knowledge of professional ethics among physiotherapy academic faculty.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Department of Physical Therapy, University Institute of Physical Therapy, University of Lahore from January 2021 to April 2021.

Materials and Methods: Non-probability convenient sampling technique was used to collect data from 104 Physiotherapy academic faculty members. Standardized and modified, self-administered questionnaire was used and collected data were analyzed in SPSS 21.0 for its analysis.

Results: The mean age of the academic faculty members was 27.7±3.74 years in which majority (73.1%) were females. About 42.3% faculty had excellent knowledge, 86.5% of the physiotherapists showed medium level of interest towards professional code of ethics. Among all the physiotherapy faculty, 48.1% faculty perceived that code of ethics of physiotherapy must be the part of syllabus in all years of under-graduation (BSPT/tDPT/DPT).

Conclusion: Significantly higher level of knowledge and good interest is found in this study with perception of adding code of ethics in syllabus of students for all years and even better to punish the students in case they don't follow the ethical conduct during their academic activities

Key Words: Academic, Code of ethics, Faculty, Professionalism, Professional ethics, Physiotherapy

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INTRODUCTION

Profession is determined by having specific area of knowledge gained by extended academic procedure. [1, 2]Ethics are the rules, regulations or standards that governs the conduct of individuals belonging to specific profession.[3, 4] Professional ethics are the constant rules that ensure that the profession keeps the confidence and trust of the public.[5] Giving respect to others, being responsible, accountable and have commitment towards profession forms the base of professional ethics.

Self-evaluation and having good interaction with colleagues is also essential.[6]

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Autonomy, non-maleficence, beneficence and justice are the four main components of professional ethics.[7, 8] There are two factors that constitutes professional ethics named as personal and background factors. Background factors includes the role of environment and teachers while personal factors includes self-motivation and interaction with other professionals.[9] Professional ethics among engineering faculty showed that teachers should avoid inappropriate jokes in class and should not use facilities provided by university for their own personal matters.[10] Professional ethics is an important component for every profession including nursing. According to an integrative review, professional ethics in nursing is rarely studied and the problems are poorly examined. professional ethics create a basis for the nursing profession.[11] Literature says; the level of professional ethics before the intervention was good in 64% of the nurses. But after the intervention 94% of the nurses showed good level of professional ethics.[12]

The commitment of health care providers to uphold a high degree of professionalism is invaluable because it provides patients with the confidence that they are in safe hands. Professional ethics in physiotherapy profession are very important but underrated in literature. Therefore, to fill this gap, the study aimed to find the interest, perception and knowledge of

professional ethics among physiotherapy academicians so that the physiotherapy teachers can be encouraged to promote behavioral and ethical considerations in students on early stages and a better growth and prosperity of this noble profession.

MATERIALS AND METHODS

Data of study was collected from University of Lahore, Superior University, University of Management and Technology, University of Central Punjab, University of South Asia, Pakistan Society for the Rehabilitation of Disabled College, King Edward Medical University, Allama Iqbal Medical College, Rashid Latif Medical College and School of Allied Health Sciences Children Hospital Lahore from January 2021 to April 2021

A qualitative, cross sectional study design was carried out for this study in which non-probability convenient sampling technique was used to collect data from 104 Physiotherapy academic faculty members. Sample size was calculated through the following formula;

$$n=(Z^2 \times P \times (1-P))/e^2$$

where:

Z=1.96 for 95% Confidence Interval

P= Expected true proportion which was kept as 0.94 (94%)

e= Desired precision or acceptable error in estimate which was kept as 0.05

By this formula, sample size calculated was 104. Data were collected from University of Lahore, Superior University, University of Management and Technology, University of Central Punjab, University of South Asia, Pakistan Society for the Rehabilitation of Disabled College, King Edward Medical University, Allama Iqbal Medical College, Rashid Latif Medical College and School of Allied Health Sciences Children Hospital Lahore. Objective, benefits and important content regarding the research work was delivered to the participants and after their consent they were distributed with questionnaire forms. Ethical conduct was maintained for this study through Ethical Review Committee of Kanan Physiotherapy and Spine Center (PT/2020/REC/IRB/080). Physiotherapy faculty from academic side aging between 24 to 60 years, working as professional physiotherapy lecturer in any government or private institute of Lahore and holding at least degree of graduation (BSPT/tDPT/DPT). Standardized and modified self-administered questionnaire from existed literature was used as study tool.[13, 14] Data were analyzed by SPSS, ver. 21.0.

RESULTS

The mean age of the academic faculty members was 27.7±3.74 years in which majority (73.1%) were females. Most of the faculty (51%) were post-graduated with last degree of MS-PT/MPhil-PT and 79.8% academic faculty were teaching in private colleges/universities of Lahore, Pakistan (Table-1).

Table No.1: Descriptive statistics of demographic variables and interest section of physiotherapy faculty regarding professional ethics (n=104)

Variable	Mean	Std. Deviation	Min.	Max.
Age (years)	27.7	±3.74	25	48

Variable	Construct	Frequency	%tage	
Gender	Male	28	26.9%	
	Female	76	73.1%	
Last Degree	BSPT/DPT/ tDPT	48	46.2%	
	MS. PT/ Mphil. PT/ tDPT	53	51.0%	
	PhD. PT	3	2.9%	
Institution	Private College/University	83	79.8%	
	Government College/University	21	20.2%	

Interest of Physiotherapy faculty regarding Professional Ethics				p-value
Reading of Physiotherapy code of ethics	No/Never	17	16.3 %	0.001*
	Yes, partially	44	42.3 %	
	Yes, entirely	43	41.3 %	
How update yourself	Once a month	38	36.5 %	<0.001*
	Once every six months	27	26.0 %	
	Once a year	28	26.9 %	
	I don't update myself	9	8.7%	
	Not applicable	2	1.9%	
Main source of updates regarding professional ethics	Internet	45	43.3 %	<0.001*
	Scientific events	10	9.6%	
	Books and journals	45	43.3 %	
	Not applicable	4	3.8%	

*__Significant G test results for the variable (p-value less than 0.05)

About 57.7% faculty perceived that professional attitude can be determined exclusively by human's personality and character, 87.5% teachers agreed to make assessments and evaluations of students' ethical behavior while teaching but only 51.9% actually was making check on students' ethical attitude towards professional ethics in their lecture times.

Majority (78.8%) staff was perceiving that it should be completely okay to punish students in their academic activities whenever they found them doing ethical misconduct either towards patients, teachers, mates and

colleagues. Most of the Physiotherapy teachers (61.5%) rated highest score (5 out of 5) towards training of code of ethics in physiotherapy field as professionals for students, teachers and clinicians, everyone. Among all the physiotherapy faculty, 48.1% faculty found it important to add code of ethics of physiotherapy must be the part of syllabus in all years of under-graduation level (BSPT/tDPT/DPT). (G-test, $p<0.001$) (Table-2).

Table No.2: Perception of physiotherapists towards professional ethics in physiotherapy profession (n=104)

Variable	Construct	Frequency	%age	p-value
Rate your knowledge of ethics in physiotherapy from 1 to 5	2	6	5.8%	<0.001*
	3	39	37.5%	
	4	44	42.3%	
	5	15	14.4%	
Professional attitude involving ethics can be determined exclusively by character & personality of physiotherapist	Yes	60	57.7%	<0.001*
	No, but are influenced by character and personality	43	41.3%	
	No, character and personality are of no concern	1	1.0%	
Ethical misconduct by peers (have you listened?)	Yes, I have experienced it	30	28.8%	<0.001*
	Yes, I heard of it	58	55.8%	
	No	16	15.4%	
Ethical behavioral assessment of students during teaching?	Yes	91	87.5%	<0.001*
	No	13	12.5%	
Do you evaluate students' ethical behavior towards profession in fair way as needed?	Yes	54	51.9%	<0.001*
	No	43	41.3%	
	Not applicable	7	6.7%	
Ethical misconduct towards patient or colleague, ever done by you ?	Yes	12	11.5%	<0.001*
	No	72	69.2%	
	I don't recall/ I don't know/ not applicable	20	19.2%	
Should students punished if they break ethical conduct during their academic activities	Yes	82	78.8%	<0.001*
	No	22	21.2%	
Rate the importance of training of code of ethics in physiotherapy as a professional (from 1 to 5)	1	2	1.9%	<0.001*
	3	10	9.6%	
	4	28	26.9%	
	5	64	61.5%	
In which year code of ethics in physiotherapy should be added as part of curriculum?	1st year	13	12.5%	<0.001*
	2nd year	4	3.8%	
	3rd year	16	15.4%	
	4th year	5	4.8%	
	5th year	15	14.4%	
	All years	50	48.1%	
	It doesn't matter	1	1.0%	

***__Significant G test results for the variable (p-value less than 0.05)**

The bulk of professionals (86.5%) cascaded in medium interest level of professional ethics as Physiotherapists whereas 51% faculty had good knowledge and 42.3% had excellent knowledge observed in the study (G-test, p<0.001) (Table-3).

Mann Whitney-U test was employed on knowledge, interest levels and demographic variables for analyzing the significant difference among them. Results were not significant but it showed some probabilities according to their mean rank values. It was analyzed that male faculty had better knowledge and interest of professional ethics than female staff. Physiotherapy faculty who had done post-graduation were having good knowledge and high interest of code of ethics and professionalism than the ones who had just done with graduations (BSPT/tDPT/DPT).

Physiotherapy professionals who were working in private colleges/universities were poor in terms of knowledge of professional ethics rather than the faculty of government institutions. Level of interest of professional ethics were almost equal in staff of both government and private institutes. Correlation coefficient (r) was ran out between knowledge and interest of professional ethics in physiotherapy academic faculty. Weak positive relationship was found (r= +0.38) but results were not significant (p=0.70) (Table-4).

Table No.3: Knowledge and Interest of Physiotherapy faculty towards professional ethics (n=104)

Variable	Construct	Frequency	%age	P-value
Interest	Low Interest	4	3.8%	0.000*
	Medium Interest	90	86.5%	
	High Interest	10	9.6%	
Know-ledge	Fair Knowledge	7	6.7%	0.000*
	Good Knowledge	53	51.0%	
	Excellent Knowledge	44	42.3%	

***__Significant G test results for the variable (p-value less than 0.05)**

Table No.4: Mann- Whitney U test and Correlation between Knowledge and interests of physiotherapy faculty in professional ethics (n=104)

	Gender	Mean rank value	p-value
Knowledge of professional ethics	Male	60.64	0.06
	Female	49.50	
Interest in professional ethics	Male	53.18	0.81
	Female	52.25	
	Last Degree	Mean rank value	p-value
Knowledge of professional ethics	BSPT/DPT/tDPT	53.46	0.37
	MS. PT/ MPhil. PT/PhD. PT	48.78	
Interest in professional ethics	BSPT/DPT/tDPT	50.68	0.86
	MS. PT/ MPhil. PT/PhD. PT	51.29	
	Type of institute	Mean rank value	p-value
Knowledge of professional ethics	Government	60.29	0.13
	Private	50.53	
Interest in professional ethics	Government	52.17	0.92
	Private	52.58	

CORRELATION COEFFICIENT (r)			
Variable 1	Variable 2	Sign (2-tailed)	Pearson correlation value
Knowledge of physiotherapy faculty about professional ethics	Interest of physiotherapy faculty about professional ethics	0.70	+0.38
Interest of physiotherapy faculty about professional ethics	Knowledge of physiotherapy faculty about professional ethics		

DISCUSSION

The mean age of the academic faculty members was 27.7±3.74 years in which majority (73.1%) were females. Most of the faculty (51%) were post-graduated with last degree of MS-PT/MPhil-PT and 79.8% academic faculty were teaching in private colleges/universities of Lahore, Pakistan. About 51% of the faculty had good knowledge and 42.3% of the faculty showed excellent knowledge in the study. Overall good knowledge and interest of physiotherapy faculty was found towards the professional ethics in the present study. Similar to the current study two studies showed that books, journals and internet are the main source of the knowledge but in contrast to the current study the results of both of the studies showed that the physiotherapists update themselves rarely or once in every six months whereas the current study showed that physiotherapists update themselves once in a month.[13, 15]

Similar to the current study another study taken out by Coelho et al. showed the same results that students should be punished if they break ethical conduct during their academic activities. The study showed the results that code of ethics towards professionalism should be teach in all semesters of the curriculum just like the current study.[16] In support of the current study another research was performed by Surjit Singh et al. in 2016, and found good knowledge in doctors working in a tertiary care hospital. The doctors were also using their knowledge for the betterment of their patients found in the study.[17] One more study by Haleh Jafari et al. in 2019 on nursing students was in favor of present study results. It was found that nurses have good knowledge and attitude towards the medical ethics. [18] In contrast to the current study Jadranka Vukovic et al. performed a study in 2018 on pharmacists, the results of the study was not consistent with present study. The study showed the results that there is a need to improve the level of education in pharmacists to have better understanding of the medical ethics in order to deal with ethical issues and to make better professional decisions.[19] Professional ethics are the base of any profession.[20]

The study summarizes that updating the professionals by themselves individually on regular basis is important to maintain good professionalism. The study was limited in sample size because it covered only Lahore city but sample size is not the only factor on which results can be generalized. In addition, for detailed exploration regarding various aspects of professionalism and code of ethics further studies with larger sample size including other professions and cities can be conducted. Professional code of ethics must be taught in syllabus and should be the part of curriculum on both national and international levels. Students of physical therapy profession should be encouraged to maintain the professional decorum in the class towards everyone and in their carrier. Teachers should strictly evaluate the students during their academic activities for better growth of them as professional healthcare providers.

CONCLUSION

Significantly higher level of knowledge and good interest is found in this study with perception of adding code of ethics in syllabus of students for all years and even better to punish the students in case they don't follow the ethical conduct during their academic activities. Male physiotherapy academicians were leading in knowledge and interest of code of ethics than female teachers meanwhile, teaching faculty in government colleges or universities were having better professional decorum than professionals from private institutions. A weak positive relationship is found between knowledge and interest which depicts that professionals with better knowledge will have more interest in adapting professional behavior towards patients, colleagues and other healthcare professionals.

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Original Article

Effects of Nursing Intervention on Knowledge and Family Functioning among Parents of Epileptic Patients

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ABSTRACT

Objective: To evaluate the effect of educational interventions on knowledge, and family functioning of parents regarding the epileptic patient's management.

Study Design: Qausi experimental study

Place and Duration of Study: This study was conducted at the Department of Neurology Faculty of Allied Health Sciences, The University of Lahore from June 2021 from October 2021.

