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Editorial

HIV / AIDS Control and its Prevention

Mohsin Masud Jan
Editor

HIV/AIDS remains a major public health issue that affects millions of people worldwide. The Human Immunodeficiency Virus (HIV) targets the immune system and weakens people's defence against many infections and some types of cancer that people with healthy immune systems can fight off. As the virus destroys and impairs the function of immune cells, infected individuals gradually become immune-deficient. Immune function is typically measured by CD4 cell count.

The symptoms of HIV vary depending on the stage of infection. The initial period is called acute HIV. People living with HIV tend to be most infectious in the first few months after being infected. In the first few weeks after the initial infection, people may experience no symptoms or an influenza-like illness, including fever, headache, tiredness, sore throat, large tender lymph nodes, a rash on the trunk. As the infection progressively weakens the immune system, they can develop other signs and symptoms, such as weight loss, fever, diarrhoea and cough. Without treatment, they could also develop severe illnesses such as tuberculosis (TB), meningitis, severe bacterial infections and cancers such as lymphomas and Kaposi's sarcoma.

The initial symptoms are followed by a stage called chronic HIV. Without treatment, this second stage can last from about three years to over 20 years (average, eight years). Typically, there are few or no symptoms at first. However, many people experience fever, weight loss, gastrointestinal problems, and muscle pains near the end of this stage. Between 50 percent and 70 percent of people also develop persistent generalised lymphadenopathy, characterised by unexplained, non-painful enlargement of more than one group of lymph nodes for over three to six months.

In the absence of treatment, an HIV infection will eventually progress to AIDS. The most advanced stage of HIV infection is acquired immunodeficiency syndrome (AIDS), which can take many years to develop if not treated. The most common initial conditions that alert people to the presence of AIDS are pneumocystis pneumonia, cachexia in the form of HIV wasting syndrome, and oesophagal candidiasis. Other common signs include recurrent respiratory tract infections.

Additionally, people with AIDS frequently have systemic symptoms such as prolonged fevers, sweats (particularly at night), swollen lymph nodes, chills, weakness and unintended weight loss. Diarrhoea is another common symptom, present in about 90 percent of people with AIDS. They can also be affected by diverse psychiatric and neurological symptoms independent of opportunistic infections and cancers.

It spreads by three main routes: sexual contact with an infected individual, significant exposure to infected body fluids or tissues such as blood and blood products, semen, and other genital secretions, or breast milk, and from mother to child during pregnancy, delivery or breastfeeding. HIV frequently spreads among intravenous drug users who share needles or syringes. There is no risk of acquiring HIV if exposed to faeces, nasal secretions, saliva, sputum, sweat, tears, urine, or vomit unless these are contaminated with blood.

HIV does not spread by coughing, sneezing, or casual contact (*e.g.*, shaking hands). HIV is fragile and cannot survive long outside the body. Therefore, direct transfer of bodily fluids is required for transmission.

Preventive measures include safe sex, needle exchange programmes, treating those who are infected, as well as both pre-and post-exposure prophylaxis. Disease in a baby can often be prevented by giving both the mother and child antiretroviral medication. Attempts to reduce intravenous drug use and to discourage the sharing of needles led to a reduction in infection rates.

Antiretroviral therapy represents an important prevention strategy. Research has indicated that pre-exposure prophylaxis, in which uninfected persons take an antiretroviral pill daily, can effectively prevent infection.

There is currently no cure. Treatment consists of highly active antiretroviral therapy (HAART), which slows the progression of the disease. Treatment also includes preventive and active treatment of opportunistic infections. Rapid initiation of antiretroviral therapy (within one week of diagnosis) appears to improve treatment outcomes. Once treatment is begun, it is recommended that it is continued without a break.

The WHO has recommended that all people living with HIV be provided with lifelong ART. This included children, adolescents, adults and pregnant and breastfeeding women, regardless of clinical status or CD4 cell count.

The benefits of treatment include a decreased risk of progression to AIDS and a decreased risk of death. Treatment also improves physical and mental health. With treatment, there is a 70 percent reduced risk of acquiring tuberculosis. Additional benefits include a decreased risk of transmission of the disease to sexual partners and a decrease in mother-to-child transmission. Treatment recommendations for children are somewhat different from those for adults. The World Health Organisation recommends treating all children less than five years of age; children above five are treated like adults.

A generally healthy diet is recommended. High intakes of vitamin A, zinc and iron can produce adverse effects in HIV-positive adults and are not recommended unless there is documented deficiency.

Original Article

The Influence of Size of Nd:YAG Capsulotomy on Refraction, Anterior Chamber Depth and Patients Symptoms

Syed Abdullah Mazhar[1], Khurram Nafees[2], Nesr Farooq[3], Sehar Zahid[4], Nazish Mazhar Ali[5] and Maria Hanif[6]

ABSTRACT

Objective: To find out the influence of size of ND:YAG capsulotomy on refraction, anterior chamber depth and patients symptoms

Study Design: Cross-sectional study.

Place and Duration of Study: This study was conducted at the Department of Ophthalmology, Shalimar Medical & Dental College Lahore from 1st December 2020 to 30th November 2021.

Materials and Methods: A detailed ophthalmic examination including refraction**,** anterior chamber depth and patients symptoms of all the included patients were done before and after Nd:YAG laser capsulotomy.

Results: Statistically, non-significant difference was observed in refraction and anterior chamber depth before and after Nd:YAG laser capsulotomy in both the group ($p<0.05$). In group 1 floater were observed in 10(25%) patients while in 30(75%) patients floaters were not observed. In group 2 floater were observed in 6(60%) patients while in 4(40%) patients' floaters were not observed. In group 1 glare was observed in 9 (22.5%) patients while in 31(77.5%) patients glare was not observed. In group 2 glare was observed in 5(50%) patients while in 5(50%) patients' glare was not observed ($p<0.05$).

Conclusion: The size of ND:YAG capsulotomy has statistically no significant influence on refraction, anterior chamber depth and patients symptoms. Better improvement in visual function and less complication can be achieved by capsulotomy with an opening of 3.5 mm.

Key Words: ND:YAG capsulotomy; Refraction; Anterior chamber depth; Patients symptoms

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INTRODUCTION

Reductions in posterior capsule opacification have been achieved by using sharp-edge optic intraocular lenses and the current phacoemulsification procedure.[1,2]

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In spite of advances in cataract surgery, posterior capsule opacification (PCO) remains the most prevalent postoperative issue[3] and it is caused by the proliferation and migration of remnant lenticular epithelial cells.[4] The standard therapy for PCO is Nd:YAG laser capsulotomy.[5] This technique has been shown to be effective and safe, complications like intraocular lens displacement, retinal detachment, IOL subluxation, increase in intraocular pressure and cystoid macular edema have been reported after the procedure.[6,7] Diffraction, sensitivity, glare and reduced image are all optical factors. Mechanical concerns are predicated on the intact posterior capsule's barrier effect, which favors a modest capsulotomy size.[8] Macular edema is induced the release of inflammatory mediators as a result of blood–aqueous barrier disruption, such as in complex cataract procedures with burst posterior capsule and vitreous loss.[9]

Following Nd:YAG laser capsulotomy, elevated IOP is related with an increased number of aqueous particles[10]. The impact of Nd:YAG laser therapy on refraction and anterior chamber characteristics has produced conflict findings in the literature.[9-12] The relationship between size of capsulotomy, visual acuity, issues of posterior segment and refraction has been studied in many studies.[11-13] According to the literature very limited data

is available about the effect of size of capsulotomy on theanterior chamber depth, refraction and patients symptoms. To our knowledge, this is only study in Pakistan to determine this association.

MATERIALS AND METHODS

This was cross sectional study carried out at the Department of Ophthalmology, Shalimar Medical and Dental College from 1st December 2020 to 30th November 2021. Consent was signed in written from all the patients included in our study. The criteria for inclusion in our study were all adults of both the gender with a PCO impairing visual acuity, cataract surgery history of three months, and had two or more lines of decreased best corrected vision while exclusion criteria was patients with any anterior segment disease and chronic eye problems like uveitis, keratoconus and glaucoma. A detailed ophthalmic examination including refraction, anterior chamber depth and patients symptoms of all the included patients was done before and after Nd:YAG laser capsulotomy. A total of 50 patients were included in this study. They were categorized into group 1 and group 2 based on sizes of capsulotomy. There were 40 patients in the group 1 with capsulotomy size ≤4 while there were 10 patients in group 2 with capsulotomy size >4. SPSS version 23 was used for the statistical analysis of the data. For comparison of data independent samples t test was used. A p-value of less than 0.05 was taken as significant.

RESULTS

In group 1, there were 16 (40%) male and 24 (60%) female while in group 2 there were 5 (50%) male and 5 (50%) female (Fig. 1) In group 1, the mean age was 61.75±11.19 years ranging from 20-80 years while in group 2, the mean age was 64.4±9.03 years ranging from 45-77 years. In group 1 the mean anterior chamber depth before laser was 3.93±0.52 mm while it was 3.97±0.33 mm after laser therapy while in group 2, the mean anterior chamber depth before laser was 3.66±0.21 mm while it was 3.85±0.11 mm after laser therapy. In group 1 the mean refraction before laser was -0.43±0.81 diopters while it was -0.50±0.86 diopters after laser therapy while in group 2. The mean refraction before laser was -0.80±0.91 diopters while it was -0.71±0.66 diopters after laser therapy. Statistically, the difference was non-significant {P>.05) in refraction and anterior chamber depth before and after laser therapy in both the group (Table 1). In group 1 floater were observed in 10 (25%) patients while in 30 (75%) patients floaters were not observed. In group 2 floater were observed in 6 (60%) patients while in 4 (40%) patients' floaters were not observed. In group 1 glare was observed in 9 (22.5%) patients while in 31 (77.5%) patients glare was not observed. In group 2glare was observed in 5 (50%) patients while in 5 (50%) patients' glare was not observed. Statistically, the variation was non-significant (P>0.05) in patients symptoms in both the group (Table 2). Night vision was good in all patients of both the group.

Table No.1: Anterior chamber depth and refraction before and after laser therapy

Parameter	Group 1	Group 2	P value
Anterior chamber depth (mm)			
Before laser	3.93±(0.52	3.66±0.21	0.731
After laser	3.97±0.33	3.85±0.11	
Refraction (diopters)			
Before laser	-0.43±0.81	-0.80±0.91	0.291
After laser	-0.50±0.86	-0.71±0.66	

Table No.2: Patients symptoms after laser therapy in both the groups

Group	Patients symptoms	Sub-category	No. (%)	P value
1	Floater	Yes	10(25%)	0.091
		No	30(75%)	
	Glare	Yes	9(22.5%)	0.231
		No	31(77.5%)	
2	Floater	Yes	6(60%)	0.711
		No	4(40%)	
	Glare	Yes	5 (50%)	0.081
		No	5(50%)	

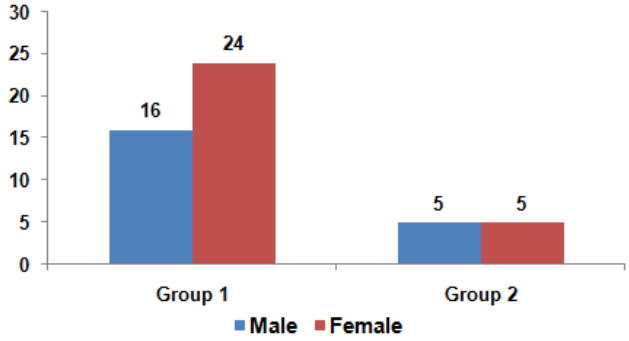

Figure No. 1: Gender wise distribution of patients

DISCUSSION

Visual acuity improvement is the primary aim of Nd:YAG laser therapy. Smaller capsulotomy apertures reduce visual acuity due to diffraction and cause light travelling through the unopened section of the capsule to be dispersed, resulting in glare and a decrease in contrast sensitivity in the eye. In scotopic condition, the capsulotomy opening should be equivalent to or bigger than the pupil size.[14] Capsotomy opening, on the other hand, should be big enough to provide adequate vision of the peripheral fundus, especially in individuals with retinal pathology. Three research studies published employed various approaches to look at the impact of Nd:YAG laser therapy on the morphology of anterior

chamber angle and found no statistically significant change in anterior chamber angle before and after Nd:YAG laser therapy.[15,16] Nd:YAG capsulotomy generated a rearward migration of the intra-ocular lens, which led in anterior chamber deepening, according to Findl and colleagues.[17] Another study reported no significant variation in anterior chamber depth.[18]

After Nd:YAG capsulotomy, two studies found a substantial reduction in mean anterior chamber depth.[19,20] In our study, in group 1 the mean anterior chamber depth before laser was 3.93±0.52 mm while it was 3.97±0.33 mm after laser therapy while in group 2, the mean anterior chamber depth before laser was 3.66±0.21 mm while it was 3.85±0.11 mm after laser therapy. Comparable results were reported by another study. Statistically, the difference was non-significant in anterior chamber depth before and after laser therapy in both the group ($p<0.05$). In accordance with our study, another study also reported similar results.[20]

In group 1 the mean refraction before laser was -0.43±0.81 diopters while it was -0.50±0.86 diopters after laser therapy while in group 2, the mean refraction before laser was -0.80±0.91 diopters while it was -0.71±0.66 diopters after laser therapy. Statistically, the difference was non-significant in refraction before and after laser therapy in both the group ($p<0.05$). In accordance with our study, another study also reported similar results.[20] Despite the fact that Nd:YAG laser capsulotomy has been shown to be effective and safe, the technique has the ability to modify the intra-ocular lens location. A hyperopic shift might theoretically be caused by posterior intra-ocular lens movement. According to several investigations, the decrease in refraction following Nd:YAG laser capsulotomy was not significant statistically.[15,16,21] On the other hand, there have been conflicting views on the relationship between refraction and capsulotomy size. A previous study also reported no significant variation of refraction with change in size of capsulotomy as reported by another study.[11,22] Another study found, on the other hand, an increased risk of hyperopia in individuals who had a capsulotomy size greater than 3.9 mm.[12]

In our study floaters and glare was higher in patients of group 1 as compared to group. In accordance to our study, another study also reported similar results.[11]

CONCLUSION

Size of Nd:YAG capsulotomy has statistically no significant influence on refraction, anterior chamber depth and patients symptoms. Better improvement in visual function and less complication can be achieved by capsulotomy with an opening of 3.5 mm. Our study recommends another study based on large sample size.

Author's Contribution:

Concept & Design of Study:	Syed Abdullah Mazhar
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Final Approval of version:	Syed Abdullah Mazhar

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

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Original Article

Preoperative Predictors and Frequency of Conversion of Laparoscopic Cholecystectomy into Open Cholecystectomy

Muhammad Imran Anwar, Sameen Tahir and Muhammad Aamir Jameel

ABSTRACT

Objective: Determining the preoperative risk factors and frequency of conversion of laparoscopic cholecystectomy into open cholecystectomy.

Study Design: Prospective study

Place and Duration of Study: This study was conducted at the Department of Surgery, Shaikh Zayed Hospital Lahore, from 1st June 2019 to 30th June 2021.

Materials and Methods: Two hundred and ninety one patients who were enrolled. Demographic data e.g. name, age, gender and address were obtained and clinical examinations were performed. All patients were admitted in surgical ward after preoperative workup and fitness for surgery. All of them were taken up on list for laparoscopic cholecystectomy. All the symptomatic patients undergoing laparoscopic cholecystectomy for gall bladder disease (gall stones, gall bladder polyp). Patients were excluded from the study who refused laparoscopic cholecystectomy.

Results: There were 167 (57.3%) females and 124 (42.6%) patients were males with mean age 35.27±14.18 years. Mean duration of disease was 4.24+3.98 years. Mean gall bladder thickness was 4.28±1.06mm. Excessive bleeding was the commonest per-operative complication found in 40 (14%) patients. Difficult laparoscopic cholecystectomy was found in 32 (11%) patients need conversion to open procedure.Post-operative wound infection found in 18 (6%) patients. Frequency of difficult laparoscopic cholecystectomy which needs conversion to open procedure was high in patients having increased thickness of gall bladder wall. In this study 32 patients (11%) were transitioned from laparoscopic cholecystectomy to open cholecystectomy. The most common cause of 21 (65.6%) was fibrosis in the Calots triangle and adhesion due to inflammation.

Conclusion: Conversion happened in 32 (11%) of the patients and mostly because of increased thickness of gall bladder. Even though other factors like bleeding per-operatively was important emphasis is made on timely conversion to avoid post-operative complications.

Key Words: Gall stones, Gall bladder polyp, Laparoscopic cholecystectomy, Open cholecystectomy

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INTRODUCTION

Gall stones are a major health problem in many parts of the world (15% of the total population of United States of America with total 20 million patients) having gallstones of 0.63/100 year.[1,2] An annual surgical incidence of 4.2% in men and 14.2% in women was reported in a Pakistani study. Open cholecystectomy procedure to treat gallstones has increased incidence in adults.

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First open cholecystectomy was performed by Carl Langebuch (Germany) in 1882 and first laparoscopic cholecystectomy by Professor Erich (Germany) in 1985 since from that time management of gall has been greatly improved. It has now been established without controversy that laparoscopic cholecystectomy can be performed safely, in mostcases of severe cholecystitis, and if completed inadvertently, the benefits over open cholecystectomy are retained.[3,4]

The benefits of laparoscopic surgery over traditional surgery include less surgical pain, shorter hospital stay, better self-correction effect, and earlier recovery.[5] But conversion from laparoscopic cholecystectomy to open cholecystectomy is still very common and the risk factors associated with conversion are very useful pre operatively.[6] Lot of research has been performed by many people about the predictive risk factors for conversion worldwide and literature reveals that conversion rate is 2% to 22%.[7,8] Predictability of features of laparoscopic cholecystectomy to open

cholecystectomy may not only improve the patient's safety but may also help reduce the cost of treatment and may assist the surgeon in determining the most appropriate (open/laparoscopic) procedure for the patient, thus reducing the patient's problem, conversion rate and total treatment costs. There are a variety of risk factors identified for the conversion of the case such as wide dense adhesions that affect the appearance of the calots triangle, which is the most common cause. Acute cholecystitis is another cause which accounts 14 to 50% cases. Another cause is contracted gall bladder which results in difficulty in grasping during procedure accounts for 12%. Other causes are painful symptoms. Operative risk factors accounts for 8 to 15% cases and includes abnormalities of anatomy, hemorrhage, aberrant vessel (hepatic artery) or duct and any kind of injury to bile duct.[9]

MATERIALS AND METHODS

This study was done in General Surgery Department of Shaikh Zayed Hospital Lahore among all patients who underwent laparoscopic cholecystectomy during period of 2 years. All the symptomatic patients undergoing laparoscopic cholecystectomy for gall bladder disease (gall stones, gall bladder polyp) were included. All patients who have gall bladder perforation, gall bladder malignancy determined by preoperative scans, previous mid line laparotomy, upper abdominal surgery and CBD stones were excluded.

RESULTS

167 (57%) were women and 124 patients (43%) were menaged 35.27±14.18. The mean duration of the disease was 4.24±3.98 years. The gallbladder thickness was 4.28±1.06mm. Excessive bleeding was a common functional problem with 40 patients (14%). Laparoscopic cholecystectomy was abandoned in 32 patients (11%) who needed to be rehabilitated to open the procedure. Post-surgical wound infection is found in 18 patients (6%). The frequency of laparoscopic cholecystectomy that needed to be adjusted to open the procedure was high in patients with a thick walled gall bladder.

Only adverse clinical factors showed significant predictive value (p 0.005) and adverse radiological predictors din not showed significant predictive value (p 0.065). Among clinical predictors history of acute cholecystitis, BMI more than 30 and symptoms duration of more than 1 year showed statistically significant association. Male gender, age more than 50, deranged LFTs and radiological factors (single or impacted stone, thick wall, small contracted gall bladder) did not show significance. Clinical predictions are the most reliable factors. The use of good clinical judgment in relation to existing difficulties and complications and understanding of available facilities and resources is essential in making a decision in every case.

32 patients (11%) were transitioned from laparoscopic cholecystectomy to open cholecystectomy. The most common cause of 21 cases (65%) was fibrosis in the triangle of calot and adhesion due to inflammation. The next most common cause is acute cholecystitis 9 (28.1%) and 3 gallbladder contractor (9.4%) cases. The patients who converted the majority of 10 (66.7%) were 41-60 years old and in patients who had laparoscopic cholecystectomy the majority of 70 (44.9%) of patients who were 30-70 years of age.

The high conversion rate in men is difficult to explain. The explanation may be that men are more likely to have a delay in seeking help and thus expose themselves to a more complex disease and problems during surgery.

Table No.1: Age distribution of patients (n=291)

Age (years)	No.	%
10-20	2	0.68
21-30	37	12.71
31-40	61	20.96
41-50	111	38.14
51-70	72	24.74
>70	8	2.74
Mean±SD	45.46±1.12	

Table No.2: Sex distribution of patients (n=291)

Sex	No.	%
Male	124	43.0
Female	167	57.0
M:F ratio	1:1.34	

Table No.3: Demographic data of patients (n=291)

Data	No.	%
Laparoscopic cholecystectomy	199	68.38
Open cholecystectomy	59	20.27
Conservativetreatment	1	0.34
Lap. to openconversion	32	10.99

Table No.4: Treatment according to sex of patients (n=291)

Data	Male		Female	
	No.	%	No.	%
Laparoscopic cholecystectomy	112	38.49	86	29.55
Open cholecystectomy	36	12.37	23	7.91
Conservative treatment	-	-	1	0.34
Lap. to open conversion	19	6.53	14	4.81

DISCUSSION

The rate of conversion of laparoscopic cholecystectomy to open cholecystectomy is very high. Nine patients

(27.2%) had severe inflammation of the gallbladder. Male sex, older than 60 years, previous upper abdominal surgery, diabetes and acute inflammation are all closely related to the high conversion rate of laparoscopic cholecystectomy to laparotomy. In patients of cholecystitis with elevated white cell count, elevated bilirubin level, fever, elevated ALT and AST all are associated with conversion of laparoscopic cholecystectomy to open cholecystectomy. These risk factors are not contraindications for laparoscopic cholecystectomy. Knowledge of these risk factors results in prediction of severity of procedure and surgeon should counsel and inform the patients regarding risk of conversion of procedure.[10,11] Inflammation is most common cause of conversion of procedure in acute cholecystitis. Other predictors of conversion are advanced age, male gender and elevated white cell count. Prospective studies with large number of cases should be carried out to know the validity of these predictors.[12] Age, obesity, history of previous surgery (upper abdominal), Sex, white blood cell count, alkaline phosphatase level, and contracted gall bladder on ultrasound all are risk factors and predictors of conversion of laparoscopic cholecystectomy to open cholecystectomy.[13] A large number of studies reported a rate of laparoscopic cholecystectomy modification to open cholecystectomy at 2 to 15%. Conversion to open cholecystectomy is not a disadvantage for the surgeon but is considered a wise decision by a vigilant surgeon.[14]

The risk of conversion of laparoscopic cholecystectomy to open cholecystectomy is related to a variety of factors such as surgeon competency, mechanical failure and other most importantly patients since literature have revealed patient risk factors such as age, gender, Body mass index (BMI) and previous surgery (upper abdominal). Radiological findings on ultrasound such as contracted gallstones, one large stone, gallbladder stiffness and pericholecystic fluid collection are associated with difficulty during laparoscopic cholecystectomy.[15] Hemorrhage during the separation of the gallbladder from the liver bed was the most common finding in our study 35.7%, and was followed by 33.3% local adhesion and gall bladder perforation was observed in 7.8% of cases. Thirty two patients had turned to open procedure had a wall thickness between 4.1 to 6mm. Similarly the conversion rate was found to be higher in patients with symptoms for over 5 years. Ultrasound of gall bladder for wall thickness is a good predictor of difficult cholecystectomy. It should beused as a measure of anticipation of serious cases and the patient should be properly advised that it may be possible to switch to open cholecystectomy.[16]

Kumar et al[17] with a conversion rate of 10.7%. Daradkeh[18] reported a conversion rate of 2.6% from LC to OC and Dalal et al[19] reported a rate of 1.27%. The literature reported a wide variation between conversion rates of laparoscopic to open cholecystectomy. This variation in rate of conversion ranges from 2% to 15%.[20] In the present study, there was no significant relationship ($p > 0.05$) between age and conversion rate, but there was a significant correlation ($p < 0.05$) of gender and conversion rate. Patients with certain risk factors before surgery may experience complications during or after surgery. Predictability of patients at high risk of converting to open cholecystectomy has few potential benefits.[21]

Sharma et al[22] found that the chances of bleeding in the liver bed, local adhesion and the difficult formation of the calot triangle were high in the previous group. Factors responsible for open transformation were thick adhesion in 21 (65.62%), abnormal anatomy of the triangle at 3 (9.31%), significant intra-operative bleeding 5 (15.6), CBD damage 1 (3.13%) visceral damage 0 (0.0%) and equipment failure in 1 conversion (3.1%). The open conversion rate of laparoscopic cholecystectomy in this study was 10.99%. The most common cause was the thick adhesion around the gall-bladder. Preventable features such as equipment failure or power breakage can be prevented with reliable maintenance[17] ERCP implementation prior to surgical intervention appeared to be associated with an increased incidence of conversion in our study. There is no significant relationship between ever and changing to open surgery according to our study. Sex (male), gall bladder wall thickness, size of gall stone, shape of gall stone, acute cholecystitis and ultrasound evidence of pericholecystic fluid have been strongly associated with conversion.[18] Ercan et al[23], Harboe et al[24], all revealed that conversion is associated with male sex. So gender is highly predictable in this study. Chandio et al[25] revealed that sex is not associated with conversion.

This study revealed any association between obesity (BMI> 30kg/m^2) and conversion, Airan et al[26] and Tang et al[27] revealed obesity as strongly associated with conversion. Hutchinson et al[28] revealed that BMI (>27.2 kg/m^2) as an important predictor of a three-fold conversion rate. The co-morbid conditions i.e. hypertension and diabetes was not dangerous for our study, similar to Alponat et al[29] and Kama et al[30] revealed that by increasing experience of the surgeon and the improvement in the surgical apparatus can lead to a reduction of the conversion rate in these patients. Nine patients (1.5%) required conversion from laparoscopic to open cholecystectomy. The rate of conversion to open cholecystectomy in our study was within the 2-22%.

Analysis of various preoperative factors has shown that patients who need to undergo open surgery are more likely to exhibit the following characteristics: male sex, 40 years of age, diabetes history, history of hospitalization with gallstones and total increase in bilirubin, direct bilirubin, or alkaline phosphatase

levels. We found that adhesions, bleeding, and sprains were associated with alteration. These findings are consistent with those of previous reports in the literature.[31-32]

CONCLUSION

Laparoscopic cholecystectomy is the gold Standard for both acute and chronic cholecystitis and 100% of the cases must begin with laparoscopic cholecystectomy. Several factor contribute to conversion to open technique among which increased gall bladder thickness is the most common. Other factors may also contribute like increased bleeding per operatively for more than 5 minutes and adhesions in the calots triangle. Conversion happened in 32 (11%) of the patients in our study and mostly because of increased thickness of gall bladder. Even though other factors like bleeding per-operatively was important emphasis is made on timely conversion to avoid postoperative complications.

Author's Contribution:

Concept & Design of Study:	Muhammad Imran Anwar
Drafting:	Sameen Tahir
Data Analysis:	Muhammad Aamir Jameel
Revisiting Critically:	Muhammad Imran Anwar, Sameen Tahir
Final Approval of version:	Muhammad Imran Anwar

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

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Original Article

Maternal Age and Low Birth Weight in Sindh Province: A Cross Sectional Survey

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ABSTRACT

Objective: To evaluate the association between maternal age and low birth weight.
Study Design: Cross sectional survey
Place and Duration of Study: This study was conducted at the various Neonatal Wards in Sindh province over a period of 9 months from January 2021 to September 2021.
Materials and Methods: Data was collected using a structured questionnaire, mothers of the 430 neonates were interviewed and birth weight of neonates was measured at the neonatal ward.
Results: Most of the mothers 254 (59.1%) were aged between 21 to 30 years. Mothers' age was observed to have significant association with low birth weight. Mothers aged between 21-30 years had 15.29 times higher odds of having low birth weight neonates with (p-value 0.041 95% CI: 0.42 – 107.11).
Conclusion: The study observed that mothers had a higher likelihood to conceive at younger age. It was concluded the younger age mothers had greater tendency to deliver low birth weight neonates.
Key Words: Maternal age, Low birth weight, Sindh

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INTRODUCTION

World Health Organization has defined the low birth weight as the weight less than 2500 grams at the time of birth[1]. Maternal age is one of the important factors affecting the fetal outcomes. Among mothers, the extreme aged (too young and too old) pregnancies are considered a major risk factor for the pregnancy and perinatal outcomes in both low- and high-income countries[2]. Maternal age, in particular, is linked to an increased risk of low birth weight (LBW) and premature delivery[3]. Consequently, besides many other factors, the low birth weight itself, is one of the major important causes of neonatal mortality[4].

MATERIALS AND METHODS

A cross sectional survey was conducted at, Neonatal wardsShaikhZaid Children Hospital Larkana, Neonatal Ward GMMMC Sukkur, Neonatal Ward Civil Hospital Khairpur, Neonatal Ward SASIMS Sindh, Pakistan. The mother/guardian/attendant of 215 low birth weight and 215 normal birth weight neonates were interviewed. Mothers' age was divided into four groups and birth weight of the neonates was categorized into low birth weight and normal birth weight with cut of value 2500 grams. Data was entered and analyzed on SPSS version 23.

RESULTS

In this study, the age of the mother was coded into four groups as ≤20, 21-30, 31-40 and above 40 years old. There were 48 (11.2%) mothers below or equal to 20 years old, 246 (57.2%) mothers aged between 21 to 30, 108 (25.1%) mothers were aged between 31 to 40 and 28 (6.5%) mothers were older than 40 years. Table 1.

Our findings revealed that out of 49 (11.4%) mothers aged ≤ 20 years, 31 (63.3%) mothers delivered low birth weight neonates and 18(36.7%) mother delivered normal birth weight neonates. which is the highest percentage of LBW neonates in four maternal age groups.

Amongst 254 (59.1%) mothers in age category 21-30 years, there were 129 (50.8%) low birth weight.

Amongst the age group 31-40 there were 109 (25.3%) mothers in total, 51 (46.8%) mothers delivered low birth weight neonates, while in the age group >40 years there were four (22.2%) mother delivered low birth weight.

Chi-square analysis compared the percentage of low birth neonates among four age groups of the mothers

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which revealed that low birth weight is significantly associated with mothers' age with p-value 0.023 with Chi-square value of 9.517. Table 2.

Maternal Age Among four groups of maternal age, the reference group was the mothers aged >40 year. Multinomial logistic regression results show that for mothers aged between 21- 30 years were the predictors to have low birth neonates. We observed that compared to mothers aged above 40 years, mothers aged between 21-30 years had 15.29 times higher odds of delivering low birth weight neonates with(p-value 0.041 95% CI: 0.42 – 107.11).

The mothers aged 31-40 years had 10.67 times higher odds of delivering LBW neonates (p-value 0.048, 95%CI: 1.12-208.26). While, the mothers aged 20 years or below had 6.74 times higher odds to deliver LBW neonates (p-value 0.176 95%CI 1.02-111.35). Table 3.

Table No.1: Frequency Distribution of Maternal Age

Independent Variable	Description	N	Percentage
Maternal Age	1. ≤20 years	49	11.4
	2. 21-30 years	254	59.1
	3. 31-40 years	109	25.3
	4. >40 years	18	4.2

Table No.2: Chi Square Association Between Birth Weight and Maternal Age

Maternal Age	LBW		Non LBW		Chi Square	
	N	%	N	%	Statistic value	p-value
≤20 years	31	63	18	36.7	9.517	0.023
21-30 years	129	51	125	49.2		
31-40 years	51	47	58	53.2		
>40 years	4	22	14	77.8		

Table No.3: Multivariate Logistic Regression Maternal Age and Low Birth Weight

Maternal Age	Wald	p-value	Multiple Logistic Regression		
			Adjusted Odds Ratio (Adj. OR)	95% Confidence Interval CI	
≤ 20 years	1.829	0.176	6.741	0.424	107.113
21-30 years	4.19	0.041	15.293	1.123	208.269
31-40 years	3.914	0.048	10.67	1.022	111.355
>40 years			Ref		

DISCUSSION

Maternal age is one of the important factors affecting the fetal outcomes. Among mothers, the extreme aged(too young and too old) pregnancies are considered a major risk factor for the pregnancy and perinatal outcomes around the world[2]. Maternal age, in particular, is linked to an increased risk of low birth weight (LBW) and premature delivery[3].

In this study, there were 48 (11.2%) mothers below or equal to 20 years , 246 (57.2%) mothers aged between 21 to 30, 108 (25.1%) mothers were aged between 31 to 40 and 28 (6.5%) mothers were older than 40 years. The distribution of mothers according to age was comparable with a study conducted in Ethopia where 120 (25.4%) mothers were in age group 31-40 compared to a similar proportion of mothers in same age group in our study 108 (25.1%). However, in our study the proportion of mothers aged between 21-30 was higher. There were 246 (57.2%) mother aged 21-30 in our study compared to 143 (30.3%) were 20-30 years. We had only 28 (6.5%) mothers older than 40 years in our study showing a much lesser number compared to 101 (21.4%) mothers were above 40 years of age, also mothers younger than 20 were only 48 (11.2%) in our study compared to 108 (22.9%) in a cross sectional study conducted with 472 samples in Ethopian capital Dilla, Ethopia[5].

In our study, most of the mothers 246 (57.2%) were aged between 21 to 30 while a research conducted in Libya by Alabed et al[6] observed that most of the mothers (49%) were aged between 19-26 years and least number of mothers were aged below 19 years24 (5.9%).

In our study 57.2% of the mothers belonged to age group 21-30 years, this observation is roughly similar to the findings of a study with 51% mothers aged between 20-29 years[7].

In our study proportion of middle aged mothers were way higher than rest of the age categories, similar finding was observed in a study conducted in Tehran, Iran, where 80.6% of mothers were between 18-35 years[8].

The majority of mothers (59.1%) belonged to age category 21-30 in our study. Nearly similar finding was observed in a study conducted in in a public hospital in Killis, Turkey [9].

We observed that the association of maternal age with low birth weight was significant not only in chi square test of association but in multivariate model as well. In multivariate analysis, we observed that the association of maternal age with low birth weight was significant, this observation in our study is in line with several studies available in the literature[7,9-12].

Mothers aged 20 or below had 6.74 times higher odds of having LBW neonates compared to mothers'

age>40, our finding is in line with a study conducted in Sub-Saharan Africa[7].

This observation was nearly similar to the research conducted by Adem et al[10] who observed that mothers aged ≤20 years had three times higher odds to have lbw neonates compared to mothers in age bracket 21-30 years(AOR = 2.9, 95 % CI: 1.55, 5.47). In contrast to our findings, Niknejadet al[11] observed that the risk of giving birth to LBW infants was higher in mothers over 35 years of age. Our observation showed that the mother aged > 40 had lesser odds of having low birth weight compared to rest of the categories, moreover, odds of LBW births were highest 15.293 in mothers aged 21-30 years taking >40 years as reference. In contrast to this observation, Tessema et al[7] observed that compared with mothers aged 15-19 years, mothers in age bracket 20-29 had 25% (AOR = 0.0.75, 95% CI: 0.71, 0.80), mothers in age bracket 30-39 had 24% (AOR = 0.076, 95% CI: 0.71, 0.82) and mother aged 40 and above had 14% (AOR = 0.86, 95% CI: 0.78, 0.95) lesser chances to have LBW neonates.

CONCLUSION

Most of the mothers 254 (59.1%) were aged between 21 to 30 years. Mothers' age was significantly associated with low birth weight. Mothers aged between 21-30 years had higher odds of delivering low birth weight neonates compared to rest of the age categories. Our study concluded the younger age mothers had higher tendency to deliver low birth weight neonates

Recommendations: In our observations, young age mothers were more likely to deliver low birth weight neonates. We strongly suggest avoiding teenage marriages and pregnancies for young girls to avoid the odds of low birth weight deliveries. Also the parents and community needs structured programs of awareness to discourage the early marriages and pregnancies during the teenage. This target is only achievable by involving the community itself. Parental involvement, community advocacy and involving the youth could be the promising ideas for the change.