Materials and Methods: 36 parents of epileptic patients were enrolled. The parents of epileptic patients who visited in the neurology clinic (OPD) were included and the parents who were already in the health profession and whose children without seizures in the last year were excluded. Family functioning was assessed by using the Family Assessment Device (FAD).

Results: Majority of patients were more than 35 years old (63.9%), females (66.7%), have secondary education (36.1%) and belongs to rural area (58.1%). After intervention it was observed a statistical significant difference in domain of FAD like problem solving, Defining Roles, Affective involvement, behavior Control and general function of family ($P<0.05$).

Conclusion: The nurse plays a vital role in improving the family functioning of epileptic family's. They are the key essentials for training parents. The Nursing intervention has positive impact on the family functioning of epileptic patients especially in problem solving, defining roles, affective involvement, behavior control and general function of family.

Key Words: Epilepsy, Family Functioning, Intervention programme, Education

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INTRODUCTION

Epilepsy is chief neurological illnesses among the children that affect approximately 50,000,000 individuals around the globe.[1] Among all the epileptic cases in the world, 80% of the population with epilepsy is from the developing countries. However, in spite of all these facts, epilepsy happen at any stage of life but half of the epileptic cases appeared in youth or adolescent. A recent survey on epilepsy conducted in the twenty three Asian nations including specially Bangladesh explored that the ratio of epilepsy is 1.5 to 14.0 % out of 1000 people in these Asian countries.[2]

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The prevalence of active epilepsy in Pakistan was 0.98% with 98.1% epilepsy treatment gap in the rural area.[3]

Epilepsy is often misunderstood and not taken seriously as compare to other diseases the reason behind it is lack of health related knowledge, poor economic condition, shortness of health facilities in the remotes areas. So that, the ratio of epilepsy is very high in the developing countries and treatment gap is very difference than the developed countries.[4] Epilepsy is an old common neurological condition. It occurs due to unprovoked spontaneous seizures. The prevalence rate in elderly people and children is 0.7-1.0%, where some patients have more signs and symptoms like jerky movements and unsatisfied behavior.[5]

Parents do not have enough knowledge to access epilepsy just like medical professionals. Sudden onset of epilepsy has strong effect on family routine life. Sometimes parents' emotional supports delay the initial diagnosis.[6] Moreover, delay and mishandling of these problems from parents can be life threatening for epileptic patients. Especially children need more attention in this condition, because they can encounter worse complications during seizure. The combination of fever and seizure in children, develop severe anxiety in their parents as the time of despair sometimes they proclaimed that their children are dying. However, it is

important for the parents or attendants should be aware for management of this disease during the critical time to save the child from developing epileptic complications. It is necessary to educate parents to manage this problem at home care.[7] Epilepsy in individual not only affects their perception and good behavior, but also effect on caregivers, involving employment and work at home, physical and emotional health, relations of health care providers with partner, other age fellows, friends, and self-confidence for caregiving.[8]

Epilepsy has significant influence on family functioning. Epilepsy can cause psychological difficulties in terms of stress, stigmatization, marital issues, low self-esteem, and social anxiety in family members. Family functioning is an important factor for intervening patient's condition and outcome.[9] It is essential that the parents maintain their coping strategies because the psychological well-being of a parent is directly related to family functioning. If a family is not able to function, there may be a profoundly negative impact on the child's psychosocial adjustment to living with a chronic condition.[10] Training of parents for improving family functioning and effective self-management behaviors are very essential. Several training programs have been developed and available for patient's self-management.[11] Parents need sufficient knowledge and awareness regarding epilepsy. It was observed that there was a direct relation between parents' knowledge and their practice.[12,13]

Due to poor knowledge of epilepsy family functioning suffers badly. Parents of epileptic patients cannot participate in active decision making, role and relationship, effective communication, due to lake of knowledge. They cannot manage actively epileptic seizure at home because they have no training and knowledge regarding epilepsy. Sufficient knowledge helps the families of epileptic patients to improve the family functioning. Therefore, there is a need educational intervention programs at community level which will be improved the knowledge and family functioning of parents with epileptic patients. The objective of the current study was to evaluate the effect of educational interventions on knowledge, and family functioning of parents regarding the epileptic patient managemen.

MATERIALS AND METHODS

This quasi experimental study was conducted at public sector hospital, Neurology Department. The study duration was from 1st June 2021 to 31st October 2021. Ethical approval was obtained from Institutional Review Board of University of Lahore. Thirty-six parents of epileptic patients were enrolled in current study after taking informed consent. The parents of epileptic patients who visited in the neurology clinic (OPD) were included and the parents who were already in the health profession and whose children without seizures in the last year were excluded. Data regarding Socio demographic characteristics for parents with epileptic patients was collected through a self-administered questionnaire. Parent's knowledge about epileptic patient care will be assessed through questionnaire developed by Joan Austin[14] "Knowledge of parents toward epilepsy". The questionnaire had questions which were of the close ended type and comprised of true/false answers. Family functioning was assessed by using the Family Assessment Device(FAD) developed by Epstin et al.[15] The scale have 7 domains including, Communication (6 items), Problem solving(5 items), Affective response(6 items), Affective Involvement(7 items), General Functioning (12 items) and Role (8 items). Responses of each items were graded as strongly agree' to 'strongly disagree' based on how the participant's family reacts most of the time. Scores on the 12 items are summed to produce a total ranging from 4 to 48. Lower scores indicate healthy functioning in terms of communication and problem solving, and higher scores reflect unhealthy family functioning.

Intervention:

Phase I: Parents were introducing about the program after the self-introduction then written consent will be taken to participate in the study. Pre-test was conducted through structured schedule questionnaire. Demographic data was collected through face-to-face interview; parent's knowledge about epileptic patient care was" Knowledge of parents toward epilepsy" questionnaire. And family functioning was assessed by using the Family Assessment Device (FAD)

Phase II: The education program was implemented over 16 weeks. The study participants attended 5 sessions, 2 sessions for theory (6 weeks) which includes epilepsy knowledge, self-management skills and social support and 3 sessions for practice of seizer management, coping with problems, improving family functioning (10 weeks). The duration of each session ranged between 30-45 minutes. At the beginning of each session researcher starts by giving a summary about previous session and explaining the objective new one. Different strategies were used including brain storming, instructions, lectures, role playing and group discussions.

Phase III: After 4 month of intervention Post-test was conducted. Post-test data was collected by using same questioners.

Statistical analysis was performed using the SPSS-26. The frequencies, proportions and comparisons of means using a paired t-test will analyze. Differences were considered statistically significant if $p<0.05$.

RESULTS

There were 13 (36.1%) participants having age less than 35 years and remaining 23 (63.9%) were having age above 35 years. Among those 13 participants; 3 (8.3%) were having poor, 4 (11.1%) average level and 6 (16.7%) good levels of knowledge. Whereas from participants above 35 years of age; 3 (8.3%) were having poor, 8 (22.2%) average and 12 (33.3%) were having good levels of knowledge. There were females 24 (66.7%) and 12 (33.3%) were males. There were 7 (19.4%) males who achieved good level of knowledge post-test and 11 (30.6%) were females. Majority of the participants were having secondary level of education 13 (36.1%). Twenty-four (66.7%) were employed and remaining 12 (33.3%) were employed. From employed participants 2 (5.6%) were having poor knowledge, 4 (11.1%) were having good knowledge and 6 (16.7%) were having good level of knowledge. Twenty-one (58.3%) from rural area while remaining 15 (41.7%) were from urban area. There was statistically insignificant (P>0.05) relationship between demographic characteristics and level of knowledge at post-test (Table 1).

It has been observed that there were statistically significant (P<0.001) changes in all dimensions except communication and affective responsiveness between pre and post intervention session. The pre-intervention mean score regarding problem solving was 2.66±0.43 and post intervention mean score was 2.00±0.42 with a mean difference of 0.66±0.63 (p<0.001). Regarding communication, the pre-study mean score was 2.38±0.22 and post-study session mean score was 2.34±0.64 (p=0.782). Concerning roles dimension the pre-intervention mean score was 2.48±0.56 and post-intervention was 2.13±0.50 (p<0.003). The affective responsiveness the mean score was observed as 2.45±0.61 before study and after 2.26±0.48 (p=0.140). The affective involvement the pre-study mean score was 2.62±0.64 and post-study the mean score decreased to 1.93±0.45 (p<0.001). The behaviour controls the mean score before 2.68±0.49 and after 1.90±0.35 (p-value < 0.001) and concerning general functioning the mean score before 2.32±0.59 and post study was 1.93±0.40; with a mean difference of 0.39±0.67 (p<0.001) [Table 2].

There was statistically significant (P<0.001) difference regarding pre-post knowledge levels. According to pre-intervention sessions there were almost 18 (50.0%) participants having poor knowledge, 12 (33.3%) participants having average knowledge and remaining only 6 (16.7%) participants having good knowledge. As far as post-intervention session is concerned there were only 6 (16.7%) participants who were having poor knowledge regarding epilepsy, 12 (33.3%) participants were having average knowledge and 18 (50.0%) participants were having good knowledge regarding epilepsy (Table3).

Table No.1: Relationship of demographic characteristics of parents and their knowledge at post intervention

Variable	Level of Knowledge				χ^2	P value
	Poor	Average	Good	Total		
Age (years)						
< 35	3 (8.3%)	4 (11.1%)	6 (16.7%)	13 (36.1%)	0.602	0.740
≥ 35	3 (8.3%)	8 (22.2%)	12 (33..3%)	23 (63.9%)		
Gender						
Male	2 (5.6%)	3 (8.3%)	7 (19.4%)	12 (33.3%)	0.625	0.732
Female	4 (11.1%)	9 (25%)	11 (30.6%)	24 (66.7%)		
Education						
Primary	1 (2.8%)	2 (5.6%)	6 (16.7%)	9 (25%)	5.300	0.506
Secondary	4 (11.1%)	3 (8.3%)	6 (16.7%)	13 (36.1%)		
Bachelor	1 (2.8%)	5 (13.9%)	4 (11.1%)	10 (27.8%)		
Masters	-	2 (5.6%)	2 (5.6%)	4 (11.1%)		
Employment Status						
Employed	2 (5.6%)	4 (11.1%)	6 (16.7%)	12 (33.3%)	0.000	1.000
Unemployed	4 (11.1%)	8 (22.2%)	12 (33.3%)	24 (66.7%)		
Residential Area						
Rural	5 (13.9%)	7 (19.4%)	9 (25%)	21 (58.3%)	2.057	0.358
Urban	1 (2.8%)	5 (13.9%)	9 (25%)	15 (41.7%)		

Table No.2: Comparison of means scores regarding family functioning domains among participants

Domains	FAD Scores			t	P value
	Before Study	After study	Mean Difference		
Problem solving (Cutoff=2.20)	2.66±0.43	2.00±0.42	0.66±0.63	6.348	<0.001*
Communication (Cutoff=2.20)	2.38±0.22	2.34±0.64	0.03±0.70	0.279	0.782

Roles (Cutoff=2.30)	2.48±0.56	2.13±0.50	0.35±0.65	3.242	0.003*
Affective responsiveness (Cutoff=2.20)	2.45±0.61	2.26±0.48	0.19±0.77	1.509	0.140
Affective involvement (Cutoff=2.10)	2.62±0.64	1.93±0.45	0.69±0.85	4.902	<0.001*
Behavior Control (Cutoff=1.90)	2.68±0.49	1.90±0.35	0.78±0.59	7.960	<0.001*
General Functioning (Cutoff=2.00)	2.32±0.59	1.93±0.40	0.39±0.67	3.550	0.001*

* Statistically significant

Table No.3: Knowledge of epilepsy levels

Knowledge level	Level of Knowledge			Test	P value
	Before the Study	After the study	Mean Difference		
Poor knowledge	18 (50%)	6 (16.7%)	12 (33.3%)	Wilcoxon Signed Rank Test	0.001*
Average knowledge	12 (33.3%)	12 (33.3%)	-		
Good knowledge	6 (16.7%)	18 (50%)	12 (33.3%)		

DISCUSSION

Epilepsy is an old common neurological condition. It occurs due to unprovoked spontaneous seizures. Epilepsy is often misunderstood and not taken seriously as compare to other diseases the reason behind it is lack of health related knowledge, poor economic condition, shortness of health facilities in the remotes areas. In current study majority of patients were more than 35 years old (63.9%), females (66.7%), have secondary education (36.1%) and belongs to rural area (58.1%). In a study conducted in an Arab experience shows that if the caregiver was female, less educated, and parent of epilepsy patients had significant effect on their QOL. Females have to face more social, emotional and physical problems.[16] In another cross-sectional study on burden of caregivers shows that majority of the caregivers were females and have tertiary education which also supports the results of current study.[17] In this study majority of the participants belong to rural area. This would be the reason behind poor management and family functioning as they have not much knowledge about epilepsy, medications, nutrition, access to medical services and treatment methods. These findings were supported by different studies which showed that majority of participants were from rural area.[18,19]

The current study focuses on the management of family functioning and coping strategies among families of epileptic patient's. After intervention it was observed a statistical significant difference in domain of FAD like problem solving, Defining Roles, Affective involvement, behavior Control and general function of family (P<0.05). It was also observed that there was significant difference between pre and post intervention results. The findings show that the families who have underwent the intervention programme, follow the instruction of nurses, follow the coping strategies to improve their family functioning, define the responsibility of each family member, how to control and avoid causes the creates problems, make their own decisions and obtain information about self-management shows that the intervention programme was effective and worthy.

The study conducted in India on the effectiveness of educational programme among epileptic patients shows significant difference in mean scores of each domain.[20] In a study conducted in Sweden also shows that the intervention programme has significant effect on the self-management support scales and subscales.[21]

Another study conducted on the effect of nursing intervention programme on self-management and social support in epileptic patient's reported that the nursing intervention plays a vital role in the improvement of management skills of patient. There was significant difference in pre and post intervention.[22]The results of current study also supported by the study conducted on nurse led self-management intervention programme shows significant difference physical role limitations, medication and health issues.[23]

The role of family functioning is very important. A study was conducted to compare the family functioning of pseudoseizures and epilepsy patients. There was significant difference was observed in affective involvement, communication and general functioning among both groups. pseudoseizures thought that they have more dysfunctional families as compared to epileptic patients. It was also suggested that the intervention programs should be conducted so that lacking in family function should be improved.[24].

CONCLUSION

The nurse plays a vital role in improving the family functioning of epileptic family's. They are the key essentials for training parents. The Nursing intervention

has positive impact on the family functioning of epileptic patients especially in problem solving, defining Roles, affective involvement, behavior control and general function of family whereas communication and affective responsiveness shows lacking. Family education and interventions programme should focus on these domains which may lead to important aspects of treatment and improvement in their lives.