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Original Article

Gender Based Comparison of Stress in Students Appearing for University Entrance Test

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ABSTRACT

Objective: To evaluate the Gender based comparison of stress in students appearing for university entrance test.
Study Design: Descriptive / cross sectional study
Place and Duration of Study: This study was conducted at the Karachi Medical & Dental College, Karachi for two months from August to September 2021.
Materials and Methods: The 498 students were enrolled from various Entrance test/ aptitude training (M-CAT/E-CAT) centers of Karachi and students were having history of psychiatric illness or history of taking drugs like anxiolytics or antidepressants were excluded from study. The Perceived Stress Scale was used to evaluate the degree of stress level in students. Data were analyzed by using SPSS- IBM 23.0 version, Counts with percentages were reported for baseline qualitative characteristics of studied samples included gender, educational board, education type, college. Mean Comparison of Perceived stress scores was done, by using ANOVA for the baseline factors. The results were having p-value <0.05, will be considered as statistically significant.
Results: The majority of participants were females 82% and 18% males, the mean age of samples was 18 (SD=±0.83) years, There were 42.1% students were having moderate stress level ranges between 14 – 26 units, and the mean perceived stress scores of sample was 21(SD=±10) and gender based comparison of perceived stress scores showed significant differences (P<0.05) in students.
Conclusion: It is observed from these observations in this research that mean gender based comparison with stress, showed significant difference (P<0.05), so we should have to work to elevate stress, so that achievements can be acquired.
Key Words: Gender, Perceived Stress, students

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INTRODUCTION

"Stress" is a word, which is used widely in everyday life and it is defined as the insight of impropriety between factors or stressors and ability of human body to cope these strains or it is defined as the undesirable response of the human body against burden or any type of strains placed on them.
Stress is developed in the human body as it faces or deals with an environment or situations, like physical or psychological challenges. These are recognized as an inevitable or irresistible and that cannot be coped up or cannot be managed easily.[1] So our body's response (physiological, biological, or psychological) to the changing surroundings or environmental stimulus or stressors, which are in any form affecting the human body. The response of Human body occurs physically, mentally, and with emotional capabilities. Stress is worthy regard to consider as dangerous to human health as it affects the normal daily activities or functioning or performance.[2,3] There are two types of stress, first is the negative form or distress and second form is positive form or eustress. Both experts different effects on the human body. The distress form or negative form, in which most people are associated with stressed out condition, which exerts effects or develop sign and symptoms like insomnia or lack of sleep, tension, irritability or anger and headache. The peoples responds destructively with collapse of the body or develops suicidal ideation or suicidal attempts or exerts negative effects on human body. The positive form or eustress, will boost or energize and motivate, which results in achievements of goals or destinations or high dignity and exerts positive effects on human body.[4] Adolescence is a transition period from childhood to adulthood during which emotional, social and cognitive development occurs. They are the more than 1.5 billion

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and considered as one fifth of the total population in the world.[5] In Adolescence, transition occurs in education level from higher secondary schools or degree colleges to professional universities (Medical / Engineering), so crises increases in the human body and this issue can be assessed by psychologically parameters, like Academic stress. This type of stress is considered as pervasive problem, which is prevalent in our society, as well as in each ethnic group in our country. As to continue their higher educations, everyone is facing or dealing with different types of pressures, like environmental/ personnel/familial.[6] The 30% to 75% is prevalence of anxiety, depression and stress in pre-adolescent children's, while in adolescent's age group is 25% to 50%.[5] As change in living trends in our societies, which will be likely responsible for development of stress in students, so incidence increased dramatically.[7] Every student have a right to achieve respect or pride in society by pursuing higher professional educations, that needs very high academic progress and this can be achieved by hard working for success as to get rid of various pressures or demands to perform best in entry exams especially in college students, so that they are not enjoying life during this life period. As every student passing joyless life, and feeling burden on family or relatives or society, which leads to development of psychological disturbances or negative effects on human health (anxiety, depression and stress), so every student is working hard as to get highest marks or percentage or grades or best scores in entry exams. The psychological disturbances (anxiety), caused by examination stress reaches at peaks, as dates comes near the exams, which leads to development of more and more symptoms. This psychological disturbances will be responsible for interference in getting good sleep, problem in memorizing or difficulty in recalling subject's knowledge, irritability, lack of appetite or nausea or vomiting. This leads to development of distress in human life. The fear of failure is one of the factor exerts negative effects on physiological functions of the human body and self-respect or self-esteem of the many students too. Every student is working hard with dedication and motivation as to achieve the higher education as a reward. The current study aimed to evaluate the stress in Degree College or higher secondary school students. Objective of study is to evaluate the gender based comparison of stress in students appearing for university entrance test (M-CAT/E-CAT). Our research will help to fill the gap by raising awareness about the stress, and highlighting the levels of stress in students by using Sheldon Cohen's Perceived Stress Scale (PSS),[8,9] who are appearing the university admission test (M-CAT/E-CAT).

MATERIALS AND METHODS

It is a descriptive cross-sectional study, and duration of study was two months, which was done in 2021, through non probability convenience sampling technique. Sample size was calculated by Rao soft calculator [10] i-e 377 (5% margin of error and 95% confidence level), but at the time of data collection, 498 students was available, so we included all. Written informed consent will be taken from each responder. Enrolled from various Entrance test/ aptitude training (M-CAT/E-CAT) centers of Karachi and students having history of psychiatric illness or history of taking drugs like anxiolytics or antidepressants were excluded from study.

The Sheldon Cohen's Scale (PSS), is used to assess the stress in the students, and it measures the degree of perceived stress. It includes 10 items version of Sheldon Cohen's Perceived Stress Scale. [9] The PSS uses a 5 point rating scale ranging from "0" to "4". 0 = Never, 1=0 = almost never, 2 = Sometimes, 3 = Fairly Often, and 4 = Very Often, and 4, 5, 7 and 8 items are reversed scored in perceived stress scale, for e.g. 0=4, 1=3, 2=2, 3=1 and 4=0 and then sum all 10 items of Sheldon Cohen's Perceived Stress Scale, with range of 0 to 40. This perceived stress scale is applicable to age group of 18 years and above this age group. The different researchers showed different reliability (0.78-0.98) of perceived stress scale (PSS). [11-13] The Sheldon Cohen's Perceived Stress Scale (PSS), with high score near 40 is considered as mentally wellbeing or out of distress. Data were analyzed by using SPSS- IBM 23.0 version, Counts with percentages were reported for baseline qualitative characteristics of studied samples included gender, educational board, education type, college. Mean Comparison of Perceived stress scores (PSS) was done, by using one way of variance (ANOVA) for the baseline factors.

The results were having p-value <0.05, will be considered as statistically significant. The permission for doing research was taken by from Ethical & scientific review committee, (Reference No: 029/18, date 10 November 2018) Karachi Medical & dental college, Karachi.

RESULTS

The data were collected from 489 samples among them including 401 (82%) female and 88 (18%) males, the mean age of samples was 18 (SD=±0.83) years, 438 (89.6%) data were received from the Sind educational board and regular students, 259(69.9%) were studying in the government college, as summarized in Table 1. There were 206 (42.1%) students were having moderate stress level with perceived stress scores (PSS) ranges between 14 – 26 units, and the mean perceived stress scores (PSS) of sample was 21(SD=±10), as summarized in Table 2. The mean comparison of perceived stress scores (PSS) of samples with respect to gender, results showed a significant differences (P<0.05), while educational board (AKU-EB, Sindh, Federal, Cambridge and others) type of education (Regular and Private), college (Government and Private) were found statistically insignificant (P>0.05) results, as summarized in Table 3.

Table No.1: Baseline Characteristics of Studied Samples (n=489)

Characteristics		N	%
Gender of student	Male	88	18.0
	Female	401	82.0
Age (years)	Mean ±SD	18±0.83	
Educational Board	AKU-EB	15	3.1
	Sindh	438	89.6
	Federal	11	2.2
	Cambridge	21	4.3
	Other	4	0.8
Education Type	Regular	259	87.8
	Private	36	12.2
College	Government	342	69.9
	Private	147	30.1

Table No.2: Perceived Stress Score (PSS) 10 Outcomes

Perceived Stress Score	N	%	Interpretation
Perceived Stress Score (PSS) 0-13	126	25.8	Low Stress level
Perceived Stress Score (PSS) 14-26	206	42.1	Moderate stress level
Perceived Stress Score (PSS) 27-40	157	32.1	High level of perceived stress.
Perceived Stress Scale (PSS)	Mean ±SD		21±10

Table No.3: Mean Comparison of PSS with respect to studied Factors

Factors		Perceived Stress Scores (PSS)		p-value
		Mean	SD	
Gender of student	Male	18	9	<0.01*
	Female	21	10	
Educational Board	AKU-EB	22	10	0.29
	Sindh	20	9	
	Federal	26	10	
	Cambridge	21	9	
	Other	25	15	
Education Type	Regular	20	9	0.90
	Private	21	11	
College	Government	21	10	0.89
	Private	21	10	

*p<0.05-statistically significant.

DISCUSSION

The aim of this study is to evaluate the Gender based comparison of stress in students appearing for university entrance test. The students are prone to develop stress in academics due to various factors or pressure sources (environmental and personal), huge curriculum and family or relative or society stressors are involved in this transition period of life, which becomes progressively problematic for adolescents who intend to continue higher education as to achieve admissions in professional degree awarding universities as to acquire education in medical or engineering institutes for saving their future. Every student is working hard with dedication and motivation as to achieve the higher education as a reward or academic success in life for getting respect and pride in society. This results in extremely high academic demands and extraordinary pressure on students and specially adolescents. According to our study results, outcome of Perceived Stress Score (PSS), low stress level (25.8%), Moderate stress level (42.1%) and High level of perceived stress (32.1%), as summarized in Table II, similar to our findings. Graves et al [14]and Brougham, Zail, Mendoza and Miller[15] were agreed too. In our study results, mean comparison of perceived stress scores (PSS) of samples with respect to gender, results showed a significant differences (P<0.05), as summarized in Table 3, like our results Graves et al [14], Schmaus, et al.[16] ,Thawabein and Quaisy [17] agreed with Harutyunyan, Musheghyan, Hayrumyan.[18] Moderate level of Perceived Stress Score (PSS) is observed mostly in female gender, that leads to the failure to achieve the academic goal or admissions in Professional universities (Medical/ Engineering). It is also observed in our society, that getting admissions in Medical colleges are merely to acquire matrimonial match for girls, so it is main reason, for developing more stress in females.[19,20] hypothalamic-pituitary-adrenal axis and Autonomic nervous system (ANS) , are considered as a two major systems, which reacts to stress in human body via fight-or-flight response and release of cortisol. Acute or chronic stress may induce problems in regulation of these systems in human body like serotonin system, epinephrine &norepinephrine system and adrenocortical system. Cortisol hormone is considered as stress hormone, as it influences the functions of human body like psychological effects, immunological effects and metabolic effects.[21] The impact of ongoing academic-related Perceived Stress Scale (PSS) to student is multidimensional and multi-systemic on human body, which is mainly distress form or negative form. It is due to educational stress, parental expectations and environmental factors or society, for best performance in getting admissions in professional universities, best for carrier growth, fear of failure or nor meeting the expectations of teacher, parents or relatives and society.[22]

More research is required in Pakistan in this age group (adolescents), who are preparing for admissions in medical and engineering universities, for their future brightness, and role of parents, consultant psychiatrics

or councilors and teachers become very important for better management or cope of perceived stress in students, who are preparing for entry test.

CONCLUSION

Despite all the limitations of the study, it is observed from these observations in this research that mostly students were having moderate stress level, and mean gender based comparison with stress, showed significant difference (P<0.05) on Perceived Stress Scale (PSS), so we should have to work to elevate stress, so that achievements can be acquired.

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Original Article

Association of Depression to Age, Trimester, Gravida, Number of Live Children and Two or More Daughters and Having No Son in Currently Pregnant Females at Bahawalpur

Saeed Akhtar[1], Azra Yasmeen[2] and Fariha Saeed[3]

ABSTRACT

Objective: To find out association of depression to age, trimester, gravida, number of live children and two or more daughters and having no son in currently pregnant females at Bahawalpur.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the antenatal clinic at Gynaecology and Obstetrics OPD at Bahawal Victorial Hospital, Bahawalpur during month of July, 2020.

Materials and Methods: This study involving 150 pregnant women aged 18-47 years who were attending antenatal clinic at Gynaecology and Obstetrics OPD at Bahawal Victorial Hospital, Bahawalpur. This hospital is a tertiary care facility with large catchment area. Specific to our study is that we excluded all the patients having history of any psychiatric illness and physical illness having some association with depression before the start of current pregnancy. So that we may be able to find out the specific association of depression with current pregnancy.

Results: Out of 150 pregnant women 23 were found having depression. This is 15.33%. Out of these 23 pregnant women 21 had mild to moderate depression, 2 had severe depression. No patient was having very severe depression. 50% of pregnant women belonged to age group 18-27 years and out them 24% (n=18) had depression. As regard trimester clarification, 1st trimester patients had 22.22% (n=10) patients of depression.

Conclusion: It is important to diagnose and treat depression in pregnant females.

Key Words: Pregnancy, Depression, Garvida

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INTRODUCTION

Pregnancy is usually a source of happiness in our society but some women report depression during pregnancy. Pregnancy leads to psychological, physical and hormonal changes, due to these changes, women can get depression.

There is considerable evidence that the status in society, poverty, illiteracy, age, poor social support, violence, large families, grand multiparity, having two or more female babies and no son, serious arguments with significant family members, lack of autonomy in decision making and a lack of access to health care facility correlate with the development of depression in pregnant women.[1-5] Antenatal depression may be associated with unplanned and unwanted pregnancy. Other risk factor for depression during pregnancy may include, previous history of psychiatric disorder, any puerperal complication, miscarriage and still birth previously.[6] Antenatal depression may remain undiagnosed and untreated, and this may negatively affect a women's health, fetal and infant development and family relationship.[7-10] In our opinion this is common in our society. Mother in law usually says that pregnancy is a normal process and I have given birth to 6 children. I cannot understand why she is weeping. Aga Khan university Hospital study has shown high rate of depression in pregnant women, that is 62%.[11] Other study of depression in pregnant women, done at Hyderabad Pakistan showed the rate of depression as 18%.[12] Nagandla et al has shown depression in pregnant women from 7.4% to 12.8%.[13] A study conducted in Oman had 24.3% rate of depression in pregnant

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females.[14] So results vary widely among different studies.

In our study we tried to delineate the patients whom may have developed depression in response to current pregnancy only. As we excluded all the patients having past history of depression, even having depression in pervious pregnancy or postnatal depression in the past. Similarly as it is known that patients of bipolar illness, schizophrenic patients, patients of generalized anxiety disorder, conversion disorder, obsessive compulsive disorder can have depression during their course of illness. In the same way patients of hepatitis and diabetes have special tendency to develop depression. We excluded all such patients from our study.

MATERIALS AND METHODS

It was a cross sectional study involving pregnant women aged 18-47 years who were attending antenatal clinic at Gynaecology and Obstetrics OPD at Bahawal Victorial Hospital, Bahawalpur. This hospital is a tertiary care facility with large catchment area. All the patients were included in the study who visited during month of July, 2020. Informed consent was taken from all the patients. Patients who had depression or other psychiatric illness like post-natal depression or psychosis during period without pregnancy were excluded. Similarly patients having anemia, diabetes, hypertension cardiovascular illness and hepatitis A, B and C were also excluded from the study. A total of 150 patients of all three trimesters were included in the study. The study approval was got from ethical committee of the Quaid-e-Azam Medical College and B. V. Hospital Bahawalpur.

Hospital anxiety and depression scale was used to assess depression. It includes anxiety (seven item) and depression (seven items) subscales and the total score ranges from 0 to 21, with a higher score reflecting a worse psychiatric status. Subscale scores of >8 represent pathological level of anxiety and depression.

Demographic data included age of the patients and trimester of the pregnancy. Data was also collected regarding weather patient is primgravida or multi gravida, number of live children, weather patient has two or more daughters and having no son. For assessment of depression we used Hamilton Rating Scale of Depression. The data was entered in SPSS version 16 and analyzed. Mild, moderate, severe and very severe types of depression were assessed in the form of frequencies. Estimates of depression prevalence among pregnant patients and association between pregnancy and depression (estimated with reported odd rations (ORs) were provided

RESULTS

Out of 150 pregnant women, 23 were found having depression. This is 15.33%. Out of these 23 pregnant women 21 had mild to moderate depression, 2 had severe depression. No patient was having very severe depression. Total 78 (50%) of pregnant women belonged to age group 18-27 years and out them 24% (n=18) had depression, 55 (36.67%) pregnant women belonged to age group 28-37 years and out of them 7.27% (n=4) had depression, 20 (13.33%) pregnant women belonged to age group 38-40 years and 5% (n=1) had depression. (Table 1)

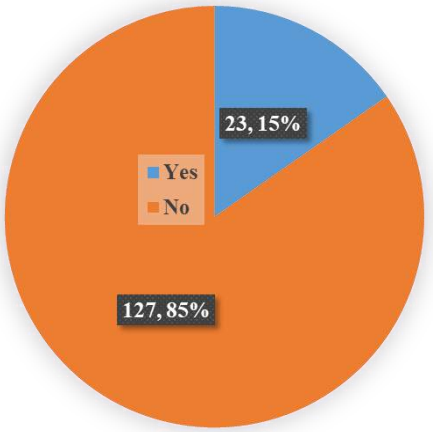

Figure No. 1: Frequency of depression

Table No.1: Association of depression with age group

Age group	Depression		Total	P value
	Yes	No		
18-27	18 (24%)	57 (76%)	75 (50)	0.013
28-37	4 (7.27%)	51(92.73%)	55 (36.67%)	
38-47	1 (5%)	19 (95%)	20 (13.33%)	
Total	23 (15.33%)	127 (84.67%)	150	

Table No.2: Association of depression with trimester

Trimester	Depression		Total	P value
	Yes	No		
1st	10 (22.22%)	35 (77.77%)	45 (30%)	0.191
2nd	5 (9.09%)	50 (90.91%)	55 (36.67%)	
3rd	8 (16%)	42 (84%)	50 (33.33%)	
Total	23 (15.33%)	127 (84.67%)	150	

Table No.3: Association of depression with gravida

Trimester	Depression		Total	P value
	Yes	No		
Primary gravida	16 (30.77%)	36 (69.23%)	52 (34.67%)	0.000
Multi gravida	7 (7.14%)	91 (92.86%)	98 (65.33%)	
Total	23 (15.33%)	127 (84.67%)	150	

As regard trimester clarification, in 1st trimester, 10 (22.22%) patients had depression, in 2nd trimester, 5 (9.09%) patients had depression and in 3rd trimester total 8 (16%) patients had depression. (Table 2) Similarly primigravidea was having 30.76% (N = 16) patients of depression. (Table 3) According to no of live children categories, the category of patients having 0-1 live children had 30% (n=18) patients of depression. (Table 4) The category of pregnant patients having two or more daughter and no son were 6 out of 150 and 4 of them were depressed.

Table No.4: Association of depression with No. of live children

No. of live children	Depression		Total	P value
	Yes	No		
0-1	18 (30%)	42 (70%)	60 (40%)	0.000
2-4	2 (3.28%)	59 (96.72%)	61 (40.67%)	
5-6	3 (10.34%)	26 (89.66%)	29 (19.33%)	
Total	23 (15.33%)	127 (84.67%)	150	

DISCUSSION

Our study investigated association of depression with pregnancy, itself and its association with age group of the pregnant women, trimester of the pregnancy, gravida, number of live children and with the factor that pregnant women has two or more daughters and having no son.

Rate of depression in pregnant women was 15.33%, that is in line with some previous studies.

An international study has shown rate of major depression disorder from 8% to 12% in pregnant women.[15]

Two Pakistani studies have shown wide difference between the percentage of depression among pregnant women. That is, a study from Karachi, Pakistan showed, 81% prevalence of depression in pregnant women,[16] while other study from Chitral, Pakistan showed, around 34% depression in pregnant females. Both the studies have higher percentage of depression, as compared to our study at Bahawalpur. In our opinion proposed reasons of this difference may be that Bahawalpur is a more religious place and our religion encourages more pregnancies and more children. So religious satisfaction may help in avoiding depression. The other reason may be that we excluded the patient, having past history of depression and other psychiatric illnesses during period prior to pregnancy or during postpartum period.

According to age groups, our study showed highest rate of 24% in age group 18-27 years. Rich-Edwards et al[17] also found that young maternal age was the strongest predictor of antenatal depression. A study from Pakistan also has shown that females in younger age group were high on depression as compared to the female in the elder age category.

Our study has shown relatively high level of depression that is 22.22% in the first trimester, as compared to 2nd and third trimester, which is 9.09% and 16% respectively. But another Pakistani Study from northern Punjab has shown higher levels of depression in third trimester.

Our study also highlighted higher level of depression in primigravida that is, 30.7% as compared to low level of depression in multigravida, that is 7.14%. Similarly, pregnant women having no or one live child were at higher level of depression, that is 30%. In comparison to women having two or more live children, that is 3.27% in women having two to four live children and 10.34% in women having five to six live children. This increase of depression in women having 5-6 children, as compared to women having 2-4 children may be due to unwanted pregnancy.

Another finding of our study is that women having two or more live daughters and no son. They were 6 in our study and out of them four were having depression. This means that not having son is important in our society and is a significant cause of depression.

Depression during pregnancy may have serious effects on the fetus, including intrauterine growth retardation.

CONCLUSION

It is important to diagnose and treat depression in pregnant females.

Author's Contribution:

Concept & Design of Study:	Saeed Akhtar
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Data Analysis:	Fariha Saeed
Revisiting Critically:	Saeed Akhtar, Azra Yasmeen
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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 the Standard Therapy versus Add-On Zinc Therapy for the Management of Hepatic Encephalopathy

Kashif Nawaz[1], Muhammad Rizwan[2], Awais Aslam[3], Atif Maqsood[2], Faizan Aslam[4] and Muhammad Absar Alam[2]

ABSTRACT

Objective: The objective of this study is to compare the frequency of decrease in number of hepatic encephalopathy episodes with patients receiving standard versus add on zinc therapy.

Study Design: randomized controlled study

Place and Duration of Study: This study was conducted at the department of Gastroenterology, Aziz Fatima Medical and Dental college, Faisalabad for a period of six months from July, 2020 to December, 2020.

Materials and Methods: Total 90 patients meeting inclusion and exclusion criteria were studied in 6 months period from July to December 2020. HE was diagnosed with use of west haven criteria. Patients were divided in two groups. On group received standard treatment including lactulose, rifaximin and protein restricted diet (control group) and other group received add on zinc therapy 40 mg daily in addition to standard treatment (Zinc group) and were followed for 3 months and number of HE episodes were noted.

Results: In control group, decrease in episodes of hepatic encephalopathy was observed in 33.33% while decrease in episodes of hepatic encephalopathy was observed in 57.78%. By using chi-square test it found that decrease in number of HE was significantly higher in zinc therapy group having p-value = 0.017. By stratification of age, it was found that there was significant association found in decrease in HE episodes and study group in less than 45 years of age having p-value = 0.018 but there was no significant association between decrease in HE episodes and study group in greater than 45 years of age having p-value = 0.430.

Conclusion: Decrease in episodes of hepatic encephalopathy was observed significantly higher in zinc therapy group. Significant association was found in decrease in HE episodes and study group in less than 45 years of age, males and number of HE episodes in previous three months.

Key Words: Liver Cirrhosis, hepatic encephalopathy, Zinc Therapy.

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INTRODUCTION

In our part of the world cirrhosis of liver is a common cause of mortality and the viral hepatitis being the most common etiological factor. Hepatic encephalopathy (HE) is one of its complications[1].

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Hepatic encephalopathy is a state of disordered central nervous system function resulting from failure of the liver to detoxify noxious agents of gut origin because of hepatocellular dysfunction and porto-systemic shunting[1]. The clinical scale ranges from day-night reversal and mild intellectual impairment to coma[1]. Hepatic encephalopathy is present in up to 70% of all patients with cirrhosis, including patients with abnormalities demonstrable only by psychometric testing[2,3]. Hepatic encephalopathy leads to death in 2.2% of cirrhotic patients during hospital stay[4]. Hepatic encephalopathy portends a worse survival for patients compared to similar patients without HE[5]. The inpatient incidence of HE is approximately 23,000/year[5]. 1-year mortality for patients with severe HE in intensive care unit (ICU) is 54%, with requirement for inotropic support[6].

The pathogenesis of hepatic encephalopathy is not completely understood but ammonia is considered to play a key role[7]. Hepatic encephalopathy is a result of several complex factors rather than a single

mechanism[4]. Etiology of hepatic encephalopathy is thought to be due to biochemical changes in the brain function as it is reversible and does not cause pathological changes in brain[8]. In advanced cirrhosis, ammonia reaches the systemic circulation via Porto-systemic shunting and the failure of the liver to metabolize ammonia. This contributes to the increased occurrence of motor dysfunction and the extra-pyramidal symptoms[7].

Most cases of hepatic encephalopathy are precipitated by infection, gastrointestinal bleeding, electrolyte imbalance, medications or other culprits[5]. Synthetic disaccharides such as lactulose and lactitol have been used as the main agents to treat hepatic encephalopathy in advanced cirrhosis[7]. Neomycin is a poorly absorbed aminoglycoside used to decrease gut bacteria-derived ammonia. Rifaximin can be added in patients not responding to lactulose[5].

Zinc deficiency is common in cirrhotics[5]. In a recent clinical trial, the zinc deficiency prevalence was 96% in patients with a median MELD score of 12[7]. Zinc is a co-enzyme in urea cycle. Ammonia conversion to urea is halted by zinc deficiency[5]. Treatment with zinc has been found to enhance the formation of urea from ammonia and amino acids[9]. The causes of low serum zinc levels in advanced cirrhotic patients are thought to be poor dietary intake via protein-restricted diet, impaired intestinal absorption and excessive urinary losses[7]. Zinc is relatively well tolerated with a rare side effect of dyspepsia[5].

The most recent study from Takuma et al. in 2010[7] randomized patients with cirrhosis and hepatic encephalopathy Grade I-II refractory to standard treatment to receive zinc treatment (n=39) in addition to lactulose and branch chain amino acids (BCAA) versus no zinc (n=40) with BCAA and lactulose. Patients were followed for 6 months to determine the effect on quality of life and hepatic encephalopathy. Hepatic encephalopathy improved in 21(54%) vs. 10 (26%) in the zinc vs. no zinc respectively, with 16 (41%) zinc-treated patients improving to HE grade zero. The role of zinc deficiency has been documented in cirrhotic patients in the development of hepatic encephalopathy. Previous studies have reported the benefit of using zinc supplements in patients with end stage liver disease in reducing the severity of hepatic encephalopathy. However, its role in patients with cirrhosis having hepatic encephalopathy has not been documented in patients in Pakistan as per my knowledge.

MATERIALS AND METHODS

This randomized controlled trial was carried out in department of Gastroenterology, Aziz Fatima Medical and Dental college, Faisalabad. All patients admitted or attended in SIH with HE meeting the inclusion and exclusion criteria were included in study after written informed consent by the guardian of the patient. Total 90 patients were studies which were randomly divided into two groups with 45 participants in each group i-e control group and zinc therapy group. Total duration of study was 6 months from July to December 2020.

Inclusion criteria:

i. Patients with liver cirrhosis diagnosed by radiological findings
ii. Age from 18 to 70 years.
iii. Six or more than six HE episodes in previous three months.
iv. HE of any grade.

Exclusion criteria:

i. Use of antibiotics & drugs having psychometric effect (benzodiazepines, antiepileptic's, psychotropic drugs, or narcotics)
ii. History of shunt surgery.
iii. Organic neurological diseases such as subdural hematoma, Wernicke's disease, encephalitis and drug intoxications.

This study was carried out in department of Gastroenterology, Aziz Fatima Medical and Dental college, Faisalabad. Liver cirrhosis was confirmed by ultrasonographic findings. History and clinical examination were carried out when patients were screened for enrollment. Previous history and recent episode of HE was assessed clinically with use of West Haven Criteria. The study included initial visit, enrollment and treatment phase during hospital stay and as outpatient department (OPD) visit. After taking informed consent eligible patients were selected and divided into two groups by using lottery method. One group received standard treatment including lactulose, rifaximin and protein restricted diet (control group) and other group received add on zinc therapy 40 mg daily in addition to the standard treatment (zinc group). Treatment was continued in both groups for three months. Both groups were followed for three months and the number of hepatic encephalopathy episodes were noted. All enrolled patients and their care-givers were educated about the potential side effects of the drugs.

Data Analysis: Data was analyzed using SPSS version 20. Chi-square test was applied to compare frequency of HE episodes between two groups. Qualitative variables like gender & decrease in hepatic encephalopathy episodes were measured as percentage & frequency. Quantitative variables like age & number of hepatic encephalopathy episodes were measured as mean and standard deviation. Effect modifiers like age, gender & previous number of HE episodes were controlled by stratification. Post stratification Chi-square test were applied

RESULTS

From 90 patients with liver cirrhosis the minimum age was found as 18 years and maximum was 70 years with mean and standard deviation of age as 39.31±18.185

years. The minimum and maximum HE episode in previous three months were found as 1 and 6 respectively having mean and standard deviation as 4.1±1.53 episodes. The minimum and maximum HE episode in last three months of study duration were found as 1 and 6 respectively with mean and standard deviation as 3.33±1.59 episodes. There were 53 (58.9%) male patients and 37 (41.1%) female patients. In control group, decrease in episodes of hepatic encephalopathy was observed in 15 patients (33.33%) while in Zinc group there were 26 patients (57.78%). By using chi-square test it found that decrease in number of HE was significantly higher in zinc therapy group having p-value = 0.017 (Table 1).

Table No.1: Comparison of Decrease in HE episodes in both groups

Group	Decrease HE episodes		Total	P-value
	Yes	No		
Control group	15	30	45	0.017
Zinc group	26	19	45	
Total	41	49	90	

Table No.2: Stratification of outcome in both groups with reference to age and gender

Characteristic	Total	Control group	Zinc group	P-Value
Decrease in HE episode <45 Years (Yes/No)	28/18	10/20	18/10	0.018
Decrease in HE episode >45 Years (Yes/No)	13/19	5/10	8/9	0.430
Decrease in HE episodes in males (Yes/No)	23/30	6/18	17/12	0.014
Decrease in HE episode in females (Yes/No)	18/19	9/12	9/7	0.317

Table 3: Stratification of outcome in both groups with reference to previous no. of HE episodes

Previous no. of HE episodes	Treatment Group	Decrease in HE episodes		Total	P-value
		No	Yes		
< 4 Episodes	Control group	11	6	17	0.251
	Zinc group	13	3	16	
≥ 4 Episodes	Control group	19	9	28	0.001
	Zinc group	6	23	29	
Total		49	41	90	

By stratification of age, it was found that there was significant association found in decrease in HE episodes and study group in less than 45 years of age having p-value = 0.018 but there was no significant association between decrease in HE episodes and study group in patients with age greater than 45 years having p-value = 0.430 (Table 2). By stratification of gender, it was found that there was significant association found in decrease in HE episodes and study group in males having p-value=0.014 but there was no significant association between decrease in HE episodes and study group in females with p-value = 0.317 (Table 2). By stratification of number of previous HE episodes it was found that there was no significant association in decrease in HE episodes and study group in less than 4 previous HE episodes having p-value = 0.251 whereas there was significant association between decrease in HE episodes and Zinc therapy group for more than 4 previous HE episodes having p-value 0.001 (Table 3).

DISCUSSION

The objective of the present research was to to compare the frequency of decrease in number of hepatic encephalopathy episodes with patients receiving standard versus add on zinc therapy. In this regard the present randomized control trial was conducted in department of Gastroenterology, Aziz Fatima Medical and Dental college, Faisalabad. This study revealed that zinc supplementation in addition to standard treatment clearly demonstrates improvement in hepatic encephalopathy episodes and its recurrence. Synthetic disaccharides are also effective in reducing blood ammonia levels by mainly inhibiting absorption of ammonia from intestine. This synergism of two agents (zinc and synthetic disaccharides) for reducing ammonia caused by different mechanisms seems to be effective in patients unresponsive to standard therapy. Several studies showed improvement in psychomotor performance with reduction in serum ammonia level in HE patients with zinc supplementation[10,11]

Previous studies[11-13] revealed significant improvement in patients with HE on zinc supplementation in addition to standard treatment that was consistent with our results. Hayashi et al[13] described that combined therapy with zinc and conventional therapy lowered blood ammonia level more than branch chain amino acids alone. They inferred from their result that zinc administration increased liver ability to metabolize ammonia.

Mean age in our study was 39.31 years whereas takuma et al[7] reported mean age of 66.5. In our study 58.9 % participants were male and 41.1 % were female. Comparison to it there were 50.63 % male and 49.4 % were female participants as previously reported[7]. In contrast to these results previous study[14] concluded that zinc supplementation failed to improve HE, the different outcomes between those studies and the present one are may be due to variable duration of zinc therapy or participants background.

Limitations of this study are that it was conducted in short period of time and was non-blinded. Although treatment bias unavoidable because our study was assessed by same person unaware of the assignment.

CONCLUSION

In conclusion, Zinc supplementation may be an effective treatment for the HE that also prevents its recurrence. However Double blinded randomized controlled trial in large population is necessary to make definitive conclusion.

Author's Contribution:

Concept & Design of Study:	Kashif Nawaz
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Data Analysis:	Atif Maqsood, Faizan Aslam, Muhammad Absar Alam
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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 Whole Walnut, Ethanolic and Aqueous Walnut Leaves Extract on Lipid Profile and Atherogenic Index in Hypercholesterolemic Rats

Rabia Azhar[1], Shazia Ali[1], Humaira Fayyaz Khan[1], Ghazala Jawwad[1] and Fareeha Farooq[2]

ABSTRACT

Objective: To compare the effect of whole walnut and walnut leaf extract (Aqueous and Ethanolic) on lipid profile and atherogenic index in Hypercholesterolemic rats.

Study Design: Experimental study

Place and Duration of Study: This study was conducted at the Islamic International Medical College, Riphah International University, in collaboration with National Institute of Health and Citilab, Islamabad, Pakistan from January to June 2015.

Materials and Methods: A total of 50 Sprague Dawley rats were in divided in five groups, HC (hypercholesterolemic control), WW (Whole walnut), AE (Aqueous extract), and EE (Ethanolic extract). Serum cholesterol, triglycerides, LDL, HDL and atherogenic ratios LDL/HDL and TC/HDL were measured at baseline, 8 and 12 weeks respectively after inducing hypercholesterolemia. Data was analyzed by ANOVA and student t test using SPSS version 19. P value of <0.05 was considered statistically significant.

Results: WW in comparison to AE group decreased serum triglycerides (p=0.01) and serum total cholesterol in (p=0.02). WW in comparison to EE group decreased only serum triglycerides significantly among all lipid profile parameters (p=0.00). A significant decrease in serum total cholesterol (p=0.00) and an increase in serum HDL (p=0.00) by EE was observed compared to AE group.

Conclusion: WW, AE and EE have specific effects on individual lipid profile parameters which is hypolipidemic as all three decreased bad cholesterol and raised the good HDL lipoproteins. Further research can delineate this therapeutic potential in cardiovascular diseases.

Key Words: Atherogenic index, Hypercholesterolemia, Juglans regia, Triglycerides, Walnuts

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INTRODUCTION

Cardiovascular diseases cause worldwide morbidity and is a leading cause of death in United States.[1] Abnormal lipid profile due to unhealthy lifestyle, diet and stress contributes to this situation. Since high cholesterol levels does not necessarily cause any symptom so many people live with it undiagnosed and untreated.

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Total cholesterol level of more than 200mg/dl is defined as hypercholesterolemia and 38% of adults in America and increases risk of stroke and heart disease.[2] Out of all the lipoproteins that circulate in blood, Low Density Lipoprotein is considered as the most dangerous. A recent large population-based study in Denmark found a higher incidence of myocardial infarction and atherosclerotic cardiovascular disease with raised small dense LDL.[3] As the field of lipidology is expanding based on increasing clinical trials and genetic epidemiology studies, serum triglycerides remains a valuable predictor of the atherosclerotic disease.[4] VLDL also transports cholesterol and has shown it to contribute fifty percent of risk among all apo-B containing lipoproteins. The good cholesterol containing lipoproteins are called High-density lipoproteins. There is recent data on HDL proteome which is unveiling them as useful markers on cardiovascular protection.[5] Serum HDL is a promising marker as more mechanistic insights into HDL metabolism are unveiling.[6] The ratios of total cholesterol to HDL and LDL/HDL are said to be best

predictors of cardiovascular disease and is more sensitive and specific than individually used LDL, total cholesterol, and HDL levels.[7]

Lipid lowering agents are used to treat hypercholesterolemia. However, use of medicinal plants for their therapeutic potential are gaining importance for being safe and cost effective.[8] Walnut (Juglans regia L,) belongs to family juglandaceae and is produced in South Asia, Japan, China, and United States. Walnut fruit as well as kernel, shell, leaves, septum, bark, epicarp have all been shown to possess anti oxidative and anti-inflammatory properties.[9]

The objective of this study was to compare the effect of whole walnut as well as walnut leaves extract (both aqueous and ethanolic) on lipid profile with ratios of LDL/HDL and TC/HDL in rats with raised cholesterol levels.

MATERIALS AND METHODS

This study was conducted at Islamic International Medical College, Riphah International University and National Institute of Health (NIH) after ethical approval. A total of 50 male Sprague Dawley rats were divided into control (C), hypercholesterolemic control (HC,) whole walnut (WW), aqueous (AE) and ethanolic extract (EE) groups. C was fed on standard rat diet throughout the study. HC was fed for initial eight weeks with high fat diet and then fed on standard rat diet till the study was completed. High fat diet (HFD) was 17 % of calories as carbohydrates, 25% as proteins and 58% calories as fat and 2% cholesterol powder[10]. WW was fed for initial eight weeks with high fat diet and then given 10% whole walnut feed (powder) mixed in standard feed daily.EE and AE were given extracts of 100gm powder of walnut leave in 1000ml of 95% ethanol and distilled water respectively.[11]

Sampling was done at baseline, 08 week & 12 weeks. Blood was centrifuged at 3000 rev/min for I5 min to obtain serum. Serum total cholesterol (TC), Serum triglycerides (TG), serum LDL and serum HDL were analyzed using Merck Germany kits (lot no 17895) on Selectra E Automated chemistry analyzer.[12] All data was shown as mean ±S.E.M. ANOVA and student t test were applied using SPSS 19. A p-value of < 0.05 was considered as statistically significant.

RESULTS

Comparison of lipid profile parameters in all groups at the end of experiment as shown in table 1. Comparison of WW and AE showed that aqueous extract significantly reduced TC and TG levels in both the groups as shown in table 2. Comparison of WW and EE revealed that EE significantly reduced only TG levels (p=0.00) as shown in table 3. Comparison of AE and EE revealed significant reduction of serum TC levels (p=0.00). Serum HDL levels were significantly increased in EE group as shown in table 4.

Table No.1: Comparison of lipid profile in all groups at the end of 12 weeks.

		Sum of Squares	df	Mean Square	F	p value
TC (mg/dl)	Between Groups	66265.150	4	16566.288	613.404	.000
	Within Groups	945.250	35	27.007		
	Total	67210.400	39			
TG (mg/dl)	Between Groups	34859.650	4	8714.913	86.848	.000
	Within Groups	3512.125	35	100.346		
	Total	38371.775	39			
LDL (mg/dl)	Between Groups	3360.400	4	840.100	118.383	.000
	Within Groups	248.375	35	7.096		
	Total	3608.775	39			
HDL (mg/dl)	Between Groups	68.900	4	17.225	7.188	.000
	Within Groups	83.875	35	2.396		
	Total	152.775	39			
TC/HDL ratio	Between Groups	136.504	4	34.126	438.670	.000
	Within Groups	2.723	35	.078		
	Total	139.227	39			
LDL/HDL ratio	Between Groups	8.131	4	2.033	70.321	.000
	Within Groups	1.012	35	.029		
	Total	9.143	39			

*= $p < 0.05$ is considered significant

Table No.2: Comparison of lipid profile in WW and AE groups

Groups		Mean ±SD	p-value
TG (mg/dl)	WW	76.13±4.74	.001*
	AE	3.30±14.63	
TC (mg/dl)	WW	51.88±6.10	.02*
	AE	45.00±4.56	
LDL (mg/dl)	WW	22.75±2.43	0.15
	AE	1.25±1.48	
HDL (mg/dl)	WW	25.50±1.64	0.36
	AE	24.87±0.83	
TC/HDL ratio	WW	2.03±0.28	0.11
	AE	1.84±0.15	
LDL/HDL ratio	WW	0.89±0.13	0.41
	AE	0 .85±0.06	

*= p <0.05 is considered significant

Table No.3: Comparison of lipid profile in WW and EE groups

Groups		Mean± SD	p-value
TG (mg/dl)	WW	76.1±4.703	0.00***
	EE	50. 6±11.73	
TC (mg/dl)	WW	51.8±6.108	0.71
	EE	52.8± 4.428	
LDL (mg/dl)	WW	22.7± 2.430	0.20
	EE	21.5±1.060	
HDL (mg/dl)	WW	25.5±1.690	0 .23
	EE	26.5± 1.510	
TC/HDL ratio	WW	2.03±0.288	0.71
	EE	1.991±0.212	
LDL/HDL ratio	WW	0.89± 0.135	0.11
	EE	0.80± 0.648	

*= p <0.05 is considered significant

Table No.4: Comparison of lipid profile in AE and EE groups

Groups		Mean± SD	p-value
TG (mg/dl)	AE	53.33± 14.60 8	0.68
	EE	50.62± 11.73	
TC (mg/dl)	AE	45.00± 4.56	0 .00*
	EE	52.83± 4.40	
LDL (mg/dl)	AE	21.25± 1.480	0 .70
	EE	21.50± 1.060	
HDL (mg/dl)	AE	24.87± 0.830	0.01*
	EE	26.50± 1.510	
TC/HDL ratio	AE	1.84± 0.153	0.14
	EE	1.99±0.21 2	
LDL/HDL ratio	AE	0.85± 0.065	0.19
	EE	0.80± 0.068	

* = p <0.05 is considered significant

DISCUSSION

Comparison of lipid profile amongst all groups revealed significant (p=0.00) difference as shown in table1. Further comparison between WW, AE and EE groups indicate that TG, TC, LDL, TC/HDL and LDL/HDL ratio are all not uniformly reduced in all three groups but have specific effects on each lipid profile parameter as shown in tables 2,3 and 4. HDL levels were significantly increased in only EE group (26.5 mg/dl; p=0.01) in comparison with AE group, along with decrease in TC (p=0.00) as shown in table 4. EE in comparison with WW whole walnuts significantly decreased only serum TG (p= 0.00) as shown in table 3. WW in comparison to AE reduced both serum TC (p=0.02) and TG (p=0.01) as shown in table 2. Similar results are reported by Uti DE et al, whereby ethanol extract of walnuts decreased total lipid, phospholipids, triacylglycerol, and cholesterol concentration in adipose, kidney, brain and heart tissues of obese rats fed.[13-15]

Sun Y et al found a decrease in serum LDL as well as cardiac markers in MI with use of walnut kernel extracts.[16] Walnut leaves consist of components like fiber, folic acid, calcium, potassium, vitamin E and C, magnesium, plant protein (e.g., arginine) and polyphenols along with fatty acids. Unsaturated fatty acids and polyphenols have antioxidant properties in rats with diabetic nephropathy and lung injury. [14,15] The possible mechanism for lowering lipid levels by walnut leaves is that phenolic acids and flavonoids. Pedunculagin is a polyphenol which belongs to the class ellagitannin. Its hydrolysis yields ellagic acid and urolithins Ellagitannins are antioxidant and anti-inflammatory in cancer, cardiovascular, and neurodegenerative diseases.

A recent study conducted by Liu X et al conducted on three large cohorts of men and women using food frequency questionnaires for four years found walnuts consumption associated with decreased risk of coronary artery disease and stroke.[17] They report lipid lowering effect due to another antioxidant substance called quercitin and cholorogenic acid. They reduce synthesis of cholesterol in the liver through suppression of HMG COA reductase enzyme and thus causes increased release of cholesterol in bile. The phenolic compounds isolated from nuts by HPLC fingerprinting have recently been shown to have antioxidant properties responsible for reducing serum cholesterol as reported by Olabiyi AA et al.[18]

Recent large-scale studies in metabolomics and lipidomic fields are investigating the complex metabolism of lipids in chronic inflammatory diseases and diabetes. Side by side nutraceuticals such as walnuts have gained special attention due to unique composition of omega 3 and omega 6 fatty acids as well as antioxidant polyphenols.

The strength of this study is the comparative analysis of three groups WW, AE and EE which has not been done before and shows differential effects on lipid

profile which can be further explored. Further studies can be carried out using different doses and timings of walnut intake as well as designing a different combination of macronutrients to understand the impact on lipid profile. Beneficial effect of walnuts using newer markers of cholesterol metabolism at molecular level offers more for future research.

CONCLUSION

The present study suggests that whole walnuts in comparison with aqueous and ethanolic extract of its leaves decreased both serum total cholesterol and triglycerides. Moreover, the ethanolic extract increased serum HDL compared to aqueous extract.

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Original Article

Practices of Blunt Abdominal Trauma in a Government Tertiary Care Hospital, Karachi, Pakistan

Different Kinds of Management with Blunt Abdominal Trauma

Aqsa Ismail, Rizwan Ahmed Khan, M. Hassan ul Haq, Bushra Tasneem, Ayesha Tasneem and Rahil M Rahman

ABSTRACT

Objective: To determine the frequencies of different kinds of management provided to the patient presented with blunt abdominal trauma (BAT) in a government tertiary care center in Karachi, Pakistan.

Study Design: prospective descriptive analytic study

Place and Duration of Study: This study was conducted at the Surgical Department, Abbasi Shaheed Hospital Karachi from July 2019 to July 2021.

Materials and Methods: The data was captured using a pre-designed and pre-tested questionnaire. Data of all patients admitted in hospital diagnosed with blunt abdominal trauma were prospectively collected. Advance Trauma Life Support (ATLS) protocols were used to treat the trauma. Laboratory and imaging investigation were done to make diagnosis and manage patients. Data was entered and analyzed using SPSS version 26.0. Descriptive statistics were reported in terms of mean ± SD/median, frequency and percentage where appropriate

Results: Total 84 BAT patients were reviewed during the study period. Mean age of patients was 31.3 ± 12.2 years. Majority of the injured patients were males (n=73, 86.9%) and were symptomatic cases (n=77, 91.7%). More than half of the cases had injuries other than abdomen as well (n=53, 63.1%). Abdomen was tender on presentation among more than half of the patients (n=51, 60.7%). X-ray (n=60, 71.4%), ultrasound fast (n=54, 64.3%) and laboratory investigations (n=54, 64.3%) were done for majority of the patients. CT-scan for abdomen was performed in nearly quarter of the patients (n=25, 29.8%). Few patients did not survive (n=10, 11.9%). 78.6% of patients were treated conservatively and 21.4 % of patients underwent surgical interventions

Conclusion: For vitally stable patients with blunt injuries, non-operative therapy has become the gold standard. Although NOM has a greater failure probability in patients with multiple solid organ injuries, in most vitally stable individuals who do not have peritoneal symptoms, it can still be taken with caution.

Key Words: Blunt abdominal trauma (BAT), hemodynamically or vitally stability, non-operative management (NOM), Injury, Focused assessment with sonography in trauma (FAST)

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INTRODUCTION

Trauma or injury is defined as bodily harm induced by an exchange of environmental energy larger than the strength of body[1]. It is seen as a major public health problem worldwide, regardless of socioeconomic background[2]. Abdominal trauma is classed as penetrating or blunt depending on the mechanism of injury[3]. Injury is the seventh biggest reason of death worldwide, and the abdomen is the third highest commonly injured organ[3].

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Blunt abdominal trauma (BAT) is missed because it is usually not obvious unless examined multiple times. Diagnosis delay and insufficient management of abdominal injuries may become lethal. Initial resuscitation, in combination with focused assessment with sonography in trauma (FAST) and computed tomography (CT) abdomen, is particularly helpful in detecting individual with limited and clinically unidentifiable indications of abdominal injury, and is recommended in recent care guidelines[4]. A patient who is hemodynamically unstable and has a positive FAST exam should undergo laparotomy right away. Ultrasonography is an adjunct of the clinical evaluation and should not intervene with primary and secondary intervention. The development of non-operative treatment has been aided by the use of CT scanning, which enables for precise identification of solid organ injury. Approximately 10% of patients experience prolonged hypovolemic shock despite vigorous fluid resuscitation and need an emergency laparotomy. There has been a growing trend toward non operative

management (NOM) of blunt abdominal trauma, which now accounts for 80% of cases with failure rates ranging from 2% to 3%. For vitally stable solid organ injuries, NOM is a routine treatment[4]. NOM of blunt splenic damage has reported success rates of 95 percent or higher in children and around 80 percent or greater in adults[5]. The majority of this data, on the other hand, comes from retrospective research, and it focuses on the failure percentage of single intra-abdominal solid organs trauma treated non-operatively. Despite the fact that NOM has a greater failure rate in cases of multiple solid organ injury, it should be used with caution in these cases[6].

In trauma management, pre-hospital transfer, initial examination, complete resuscitative efforts, and accurate diagnosis are critical. The mortality rate was only 2% with timely diagnosis and treatment (within 8 hours), however delays of 8 to16 hours resulted in a 9% mortality rate (a four-time increase), and when these injuries were detected >24 hours after admission, the mortality rate was 31% (a 15-time increase)[7].

MATERIALS AND METHODS

This prospective descriptive study was conducted at surgical department of Abbasi Shaheed Hospital Karachi after approval from the institutional ethical review board. The data was captured using a pre-designed and pre-tested questionnaire. The study included patients of either gender between the ages of 20 and 60 who arrived to the emergency with a diagnosis of blunt abdominal trauma confirmed by ultrasound. Individuals with penetrating trauma, those who died on arrival, pregnant women, and those who left during resuscitation against medical advice were all excluded from the present study. Data of all patients who were admitted in Surgical Department of Abassi Shaheed hospital diagnosed with blunt abdominal trauma from July 2019 to July 2021 were prospectively collected with designed Performa.

Trauma patients presented to emergency department were firstly resuscitated at trauma management room following the Advance Trauma Life Support (ATLS) protocols. All patients were investigated by x-ray examinations & ultrasound FAST scan for diagnosis when admitted to emergency as per standard procedure. After performing first resuscitation and considering the hemodynamic stability, patients were carefully assessed. Further investigations such as diagnostic peritoneal lavage and CT Scan abdomen were done based on clinical finding. Physical examination and abdomen examination findings included abrasions, bruising on abdomen, localized or generalized tenderness. An exploratory laparotomy were conducted in all BAT patients with peritonitis, tenderness, hemodynamic instability, or a free fluid finding on the FAST. Intra-abdominal solid viscus injuries were documented on ultrasound in hemodynamically stable patients and laparotomy findings in unstable patients. Patients' clinical and demographic characteristics that included age, gender, socio-economic status, types of injury, presence of gut sound, body mass index and final outcome were recorded on pre-designed Performa. Data were entered and analyzed using SPSS version 26.0. Mean ± SD/Median were computed for the quantitative variables based on the distribution of data. Normality of the data were checked by Shapiro- Wilk test. Frequency and percentage were computed for all the categorical variables**.**

RESULTS

Total 84 BAT patient were reviewed during the study period. Mean age of patients was 31.3 ± 12.2 years.

Table No.1: Descriptive statistics of study subjects

Variables	**Frequency (%)**
Age (in years)[#]	31.3 ± 12.2
Gender	
Male	73(86.9)
Female	11(13.1)
Symptomatic cases	
yes	77(91.7)
no	7(8.3)
Injuries other than abdomen	
yes	53(63.1)
no	31(36.9)
Presence of gut sounds	
yes	60(71.4)
no	24(28.6)
Abdomen tenderness	
yes	51(60.7)
no	30(35.7)
not examined	3(3.6)
Abdominal wall sign	
yes	31(36.9)
no	53(63.1)
Injuries other than abdomen	
Head	11(13.1)
Chest wall	42(50)
Ribs	13(15.5)
Pelvis	18(21.4)
Investigations done	
X-ray	60(71.4)
Ultrasound fast	54(64.3)
laboratory investigations	54(64.3)
CT-scan for abdomen	25(29.8)
Outcomes	
alive	74(88.1)
dead	10(11.9)

#: Age is presented as mean ± standard deviation

Majority of the injured patients were males (n=73, 86.9%) and were symptomatic cases (n=77, 91.7%). More than half of the cases had injuries other than abdomen as well (n=53, 63.1%). Nearly quarter of the

participants had no gut sounds (n=23, 27.4%) and abdominal wall sign was present in 31 (36.9%) patients. Abdomen was tender on presentation among more than half of the patients (n=51, 60.7%) (Table 1). Figure 1 shows the frequency of injury mode.

X-ray (n=60, 71.4%), ultrasound fast (n=54, 64.3%) and laboratory investigations (n=54, 64.3%) were done for majority of the patients. CT-scan for abdomen was performed in nearly quarter of the patients (n=25, 29.8%). Few patients did not survive (n=10, 11.9%) (Table 1). Figure 2 shows the frequency of approach used for the management of the patients.

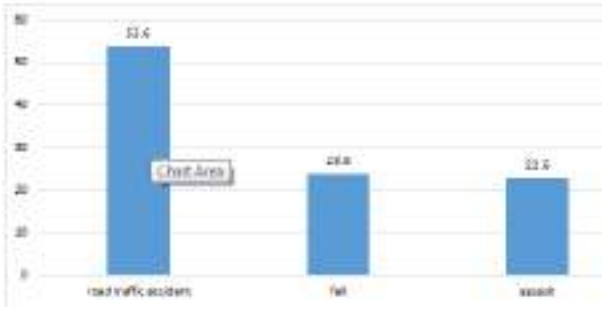

Figure No.1: Frequency of injury mode

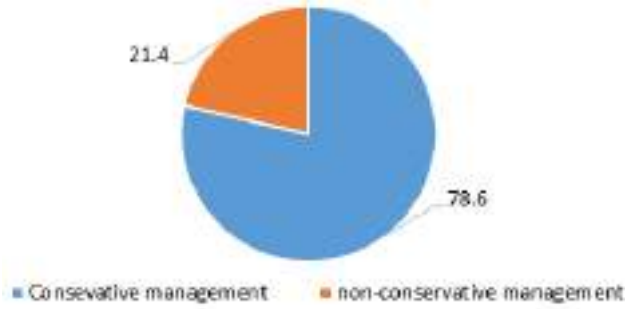

Figure No.2: Types of management provided to blunt abdominal Injury patients

DISCUSSION

Total 84 BAT patients were reviewed during the study period. Mean age of patients was 31.3 ± 12.2 years. This is in accordance with a research conducted by Mehta et al. they reported that 40% of patients who sustained BAT were between the age of 21-30 years[8]. One possible reason for affecting young population is that in developing countries, such as Pakistan, have a high rate of traffic and industrial trauma. We observed that the majority of the injured cases were males. This is in line with the researches of Mehta et al[8] and Bushra Khan et al[1]. Road traffic accidents (RTA) were the most frequent source of abdominal injury in our analysis, followed by falls. This is in accordance with the research of Mehta et al. They reported motor-vehicle accidents were responsible for 53% of all trauma cases[8].

In the present study FAST was performed in 64.3 % of patients while CT Scan abdomen were performed in 29.8 % of patients. Ultrasonography, has been shown in some studies to be a viable alternative to CT scans, which are regarded as the gold standard in the field of radiology. In a randomized analysis, Rose et al. found that 52% of the control group (who did not get ultrasound in the casualty room) eventually had CT, in comparison to just 36% of the ultrasound group. They came to the conclusion that evaluating patients with blunt abdominal injuries by utilizing with abdominal ultrasound could reduce the CT scan need[9,10]. In a study conducted on 4,029 participants, 122 were hypotensive at the time of admission, Lee et al. found that FAST ultrasonography showed 85% sensitivity, 60% specificity, and 77% accuracy in forecasting the requirement for surgery in the hypotensive cohort. Finally, researchers observed that in hypotensive patients with acute abdominal injuries, a positive FAST ultrasound may result in direct triage to therapeutic laparotomy without the necessity for a CT scan of the abdomen[10]. Miller et al., in contrast to these results, suggested that using FAST ultrasonography as a screening technique in hemodynamically stable patients may lead to a misdiagnosis of intra-abdominal injuries, putting the therapy and outcome at danger. As a result, such patients must get a CT scan on a regular basis[11].

To rule out extra-abdominal injuries, the surgeon should seek for additional sources of trauma. Abdominal injuries were associated to a variety of extra-abdominal injuries. In our study the most prevalent accompanied extra-abdominal injuries, were chest wall (50%), Pelvis (21.4%) and rib fractures (15.5%). Similarly, Arumugam S et al[2] also discovered that chest injuries to be the most commonly related upper extra-abdominal injuries in polytrauma patients followed by limbs and head injuries. Furthermore, Mehta et al. also discovered that rib fractures (20 percent) and soft tissue injuries (20 percent) were the most common extra abdominal injuries in their study[8].

In our research, 78.6% of patients were treated conservatively, while 21.4 percent required surgical intervention. According to Arumugam S, et al[2], 27% of their patients had laparotomies. Another Turkish study found that emergency laparotomies were performed in 13% of blunt abdominal trauma cases[12]. Howes, et al observed that 8% of trauma victims with abdominal injury needed a laparotomy[13]. Multiple researches indicated that NOM for solid organ injury is beneficial amid the last three decades, with a reported success rate of >90%[14,15].

Eelderliness, ISS, and cerebral injury may all have an impact on NOM's success rate, among other variables[15,16]. In a study of 558 individuals with traumatic splenic injury conducted at a single institute, found that NOM failed in 22% of patients who were above 55 years, compared to 6% of patients under 55 years[16]. In practically all instances, Bee et al.7 found that the failure rate was independently determined by ISS[16].

In numerous researches, the reasons of failure have been explained in various ways. One-third of patients had failure due to causes other than solid organ injury, according to Velmahos et al[17]. Bicycle collision were linked to a higher risk of NOM failure, according to Holmes et al[18], who also discovered that In isolated organ injury, the percentage of NOM failing was 10.9-o 38.2%, whereas in multiple organ injury, it was 54.4-70%.

Mortality in our study was 11.9%. Musau et al[19] found that 12.5% of patients with abdominal injuries died. Another prospective study on blunt abdominal injuries found a 26% overall death rate, with half of the patients dying from sepsis-related multiple organ failure[13]. Mortality rate ranged from 2.4% to 4 % in other studies[2,8]. The rationale for the greater risk of mortality in our study could be due to patients' delayed presentation. Arumugam S et al. also reported that, cause-specific mortality was rather high, with serious head injuries (58%) and sepsis accounting for the majority of deaths (33%).

This study has various limitations, the sample size is very small, and needs to be increased. A larger sample size is required to truly evaluate the various management procedures for the treatment of blunt abdominal trauma and their rate of success.

CONCLUSION

For vitally stable patients with blunt injuries, non-operative therapy has become the gold standard. Although NOM has a greater failure probability in patients with multiple solid organ injuries, in most vitally stable individuals who do not have peritoneal symptoms, it can still be taken with caution.

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Original Article

The Effects of Virtual Reality on Burden, Quality of Life and Satisfaction in Informal Caregivers of Stroke Survivors

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ABSTRACT

Objective: To determine the effects of virtual reality on burden, quality of life and satisfaction in informal caregivers of stroke survivors.

Study Design: Randomized control trial study

Place and Duration of Study: This study was conducted at the Rawal General Hospital Rawalpindi from Aug 2020 to March 2021 for a period of six months.

Materials and Methods: A Total of 66 participants were included divided into three groups, Group A had undergone virtual reality therapy using Kinect (XBOX360) while playing the game Kinect adventure. The participants of Group B undergo cognitive Behavioral Therapy. The participants of group C were provided with both CBT and VR training. Assessments were taken at baseline and after 4 weeks using tools as The Caregiver Strain İndex, 36-Item Short Form Health Survey and the Adult carer questionnaire. Data analysis was done through SPSS-21.

Results: Analysis show significant effects of virtual reality on burden, quality of life and satisfaction in informal caregivers of stroke survivors for within group analysis and between group analysis with p value <0.05.

Conclusion: It is concluded that VR&CBT combined is effective in improving quality of life reducing caregiver's burden and increasing satisfaction.

Key Words: Cognitive Behavioral Therapy, Quality of Life, Virtual Reality

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INTRODUCTION

Stroke, or a Cerebrovascular accident (CVA) is a neurological dysfunction that often renders patients with different levels of disability which in turn need inpatient treatment along with prolonged care at home for complete function and recovery.[1] A stroke attack occurs as a result of interruption of blood supply and oxygen to the brain cells for a period of time can result brain cell death in the affected area. Stroke can result in the development of symptoms such as sudden, severe headache, loss of balance, slurring of speech, drooping of eyelids or mouth paresis or paralysis of the affected side, difficulty in comprehending and articulating speech sudden blurring or loss of vision.

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Therefore, the caregivers are put under the pressure to handle multiple responsibilities resulting in burden, especially when the needs of the caregivers are ineffectively addressed during the recovery phase of the patient. Stroke can often result in severe and long-lasting disabilities, especially in older people. This manifestation can result in loss of independence and the impending need for long-term care either at home or even in a nursing home depending upon the extent of disability or post stroke manifestations. Major disability may always involve impairment of several functions i.e. more than one for example, diminished power in the right side is very common .Moreover some of these limitations which may be seen in patients with stroke are due to poor motor control, muscle weakness and soft tissue tightening, sensory disturbances and balance disturbances, etc.[2] These conditions are particularly increasing the risk of falls for the patients. Weakness/ paresis could be considered the most prevalent impairments during the early stages post stroke as they result in disuse atrophy of limbs. Chronic pain, immobility and some other sensory impairments can also result in the above-mentioned atrophy state.[3] Symptoms can be ranging from varying degrees of minor weakness to a severe weakness/paresis or in the most severe cases of all consequently paralysis of one side of the body[4]. Depression is also a very frequent

disorder for post stroke patients. It often develops as a result of biochemical alterations of the brain. When the brain is damaged, the stroke victim may not be able to feel or sense positive or good emotions. Depression can also be a result of normal psychological reaction due to losses or disabilities caused by the stroke. The stroke survivors not only experience physically degrading changes, but many people experience changes in personality ranging from minor disturbances such as apathy to even total neglect.[5]

The demands of caregiving can result in a decrease in leisure time, socializing, adequate time for sleep, and mental relaxation for informal caregivers. It also affects their work lives due to decrease in working hours as to look after the patient, or even resignation due to poor work performance or overwhelming work burden, o ultimately in an early retirement. An increase in expenses due to the patient care including medications etc. and a decrease of the income of caregivers have also been reported in the 12-15 months post hospital discharge. It can also be due to the raise in care related expenses. In addition to that, factors such as prolonged time of care, or having higher levels of closeness or intimacy with the stroke survivor, physical disabilities and the costs to compensate for those changes, cognitive changes, and behavioral disturbances of the patient, diminished mobility, dependency for ADLs results in immense pressure and burden for the caregivers. There are many cases where caregivers have reached to the denial phase because of their dreadful experiences.[6] Stress coping strategies may include Virtual Reality (VR), Physical Exercise (P.E) and CBT (Cognitive Behavioral Therapy)

Virtual reality is the use of equipment to create virtual surroundings that make the user the feel of being absorbed in it. These atmospheres (3D designs or real videos) are multisensory (visual and auditory) and are produced by us with the purpose of treating changed psychosomatic pathologies.

The idea is to make a logic of being there: that the patient senses the identical emotions and has the similar feelings and responses that he would have in real life [7]. Cognitive behavioral therapy is a psycho-social intervention that aims to improve mental health. CBT focuses on challenging and changing unhelpful cognitive distortions and behaviors, improving emotional regulation and the development of personal coping strategies that target solving current problem. As per APA only 8-10 sessions are enough to create a significant improvement in patients.[8] Stroke survivors becoming disabled partially or completely, creates a high level of burden among caregivers. This burden gradually produces a negative effect on life of caregivers. In accessible literature very few researches have been conducted on this topic and none have been conducted on the effectiveness of VR on post stroke's informal caregiver's burden, QoL and satisfaction collectively. This study helps to determine the effect of usage of accessory tools such as virtual reality in eradication of caregiver's, burden or in satisfaction and improvement of quality of life.

MATERIALS AND METHODS

The study had approval from the Research Ethical Committee with REC.no: 00753 of Riphah International University and registered with IRCT20211123053152N1. Sixty-six participants were recruited with their consent and divided them into three groups A, B & C randomization. Randomization was done through sealed envelope method. Caregivers were recruited, from Physiotherapy department of Rawal General Hospital, of both genders aged between 20 to 40 years, taking care of patients for more than 3 months and having caregiver strain index above 7. Caregivers who were no longer primary caregiver or taking care of more than one patient or were suffering from any neurological or orthopedic disorder were excluded. We had also used blinding assessor process. We had accessed the participants prior to intervention in 1st weeks and after the intervention in 4th week to see the difference. Intervention was done for 4 weeks with 3 days every week. The participants of Group A had undergone virtual reality therapy using Kinect (XBOX360) while playing the game Kinect adventure. The procedures were explained to the subjects, and a demonstration of games was given by the therapist before starting the intervention. The intervention goes on for 4 consecutive weeks. The subject plays the game for 25 to 30 minutes for 3 times in a week. The participants of Group B undergo the Psychotherapy using Cognitive Behavioral therapy. Caregiver takes the CBT from the Psychologist for 25 to 30min per day for 3 times a week for a full month. The participants of group C were provided with both CBT and VR training for hour, 3 times in a week for a month. Total of 87 caregivers were assessed for eligibility. 11 were excluded in which 5 were not meeting the inclusion criteria and 6 declined to participate. 66 Caregivers participated in this research in which 48 were given intervention. We had also used blinding assessor process. We had accessed the participants prior to intervention in 1st weeks and after the intervention in 4th week to see the difference. Intervention was done for 4 weeks with 3 days every week.

The IBM SPSS 21 version was used for all statistical analysis. Normality test was applied on General health, limitation of activities, physical health problem, emotional health problem, social activities, pain, energy and emotion, social activities, Adult carer QOL and CSI. Non-parametric test was applied on the data because the p-value was <0.05. Non-Parametric; Wilcoxon signed rank test was applied for within group analysis. Kruskal Willis test was used for comparison of all three.

RESULTS

The mean age of GPA(VR)was 29.91±5.51, GPB(CBT) was 29.8±4.8 and GPC(VRCBT) was 29.8±4.58. Among total individuals, 26(27.3) were females and 22(22.7) were males. There were 15(18.2) caregivers who were taking care for the patient for 3 months, 12(8.3) for 4-6 months and 21(23.5) caregivers were taking care for 6-1 years. CSI frequency of Group A VR is 19(14.2) and in Group B CBT is 13(6.2) and VRCBT is 16(10.3).

Wilcoxon Sign Rank test was used for within group Analysis. General health, limitation of activities, physical health problem, emotional health problem, social activities, pain, energy and emotion, social activities, Adult carer QoL and CSI and it shows significant effect with p value <0.05. Kruskal Willis test was used for between group Analysis and it shows significant effect with p value <0.05.

Table No.1: Wilcoxon Sign Rank between groups Analysis

Variables		(VR GROUP A) MR	(CBT GROUP B) MR	(VRCBT GROUPC) MR	P value
General Health	Pre-Test	10.74	8.50	10.12	0.00
	Post Test	8.50	7.20	8.91	
Limitation of activities	Pre-Test	10.74	9.22	12.70	0.00
	Post test	8.22	8.50	10.32	
Emotional health problems	Pre test	9.50	8.25	9.23	0.00
	Post test	8.21	6.41	7.11	
Social activities	Pre test	9.50	8.25	9.23	0.00
	Post test	7.21	6.41	7.11	
Pain	Pre test	10.1	7.5	11.2	0.00
	Post test	8.3	6.41	9.5	
Energy and emotion	Pre test	10.4	9.4	12.1	0.00
	Post test	7.3	7.41	10.6	
Adult carer QoL	Pre test	9.50	6.23	9.23	0.00
	Post test	7.21	5.4	6.11	
CSI	Pre-Test	8.50	9.25	11.23	0.00
	Post test	5.1	7.41	8.50	

Table 2: Kruskal Wallis test for within group Analysis

Variables		(VR GROUP A) MR	(CBT GROUP B) MR	(VRCBT GROUP C) MR	P value
General Health	Pre-Test	35.4	34.2	30.8	0.661
	Post Test	32.8	33.6	22.0	0.00
Limitation of activities	Pre-Test	32.5	32.5	35.5	0.508
	Post test	30.0	29.2	23.5	0.00
Emotional health problems	Pre test	32.5	33.5	35.5	0.775
	Post test	22.5	22.5	20.5	0.000
Social activities	Pre test	33.5	33.5	33.5	0.563
	Post test	31.5	32.2	29.6	0.001
Pain	Pre test	31.5	35.1	33.8	0.691
	Post test	23.5	21.5	22.5	0.000
Energy and emotion	Pre test	30.9	34.2	35.3	0.787
	Post test	23.5	21.5	22.5	0.000
Adult carer QoL	Pre test	32.4	33.3	34.6	0.617
	Post test	27.4	29.3	21.6	0.001
CSI	Pre-Test	31.0	34.0	35.4	0.991
	Post test	21.5	22.0	21.0	0.045

DISCUSSION

The goal of present study was to inspect the effects of VR and CBT in caregivers of chronic stroke patients. The current study data specifies that VR and CBT is effectual to increase QoL, caregiver burden and contentment. All subjects with better caregiver burden at pretest has shown better progress after following VR and CBT. Present study stipulates that there was statistically substantial results after attentive treatment

with VR and CBT. In existing study, caregivers burden shown individual getting VR and CBT following 4-week exercise program presented noteworthy development in burden which is also reinforced by study carried by Gianluca Pucciarelli et al (2017) displayed that QOL in stroke caregivers did not meaningfully alter: (9).Though our study presented momentous development in QoL of caregiver with VR and CBT. Another randomized comparative study led by Ann-Cathrin Jönsson et al (2005) scrutinized variations of quality of life (QoL) covering physical and psychological features of stroke survivors and their informal caregivers. QoL of 304 successive stroke patients and their 234 informal caregivers were measured 4 months after stroke onset. SF-36 was continual for both groups after 16 months the patients' mean QoL scores enhanced between 4 and 16 months after stroke in the socio-emotional and psychological SF-36 areas and reduced in the area of physical function while our study's outcome exhibited important development in QoL by examining numerous aspects of QoL by SF 36.[10] In current study, burden of family members or caregivers and QoL were suggestively associated, a study directed by Camila Caminha et al 2018 showed that no substantial associations amid burden and quality of life, and variables in the emotional and societal spheres, age of caregivers, or care period [11]. Moreover, Eva M. Wijma et al worked on virtual reality involvement to improve acceptance and empathy for people with dementia in informal caregivers showed TDL(a form of VR) could support informal caregivers in their caregiving role: [12] A study in 2016 by Linda Helena Jütten et al on testing the effectivity of the mixed virtual reality training into dementia for informal caregivers of people with dementia and the consequence of both these studies were dependable with the effects of VR on stroke patients, in our research[13]. A study by Losada Andrés (2015) on Cognitive–behavioral therapy (CBT) for dementia family caregivers with depressive symptoms presented that substantial variations at post involvement were established in leisure and dysfunctional thoughts after CBT. Our study displayed similar outcomes afterwards cognitive rehabilitation.[14] Montse Romero Mas et al (2020), an article was published on Designing virtual communities of practice for informal caregivers of Alzheimer's patients. Virtual reality intervention was proved to be beneficial in promoting understanding and reducing burden on caregivers of Alzheimer's patients:[15] Milicia Petrovich and Andrea Gaggioli(2020), an article published in Front Public Health written on the effectiveness of digital mental health tools i.e. VR for caregivers (informal) of older adults. Caregivers reported that digital mental health tools such as V.R etc. have an overall positive impact on their health. Skills such as coping skills, emotion regulation and physical skill building were greatly enhanced.

CONCLUSION

In conclusion, stroke survivors as they become disabled partially or completely, creates a high level of burden among caregivers. This burden gradually produces a negative effect on of life of caregivers. So, the VR and CBT used combined has significant effect to eradicate burden, improve quality of life and increase satisfactions in informal caregivers of stroke survivors.

Author's Contribution:

Concept & Design of Study:	Marrium Batool
Drafting:	Mirza Obaid Baig, Maham Nasir
Data Analysis:	Maham Nasir, Iqra Shabbir
Revisiting Critically:	Marrium Batool, Mirza Obaid Baig
Final Approval of version:	Marrium Batool

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

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Original Article

Urea A Significant Clinical Marker of Vaso-Occlusive Crises in Sickle Cell Disease

Clinical Marker of Vaso-Occlusive Crises in Sickle Cell Disease

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ABSTRACT

Objective: To measure serum urea level of Sickle Cell Disease (SCD) patients in pain free steady state and compare it with the levels taken at start, during and on recovery of Vaso-occlusive crises (VOC).

Study Design: Prospective observational study

Place and Duration of Study: This study was conducted at the Lifecare Molecular & PCR Lab Services from May 2018 till May 2020 for a period of more than two years.

Materials and Methods: 25 diagnosed cases of SCD aged 12 to 22 years were included. It was a multidisciplinary approach study including the anesthetist for pain management when required. UCE (Urea, creatinine and electrolytes) was taken in the steady pain free state, at the start, during and on resolution of VOC. The steady state urea level was compared with the other samples taken during VOC using a student's unpaired two-tailed 't' test, a p value <0.005 was taken as significant.

Results: 36 episodes of VOC were analyzed. Mean serum urea level in steady state was 2.8 +- 0.8 mmol/L which dropped to 1.9 +- 1.1 at the time of presentation, reached to 1.5 +- 0.9 ($p< 0.0005$) during VOC with gradual return to steady state level as the crises settled.

Conclusion: A significant drop in urea levels during VOC with a return to steady state level was seen defining VOC and its resolution.

Key Words: Sickle cell disease, Urea, VOC, Painful crises, Nitric Oxide, Arginine

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INTRODUCTION

SCD is amongst the most common genetic disease in United States, effecting 1 in 500 African Americans. About 1 out of every 12 African Americans carry autosomal recessive mutation, with approximately 300,000 effected children born annually [(1)]. We could not come across any study on the epidemiology of SCD in Pakistan. SCD is one of the common hemoglobinopathy seen especially in Africa, black Americans and people living in middle-east Asia.

It has numerous presentations but one of the most common is Painful crises or Vaso-occlusive crises (VOC) of the bones, which may be mild to severe and usually lasts for few days to one week. SCD is a group of hereditary genetic disorder in which there is mutation of one or both beta globin chains resulting in the formation of abnormal hemoglobin (Hb) [(2)]. Either both the chains have sickle cell mutation or one chain has sickle cell abnormality while other chain has an abnormality for some other hemoglobinopathy. SCD has two groups, one homozygous group where both chains have sickle cell genes, then it is called sickle cell anemia or homozygous sickle cell disease, while the other is heterozygous group where if sickle cell gene combines with some other hemoglobinopathy like Hb-C, D, E or quantitative globin chain disorders like beta thalassemia trait, then it becomes heterozygous SCD or named according to the other hemoglobin disorder [(3)]. In both cases one abnormal gene has to be sickle cell gene. The abnormality of sickle gene occurs due to the replacement of glutamic acid with valine in position six on the β -chains [(4)]. During deoxygenation phase of Hb in peripheral tissues and organs, red cells containing sickle Hb precipitate, becomes rigid and cell assumes a sickle appearance [(5)]. This rigid and abnormal shaped red cell can obstruct blood flow through small vessels especially in bones, thereby causing painful Vaso-occlusive crises (VOC), which is the most common clinical presentation of the disease leading to loss or working days in addition to bone, tissue, and organ damage. This hemoglobinopathy causes a significant

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decrease in life span of the sickle cell resulting in chronic hemolytic anemia [6]. Although this appears simple but there is great variability in the clinical expression of the disease even in same family with same phenotype [7]. This variability can be due to epigenetic, genetic, environmental and social factors either alone or in various combinations. Most frequent presenting symptoms in SCD is pain during the VOC process for which NSAIDS, Opioids both oral and parenteral and sometimes hospital admission is required. Due to better understanding and treatment of the disease, patients now live longer but the disease has become more complex and sometimes it is difficult to differentiate real VOC from pain due to other reasons like pain due to avascular necrosis of bones and joints. Some of these patients also become dependent on pain medications especially morphine or may use this symptom for some gain. It is thought sickling of red cells initiate the beginning of VOC [8]. These sickle cells are adhesive and binds to several endothelial receptors and proteins like endothelial cell P -selectin, E -selectin, intercellular adhesion molecule -1, vascular cell adhesion molecule -1, CD36 leading to activation and recruitment of monocytes, polymorphonuclear neutrophils and platelets[9]. Thus, occlusion of microcirculation on a background of chronic hemolysis is important factors that stimulate the cytokine storm leading to the clinical and subclinical VOC episode [10]. NO is a soluble gas with a half-life of seconds and is synthesized continuously in endothelial cells from the amino acid L-arginine by isoforms of the NO synthase enzyme producing relaxation of smooth muscles causing vasodilation, and increased regional blood flow [11]. NO also induces cellular events in a coordinated program which promotes blood flow, primarily by decreasing aggregation of platelet, expression of cell adhesion molecules on endothelial cells, and secretion of procoagulant proteins [12]. This reduction in NO also contributes to VOC. Biochemically Arginine is catabolized by enzyme arginase to urea which is then cleared by the kidneys [13]. Arginine is required to produce NO by enzyme NO synthetase. Arginine can also be acted upon by enzyme Arginase to produce ornithine and urea [14]. This arginase enzyme is released by the hemolysis of red cells particularly the young cells which are predominant in SCD. As a result, the concentration of arginine decreases in the blood leading to a probable decrease in serum Urea [15]. The ongoing chronic hemolysis in these patients may also be a contributing factor for a decrease in serum urea particularly during and recovery from VOC. Early detection and treatment of VOC is important in the management of VOC as it may lead to further complications of the disease. Our aim was to compare the variation of urea concentration in steady state, at the start of VOC, during and on recovery. In addition, it may also help us to clinically differentiate true painful crises of VOC from non-VOC pains like joint pains and or malingering by the patient.

MATERIALS AND METHODS

25 SCD patients, 18 males and 7 females attending Lifecare Molecular & PCR Lab Services, Karachi for their blood investigations were included in the study between May 2018 & April 2020 after Informed consent. The normal range of urea nitrogen in blood or serum is 5 to 20 mg/dl, or 1.8 to 7.1 mmol urea per liter. The wide range in this level is due to protein intake, endogenous protein catabolism, state of hydration, hepatic urea synthesis, and renal urea excretion. Their steady state urea, electrolytes, creatinine & urea (UCE) was collected in the steady state (the pain free period between the VOCs) as a baseline value for comparison when the same parameters were taken at the start, during and at recovery from VOC. Blood was collected in plain tube by venipuncture and UCE was done on chemical analyzer of total lab automation. Statistical significance was calculated using the student's unpaired two -tailed 't' test and the data presented as mean + standard deviation. A p value of <0.05 was considered as significant.