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Original Article

Post-Operative Outcome of Open Cholecystectomy in Spinal versus General Anesthesia

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ABSTRACT

Objective: The purpose of this study is to compare the post-operative outcome of open cholecystectomy in spinal vs general anesthesia.

Study Design: Comparative/control randomized study

Place and Duration of Study: This study was conducted at the Surgery Department of Khairpur Medical College Hospital, Khairpur from January 2021 to June, 2021 for a period of six months.

Materials and Methods: One hundred and twenty patients of both genders were presented in this study. Patients were aged between 18-65 years. Patients who had ASA grade I and II and underwent open cholecystectomy were presented. Detailed demographics of enrolled cases including age, sex and body mass index were recorded after taking informed written consent. Patients were equally divided into two groups. Group I had 60 patients and received spinal anesthesia for open cholecystectomy and group II received general anesthesia in 60 patients. Post-operative VAS pain score, complications, effectiveness, hospital stay and patients' satisfaction were recorded and compared among both groups.

Results: There were 35 (58.3%) male patients and 25 (41.7%) females in group I with mean age 36.18±8.76 years while in group II 33 (55%) were males and 32 (45%) females with mean age 37.13±4.88 years. Mean BMI in group I was 24.09±7.24 kg/m^2 and in group II mean BMI was 25.04±4.44 kg/m^2. Forty-eight (80%) cases in group I had ASA 1 and 45 (75%) patients in group II had ASA I. Mean operative time in group I was 40.03±3.61 minutes and in group II mean time was 44.07±6.18 minutes. Post- operative less pain score was observed among patients of group I 1.09±5.11 as compared to group II 3.07±4.13. Rate of complications nausea/vomiting, dizziness and hospital stay were significantly higher in group II. Recovery 48 (80%) and patients satisfaction 44 (73.3%) were higher among patients of group I as compared to group II 42 (70%) and 38 (63.3%).

Conclusion: The use of spinal anesthesia in open cholecystectomy was effective as compared to general anesthesia in terms of post-operative pain, complications and hospital stay.

Key Words: Open cholecystectomy, Spinal, General anesthesia, Complications

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INTRODUCTION

The gold standard for surgical therapy of symptomatic cholelithiasis was laparoscopic cholecystectomy (LC) Because of the procedure's minimally invasive nature, it's more likely to be given to patients who will have less postoperative pain, spend less time in the hospital, and return to work sooner.[1-3]

Surgery for LC is done under general anesthesia, (GA) and the procedure may cause nausea and vomiting as well as postoperative pain. In comparison to general anesthesia, spinal anesthesia was a less invasive anesthetic approach with reduced death and morbidity rates.[4] Laparoscopic surgery patients who had spinal anesthesia were more likely to be awake and have a better quality of life after the procedure, as well as to be able to walk around more quickly after the procedure.[5,6]

Laparoscopic cholecystectomy is typically performed under GA and comes with the possibility of postoperative discomfort, nausea, and vomiting (nausea and vomiting) (PONV). Meta-analysis by Rodgers et al. found that using neuraxial methods for several surgical operations reduced mortality, vein thromboembolism and myocardial infarction among other problems.[7]A very safe anesthetic approach is spinal anesthesia (SA), which is widely utilized. In comparison to GA, SA has

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a number of advantages. They include being awake and oriented at the end of the treatment, reduced postoperative pain and the ability to ambulate earlier than patients who get general anesthetic. Selective spinal anesthesia also reduces the risk of nausea and vomiting compared to general anesthesia.[8] Surgery-associated neuroendocrine stress and unfavorable surgical reactions are better mitigated by SA than by GA. Patients having laparoscopic procedures benefit from selective spinal anesthesia, which reduces the risk of tooth and oral cavity damage during laryngoscopy, sore throat, and pain associated with intubation and/or extubation.[9] Several studies have examined whether SA may be used to treat LC in patients who are also candidates for GA.[10,11]

Regional anaesthetic hasn't acquired popularity or been consistently utilized as the exclusive type of anesthesia in laparoscopic surgeries, which is surprising in the era of minimally invasive medicine. As Johnson pointed out, "the difference between laparoscopic surgery and conventional surgery is likely to be modest because all laparoscopic treatments are essentially a change in access".[12] In order to prevent aspiration and respiratory distress due to the induction of carbon dioxide pneumoperitoneum, which is not well tolerated in a patient who is awake throughout the procedure, this statement is primarily founded on the notion that laparoscopy demands endotracheal intubation.[13].

MATERIALS AND METHODS

This comparative study was conducted at Surgery Department of Khairpur Medical College Hospital, Khairpur over a period of six months from 1st January 2021 to 30thJune 2021 and comprised 120 patients. Detailed demographics of enrolled cases were recorded after taking informed written consent. Patients with spinal deformity, back infection, bleeding disorders and those did not give any written consent were excluded.

Patients were aged between 18-65 years. Patients had ASA grade I and II underwent for open cholecystectomy were presented. Patients were equally divided into two groups. Group I had 60 patients and received spinal anesthesia for open cholecystectomy and group II received general anesthesia in 60 patients. Hyperbaric bupivacaine hydrochloride was injected intrathecally at the L3-L4 or L4-L5 intervertebral area under aseptic conditions into patients randomized to spinal anesthesia. To induce deep spinal anesthesia, the patient was placed in the trendelenburg position for three minutes. Propofol (2-3 mg/kg), fentanyl citrate (5 g/kg), and atracuriumbesylate (0.5 mg/kg) were used to induce anesthesia in patients who were randomly assigned to receive it. Using sevoflurane (1–2 percent) and propofol (2–4 mg/kg/h), the anesthesia was stabilized. During the procedure, all patients' hemodynamics was closely monitored. After surgery, 25 mg of neostigmine methyl sulfate and 1 mg of atropine sulfate were administered to combat any residual neuromuscular block.

Post-operative VAS pain score, complications, effectiveness, hospital stay and patient's satisfaction were recorded and compared among both groups. Complete data was analyzed by SPSS 26.0 version.

RESULTS

There were 35 (58.3%) male patients and 25 (41.7%) females in group I with mean age 36.18±8.76 years while in group II 33 (55%) were males and 32 (45%) females with mean age 37.13±4.88 years. Mean BMI in group I was 24.09±7.24 kg/m^2 and in group II mean BMI was 25.04±4.44 kg/m^2.Forty eight (80%) cases in group I had ASA 1 and 45 (75%) patients in group II had ASA I. Mean operative time in group I was 40.03±3.61 minutes and in group II mean time was 44.07±6.18 minutes (Table 1).

Post- operative after 8 hours less pain score was observed among patients of group I 1.09±5.11 as compared to group II 3.07±4.13 by using visual Analog score (Table 2). Rate of complications nausea/vomiting, dizziness and hospital stay were significantly higher in group II (Table 3). Recovery 48 (80%) and patients satisfaction 44 (73.3%) were higher among group I as compared to group II 42 (70%) and 38 (63.3%) [Table 4].

Table No.1: Baseline detailed demographics of enrolled cases

Variable	Group I	Group II
Mean age (years)	36.18±8.76	37.13±4.88
Mean BMI (kg/m^2)	24.09±7.24	25.04±4.44
Gender		
Male	35 (58.3%)	33 (55%)
Female	25 (41.7%)	32 (45%)
ASA		
I	50 (80%)	45 (75%)
II	12 (20%)	15 (25%)
Mean operative time (min)	40.03±3.61	44.07±6.18

Table No.2: Post-operative comparison of pain score among both groups by using VAS

Mean pain score (VAS)	Group I	Group II
After 2 hours	6.11±7.18	7.07±6.21
After 4 hours	3.11±7.05	5.24±6.07
After 8 hours	1.09±5.11	3.07±4.13

Table No.3: Frequency of complications

Variable	Group I	Group II
Hospital stay (days)	1.02±8.16	2.51±7.24
Complications		
Nausea/Vomiting	6 (10%)	8 (13.3%)
Dizziness	3 (5%)	5 (8.3%)
Pruritus	2 (2.5%)	2 (2.5%)
Urinary retention	1 (1.75%)	1 (1.75%)

Table No.4: Post-operative comparison of efficacy and satisfaction among both groups

Variable	Group I	Group II
Recovery		
Yes	48 (80%)	44 (73.3%)
No	12 (20%)	16 (26.7%)
Patients satisfaction		
Yes	42 (70%)	38 (63.3%)
No	18 (30%)	22 (36.7%)

DISCUSSION

Open cholecystectomy is commonly performed under general anesthesia because it helps to relax the patient's muscles enough for the procedure. However, it comes with a slew of risks, particularly if the patient has other health issues. Patients with bronchial asthma who undergo tracheal intubation run the risk of suffering life-threatening spasms, necessitating postoperative ventilation and thus an expensive hospital stay. Other risks that can be avoided in a regional anesthetic environment include oral and teeth harm during laryngoscopy, sore throat, and stomach inflation due to mask ventilation.[14]

There were 35 (58.3%) male patients and 25 (41.7%) females in group I with mean age 36.18±8.76 years while in group II 33 (55%) were males and 32 (45%) females with mean age 37.13 ±4.88 years. Mean BMI in group I was 24.09±7.24 kg/m^2 and in group II mean BMI was 25.04±4.44 kg/m^2. These findings were comparable to the previous studies.[15,16] 48 (80%) cases in group I had ASA 1 and 45 (75%) patients in group II had ASA I. Mean operative time in group I was 40.03±3.61 minutes and in group II mean time was 44.07±6.18 minutes. Pain following surgery is a universal phenomenon; it is often underestimated and undertreated. In open cholecystectomy, postoperative discomfort is critical because of the potential for respiratory complications. The first reason is that the open cholecystectomy incision is placed in such a way that it impairs the patient's respiratory movement, leading to a weak cough reflex and atelectasis or pneumonia as a result.[17] As a second point, intubation can cause edema and fluid exudation by traumatically altering the airway, but it can also introduce bacteria into the lower airway, increasing a patient's vulnerability to respiratory infections.

In this study we found that less pain score among patients of group I 1.09±5.11 as compared to group II 3.07±4.13 by using visual Analog score. This was comparable to previous studies in which spinal anesthesia was effective and superior.[18,19] Rate of complications nausea/vomiting, dizziness and hospital stay were significantly higher in group II. This is in line with the findings of Yousef[20], however Tzovaras[22] found no difference between our SA and GA groups in terms of early discharge and shortened length of hospital stay.

A meta-analysis by Yuet al[15] demonstrated that LC under SA was superior to LC under GA in postoperative pain within 12 h (visual analogue score (VAS) in 2–4 h, WMD = −1.61, P = 0.000; VAS in 6–8 h, WMD = −1.277, P = 0.015) and postoperative complications (postoperative nausea and vomiting (PONV) WMD = 0.427, P = 0.001; Overall Morbidity WMD = 0.691, P = 0.027).

Recovery 48 (80%) and patients satisfaction 44 (73.3%) were higher among group I as compared to group II 42 (70%) and 38 (63.3%).[22] Our findings thus far support the preliminary findings of our pilot study, which showed that spinal anesthetic can be used safely and effectively for this purpose. In addition, spinal anesthesia appears to be more successful than regular general anesthesia in controlling postoperative pain during the patient's hospital stay than the standard anesthesia. The recovery of patients after laparoscopic cholecystectomy under spinal anesthesia, on the other hand, was reported to be as excellent as the current standard anaesthetic procedure after discharge. Elective laparoscopic cholecystectomy in healthy individuals may soon benefit from spinal anesthesia as the gold standard anesthetic strategy, based on these early results. Spinal anesthesia is more successful than general anesthetic in reducing post-operative pain, analgesic demand, respiratory issues, and hospital stay for patients undergoing open cholecystectomy, not only because it is safer[23].

CONCLUSION

The use of spinal anesthesia in open cholecystectomy was effective as compared to general anesthesia in terms of post-operative pain, complications and hospital stay.

Author's Contribution:

Concept & Design of Study:	Zahoor Hussain
Drafting:	Anwar Ali Bozdar, Siraj-ud-Din
Data Analysis:	Abu Baker, Ghulam Ali Narejo, Aijaz Hussain Memon
Revisiting Critically:	Zahoor Hussain, Anwar Ali Bozdar
Final Approval of version:	Zahoor Hussain

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

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Original Article

Effect of Nurse-Led Self-Management Support Intervention on Quality of Life among Kidney Transplant Patients

Rashida Jabeen, Kousar Perveen, Muhammad Afzal and Sadia Khan

ABSTRACT

Objective: To find out the impact of nurse-led self-management support interventions on quality of life among kidney transplant patients.

Study Design: Qausi experimental study

Place and Duration of Study: This study was conducted at the Rukhsana Akhtar Bahria International Orchard Hospital Lahore, Pakistan from June, 2021 to October, 2021 for a period of 05 months.

Materials and Methods: Thirty-six patients were selected by using purposive sampling technique. After taking informed consent all kidney transplant patients aged between 18 years to 60 years, visited the post-transplantation OPD and continuously in follow-up sessions were included.

Results: The mean age was 31.44±9.31 with 55.6% females. 27.8% can read/write and 52.8% belongs to urban area. 69.44% of donors were non-relatives. There was significant difference in the KDQOL before and after 4 month intervention. Over all their general health remain same after transplantation ($p>0.05$) but there physical function, emotional function, social function, daily activities and physical and emotional problems showed significant difference after intervention ($p <0.05$). 11.1% participants were having excellent quality of life and but after intervention it has increased to 44.4% ($p<0.05$).

Conclusion: Nurse led self-management program had significant impact on increasing the quality of life of kidney transplant patients. Nurses are the important factor for educating patients which can lead to significant change in their behavior and quality of life as well.