RESULTS

Table 1 shows a total of 25 patients with SCD completed enrollment, and because the enrollment was consecutive, no attempt was made to choose the patients by genotype. They comprised of 18 male (28 episodes) and 7 females (8 episodes). Eight males had one episode and ten had two episodes while from seven females six had one and one had two episodes. Patient's age ranged from 12-22 years (mean 16.25 years). Table 2 shows patient's serum urea dropped significantly to mean level of 1.5 +- 0.9 mmol/l from steady state level of 2.8 +- 0.8 mmol/l ($p<0.0005$) and then remained at this value for nearly two or three days to regain its near steady state level on fourth to sixth day for recovery.

Table No.1: Demographic & VOC numbers of SCD patients [n=25]

SCD n = 25	**Age in years**			**Total VOCs n =36**		
	Range	Mean	Median	Pts with only one episode of VOC	Pts with multiple episodes of VOC	Total VOCs
Males n = 18	12-22	16.7	16	8	10 (10 X 2 VOC =20)	28
Females n =7	12-18	14.37	15	6	01 (1 X 2 VOC =02)	08

Table No.2: Details of serum urea level as per stage of VOC

Serum Urea (NV 3.2 – 7.3 mmol/L)			**Phases of VOC**			**P value. Comparison b/w**	
		Steady State	Start of VOC	During VOC	Recovery from VOC	Steady state & during VOC	Steady state & recovery state
Total Patients n=25	Mean +- SD Range	2.8 +- 0.8 1.1-5.3	1.9 +- 1.1 0.3 - 5.3	1.5 +- 0.9 0.5 – 5.0	2.5 +- 1.0 0.7 – 5.4	p <0.0005	p .091
Male Patients n=18	Mean +- SD Range	3.5-0.7 2-53	2.4 +- 1 0.4 – 4.8	2.4 + - 1.1 0.6 - 5.0	3.0 +- 1.2 1.1 – 5.4	p <0.0005	p 0.066
Female patients n=7	Mean +- SD Range	2.4 + 0.6 1.1 – 3.6	1.6 +- 0.9 0.3 – 4.3	1.8 +- 0.7 0.4 – 3.8	2.1 +- 0.9 0.6 – 4.2	p <0.0005	P 0.143
Pts with single episodes n=19	Mean +- SD Range	2.8 + 0.9 1.1 – 5.3	2.0 +- 1.0 0.3 – 5.3	2.1 +- 0.7 0.4 – 5.2	2.6 +- 1.2 0.6 – 5.4	p <0.0005	p 0.059
Pts with multiple episodes n=6	Mean +- SD Range	2.8 + 0.7 1.6 – 4.3	1.4 +- 0.7 0.4 – 3.4	1.6 + - 0.7 0.5 – 3.5	2.3 +- 1.0 0.6– 4.3	p <0.0005	P =0.047

DISCUSSION

To the best of our knowledge, we have not come across any study which deals with urea and sickle cell disease during VOC. The major findings in our study were the low serum urea levels in the steady state and a drop during VOC and return to baseline steady level on resolution of VOC. We have observed this phenomenon in sickle cell patients presenting with VOC. Many factors contribute to low serum urea levels in the steady pain free state in these patients. A study by Olaniran [(16)] shows that a major factor of low urea levels is the kidney damage done by the SCD commonly known as sickle cell nephropathy (SCN), but under-recognized complication. In an original article by Geraldo [(17)], the main abnormalities identified, were urinary concentrating and incomplete distal acidification defect. There was also an increase in the potassium transport and decrease in water reabsorption, evidencing the occurrence of distal tubular dysfunction leading to a lower serum urea concentration, particularly in acute hemolysis on background of chronic hemolysis which is seen in SCD patients for most of the time during crises [(17)]. Our study shows that it is worth monitoring serum urea concentrations during steady phase and VOCs when it is related to the improvement in the painful crises due to VOC. One study was done in Basra Iraq where AL-Nama et al mentioned that serum urea in pediatric sickle cell patients is lower than the normal children, but they did not mention the cause of this decrease [(18)]. Another study was done by Michael et al which shows that SCD significantly changes Kidney structure and function causing multiple renal syndromes and diseases [(19)]. Such variety of renal issues shows the significant and unique but complex vascular abnormalities of SCD and the tendency sickled red cells in the renal medulla due to its hypoxic, acidotic, and hyperosmolar conditions. These all abnormalities cause a low serum urea concentration even in steady state.

The second factor which causes low serum urea and the variation particularly during a VOC episode is the decreased availability of arginine amino acid during VOC. Our observation has been substantiated by a study done by A. Kyle Macka [(20)]. A study by Nadr et al has shown that arginine amino acid is metabolized into ornithine through one path and via a second pathway into urea. When sickled red cell is hemolyzed particularly in VOC, an enzyme arginase is released in the blood which degrades arginine causing a decreased production of urea during the episode when hemolysis increases. Hemolysis also releases free Hb which is a great scavenger of Nitric Oxide. This NO is a vasodilator and its deficiency causes more damage during the VOC [(21)]. Our opinion is that at the start of VOC these changes start and causes urea level to decrease gradually and remains low as long as the process is continuing Once the process starts improving and majority of sickled cells are consumed in the episode, new RBC enter the circulation and sickling and hemolysis decreases thereby the concentration of arginase and free Hb also decreases. This may result in the upsurge of serum urea level near or at the steady state level. This bouncing back of serum urea level indicates that the process of VOC is improving. It has

also been seen in a study in which they measured GFR of two groups and found that absolute values for GFR corrected for BSA were significantly higher in SCD group compared to normal group and SCD children had more tendency to hyperfiltrate than normal children [22]. Our study is further supported by a study from Nath KA and et al [23] on renal functions in sickle cell disease patients and shows development of renal interstitial disease which seems to cause problems in urea and other constituents when the renal concentrating capability is compromised. This study supports our view that on a background of sickle cell induced nephritis, an acute VOC further aggravates it and causes a decrease in serum urea concentration.

CONCLUSION

The phenomenon of significant drop in serum urea levels occurs during a VOC and its serial monitoring may be a useful marker to judge the commencement, progress & resolution of the VOC. Improvements in serum urea towards steady state levels proves to be a good indicator for the recovery from VOC. It is also recommended that levels of arginine in the blood in SCD patients in the steady and VOC stages should also be conducted to further strengthen study.

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Original Article

Acquired Cystic Kidney Disease among End-Stage Renal Disease Patients on Hemodialysis

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ABSTRACT

Objective: To determine the prevalence of acquired cystic kidney disease in end-stage renal disease patients on hemodialysis.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Nephrology Department, Khyber teaching hospital, Peshawar from July 2021 to January 2022, for a period of seven months.

Materials and Methods: This study was conducted on 124 subjects fulfilling the inclusion criteria for end stage renal disease. The patients were sent to radiology department for the diagnosis of acquired cystic kidney disease using ultrasonography by an expert radiologist. All subjects information was stored and analyzed using IBM SPSS 20. Variables like gender, age, duration of hemodialysis was stratified with acquired cystic kidney disease. Chi Square test was used for association.

Results: This study was conducted on 124 patients presented with end stage renal disease. The mean age of the subjects was 38.63±16.81 years. There number of males were 81 (65.3%) and females were 43 (34.7%). The prevalence of acquired cystic kidney disease was 17.7%. There was no significant difference between gender and acquired cystic kidney disease ACKD ($P > 0.05$). A significant difference was observed ($P < 0.05$) between age groups and acquired cystic kidney disease. A total of 8 (10.3%) subjects had acquired cystic kidney disease in the age range of 18-35 years, while in the age range of 36-75 years; a total of 14 (30.4%) subjects had acquired cystic kidney disease. Significant difference ($P < 0.05$) was found between acquired cystic kidney disease and the duration of hemodialysis.

Conclusion: In our study the prevalence of 17.7% was recorded for ACKD among the subjects of ESRD. There was a significant relationship between the age and hemodialysis duration with ACKD.

Key Words: Acquired Cystic Kidney Disease (ACKD), End Stage Renal Disease (ESRD)

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INTRODUCTION

Kidneys are the vital organ of human body, any amount of damage to this vital organ can results in fatal consequences.

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Chronic kidney disease (CKD) is a serious condition having immediate as well as long term consequences. This disease is often diagnosed incorrectly by medical professionals due to which its impact on subjects around the globe is substantial i.e. recorded up to 16%[1,2]. Glomerular filtration rate (GFR) and albuminuria both are important and are considered quite significant in the management, diagnosis, and staging of CKD[3]. The functionality of the Kidney is commonly measured by GFR while albuminuria indicates the ongoing damage to the kidney. The readings of GFR < 60mL/min/ 1.73m^2, and albuminuria more than 30 mg/24hrs exceeding 3 months duration are considered the important markers of permanent kidney damage, depending upon the different stages of CKD and the need of immediate medical attention[4].

The relationship between CKD and conditions like diabetes and hypertension are frequently observed in different studies on CKD and it's quite prevalent in underdeveloped regions of the world as compared to developed countries[5]. The development of bilateral and multiple kidney cysts is frequently observed in CKD

subjects already on peritoneal dialysis or hemodialysis[6]. Subjects of any age group with pre-existing medical history of CKD are at higher risk of getting Acquired Cystic Kidney Disease (ACKD) which is associated with end-stage renal disease (ESRD) [7].

ACKD is characterized by different sizes of fluid-filled kidney cysts among subjects suffering from ESRD with no history of the inherited cystic disease [8]. This condition generally involves both kidneys with significant prevalence in ESRD cases. Subjects with ACKD are commonly differentiated from autosomal dominant polycystic renal disease (ADPKD) because the kidneys are small as compared to the larger kidneys found in all ADPKD cases. Amongst ACKD subject's involvement of additional body organs and family history of cystic kidney disease are not reported [9,10].

The complications usually arise as the cysts advances in number, size, and complexities i.e, such as cyst infections, renal cell carcinoma (RCC) associated with distant metastasis, intra-renal hemorrhage, and sometimes erythrocytosis. Regular surveillance is required in such cases to avert major complications and malignant transformation in such cystrs[11].

The frequency of ACKD was observed at 13% world-over in subjects with ESRD [12]. However, multiple studies from different places have reported variable number of cases manifesting as ACKD in ESRD patients on hemodialysis as well as on peritoneal dialysis[13].

As the ACKD is a burden on healthcare setup along with risk of life threatening complications for the patients, its early diagnosis and management is a challenge and inevitable for medical practitioners. Due to the insufficient amount of literature available on this topic our primary aim is to establish the frequency of acquired cystic kidney disease (ACKD) among subjects with end-stage renal disease (ESRD) and to develop sound protocols for the prevention and surveillance of acquired cystic kidney disease.

MATERIALS AND METHODS

The cross sectional type of the study was carried after taking approval from ethical committee of the health institute (ABC hospital). The duration of the study six months, it was conducted from July 2021 to January 2022. Subjects were asked to give a written consent for participation in the study. In this study, subjects with both gender, in the age range of (18-75) years, identified as end-stage renal disease subjects on one hemodialysis session once in a week during last 6 months were enrolled. Subjects presenting with Autosomal dominant polycystic kidney disease (ADPKD) and Medullary sponge kidney (MSK) disorder were excluded from this study. Acquired Cystic Kidney Disease (ACKD) was diagnosed by an experience radiologist.

A sample size of 124 subjects was calculated using sample size calculator available at https:// www. openepi.com, with anticipated proportion of 13.3%[12], margin of error 6% and confidence interval 95%.

All the collected data was analyzed with IBM SPSS 20. The determination of frequencies and percentages were accomplished for qualitative data. The determinations of Mean + Standard Deviation were achieved for quantitative data. Chi-Square test was performed for association, keeping the P value at ≤ 0.05.

RESULTS

This study involved 124 subjects presenting suffering from end stage renal disease. The mean age of the subjects was 38.63±16.81 years. The hemodialysis mean duration was 3.12±1.81 years. The prevalence of male subjects was higher with 81 (65.3%) than female subjects which were 43 (34.7%) in number (FIG 01).

The prevalence of acquired cystic kidney disease was 17.7%. No significant difference between acquired cystic kidney disease and gender was observed ($P > 0.05$).

A significant difference ($P < 0.05$) was observed regarding age groups and acquired cystic kidney disease, a significant difference ($P < 0.05$). Age range 18 to35 years, 8 (10.3%) subjects had acquired cystic kidney disease, while in the age range 36 to 75 years 14 (30.4%) subjects had acquired cystic kidney disease (Table 1).

We also found significant difference ($P < 0.05$) between the acquired cystic kidney disease and duration of hemodialysis and. The prevalence of subjects having more than 4 years of hemodialysis was higher than those between 1 and 3 years (37.5% vs 8.3%) (Table 2).

Table No.1: Stratification of ACKD with Age

Acquired Cystic Kidney Disease	Age Groups		Total	P value
	18 to 35	36 to 75		
Yes	8	14	22	0.004
	10.3%	30.4%	17.7%	
No	70	32	102	
	89.7%	69.6%	82.3%	
Total	78	46	124	
	100.0%	100.0%	100.0%	

Table No.2: Stratification of ACKD with Duration of Hemodialysis

Acquired Cystic Kidney Disease	Hemodialysis Duration		Total	P value
	1 to 3 years	> 4 years		
Yes	7	15	22	0.0001
	8.3%	37.5%	17.7%	
No	77	25	102	
	91.7%	62.5%	82.3%	
Total	84	40	124	
	100.0%	100.0%	100.0%	

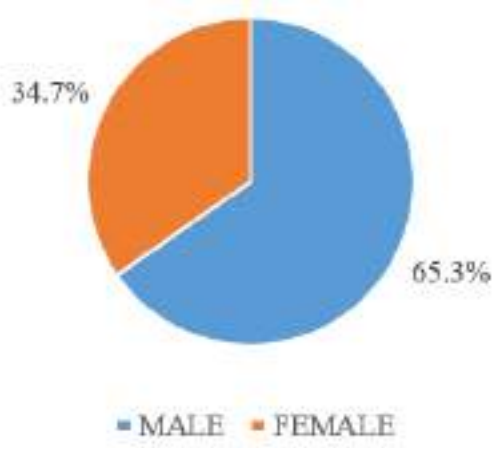

Figure No.1: Gender Distribution

DISCUSSION

Numerous studies were conducted on dialysis subjects to record the prevalence and complications of acquired cystic kidney disease among these patients [14]. Dunnill et al. in their study primarily described acquired cystic kidney disease (ACKD) after doing autopsies in 30 subjects suffering from chronic kidney disease that had been on long-term dialysis. Numerous renal cysts were found in large portion of these specimens[15]. The prevalence of ACKD among hemodialysis subjects in our study was observed in 17.7%, which is comparable with most of reports published worldwide. For example, the prevalence of ACKD in domestic surveys was 10% in Pakistan and 20.3% in Iran[16,17]. Another study from Pakistan showed the prevalence of ACKD 13.3%[12]. A small number of studies revealed several examination techniques i.e. computed tomography or autopsy, results in a greater ACKD prevalence in contrast to ultrasound[12].

A significant association has been observed in age and ACKD. Subjects in age range of 18 - 35, 8 (10.3%) subjects had ACKD, while in the age group of 36 -75, 14 (30.4%) had ACKD. This infers that the higher rate of ACKD is associated with advancement in age. Our finding are comparable to one of the local study[12] which reported similar prevalence.

In different studies it has been observed quite consistently that the incidence of ACKD increased with duration of CKD[18, 19]. In our study we saw similar pattern of presentation, 8.3% of subjects were observed with acquired cystic kidney disease on hemodialysis for the duration of less than four years while 37.5% of subjects with hemodialysis greater than four years. This was also backed by Matson et al,[20] who observed that the prevalence of ACKD was only 10–20% after one to three years of hemodialysis, rising in 3-5 years of regular hemodialysis to 40–60% cases, and after 5-10 years of hemodialysis more than 90% of subjects had ACKD. In a different study, the prevalence of ACKD among 54 children on peritoneal dialysis for around four years, five to nine years, and greater than 10 years were 9%, 50%, and 80%, respectively[19].

Acquired cystic kidney disease is frequent in both genders, but cystic variations are highly prevalent among male subjects. Ishikawa et al[14] in their study observed the higher incidence of ACKD among males because of gender-specific elements. As compared to Ishikawa et al, we had similar results; in our research the ACKD prevalence was higher among males as compared to female subjects, though the number of male patients were higher in our study. In a study by Gnionnahe et al[21] they found a insignificance for the higher prevalence of ACKD in men. By race, African American men and women are at higher risk for ACKD than women or white race.

Renal cell carcinoma is a dreadful consequence of ACKD, with a 0.18% annual frequency compared to 0.005% in the overall population. In roughly half of all cases with acquired renal cyst disease, renal carcinomas are multicentric, and in around 10 % of cases they are bilateral[22]. During long term dialysis, malignancy frequently develops approximately after eight to ten years[12]. Therefore renal ultrasonography is indicated in all ESRD subjects who are on dialysis for more than 3 years duration for early detection of precancerous lesions. In cystic kidney disease patients suspected of malignancy, the most sensitive test is a CT scan with contrast medium[16,12].

CONCLUSION

The study conducted in our setup showed the prevalence of ACKD to be 17.7% among ESRD subjects, which is comparable to various national and international studies[10,12,16,17]. We observed a significant association between age and ACKD, with increasing age the incidence of ACKD in ESRD subjects also increased.

Another important finding in our study was duration of Dialysis with ACKD. It shows a significant association with prolong duration of hemodialysis. We recommend further studies to be conducted in various tertiary care hospitals and renal setups to explore the incidence ACKD and its association with malignancy.

Author's Contribution:

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Original Article

Antibiogram Pattern of Urinary Tract Infections

Pattern of Urinary Tract Infections

Muhammad Tayyab Naeem[1], Abdul Rauf[1], Fazal-ur-Rehman Khan[1], Hammad Shafi[2], Saba Rasool[3] and Zeeshan Shaukat[4]

ABSTRACT

Objective: To determine the susceptibility pattern of three most common uropathogens; E. Coli, Enterococci sp and Klebsiella sp.

Study Design: A cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Urology, National Institute of Kidney Diseases, Shaikh Zayed Hospital, Lahore from 1st March to 30th June 2021.

Materials and Methods: One hundred and thirty patients were selected with confirmed UTI symptoms. Early morning mid-stream urine was collected in sterile wide mouth containers and exposed to CLED (a differential media) to get pure growth. The isolated microbes were subjected to Kirby-Bauer disk diffusion method to obtain antibiotic susceptibility pattern of each uropathogen. Muller Hilton agar plate was used to receive susceptibility pattern to test antibiotics. Uropathogens were declared sensitive, intermediate or resistant by using CLSI.

Results: E.coli, Enterococci sp and Klebsiella sp were found 46.20%, 33.10% and 21.70%, respectively in 130 clinically verified UTI patients. Escherichia Coli showed 90% sensitivity to Colistin and 86.70% to Nitrofurantoin. Whereas, Enterococci sp manifest 100% sensitivity to Linezolid, Teicoplanin and Gentamycin. Klebsiella sp exhibited maximum sensitivity to Aminoglycosides group (Amikacin 92.6% and Gentamycin, 92.6%).

Conclusion: E. coli was the most common pathogen in the urine of the UTI patients. Irrational consumption of antibiotics is increasing and the pipeline to develop new antibiotics is dry. Antibiotics should be used rationally in clinical setups employing locally designed antibiogram patterns.

Key Words: Antibiogram, Uropathogens, Antibiotics, Culture

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INTRODUCTION

Almost 150 million people are suffering from UTI in the world.[1] Incidences of patients suffering from UTI are exected to be 18/1000 per year in general population and ranked on second highest infections globally.[2] In Pakistan the UTI cases are on the rise which accounts for 18-20 % of clinical diagnosis. Apart from financial constraint it significantly affects the quality of life of the patients.[3] It is more prevalent in women of reproductive age which is influenced by educational and marital status.[4] In comparison with males (7.4%), females (14.6%) are more prone to UTI.[5]

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E.coli, Enterococcos sp and Klebsiella sp are the most common causative agents.[6] E.coli has the ability to form intracellular capsules that enables them to evade the hummoral immune response.[7] E.coli is followed by Enterococcos sp in term of most common cause of UTI.[2] Enterococcos sp has intrinsic affinity to invade cells and form intracellular colonies to prevent host responses revealed by confocal microscopy.[8] Enterococcos feacalis in Enterococcos sp has tropism in kidney which may persists in kidney for about two weeks causing pyelonephritis as presented in Murine Models.[9] Unjudicious use of antibiotics to treat UTI has birth out the escalating prevalence of resistant uropathogens.[10] Unauthorized prescription of antibiotics, lack of appropriate surveillance of Drug Regulating Authority of Pakistan (DRAP) and patient's education has given rise to resistant uropathogens.[11] Antibiogram is the generation of antibiotic susceptibility pattern of different uropathogens for rational use of antibiotics.[12] It is essential to ensure rational use of antibiotics as the clinical pipeline for new antibiotics is dry.[13] In view of the above there is a dire need to carry out investigations on uropathogens of the UTI patients and determine the local antibiogram pattern for susceptibility of various antibiotics. Consequently, a study was designed at NIKD, SHZ Lahore to find out the local antibiogram pattern of uropathogens.

MATERIALS AND METHODS

This cross–sectional study was devised on UTI patients presented with complaints of burning micturation at NIKD, SZH, Lahore from March to June 2021. Consecutive sampling technique was opted for the study. 250 patients with burning micturation complaints were enrolled for this study. However, finally 130 patients were selected with confirmed UTI clinical symptoms like burning micturation, dysuria along with uropathogen growth of about 10^5CFU/ml (Krass Criteria) in urine culture.

Identification and Isolation: Urine sampling was done under sterile conditions. Patients were provided with sterile containers with the instructions to void mid-stream urine in the morning into these containers that were tightly packed and sent to the Microbiology Department of SZH, Lahore. A sterile loop was entered into each container and 2 microliter film was produced in the loop and then placed on the CLED agar (Cystine-Lactose-Electrolyte Deficient). It was then placed inside the incubator at 35-37°C for 48 hours. Colony forming units were apparent on the CLED after 48 hours. Colonized bacterial growth was then placed on to the nutrient enriched agar (Muller Hilton Agar) to enhance the bacterial growth and then the antibiotic susceptibility plate is placed over the bacteria enriched Muller Hilton Agar for 48 hours. Disk Diffusion Test was performed by allowing the antibiotics to diffuse the bacteria enriched agar and zone of inhibition was measured by CLIS criteria to declare the sensitivity of a uropathogen to a specific antibiotic by measuring the zone of inhibition.Uropathogens were identified by Biochemical and Gram stain test.

Antibiotic Susceptibility Test: E. coli was exposed to Colistin, Amikacin, Fosfomycin, Gentamycin, Nitrofurantoin and Polymycin B antibiotics. Enterococci sp was subjected to Ampicillin, Amoxicillin, Linezolid, Teicoplanin, Vancomycin, Nitrofurantoin, Fosfomycin and Gentamycin. While Klebsiella was exposed to Pipracillin/Tazobactam, Colistin, Amikacin, Gentamycin, Imipenem and Polymycin B and antibiotic susceptibility pattern of each uropathogen was calculated. For the data interpretation Microsoft Excel was used to generate histograms.

RESULTS

Escherichia coli is found in 46.20% of the cases. Enterococci sp accounts for 33.10% that is the second highest infection revealed in our analysis whereas, Klebsiells sp is present in 21.70% of urine analysis of the UTI patients (Fig. 1).

Aminoglycosides sensitivity pattern for E.coli is following: Amikacin, Gentamycin and Nitrofurantoin show 85%, 88.3% and 86.70% sensitivity respectively. Fosfomycin is susceptible in 56.70% in E.coli sp. While Polymycin B and Colistin susceptibility is detected in 85% and 90% of the UTI cases (Fig. 2).

Linezolid, Teicoplanin and Gentamycin are sensitive in 100% of cases. Enterococci sp is sensitive to following antibiotics: Ampicillin (74%), Amoxicillin (72%), Vancomycin (91%), Nitrofurantoin (86%), Fosfomycin (65%), Linezolid (100%),Teicoplanin(100%) and Gentamycin (100%) [Fig. 3).

Sensitivity of Klebsiella sp to various antibiotics is following: Pipracillin/Tazobactam (81.48%), Colistin (81.48), Amikacin (92.60%), Gentamycin (92.60%), Polymycin B (88.80%) and Imipenem (96.29%) (Fig. 4).

Figure No.1: Percentages of different uropathogens

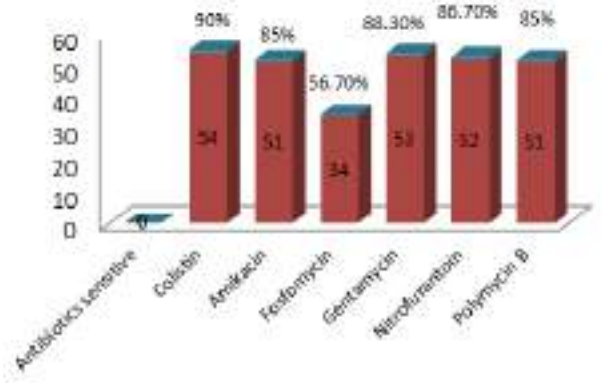

Figure No.2: Susceptibility pattern of E. coli to various antibiotics.

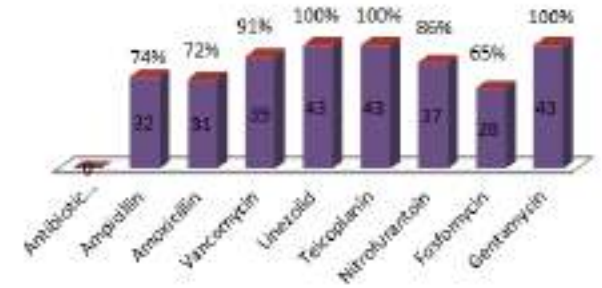

Figure No.3: Percentages of Enterococcos sp susceptibility to various antibiotics

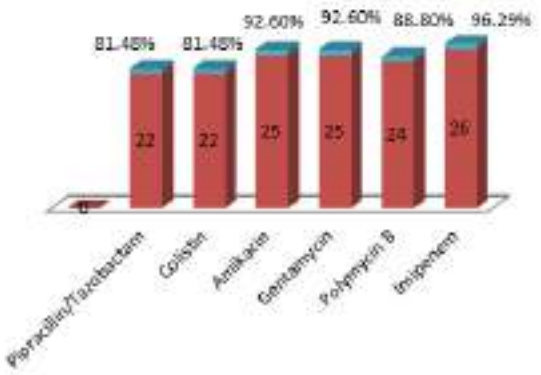

Figure No.4: Percentages of Klebsiella sp sensitive to each antibiotic

DISCUSSION

The current study reveals that out of 130 UTI patients, E.coli was found in 46.20% cases. E.coli showed highest vulnerability to Colistin (90%), Amikacin (85%) and Polymycin B (85%) in our analysis. Kumar et al., (2013) have reported the ability of Nitrofurantoin to E.coli as an effective antibiotic which is consistent with our study.[15] Antibiogram pattern of Aminoglycosides (Amikacin and Gentamycin) of this study showed similar results with the findings of Daoud et al. However, Fosfomycin has not been proven as effective as declared by Daoud et al.[16] Outcome of the present work regarding efficacy of Colistin against E.coli shows consistency with the findings of Dharati et al.[17] The present work shows that Amikacin is a rational treatment plan for urinary E.coli.[18] Current investigation reveals that Polymycin B is effective against E.coli which is parallel with the work reported by Ezadi.[19] Enterococcos sp accounts for 33.10% of the cases. Glycopeptides like Vancomycin and Teicoplanin shows 91% and 100% efficacy while Aminoglycosides like Nitrofurantoin has 86% effective against urinary Enterococcos sp in terms of antibiotic sensitivity and our findings are articulated with the work done by Maria.[20] and Muzammil et al. However, Teicoplanin sensitivity is seen in 72% of Enterococci sp in analysis retrieved by Muzammil et al.[21] Enterococcos sp are found 100% susceptible to Gentamycin which is an essential antibiotic in armamentarium against urinary Enterococci sp that is in line with the analysis of Kumari.[22] Linezolid and wide spectrum pencillinase inhibitors (Ampicillin and Amoxicillin) are effective against urinary Enterococci sp and our findings endorse the work of Muzammil (2020).**21.** Barros (2009) has reported the efficacy of Ampicillin (67%) and Amoxicillin (78%) against Enterococci sp similar to the findings of our study.[23] Teicoplanin and Linezolid have come up with stupendous result and encouraging efficacy against Enterococci sp as delineated in our study.[24]

As far as the Klebsiella sp are concerned**,** it holds a share of about 16% of total cases.[25] Present study endorses the effectiveness of Amikacin for Klebsiella sp by 92.60% similar to the efficacy ratio calculated by Virawan.[25] Present work indicates 81.48% efficacy of Klebsiella sp for Colistin that is parallel with the results presented by Kathia et al.[26] Polymycin B showed 88.80% effective regimes for Klebsiella sp in the current study while Bukhari (2019) has asserted 100% efficacy of Polymycin B for Klebsiells sp.[17] Pipracillin/Tazobactam and Imipenem are an effective antibiotics for management of urinary Klebsiella sp as prsented by the study of Abdullah et al.[27] Aminoglycosides (Gentamycin and Amikacin) have intrinsic activity to nullify urinary Klebsiella sp symptoms with reference to our investigation.[26,28] and our study is in contrast with the Bouamri et al., (2015) who have claimed 21% efficacy for Gentamycin and 11% efficacy for Amikacin.[29]

CONCLUSION

The present study reveals that E.Coli, Enterococcos sp and Klebsiella sp are the most common pathogens found in the UTI patients. E.coli and Klebsiella sp responded maximally to Polymycins and Aminoglycosides while, Enterococcos sp showed efficacious response to Glycopeptides, Oxazolidinone (linezolid), Penicillins and Aminoglycosides.

Author's Contribution:

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Original Article

Prevalence of Tongue Lesions in Patients Visiting Private Dental Practices of Pakistan: A Multicenter Study

Daud Mirza[1], Bhunesha Devi[4], Saima Salman[5], Arsalan Khalid[2], Syed Ahmed Omer[3] and Jawaria Zeeshan[1]

ABSTRACT

Objective: To determine the prevalence of lesions of tongue and their association with gender among dental patients.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Different private dental clinics of Sindh and Punjab province from November 2020 to October, 2021 for a period of one-year.

Materials and Methods: The current study comprised of 1500 subjects which were clinically examined in different dental clinics of Sindh and Punjab province (n=768 Male) and n=732 females) Diagnosed patients of tongue lesions, aged between 10 - 90 years of age were selected by using the convenience sampling technique. The existence of various types of lesions was determined by examination of the oral cavity.

Results: The frequency of tongue lesion was 14.4%. Coated tongue was found be the most common lesion diagnosed in the present study affecting 89 (41.2%) participants followed by traumatic ulcers 47(21.7%), geographic tongue 38(17.5%) and fissured tongue 17(7.87%). The prevalence was higher among females than males. Among the systemic conditions hypertension was found to be most common followed by diabetes mellitus.

Conclusion: Tongue lesions are the major health concern for any dental practitioner. Most of the lesions are easily diagnosed by an experienced clinician except for malignant pathology which requires microscopic examination.

Key Words: Prevalence, tongue, coated tongue, geographic tongue.

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INTRODUCTION

Tongue a strongest muscular organ[1] is covered by different types of mucosal layers. It plays an important role in taste, swallowing, speech, suckling, general sensation.[2] Lesions of tongue are an important health issue as it comprises substantial amount of oral lesions.[3] During tongue examination the important clinical features that need to be given utmost importance are size, shape, colour and texture, thickness surface epithelium texture as they help in ruling out if the condition or lesion of the tongue is related to a local factor or is a result of a manifestation of systemic diseases.[4] Literatures have shown the association of tongue lesions as a manifestation in syndrome like Vanderwoude and Melkersson Rosenthal.[5]

Tongue lesions form an important part of oral mucosal lesions. Different epidemiological studies on oral mucosal lesions have been conducted around the world among different populations.[6,7] Study conducted among Jordanian dental patients showed higher prevalence in females than males.[8] Another study conducted by Sujata and colleagues showed fissured tongue to be the most prevalent condition observed in Libyan dental patients. A case control study on the occurrence of tongue lesions in psoriatic patients is still controversial but researches have shown the evidence that fissured tongue and benign migratory glossitis were the condition noticed in psoriasis patients.[9] Studies on tongue lesions have found to be insufficient in Pakistan; hence our study setting will provide a base-line data for treatment planning and patient education to the oral health care professionals

The aim of this study is to investigate the frequency and risk factors associated with tongue lesions with respect to gender and age among dental patients of Sindh Province.

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MATERIALS AND METHODS

The current cross-sectional and multi-centered study was done on dental patients, who attended different private dental clinics of Sindh and Punjab province from November 2020 to October, 2021. The study design and approval was taken by the mutual consent from the owners of private dental practices and a written informed consent was obtained from the subjects. The current study comprised of 1500 subjects (n=768 Male) and n=732 females) among which the diagnosed patients of tongue lesions, aged between 10 - 90 years of age were selected by using the convenience sampling technique. The existence of various types of tongue lesions was determined by clinical examination for any surface changes, specific lesions, size and movement. The inclusion criteria for this study was tongue lesions present in both genders and exclusion criteria included patients under 10 years of age and those who did not give the consent for the study. Data analysis was done using Statistical Package for Social Sciences version 24. (SPSS Inc., Chicago, IL, USA). Chi-square test was applied to cross tabulate different variables such as gender & age with tongue lesions. p value < 0.05 was considered to be statistically significant.

RESULTS

The present study group comprised of 1500 diagnosed patients of tongue pathologies, out of which 767(51.1%) subjects were males and 733 (48.9%), females. Patient's age ranged from 10 – 90 years. Mean age found was 35.07 years with SD of 15.49 years as shown in Table 1. Of the total patients examined, 216 patients were diagnosed with various tongue lesions. Distribution of various lesions is presented in Table 2.

Table No.1: Distribution of Gender.

Gender	n%	SD±	Mean age
Male	767 (51.1)	15.49	35.07
Female	733 (48.9)		
Total	1500 (100.0)		

The prevalence of tongue lesions in present study was 14.4%. The most common lesion diagnosed in present study sample was coated tongue affecting 89 (41.2%) of the subjects followed by traumatic ulcers 47(21.7%), geographic tongue 38(17.5%), fissured tongue 17(7.87%). The least cases 1(0.46%) observed were oral lichen planus, cleft tongue, ankyloglossia and hairy tongue category (See Table 2). The cross-tabulation of tongue lesion with gender showed insignificant findings p-value <.354. Various systemic conditions were also seen in patients with tongue lesions. The most common systemic condition observed in patients with tongue lesions was hypertension, followed by diabetes Mellitus, thyroid deficiency and stress/anxiety patients.

Table No.2: Frequency of tongue lesions with respect to gender.

Tongue Lesions	Gender		Total
	Male	Female	
Geographic tongue	23(10.6%)	15(6.9%)	38 (17.5%)
Median rhomboid glossitis	2(0.92%)	2(0.92%)	4(1.85%)
Fissured tongue	8(3.7%)	09(4.16%)	17(7.87%)
Coated tongue	36 (16.6%)	53(24.5%)	89(41.2%)
Cleft tongue	1(0.46%)	-	1(0.46%)
Ankyloglossia	1(0.46%)	-	1(0.46%)
Leukoplakia	-	1(0.46%)	1(0.46%)
Traumatic ulcer	20(9.25%)	27(12.5%)	47(21.7%)
Oral Lichen Planus	1(0.46%)	-	1(0.46%)
Hairy tongue	-	1(0.46%)	1(0.46%)
Depapillated tongue	3(1.38%)	5(2.31%)	8(3.70%)
Candidiasis	5(2.31%)	3(1.38%)	8(3.70%)
Total	**100 (46.29%)**	**116 (53.7%)**	**216 (100%)**

* in 1284 patients tongue lesions not detected
* p-value <.354 (insignificant)

DISCUSSION

The present study based on various types of tongue lesions was assessed in both males and females among dental patients of Sindh & Punjab Province. There is scarcity of studies regarding tongue lesions prevalence in Pakistan. Therefore, this will provide the base line data for the researchers. Tongue pathologies sometimes are the oral manifestations of some systemic diseases which need to be diagnosed in time for therapeutic purpose. This is very important for dental clinician to know the diagnosis otherwise it will become a challenge for a dental practitioner.[5]

The prevalence of tongue in present study was 14.4%, study conducted in our neighboring country India showed prevalence of 13.75%, while similar studies on oral lesions done in King Saud University, Saudi Arabia revealed low prevalence 3.96%.[10] Darwazeh and colleagues reported higher prevalence of tongue lesion 23.7% which is in accordance with Voros study conducted in Hungarian children 35.11% .[11] Variation in tongue lesion's distribution between both the genders was also seen. The tongue lesions were more common among males (51.13%) than females (48.86%). This was in accordance with a retrospective study conducted in Ajman which showed that the tongue lesions were more common among males (77%) versus females (23%).[4] Similar type of retrospective study was

conducted in Nigerian subjects showed male preponderance.[12] However, it disagreed with Sura Ali Fouad study that demonstrated that tongue lesions were more frequently seen females.[13] This study was also supported by Kittipong research which showed tongue lesions to be 1,285 (59.68%)in females subjects than males 865(40.18%).[14]

As far as the type of lesions of tongue is concerned, coated tongue was the commonest lesion reported in dental patients. This finding was in accordance with Patil S and Colleagues[3] study. Another study conducted by Avcu, Kanli[1] found coated tongue to be the most prevalent tongue lesion followed by fissured tongue.[15] Study conducted in Jodhpur Dental College General Hospital in India showed high prevalence of coated tongue 28%. This finding also supported our present study.[3] Research conducted in Chulalongkorn University on tongue lesions constituted 4.87 % of all biopsy cases from Thailand[14] which is comparable to 3.51% by Shamloo and colleagues [16] 4.00% by Lasisi et al,[12] 6.30% by Alaeddini et al.[17]

In the study of Maher AL Shayeb[4] fissured tongue (40%) was the commonest lesion found followed by geographic tongue (14.3%), strawberry tongue (8.6%) and Hairy tongue (7.1%). However, in majority of the clinical studies fissured tongue was seen to be the most common tongue lesion. However, the prevalence of geographic tongue in a study conducted by Picciani et al[18] was 2.1%, which was within the global normal range of 0.6 - 4.8%.[18] Another study conducted among United States population reported 2% prevalence of geographic tongue.[19]

In the present study, the lesions were found to be most common among middle aged 31-60 years (47.33%) groups, followed by 0-30 years (46.4%) and 61-90 years (6.26%). This was in accordance with the Bajaranga study where most of the tongue lesions occurred in the age range of 21-40 years (39.1%) followed by 41-60 years (29.7%) and 61-80 years (19.6%).[20] A study conducted by Fuaod and Associates on Iraqi subjects, showed that in a total of 130 patients, 75 patients were in the age group of 20-39 years followed by 40-59 years and 60-79 years with 34 and 10 patients respectively.[13] In the current study the correlation of systemic disease with tongue lesions was also investigated. The most common systemic disease observed in our study was hypertension followed by diabetes mellitus, thyroid deficiency, stress, gastrointestinal diseases (GIT) and Liver Diseases. Study on Libyan patient also reported diabetes and hypertension in their patients which also supported our findings.

CONCLUSION

The presence of different types of tongue lesions in the current study demonstrates the importance of the timely assessment and diagnosis of the tongue lesions. As there has been a lack of research done on tongue lesions in Pakistan, further studies and surveys on large samples are recommended to evaluate the correlation of tongue lesions with systemic diseases.

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 Frequency of Upper Gastrointestinal Bleeding With and Without the Use of Proton Pump Inhibitors in Patients of Chronic Kidney Disease Undergoing Hemodialysis

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ABSTRACT

Objective: To analyze the effect of proton pump inhibitors (PPIs) on incidence rate of upper gastrointestinal tract bleeding (UGIB) in patients with chronic kidney disease undergoing hemodialysis.

Study Design: A retrospective cohort study

Place and Duration of Study: This study was conducted at the Nephrology department of Nishtar Medical University & Hospital Multan from 22nd June 2020 to 22nd Dec 2020.

Materials and Methods: Clinical data of 300 patients suffering from end-stage renal disease and who began hemodialysis between 2015 to 2020 was categorically reviewed. The study compared the incidence of upper gastrointestinal tract bleeding in 80 patients treated with PPIs to another 220 patients who didn't undergo this treatment (control group).

Results: 41 patients had UGIB during the study period, at the rate of 14.4 per 1000 persons per year. In the patients given anti-platelet or warfarin therapy, the incidence was 20.7 per 1000 persons per year. A meantime of 26.3± 29.6 months was found between the start of dialysis and the appearance of UGIB. Kaplan-Meier analysis revealed a significantly lower probability of UGIB occurrence in PPI group as compared to control group. Univariate analysis demonstrated an association of anti-platelet and anti-coagulation, PPI use, and coronary artery disease with UGIB. After adjusting confounding variables involved in the potential occurrence of UGIB, PPI was highly effective in lowering UGIB when compared with the control group.

Conclusion: Treatment of patients with chronic renal disease undergoing dialysis with PPIs leads to reduced occurrence of UGIB.

Key Words: Dialysis, Chronic Renal Disease, Proton Pump Inhibitor

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INTRODUCTION

Bleeding complications are highly prevalent in end-stage renal disease (ESRD)[1]. Upper gastrointestinal bleeding (UGIB) mainly occurs in dialysis patients, it is related to increased risk of mortality and rebleeding compared to the normal population[2].

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Pathogenesis and origin of UBIG have not been explained, though anaemia, platelet dysfunction and abnormal blood coagulation may lead to bleeding[3]. As hemodialysis patients (HD) are constantly exposed to anticoagulants, they have more tendency of UGIB as compared to patients undergoing peritoneal dialysis (PD) [4]. With time there has been a decline in the prevalence of UGIB in the general population. However, according to a study among ESRD patients, the incidence of UGIB has not been lowered in last 10 years[5]. As per estimates, 3% to 7% mortality in ESRD patients is due to UBIB. There are multiple strategies for reducing UGIB; among these, proton pump inhibitors have been proven significant and are recommended for high-risk UGIB patients who take non-steroidal anti-inflammatory drugs (NSAIDs), aspirin and dual anti-platelet therapy[6].

Increased administration of acid-suppressive regime in ESRD patients leads to an increase in gastrointestinal (GI) symptoms[7]. Among patients undergoing PD and HD, frequencies of GI disease were 9.3% and 10.1%[8].

PPIs are safe for administration in ESRD patients and, when given with acid suppression therapy, rarely results in adverse effects. Studies show that in patients with GI disease, low dose PPIs are being increasingly prescribed. In this study, we will assess the effect of proton pump inhibitors (PPIs) on the incidence rate of upper gastrointestinal tract bleeding (UGIB) in patients with chronic kidney disease undergoing hemodialysis.

MATERIALS AND METHODS

A retrospective cohort study was conducted at the Nephrology Department of Nishtar Medical University & Hospital Multan for 6 months. Clinical data of 300 patients suffering from end-stage renal disease and who began hemodialysis between 2015 to 2020 was categorically reviewed. All the included patients underwent upper gastrointestinal endoscopy for GI symptoms. Those below 18 years, had a renal transplant, had a history of peptic ulcer and gastric surgery, liver cirrhosis, malignancy, less than three months of dialysis, less than six months follow up duration and those prescribed NSAIDs,corticosteroid and histamine H2-receptor antagonist were excluded. Subjects were divided in two groups: the first group contained those who were given PPIs, and the second (control group) contained those who were not being prescribed PPIs. The study was approved by the ethics committee of the hospital.

Diagnosis done by gastroenterologist and absence of any other bleeding pathology was considered as UGIB. If an ESRD patient was a suspect of clinical GI bleeding like melena, idiopathic decrease in haemoglobin>2g/dL, hematochezia or hematemesis, endoscopy was performed by a gastroenterologist. Bleeding was defined as the presence of visible vessels, bleeding in the stomach, adherent clot and high-risk stigmata in endoscopic findings. Subjects with gastric varices or oesophagal bleeding were not included in the study. Repeating endoscopy due to doubt of rebleeding and the occurrence of stigmata in the stomach was defined as rebleeding.

SPSS version 18.0 was used for performing a statistical analysis. Data was ranged and represented as median or mean ± SD. Analysis of continuous data was done using Student's t-test or Mann-Whitney U test for equal or unequal variance respectively, and Pearson's χ^2 test was used for investigating categorical variables. Kaplan-Meier survival estimates were used for estimating cumulative non-bleeding rates in both groups, and the difference between the curves was estimated using the log-rank test. Independent predictors of UGIB were evaluated using Cox's proportional hazard model analysis. P-value less than 0.05 was considered statistically significant.

RESULTS

In this study, clinical data of 300 patients suffering from end-stage renal disease and who began hemodialysis between 2015 to 2020 were retrospectively reviewed. The clinical and demographic data of the cohort include: mean age= 63 ± 14 years, male=69%, patients undergoing hemodialysis =94%, diabetics= 65%, smokers=2 %. 86 patients had coronary artery disease, 167 were given aspirin, 15 were given warfarin, and 32 were treated with dual anti-platelet therapy. Out of 300 patients, 80 were in the PPI group (50 patients were given pantoprazole orally 20 mg once daily and 30 were given rabeprazole 10 mg once daily orally), and 220 were in the control group. The difference in sex, age, mode of dialysis, renal disease, smoking, body mass index (BMI), and anti-platelet and warfarin use between both the groups was not significant. The basic characters of groups are mentioned in Table 1.

Table No.1: Basic Characters Of Groups

Characteristics	PPI group	Control group
Age (years)	64.8±13.8	63.6±14
Follow up (month)	56.8±34.6	67.5±38.5
Sex, male	50 (62.5)	157 (71.4)
Hypertension	51 (63.7)	167 (76.0)
Diabetes	49 (61.2)	148 (67.3)
Smoking	5 (6.25)	1 (0.45)
Hemodialysis	72 (90)	210 (95)
BMI (kg/m2)	24.3±4.1	24.4±4.6
History of cardio vascular events		
Cerebrovascular event	17 (21.25)	29 (13.18)
Coronary heart disease	25(30.86)	58 (26.36)
Chronic liver disease	1 (1.25)	4 (1.81)
Aspirin use	62 (77.5)	165 (75)
Dual anti-platelet therapy	9 (11.25)	22 (10)
Warfarin	2 (2.5)	4 (1.81)
Helicobacter pyroli		
Positive	20 (25)	30 (13.36)
No test	60 (75)	190 (86.36)
Basic laboratory tests		
Haemoglobin (g/L)	9.2±1.7	8.8±1.7
Hematocrit (%)	27.4±5.4	25.1±4.1
Creatinine (mmol/L)	6.8±3.9	7.1±3.1
Protein (g/L)	7.4±.8	7.1±.8
Albumin (G/L)	3.1±.8	2.9±.5
C-reactive protein(mg/L)	10.0±17.8	9.5±16.2
Death	5	24

41 patients had UGIB during the study period, at the rate of 14.4 per 1000 persons per year. In the patients given anti-platelet or warfarin therapy, the incidence was 20.7 per 1000 persons per year. The mean duration between UGIB events and the start of dialysis was 26.3± 29.6 months. Sources of UGIB are mentioned in Table 2. Among ESRD patients the most common cause of UGIB was gastric lesions, accounting for half of the bleeding sources. 18 patients came with hematochezia or melena, 13 patients came with hematemesis, while endoscopy was performed on 10 patients because of idiopathic anaemia. At the time of

admission, haemoglobin level was 6.6 ± 1.8 g/dL, and red cell transfusion was given to 40 patients. Rebleeding occurred in 2 patients, 1 in each group. 1 death occurred in the control group due to UGIB.

Table No.2: Causes

Cause	Subjects
Gastric Ulcer	13
Duodenal Ulcer	8
Duodenal and Gastric Ulcer	2
Dieulafoy's Lesion	5
Mallory-Weiss Tear	4
Gastric Erosion	4
Duodenal Erosion	4
Gastric cancer	1

The frequency of anti-platelet therapy and warfarin use was significantly higher in patients with UGIB as compared to those without it. 2 patients in the PPI group and 39 in the control group had bleeding. According to Kaplan Meier analysis possibility of UBIG was much less in the PPI group as compared to the control group. According to the subgroup analysis, the use of PPI with anti-platelet or warfarin therapy risk of PPI was decreased significantly.

According to the Univariate analysis, anti-platelet and warfarin therapy, no use of PPI and coronary artery disease were related to UGIB. After adjusting sex, age, hypertension, coronary heart disease, diabetes, smoking, mode of dialysis, albumin and haemoglobin, use of PPI significantly reduced UGIB. Table 3.

Table No.3: Univariate analysis

Variable	HR	95% CI	P-value
PPI	14.688	1.83-101.63	.011
Warfarin	5.728	1.56-14.24	.005
Anti-platelet therapy	2.456	1.37-1.43	.002
Coronary artery disease	2.077	.953-4.531	.093
Cerebrovascular disease	1.591	.973-2.286	.066
Smoking	2.154	.658-7.042	.203
Diabetes	1.021	.47-2.2	.898
Hypertension	1.418	.58-2.91	.496
Age	1.001	.97-1.02	.87

DISCUSSION

In this study, it was found that ESRD patients had a relatively high incidence of UGIB, which was significantly reduced upon the administration of PPIs. In this study, incidence of UGIB among ESRD patients was 14.4 per 1000 person per year and duration from the start of dialysis to UGIB was 26.3± 29.6 months. In the PPI group, the incidence of UGIB was much lower as compared to control group. These effects were similar in the patient's given warfarin or anti-platelet therapy. Results indicate that in patients with ESRD, administration of PPIs lowers the incidence of UGIB events.

Dialysis patients are at a higher risk of UGIB as compared to the normal population. A study conducted in the United States shows that in ESRD patients incidence of UGIB was 22.8 per 1000 person-year[9], which is higher than the incidence in the PPI group and the same as incidence in control group. Another study showed that in HD patients incidence of UGIB was 42.0 per 1000 person per year, which is more than incidence in this study[1]. The results are associated with the exclusion of patients given steroids or NSAIDs and liver cirrhosis patients and inclusion of patients undergoing peritoneal dialysis. Though there is uncertainty regarding risk factors associated with UGIB in ESRD patients, it was found that administration of anti-platelet drugs and warfarin therapy are significantly related. A study revealed that inability to move and history of cardiovascular and smoking are related to an increased risk of UGIB[10]. Another study showed UGIB is significantly associated with the administration of NSAIDS, coronary artery disease, diabetes, HD patients and cirrhosis[11]. It was also found that congestive heart failure, PD, diabetes and albumin were associated with peptic ulcers in ESRD patients[12].

Studies have shown that low dose PPIs are given as prophylactic agents for relieving gastric symptoms and ulcers. Prophylactic administration of omeprazole to dialysis patients effectively reduced the incidence of peptic ulcers[13]. This is first study, to our knowledge, suggesting pr effectiveness of PPI in preventing UGIB in dialysis patients as many studies have found an association between PPIs and bone metabolism[14], vascular calcification[15], and fractures[16]. As it's a retrospective study, so patients were not randomized. Many subjects in the PPI group showed gastric symptoms. The difference in sex, age, cardiovascular disease, smoking or diabetes between both groups was not significant. This study assessed mortality in both groups, while bone mineral density and vascular calcification were not assessed. In our study data concerning ambulatory status was not included.

There are several limitations of this study. First, general conclusions could not be drawn as it was not a randomized controlled study. However, it is difficult to conduct such a study in practice because of ethical considerations. Second, Helicobacter pylori was examined in a few patients only. Third, patients given H_2 receptor antagonists were excluded. It has been found that during the dual anti-platelet regime, H_2 receptor antagonists are the potential alternative of PPIs for preventing UGIB without more risk of

cardiovascular abnormalities. Finally, long term side effects of PPIs were not assessed as vascular calcification, mineral bone disease, serum magnesium and bone fractures were not considered.

CONCLUSION

It was found that in ESRD patient's risk of UGIB is more in control group as compared to PPI group. Moreover, PPI is considered effective and safe for preventing UGIB in dialysis patients and do not increase mortality. More large scale studies are required for confirming our results.

Author's Contribution:

Concept & Design of Study:	Poonum Khalid, Ghulam Abbas
Drafting:	Arslan Akbar Saeed, Poonum Khalid, Muhammad Muzammil
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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

Analysis of Different Factors Associated with Re-Laparotomy after Cesarean Section Deliveries at a Tertiary Care Hospital

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ABSTRACT

Objective: To evaluate the risk factors associated with re-laparotomy after cesarean section.
Study Design: Prospective case-controlled Analysis
Place and Duration of Study: This study was conducted at the Gynecology department of Nishtar Medical University & Hospital Multan from Aug 2020 to Jan 2021 for a period of six months.
Materials and Methods: The study involved all the cases who underwent re-laparotomy after a cesarean section. The study cases were matched with control subjects who underwent cesarean section without re-laparotomy after cesarean. The study participants were compared for demographic information, obstetric clinical data, and indications of the cesarean section.
Results: Out of a total of 837 cesarean section deliveries conducted in the hospital within the study period, 19 (2.2%) underwent exploratory re- laparotomy. The average time between primary surgical procedure and re-laparotomy was 1.2 ± 0.5 days. Postpartum hemorrhage (PPH) was the major indication of re-laparotomy reported in 12 (63.1%) women. The leading indications of cesarean section were multiple prior cesareans (18, 31%), fetal distress (9, 15.5%), placental previa (7, 12%), and placental abruption (6, 10.3%). Upon multivariate logistic regression, Placenta previa (OR 5.97; CI 0.96- 21.3), fetal macrosomia (OR 5.61; CI 0.91-23.1), and pre-Eclampsia were found to be significant risk factors of re-laparotomy.
Conclusion: In the present study, re-laparotomy was conducted in 2.2% of cases during the study period. Placenta previa, fetal macrosomia, and pre-Eclampsia were the strongest risk factors causing re-laparotomy after cesarean section.

Key Words: Cesarean section, relaparotomy, risk factors, obstetric complications

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INTRODUCTION

Globally, the rate of cesarean section deliveries is constantly on the rise both due to maternal factors, such as obesity and late pregnancy age, and obstetric practices like epidural anesthesia and labor induction[1, 2]. According to the Center for Disease Control and Prevention report of 2020, 31.7% of overall births in the USA are by cesarean section [3].

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The increasing rate of cesarean section is caused by both planned and unplanned (emergency) cesarean deliveries. Although unplanned or emergency cesarean section has a larger share in maternal morbidity rate. Any cesarean section triggers a series of future cesarean delivery as contemporary obstetric intervention and obstetricians prefers repeat cesarean to a subsequent trial of labor [4].

Recent data has found a correlation between maternal complications and the number of deliveries through cesarean sections [5]. Therefore, as the trend of cesarean delivers rises, obstetrician fears the risk of escalating maternal complications. In this regard, re-laparotomy after cesarean delivery is a life-threatening procedure that not only poses a high risk of maternal mortality but also acts as a critical challenge for the obstetrician. Thus, in the last two decades, multiple studies have been conducted to report the incidence rate of re-laparotomy and investigate the associated factors [6, 7]. However, Pakistan lacks behind in this critical research area. Similarly, only a few studies have conducted comparative research to investigate the risk factors

associated with re-laparotomy after cesarean delivery. Therefore, the present study was designed to evaluate the risk factors associated with re-laparotomy after cesarean section by comparing the clinical obstetric data of re-laparotomy cases with the control subjects.

MATERIALS AND METHODS

This prospective study was conducted at the gynecology department of Nishtar Medical University & hospital from Aug 2020 to Jan 2021. During this period all the cases who had undergone exploratory re-laparotomy were included in the study. For each case, 2 control subjects who had just undergone cesarean section without re-laparotomy within the same study period were randomly chosen from the data registry. All the participants were approached through their contact numbers are were informed of the study objectives and their consent was sought. The ethical approval was taken from the ethical review committee of the hospital. The women from both groups were investigated for maternal age; gestational age; parity, gravidity; history of a mode of deliveries, miscarriages; elective v/s emergency primary operation; birth weight, duration of cesarean operation. Additionally, indications of cesarean and re-laparotomy were also observed. The data was then analyzed to predict the risk factors of re-laparotomy. Preterm delivery was characterized as births that took place before 34 weeks of gestation [8]. Both essential hypertension and pregnancy-induced hypertension were considered hypertensive disorders complicating pregnancy. Operative time was considered from skin incision to closure of skin incision. Lastly, fetal macrosomia was defined as birth weight greater than 4kg [9], and fetal distress was detected through cardiotocography (CTG).

Statistical analysis

SPSS (version 18) was used for statistical analysis. Fisher exact test was used to find a statistical difference between categorical variables whereas student's t-test was used to determine statistically different continuous variables. Multivariate analysis was conducted by including all the independent variables. The analysis was then presented as odd ratios (OR) and confidence interval (CI). A p-value (2-sided) of less than 0.05 was considered statistically significant.

RESULTS

During 6 months, a total of 837 caesarian sections were conducted. Out of which, 19 (2.2%) underwent re-laparotomy. The majority of patients, 17 (89.4%) required re-laparotomy in less than 24 hours of cesarean section while the remaining 2 (10.5%) were the cases of sepsis who were opened after 2-3 days. However, 1 patient (5.2%) patient presented with urinary incontinence due to Utero-Vesical fistula after 4 four weeks of cesarian section and relaparotomy was performed after 3 months (12 weeks) of the primary surgery. Therefore, the average time in between primary surgical procedure and re-laparotomy was 1.2 ± 0.5 days. An average of 3.7 ± 1.5 blood units were transfused to all patients. Postpartum hemorrhage (PPH) was the major indication of re-laparotomy reported in 12 (63.1%) women followed by pelvic hematoma (3, 15.7%), pelvic abscess (2, 10.5%), rectus sheath hematoma (1, 5.2%). Among the cases that underwent re-laparotomy, maternal mortality was reported in 3 (15.7%) cases ultimately due to disseminated intravascular coagulation (DIC) whereas no fetal death or immediate neonatal death was found. Among other 818 mothers who had cesarean delivery but didn't require re-laparotomy, 4 (0.48%) women died through the same period.

Table I represents the demographic and obstetric data of the study and control group. The patients in study groups had significantly increased number of prior cesarean section than control group (100% vs 54%, p=0.003); emergency cesareans (21% vs 15.7%, p=0.04); and duration of cesarean section (42.5± 22.8 vs 27.6 ± 13.4, p=0.003).

The leading indications of cesarean operations were multiple previous cesareans (18, 31%), fetal distress (9, 15.5%), placental previa (7, 12%), and placental abruption (6, 10.3%) (Table 2).

Multiple logistic regression was conducted to explore the strongest predictors of re-laparotomy while considering the control group as a reference. Placenta previa (OR 5.97; CI 0.96- 21.3), fetal macrosomia (OR 5.61; CI 0.91-23.1), and pre-Eclampsia were found to be significant risk factors of re-laparotomy (Table 3).

Table No.1: Comparison of demographic and obstetric data between two groups (N=57)

Variables	Study group (n=19)	Control group (n=38)	P-value
Maternal age, years	34.3± 5.4	32.1 ± 5.3	0.7
Gestational age, weeks	36.4 ± 1.8	37.5 ± 2.56	0.96
Parity	2.2 ± 1.65	4.8 ± 1.4	0.6
Gravidity	2.2 ± 1.9	1.89 ± 1.2	0.2
History of CS, n (%)	19 (100%)	21 (54%)	0.003
Emergency CS, n (%)	4 (21%)	6 (15.7%)	0.04
Duration of CS, min	42.5± 22.8	27.6 ± 13.4	0.003
Preterm delivery, n (%)	(14.5%)	(11.2%)	0.07
Fetal weight, g	3.3 ± 0.67	3.1 ± 0.431	0.7

Table No.2: Factors responsible for Caesarian section (N=58)

Factors	N (%)
Placenta previa	7 (12%)
Fetal macrosomia	4 (6.8%)
Eclampsia	3 (5.1%)
Fetal distress	9 (15.5%)
Tender scar	1 (1.7%)
Multiple CS	18 (31%)
Twin fetal pregnancy	2 (3.4%)
Placental abruption	6 (10.3%)
The secondary arrest of labor	5 (8.6%)

Table No.3: Multivariate analysis of potential predictors of re-laparotomy (n=58)

Variables	Control group (n=38)	Study group (n=19),OR (95% CI)	P-value
Placenta previa	1.0	5.97 (0.96-21.3)	0.003
Parity	1.0	0.76 (0.32-1.74)	0.64
History of CS	1.0	0.65 (0.142-1.85)	0.71
Fetal macrosomia	1.0	5.61 (0.91-23.1)	0.031
Pre-Eclampsia	1.0	4.3 (0.91-15.3)	0.03
Arrest of labor	1.0	2.2 (0.5-6.3)	0.23

DISCUSSION

In our study site, the rate of re-laparotomy was 2.2% during the study period. This rate doesn't comply with the majority of previous studies that reported a re-laparotomy rate in between 0.2-0.7% [10,11]. The incredibly higher rate in our study can be justified by unaware women with low literacy rate who doesn't acquire proper antenatal care which consequently increases the rate of emergency cesareans. These emergency cesareans significantly multiplied the incidence of re-laparotomy (p=0.04). Seal et al conducted a similar study and found that among 66 cases of re-laparotomy, 63 (95.5%) had a history of unplanned cesarean delivery. Under this concept, the reporting of low rates of re-laparotomy being conducted in developing countries with high literacy rates, good health care services, and a low rate of unplanned cesareans is understandable.

The majority of patients in the present study reported PPH as the leading indication of re-laparotomy, affecting 63.1% of women. This finding goes hand in hand with the results of previous studies that found intra-abdominal bleeding as the most prevalent factor behind re-laparotomy; however, the rate of women with this presentation varies. In this regard, the PPH rate reported in our study is comparable with some previous studies [12,13]. Similarly, Kessous et al. documented 70% with an indication of re-laparotomy for laparotomy [14]. Given this high prevalence, high-risk women are recommended to be actively managed either through oxytocin infusion or rectal misoprostol [15, 16]. An average of 2.3 hours gap was taken between primary surgical procedure and re-laparotomy, in agreement with previous studies [17]. 2 (10.5%) cases presented with pelvic access, as an important indication of re-laparotomy, which was managed through drainage, evacuation, and antibiotics.

The above-discussed study concluded placenta previa, pre-Eclampsia, and fetal macrosomia as the strongest predictor of re-laparotomy in women who underwent cesarean section. These findings are approved by previous authors. For instance, Hasegawa et al. confirmed placenta previa as a risk factor for not only re-laparotomy following cesarean section but also associated with feto-maternal mortality and morbidity [18]. Kessous et al agreed with considering pre-eclampsia as a significant risk factor of re-laparotomy and extended the list of risk factors by adding PPH, cervical tear, placental abruption, uterine rupture [14]. Similarly, Levin et al found out the duration of cesarean section, the experience of an obstetrician, and placental abruption as significant predictors of re-laparotomy [10]. Sak et al. analyzed 113 cases of re-laparotomy and reported HELLP syndrome, previous cesareans, and placental abruption as considerable indicators of re-laparotomy [19].

The current study reported 3 cases (15.7%) of maternal mortality with no fetal death. The mortality rate is unfortunately very high when compared with previous reports. Gedikibasi et al. examined 35 cases of re-laparotomy and reported only 1 case of maternal mortality [20]. This study was conducted at a tertiary care hospital where more complicated cases are admitted or referred. In developing countries with low resources like Pakistan, statistics of tertiary care hospitals dealing with high-risk obstetrics cases vary. Neglected high risk cases are referred and are usually late by the time they arrive tertiary care hospital. This leads to greater probability of bad outcome in emergency care. This can be a factor for increased mortality rate in our study.

This study is limited in terms of smaller sample size and absence of a follow-up period after re-laparotomy. Therefore, more such multi-center studies with a larger sample size should be conducted in Pakistan which will contribute significantly to the improvement of clinical practices and decrement of feto-maternal mortality and morbidity.

CONCLUSION

In the present study, re-laparotomy was conducted in 2.2% of cases during the study period. Placenta previa,

fetal macrosomia, and pre-Eclampsia were the strongest risk factors causing re-laparotomy after cesarean section.

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Original Article

Hemodynamic Changes in Patients Undergoing Percutaneous Transvenous Mitral Commissurotomy (PTMC)

Muhammad Shahid[1], Hadi Yousuf Saeed[2], Fawad Qadir[2], Zahid Iqbal[3], Liaqat Ali[1] and Hafiz Abdul Kabir[2]

ABSTRACT

Objective: To analyze the impact of PTMC on hemodynamic and anatomic outcomes.
Study Design: A descriptive observational study
Place and Duration of Study: This study was conducted at the Cardiology Department, Nishtar Medical University & Hospital Multan & CPE Institute of Cardiology, Multan from June 2020 to June 2021.
Materials and Methods: The study included fifty patients with isolated rheumatic mitral stenosis who underwent PTMC. The study included fifty patients with isolated rheumatic mitral stenosis who underwent PTMC. Mitral valve area, TMVG, and size of LA are measured in all patients through 2D transthoracic echo (with Toshiba Xario 2100). Echo was done before and 24 hours after PTMC. LA pressures before and after PTMC were measured in the cath lab.
Results: The mean age of the subjects was 35.24±8.75 years. A number of male patients were 29 while that of females was 21. MV area before PTMC was .92±.087 cm^2 which expanded to 1.68±.15 $cm^{2\ six}$ weeks after PTMC. LA pressures after PTMC was also significantly reduced, it decreased from 25.8±7.4 mmHg before PTMC to 10.87±5.7 mmHg after it (p-value <0.001). Pulmonary artery systolic pressure and TMVG were also significantly reduced after PTMC.
Conclusion: For managing patients with rheumatic MS, PTMC is found to be effective and safe. It significantly improves hemodynamic and anatomic outcomes in these patients.
Key Words: Percutaneous transluminal mitral commissurotomy (PTMC), left atrial pressure, rheumatic mitral valve stenosis.

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INTRODUCTION

Mitral valve stenosis (MVS) is one of the most common complications of rheumatic fever (RF)[1] Although in developed states, the rate of RF has decreased dramatically[2], but still a prevalent health condition in developing nations. In Pakistan, about 2.2% of people suffer from RF, while every 1.8 in 1000 people are reportedly diagnosed with rheumatic heart disease (RHD)[3,4].

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Symptoms of RHD appear long after the occurrence of the disease. Mitral stenosis results in pulmonary hypertension as flow across the valve decreases leading to blood backflow.[5] In most patients symptoms of RHD (NYHA class IV) are observed after fifteen years. In MS with a favorable prognosis, the standard treatment procedure is
Percutaneous trans luminal mitral commissurotomy (PTMC).[6,7]At advanced stages like high Wilkin's score or moderate to severe mitral regurgitation, surgery is mostly recommended. The success of PTMC is usually determined by the Trans-mitral valve gradient (TMVG). The success of the procedure is indicated by the major difference in pre and post-operative value of TMVG value.

MATERIALS AND METHODS

A descriptive observational study was conducted from June 2020 to June 2021 in NMU & CPE Institute of Cardiology. The study included fifty patients with isolated rheumatic mitral stenosis who underwent PTMC. Those aged more than 50 years, having spinal deformity and both aortic and mitral valve disease were excluded. Written consent was taken from all the

included patients. Approval from the ethical board was also sought before conducting the study.

Mitral valve area, TMVG, and size of LA are measured in all patients through 2D transthoracic echo (with Toshiba Xario 2100). Echo was done before and 24 hours after PTMC. LA pressures before and after PTMC were measured in the cath lab. SPSS v23 was used for all readings. Pre and post-PTMC values were compared using paired sample statistics.

RESULTS

The mean age of the subjects was 35.24±8.75 years. The number of male patients was 29 while that of females was 21. In 13 patients with mitral stenosis, pre-operative arterial fibrillation was diagnosed. MV area before PTMC was .92±.087 cm^2 which expanded to 1.68±.15 cm^2 six weeks after PTMC. LA pressures after PTMC was also significantly reduced, it decreased from 25.8±7.4 mmHg before PTMC to 10.87±5.7 mmHg after it (p-value <0.001). Pulmonary artery systolic pressure and TMVG were also significantly reduced after PTMC. (Table 1)

Table No.1: Study variables - Pulmonary artery systolic pressure and TMVG after PTMC

Study Variable	Pre-PTMC	Post-PTMC	P-value
Mitral Valve Area (cm^2)	.92±.087	1.68±.15	<.001
LA area (cm)	4.68±.88	4.42±.07	.001
LA Pressure (mmHg)	25.8±7.4	10.87±5.7	<.001
TMVG (mmHg)	16.78±3.72	5.66±1.43	<.001
Pulmonary Artery Systolic Pressure (mmHg)	53.22±30.44	30.76±9.0	<.001

DISCUSSION

The rheumatic mitral stenosis is highly related to changes in the anatomy of LA and electrophysiological shifts resulting from an increase in LA afterload and its direct association with RHD.[8,9] There also is an increased risk of AF because of these changes. In this study, 26% of patients had AF before PTMC. Another study showed that 23.55 patients had PF pre-PTMC.[10] Inoue et al was the first to report PTMC in 1984 and since then it became the treatment of choice for managing moderate to severe MS.[11] It is significant in reducing mortality and morbidity.[12,13] Moreover, according to the studies PTMC is also significant in reducing the risk of AF in the long term.[14] The focus of our study was to analyze the impact of PTMC on hemodynamic factors. The present study shows that TMVG was significantly reduced from 17.88±2.71 before PTMC to 4.65±1.44 mm Hg after it. LA area was also reduced from 4.68±.88 cm to 4.42±.07 cm.

Another study also demonstrates the significant impact of PTMC on hemodynamic outcomes. According to the results, MV area increased from .8± .088 cm^2 pre PTMC to 1.77±0.14cm^2 after it. LA diameter decreased from 5.66±.83cm before PTMC to 4.33± .07 cm after it. Right ventricular systolic pressure (RVSP) also changed from 62.34±10.98 mmHg before PTMC to 57.51± 9.67 mmHg 24 hours after it and to 46.49±7.83 mmHg 6 months after it.[10] Another study also found that PTMC significantly improves hemodynamic and anatomic factors in MS patients. It was found that the diameter of LA was reduced from 46.33±6.35 mm to 41.19±5.66 mm after PTMC, and PAP was also significantly reduced from 55.23±30.65 mmHg to 29.77±9.10 mmHg.[15]

Another study was conducted on follow-up of the patients who had undergone PTMC, it was found that young age is associated with good outcomes and in 71% of patients, improvement was seen. Within 6 months of the procedure, the restenosis rate was 8.33% and the mortality rate was 7.14%. Moreover, patients undergoing PTMC for restenosis had a better survival rate than those undergoing MV replacement.[16] Studies have shown that long-term follow-up shows favorable results of PTMC.[17] The limitation of our study is that patients were followed up for 1 week only and not for the long term.

CONCLUSION

For managing patients with rheumatic MS, PTMC is found to be effective and safe. It significantly improves hemodynamic and anatomic outcomes in these patients.

Author's Contribution:

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Original Article

Non-Alcoholic Fatty Disease of Liver in Obese Persons, an Underappreciated Risk

Mohammad Mohsin Rana[1], Burhan Rasheed[2], Muhammad Bilal Kundi[1], Muazzam Fuaad[1], Tahir Baig[2] and Mohammad Saleem Akhtar[1]

ABSTRACT

Objective: To assess the incidence of NAFDL among local obese population, relate it with USG grading of fatty change in liver and to highlight the issue and sensitize both general population and the medical community to recognize its importance for early diagnosis and interventions.

Study Design: Observational cross section study

Place and Duration of Study: This study was conducted at the Rai Medical College teaching Hospital, Sargodha from Jan. 2021 to Dec, 2021 for a period of one-year.

Materials and Methods: The patients attending the medical OPD between the ages of 20-70 years, both genders were selected for this Observational study, convenient sampling. Ideal body weight, BMI and B-Mode USG were recorded to measure hepatic size and parenchymal echogenicity as per standard.

Results: 1010 Patients, 700 females, 310 males participated. All the % calculations are for the total number of patients. When assessed by USG, in the Normal weight category only 3% had normal parenchymal echotexture of liver (nPEL), 19% had Grade 1 Fatty liver (FL), 3% had Grade 2 FL and none had Grade 3 FL. In overweight category none had nPEL, 26% had Grade 1 FL, 32% had Grade 2 FL and none had Grade 3 FL. In obese category none had nPEL, 7% had Grade 1 FL, 10% had Grade 2 FL and none had Grade 3 FL. When assessed by USG, in the <25 BMI category 1% had nPEL, 12% had Grade 1 FL, 4% had Grade 2 FL and none had Grade 3 FL. In 25.0-29.9 BMI category none had nPEL, 25% had Grade 1 FL, 19% had Grade 2 FL and none had Grade 3 FL. In 30-35 BMI category none had nPEL, 16% had Grade 1 FL, 8% had Grade 2 FL and none had Grade 3 FL. In >35 BMI category none had nPEL, 8% had Grade 1 FL, 8% had Grade 2 FL and none had Grade 3 FL.

Conclusion: Early detection of HPE changes and sensitization to its future implication as a risk factor for CLD and even HCC among both medical community and general public must be the priority in our professional circles. It shall be highlighted in all clinical conferences because early interventions in terms of lifestyle modifications targeted to not only weight reduction but more importantly weight maintenance have a great potential for reversal of all these changes.

Key Words: Obesity, BMI, NAFDL, IR, Metabolic Syndrome

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INTRODUCTION

Inspite of the efforts of all the divine sermons, health professionals' warnings, social reformists appeal, chronic and excessive alcoholism remains the leading cause of CLD followed by chronic HCV infection and its sequel, the CLD, in our population. Excess fat deposition in the liver and other tissues is a well-known metabolic consequence of IR.

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Now Non-Alcoholic Fatty liver technically called Non-Alcoholic Steohepatitis (NASH) and NAFDL are becoming the leading hepatic pathologies in both. [1-3]

Visceral adiposity is an independent risk factor for insulin resistance, Type 2 Diabetes mellitus (T2DM) and associated cardiovascular (CV) risks. Taylor has proposed that ectopic fat deposition in the liver and islets underlies the development of hepatic insulin resistance and βcell dysfunction.[4-6] Grey scale ultrasound is a reliable, non-invasive, cheap and readily available parameter used worldwide for estimation of hepatic fatty change and severity grading.[7, 8]

Obesity is a known phenomenon from the known human history. Untill recently, in most of the cultures it was a desired beauty feature and a reflection of upper socioeconomic class. All the Egyptian, Persian, European and Indian queens and princesses are always portrayed a little bit plump. All the goddess sculptures have quite a contour of tummy and bumps. Industrial

revolution led us into an era of ever-expanding ease of procuring diet, the food and beverage industry packed our dining tables with concentrated calories foods, appetizers and delicacies. This resulted into epidemic of obesity with all its known complication, from metabolic syndrome (MS) making Ischemic Heart disease (IHD) (CHD and Cerebro-vascular Accidents (CVA) being the top killers to a range of pelvic and intestinal malignancies, musculoskeletal issues, fertility and obstetric problem and surgical issues. The worldwide prevalence of overweight and obesity has doubled since 1980 to an extent that nearly a third of the world population, 1.9 billion, and out of these 609 million were adolescents or young adults, a staggering 39%, was classified as overweight or obese by 2015 figures.

MATERIALS AND METHODS

This study was carried out on all of our consenting and affording obese patients presenting to Medical OPD between the ages of 20-70 years, both genders.

After securing informed consent, basic biodata, validating the diagnosis of obesity on anthropometric criteria and applying exclusion criteria, abdominal USG findings were recorded. Ideal body weight, BMI and B-Mode ultrasound evaluation was done to measure hepatic size and assess parenchymal echogenicity as per standard tables and calculations.

Inclusion Criteria: 20-70 years age, both sexes, Obesity.

Exclusion Criteria:

Seriously sick patient or terminally ill patient.
Non treated Chronic HBV and HCV disease
Established cirrhosis of liver
Alcohol use in last 3 years
Any other cause of hepatomegaly or CLD
Pregnancy
Ascites of any etiology
Major end organ disease, liver, kidney, heart, lungs
Active steroid use in last 6 months
Hypothyroidism
Human Immunodeficiency Virus
Gastrointestinal by-pass surgery
History of liver surgery.

Study Design: Observational cross section study.

Study Period: From January to December, 2021.

Sample Size and Sampling Technique: A sample size of 392 patients was calculated as minimum required to maintain a 5% margin of error and 95% confidence interval using WHO sample size calculator.

Statistical Analysis: Data analysis was conducted using Microsoft Excel version 2016 and Statistical Package for Social Sciences software version 25. Descriptive statistics (i.e. frequency distribution, percentages, mean and standard deviations) was the primary analytical methods.

We calculated the incidence of NAFLD in different age decades in both sexes and in different weight and BMI groups.