Key Words: Renal Diseases, KDQOL, Self-management, Kidney transplantation

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INTRODUCTION

Kidney transplantation is the best choice for end-stage renal disease patients. End -stage renal decease or chronic kidney disease is one of the chronic conditions contributing to the major part of the global prevalence of the non-communicable disease, and reduced kidney function indicate by GFR of less than 60 mL/min per 1·73 m^2, as a minimum 3 months period, irrespective of the underlying cause.[1] Chronic kidney disease is a universal matter of concern that affecting around 15% of the population globally.[2]

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In Asian countries, the prevalence of CKD is very high and China shows the highest with 18.3%, Taiwan 9.83%, 10.6% in Nepal and 23.3% in Pakistan.[3] In Pakistan, an estimated prevalence rate of end stage kidney disease is 100 per million populations. Kidney transplant rate is 8-10 cases per million populations, 10% of patients are on hemodialysis, 3% undergo peritoneal dialysis.[4]

However, kidney transplant patients have to be compelled to adhere to a lifelong follow up, and optimum self-management is important for enhancing the quality of life whereas this has direct to an improving interest in optimizing patients' self-management skills.[5] In comparison to dialysis, kidney transplantation is the preferred care option for patients with end-stage renal disease since it provides greater quality of life.[6]

When more patients live with chronic illnesses and comorbidities, there is a growing emphasis on efficient self-management and streamlining quality of life.[7] Quality of life is a multi-dimensional concept that consists of domain names associated with physical, emotional, and social functioning and daily activities etc. Therefore, Quality of life is usually impaired in patients who have renal transplant because of renal

transplant patients have anxiety, lack of social, physical and emotional support and diminished ability to take care of themselves.[8]

After transplantation, kidney transplant patients need to learn to adapt to optimal physical function, changing emotional challenges and social roles.[9] One of the most important roles of nurses is to assist patients with self-management during the post-transplant period, thereby improving quality of life in many areas, including physical function, social function, emotional function, physical and emotional problems, and daily activities.[10] Moreover, Nurse Led self-management support intervention effect on kidney patients in terms of manage physical function, social and emotional function etc. Similarly, nurses play vital role in providing care to the patients but there is lacking of interventional studies on the impact of nurse led self-management support intervention on quality of life among kidney transplant patients. Literature suggests that nurses and patients have a lack of awareness and capacity when it comes to self-management and improving quality of life. But, after a nurse-led self-management support intervention, remarkable improvements in both quality of life and self-management skills can be made, leading to an increase in overall patient quality of life outcomes.[11] A descriptive post transplantation survey among the 60 patients managed by hemodialysis at the hospital of Andhra Pardesh, India found that Nurse led intervention shown the significant improvement in the knowledge of participants regarding self-care management effect.[12] Nurse Led Self-management support intervention will considerably enhance the quality of life among the renal transplant patients. Additionally, nurses play vital role in providing care to the patients therefore this study was conducted to find out the impact of nurse-led self-management support interventions on quality of life among kidney transplant patients.

MATERIALS AND METHODS

This qausi experimental study according to trend guidelines[13] was conducted at Rukhsana Akhtar Bahria International Orchard Hospital Lahore, Pakistan from 1st June to 31st October 2021. The study was approved by the Institutional Board of University of Lahore. Thirty-six patients were selected by using purposive sampling technique. After taking informed consent all kidney transplant patients aged between 18 years to 60 years, visited the post-transplantation OPD and continuously in follow-up sessions were included in study. Terminally ill patients/hospitalized in Intensive care unit, having any comorbidity like uncontrolled diabetes mellitus, uncontrolled hypertension, cognitive limitations, acute psychiatric problems, mentally retarded, blind or deaf etc. and who will undergo dialysis or will predict to start dialysis within 3 months were excluded.

Intervention was divided into three phases. In first phase two nurses from kidney transplant unit of hospital was invited to participate in the study voluntarily (written consent taken), as a facilitator for data collection (pre-and post-assessment). Nurses received three training sessions pre intervention for data collection process. Nurses was then asked to recapitulate the material in their own worlds and the use the nurse led self-management support intervention, living a health life with chronic disease self-management skills guidance to facilitate comprehension and continuity. The training was dual-purpose; on the one hand, it comprised an explanation on how to collect data and on the other hand, nurses were trained in using intervention protocol techniques. After completion of training these two nurses collect the pre and post data from the participants. In second phase of intervention was applied on patients 16 weeks. Patient was introduced about the Nurse Led self-management support intervention for improving quality of life. Which includes taking care of the expected health problems by coping with challenges confidently, perform routine activities of their lives by improving physical activity, manage emotional changes like stress, anxiety, fear and depression, adopt the dietary modifications, manage the sleep pattern effectively, and maintain effective communication with family and colleagues. The study participants attended sessions on consecutive days. The duration of each session ranged between 45-60 minutes. At the start of each session researcher start by means of giving a summary approximately previous session and explaining the goal new one. Different strategies were used including brain storming, instructions, Videos, lectures, role playing and group discussions. In Phase III after 4-month of intervention post-test about Kidney transplants patient's knowledge of improving quality of life by self-management was collected through same instrument Kidney disease quality of life questionnaire KDQOL-36TM 16 varying dimension such as physical function, Social function, emotional function etc. was assessed through questionnaire.

Data will be entered and analyzed in SPSS-21. Paired sample T-test was applied to compare the scores of all the domains of quality of life i.e. physical functioning, social functioning, emotional functioning, physical and emotional problems and daily activities. P-Value ≤ 0.05 was considered as statistically significant.

RESULTS

The mean age of participants was 31.44+9.31 with 55.6% were females and 44.45% were male. Majority were married 27 (75.0%) and unmarried were 9(25.0%). Four (11.1%) were illiterate, 10(27.8%) were able to read or write, 8 (22.2%) have done matriculation, 6 (16.7%) participants had completed secondary level of education, 5(13.9%) were bachelors

and only 3(8.3%) were masters. In relation to residential area most of 52.8% were from urban area whereas 47.2% were from rural area. In relation to type of kidney donor most of 69.44% were non relative and 30.56% were relative (Table 1).

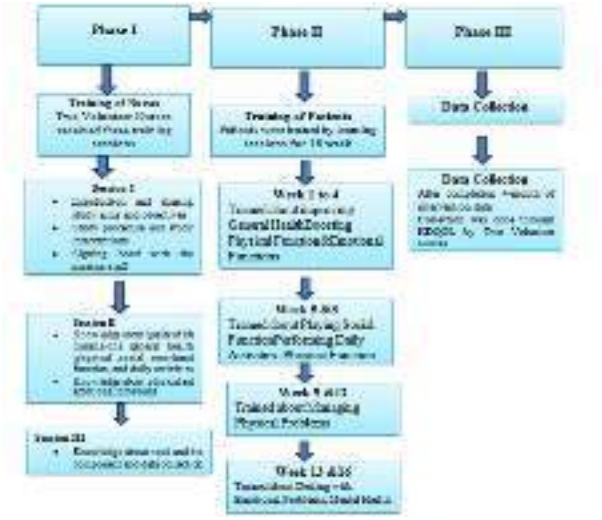

Figure No.1: Flow diagram of intervention

The mean score was significantly more than that before study group regarding all domains and total score except general i.e. 5.97±2.20 before intervention and 5.97±2.20 after intervention with a mean difference of 0.52±2.78; 16.72±2.92 before intervention and 21.64±1.42 after intervention with a mean difference of 4.92±3.25 (p<0.001); 15.50±3.87 before intervention and 23.19±2.54 after intervention with a mean difference of7.69±4.63 (p<0.001); 17.64±4.08 before intervention and 24.94±2.43 after intervention with a mean difference of 7.31±4.33 (p<0.001); 23.14±4.52 before intervention and 28.89±3.45 after intervention with a mean difference of 5.75±5.49 (p<0.001); 28.39±2.57 before intervention and 32.52±3.75 after intervention with a mean difference of 4.14±5.05(p<0.001) and 107.36±10.14 before intervention and 137.69±5.90 after intervention with a mean difference of 30.33±11.85 (p <0.001) with respect to general health, physical functioning, emotional functioning, social functioning, daily activities, physical and emotional problems and total score respectively (Table 2).

Table No.1: Demographic characteristics of patients

Variables	No.	%
Age	31.44+9.31	
Gender		
Male	16	44.4
Female	20	55.6
Marital Status		
Married	27	75.0
Unmarried	9	25.0
Education		
Illiterate	4	11.1
Read/Write	10	27.8
Matriculation	8	22.2
Secondary	6	16.7
Bachelor	5	13.9
Masters	3	8.3
Residential Area		
Urban	19	52.8
Rural	17	47.2
Type of kidney donor		
Relative	11	30.56
Non Relative	25	69.44
Post kidney transplantation length of time (years)		
Less than 1	8	22.22
1 to 3	19	52.78
4 to 6	6	16.67
Greater than 6	3	8.33

Table 3 shows the frequency and percentage of interpretation of KQDOL levels before and after the intervention which indicates that 50% participants had poor quality of life before the study whereas it decreases to 19.4% after the study, 38.9% had average quality of life before the study and afterwards it was 36.1%, and only 11.1% participants were having excellent quality of life and after the intervention it has increased to 44.4% (p=0.001).

Table No.2: Comparison of means scores regarding KQDOL domains among patients underwent kidney transplant

Domains	Before Study	After study	Mean Difference	t	P value
General health	5.97±2.20	5.97±2.20	0.52±2.78	-1.138	0.263
Physical function	16.72±2.92	21.64±1.42	4.92±3.25	-9.064	<0.001*
Emotional Function	15.50±3.87	23.19±2.54	7.69±4.63	-9.976	<0.001*
Social Function	17.64±4.08	24.94±2.43	7.31±4.33	-10.128	<0.001*
Daily Activities	23.14±4.52	28.89±3.45	5.75±5.49	-6.285	<0.001*
Physical & Emotional Problems	28.39±2.57	32.52±3.75	4.14±5.05	-4.913	<0.001*
Total	107.36±10.14	137.69±5.90	30.33±11.85	-15.360	<0.001*

*Statistically significant

Table No.3: Comparison of pre and post difference in KQDOL Levels (Wilkoxon signed rank test)

KQDOL level	Before the Study	After the study	Difference	P value
Poor	18 (50%)	7(19.4%)	11(30.6%)	0.001*
Average	14(38.9%)	13(36.1%)	1 (2.8%)	
Excellent	4 (11.1%)	16(44.4%)	12 (33.3%)	

DISCUSSION

Self-management support intervention helps patients to improve the skill, confidence, encouragement and power to enhance their managing their chronic condition. Additionally, nurses play vital role in providing care to the patients therefore this study was conducted to find out the impact of nurse-led self-management support interventions on quality of life among kidney transplant patients. The results of current study reveals that Nurse led self-management program had significant impact on increasing the quality of life of kidney transplant patients. The mean age of patients was 31.44±9.31. The patient's characteristics showed that (55.6%) females, 27.8% can read/write and 52.8% belongs to urban area. 69.44% of donor were non-relatives. A study conducted by Rizvi et at[14] reveal the demographic information of donor which shows that male donors were higher in number and 54% of donors were siblings, 3.5 % were close relatives, 8.4% were spousal.

In current study pre and post Nurse led intervention for self-management was applied. There was significant difference in the KDQOL before and after 4-month intervention. Over all their general health remain same after transplantation ($p>0.05$) but their physical function, emotional function, social function, daily activities and physical and emotional problems showed significant difference after intervention ($p<0.05$).11.1% participants were having excellent quality of life and but after intervention it has increased to 44.4% ($p<0.05$).

The result of a pilot study conducted by Been-Dahmen et al[15] reveals that recipients who receive intervention admire the intervention, become more competent in solving their problems and social interactions. There was an improved quality of life among intervention group. It was concluded that Nurse-led-self management approach was successfully accepted by patients and professional as well.

Another study reported that self-management program had significant impact on patient's quality of life. There was significant improvement in patient activation, health related quality of life, health status and self-management skill as well.[16]

A study conducted among Korean adults to investigate Chronic Disease Self-Management Program which was followed for 18 weeks. The result of this study reveals higher levels of self-efficacy and physical activity at the end of study. The participants who have low health related literacy have greater impact and benefit than those who have high literacy.[17]

Kafami et al[18] conducted study on self-management programe on multiple sclerosis patients shows that after two months of intervention there was significant difference in health status of two groups which is in accordance to current study.

A qusai experimental study was conducted on 86 patients with cardiovascular diseases showed that the self-management intervention had significant effect on changing patient's lifestyle as well as medication regimen and choosing better diet plan[19].

CONCLUSION

The nurse led self-management support intervention has potentially significant positive effect on the quality of life of kidney transplant patients. Nurses are the important factor for educating patients which can lead to significant change in their behavior and quality of life as well. It was also recommended that higher authorities should pay more attention to nurse led self-management support programs so that we can improve patient's health, independence and satisfaction.

Author's Contribution:

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

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Original Article

Burden of Non-Cardiac Patients Attending Cardiac OPD at Tertiary Care Hospital

Jawad Ahmed Qadri, Suhail Ahmed Bijarani, Muhammad Ilyas Siddiqui, Wali Muhammad Nizamani, Faiza Memon and Sindhia Javed Junejo

ABSTRACT

Objective: To determine the burden of non-cardiac chest pain reported at the tertiary care hospital.
Study Design: Descriptive Cross sectional study
Place and Duration of Study: This study was conducted at the Cardiac OPD of Liaquat University Hospital, Hyderabad/Jamshoro from September 2018 to November 2018 for a period of 03 months.
Materials and Methods: Non-probability (Purposive) sampling technique was applied and the data was collected on pre-tested structured questionnaire after taking written informed consent from the patients presented in cardiac OPD. Ethical approval was taken from the ethical committee of LUMHS, Jamshoro. Statistical package for Social Sciences (SPSS) version 22 was used to analyze the data.
Results: During the study data collection period a total number of a total 182 (43%) out of (n=424) presented with non-cardiac chest pain who fulfilled the inclusion criteria while the overall response rate were (n=154) 84.6% and all those were included in the present study. Among the participant majority 83(54%) were female compared to 71(46%) males. The age of patients ranges from 19 years to 70 years with the mean age of 43.4 years. Most 32% of patients belongs to age group of 39-48 years whereas only 13% belongs to 59 and above year age group. Majority, (34.5%) of participants having only primary education and 6% of them had some higher-level education. While half (51%) of them belongs to lower middle class families or having lower middle class economic status.
Conclusion: Substantial numbers of patients were suffering from Non-cardiac chest pain (NCCP) among them female patients visited more than males, whereas majority of the patients were belonging to their middle age i.e. 39 to 48 years.
Key Words: Chest pain, non-cardiac chest pain, Tertiary care hospital

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INTRODUCTION

Chest pain is a most commonly reported complaint in the hospital`s emergency departments or coronary care unites, which could be an important and main symptom of life threating conditions, such as acute coronary symptom[1]. Majority of the patients visiting the emergency department with symptoms of acute chest pain do not have a cardiac cause for their presentation[2]. There are many reasons of non-cardiac chest pain such as trauma of the chest wall or inflammation and disease of the underlying organs other than heart[3].