RESULTS

In this study, out of 1010 patients, 700 were females and 310 were males, completed the study. These were divided into Normal Weight, Overweight and Obese categories as per standard. BMI Groups are divided into <25, 25-29.9, 30-35 and >35.

Table No.1: Ideal Body Weight and Liver Fat. All % calculated for total number of patients in the group. (N 1010)

Weight Category	Total Patients	Liver Fat			
		Nor. Liv.	F. Liv. 1	F. Liv. 2	F. Liv. 3
Normal	170	70	90	10	0
		(6.93±1.17%)	(8.91±1.20%)	(0.99±1.01%)	(0.00±0.00%)
Overweight	440	170	90	80	100
		(16.83±0.95%)	(8.91±0.99%)	(7.92±1.21%)	(9.90±1.00%)
Obese	400	0	240	160	0
		(0.00±0.00%)	(23.76±0.76%)	(15.84±1.09%)	(0.00±0.00%)

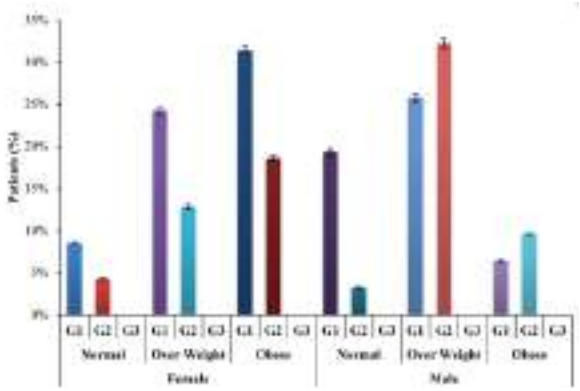

Figure No.1: Obesity and Nafdl

On USG, in the Normal weight category only 7% had nPEL, 9% had Grade 1 FL, 1% had Grade 2 Fatty liver and no person had Grade 3 FL. In overweight category17% had nPEL, 9% had Grade 1 FL, 8% had Grade 2 FL and 10% person had Grade 3 FL. In obese category no person had nPEL, 24% had Grade 1 FL, 16% had Grade 2 FL and no person had Grade 3 FL. Same is presented graphically in Graph A.

Two important trend needs to be noted, inspite of the body weight being in the normal range around 10% still had FL, on the other hand all in obese category had FL. The Grade 3 fatty changes were not seen in obese persons while 10% in overweight category had G3 FL.

As expected % of persons having FL follows the increase in weight both in G1 and G2, it was not seen in G3. Deposition of fat in liver is a multifactorial process, genetic background, sedentary lifestyle, fructose intake and pattern of fat storage reflected in Waist: Hip Ratios and Waist Circumference, both gender dependent, being the notable ones.

When BMI figures are combined for both gender, in the <25 BMI category 1% had nPEL, 12% had Grade 1FL, 4% had Grade 2 FL and none had Grade 3 FL. In 25-29.9 BMI category none had nPEL, 25% had Grade 1 FL, 19% had Grade 2 FL and none had Grade 3 FL. In 30-35 BMI category none had nPEL, 16% had Grade 1 FL, 8% had Grade 2 FL and none had Grade 3 FL. In >35 BMI category none had nPEL, 8% had Grade 1 FL, another 8% had Grade 2 FL and none had Grade 3 FL. Same is presented graphically in Graph B.

Table No.2: BMI and liver fat. All % calculated for total number of patients in the group. (N 1010)

BMI	Total Patients	Liver Fat			
		Nor. Liv.	F. Liv. 1	F. Liv. 2	F. Liv. 3
< 25	170	10	120	40	0
		(0.99±0.67%)	(11.88±0.63%)	(3.96±0.62%)	(0.00±0.00%)
25 – 29.9	440	0	250	190	0
		(0.00±0.00%)	(24.75±0.60%)	(18.81±0.58%)	(0.00±0.00%)
30 – 35	240	0	160	80	0
		(0.00±0.00%)	(15.84±0.71%)	(7.92±0.91%)	(0.00±0.00%)
> 35	160	0	80	80	0
		(0.00±0.00%)	(7.92±0.80%)	(7.92±0.76%)	(0.00±0.00%)

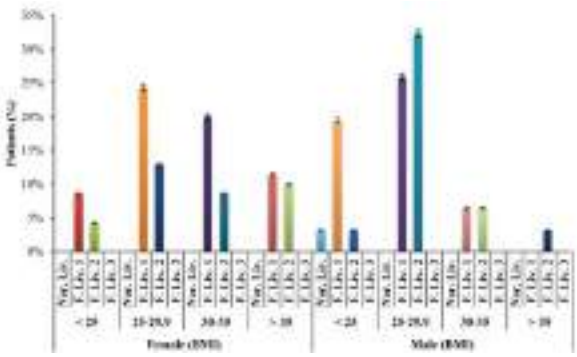

Figure No.2: BMI and NAFDL

DISCUSSION

Body mass index (BMI) is typically used to define overweight and obesity in epidemiological studies. Greater cardio-metabolic risk has also been associated with the localization of excess fat in the visceral adipose tissue and ectopic depots (such as muscle and liver), as well as in cases of increased fat to lean mass ratio (e.g. metabolically-obese normal-weight).[5] The age-standardized prevalence of being overweight or obese has increased almost 50% and 80% respectively over the past 35 years with female predominance. In low-income countries it's generally higher among middle-aged adults from wealthy and urban environments (especially women); whereas in high-income countries it affects both sexes and all ages, but is disproportionately greater in disadvantaged groups associated with adoption of an energy- and fat-rich diet and a sedentary lifestyle. It's one of the leading underlying causes of both NASH and NAFDL. Abdominal USG is the widely available, affordable, non-invasive tool to pick fatty infiltration of liver.[9]

Obesity andT2D both predispose to development of NAFLD. Early in the course, histologically, it's called steatosis or nonalcoholic fatty liver (NAFL). With hepatocytes degeneration and inflammation it's called nonalcoholic steatohepatitis (NASH). With advancement, fibrosis typical of cirrhosis sets in. All is clubbed together as NAFDL. Normally slowly progressing (on average 14 years to progress to next stage of fibrosis), in upto 20% of cases it progress rapidly to advanced fibrosis. Risk factors for rapid progression of fibrosis in NAFLD includes the existence of NASH on histology, advancing age, moribund obesity, excessive fructose intake, presence of insulin resistance and poorly controlled DM reflected as high HbA1c levels, post-menopause years and high ALT.[10]

Two important trend needs to be noted, inspite of the being in the <25 BMI category only 1% had normal liver but 12% had Grade 1 Fatty liver and 4% had Grade 2 Fatty liver. In 25 and above categories none had normal liver. The Grade 3 fatty changes were not seen in any of the BMI categories. In both 25-29.9 and 30-35 BMI categories maximum numbers had G1 and G2 changes as expected. This was not seen in >35 BMI group, this phenomenon is well explained on the basis of "Metabolically Healthy Obese Persons" who are not at risk of developing DM, HTN and Lipid abnormalities. Deposition of fat in liver is a multifactorial process, genetic background, sedentary lifestyle, fructose intake and pattern of fat storage reflected in Waist: Hip Ratios and Waist

Circumference, both gender dependent, being the notable ones. These results very loudly justify the need for similar studies. NAFDL is now an established entity with its significant role established as an underlying pathophysiological mechanism underlying the development of IR and its metabolic consequences leading to early and advanced atherosclerotic sequel.

In Men incidence of fatty liver remains stable from 30s through 60s but women catchup during 60s to match men.[10] Global burden of NAFLD related CLD is now estimated to be around 25%. The focus has now shifted from simply reflecting metabolic Syndrome (MetS) to the major underlying pathophysiologic mechanism of Insulin resistance in a bidirectional cause and effect mode for T2DM.[11]

The American Association of Liver Diseases predicts that NAFLD will surpass the chronic alcoholism as the as the leading cause for CLD and the indication for liver transplant due to the twin epidemics of obesity and DM. As Asians especially Indian populations are known to have more intra-abdominal adipose tissue for the same weight and height than white Caucasians (9-32% prevalence), almost half are reported to have clinical evidence of full-blown MetS. NAFLD precedes MetS starting from early childhood and keeps on increases with age[12]. The adult treatment panel III (ATP III) is considering to include NAFDL in the list of inclusion criteria for MetS. This alarming prevalence has led to a separate definition of MetS for children and adolescents. Recently NAFDL variant in lean individuals are being recognized increasingly.[13]

Ultrasonographic changes in liver and/or serum Alanine Aminotransferase (ALT) are used in all epidemiological studies of NAFDL inspite of the well-known limitations at both end of spectrum: US detects changes only when liver fat is more than 30% and ALT levels may be normal in advanced disease called "burned-out NASH".[11] The overall sensitivity and specificity of ultrasound in detection of moderate to severe fatty liver have been shown to be accurate and comparable to those of histology. [7,8] Liver biopsy is the gold standard for documenting and assessing the severity of NAFLD: The magnetic resonance (MR) techniques are very good non-invasive surrogate for initial assessment and for monitoring change over time and with interventions.[14] Quantitative assessment of liver fat by MRI-PDFF is now increasingly being recommended as an endpoint in NAFLD/NASH trials.[15,16].

CONCLUSION

After reviewing the literature and interpreting this study, it is very clear that HPE changes in the NAFLD is not only a simple reflexion of excess fat deposition like in other organs like subcutaneous tissue and around the abdominal viscera. USG is most cost-effective due to its wide availability, reliability in diagnosing and reproducibility in following changes both for better or worse, being cheap and non-invasive nature makes it ideal for early diagnosis of HPE in NAFDL cases in obese persons. Early detection of HPE changes and sensitization to its future implication as a risk factor for CLD and even HCC among both medical community and general public must be the priority in our professional circles. It shall be highlighted in all clinical conferences because early interventions in terms of lifestyle modifications targeted to not only weight reduction but more importantly weight maintenance have a great potential for reversal of all these changes.

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

Effect of Proprioceptive Exercises on Pain and Function in Non-Specific Chronic Neck Pain

Noshaba Kanwal[1], Qurat ul Ain[1], Tasneem Shehzadi[1], Sidra Faisal[1], Atiya Fatima[1] and Misbah Waris[2]

ABSTRACT

Objective: To determine the effect of proprioceptive exercises on pain and function in Non-specific chronic neck pain.

Study Design: Randomized control trial

Place and Duration of Study: This study was conducted at the Muhammad physical therapy clinic and rehabilitation center, Multan from June 2020 to January 2021 for a period of one and a half year.

Materials and Methods: Through non-probability convenient sampling technique 34 participants with chronic Non-specific neck pain were randomized in two groups through lottery method. Group A received conventional treatment with proprioception exercises while Group B received conventional treatment only. Pain and disability were measured by using numeric rating pain scale and Neck disability index scales were respectively. Exercise regime distributed in six weeks period alternate session in week exercise, 10-12 repetitions with 1-minute rest interval, and lasted 45 minutes in both groups. Pre-treatment and post-treatment measurements were taken.

Results: Mean age for treatment group and control group was 31.85±4.94 and 30.85±6.93 years respectively**.** Mean of numeric rating pain scale in treatment group before treatment was 2.71±0.48 and post treatment mean was 0.85±0.37, p value was 0.00. In control group pretreatment mean of numeric rating pain scale was 2.71±0.48 and post treatment mean 1.85±0.37, p value was 0.001. For treatment group pretreatment mean for neck disability score was 4.28±0.75 and post treatment mean was 1.57±0.53, p value was 0.00. In control group pretreatment means neck disability score was 4.28±0.75 and post treatment was 3.28±0.75, p value was 0.04.

Conclusion: Proprioceptive exercises were effective on improving pain and function in non-specific chronic neck pain.

Key Words: Neck disability index, Numerical pain rating scale, proprioceptive exercise

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INTRODUCTION

Neck pain is an illness that most individuals endure. As a consequence, in the spinal parts, instability increases, resulting in failure towards the neutral position is maintained.(1) chronic neck pain which is caused by damage and loss of neck muscles functions like a proprioceptive damage in such kind of pain.(2)

Active Joint Position Sense can be tested by using a laser pointer in neck region.(3)

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It can be tested by using a laser pointer in neck region by attaching a laser pointer to head of patients and instruct a patient to relocate head from right rotation to initial neutral position with closed eyes.(3) Most nonspecific pain in the neck is not associated with a major illness or with neurological symptoms of compression of the nerve. (4) people who have neck pain oculomotor and eye head coordination assessment is necessary for neck region vertebrae ,because cervical spine sensory neuron have important role in maintaining eye head movement.(3) Strengthening exercises in individuals with joint pain can improve joint stability and power due to the ability of the muscle to generate Higher strength by enhanced strength of the muscle control.(9) The muscles of body are strengthen by strengthening exercises, reduce stress on joint during movement. clinical outcomes such as pain relief ,physical function ,and quality of life improved by strengthening exercises.(9) (4) The aim of the proprioceptive insole is to activate correction reflexes with an immediate response to stabilization and equilibrium parameters affecting muscular proprioception in the feet.(10) highlighting shifts in the

lateral location of the pressure core, the pressure surface and the anteroposterior oscillations of the pressure Centre.[11]The plant pressure proprioceptive sensitivity enables the organization of an Optimum kinesthetic response and optimizes postural techniques in combination with the other sensory inputs.[12] Beom-Ryong Kim et al 2017 conducted a study to see the effect of proprioceptive exercises on pain, respiratory function and neck disability scale, muscle strength in people who have chronic low back pain. Result showed that proprioceptive exercises were effective in improving in pain by reduction its severity, reduction in functional disability index and enhance pulmonary functions.[5] Michael A McCaskey et al 2014 conducted a study on chronic neck pain to assess pain and function of cervical region proprioceptive exercises were used for assessment of neck muscle function. It suggests that proprioceptive is no more effective than conservative physiotherapy.[6]Tomas Gallego izquierdo, PT, PhD et all 2016 conducted a study to compare on neuromuscular control, pressure pain sensitivity and perceived pain and disability in patients with chronic neck pain to compare the effects of cranio-cervical flexion training and proprioceptive training. The result indicates that proprioception training have positive effect on function of deep cervical flexor.[7]Exercises were seen to boost efficiency in tasks with sensor motors, relieving neck pain and decreasing postural sway.[8] Soon-young Bong et all, 2016 conducted a study to assess the effect of proprioceptive exercises in people who have chronic low back pain to evaluate the pain and functional disability index. Result showed that proprioceptive exercises were effective in reduction of pain and functional disability scale.[13]Kim jin et all 2015 conducted a study to check pain and balance in people who have low back pain. Patients were treated with proprioceptive exercises and swiss ball training. Result showed that proprioceptive exercises were effective in improving pain and balance as compared to swiss ball training.[14]

MATERIALS AND METHODS

This Randomized controlled trial was conducted at Muhammad physical therapy clinic and rehabilitation center, Multan from June 2020 to January 2021. Through non-probability convenient sampling technique 34 participants with chronic Non-specific neck pain were randomized in two groups through lottery method. **Group A** received conventional treatment with proprioception exercises while **Group B** received conventional treatment only. Patients with the age 20 to 45 years with non-specific neck pain for more than three months of both gender were included in the study. Patients with any systemic or congenital disease were excluded. NPRS and NDI were used as data collection tool. 34 patients were assessed at the end of the sixth treatment weeks. Patients were assessed by performing spurling test and neck distraction test, excluding red flags. Group A received proprioception exercises plus conventional treatment of strengthening exercise which were performed with prone and supine position by placing a towel under head, press towel for 5 seconds with 10-12 repetition. Proprioception exercises were performed as A) Head relocation which involves the relocation of head back to natural head posture and to predetermine positions in range first with eyes open and closed with all cervical movements. b) Gaze stability coulometer exercises with stationary head and movement of eye balls progressing to movement of head with visual fixation on a target. (c) Eye head coordination exercises which include rotation of eyes and head to the same side in right and left directions. Then progressed with in opposite direction. While **Group B** received conventional treatment only. NPRS for pain and NDI for disability was used .Pre and post measurements were taken after six weeks. The data was analyzed using SPSS Independent sample t- test was used to compare the effects between two groups. Paired sample t test was used to compare within groups. Descriptive statistics were used.

RESULTS

Normality of data was calculated Shapiro-wilk test showed p value greater than 0.05, Parametric test were used.

Mean change of NDI scale of treatment group was 2.71 with a p value 0.000.pre-treatment mean of NDI scale of control group was 4.28 and post-treatment mean 3.28.

Table No.1: Descriptive Statistics of Demographics

Demographic characters	Treatment group	Control group
Age	31.85±4.94	30.85±6.93
Gender	1.71±0.48	1.57±0.53

This table shows descriptive statistics of demographics.

Table No.2: NPRS Paired sample statistics

Measure	Group	Pre-treatment Mean ± SD	Post-treatment Mean ± SD	Mean change Mean ± SD	P value
NPRS	Treatment control	2.71±0.48 2.71±0.48	0.85±0.37 1.85±0.37	1.85±0.69 0.85±0.37	0.000 0.001
NDI	Treatment control	4.28±0.75 4.28±0.75	1.57±0.53 3.28±0.75	2.71±0.48 1.00±0.57	0.000 0.045

Table No.3: Independent sample t-test

	Levene Test For Equality of Variances		**t test for equality of means**			
	F	SIG	t	df	Sig(2-tailed)	Mean difference
NPRS						
equal variances assumed			-4.95	12	0.000	-1.00
equal variances not assumed	0.000	1.000	-4.95	12.00	0.000	-1.00
NDI						
Equal variances assumed			-4.15	12	0.001	-1.71
Equal variances not assumed	0.046	.834	-4.15	11.98	0.001	-1.71

This table showed mean difference of NPRS is 1.00, with a significant 2-tailed value 0.000, and mean difference of NDI was 1.71 with a significant 2-tailed value 0.01.

DISCUSSION

The current study was performed on 34 subjects with aim to know the individual effects of proprioceptive exercises on pain and function in chronic nonspecific neck pain A characteristic of some patients with neck pain is compromised proprioception and postural function, and many therapeutic measures have been proposed to impairments, such as head-neck recognition exercises, oculomotor exercises or equilibrium training exercises, are discussed specifically.[7]

In previous study proprioceptive exercises were used in low back pain individuals for pain, pulmonary function and disability function. The result of this study showed that pain and disability decreases with VAS score and disability score. In current study proprioceptive exercises were used for chronic non-specific neck pain. Result showed that pain, disability decrease, NPRS score (p=0.000) and disability score (p=0.000) in chronic Non-specific neck pain. NPRS pre-treatment value was 2.71±0.48 and post-treatment was 0.85±0.37 in treatment group.[5]

Tae-woo-king et all, studied an effect of proprioceptive exercises on patients of whiplash injury and measured the neck disability index, endurance of deep neck flexor muscles. The result of this study showed marked improvement in functional activities. and pain decrease with a NPRS score (0.000) in chronic non-specific neck pain.[15] In current study proprioceptive exercises proved to improve pain among patients with chronic non-specific neck pain. IZQUIERDO TG et all carried a study on proprioceptive training in patients of chronic non-specific neck pain. Results showed that disability decreases and improvement in function in chronic non-specific neck pain. In recent study disability decrease with a NDI score. Pre-treatment value in treatment group was 4.28±0.75 of NDI , while post treatment value was 1.57±0.53 [7]

ojoawo et all, carried a study on pain intensity, disability of knee. Proprioceptive exercises and isometric strengthening exercises were used. Pain was reduced due to increase in joint lubrication, decreased stiffness and muscle strength increased.it was seen proprioceptive exercises significantly reduced pain intensity and disability. The result showed that pain score (p=0.001) and disability score (p≥0.01).[16] In current study proprioceptive exercises were found to reduce pain.

In previous study cupping massage was used for non-specific neck pain. Fifty patients were included in study. Participants were divided into two groups' treatment and control. Treatment group received 5 cupping session per week for three weeks. Outcome measures VAS was used for pain. The result of this study was found that pain reduced significantly (p=0.019) functional disability (p≥0.001) quality of life subscales for pain (p=0.002). It was found that cupping massage improve functional activities of daily life and pain. [17] In current study pain reduced (p=0.000) functional activities like driving improved significantly (0.002), lifting (0.001).Disability reduced (0.000).proprioceptive exercises were found effective in pain, functional activities, neck pain·

On neurophysiological substrates, Proprioceptive Neuromuscular Facilitation (PNF) functions. It improves proper neuromuscular activation through the use of neurophysiological techniques, resulting in the regulation of sensory-motor conduction stimulation and proprioceptive stimulation[18]

In previous study proprioceptive exercises were used in muscle strength, range of motion, stability of joints and function of upper limb and pain of adhesive capsulitis.it improves strength of muscles of upper extremity. proprioceptive exercises were found in improving pain and functional activities with a pain score and disability (p=0.01).In current study quality of life, functional activities and pain improve with a NPRS score (p=0.000) and NDI score (p=0.000).[19] The system activates proprioceptors inside the nerves and the muscles Tendons, thus enhancing their roles and increasing Muscle power, endurance, balance and synchronization, optimizing the motor units' responses efficiently.[20]

CONCLUSION

Proprioceptive exercises were effective in reducing pain and disability and improving function in Non-specific chronic neck pain.

Author's Contribution:

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Original Article

Comparison of Muscle Energy Technique versus Kinesio Taping Technique to Reduce Pain and Improve Lower Limb Functional Activity in Patients with Plantar Fasciitis

Fatima Tariq[1], Shabana Ashraf[1], Fatima[1], Aqsa Waris[1] and Rabiya Noor[2]

ABSTRACT

Objective: To compare the effectiveness of muscle energy techniques versus calcaneal taping for reducing pain and Improve Lower limb Functional Activity in Patients with Plantar Fasciitis.

Study Design: Randomized clinical trial study

Place and Duration of Study: This study was conducted at the Haq Orthopaedic Hospital and Surraya Azeem Hospital, Lahore from July, 2018 to July, 2019 for a period of one-year.

Materials and Methods: Through non-probability convenient sampling technique 52 Subjects were recruited and allocated in two groups by using Lottery method of Randomization. Subjects diagnosed having plantar fasciitis for more than 6 months and age between 20-60 years were included in study. Those with any foot surgery or neurological deficit or with any referred pain to foot were excluded from the study. Group A received taping along with conventional treatment group B received MET along with Conventional physiotherapy protocol (therapeutic ultrasound, foot intrinsic muscles' strengthening exercises, TA stretching exercise). Total 7 sessions were given on alternate days with each session for about 30 minutes. Assessment was done prior to (pre) and at the end (post) of treatment through Visual Analogue Pain Scale (VAS) and Foot Function Index (FFI).

Results: The total mean±SD of total score of post treatment FFI was 13.5296±5.25312 for group A and 21.2712±9.30238 for group B with p value of 0.001. The pain measured on the VAS showed mean± SD of 1.42±0.758 for group A and 2.92±1.354 for group B with p-value of 0.000. Paired t-test shows p-value of 0.000 which is highly significant.

Conclusion: Taping is more effective than muscle energy techniques to reduce pain and improve lower limb functional activity when given along with conventional physiotherapy protocol.

Key Words: Plantar Fasciitis, Calcaneal Taping, Muscle Energy Techniques, Heel pain, Active stretching, Foot Function Index, Kinesio taping

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INTRODUCTION

'Plantar Fascitis' is a heel disorder with pain and inflammation which is triggered by repeated trauma on the bottom of calcaneum or at the plantar fascia's origin.[1]

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Plantar Fascitis (PF) was categorized as an overuse syndrome arising due to the plantar fascia's micro tear at its origin.[2] It happens mostly in those people who spend most of the time in standing position or have restricted dorsi flexion of ankle joint.[3] It is more prevalent in females, accounting for 11-15% of all pathologies of the foot. Plantar heel pain is the most prevalent disorder treated in physical therapy clinics and accounts for up to 40% of all patients in podiatric hospitals.[4] Taping is very effective for reducing pain in plantar fasciitis. It can be used both in acute and chronic stages of PF. It removes stress from the fascia, promotes the natural arch of the foot and gives support to the muscles around the foot.[5] There are several kinds of taping methods available efficient for relieving pain like windlass taping, medial longitudinal arch taping, calcaneal taping and mulligan taping.

Patients receive immediate pain relief and increase in range of motion by calcaneal taping technique. Muscle Energy Technique (MET) is one of the neuromuscular re-education methods used for the treatment of musculoskeletal dysfunctions. It includes soft tissue or joint manipulation or mobilization methods. MET eliminates trigger points and helps to reduce hypertonia and lengthens the muscles that are tight. This method is used for strengthening weakened muscles, reducing localized edema or mobilizing limited joints.[6] Calcaneal taping and MET both are efficient methods to manage heel pain in the plantar fasciitis. The basic aim of the research is to discover the influence of MET and taping in patients with plantar fasciitis and to compare their efficacy. These methods assist to manage the ankle joint's pain and to increase the functional movement of lower limbs.[7]

MATERIALS AND METHODS

This randomized clinical trial was ethically approved by the committee of University of Health Sciences, Lahore. All participants gave written informed consent. The data was collected from Surraya Azeem Hospital and Haq Orthopaedic Hospital, Lahore. The duration of this study was 1 year from 1-06-2018 to 1-06-2019. 52 patients diagnosed with plantar fasciitis were included. Non probability convenient sampling technique was used for the selection of patients. The inclusion criteria were patients diagnosed having plantar fasciitis for more than 6 months with the age of 20-60 years. Patients who had undergone any surgical procedure for feet in the last 6 months or if any Red flag signs were present in which manual therapy is contraindicated or if the patient had any neurological deficits or had referred pain e.g. sciatica or diabetes or who had used steroid injections for the management of PF before or the Individuals who had adhesive tape allergy and Prior foot taping exposure within last 6 months were excluded from the research.[8] The patients who had foot pain due to any other musculoskeletal issues e.g. gout or inflammatory joint diseases were also excluded from the research. The patients who were taking pain killers to manage the pain caused due to plantar fasciitis were also excluded from the research.[9]

Data Collection: Patients were divided in 2 groups. Group A patients were treated with calcaneal taping, applied to the plantar fascia, along with physiotherapy traditional program (therapeutic ultrasound, foot intrinsic muscles' strengthening exercises, TA stretching exercise).[10] Group B was treated with MET (applied to gastrocnemius and soleus) and conventional physiotherapy protocol. Total 7 sessions were given on alternate days with each session for about 30 minutes.[11] Therapeutic ultrasound was used at the painful area for 5 minutes and intensity was kept at 3 MHz.[12] Assessment was done prior to (pre) and at the end of the treatment (post) through Visual Analogue Pain Scale (VAS) and Foot Function Index (FFI) for measuring pain intensity and disability. Foot function index is a self-administered questionnaire and consists of 23 items and is divided into three subscales. It is used to measure the effect of foot pathology on function in terms of pain, disability and activity restriction.[12]

Technique to apply MET: MET was implemented with patient in the supine position and foot extended over the edge of the plinth holding the knee in extension for gastrocnemius and knee in flexion for soleus (figure 1). The therapist's hand dorsiflexed the ankle joint of the patient until a resistance or pain was felt. This position was kept and the subject was requested to exert effort (isometric contraction) towards plantar flexion for a period of 5-7 seconds, then resistance was released slowly and relaxation was provided for a period of 5 seconds. Ankle was passively dorsiflexed to a fresh barrier during this relaxation period. For each therapy session a set of 10 repetitions were provided individually for gastrocnemius and soleus muscle.[4]

Figure No.1: MET technique for Gastrocnemius and soleus

Technique to Apply Calcaneal Tape: Measurements were taken from heel to the ball of the foot. The tape was cut to that length. The last 2 inches were left as uncut as an anchor and remaining tape was cut in a fan like manner. The base of the tape was anchored to the tendoachilles. The tails of the tape were applied with a stretch of 75% to the toes. Then a piece of tape was measured around the foot. This strip of tape was anchored at the outside edge of the foot. The arch was taped from outside to inside, pulling up a little at the end with the tape. The end of the tape was laid on top of the foot without any strain. Then, the tape was rubbed to activate the glue. (figure 2) Both zinc oxide tape and kinesiological tape were used in this research.[13]

Figure No.2: Method of Calcaneal Taping

Strengthening exercises for foot muscles

1. Towel curl up exercise in which the person hold the towel in his hand and pulled it to his upper body.
2. Curl up exercise for the toes in which the marbles were picked from the ground and placed in the bucket.
3. Active range of motion exercises of the ankle in supine (it included dorsiflexion, plantarflexion, inversion and eversion)[14]

Stretching Exercises: Active stretching exercise of the TA was performed in standing position. The patient leaned against the wall to stretch the muscles. Each stretch was held for 20 seconds. All these exercises were repeated 10 times each.[14]

Statistical Analysis: IBM SPSS v20 was used to analyze the data. Before the application of statistical tests, data was screened for normal distribution. Qualitative variables (age and duration of symptoms) were evaluated as pie and bar charts. The data was found to be parametric so for comparing mean± standard deviation score at pre post level for Foot Function Index and VAS, independent sample t test was employed. A p-value less than 0.05 was considered significant. Paired t- test was used to analyze difference in mean values of VAS and FFI scores between group A and B

RESULTS

In this study 52 participants were enrolled of which 46.2% were males and 53.8% were females. Results showed that 19.2% of participants were of age 20-30 years, 34.6% were of 31-40 years, 30.8% were of 41-50 years and 15.4% were of 51-60 years of age group.

Table No.1: Pre and post treatment comparison between group A and B

Variables	Treatment groups		P-value
	Group A (taping)	Group B (MET)	
Total score of pre FFI (mean ± SD)	46.20±12.247	51.29±11.53	0.129
Total score of post FFI (mean ± SD)	13.53±5.25	21.27±9.30	0.001
Pre score of the pain on VAS(mean ± SD)	7±1.497	7.15±1.617	0.723
Post score of the pain on VAS (mean ± SD)	1.42±0.758	2.92±1.354	0.000

17 of the participants included in research had pain from last 6-12 months, 14 from last 12-18 months, 10 from 18-24 months while 11 participants had pain present in their foot since more than 2 years

The mean ± standard deviation for total score of foot function index and visual analogue pain scale measured before and after applying the treatment shows statistically significant difference as shown in table 1. The p-value measured after the treatment shows the results are highly significant.

Paired t- test was used to analyze difference in mean values of VAS and FFI scores between group A and B which shows p-value of 0.00. (Table 2)

Table No.2: Comparison between group A and B by paired sample t-test

	Mean	Std. Deviation	T	P value
Total score of pre FFI	48.7456	12.05583	29.364	.000
Total score of the post FFI	17.4004	8.43934		
Pre Score of the pain on VAS	7.08	1.545	26.841	.000
Post Score of the pain on VAS	2.17	1.324		

DISCUSSION

The aim of the current study was to compare the effectiveness of muscle energy techniques versus calcaneal taping for reducing pain and to increase the

functional activity of lower limbs in the patients of plantar fasciitis. The majority of patients who presented in the current study of plantar fascitis were females. This is in accordance with the study by joschua dubin 2007 which suggests[15]. In current study it was found both MET and taping were beneficial in decreasing the VAS score in both groups. Pre VAS score of group A was found to be 7 and in group B it was found to be 7.15 after the treatment it was reduced to 1.42 for Group A and 2.92 for Group B.

Another study was conducted for comparing the effectiveness of calcaneal taping and muscle energy techniques with a common treatment of Ultrasound therapy, strengthening exercises of the intrinsic muscles of foot and TA stretch to both groups for the treatment of PF. The treatment was given for two weeks and the outcome measures were calculated with the help of Visual Analogue Scale (VAS) and Foot Functional Index (FFI).Improvement was found in both the Groups but calcaneal taping showed significant results than METS.[16] Another study conducted by Sweeting D in 2011, effects of taping and MET techniques were compared and it was found that both techniques improved the pain. Results also showed that Stretching and strengthening exercises are important for the management of PF. The purpose of the stretch is to reduce the stress placed on plantar fascia.[17] The study showed significant decrease in pain in both the groups but more decrease in painis seen in group A (p value = .000). Chitara 2015 concluded the similar results where taping technique is effective in reducing the pain.[18] The study showed statistically significant decrease in pain with the application of MET by using independent t test with the pre post values 7.15±1.617 and 2.92±1.354 respectively and improvement in lower limb functional activity with the pre post values 51.29±11.53 and 21.27±9.30 respectively in patients with PF. It is in accordance with the chitara et al., 2017 who concluded the effectiveness of MET techniques in reduction of pain in patients with PF.[18] Taping is found to be very effective in reducing pain and for the improvement of lower limb functional activity. The study showed significant decrease in pain with the application of calcaneal taping technique with the pre post values 7±1.497 and 1.42±0.758 respectively and improvement in lower limb functional activity with the pre post values 46.20±12.247 and 13.53±5.25 respectively. It is according to the research of Selkow et al., 2009 which have hypothesized a neurological explanation for the analgesic effects of MET.[19]

CONCLUSION

In the patients of plantar fasciitis, two weeks of treatment at alternate days either with MET or taping is helpful to reduce pain and improve functional activity of lower limbs. But Calcaneal taping (along with physiotherapy traditional protocol) is found to be more efficient than MET in short term plantar heel pain management.

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Original Article

Non-Prescription Use of Proton-Pump Inhibitors for Self - Treating Frequent Heartburn

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ABSTRACT

Objective: Determine the Prescription Patterns of Proton Pump Inhibitors (PPI) at the outpatient department (OPD) of a tertiary care hospital of Sindh.

Study Design: Retrospective study

Place and Duration of Study: This study was conducted at the Department of Pharmacologhy and Medicine, Peoples University of Medical and Health Sciences for Women from February 2019 to August 2020.

Materials and Methods: Previous records of 300 outpatient department (OPD) subjects were checked during the study period. OPD sample was selected by probability non – purposive convenient sampling. Age, gender and GI symptoms PPI used for were entered in proforma. PPI class, duration of use, frequency of use, and prescription or non-prescription patterns were noted. Data variables were saved in a pre – structured proforma. Data was analyzed on SPSS (version 21.0) and Microsoft Excel sheet. Data was presented as tables showing frequency and % of variable.

Results: Omeprazole was used by 31% followed by dexlansoprazole 29%, esomeprazole 21%, pantoprazole 7.3%, lansoprazole 7.6% and rabeprazole by 4% of subject's respectively (table - 2). PPI were being used as long durations as >5 years noted in 18.6% on irregular basis (35.6%) and without prescription (63.0%).

Conclusion: We found injudicious use of proton pump inhibitors on irregular basis without prescription that needs to be controlled by the health authorities.

Key Words: Proton Pump inhibitors, Injudicious Use, Non - prescription

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INTRODUCTION

Proton pump inhibitors (PPIs) are one of widely used drug agents primarily indicated for the acid peptic disorders. It is the widely purchased by prescription but more so non-prescription as over the counter drugs that is illegal. PPIs are prescription sold drug agents only despite this is available freely.[1,2] Although PPIs are an excellent drug of its class but injudicious use has created problem of toxicity and adverse drug reactions. PPIs are indicated for the acid peptide disorders, gastro-esophageal reflux disease (GORD), gastric and duodenal ulcers, Zollinger – Ellison syndrome (ZES), esophageal ulceration, and Barrett's esophagus. Maintenance low dose PPIs prevents the recurrence of acid related disorders of upper GI system. PPIs have shown promising results in the eradication of H.pylori. PPIs are now over-prescribed and over – used for gastric acid disorders. PPIs are also indicated as co-therapy for nonsteroidal anti-inflammatory drug (NSAID) and aspirin. Injudicious uses are frequent for the functional dyspepsia, mild gastric problems, and un-investigated dyspepsia without making a proper diagnosis. Non-ulcer dyspepsia (NUD) or with mild dyspepsia are often not benefited from PPIs but still people are using without prescription.[2,3] It has noted the majority of patients attending the OPDs have already used a variety of PPIs before reaching to the medical officers. Masses are using the high dose PPIs for poorly defined gastric problems or as digestant after hot spicy foods that has become a public dilemma. Such inappropriate and injudicious PPIs use has accelerated adverse effects that are unnoticed and not understood

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properly creating new health problems and are threatening normal health of public. Currently, the PPIs are the over used by prescription and non-prescription.[4-5] Many subjects are taking the drug as self-determined regimen on irregular basis.[6,7] Although intermittent therapy with H_2- blockers is ideal and considered safe but is denied. In general, a pressure is developed by the pharmaceutical industry on the general practitioners (GPs) to prescribe the PPIs to each of the patient 'inappropriately'.[8] PPIs have side effects as diarrhea, gut upset, headache and malabsorption. Headache and diarrhea are noted in up to 10% subjects. PPIs use is linked to increased risk of malabsorption, vitamin and iron deficiency, bacterial growth, community acquired pneumonia, C – difficile colitis and C – jejuni gastroenteritis.[7,8] PPIs interact with vitamin, mineral, calcium supplements and occasionally cause adverse drug reactions resulting in hepatic, renal, bone marrow, skin and even anaphylaxis.[9-11] Data is lacking on the injudicious use of PPIs, patterns of its use, duration and side effects. National data is seriously lacking although the problem has deep rooted. In this context, the present observations study was conducted on the dose and duration of proton pump inhibitors in the general patient population. The present study determined the clinical and practice use on PPIs use, duration of uses, dosing frequency and prescription patterns in patients attending the OPD of our tertiary care hospital.

MATERIALS AND METHODS

The present retrospective study took place at the Department of Pharmacology and Medicine, Peoples University of Medical and Health Sciences for Women from February 2019 to August 2020. Study protocol was discussed in detail by the researchers. Hundreds of patients were screened as per inclusion criteria. Inclusion criteria were records of drug prescriptions, laboratory investigations, outpatient department (OPD) patients, complete clinical history, PPIs intake irrespective of duration, and age 40 – 60 years. Finally, 300 patients qualified the inclusion criteria and were included in the study protocol. Patients were selected according to the convenient sampling. Patients with major systemic disease such as; chronic liver diseases, chronic lung disease, chronic valvar cardiac disease, chronic malabsorption syndrome, pulmonary tuberculosis, etc. were excluded. Patients without proper records and prescription slips were also excluded. Volunteers were interviewed that the participation is on personal willingness, and there will be no extra expenses of any investigations. They were taken into confidence that if they are not willing, it will not affect their therapy. Patients with proofs of PPIs intake of different symptoms and durations were further screened. Symptoms of PPIs intake were confirmed by interviews and from prescription records. Clinical history of epigastric pain, heart burn, dyspepsia, nausea, vomiting, hematemesis, indigestion, bloating and retching (34.3%) was taken in detail. Age, gender, PPIs class, duration of PPIs, frequency of PPIs (regular or irregular intake) use, and prescription or non – prescribed, were noted in a pre – structured proforma. Type of PPIs taken was enquired and checked from prescriptions and included; omeprazole, esomeprazole, pantoprazole, dexlansoprazole, lansoprazole and rabeprazole. PPIs intake details were saved in the proforma. Saved data in proforma was kept confidential. The data was copied and pasted on Microsoft Excel Sheet. Statistical analysis was performed on Statistical Package for Social Sciences (SPSS) 21.0 (ver.) (Microsoft Windows Release) (IBM, Inc., Chicago, IL, USA) using Student`s t – test and Chi – square testing. Result output of continuous data was presented as mean±SD. And results of Categorical data were presented as frequency and %. Analysis of significance was calculated at 95% CI ($P \leq 0.05$).

RESULTS

Table –1 show age distribution and gender patterns of study subjects (n=300). 21 (7%) subjects belonged to 2nd decade, 53 (17.6%) to 3rd decade, 67 (22.3%) to 4th decade, 45 (15%) to 5th decade, 77 (25.6%) to 6th decade and 37 (12.3%) to ≥6 decade. Mean±SD age was noted as 47.1±10.5 years. Male to female ratio was 1:1, comprised 150 of each gender.

Table No.1: Age and gender distribution of study groups (n=300)

Age (years)	Frequency	%	P
- 12 – 19.9	21	7.0	0.001
- 20 – 29.9	53	17.6	
- 30 – 39.9	67	22.3	
- 40 – 49.9	45	15	
- 50 – 59.9	77	25.6	
- ≥60	37	12.3	
Gender			
- Male	150	50%	0.91
- Female	150	50%	

Table No.2: Frequency of GI symptoms (n=300)

	Frequency	%
Epigastric pain	239	79.6
Heart burn	287	95.6
Dyspepsia	132	44.0
Nausea	39	13.0
Vomiting	76	25.3
Hematemesis	89	29.6
Indigestion	197	65.6
Bloating	53	18.6
Retching	103	34.3

PPI were being used for the epigastric pain (79.6%), heart burn (95.6%), dyspepsia (44%), nausea (13%), vomiting (25.3%), hematemesis (29.6%), indigestion (65.6%), bloating (18.6%) and retching (34.3%).

Omeprazole was used by 31% followed by dexlansoprazole 29%, esomeprazole 21%, pantoprazole 7.3%, lansoprazole 7.6% and rabeprazole by 4% of subject's respectively (table - 2). PPI were intake for long durations as >5 years noted in 18.6% (Table - 3) on irregular basis (35.6%) and without prescription (63.0%).

Table No.3: Information of PPI use (n=300)

PPI Class	Frequency	%
- Omperazole	93	31.0
- Esomeprazole	63	21.0
- Dexlanzoprazole	87	29.0
- Pantoprazole	22	7.3
- Lansoprazole	23	7.6
- Rabeprazole	12	4.0
Duration		
- <1 months	32	10.6
- <6 months	31	10.3
- < 1 years	67	22.3
- 1- 2 years	53	17.6
- >2 years	61	20.3
- >5 years	56	18.6
Frequency of Use		
- Daily	193	64.3
- Irregular	107	35.6
Prescribed Use		
- Prescribed	111	37.0
- Non – prescribed	189	63.0

DISCUSSION

The present observational study was conducted for PPIs use and duration, dosing frequency and prescription patterns in patients in patients attending the out patients department of a tertiary care hospital. In present study, the mean±SD age was noted as 47.1±10.5 years. The findings are in agreement with previous studies.[12-14] Madi et al[12] found the age of participants was 40–59 years that is highly comparable to our present study. Age finding of present is also consistent with previous studies.[13,14] Of 300 study participants, 150 were male and female each showing male to female ratio 1:1. The findings are inconsistent of a recent study[12] that reported majority of patients were male. Reason could be different sample size, different study settings, geographical patterns of health provision and data collection. Equal ratio of male to female is because of although the male the only bread earners, and are tolerating the major stress of life in the setting of economic crisis of corona virus pandemic but female have been at risk of anxiety by staying at home due to financial crisis equally. Peptic ulcer disease is the major indication of PPIs, but the erupting tense financial crisis has created much worry and anxiety that begot the hyperacidity due to stress. In present study, the PPIs were being used for the epigastric pain (79.6%), heart burn (95.6%), dyspepsia (44%), nausea (13%), vomiting (25.3%), hematemesis (29.6%), indigestion (65.6%), bloating (18.6%) and retching (34.3%).The findings are in keeping with previous studis[12-14] that had mentioned similar acid related gastric problems. In present study, the omeprazole was frequently used PPI found in 31% followed by dexlansoprazole 29%, esomeprazole 21%, pantoprazole 7.3%, lansoprazole 7.6% and rabeprazole by 4% of subject's respectively (table - 2). The findings are in line with previous studies.[12-16] Madi et al[12] reported omeprazole was frequent prescribed PPIs followed by esomeprazole and pantoprazole. In present study, the dexlansoprazole was found in 29% second to omperazole; that is because of its new entry as a magical pill that captured major share of PPIs market being new addition to the already available pool of PPIs. Madi et al[12] found 65% use of esomeprazole and pantoprazole that is in contrast to present study. In present study the rabeprazole accounts for 4% prescriptions that are in contrast to only 1% in a previous study.[12] Currently, the burden of PPIs has increased in the society because of stressful life full of financial constraints putting the pocket open to extra expenses. Patterns of PPIs use noted in present study is in agreement with previous studes.[15-19] However, Pendhari et al[14] has produced inconsistent results as they found high use of rabeprazole that is in contrast to present and previous studes.[12-19] In present study, the PPIs were intaken for long durations as for as >5 years noted in 18.6% (Table - 3) on irregular basis (35.6%) and without prescription (63.0%). This is a crucial state of serious concerns. A previous study[12] reported using PPIs for >1 years in 8% of participants. Hence findings are supporting the present study. In presnet study the without prescription PPIs were found in 63.0% on irregular basis in 35.6% participants that is an alarming situation. A previous study[21] reported the stress ulcer prophylaxis was major indication in 77% of the patients who were prescribed PPIs for >1 year. Using PPIs for more than 5 years as noted in present study is beyond the recommended duration of any of medical indications. It is reported the adverse effects of PPIs are substantially increased when PPIs are used for >1 year.[12] The findings are consistent with previous studies.[17-21] In light of evidence based finding of present study supported by previous literature, it is an alarming situation of PPIs over – and injudicious use that must be condemned. Institutional pharmacovigilance programs and awareness seminars should be arranged for the medical practitioners and non-prescription sale of drugs must be stopped immediately for overcoming the adverse drug reactions of proton pump inhibitors.

CONCLUSION

The present study shows proton pump inhibitors were being used for long durations as >5 years (18.6%) on irregular basis (35.6%) and without prescription

(63.0%). The injudicious use of proton pump inhibitors on irregular basis without prescription needs to be controlled by the health authorities urgently. Further studies on the patterns of proton pump inhibitors use are warranted.

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Original Article

Lycopene Ameliorates Glycemic Control in Fructose Induced Diabetes Mellitus in Wistar Albino Rats

Jawad Mumtaz Sodhar[1], Shagufta Memon[3], Majid Ali Hingoro[4], Palwasha Abbasi[5], Mashal Siddiqui[6] and Umair Ali Soomro[2]

ABSTRACT

Objective: Experiment determining the blood glucose regulating effects of lycopene in high fructose fed diet (HFD) induced diabetes mellitus (DM) in Male Albino Wistar Rat.

Study Design: An Experimental study

Place and Duration of Study: This study was conducted at the Departments of Basic Medical Sciences, Suleman Roshan Medical College, Tando Adam from April 2021 to September 2021 for a period of six months.

Materials and Methods: Sixty male Wistar albino rats were divided into –ve and +ve controls (groups A and B) and Experimental groups – HFD induced DM treated with lycopene (groups C and D). Each group comprised 15 rats. DM was induced by feeding HFD (21% w/v) till induction of fructose. Glycemic and lipid variables were estimated by standard biochemical analysis from the blood sera of rats. Data was analyzed in SPSS 21.0 (IBM, Incorporation, USA) at 95% CI ($P<0.05$).

Results: Lycopene therapy improves the RBS, FBS and HbA1c% in experimental rats. Lycopene therapy also reduced the serum cholesterol, triglycerides and LDLc with rise in serum HDLc concomitantly ($P=0.0001$).

Conclusion: In conclusion, the lycopene therapy improves blood glucose and lipid level in high fructose diet induced diabetes mellitus in rat model.

Key Words: Lycopene, Fructose, Glycemic control, Lipids, Rats

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INTRODUCTION

Herbs and phytochemicals have attracted much interest as remedy for various disorders in recent years including the scientific community. Much interest is growing to prove evidence, safety and effectiveness of herbs in complementary medicine. Herbs and phytochemicals are being analyzed in majority of scientific research studies making them available for alleviation of various metabolic disorders.[1] Accumulating information on bioactive compounds of herbs origin is gathering for the treatment of diabetes mellitus (DM), also proving their mechanisms of actions and safety, clinical use based on clinical evidence of their effectiveness.[1,2] Phytochemicals obtained from herbs and plants are recognized a potential source of newer drugs, the main example of this is the metformin. Phytochemicals are capable of lessening hyperglycemia and hyperlipidemia of DM.[2] This makes the herbs of utmost value and an interesting candidate for metabolic disorders such as the DM. Herbs as add on therapy potentiate their therapeutic effects too. One of such nutraceutic phytochemical is a β-carotenoid rich red pigmented substance called lycopene derived from tomatoes, red fruits, apricots, papaya, guavas, grape fruits, watermelons, grapes and vegetable and is also present in human plasma.[1,3] Lycopene is a linear polyene acyclic hydrocarbon isomer of β-carotene.[1,3] Certain microorganisms contain lycopene. Lycopene functions through both non-oxidative and oxidative mechanisms. Lycopene is capable of quenching the reactive oxygen species (ROS) free radicals and maintains redox homeostasis within body cells. Lycopene prevents oxidative process of proteins, DNA, phospholipids and lipids. It opposes carcinogenesis through multistage anti – oxidant

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mechanisms. Lycopene is capable of quenching and scavenging the ROS.[4,5] Lycopene has higher antioxidant activity than β-carotene. Lycopene and lycopene rich food supplements have attracted growing interest protecting against various metabolic diseases such as DM.[1] Lycopene also retards formation of advanced glycation end products (AGEs).[6,7] Evidence shows the lycopene used in combination with metformin improves the glycemic control.[1] Currently, the DM prevalence is increasing in the country due to aberrant dietary habits, obesity, urbanization and sedentary life style. Hence there is dire need to analyze the new and available herbals products of their blood glucose and lipid regulating effects and lycopene is an ideal newer agent. The present experimental study evaluated the blood glucose and lipids ameliorating effects of lycopene in fructose induced diabetes mellitus in Wistar Albino rats.

MATERIALS AND METHODS

Ethical approval of research protocol of conducting the present experimental study was taken from the institute. Research design was completed at the Departments of Basic Medical Sciences, Suleman Roshan Medical College, Tando Adam, Sindh.

Experimental study was conducted at the Animal house of Sindh Agriculture University. We purchased rats from the Animal house (SAUT) of Albino rats of Wistar strain. Experiment was conducted from the April 2021 to September 2021. Sixty male albino of Wistar strain were purchased according to the inclusion and exclusion criteria. Albino rats of 150 – 200 grams, male gender, moving in the cages and eating properly, with proved diabetes mellitus (DM) induction with high fructose diet (HFD – 21% w/v) were included. Fructose was given in dose of 10 g/kg bwt diluted in water to give – 21% w/v solution.[8] Present study strictly excluded the female rats, lazy and not feeding properly male rats. Rats not developing DM with HFD (21% w/v). Experimental rats were handled according to the NIH, USA guidelines for animals. Animals were housed in stainless steel – cages provided with proper feeders and drinkers within the cages. Temperature was maintained at 25 ± 3 °C. Light/dark cycles of 12/12 hours were maintained. Experiment lasted for eight weeks. Feeds and water was available ad – libitum in the cages. Negative control (group – A) were given normal chow diet. Positive control (group B) was given normal diet + HFD. Experimental rats group C and D were fed normal chow diet fortified with HFD and treated with lycopene 4 and 8 mg/kg/day[9] p.o. respectively. Lycopene was got from the pharmacy department of institute. Therapy continued for eight weeks. After the experiment was over, the rats were handled carefully for the blood sampling. A lancet was delicately inserted behind the eye ball and blood coming from the retro orbital venous plexus was collected into the sterilized tubes. 2 ml blood was taken into tubes. Sera were stored at -20^{0}C. Blood glucose, glycated hemoglobin A1, serum creatinine, and blood lipids were analyzed in post graduate laboratory. Data was saved in proforma that was designed with research protocol. Results were entered in Microsoft Excel sheet. Data values were entered in SPSS 21.0 for statistical analysis. One – way analysis of variance, descriptive statistics, and post Hoc Bonferroni test analyzed the continuous result variables. Resutls were presented in tables as mean+/- SD. 95% CI (P<0.05) was used for data analysis of statistically significant.

RESULTS

Lycopene therapy ameliorates the random blood glucose (RBS) and fasting blood glucose (FBS) and the glycated hemoglobin A1 (HbA1c) (%) in experimental rats (table – 1).

Table No.1: Glycemic control in different rat groups

Parameter	Rat groups				
	A	B	C	D	P
RBS (mg/dl)	118.4±3.7	264.3±28.1	229.5±23.0	209.7±14.1	0.0001
FBS (mg/dl)	65.5±7.3	258.1±29.3	172.1±21.3	133.1±19.1	0.0003
HbA1c (%)	4.7±0.7	8.7±0.7	7.6±0.5	6.75±0.5	0.0001

Table No.2: Blood lipid profile in different rat groups

Parameter	Rat groups				
	A	B	C	D	P
Total Cholesterol	121.9±9.9	388.1±29.3	267.1±15.1	193.1±17.7	0.0001
Triglycerides	175.2±17.1	401.1±12.1	353.3±30.7	252.1±25.1	0.0003
LDLc	119.5±9.3	263.1±27.5	235.9±26.1	163.5±11.3	0.0001
HDLc	40.9±1.2	23.2±1.7	25.1±1.8	37.3±3.1	0.0001

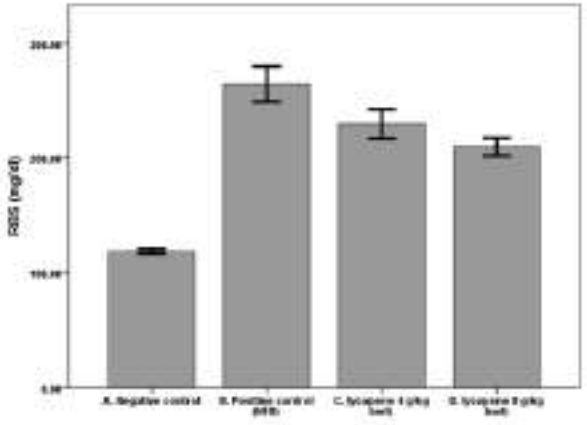

Figure No.1: Random blood glucose (RBS) (mg/dl)

RBS in positive control group B was 264.3±28.1 mg/dl that was decreased by lycopene therapy in experimental

groups C and D significantly noted as 229.5±23.0 and 209.7±14.1 mg/dl respectively (P=0.0001). FBS in positive control group B was 258.1±29.3 mg/dl that was decreased by lycopene therapy in experimental groups C and D significantly noted as 172.1±21.3 and 133.1±19.1 mg/dl respectively (P=0.0003). HbA1c in positive control B was 8.7±0.7% that was decreased to 7.6±0.5 and 6.75±0.5 in experimental groups C and D (P=0.0001). Lycopene therapy also reduced the serum cholesterol, triglycerides and LDLc with rise in serum HDLc concomitantly (P=0.0001).

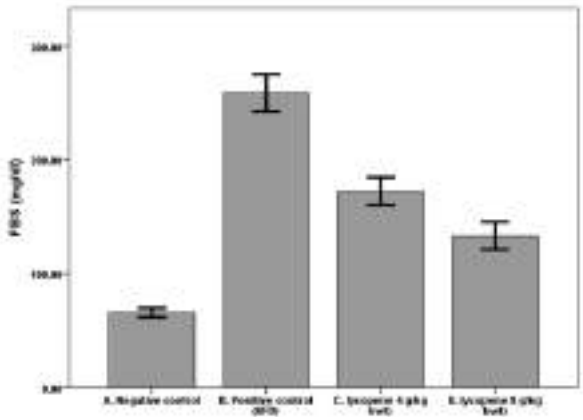

Figure No.2: Fasting blood glucose (RBS) (mg/dl)

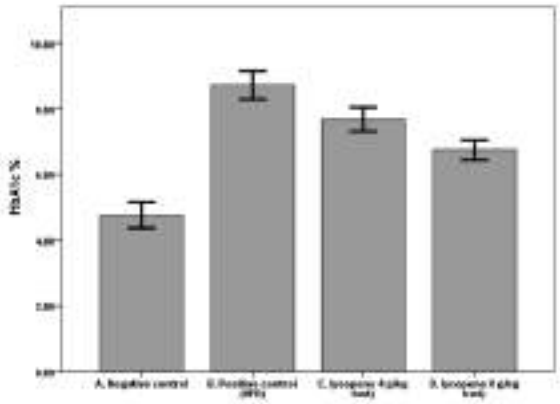

Figure No.3: Serum Glycated HbA1 (HbA1c) (%)

DISCUSSION

The present experimental study determined blood glucose and lipid regulatory effects of lycopene in high fructose fed diet Wistar Albino male diabetic rat model positively. The present study proves glucose and lipid lowering effects of lycopene in HFD induced diabetes mellitus. The findings are in agreement with previous studies.[10-12] Present study is the first from our institute reporting on the topic. Prevalence and incidence of DM is increasing in the country hence there is dire need innovation in the diabetic therapy beside allopathic drug therapy. Rising DM populations in Pakistan has raised its position to fifth rank and high prediction for the future.[13,14] Lycopene is red pigmented fruit and vegetable derived agent that has proved astonishing results in previous studies.[1,3] Lycopene is present in tomatoes and tomato – products, grapefruits, pink guava, minestrone soup, pizza, spaghetti, etc.[1,3] Present study consumed lycopene in doses of 4 and 8 g/Kg bwt in HFD rats that proved noticeable biological potential on blood glucose and lipid levels. Leh et al[15] (2021) reported the lycopene intake in diabetic population in doses of 0.04 and 0.05 mg/Kg bwt and reported highly significant pharmacological effects on blood lipids and glucose. The findings of above study are concordant to present study. A previous study[1] proved lycopene rich yogurt therapy positively lessened the hyperglycemia, dyslipidemia and oxidative markers in diabetic rats. Lycopene combined with curcumin produced highly significant lipid and glucose regulatory effects in another study. They also reported dampening of oxidative stress.[16] The present study provides scientific insights on the potential of lycopene as therapeutic agent; the findings are supported by previous study. Lycopene has gained much scientific attention and research interest against the metabolic syndrome and associated grave complications like diabetes mellitus.[17,18] Supporting the present study, previous studies[19,20] found improvement in glucose intolerance and insulin resistance in HFD mice model. A recent review[21]reported lycopene maintained pancreatic function and metabolic defects in in – vivo models. Ozmen et al[22] witnessed the lycopene prevents the vacuolization and loss of insulin cells in pancreatic Islets in diabetic rats. Lycopene therapy increased circulating insulin levels with improved glycemia and dyslipidemia. Lycopene therapy attenuated dyslipidemia in a previous study[23], has been witnessed. The findigns of above studies are in line keeping with present study. Lycopene has also been proved as scavenger of reactive oxygen species (ROS), HO^-, OCl^-, and other species.[1,24-26] Anti-oxidative effects of lycopene have been proved in another previous study.[27] The findings of above studies are matchless to our present study as the oxidative status was not detected due to financial issues. Considering literature, it shows lycopene is an interesting panacea against development of DM and its complications. Findings of present study reinforces the need for future animal and human studies investigating the lycopene effects scientifically. Extrapolating the results of present study, it is inferred lycopene is a nutraceutical herb of prime importance for the diabetes mellitus. Lycopene is an herbal nutraceutic agent that needs further research to make it available for the DM therapy.[1,3] Findings of lycopene therapy of present study, prove glycemic and lipid regulatory potential that may be exploited for clinical use, however, this needs further research. Lycopene may then be used as alternative add – on therapy for diabetes mellitus.

CONCLUSION

In conclusion, the lycopene therapy improves blood glucose and lipid level in high fructose diet induced diabetes mellitus in rat model. Euglyemic and hypolipidemic potential of Lycopene is a very important finding that demands further clinical research making it conveniently available as an alternative add – on therapy for diabetes mellitus. Future studies are recommended to validate the finding of present study.

Author's Contribution:

Concept & Design of Study:	Jawad Mumtaz Sodhar
Drafting:	Shagufta Memon, Majid Ali Hingoro
Data Analysis:	Palwasha Abbasi, Mashal Siddiqui, Umair Ali Soomro
Revisiting Critically:	Jawad Mumtaz Sodhar, Shagufta
Final Approval of version:	Jawad Mumtaz Sodhar

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

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Original Article

ESWL with URS Lithoclast

Extracorporeal Shock Wave Lithotripsy versus Ureteroscopy Lithoclast in Management of Upper Ureteric Stones

Nisar Ahmad, Khalid Khan, Saqlain Amjad, Ajmal Rasheed and Usama Iftikhar

ABSTRACT

Objective: To compare the efficacy of Extracorporeal Shock Wave Lithotripsy (ESWL) with URS Lithoclast in management of upper Ureteric stones

Study Design: Retrospective study

Place and Duration of Study: This study was conducted at the Department of Urology, Sahiwal Teaching Hospital, Sahiwal, from June, 2021 to January, 2022 for a period of eight months.

Materials and Methods: Two groups were formed of total 70 patients. In the group undergoing ureterorenoscopy surgery was done by giving general anesthesia. Swiss pneumatic lithoclast, 0.8 mm or 1 mm probe, was used to break down the stone. SWL was performed on all patients using the standard procedure using Storz Modulith SLX-MX electromagnetic lithotripter equipment (3rd generation). A shock wave was delivered to the patient every 60 seconds until the desired result was achieved. If the stone was > 1.5 cm, a double J stent was typically used. The procedure was performed by a consultant doctor who specializes in the ESWL machine.

Results: Stone-free rate after first and second session in SWL was lower than URS group, but the difference was not statistically significant. The mean procedure time of SWL and URS was 65.88±2.05 and 87.98±9.22, respectively, (p=0.000). The mean number of sessions and hospital stay in both the groups was almost equal, (p≥0.050). The clavien grading system was applied to examine the complications in both the groups.

Conclusion: It can be concluded that stone free rate of proximal Ureteric stones after single session of ESWL and URS showed significantly better outcome in URS group of patients

Keywords: Extracorporeal shock wave lithotripsy, ureteroscopy, Lithoclast, management, upper Ureteric stones, laparoscopy, invasive, non-invasive.

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INTRODUCTION

Urolithiasis is most common reasons of urinary tract morbidity in the world. The emergence of minimally invasive procedures has changed the treatment of urinary tract stones during the last few decades [1,2]. In past few decades ureteral stones were treated by open ureterolithotomy. After that due to establishment of more refined procedure, such as use of shock wave lithotripsy devices i.e., semi-rigid ureteroscopes, flexible ureterorenoscopy and laparoscopic procedures, to treat ureteral stones the therapeutic approach changed dramatically. All of these modalities, if administered properly, can be highly effective in children and adults[3,4]. The choice of procedure is up to the preferences of the patient and surgeon [3,4].

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Treatment of proximal ureteral stones can be done by minimally invasive technique, shock wave lithotripsy, and can be done on outpatient basis. But, a long treatment duration, a high rate of retreatment, and poor patient compliance in some cases are the major drawbacks of shock wave lithotripsy [4,5]. In past few years the surgeons prefer the ureterorenoscopic treatment of ureteral stones and it has become more popular approach. Due to high stone free rate (>90%), for the patients with distal ureteral calculi, ureterorenoscopy is highly recommended. [6] For proximal ureteral stone, due to larger working distance in males, surgeons are cautious of using semi-rigid URS, in comparison to females. [7] Because of difficulty in entrance and migration of stones towards proximal end during procedures, the success rate of ureterorenoscopy is considerably low in comparison to distal ureteral stones. It is also said that the expenses of lithotripsy group's treatment were way low in comparison to the ureterorenoscopy group. [8] The discussion for best treatment approach for ureteral stones is still not over [8]. Patients unable to visit hospital frequently prefer ureterorenoscopy treatment strategy due to its high rate of success in first time, as compare to shock wave lithotripsy [9]. In developing

countries like Pakistan where people have low income and are unable to afford treatment approaches like ureterorenoscopy or shock wave lithotripsy due to high rates of private hospitals, patients choose one technique according to their economic status[10]. Patients' financial loads are still discussed in the literature [8, 10].
Financial burdens and outcomes of these restrictions of the patients were also observed in this study for stone free rates. No study in the past excluded the patients that are obese, with distance more than 10cm between skin to stone distance and patients with stone density more than 1000 HU for comparative analysis of ureterorenoscopy and shock wave lithotripsy modalities for treatment of proximal ureter stones. In this study these complicating elements were also excluded. Due to which our study is first to do comparative analysis on the use of ureterorenoscopy and shock wave lithotripsy for treating proximal ureteral stones with all those elements mentioned above excluded.

MATERIALS AND METHODS

Two groups were formed of total 70 patients. Clearance was received from the ethics from department of urology, Sahiwal Teaching Hospital, Sahiwal before the beginning of this retrospective assessment. After proper counseling of patients on the benefits and downsides of both treatment procedure and are allowed to choose between ureterorenoscopy or shock wave lithotripsy according to departmental policy. Radiological tests as X-ray KUB, computed tomography (CT) and urine ultrasonography was done along with acquiring the physical examination and medical history in order to diagnose the patients. The stone size was determined using largest stone size. Patients with proximal ureteral stones already had CT scan were included in this study in order to know about the density of the stone and distance of skin to stone. Patients with distal and mid-ureter stones, proximal radiopaque and single ureteral stone with a size less than 2cm, multiple ureteral stones,; age more than or equal to 18 years, body mass index of 30 kg/m^2, congenital genitourinary anomaly, skin-to-stone distance of > 10 cm, stone size more than 2 cm, stone density of more than 1000 HU, urinary tract infection (UTI), distal ureteral obstruction and coagulation disorder were all included in this study.
In the group undergoing ureterorenoscopy surgery was done by giving general anesthesia. Swiss pneumatic lithoclast, 0.8 mm or 1 mm probe, was used to break down the stone. If the stone is disintegrated completely with smallest residual procedures on each operational inspection and cleared of the ureter the procedure is considered as a success. However, if the stone is not broken down completely or pass to the kidney the procedure is considered as a failure. After two weeks and three months, post-procedural follow-up visits were conducted using plain X-ray KUB and urine ultrasonography to determine if any dilatation of ureter or residual fragment > 4mm following the URS procedure (kidneys, ureter, and bladder). For up to a year, the patients were examined using ultrasonography for hydro-nephrosis.
SWL was performed on all patients using the standard procedure using Storz Modulith SLX-MX electromagnetic lithotripter equipment (3rd generation). A shock wave was delivered to the patient every 60 seconds until the desired result was achieved. If the stone was > 1.5 cm, a double J stent was typically used. If gross residual stones were visible on X-Ray KUB and urine ultrasonography 2 to 4weeks after 1st SWL session, a second SWL session was performed. The stone free rate was defined as no trace of a stone on a plain KUB X-ray or ultrasound 3months after last SWL session.
SPSS 23 was used for statistical analysis of the data obtained. Frequency and percentage was calculated for qualitative variables while mean and standard deviation was calculated for quantitative variables. Chi square test was applied to check the significance between two groups. P value of less than or equal to 0.05 was considered as statistically significant.

RESULTS

Seventy patients were enrolled in our study. The patients were equally randomized into two groups as n=35 SWL and n=35 URS.

Table No.1: Demographic characteristics of both the groups

Variable	Group		P-value
	SWL (n=35)	URS (n=35)	
Age (years)	36.37±4.79	36.77±5.01	0.734
BMI (kg/m^2)	25.16±2.01	25.39±2.04	0.634
Gender			
Male	n=26 (74.3%)	n=25 (71.4%)	0.788
Female	n=9 (25.7%)	n=10 (28.6%)	
Stone size (mm)	11.98.1.08	12.31±1.22	0.239
Location of stone			
Right side	n=8 (22.9%)	n=10 (28.6%)	0.874
Left side	n=27 (77.1%)	n=25 (71.4%)	
Skin to stone distance (cm)	9.64±0.84	9.54±0.78	0.618
Hounsfield unit of stone	800.34±20.43	799.08±24.54	0.817
Hypertension	n=8 (22.9%)	n=3 (8.6%)	0.101
Diabetes mellitus	n=11 (31.4%)	n=8 (22.9%)	0.420

There was no statistical difference between demographic characteristics and both the groups, (p≥0.050). (Table. 1).

Table No.2: Procedural outcomes of both the groups

Outcome	Group		P-value
	SWL (n=35)	URS (n=35)	
Stone-free rate after first session	n=25 (71.4%)	n=29 (82.9%)	0.255
Stone-free rate after second session	n=28 (80.0%)	n=30 (85.7%)	0.145
Stone-free rate after third session	n=31 (88.6%)	--	--
Procedural time (minutes)	65.88±2.05	87.98±9.22	0.000
No. of session (procedure)	1.24±0.38	1.34±0.39	0.270
Hospital stay (days)	1.21±0.41	1.32±0.48	0.281
Stone retropulsion into kidney	--	n=2 (5.7%)	--

Table No.3: Clavien grading of both the groups

Clavien grade	Group		P-value
	SWL (n=35)	URS (n=35)	
0=No complications	n=16 (45.7%)	n=5 (14.3%)	0.109
1=Deviation from normal post procedural course without need for intervention	n=2 (5.7%)	n=6 (17.1%)	
2=mild complications needing intervention	n=8 (22.9%)	n=11 (31.4%)	
3a=post-procedural complications needing intervention without use of general anesthesia	n=2 (5.7%)	n=2 (5.7%)	
3b=Complications needing intervention under general anesthesia	n=2 (5.7%)	n=4 (11.4%)	
4a=life-threatening complication needing intensive care management (single organ dysfunction)	n=2 (5.7%)	n=5 (14.3%)	
4b= life-threatening complication needing intensive care management (multiple organ dysfunction)	n=3 (8.6%)	n=2 (5.7%)	
5=Death	n=0 (0.0%)	n=0 (0.0%)	

Stone-free rate after first and second session in SWL was lower than URS group, but the difference was not statistically significant. The mean procedure time of SWL and URS was 65.88±2.05 and 87.98±9.22, respectively, (p=0.000). The mean number of sessions and hospital stay in both the groups was almost equal, (p≥0.050). (Table.2). The clavien grading system was applied to examine the complications in both groups and presented in table 3.

DISCUSSION

Over the recent decades a lot of advancements have been achieved in the treatment of urinary stones. In most recent advancements, minimally invasive techniques such as totally non-invasive SWL and endoscopic surgeries are at the top. As a result of these novel techniques, open surgeries have almost become obsolete [11,12]. While choosing the type of technique i.e. URS, SWL, laparoscopic or open, for urinary lithiasis, multiple factors are to be considered such as size, location, composition of stone, patients' choice and surgeon's inclination. In current guidelines URS and SWL are considered to be the treatment of choice for Ureteric stones [12]. ESWL is a non-invasive type procedure commonly performed in outpatient settings which has its own demerits such as high treatment rate, long treatment time and low compliance by the patients [9,12]. Standard guidelines indicate that ESWL is treatment of choice for stones <1cm but no definite guidelines are available over its use in stones of size more than 1cm in proximal ureter [13m 14].

With recent advancements small-caliber-semi rigid-ureteroscopes have been introduced. As an alternate to ESWL, a combination of intracorporeal lithotripsy and URS has been seen effective [13]. A previous study conducted in population of Pakistan indicated that even though ESWL is a preferred choice for proximal ureteral stones, the combination of URS and intracorporeal lithotripsy is also a safe option for relatively quicker relief from symptoms in treatment of proximal ureteral stones [15].

The use of URS has been shown to be associated with higher stone free rates in patients with stones smaller than 10mm in distal ureter and stones >10mm in proximal ureter [10]. Among the deciding factors for efficacy of URS, size, position are the most important but experience and skill of the surgeon is also of high significance [17]. Patients' preference is the most common deciding factor in making a choice of the treatment to be used. Due to invasive nature of URS and risk of anesthesia complications most patients opt for non-invasive or minimally invasive options, whereas some patients might prefer quickest removal of stones and relief of symptoms, thus avoiding multiple session that could be required in cases of ESWL [18,19]. In a past study where URS was compared to ESWL, although stones free status was greater among URS

patients, it was associated with higher complications rate and longer hospital-stay [19].

Similarly, Lee et al. [20] reported no significant difference when comparing URS with ESWL in terms of patients' satisfaction. In an Egyptian study mean cost of URS and ESWL were assessed to be EGP 6500 and EGP 5700 respectively (EGP=Egyptian Pound) [21]. Similarly cost for ESWL was lower than URS in study by Lee et al. [20]. However, types of ESWL devices used in these studies are different therefore no definite recommendations can be made. The results of current study are needed to be studied further with larger sample size and multicenter prospects. This study had a limitation of small sample size and being a retrospective single center study. Patients' satisfaction with URS or ESWL was not taken into account in this study.

CONCLUSION

It can be concluded that stone free rate of proximal Ureteric stones after single session of ESWL and URS showed significantly better outcome in URS group of patients with comparable rate of complications in both groups, with hospital stay and treatment expenses being significantly lower in ESWL group.

Author's Contribution:

Concept & Design of Study:	Nisar Ahmad
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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

Incidence of Distant Metastasis in Oral Squamous Cell Carcinoma on 18f FDG PET CT Scan

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ABSTRACT

Objective: To evaluate the incidence and pattern of distant metastasis in squamous cell carcinoma of the oral cavity
Study Design: Retrospective study
Place and Duration of Study: This study was conducted at the Study was conducted in the department of oral and maxillofacial surgery/Radiology department, Jinnah Postgraduate Medical Centre, Karachi, from January, 2018 to June, 2021 for a period of six months.
Materials and Methods: A total of 416 patients were enrolled in study. Main variables of the study were area of residence, type of cancer, treatment given, recurrence rate, staging of cancer and metastasis. Data was analyzed using SPSS version 23. Mean for numerical data and frequency for categorical data was calculated. After applying test of significance p value ≤0.05 was taken as significant.
Results: Four hundred and sixteen squamous cell carcinoma patients were examined in our study. Mean age of the patients was 69.44±18.31 years and most of the patients (49.8%) were between 46-64 years. Most patients belonged to urban areas (55.8%). Mean weight of the patients was 60.56±14.89 kg and mostly (31.0%) weighed in between 51-60 kg. The most common type of cancer we found was buccal mucosa (45.7%) and tongue (43.5%). Amongst the 416 patients, 13.2% patients were diagnosed as having distant metastasis. The most common site that produced metastasis was buccal mucosa especially of the right side (34.6%). Radiotherapy and chemotherapy was given in 50.9% and 58.2% patients respectively. Recurrence was found in 45.5% patients. Most common time to occurrence was between 6-12 months observed in 40.0% patients. The most common tumor stage was observed T3 (41.8%) followed by stage IVA (38.2%) tumor stage, N0 (21.8%) was the most common nodal stage and M0 (43.6%) was the most common M stage. Lungs and mediastinum were the most common organs of distant metastasis at 25.5% and 14.5% respectively.
Conclusion: A high proportion of squamous cell carcinomas of the oral mucosa in our population developed distant metastasis with the most common primary site being the right buccal mucosa and most common metastatic site being the lungs as expected. We also found a considerable number of patients that developed extra pulmonary metastasis in liver, bones and brain which might be due to the higher stage at which patients present and possibly more aggressive characteristic of the tumors.

Key Words: Squamous cell carcinoma, oral cavity, head and neck cancer, distant metastasis.

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INTRODUCTION

Squamous cell carcinoma (SCC) is 6th most common cancer having the highest incidence rate in South Africa[1].

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Its locoregional control is 50% at 5 years and distant control is 85%[2]. Alcohol, tobacco and lack of antioxidants in diet are the main causes of squamous cell carcinoma. In Indo-Asian population areca nut chewing is the leading cause. Less frequent causes are poor dental hygiene, human papilloma virus, irritation with sharp dentures and genetic susceptibility[3]. Oral cavity has many subsites including tongue, hard palate, floor of mouth, gingiva covered upper and lower alveoli, retromolar trigone, buccal mucosa, inner side and anterior boundary of lips[4].

There are many challenges in pretreatment staging, diagnosis and evaluation of patients after treatment[5]. Clinical signs may be nonspecific depending on the site of cancer like pharynx, oral cavity, larynx, paranasal sinuses, nasal cavity, thyroid and salivary gland[6]. Sometime occult cancers were found that escaped detection by endoscopy, physical examination and

cross-sectional imaging. Many techniques like magnetic resonance imaging, contrast enhanced computed tomography and PET scans are used worldwide to diagnose the baseline extent of tumor and post treatment response[7]. PET scan is a sensitive modality for detecting distant metastasis, lymph node metastasis, residual/recurrent disease as compared to MRI and CT scan as it is functional imaging rather than anatomic imaging[8].

Systemic metastasis in oral squamous cell carcinoma (OSCC) is associated with a dismal prognosis, systemic chemotherapy and 10 months overall median survival[9]. Mortality rate of patients from distant metastasis is 15-20%. Incidence of distant metastasis in autopsy reports is 3-4 times higher as compared to clinical evaluation[10]. About 90% of malignancies arise from subsites within the oral cavity. The aim of this study is to evaluate the role of imaging in diagnosis of distant metastasis and consequent management of head and neck squamous cell carcinoma.

MATERIALS AND METHODS

This retrospective study was conducted in the department of oral and maxillofacial surgery/Radiology department, Jinnah Postgraduate Medical Centre, Karachi, from January 2018 to June 2021. Study was conducted after approval from the Institutional Review board. Informed written consent was obtained from every possible patient. Non probability consecutive sampling technique was used. Sample size was calculated using an online software openepi.com with confidence interval 95% and margin of error 0.5%. Inclusion criteria was patients with biopsy proven squamous cell carcinoma of oral cavity who were undergoing staging or post treatment imaging. Patients with SCC of other sites were excluded.

Primary surgery was performed in patients with operable oral cavity cancers. Adjuvant intensity modulated radiotherapy (IMRT) was performed in some cases upto 5 fractions per week. After completion of treatment with IMRT patients were followed up with imaging every 3 months for one year. In the second year follow up was extended to every 4 months and biannually after that. Loco regional control and toxicity were assessed with endoscopy and clinical examination. SPSS version 24 was used for data analysis, mean and standard deviation was calculated for numerical data like age and frequency and percentages were calculated for categorical data like gender. Test of significance like test and chi square test were applied to see association among variables. P value less than or equal to 0.05 was considered as significant.