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The Non-cardiac chest pain is usually similar in characteristics of the cardiac chest pain but it is mainly due to the gastrointestinal or musculoskeletal problems and are non- lethal[4]. A cross-sectional study conducted in the four districts of the Sindh Province of Pakistan, revealed that there is substantial lack of essential equipment and provider knowledge to provide necessary and effective emergency care[5]. The institute of Health Metrics and Evaluation reported that ischemic heart disease, cerebrovascular disease was the leading cause of deaths in Pakistan[6]. Globally 15% of deaths are contributed to the cardiovascular problems such as, cardiac arrest and MI and the majority of these deaths are occurring in the low middle-income countries. [7-8] According to the Institute of Health Metric and Evaluation (IHME), profile of Pakistan in 2017 reported 29% rise in deaths due to IHDs whereas 20.7% rise death toll due to CVA or stroke in Pakistan[9]. In Pakistan, where very limited health care resource are available and having high burden of communicable and non-communicable diseases. There is need to determine the burden of the non-cardiac patients, visiting the emergency department and cardiac care unit (CCU) of the tertiary care hospital.

MATERIALS AND METHODS

A total 154 patients presenting with acute chest pain at OPD of Liaquat University Hospital, Hyderabad. Having no any underlying cardiac disease conformed by consultant and ECG, Troponin I Tests (normal & negative) and given the consent to be part of the study visiting cardiac OPD. During the study period September 2018 to Number 2018 of Liaquat University Hospital, Hyderabad were included. Ethical approval was taken from the ethical committee of LUMHS, Jamshoro. The data was collected on a pre-tested structured questionnaire. We have used SPSS version 16.0 software for both data entering and analysis. Frequencies and standard deviations were calculated and categorical variable were analyzed using chi-square test. P-value of ≤0.05 was taken as statistically significant.

RESULTS

A total 154 patients with non-cardiac pain (NCCP) fulfilling the inclusion criteria had given the consent and willing to participant in the study were included. Among the participants majority 83(54%) were female compared to 71(46%) males. The age of patients ranges from 19 years to 70 years with the mean age of 43.4 years, as shown in Table 1.

Information inquired from the participants about the risk factors, comorbid features and underlying conditions related to the chest pain. Majority (73%) of the male participants were smokers while (15 %) female participants having smoking habits. Majority 54% of participants reported that they sweat excessively in routine life, while 58% reported that often they feel like chocking. Most (64%) of participants were complaining of feelings hot flushes or chills, as shown in Table 2. Regarding the characteristics of their chest pain, 12% participants reported suffering from chest discomfort for more than three times during the last year. About the severity, majority (36%) of them reported that their chest pain was moderate in severity.

Table No.1: Socio-demographic and economic features of participants (n=154)

		Female 83 (54%)		Male 71 (46%)		Total	
		n	(%)	n	(%)	n	(%)
Age of participants	19-28 years	12	(14.4)	12	(17)	*24*	*(15.6)*
	29-38 years	23	(27.7)	16	(22.7)	*39*	*(25.4)*
	39-48 years	27	(32.5)	23	(32.3)	*50*	*(32.4)*
	49-58 years	11	(13.3)	10	(14)	*21*	*(13.6)*
	59 and above	10	(12)	10	(14)	*20*	*(13)*
Education of participant	No education	17	(20.5)	10	(14)	*27*	*(17.4)*
	Primary	25	(30)	28	(39.4)	*53*	*(34.3)*
	Secondary	23	(27.7)	23	(32.3)	*46*	*(30)*
	Tertiary	11	(13.3)	8	(11.3)	*19*	*(12.3)*
	Higher level	7	(8.5)	2	(3)	*9*	*(6)*
Economic status of participants	Poor	20	(24)	29	(41)	*49*	*(32)*
	Lower middle	43	(52)	36	(50.7)	*79*	*(51.3)*
	Upper middle	20	(24)	6	(8.3)	*26*	*(16.7)*

Table No.2: Participant replies of question related to risk factors of chest pain (n=154)

Variable	Female 83 (54%)		Male 71 (46%)		Total		P-value
	n*	(%)	n*	(%)	n*	(%)	
Are you a smoker?	13	(15.7)	52	(73)	65	(42)	0.00
Do you use aspirin regularly?	39	(47)	40	(56)	79	(51.3)	0.247
Do you use NSAIDs regularly?	53	(64)	50	(70.5)	103	(67)	0.388
Do you use angesid?	41	(49.4)	32	(45)	73	(47.5)	0.592
Did you have chest pain on pressure?	43	(52)	26	(36.7)	59	(38)	0.059
Do you sweat excessively?	49	(59)	35	(49)	84	(54.5)	0.226
Do you often feel like chocking?	48	(58)	41	(58)	89	(58)	0.992
Do you have hot flashes or chills?	56	(67.5)	42	(59)	98	(64)	0.285
Do you have any one in your family having heart diseases?	45	(54)	42	(59)	87	(56.5)	0.538
Do you have Diabetes Mellitus?	44	(53)	34	(48)	78	(51)	0.526
Are you suffering from depression?	46	(55.5)	40	(56)	86	(56)	0.976
In last 4 weeks, have you had sudden feeling fear or panic?	51	(61.5)	42	(59)	93	(60)	0.772
If yes, have you experienced it before?	33	(35.5)	20	(21.5)	53	(34.4)	0.160
Do you feel excessive stress in routine life?	61	(73.5)	47	(66)	108	(70)	0.324

*** All above are reply in yes**

Table No.3: Participant replies of questions related to chest pain (n=154)

Variable		Female 83(54%)		Male 71(46%)		Total	
		n	(%)	n	(%)	n	(%)
How many times have you had chest discomfort in the past 12 months?	Once in a month	21	(25.3)	19	(27)	40	(26)
	Twice in a month	18	(21.7)	25	(35)	43	(28)
	Thrice in a month	15	(18)	11	(15.5)	26	(17)
	> three times in a month	13	(15.7)	6	(8.5)	19	(12)
	Almost daily	16	(19.3)	10	(14)	26	(17)
How severe your chest pain is?	Mild	26	(31.3)	23	(32.4)	49	(32)
	Moderate	30	(36.2)	26	(36.6)	56	(36)
	Severe	27	(32.5)	22	(31)	49	(32)
At what location you feel chest pain commonly.	Epigastric region	39	(47)	27	(38)	66	(43)
	Central chest	5	(6)	9	(12.3)	14	(9)
	Right Arm	22	(26.5)	19	(27)	41	(26.6)
	Left Arm	17	(20.5)	16	(22.7)	33	(21.4)
What type of pain you feel in your chest?	Gripping	16	(19.3)	15	(21)	31	(20.1)
	Stabbing	20	(24.1)	14	(19.7)	34	(22.2)
	Heavy feeling	19	(22.6)	19	(27)	38	(24.6)
	Burning	28	(34)	23	(32.3)	51	(33.1)
How long your chest pain usually lasts?	Less than five minutes	8	(9.6)	10	(14)	18	(11.7)
	Five to Ten minutes	9	(11)	8	(11.3)	17	(11)
	Less than fifteen minutes	10	(12)	6	(8.4)	16	(10.4)
	Fifteen to thirty minutes	28	(33.7)	27	(38)	55	(35.7)
	Less than an hour	23	(27.7)	17	(24)	40	(26)
	More than an hour	5	(6)	3	(4.3)	8	(5.2)

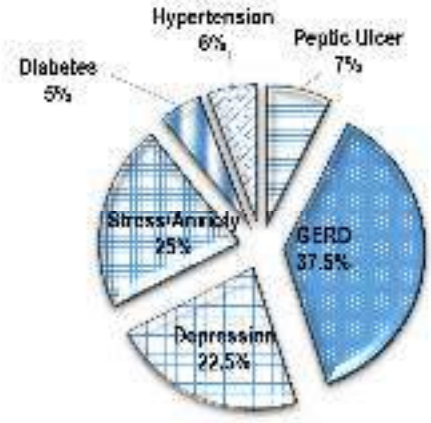

Figure No.1: Proportional distribution of patients suffering from other diseases (n=154)

Location of pain was epigastric region reported by most (43%) of the participants. Among the type of chest pain, majority (33.1%) said they feel burning like pain in chest (Table 3). Although the participants were suffering from other health problems like GERD (37.5%) followed by stress/anxiety (25%) and depression (22.2%) along with chest pain problem. (Figure 1).

DISCUSSION

Pakistan has several changes in the health care delivery system and having very less number of emergency services throughout the country. Emergency services has vital role in decreasing disabilities and mortalities.[10] there is urgent need of time to provide appropriate adequate and effective emergency medical care.[11] The major problem accompanying with increasing frequency of patients visiting the emergency or coronary care units is Non-cardiac chest pain.[12] A huge number of people spend many years of their life in a fear of fetal consequences of cardiac disorder without having any cardiac illness.[13] Awareness about diseases and healthy life style related with level of education and economic status. In the present study, majority (34%) patients were having primary education only and 51% belongs to lower middle class of families.

This study planned to assess the burden of non-cardiac chest pain among patient visiting the cardiac OPDs of Tertiary care unit. Initially patients were divided into two groups i.e. one with chest pain due to cardiac problems and presented with chest pain due other than any cardiac problem. The analysis showed that more than half (56%) of total patients visited to cardiac OPDs of tertiary care center presented with chest pain as chief complain. These findings are consistent with the similar study conducted in rural areas of Sindh by Sial et al. in 2018 reported two-third (71.6%) of their patients who visited the cardiac emergency room having chest pain as chief complain[14]. Whereas, these findings are much higher and inconsistent with the findings of studies published in Pakistan (Paichadze e al. 2015), UK (Amsterdam et al 2010) and Europe (Groarke et al. 2013 and Martínez et al. 2008).These studies demonstrated the prevalence of chest pain patients in emergency units between 2.4 and 20%[15-18]. Age of patients is an important and always crucial determinant

of non-communicable diseases like Myocardial Infarction (M.I.) and other coronary artery diseases[19]. Incidence cardiac problems, GERD, Hypertension and Diabetes etc. increases with the increasing age[19]. Such increase in incidence of diseases in working age group may lead to increase in burden on economy of family and have negative impact on personal life[20].

In this study, more females (54%) visited the cardiac OPDs with complaints of chest pain comparison with the males (46%). These findings are consistent with those by Mourad et al. 2018 reported that 51% of their participants with NCCP were females[21]. Paichadze et al. 2015 and Sial et al. 2018 reporting the less women visitors in their study i.e. 39%, 40%, 39% respectively[14-15]. In the current study, we analyzed that most (29%) patients suffered from GERD and 6% from peptic ulcer for which they recently took treatment. Similar findings regarding causes of NCCP over the years identified by researchers. Among these causes GERD is found as the most common cause followed by esophageal hypersensitivity and dysmotility, musculoskeletal pain, MDD, and pericarditis by different studies of Paichadze et al. 2015, Achem et al. 2011 and Al-Ani et al. 2015[14,22].

CONCLUSION

Substantial numbers of patients were suffering from Non-cardiac chest pain (NCCP) among them female patients visited more than males, whereas majority of the patients were belonging to their middle age i.e. 39 to 48 years. Majority of patients were in their middle age i.e. 39 to 48 years.

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Original Article

Prevention and Control of Dengue Fever among Urban Population

Prevention and Control of Dengue Fever

Erum Ghani, Suhail Ahmed Bijarani, Muhammad Ilyas Siddiqui, Gulzar Usman, Wali Muhammad Nizamani and Sindhia Javed Junejo

ABSTRACT

Objective: To assess the perceptions of urban community about Dengue Fever and its preventive & control measures among the patients visiting OPD.

Study Design: Descriptive cross-sectional study

Place and Duration of Study: This study was conducted at the public sector secondary level health care facility Shah Bhittai Hospital Latifabad Hyderabad from January, 2020 to June 2020 for a period of six months.

Materials and Methods: A sample size of 308 was obtained and participants were selected by using non-probability purposive sampling technique and all the patients above 18 years of age of both gender, residing at urban area of district hyderabad, having fever visiting at outpatients department of Shah bhittai Hospital Hyderabad were included after getting the informed and written consent. Ethical approval was taken from the ethical committee of LUMHS, Jamshoro. The data was collected on a pre-tested structured questionnaire. We have used SPSS version 16.0 software for both data entering and analysis.

Results: A Total 308, participants, who fulfilled the inclusion criteria were included in this study. Out of them majority (82.5%) of participants were female while (17.5%) were males, whereas majority of the participants belongs to the lower class (73.4%) while 24.4% were having middle class economic status. A substantial number of responded (80%) heard and considered dengue fever as a serious illness.

Conclusion: There is satisfactory awareness and practices towards preventive measures against dengue fever while inadequate knowledge about cause, mode of transmission of dengue fever.

Key Words: Dengue, vector-borne, urban population

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INTRODUCTION

Dengue fever is a rapidly spreading vector-borne viral disease and an emerging public health problem with high morbidity and mortality worldwide and caused by the dengue virus (DENV) and transmitted to humans by the bite of infected female mosquito of specific species i.e.; Aedes aegypti and Aedes albopictus.[1] Which also acts as vector in transmitting yellow fever, zika infection and Chikungunya like serious diseases.[2]

Despite of adapting modern control measures of vector borne diseases there is dramatic increases in dengue infections, approximately 400 million cases reported yearly in which 500,000 become complicated and requires hospitalization while 25,000 died annually worldwide[3]. Ministry of health Pakistan declared the second high alert disease in the country. [4] In 2017 the largest outbreak of dengue fever were reported in Khyber Pakhtunkhuwa province in which a total of 24,807 dengue cases reported out of which 69 people loss their life.[5] Whereas in hyderabad, dengue outbreak took place in 2013 and 2016 in which 576 and 182 cases of dengue fever reported respectively.[6] According to WHO the number of dengue cases increased over eight fold during the last two decades, i.e. from 505,430 cases in 2000 to over 2.4 million in 2010 and in 2019 it reaches to 5.2 million cases, as well as increased in number of reported deaths from 960 in 2000 to 4032 in 2015.[7] Presently it is estimated that 50% population of the world are living in dengue epidemic area and are at risk of dengue arboviral diseases.[8-9] The presence of the enhancing factors for the spread of dengue fever such as, urbanization, population growth and lack of preventive measures pushing the country at the highest risk for the epidemic and outbreaks of the dengue fever.[10] A critical risk factor associated with the incidence of DF outbreaks is marshy land and built-up environment in urban areas in many countries like Malaysia and Thailand. [11-12] It has been observed from the available data that there is a major threat of this

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viral disease throughout the country that need to be considered and preventive measures should be taken timely so lives of the peoples can be saved.[13-14].

MATERIALS AND METHODS

A sample size of 308 was obtained and participants were selected by using Non-probability purposive sampling technique and all the patients above 18 years of age of both gender, residing at urban area of district hyderabad, having fever visiting during the study period (from January 2020 to June 2020) at outpatients department of Shah Bhittai Hospital Hyderabad were included after getting the informed and written consent. . Ethical approval was taken from the ethical committee of LUMHS, Jamshoro. The data was collected on a pre-tested structured questionnaire. We have used SPSS version 16.0 software for both data entering and analysis. Frequencies and standard deviations were calculated and categorical variable were analyzed using chi-square test. P-value of ≤0.05 was taken as statistically significant.

RESULTS

In this study a total 308 patients were included who presented with the complaint of fever during the data collection period at OPD of Shah Bhittai Hospital, Hyderabad and fulfilled the inclusion criteria. Regarding the socio-demographic status of the respondents were as, the majority (82.5%) of participants were female while (17.5%) were males, whereas majority (73.4%) of the participants belongs to the lower class while (24.4%) belongs to middle class while very few (2.2%) were having upper middle class economic status. Majority, (35.5%) of participants having only primary level education and 23.3% of them secondary level education while 24% were uneducated. Regarding the knowledge of dengue fever majority 248 (80.5) of the participants heard about dengue fever while 45 (19.5%) didn't heard. A substantial number of participants 262 (85.1) recognized dengue fever as a serious illness whereas 28 (9.0%) participants considered it as a non-serious health illness and 18(6.0%) respond don`t know. More than half 194 (62.2%) of the participants assumed that person suffering with DF can be treated at home while 90 (30%) answered no, whereas 90(30%) didn`t know about it. Regarding the breeding place for the mosquitoes 170(55.2%) of the respondents believe that water storage places are the main breeding places as shown in table 1.

Regarding the preventive measures against the dengue fever, it was observed that 160 (51.9) respondents were in favor of using of smoke to drive away mosquitoes while 88(28.5%) were not in favor of using smoke and 60(19.6%) choose don't know option. A substantial number of participants 122(38%) don't know that by tightly covering of water containers can reduce the mosquitoes while 107(34.7%) had knowledge and doing this practice at their homes. Other preventive measures practices use by the participants as, 265(86%) insecticide sprays, use of fans 185(60%),use of impregnated nets 191(62%), use of repellent cream 128(38.9), and mosquito mats/coils were used by 236(76.6) as a preventive measure from the mosquito bites as shown in table no: 2.

Most common signs and symptoms of dengue fever that respondents chosen fever which were 190(61.6%) while headache was 31(10%) and pain in bones and joints 49(16%).Majority of the participants had good knowledge regarding the sign & symptoms of dengue fever as, Fever 190(61.6%), pain in joints & bones 49 (15.9%) and headache 31 (10%) had been responded as the main sign & symptoms of the dengue fever respectively as shown in figure no:1.

Table No. 1: Knowledge about Dengue Fever

Variable	Frequency (%) Yes	Frequency (%) No	Frequency (%) Don`t Know
Heard About Dengue fever	248 (80.5)	45 (14.6)	15 (4.9)
Dengue fever is a serious illness	262 (85.1)	28 (9.1)	18 (5.8%)
Dengue fever can be treated at home	24 (7.8)	194 (63.0)	90 (29.2)
Occurrence mostly in monsoon rainy season	162 (52.6)	78 (25.3)	68 (22.1)
Extra Bushes	170 (55.2)	68 (22.1)	70 (22.7)
Fresh water	172 (55.8)	35 (11.4)	101 (32.8)
Increase breeding in Humidity and Hot climate	132 (42.9)	144 (46.8)	32 (10.4)

Table No. 2: Preventive measures against Dengue Fever

Variable	Frequency (%) Yes	Frequency (%) No	Frequency (%) Don`t Know
Use of smoke to drive away mosquitos	160	88	60
Covering of water containers	107	84	122
Use of insecticide spray	265	43	0
Use of fans to reduce mosquitoes	185	91	32
Use of impregnated nets	191	80	37
Use of mosquitoes repellent creams	128	160	20
Use of mosquitoes mats/coils	236	64	8
Covering of whole body with clothes	156	80	72
Cleaning of Garbage/Trash	191	47	70

Disposal of waste at proper place	262	0	46
Cleanliness around the houses reduces breeding of mosquitos.	268	0	40
Elimination of stagnant water	252	0	54

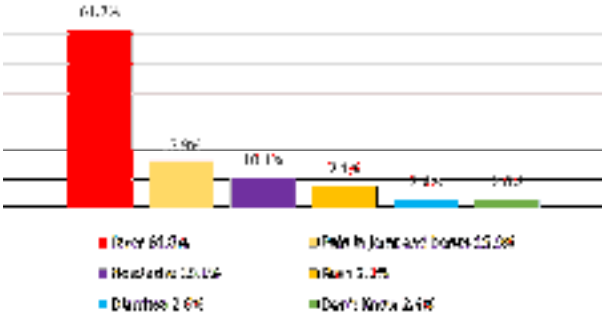

Figure No.1: Signs and symptoms of dengue fever

DISCUSSION

Our study which was conducted in the secondary level health care facility in the urban area of the district Hyderabad, Sindh, Pakistan. A total 308 participants visiting the facility and fulfil the inclusion criteria of study and gave the consent were included to assess the basic knowledge about the dengue fever and found that a substantial number of the participants possess basic information regarding the dengue fever and consider the illness to be a grave and follows approximately affordable preventive measures and pursuing treatments these findings are inconsistent with the study conducted in Tanzania. [15] Regarding the early symptoms of DF, majority of the participants identified Fever of more than two days accompanied with headache and or joint pain as main symptoms of the DF suggesting that the basic knowledge of the participants is satisfactory. Similar results were found in studies conducted in Vietnam and in patialia india.[16-17] Many respondents could not correctly identify typical symptoms of DF apart from fever and headache. Several respondents couldn't identified other symptoms of DF, similar findings were found in a study conducted in Nepal, [18] which might be due to low literacy rates. A substantial number of the respondents (80%) had heard about the DF though the mass media which proves that use of mass media for sharing the information regarding the major public health issue and for health education purpose. In the present study, two important sources of information were television i.e. 54.1 percent. In the present study the most important source of information were television 54.1 percent similar finding were reported in a study conducted in New Delhi, India by Chinnakali et.al.[19] In our study a majority of participants (83%) were believed that to control of mosquito borne diseases is the responsibility of government which is inconsistent to a study of Jamaica by Alobuia et al.[20 -21] Studies published also suggest that efforts to mobilize the communities are essential for the sustainability for the vector-borne diseases.[19-20-21] In our study only 3.8 percent of the respondents had received the information regarding the DG from the health care providers it could be due to overburden and lack of time in the OPDs it also indicate that there is need of mobilizing the healthcare providers for the importance of giving the health education to the patients visiting the health facilities. At present there is no specific treatment or vaccine for the DF, hence the backbone to control this vector-borne disease is adapting preventive measures at mass level such as, abolishing of breeding places, covering of water containers and use of nets, insecticide sprays and repellent creams to prevent mosquito bites.

CONCLUSION

The study concluded that, there were satisfactory knowledge and practices towards the preventive measures, however there were gaps in causes, mode of transmission of dengue fever.

Author's Contribution:

Concept & Design of Study:	Erum Ghani
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Knowledge of Bitewing Radiographs Among Faculty of Public Sector University Karachi, Pakistan

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ABSTRACT

Objective: To evaluate Knowledge of Bitewing Radiographs among faculty of public Sector University Karachi, Pakistan.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Jinnah Sindh Medical University (JSMU) and Jinnah Postgraduate Medical Center (JPMC), Karachi during June 2021.

Materials and Methods: A questionnaire-based survey was conducted with permission of JSMU Ethical Committee. A questionnaire was disseminated in faculty of the institute. The questionnaire included consent form, demographic details and questions related to bitewing radiographs. Data was analyzed using SPSS version 21.

Results: Total 73 complete responses were received and analyzed**.** Nearly one-third were attending specialization (n=23, 31.5%). All of the participants heard about bitewing radiograph. 41(56.2%) did not prescribe bitewing radiograph in their practice. Majority responded that occlusion radiograph and bitewing radiograph are not the same thing (n=67, 91.8%). Most of the participants were using periapical radiograph n=70, 95.9%) and few reported that were using bitewing (n=2, 2.7%) and occlusal radiograph (n=1, 1.4%).

Conclusion: Although dental practitioner had awareness of bitewing radiograph but it is particularly underutilized among practitioners at our institute for diagnosing dental caries. Therefore, trainings sessions should be could conducted to improve the clinical practices to establish appropriate diagnosis of dental caries and providing the timely management to patients.

Key Words: Dental caries, dental practitioner, bitewing radiograph, periapical radiograph, public sector hospital, Karachi, Pakistan.

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INTRODUCTION

One of the most frequently occurring oral disease caused by bacteria is dental caries [1]. American Dental Association classified dental caries as normal, initial, moderate or extensive based on the lesion severity [2]. It is well recognized that prompt diagnosis is essential for initiating effective management plans to increase the success chance and lessening the healthcare costs. This concept is also applies to oral diseases including dental caries. However, because of lacking in timely diagnosis, these lesions are mostly identified in late stages when restoring is the merely effective option [3].

The identification of proximal caries with proper and timely diagnosis is a challenging task for general dental practitioners in their routine practice [4, 5]. the diagnosis established with the correlation of clinical and imaging findings. In this context, radiography is the dentists' chief diagnostic support among various domains of dentistry which may establish diagnosis for intra and post-operative conditions for various dental procedures [6]. Disregarding the radiographs use shown the underestimation of dental caries, particularly in proximal and occlusal surfaces [7].

There are many modalities for detection of dental caries with each modality has its own limitations. The most frequently using technique for detecting caries is visual-tactile. Further non-invasive methods for early detection have been emerged and studied including Fibre-optic Transillumination (FOTI), DIAGNOdent (DD), Quantitative Light-induced Fluorescence (QLF) and Electrical Conductance (EC) [8]. Nevertheless, because of lacking in light dispersion, use in the clinical setting, and inadequate capacity of bacteriological

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byproducts, none of these techniques in their existing way are smart enough for early identification of caries. The Finnish Current Care Guidelines to manage dental caries delineate radiographic imaging as reasonable in kids even if caries lesion penetrates into dentin as identified through visual clinical evaluation. Radiographic imaging is also permissible even if there is a basis to suspect that there may be raised dental caries risk and radiographic images have not been taken in years [9].

Bitewing radiography is an imaging technique through which premolar, molars and alveolar bones are distinctly bilaterally appear on the radiograph. Radiographic imaging is done by inserting a receptor inside and corresponding to the dental arch next to the anticipated part, typically through a particular holder which benefits placing of the X-ray tube[10]. Since carious lesions are repeatedly existing on the proximal planes, it is suggested to carry out not only a visual and medical assessment but likewise prescribe bitewing X-rays [11].

It is documented that in a perfect clinical setting (with sufficient light, and hygienic and dehydrated teeth), clinical inspections conducted without adjunctive radiography have been observed to miscalculate the definite illness severity [12]. It was observed in China that clinical evaluation alone without bitewing radiograph caused the underrating of caries lesion nearly by 50% [13]. Since dental carries impose other serious complaints such as toothache, dental abscesses, loss of function, poor diet, and tooth loss and it is underestimated when radiographic evaluations are not used. Therefore, it is very necessary to ascertain its knowledge among our local dental practitioners.

MATERIALS AND METHODS

This cross-sectional survey was performed at Sindh institute of Oral Health Sciences, Jinnah Sindh Medical University, Karachi during the month of June 2021 with acquiescence of hospital ethics committee. The survey included all of dental faculty and general dental practitioner working at the institute. Survey participants who were not giving consent to participate were excluded from the study. The written consent was gained from the participants which was the first component of the survey questionnaire.

A questionnaire distributed to all of the targeted population of the institutes. Reminders were sent to participants who did not respond and their responses was expected within a week and this way the link of the survey was closed when all of the participants responded within one week of the reminders. The first part of the questionnaire was consent form those who were filling were suggested to fill out the survey further. Second component included demographic such as dental specialization, years of practicing. Third part included questions related to their practice of prescribing bitewing radiographs and their perceptions regarding bitewing radiographs. In fourth part, their preference for using bitewing radiograph in different dental conditions was determined. The questionnaire is attached as supplementary material.

The collected data was imported to SPSS version 21 for statistical analysis. Categorical data was summarized as frequency and percentages whereas mean ± standard deviation was calculated to present continuous variables. Appropriate tables and graphical representation was used to present the data.

RESULTS

Total 73 complete responses were received and analyzed. Nearly one-third were attending specialization (n=23, 31.5%). 19(26%) had no specialization. Among 54(39.7%) participants who had specialization or attending specialization, most of them had specialist of operative dentistry (n=28, 51.9%) followed by maxillofacial surgery (n=7, 13%), ortho (n=6, 11.1%), basic science (n=6, 11.1%), prosthodontics? (n=4, 7.4%), periodontics (n=3, 5.6%). Majority had experience of less than 5 years (n=31, 42.5%) whereas some people also had experience of 5-9 years (n=26, 35.6%), 10-19 years (n=14, 19.2%) and ≥20 years (n=2, 2.7%).

Figure 1 shows the frequency of doctors who had practice of prescribing bitewing radiographs. Among 32 (43.8%) who reported that they prescribe it to their patients, 19(59.4%), 12(37.5%), and 1(3.1%) were prescribing several times a year, month and week respectively. In response of question, do they think that occlusion radiograph and bitewing radiograph are same thing, most of them said they did not think so (n=67, 91.8%). Most of the participants were using periapical radiograph n=70, 95.9%) and few reported that they were using bitewing (n=2, 2.7%) and occlusal radiograph (n=1, 1.4%).

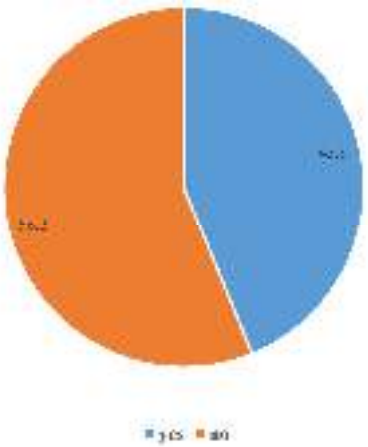

Figure No.1: Proportions of participants prescribing bitewing radiographs to patients in their practice

Survey respondents reported that they were using radiographs because of the following reasons; their

expertise in interpreting it (n=4, 5.5%), personal preferences (n=15, 20.5%), clarity in diagnosing (n=25, 34.2%), assistant training (n=1, 1.4%) and ease of availability (n=21, 28.8%). Table 1 shows their level of preference of using bitewing radiograph versus periapical radiograph for the different dental defects.

Table No.1: Dental practitioner preference of prescribing bitewing radiograph over periapical radiograph

Dental conditions	Least preferred	Slightly preferred	Neutral	Preferred	Most preferred
Vertical bone loss	28(38.4)	20(27.4)	9(12.3)	7(9.6)	9(12.3)
Horizontal bone loss	11(15.1)	17(23.3)	13(17.8)	14(19.2)	18(24.7)
Occlusal carries	18(24.7)	7(9.6)	6(8.2)	19(26)	23(31.5)
Proximal carries	1(1.4)	4(5.5)	7(9.6)	10(13.7)	51(69.9)
Overhang restoration	5(6.8)	3(4.1)	9(12.3)	14(19.2)	42(57.5)
Foreign body impaction	15(20.5)	6(8.2)	25(34.2)	8(11)	19(26)
Calculus	30(41.1)	11(15.1)	5(6.8)	11(15.1)	16(21.9)
Apical periodontitis	45(61.6)	11(15.1)	7(9.6)	3(4.1)	7(9.6)

DISCUSSION

Dental radiography is the primary part of understanding process of mass fatality events. It provides unbiased indication of the dentition formerly and subsequently death. Radiographs are a beneficial instrument for dental practitioners for a range of purposes including diagnosing caries for evaluating bone loss in periodontal disease. Radiographs may be tremendously beneficial throughout the dental management of a patient as the job of identifying caries is chief work of a dentist. Establishing a diagnosis of caries relies on a combination of detailed clinical investigation and the practice of different tests, the commonest of which is bitewing radiography.

It is not possible to underrate the radiographs utilization, particularly bitewings, for the identification of caries (specifically in kids). According to the Faculty of General Dental Practice (FGDP), bitewings are a crucial aids for clinical evaluation [14]. This kind of narrative emphasizes the radiographs significance for caries recognition and consequently the concern of subsequent reporting and disease evaluation.

In the present study, nearly half of the participants (43.2%) reported that they prescribe bitewing radiograph in their practice. However, another Pakistani survey conducted among dental practitioner reported that 96.4% of the practicing dentist had x-ray unit in their working institute/clinic [15]. It is quite alarming to conclude that there is underutilization of bitewing radiographs in our local settings. On the other hand, an international survey reported that 79.4% of the participated dentist were using digital radiological imaging[16]. A cross-sectional study performed in Norway to reveal the diagnostic value of the bitewing radiograph demonstrated that in 90% of the cases bitewings are consistently advised with a clinical checkup[17]. However, some studies have interrogated whether consuming radiographs for increasing the sensitivity of visual inspection have concurrently lessen its specificity and presented numerous cases of false positives, leading to an overestimation of caries and consequently overtreatment [18, 19].

Periapical method offers complementary evidences at a comparatively small price and radiation dosage. Each periapical X-ray displays all teeth in single portion of either the upper or lower jaw. Periapical X-rays discover any rare variations in the root and nearby bone structures. However, in spite of its extensive use, it is unable to portray the compound anatomic outline of teeth as image overlapping inherent to conventional 2-dimensional radiography [20]. On other hand, bitewing illustrates a tooth from its crown to the level of the backup bone. Bitewing radiography identify deterioration in between of teeth and alterations in bone thickness occurred because of gum problems. Bitewing X-rays may also aid in determining the appropriate fitting of a crown or further restorations. It may comprehend any wear or breakdown of dental fillings as well. It was reported observer performance was greatest with intraoral bitewing use for making diagnosis of interproximal caries [20, 21].

In our study, majority of respondents were using periapical (95.9%). Awareness level of dentist was investigated in a survey conducted in Tanzania which reported that the periapical X-ray was suggested for 65.5% patients, 28.9% were advised for orthopantomograms and 5.6% remaining was advised for both OPG and periapical X-rays[22]. However, a study was performed to compare accuracy of bitewing and periapical methods for early diagnosis of interproximal caries keeping consensus reference as gold standard and it was observed that bitewing showed a meaningfully higher sensitivity than periapicals for all stages of caries. Positive-predictive value and negative-predictive value of bitewing were also considerably higher than periapical and hence it was concluded that bitewings offer a substantial benefit over periapical for establishing early diagnosis of interproximal carious lesions [23].

In this survey, most of the faculty reported that they were using radiographs for clarity in diagnosis (34.2%), ease of availability (28.8%) and personal preferences (20.5%). A survey from Tanzania reported that dentists were using imaging X-rays because they felt it was a great aid for confirming the diagnosis (37.9%), diagnosis and management could be more accurate

(35.4%) and it was part of patients' management (16.1%). 22.7% also reported that dental x-rays could also play part in knowing the patients' age [22]. It was revealed in a cross-sectional survey conducted in Sweden that dentists were preferring digital radiographs due to following reasons; image processing (87%), improved image quality (66%), improved communication with patient (86%), improved diagnosis (74%), ease of work (91%) and lesser radiation dose is required (85%) [24].

The present study shows a single center experience of a public sector institute which may not generalized to all dental practitioners in Pakistan. Moreover, the study was descriptive in nature so possible factors associated with practice of prescribing the bitewing radiographs were not assessed. The studies also did not uncover the barriers which stop dental practitioner to prescribe the radiographs. To reveal the basic knowledge of bitewing and practices of prescribing it among Pakistani dentist, we prose a future nation-wide survey with larger sample size.

CONCLUSION

Although dental practitioner had awareness of bitewing radiograph but it is particularly underutilized among practitioners at our institute for diagnosing dental caries. Therefore, trainings sessions should be could conducted to improve the clinical practices to establish appropriate diagnosis of dental caries and providing the timely management to patients.

Author's Contribution:

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

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Original Article

Comparison of Efficacy of Lisinopril and Losartan for Reducing Microalbuminuria Levels in Patients with Type-2 Diabetes Mellitus

Roney Javed, Suresh Kumar, Naresh Kumar Khurana, Anil Kumar, Asma Hameed and Naeem Khan Durrani

ABSTRACT

Objective: To compare the efficacy of losartan and lisinopril for reduction of microalbuminuria in patients with type-2 diabetes mellitus.

Study Design: Randomized Control Trial study

Place and Duration of Study: This study was conducted at the Department of Medicine, Bolan Medical Complex Hospital, Quetta, Pakistan from July 2019 to January 2020.

Materials and Methods: A total of 110 with diagnosed type II diabetes mellitus and albumin to creatinine ratio 30–300 mcg/mg creatinine in the 1st early morning urine, age 18-75 of both genders were included. Patients with hypersensitivity to ACE inhibitors or Angiotensin Receptor Blocker, CRF, pregnancy and uncontrolled hypertension were excluded. All the patients were randomly divided into two groups by the lottery method. Group A was treated with 100 mg of Losartan potassium for 12 weeks while Group B patients were given 5 mg of Lisinopril for 12 weeks.

Results: The mean age of patients in group A was 39.60 ± 10.12 years and in group B was 41.0 ± 8.05 years. Majority of the patients 56 (50.91%) were between 18 to 45 years of age. Out of 110 patients, 47 (42.78%) were males and 63 (57.27%) were females with male to female ratio of 1:1.3. Efficacy of Group A (losartan group) was seen in 48 (87.27%) patients while in Group B (lisinopril group) was seen in 37 (67.27%) patients (p-value = 0.012)

Conclusion: This study concluded that efficacy of losartan is higher than lisinopril for reduction of microalbuminuria in patients with type-2 diabetes mellitus.

Key Words: type II diabetes, microalbuminuria, losartan

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INTRODUCTION

Diabetes mellitus (DM) is a growing public health concern with multiple complications, affecting more than 415 million individuals around the globe and expected to reach 642 million individuals by end of 2040 [1-2]. Past examinations detailed the predominance of DM in Pakistan going from 7.6% to 11% and assessed to reach 15% of absolute populace by 2030 [3]. Different miniature and full-scale vascular inconveniences are related with sickness movement particularly diabetic nephropathy (DN) that outcomes from the durable impacts of DM on the glomerular microvasculature of the kidney [4]. Around 30-40% of type II diabetic patients foster DN notwithstanding severe blood glucose and additionally circulatory strain control [5]. The principal markers of DN are constant albuminuria, hypertension, and reformist renal harm[6,7]. Angiotensin changing over compound (ACE) inhibitors e.g., lisinopril seriously block the renin angiotensin framework, and decrease the glomerular slender strain and turn away improvement of microalbuminuria to plain proteinuria. Some different examinations likewise detailed a practically identical beneficial effect of angiotensin II receptor blockers (ARB) e.g., losartan in relapse of microalbuminuria to unmistakable proteinuria [8]. In a new report, Sandhu GA et al thought about the adequacy of ACE inhibitor (Lisinopril) and ARB (Losartan Potassium) as far as decrease in microalbuminuria in Type II DM patients. Viability of medication was seen in 86.7% patients (n=26) in Losartan potassium bunch while 66.7% patients (n=20) in lisinopril bunch [9].

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DN builds the danger for sudden passing, cardiovascular infection, and other serious diseases that outcome in continuous hospitalizations and expanded health-care use. Decrease in microalbuminuria is a significant prognostic factor in the administration of DN [10]. Another metanalysis reasoned that ACEIs and ARBs are likewise compelling for treating microalbuminuria[11]. Thus, in view of as of late distributed writing, both are regularly utilized in our setting for treating raised microalbuminuria, however as far as I could possibly know, no review has done that thought about the viability of these medications for treatment of microalbuminuria in Type II DM patients of our populace. The reasoning of this review is to analyze the impacts of ACE inhibitors and ARBs on microalbuminuria in Type II DM patients. The review results will assist with deciding the better treatment choice for treating microalbuminuria in patients with DN and will be utilized as medication of decision for the treatment of these patients in future.

Better treatment option will ultimately help to reduce morbidity and mortality associated with diabetic nephropathy.

MATERIALS AND METHODS

Study design: This Randomized Control Trial was conducted in Department of Medicine, Bolan Medical Complex Hospital, Quetta during 20th July 2019 to 21st January 2020.

Sample size: The sample size was calculated using the WHO Sample Size Calculator:

Sample Size: Eighty patients n=110 (55 patients in each group).

Sample technique: Non-probability, consecutive sampling.

Sample selection:

Inclusion Criteria:

a. Patients with diagnosed type II diabetes mellitus and albumin to creatinine ratio 30–300 mcg/mg creatinine in the 1st early morning urine as described in operational definition
b. Age between 18 to 75 years.
c. Both Genders

Exclusion Criteria:

a. Patients with chronic heart failure
b. Pregnant and lactating female
c. Patients with known hypersensitivity to ACE inhibitors or Angiotensin Receptor Blocker
d. Patients with uncontrolled hypertension.
e. Patients who are being treated with any investigational drug within the last 30 days.

Data collection procedure: Study was started after taking prior approval and permission from the hospital ethical committee. Blood sample of all the patients diagnosed with DM type-2 presented to the hospital were taken and sent to laboratory for performing fasting blood glucose and 1st morning Urine sample was taken and analyzed for albumin to creatinine ratio of these patients. Patients with type II DM and microalbuminuria as defined in operational definition and fulfilling the other inclusion criteria were enrolled for study. By taking informed written consent from all the patient, the thorough physical examination was performed after taking detailed clinical history. All the patients were randomly divided into two groups by the lottery method. Group A was treated with 100 mg of Losartan potassium for 12 weeks while Group B patients were given 5 mg of Lisinopril for 12 weeks. After 12 weeks therapy the efficacy of the drug was determined in both groups as per our operational definition. For this purpose, albumin to creatinine ratio was determined from the hospital laboratory by analysis of 1st early morning urine after 12 weeks of treatment. All the data collection was performed by the trainee researcher himself to main data quality and compliance and study results were recorded in the prescribed proforma attached as annexure I.

Data analysis procedure: Data was entered and analyzed on SPSS version 20.0. Frequency and percentages were computed for qualitative variable like gender and efficacy among two groups. Quantitative variables like Age, fasting blood glucose level, height, weight, BMI & baseline albumin to creatinine ratio (microalbuminuria) and at 12-week therapy were presented by mean and standard deviation. Chi square test was used to compare the efficacy of both groups. P value ≤ 0.05 was considered significant.

RESULTS

The age range of patients in this research was from 18-75 years. The mean age of patients was 40.35 ± 8.65 years. In group A the mean age of patients was 39.60 ± 10.12 years and in group B was 41.0 ± 8.05 years. As shown in Table I, most of the patients were between 18 to 45 years of age and number of patients were 56 (50.91%).

There were 110 total patients and out of those 110 patients, the number of males patients were 47 (42.78%) and number of females patients were 63 (57.27%), the male to female ratio were 1:1.3. As shown in Table 2, the mean BMI was 29.12 ± 3.41 kg/m^2. Mean height was 165.86 ± 14.76 cm. Mean weight was 75.63 ± 8.35 cm. Most of the patients 64 (58.12%) were with the BMI of ≤ 30 kg/m^2.

Efficacy of Group A (losartan group) was seen in 48 (87.27%) patients while in Group B (lisinopril group) was seen in 37 (67.27%) patients (p-value = 0.012).

Stratification of efficacy with respect to age groups is shown in Table 3. The P-value of patients with the age group of 28-45 years was 0.350 and 46-75 years was 0.021. Results showed that the age group of 28-45 years showed more positive results compared to the other age group in both group A and Group B. The number of patients in both group A and B was 55.

Table No.1: Age distribution for both groups (n=110)

Age (years)	Group A (n=55)		Group B (n=55)		Total (n=110)	
	No. of patients	%age	No. of patients	%age	No. of patients	%age
18-45	37	67.27	39	70.91	56	50.91
45-75	18	32.78	16	29.09	34	49.09
Mean ± SD	39.60 ± 10.12		41.0 ± 8.05		40.35 ± 8.65	

Table No.2: Percentage of patients according to BMI (n=110)

BMI	Group A (n=55)		Group B (n=55)		Total (n=110)	
	No. of patients	%age	No. of patients	%age	No. of patients	%age
≤30 kg/m^2	32	58.18	32	58.18	64	58.12
>30 kg/m^2	23	41.82	23	41.82	46	41.82
Mean ± SD	29.15 ± 3.42		29.05 ± 3.34		29.12 ± 3.41	

Table No.3: Stratification of efficacy with respect to age groups

Age of patients (years)	Group A (n=55)		Group B (n=55)		P-value
	Efficacy		Efficacy		
	yes	no	yes	no	
28-45	31	06	27	12	0.350
46-75	17	01	10	06	0.021

Table No.4: Stratification of efficacy with respect to gender

Gender	Group A (n=55)		Group B (n=55)		P-value
	Efficacy		Efficacy		
	yes	no	yes	no	
Male	22	02	15	08	0.027
Female	26	05	22	10	0.159

Table No.5: Stratification of efficacy with respect to BMI

BMI	Group A (n=55)		Group B (n=55)		P-value
	Efficacy		Efficacy		
	yes	no	yes	no	
≤30 kg/m^2	29	03	23	09	0.055
>30 kg/m^2	19	04	13	09	0.082

Stratification of efficacy with respect to age groups and gender is shown in Table 4. The P-value of the gender male was 0.027 and female was 0.159. Female showed more positive results than male in both Group A and group B. The number of patients in both groups were 55.

In Table 5 the stratification of efficacy showed with respect to BMI. The P-value of BMI ≤30 kg/m^2 was 0.055 and the number of patients in group A was 55 and group B was also 55. The number of yes efficacies in those patients in group A was 29 and in group B, it was 23 and the negative numbers were 3 and 9, respectively. The P-value of BMI >30 kg/m^2 was 0.082. The number of yes efficacies in those patients in group A was 19 and in group B, it was 13 and the negative numbers were 4 and 9, respectively.

DISCUSSION

The risk for cardiovascular and renal disease increases in type II diabetes after the growth of microalbuminuria[12-14]. In type II diabetes the prevalence rate of renal disease (end-stage) has increased in many areas globally [15,16]. According to recent studies, for the protection of renal and possibly cardio protection, the main treatment goal is the regularization and reduction of proteinuria [17]. In the diabetic animal model, the inhibition of (RAS) renin-angiotensin system (by ACE inhibitors or (AIIAs) angiotensin II antagonists) prevents the growth of proteinuria or lowers the level of proteinuria which results in less damage of renal structure [18,19]. ACE inhibitor therapy reduces the albumin excretion rate (UAER) in type II diabetic patients with microalbuminuria, and as determined by serum creatinine, it also prevents the growth and development of renal disease [20]. AIIAs selectively block the AT1 receptor which reduces microalbuminuria in these patients to the same level as ACE inhibition [21].

I have conducted this study to compare the efficacy of losartan and lisinopril for reduction of microalbuminuria in patients with type-2 diabetes mellitus. Age range in this study was from 18-75 years with mean age of 40.35 ± 8.65 years. In group A the mean age of patients was 39.60 ± 10.12 years and in group B was 41.0 ± 8.05 years. Majority of the patients 56 (50.91%) were between 18 to 45 years of age. Out of

110 patients, 47 (42.78%) were males and 63 (57.27%) were females, with male to female ratio of 1:1.3. Efficacy of Group A (losartan group) was seen in 48 (87.27%) patients while in Group B (lisinopril group) was seen in 37 (67.27%) patients (p-value = 0.012). In a recent study, Sandhu GA et al compared the efficacy of ACE inhibitor (Lisinopril) and ARB (Losartan Potassium) in terms of reduction in microalbuminuria in Type II DM patients. Their study results showed that mean microalbuminuria levels (mcg/ mg) at 12 weeks of study was reduced from 193±67.5 to 36.33±54.68 in Losartan potassium group and from 209.5±72.0 to 72±83.42 in lisinopril group. Efficacy of drug was observed in 86.7% patients (n=26) in Losartan potassium group while 66.7% patients (n=20) in lisinopril group [(9)].

In patients with type II diabetes, the effect of Reno protective on ARB and ACE inhibitors were studied and, in a study, done by Barnett AH, 250 individuals with type II diabetes and initial stage of nephropathy were casually assigned to receive either the ARB telmisartan, in 120 patients (80 mg/d) or the ACE inhibitor enalapril, in 130 patients (20 mg/d). The main endpoint was the difference in the (GFR) Glomerular filtration rate amongst the standard value and the last obtainable value throughout the five (5) years therapy period. GFR reduced after five (5) years with telmisartan by 17.9 ml per minute, per 1.73 m2 of surface region of body and with enalapril by 14.9 ml per minute, per 1.73 m2, with a therapy difference of 3.0 ml per min, per 1.73 m2. In type II diabetic patients this difference was not sufficient (based on predefined criteria) to conclude that telmisartan is better than enalapril in offering long term renoprotection. For decrease in BP in such patients, combination of lisinopril and candesartan was more effective than monotherapy and the similar trend was evident for the decrease in rate of urinary albumin excretion [(22)].

CONCLUSION

This study concluded that efficacy of losartan is higher than lisinopril for reduction of microalbuminuria in patients with type-2 diabetes mellitus. Majority of the patients 56 (50.91%) were between 18 to 45 years of age. Out of 110 patients, 47 (42.78%) were males and 63 (57.27%) were females.

Author's Contribution:

Concept & Design of Study:	Roney Javed
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Revisiting Critically:	Roney Javed, Suresh Kumar
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Impact of Malocclusion on Oral Health Related Quality of Life in Young People

Sadia Nisar Ahmed[1], Ariffullah Khan[2], Reham Zaman[3], Farid Ullah[4], Muhammad Naeem[2] and Nazish Falak[1]

ABSTRACT

Objective: To evaluate the self-assessment dental look pleasure among youngsters.
Study Design: Questionnaire based descriptive cross-sectional study.
Place and Duration of Study: This study was conducted at the Department of Orthodontics at Bacha Khan College of Dentistry Mardan from 15th July 2021 to 18th October 2021.
Materials and Methods: This study was conducted on patients in aged 15 to 25 years who wants orthodontic treatment. Data was analyzed using SPSS-22. Mean±SD, frequencies, and percentages were calculated. Chi-square and t-tests were applied as per necessity of data, and $p \leq 0.05$ was measured as significant.
Results: A total 217 (72.3%) sample size had good psychological well-being regarding their dental aesthetic appearance whereas 60 (20%) had satisfactory and 23 (7.7%) had poor psychological well-being regarding their dental appearance respectively.
Conclusion: More than half of the total sample voiced desire with their dental aesthetic. Male patients were more pleased as compared to female patients, which is obviously due to the nature, thinking and misconception of our society that only those will have groom/bride who have beautiful looks.

Key Words: Dental appearance satisfaction, Oral subjective Impact Scale (OASIS), Self-assessment, Oral Health-Related Quality of Life (OHRQoL)

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INTRODUCTION

The conception of Oral Health-Related Quality of Life (OHRQoL) parallels to the effect of dental condition or disease of a person's daily comfort, working or overall quality of life (QoL).[1] The concept of OHRQoL practices patient focused consequence events to recognize the effect of oral health on features of everyday life in terms of a person's efficient, social, and emotional well-being.[2] Factors influencing dental health, counting malocclusion, are vastly dominant, and have significances not only for economic and physical comfort, but can also affect QoL by disturbing appearance, interpersonal relationships, function, self-confidence, socializing and psychological well-being.[3]
Studies on social, physical and psychological effect of malocclusion on OHRQoL explain the impacts of malocclusion on commons and offers a better indulgent of the claim for orthodontic management outside the dimension of scientific limitations. Furthermore, since psychological and social impacts are usually the main reasons for pursuing orthodontic treatment, OHRQoL can be measured the best dimension for orthodontic management requirement and consequence.[3] Such study may be of great value to health planners, oral health care providers and researchers.[4] Malocclusion varies from the common dental circumstances in that it is "a set of dental deviations" somewhat than a illness, and orthodontic treatment does not remedy a disorder but somewhat modifies disparities from an uninformed model. [5]Malocclusion can be alleged otherwise by the person pretentious, and a person's point of knowledge about their malocclusion might not be associated to its condition of sternness.[4]
Hence, once assessing the effect of a malocclusion, it is vital to reflect the unlike fields that may be overdone and their associations to the intensity of malocclusion. Few folks with a Spartan malocclusion are pleased with or are having no problems regarding to their dental esthetics, while others may be anxious regarding slight anomalies in their occlussion.[3] Essential valuation for orthodontic management is conventionally evaluated by means of tools such as the Oral Aesthetic Subjective Impact Scale (OASIS). [3, 6] Preceding investigations finding the association between malocclusions and OHRQoL, as well as the influence of orthodontic treatment on OHRQOL has been vague. Few

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researchers found a robust association among orthodontic treatment need or malocclusion and OHRQoL[7-9], but others stated no strong association.[4, 10, 11]

This current study was carried out to evaluate OHRQoL in youngsters aged 15 to 25 years who wants orthodontic treatment visiting Bacha Khan College of Dentistry, Mardan and to measure the association between orthodontic treatment need, gender, age and education level, and OHRQoL.

MATERIALS AND METHODS

A questionnaire based descriptive cross-sectional study was conducted among 300 young adults aged 15 to 25 years; appearing at department of orthodontic. Participants completed the OASIS questionnaire. Ethical approval for the study was taken from the Institutional Review Board of Bacha Khan College of Dentistry, Mardan.

Exclusion Criteria: Students with history of jaw trauma or those who are receiving orthodontic treatment and those who have received orthodontic treatment were excluded from the study.

Questionnaire and Data Analysis: The Oral Aesthetic Subjective Impact Scale (OASIS)[12] is a new self-assessment tool which has been used to amount the observant orthodontic treatment requirement. It is a consumer grounded scale, built on a socio-psychological effect of dental appearance. This scale measures the influence of exterior impacts by asking queries about their sensitivities of others and themselves, as well as about their former behavior associated to the presence of their dental aesthetic.[12] The OASIS is composed of five inquiries addressing worries and self-assessment of dental aesthetic look, and how dental anomalies harmfully distress person's life and the social relationship. Each asked question is scored on a 1 to 5 Likert scale. Five questions were asked from each student and according to their answers scoring was compiled. Total score was a sum of all five items, ranging between 5 and 25. A score of 16 or above indicated severely psychologically affected patient. Score between 5 and 10 was consider as good, 11–15 as satisfactory and 16–25 as poor psychological well-being respectively. The data was entered and analyzed using SPSS-22. Chi-square test was applied to compare psychological well-being in both genders.

RESULTS

Among the 300 subjects, 92 (30.7) were males and 208 (69.3) were females. Mean age was 21±1.45 years; 41 (13.7%) were 15 years, 32 (10.7%) were 16 years, 91 (30.3%) were 17 years, 24 (8%) were 18 years, 12 (4%) were 19 years, 17 (5.7%) were 20 years, 11 (3.7%) were 21 years, 19 (6.3%) were 22 years, 23 (7.6) were 23 years, 21 (7%) were 24 years and 9 (3%) were 25 years old respectively (Table 1).

Table No.1: Age and gender distribution [n (%)]

Mean+SD 21+1.30				
Age		Male	Female	Total
	15	7 (7.6)	34 (16.34)	41 (13.7)
	16	10 (10.9)	22 (10.57)	32 (10.7)
	17	12 (13.04)	79 (37.98)	91 (30.3)
	18	9 (9.7)	15 (7.21)	24 (8)
	19	11 (11.9)	1 (0.48)	12 (4)
	20	8 (8.7)	11 (5.3)	17 (5.7)
	21	8 (8.7)	3 (1.44)	11 (3.7)
	22	6 (6.5)	13 (6.25)	19 (6.3)
	23	9 (9.7)	14 (6.73)	23 (7.6)
	24	10 (10.9)	11 (5.3)	21 (7)
	25	2 (2.17)	7 (3.36)	9(3)
	Total	92 (100)	208 (100)	300 (100)

A total 217 (72.3%) sample size opted good psychological well-being concerning their dental aesthetic look whereas 60 (20%) had satisfactory and 23(7.7%) had poor psychological well-being concerning their dental look respectively (Table 2).

Table No.2: Distribution of OASIS

OASIS Categories		Frequency	Percent
	Good	217	72.30
	Satisfactory	60	20.00
	Poor	23	7.70
	Total	300	100.0

A total of 145 (69.71%) sample size had good psychological well-being concerning their dental look and thought that they don't need orthodontic treatment while 51 (24.51%) and 12 (5.77%) sample size had satisfactory and poor psychological well-being, they wanted to have orthodontic treatment. Whereas, 72 (78.27%) male students had good psychological well-being concerning their dental look thought that they don't need orthodontic treatment while 9 (9.8%) and 11 (11.95%) male students had satisfactory and poor psychological well-being concerning their dental look, they wanted to have orthodontic treatment (Table 3).

Table No.3: Gender-wise distribution of Oral Aesthetic Subjective Impact Scale (OASIS) in participants

Gender	OASIS Categories			Total	P value
	Good N (%)	Satisfactory N (%)	Poor N (%)	N (%)	
Female	145 (69.71)	51 (24.51)	12 (5.77)	208 (100)	<0.01
Male	72 (78.27)	9 (9.8)	11 (11.95)	92 (100)	
Total	217 (72.3)	60 (20)	23 (7.70)	300 (100)	

DISCUSSION

Self-evaluated dental appearance is gradually receiving consideration since of its suggestion in dental care and patient-oriented healthcare delivery preferred growth.[13] The OASIS is based on a Likert scale which is believed to place limited cognitive stresses on the respondent.[14] Though primarily established for use in children, has been used in a number of adult studies.[15] Self-assessment dental aesthetic presence is gradually receiving care because of its inference in dental care and patient-oriented healthcare distribution preferred growth.[16]

In the current study more than half (72.3%) of the students stated Good response concerning their dental aesthetics, similar to the study piloted by Naveh GR et al[17] among dental patients in Israel (62.7%) with sample size of 407 adults aged above 21 years, Akarslan et al[18] reported from Turkey (57.3%) and Tin et alq[19] observation among Malaysian adults (47.2%). Findings of the current study were higher than by Meng et al[20] findings among varied sample of adults in Florida, Alkhatib et al[21] observation among age group of 16–34 years in United Kingdom, and Hamamci et al[23] report from Turkish University students.

Interestingly male patients were little more concern about their dental appearance against the study conducted by Khan et al[22] conducted on students of government high schools children aged 13-17. It may be due to the aged difference as at low age looks doesn't matter the most for adolescents, and they are mostly busy in their own world.

CONCLUSION

More than half of the total sample voiced desire with their dental aesthetic. Male patients were more pleased as compared to female patients, which is obviously due to the nature, thinking and misconception of our society that only those will have groom/bride who have beautiful looks. The result suggest for a well-trained psychiatrist should be hired in every school/colleges to have a lecture with young generation and should be encourage to speak about their thinking and deficiencies they feel in themselves.

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