RESULTS

Four hundred and sixteen squamous cell carcinoma patients were examined in our study. Mean age of the patients was 69.44±18.31 years with the majority (49.8%) of patients between 46-64 years. Most belonged to urban areas (55.8%). The mean weight of the patients was 60.56±14.89 kg and 31.0% patients were between 51-60 kg. (Table. I).

Table No.1: Demographic characteristics of patients

Variable	Mean±S.D	N (%)
Gender		
Male		351 (84.4)
Female		65 (15.6)
Age (years)	69.44±18.31	
27-45		167 (40.1)
46-64		207 (49.8)
65-83		42 (10.1)
Area of residence		
Urban		232 (55.8)
Rural		184 (44.2)
Weight (kg)	60.56±14.89	
30-50		113 (27.2)
51-60		129 (31.0)
61-70		86 (20.7)
>70		88 (21.2)

S.D: standard deviation

Table No.2: Sites of metastasis

Variable	N (%)	(95% C.I)
Tongue	181 (43.5)	(32.02-45.04)
Buccal	190 (45.7)	(30.03-48.03)
Hard plate	39 (9.4)	(6.41-12.11)
Retro molar trigone	6 (1.26)	(0.44-3.83)

Table No.3: Sites of distant metastasis and treatment

Variable	N (%)	(95% C.I)
Sites of distant metastasis		
Right buccal mucosa	19 (34.6)	(32.2-42.1)
Left buccal mucosa	13 (23.7)	(22.3-25.4)
Right retro molar trigone	3 (5.4)	(1.9-4.2)
Left retro molar trigone	3 (5.4)	(1.7-4.3)
Hard palate	4 (7.3)	(3.4-8.8)
Tongue – right border	6 (10.9)	(6.2-15.3)
Tongue – left border	5 (9.1)	(9.1-12.7)
Base of tongue	2 (3.6)	(1.3-5.5)
Radiotherapy		
Yes	28 (50.9)	(32.21-60.16)
No	27 (49.1)	
Chemotherapy		
Yes	32 (58.2)	(40.02-68.50)
No	23 (41.8)	
Recurrence		
Yes	25 (45.5)	(46.07-74.09)
No	30 (54.5)	
Time to recurrence		
6-12 months	21 (38.2)	(35.2-45.6)
13-19 months	22 (40.0)	(31.4-46.8)
19-25 months	12 (21.8)	(19.5-28.6)

Table No.4: Stages of carcinoma

Variable	N (%)	(95% C.I)
Stages		
I	7 (12.7)	(9.2-13.4)
II	8 (14.5)	(6.4-15.8)
III	10 (18.2)	(8.6-20.6)
IVA	21 (38.2)	(35.5-46.8)
IVB	9 (16.4)	(8.4-20.8)
T class		
Tx,To,T1s	8 (14.5)	(12.3-20.5)
T1	6 (10.9)	(8.5-19.7)
T2	9 (16.4)	(14.4-24.5)
T3	23 (41.8)	(30.2-40.7)
T4a	9 (16.4)	(10.6-23.6)
N class		
Nx	10 (18.2)	(14.8-24.2)
N0	12 (21.8)	(17.2-30.1)
N1	10 (18.2)	(14.3-27.4)
N2	23 (41.8)	(30.2-39.6)
M class		
Mx	15 (27.3)	(23.4-38.1)
M0	24 (43.6)	(25.7-52.6)
M1	16 (29.1)	(31.6-45.2)

Table No.5: Sites of metastases in (n=55) patients

Sites of metastases	N (%)	(95% C.I)
Skeleton	7 (12.7)	(6.1-12.9)
Cervical lymph nodes	4 (7.3)	(4.6-15.6)
Axillary lymph nodes	4 (7.3)	(3.4-12.4)
Mediastinum	8 (14.6)	(12.2-18.4)
Lungs	14 (25.5)	(16.8-32.1)
Liver	7 (12.7)	(6.5-11.5)
Brain	7 (12.7)	(8.6-13.6)
Adrenals	2 (3.6)	(2.7-6.2)
Peritoneum	2 (3.6)	(1.3-4.4)

The most common sites of carcinoma were buccal mucosa 190 (45.7%) and tongue 181 (43.5%). (Table. 2). among 416 patients 55 (13.2%) patients diagnosed with distant metastasis and most common primary site was buccal mucosa especially of the right side 19 (34.6%). Radiotherapy and chemotherapy was given in 28 (50.9%) and 32 (58.2%) patients respectively. Recurrence was found in 25 (45.5%) patients, while the most common time of occurrence was between 6-12 months observed in 22 (40.0%) patients. (Table. 3).

Among 55 patients stage IVA was the most common stage observed in 21 (38.2%) patients, T3 was the most common tumor stage observed in 23 (41.8%), N0, 12 (21.8%) was the most common nodal stage and M0 24 (43.6%) was the most common M stage. (Table. 3).

Of the 55 patients, lung and mediastinum were the most common sites of distant metastasis 14 (25.5%) and 8 (14.5%), respectively. (Table. 4).

DISCUSSION

According to current studies after the diagnosis of distant metastasis in OSCC, median time to death is 64 months. Due to lack of studies on distant metastasis in OSCC patient's data is limited.

Lungs is the most common site of distant metastasis and CT chest is considered adequate staging for newly diagnosed cases with early-stage disease. But while reading PET-CT scans of such patients it was observed that they presented with extra-pulmonary metastases in the presence of no other detectable primary. So it was decided to perform a study to see the incidence of other metastases which might be due to different demographic of our patient population.

In our group of patients all were treated with IMRT and for locally advanced SCC and concomitant cisplatin-based chemotherapy was used. About 10% of SCC patients developed distant metastasis (Table IV), these results are in line with studies by Juet al[11] and Arons et al[12].

Brougham et al[13]carried out a study on frequency and metastatic stage of squamous cell carcinoma and reported median age of patients was 74 years and approximately 2.6% of patients were observed with SCC, among them common location was lip and cheek. In another study by Zbärenet al[14] reported metastasis in 40% of cases, among them 15% were diagnosed in bones, 425 in liver and 705 in lungs.

In our study we observed male gender is more prone to cancers of oral cavity as compared to females. This may be due to greater exposure to carcinogenic agents like tobacco and alcohol which culturally are found more commonly amongst males in South East Asia. But a study conducted by Struhlet al[15] reported that there is no difference in incidence of oral cancers between male and female genders. Both genders have equal prevalence ate of 14%. Similarly in our study most of the patients were between 46-64 years of age.

A study was conducted by Kotewallet al[16] and reported that the most common site of distant metastasis is lungs followed by liver which shows that no organ is immune to squamous cell carcinoma. In this study pulmonary lesions were observed in 80% of cases. Similar findings were reported by Peltier et al[17] that in human body no organ is immune to squamous cell carcinoma of head and neck and most common site of metastasis is lungs.

Some contrast studies are also available with conclusion that incidence of distant metastasis is low in squamous cell carcinoma of head and neck. In 2006 Garavello et al[18] conducted a study on patients of squamous cell carcinoma and reported distant metastasis in 9.2% of patients and most of cases were observed in younger age (below 45 years). Another similar study was conducted by Gowenetal[19] and reported that incidence of squamous cell carcinoma varies between 3-50% and mostly observed in immune compromised patients. Most commonly affected sites were liver, bone and lungs and metastasis which were observed in 9.3% of cases.

O'Brien et al[20] carried out a study on this topic and concluded that below clavicle metastasis was observed in 46.7%. Lungs and esophagus were the most common sites. Brain is also a prone site that can be affected with

metastatic lesions. Auerbachet al[21] reported distant metastasis in 36% of patients and autopsy proved epidermoid lung cancer in major proportion of patients.

CONCLUSION

A high proportion of squamous cell cancers of oral cavity developed distant metastasis (13.2%) with the most common metastatic site being the lungs. There were also a significant proportion of patients who had metastasis to liver, bones and brain which might be related to the more aggressive characteristics and later stage of presentation in our patient population.

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Original Article

Tolerability and Efficacy of Apixaban Versus Rivaroxaban for Non-Valvular Atrial Fibrillation

Mahboob Ur Rehman[1], Fazlul Aziz Mian[1], Farhan Faisal[1], Anwar Ali[2], Amjad Abrar[2] and Ali Raza[1]

ABSTRACT

Objective: The main objective of the study is to find the tolerability and efficacy of apixaban Vs rivaroxaban for non-vulvular atrial fibrillation

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Pakistan Institute of Medical Sciences Islamabad during August 2020 to July 2021 for a period of ten months.

Materials and Methods: Bunch I patients will be given rivaroxaban 15mg everyday two times per day for one month then 20mg day to day for quite some time and Group II patients will be given 5mg two times day to day all through the treatment period.

Results: The information was gathered from 120 patients. Out of 120 members, 60 were treated with rivaroxaban, while 60 were treated with Apixaban. Middle age was 26 years in the gathering I and 25.3 years in the gathering II (p=0.705). Female cases counted for 41 (86%) and 19 (14%) in I and II gatherings, individually.

Conclusion: It is reasoned that oral anticoagulant drugs for counteraction of stroke in non-valvular AF have been developed and adding new choices and benefits for patients and doctors like less recurrence of medication and food associations, no requirement for checking, expansive helpful list and endured better by patients.

Key Words: Tolerability, Apixaban, Rivaroxaban, Non-Valvular Atrial Fibrillation

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INTRODUCTION

Atrial fibrillation (AF) is the most well-known supported heart arrhythmia and is found in 1-2% of everybody. The quantity of patients with AF in the United States was 2.2 million of every 2010 and is relied upon to ascend to 12 million by 2050. Ischaemic stroke and foundational thromboembolism are the most extreme and deadly complexities of AF. AF is liable for 15% of the ischaemic stroke cases among all age gatherings and this rate increments up to 30% in individuals more established than 80 years [1]. Warfarin is a vitamin K adversary (VKA) that has been utilized in the avoidance of AF for more than 50 years.

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Randomized preliminaries have shown that warfarin is better than fake treatment, ibuprofen and the mix of anti-inflamatory medicine clopidogrel in forestalling stroke. Warfarin use is trying because of its tight restorative record and it has numerous food and medication collaborations. The quantity of patients with atrial fibrillation (AF) who need stroke anticipation keeps on rising [2]. The pervasiveness of AF increments with age and is related with a higher gamble of ischemic stroke. The utilization of warfarin decreases the gamble of ischemic stroke in patients with AF, yet they need incessant observing and portion change. Ischemic stroke is considered as a central neurological deficiency from non-horrendous and non-hemorrhagic causes. AF is the reason for ischemic stroke in 15% of any age and 30% of individuals more than 80 years old. The gamble of ischemic stroke increments altogether with anticoagulant suspension [3].

The significance of a protected and successful avoidance rule with the best antiplatelets and anticoagulants blend is a significant objective for medication. Oral direct component Xa inhibitors (xabans) are endorsed by the United States Food and Drug Administration (FDA) for the counteraction of stroke. Warfarin is a main bad guy of vitamin K. Xabans have an alternate impact in the thickening course. They act straightforwardly upon factor Xa. They have less medication and food collaborations, and

their area in the coagulation course guarantees their productivity [4].

During the past decade, non-vitamin K trouble makers (NOACs) have shown to be either preferred or noninferior over warfarin for stroke expectation in AF, both in tremendous randomized controlled starters and in evident observational assessments. NOACs as of now address a large portion of new answers for oral anticoagulation in patients with AF in a couple of countries, including the United States, United Kingdom, and Denmark [5].

Rivaroxaban and apixaban are right now the most broadly started NOACs, however no straight on randomized preliminary have straightforwardly analyzed these 2 medications. The two medications are factor Xa inhibitors, however they have different pharmacokinetic profiles that could influence their security and viability [6]. Apixaban is probably going to be liked over rivaroxaban among patients with low renal capacity and high draining gamble, and these attributes are just somewhat recorded in libraries. Instrumental variable (IV) strategies, in which an element (the instrument) predicts treatment decision however has no immediate impact on results, can address unmeasured frustrating [7].

MATERIALS AND METHODS

This cross sectional comparative study was conducted in Pakistan Institute of Medical Sciences Islamabad during August 2020 to July 2021.

Sample Size: 120 patients

$$n = \frac{\left[z_{1-\alpha}\sqrt{2\bar{P}(1-\bar{P})} + z_{1-\beta}\sqrt{P_1(1-P_1)+P_2(1-P_2)}\right]^2}{(P_1-P_2)^2}$$

Where,

α = level of significance (1%)

β = power of study (99%)

P_1 = 0.25 (population in Group I)

P_2 = 0.75 (population in Group II)

n = 120 (60 in each group)

Data Collection Method: After consent from clinic moral council, complete 120 patients meeting the consideration and rejection models was signed up for Pakistan Institute of Medical Sciences Islamabad during August 2020 to July 2021. Itemized history and actual assessment was done to meet the incorporation and rejection rules. Informed assent was acquired.

The information was gathered into two gatherings:

Bunch I: Treated with Rivaroxaban

Bunch II: Treated with Apixaban

Bunch I patients will be given rivaroxaban 15mg everyday two times per day for one month then 20mg day to day for quite a long time and Group II patients will be given 5mg two times day to day all through the treatment period. Determination was made with a clinical show predictable with AF. Both the gatherings was followed during hospitalization and after release of the patient for 30 days for the advancement of any difficulties. Viability was characterized as ischemic stroke or fundamental embolism. Security was characterized as intracranial discharge or gastrointestinal dying. Post release follow up was done month to month on OPD premise.

Statistical Analysis: All the data was analyzed by SPSS 20.0 system for Windows.

RESULTS

The data was collected from 120 patients. Out of 120 members, 60 were treated with rivaroxaban, while 60 were treated with Apixaban. Middle age was 26 years in the gathering I and 25.3 years in the gathering II (p=0.705).

Table No.1: Demographic characteristics of selected patients

Baseline characteristics	All patients	Rivaroxaban	Apixaban	p-Value
AGE (mean, min-max)	25.3 (15–45)	26 (15–36)	27 (15–45)	
Gender				
Male	13 (18%)	14 (14%)	15 (21%)	
Female	47 (82%)	46 (86%)	45 (79%)	
Risk Factor				
OCP	08 (18%)	03 (14%)	05 (21%)	
Anemia	13 (29%)	06 (29%)	07 (29%)	
Dehydration	06 (13%)	04 (19%)	02 (08%)	.613
Pregnancy/Puerpureum	22 (49%)	10 (48%)	12 (50%)	
Ischemic stroke	25 (56%)	12 (57%)	13 (54%)	.843
Hemorrhagic stroke	17 (38%)	08 (38%)	09 (38%)	.968
Myocardial infarction	13 (29%)	06 (29%)	07 (29%)	.965
Intracranial hemorrhage	17 (38%)	08 (38%)	09 (38%)	.968
Duration (months) mean (min-max)	03 (03–12)	03 (03–12)	03 (03–12)	.058

Table No.2: Complications and clinical outcomes in both groups

Variables	All patients	Rivaroxaban	Apixaban	*P*-value
Overall	32(71%)	15 (71%)	17 (71%)	
Partial	11(24%)	03 (14%)	08 (33%)	.377
Complete	21(47%)	12 (57%)	09 (38%)	
At 12 months				
Overall	45(100%)	21 (100%)	24(100%)	
Partial	05 (11%)	02 (10%)	03 (13%)	.754
Complete	40 (89%)	19 (90%)	21 (87%)	
All bleeding events	08 (18%)	02 (10%)	06 (25%)	.161
Clinically relevant non major bleeding	02 (4%)	00	02 (8%)	

Female cases counted for 41 (86%) and 19 (14%) in I and II gatherings, individually. Risk factors, clinical show, impacted vessels and AF for the two gatherings are portrayed in Table I. Results from the two gatherings were tantamount and measurably no huge contrasts were noticed (p-value more than 0.05).

DISCUSSION

Nonvalvular atrial fibrillation (NVAF) is normal in patients with ongoing kidney sickness, and the predominance notably increments as renal capacity declines. An expected 13%-27% of patients with end-stage renal sickness (ESRD) have NVAF, a significantly higher predominance than in everyone [8]. Moreover, constant kidney sickness builds the stroke risk autonomous of other gamble factors in patients with NVAF. Regardless of an expanded thromboembolism risk in patients with ESRD and NVAF, anticoagulant use in this populace has been dubious in light of the fact that it needs adequate advantages, and anticoagulant clients have had more antagonistic impacts than nonusers. Also, stroke anticipation is perplexing on the grounds that renal brokenness is an autonomous gamble factor for significant draining [9].

Significant gamble factors for dying, for example, levels of creatinine, hemoglobin, weight record, pulse, and liver capacity, are not normally accessible in libraries, and definite renal capacity has not, as far as anyone is concerned, been accessible in any past examination. Involving substitute markers for draining gamble and decreased renal capacity, for example, emergency clinic release analyze, is probably going to cause remaining frustrating; for example, variety in renal capacity among patients regardless of constant kidney sickness analysis is still liable to impact therapy choice and results [10-11].

Rivaroxaban had no critical relationship to significant draining when we analyzed rivaroxaban and apixaban involving individual-level treatment as openness in the current review, proposing that unmeasured puzzling might have caused precise misstatement of the genuine draining gamble with rivaroxaban in past examinations. Interestingly, an IV can, under a few significant suppositions, adapt to unmeasured perplexing between openness bunches [12].

CONCLUSION

It is concluded that oral anticoagulant drugs for anticipation of stroke in non-valvular AF have been developed and adding new choices and benefits for patients and doctors like less recurrence of medication and food associations, no requirement for observing, wide helpful record and endured better by patients. Treatment with rivaroxaban 20 mg whenever everyday was related with genuinely huge expansions in major extracranial dying, including major gastrointestinal dying.

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

Practices about Infections and Immunization

Knowledge, Attitude and Practices about Infections and Immunization in Patients with Autoimmune Inflammatory Disease and Oncological Disease Patients in Pakistan

Zia Ullah Ehsan Kakar[1], Muhammad Muddasser Khan Panezai[1], Uzma Rasheed[1], Obaid Ur Rehman[1], Aimal Khan[2] and Somaya Sha[1]

ABSTRACT

Objective: Among patients with autoimmune inflammatory related diseases patients in Pakistan, the primary goal of the research is to determine their knowledge, attitudes, and behaviors about illnesses, vaccination, and other topics.
Study Design: Cross-sectional study
Place and Duration of Study: This study was conducted at the Pakistan Institute of Medical Sciences Islamabad during March, 2021 till December, 2021 for a period of nine months.
Materials and Methods: One hundred patients, equally divided across sexes, took part in the research and contributed the data gleaned from it. All patients with autoimmune inflammatory illness and cancer were eligible for participation in the trial, however those who did not wish to participate were excluded.
Results: A total of one hundred patients were polled to gather data. At the time of the study's conclusion, the average age of the participants was 39.6915.86 years. The virus that causes herpes zoster affected seven persons. Four of the participants came down with the flu. Five of the individuals tested positive for pneumonia. They both suffered dengue fever and malaria, but they both recovered. The individual who had a herpes genitalis infection in the previous five years was also included in the study. Patients were provided conventional disease-modifying antirheumatic medications (DMARDs) for 59.7 percent of the total and biological medicines for 9.8 percent of the total after the study's outcomes. Thirty-three (32.9 percent) of the patients were taking glucocorticoids in significant dosages.
Conclusion: It has been concluded that the expertise, approach, and practise of the respondents produced good results. Autoimmune illnesses have a complicated multifactorial origin, and a wide range of variables might play a role in their start and progression.
Key Words: Knowledge, Attitude, Infections, Immunization, Patients, Autoimmune Inflammatory Disease

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INTRODUCTION

In the opinion of specialists, the elderly and those with weaker immune systems are at a high risk of infection. There are 1.6 million deaths per year from pneumococcal disease in both developing and developed countries, more than the annual death toll of seasonal influenza. Innumerable lives have been saved and lifelong disabilities avoided thanks to the effectiveness of immunizations as a public health intervention [1]. Because of their effectiveness, safety, and cost savings, vaccines have significantly reduced the number of cases of infection and the mortality and morbidity they cause. Consequently, the incidence of infections has decreased, as well as mortality and morbidity associated with infections. Vaccines are frequently derived from microbes, their toxins, or proteins on their surface that serve as antigens that have been weakened or killed. It's common knowledge that there are four different kinds of vaccines: live, inactivated, subunit, and toxoids (inactivated toxic compounds) [2]. Because of the SARS-CoV2 pandemic, new vaccines, such as mRNA and virus-vectored vaccines, have been developed and are currently being tested. In addition to the antigen, vaccines may include adjuvants, stabilisers, and preservatives, which may contain traces of antibiotics and are used to prevent

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bacterial or fungal contaminations during the manufacturing process.[3]

In terms of the non-monetary factors that determine poverty, such as education and health, the country's socioeconomic foundation is weak[4]. According to international standards, Pakistan's literacy rate is only 58%. Many cases of HIV/AIDS go unreported and undiagnosed as a result of the social stigma attached to the disease, as well as the lack of adequate surveillance, voluntary counselling, and testing systems [5]. As a result of its low rate of condom use, large number of long-distance truck drivers (who are at high risk of HIV infection), thriving commercial sex industry, limited blood transfusion safety protocols, high prevalence of sexually transmitted infections (STIs), limited access to quality STI care, and growing number of injection drug users (IDUs), Pakistan is considered an extremely high-risk country for HIV infection [6].

The prevalence of autoimmune and auto-inflammatory diseases in developed countries is estimated to be one in every fifteen people, and in many cases, they pose a serious health and financial burden to both patients and the public. Long-term outcomes for many patients with autoimmune diseases remain poor despite significant advances in the development of new treatment methods[7]. There is still a high risk of infection in people with rheumatological illnesses. The development of vaccinations has made important contributions to the prevention of infection in the area of rheumatic illnesses. In spite of the fact that vaccination is a powerful immune system stimulant, it may also create or aggravate immunological disturbances that appear as serological indications of immune system dysregulation or clinically manifest autoimmune disease [8].

MATERIALS AND METHODS

This cross-sectional study was conducted in Pakistan Institute of Medical Sciences Islamabad during March 2021 till December 2021. A sample of 100 patients, including male and female, have been surveyed for this study. There were no exclusions for individuals with autoimmune inflammatory sickness and cancer, as well as those who did not wish to participate were excluded. Use of an organized questionnaire was used to collect the data needed. Information on socio-demographic status, health status, and knowledge of sickness are all included in this easy-to-use survey. Information on participants' demographics, such as gender, marital status, and education level was requested in the first phase of the survey. The participant's health was the focus of the second portion. Knowledge, attitudes, and practises were divided into three different parts. In the knowledge phase, participants were asked a series of questions regarding the transmission of disease, the symptoms, and whether or not disease can be treated and cured (see below). If they considered this was a public health concern and should be addressed in order to create awareness, they were questioned about this in the attitude component. Additional questions were addressed concerning people's perceptions of folks with an autoimmune condition, and the results were rather interesting.

SPSS version 20 was used to collect and analyze the data. For each variable, the average and standard deviation were used to summarize the data.

RESULTS

The data was collected from 100 patients. At the time of the research, the average age of the participants was 39.6915.8639.69± 15.86 years. Seven people were infected with the virus that causes herpes zoster. There were four cases of influenza among the patients. Five people were diagnosed with pneumonia. A dengue patient was one of them. During that time, one had a herpes genitals infection. Conventional disease-modifying antirheumatic medications (DMARDs) were prescribed to 59 patients (59.7 percent of the total) and biological agents were prescribed to nine patients (9.8 percent of the total). Patients were using glucocorticoids in 33% of cases.

Table No.1: Demographic and disease characteristics of the participants

Demographic data	**Number (%)**
Age (years)	39.69 ± 15.86
Gender (males)	79 (33.6)
Disease course (years)	4.48 ± 5.96
Education level (primary school)	22
Education level (university)	78
Diagnosis	
Rheumatoid Arthritis	23 (9.8)
Systemic sclerosis	15 (6.4)
Other CTDs	13 (5.5)
Vasculitis	10 (4.3)
Spondyloarthritis	19 (8.1)
Gout	40 (17)
Glucocorticoids	14 (60.9%)
cDMARDs	15 (67.7%)
Biological agents	9 (3.8%)

A only fifteen people (6.4 %) had had a vaccine in the five years prior to the study's start. Pneumococcal and influenza vaccinations had not been administered to any of the patients in the prior five years. Because they had not been given, 53 of the patients were unable to get these vaccines (53.6 %). The Rabie vaccine was given first, followed by the HBV, tetanus, and HPV immunizations in this clinical research. Only one of the nine patients who got biotherapeutic drugs had previously been vaccinated in the prior five years.

Table No.2: Questions and answers about disease perception and vaccination

Number	Question	Yes Or I agreed Number (percentage)	No Or I disagreed Number (percentage)	I didn't know Number (percentage)
Knowledge and attitudes about vaccination				
Q2	Have you already heard of the flu vaccination before?	59 (67.7)	76 (32.3)	-
Q3	Pneumococcal vaccination, had you aware of it?	62 (26.4)	173 (73.6)	-
Q4	Herpes zoster vaccine has been around for a while, right?	43 (18.3)	192 (81.7)	-
Q5	Which of the aforementioned vaccinations can you get?	10 (43.8)	132 (56.2)	-
Q12	If I get vaccinated, I won't get sick with the flu.	26 (11.1)	117 (49.8)	92 (39.1)
Q13	A person who hasn't had a flu shot is much more likely to become sick than someone who's had a flu shot.	43 (60.9)	23 (9.8)	69 (29.3)
Q14	As a result of getting pneumococcal vaccine-tion, I am less likely to develop pneumonia.	15 (48.9)	30 (12.8)	90 (38.3)
Q17	There are no risks to vaccination.	10 (43.4)	38 (16.2)	95 (40.4)
Q18	Getting vaccinated is fraught with danger.	22 (9.4)	16 (49.4)	97 (41.2)
Q19	Access to information regarding immunization is readily available to me.	75 (31.9)	35 (14.9)	25 (53.2)
Q15	The influenza and pneumococcal vaccines are both covered by most health insurance plans.	29 (12.3)	22 (9.4)	84 (78.3)
Q16	Regardless of the price, I will not be vaccinating myself against influenza and pneumonia.	36 (15.3)	139 (59.1)	60 (25.5)
Q20	Due to my age and health conditions, I know that I must get a flu vaccination.	41 (17.4)	33 (14)	16 (68.6)
Q21	Because of my age and condition, I'm not sure whether I should be vaccinated against pneumococcal illness.	79 (33.6)	15 (6.4)	14 (60)
Q22	Influenza and pneumococcal vaccinations have been administered to members of my family or close acquaintances in the past.	34 (14.5)	47 (20)	154 (65.5)
Q6	Do you know of a doctor who recommends that you get the vaccines listed here?	9 (3.8)	221 (94)	5 (2.2)
Q24	In the event that my doctor recommends that I get an influenza or pneumococcal vaccination, I am open to doing so.	91 (38.7)	44 (18.7)	90 (38.3)
Vaccination uptake status				
Q1	Vaccination uptake			
	Influenza	1		
	Pneumonia	0		
	Herpes zoster	0		
	HAV	0		
	HBV	3		
	HPV	2		
	Rabies	4		
	Tetanus	2		
	Others	3		
Q2	Reasons given for non-vaccination			
	Unnecessary	21 (8.9)		
	too expensive	7 (3.0)		
	Troublesome	20 (8.5)		
	No reason	24 (52.8)		

DISCUSSION

The 3% of RD patients were never inoculated because the vaccine was too costly, according to one research [9]. The percentage of patients who did not know that influenza vaccination is free was greater among those who had never been vaccinated, although the majority of patients were aware.

Many vaccine-preventable illnesses are more common in people with autoimmune inflammatory rheumatic diseases, including influenza, pneumonia, herpes zoster, and HPV infections. As a consequence, patients with this illness must take extra precautions to prevent infection [10]. Immunizations are a major source of concern since they may aggravate or accelerate the course of pre-existing autoimmune diseases. A risk/benefit analysis of the recommended vaccines for people with autoimmunity is used to determine whether or not vaccinating them is useful in most cases. Vaccine-associated disease exacerbations have been reported in just a few studies [11]. HPV vaccination has been linked to an increase in SLE start and aggravation, although bigger studies have revealed no difference in incidence or exacerbation rates between vaccinated and non-vaccinated individuals. Vaccines do not raise the chance of developing SLE. Researchers who looked into the possibility that vaccines can cause or exacerbate MS found no evidence of a link. For example, there was no evidence that vaccines against hepatitis B, tetanus, and influenza exacerbated the symptoms of multiple sclerosis.[12]

As a consequence of immunizations, death rates throughout the world have been reduced by a wide variety of infectious diseases. Recently reported cases such as the measles epidemic have revealed, however, that reaching an adequate vaccination coverage throughout the global population remains a tough challenge [13].

Most patients said that gastroenterologists and family physicians were the primary sources of information on vaccines. A patient's primary source of information while dealing with a chronic health condition is often their family doctor. Additionally, in Poland, vaccinations are provided by a general practitioner in the office. Flu vaccine advice from a physician was shown to be undervalued by parents of children with chronic diseases in research [14].

CONCLUSION

It has been concluded that now the knowledge, attitude, and practise of the participants produced excellent results. Autoimmune illnesses have a complicated multifactorial origin, and a wide range of variables might play a role in their start and progression. As a result, vaccinations have also been investigated and tracked over time in order to determine if there is a relationship between vaccination and the development of autoimmune illnesses or immune-mediated phenomena. However, certain areas of knowledge, such as the transmission of hepatitis B and C, and attitudes, such as the necessity for post-exposure consultation with a specialist, need to be rectified or modified in order to be effective.

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Original Article

Comparison of Morphometric Parameters of Third Ventricle among Males and Females and Its Relevance with Age

Amatul Sughra[1], Syeda Bushra Ahmed[1], Sumera Tabassum[2], Tanweer Fatima[3], Maria Mohiuddin[4] and Khalida Parveen[5]

ABSTRACT

Objective: To calculate and estimate the 3rd ventricular measurements in different age groups including both genders.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Anatomy with the collaboration of Radiology Department J.P.M.C Karachi from November 2019 to December 2020.

Materials and Methods: Patients with any gross pathology of brain was excluded whereas MRI with no clinical manifestation of 206 patients were included. 3rd ventricle was measured for its dimensions on MRI via Tesla 1 weighted (T1-weighted), Tesla 2 weighted (T2-weighted) and Fluid Attenuated Inversion Recovery (FLAIR) on coronal, sagittal and transverse plane on different levels by 3D technique. Dimensions of 3rd ventricles were measured by measuring the length, width and height of third ventricle.

Results: Out of the 206 participants 106 (51.5%) were in group A and 100 (48.5%) were in group B. In total, males were 102 (49.5%) and 104 (50.5%) were females. Mean age of group A was 29.3 ± 6.88 while group B mean age was 51.7 ± 6.58. The result showed that length of 3rd ventricle was found greater in females as compared to males while width and height found greater in male than females. However in comparison with age third ventricle height was found to be decreased in size while width and length was increased with advancement of age.

Conclusion: Study showed that variations are found in measurements of 3rd ventricle in different subjects with age and gender and when we compared it with the studies in different areas and population. This will be helpful for surgeons, neuro-physcians and radiologists to investigate, manage and treat a disease of brain.

Key Words: Ventricles, Dimensions, Tesla.

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INTRODUCTION

Ventricular system is an intercommunicating system present with in the brain. It consist of lateral ventricle, 3rd ventricle and 4th ventricle. Lateral ventricle is communicated with 3rd ventricle via foramen Monro whereas cerebral aqueduct of Sylvius communicates the 3rd and 4th ventricle.

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4th ventricle communicates through the sub-arachnoid space via two lateral openings; foramen Lushka and one central opening foramen Megendi. 4th ventricle becomes narrow inferiorly to continue as central canal of spinal cord.(1)

The 3rd ventricle is a narrow midline cavity, which is present in between two thalami and hypothalamus. It is bounded superiorly/ roof by tela choroidea and body of fornix along with thalamus. Inferiorly optic chaisma, tuber cinereum, infundibulum and mammillary bodies along with hypothalamus form floor. Posteriorly it is bounded by pineal gland, habenular nuclei and posterior commissure. Anteriorly it is bounded by anterior commissure and lamina terminalis. Tela choroidea of 3rd ventricle produce cerebrospinal fluid (CSF) along with lateral and 4th ventricles.(2, 3)

Human brain develops in early life up to 3rd to 4th decades, however with the advancement of age degenerative changes progress, this leads to cortical atrophy and ventricular dilatation. Due to these changes, it remains difficult for physician, neurologist and radiologist to rule out the normal morphometric changes with diseased brain. Third ventricle dilatation compressed the thalamus and hypothalamus which are

essential parts of diencephalon. [4,5] Previously, invasive techniques pneumoencephalograms and contrast ventriculography were used but now computed tomography (C.T Scan) and magnetic resonance imaging (MRI) are in used which are non-invasive techniques.[4,6] However electromagnetic waves of MRI have better sensitivity and safety over ionized radiations of C.T Scan. [7,8] It provides best imaging of fluid and soft tissues of brain. Images can be taken on sagittal, oblique and axial planes without moving patients. [9] All healthy subjects with age group of 20 to 60 were included except participants with any metallic implants and brain related disorders. Objective of this study was to calculate and estimate the 3rd ventricular measurements in different age groups including both genders.

MATERIALS AND METHODS

This cross-sectional study was conducted on MRI of 206 patients in Anatomy Department B.M.S.I in association with Radiology Department J.P.M.C Karachi from November 2019 to December 2020. Subjects were divided into two groups containing both genders. Groups A comprise of ages 20 to 40 and group B comprises of 41 to 60. After the consent and complete history participants were counseled and prepared for the procedure. Procedure of MRI completed within 25-30 minutes. MRI was taken on Tesla 1 weighted (T1-weighted) Tesla 2 weighted (T2-weighted) on transverse and Fluid Attenuated Inversion Recovery (FLAIR) on coronal plane via 1.5 Tesla MRI Toshiba scanners at JPMC. Each sequence took 7 minutes to be completed and thickness of each was 5 to 10 mm. Measurements were taken by using Micro Dicom software.

The dimensions of third ventricle were taken by length, height and width. Length was measured from anterior wall (pre-commissure) to posterior wall (pineal gland root) of ventricle in ventro-dorsal dimension on axial plane, height was measured in craniocaudal direction (roof to floor), the distance between the two lateral wall was measured for width (coronal plane was used for measuring the height and width). [10]

Analysis was done by using SPSS version 19.0. Student t-test was used for comparison between two groups.

RESULTS

Of the 206 participants, they were divided into group A (20-40) and group B (41-60). Group A consist of 106 (51.5%) participants and group B consists of 100 (48.5%) participants. In which 104 (50.5%) were female and 102 (49.5%) were male. As presented in figure 1.

Measurement of mean length, height and width of 3rd ventricle with their significant and non-significant values are present in table # 1. These are showing the comparative measurements in group A and B in between both genders. However, the width of group A showing the significant difference as shown in table 1.

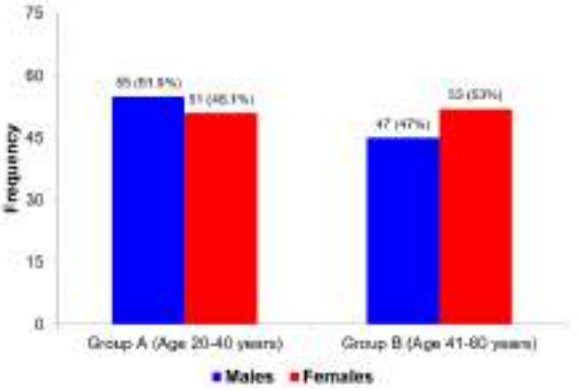

Figure No.1: Showing the age and gender distribution

Table No.1: Comparative measurements of 3rd ventricle in both genders in Group A (20-40 years) & Group B (41-60) years

	Male (n=55)	Female (n=51)	P-value
Group A (20-40) years			
Length	4.7 ± 0.98	4.9 ± 0.88	0.257
Height	20.2 ± 1.00	20.0 ± 0.77	0.203
Width	4.6 ± 0.58	4.3 ± 0.71	0.009
Group B (41-60) years			
Length	5.9 ± 2.80	5.1 ± 1.42	0.098
Height	19.7 ± 1.72	19.5 ± 1.52	0.412
Width	5.1 ± 1.90	4.8 ± 1.44	0.461

Table No.2: Comparative measurements of 3rd ventricle in different age groups in Male of group A & B

	Male		P-value
	Age (20-40) years	Age (41-60) years	
Length	4.7 ± 0.98	5.9 ± 2.80	0.010
Height	20.2 ± 1.00	19.7 ± 1.72	0.085
Width	4.6 ± 0.58	5.1 ± 1.90	0.090
	Female		
Length	4.9 ± 0.88	5.1 ± 1.42	0.430
Height	20.0 ± 0.77	19.5 ± 1.52	0.020
Width	4.3 ± 0.71	4.8 ± 1.44	0.010

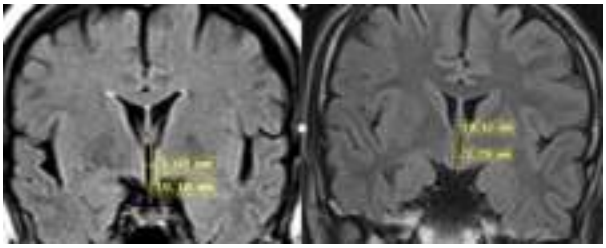

Figure No.2: Length and Width of Group A Male & Female

On comparison of group A male with group B male and group A female with B female the mean measurements showed significant and non-significant differences which are shown in table 2. Significant difference in length of group A males when compared with males in group B as shown in table 2. Similarly (Table 2) significant difference was observed on comparison of group A and B female.

DISCUSSION

This cross-sectional study was conducted on both genders in different age groups for study of normal measurements of 3rd ventricle on MRI. We found variation in measurements of 3rd ventricle when compared in different age groups in both genders. 3D quality of MRI along with electromagnetic waves shows better effects and sensitivity over brain soft tissues. It provides pioneer measurements of brain tissue and ventricles.[11-13] MRI also provide measurements on different planes and dimensions, which facilitate the neuro-physcians, surgeon and radiologist to rule out and treat a diseased or pathological condition. [14]

When length of the third ventricle was compared it was found larger in female as compared to male but width and height were found greater in males as compared to females as shown in figure # 2, similar results were reported by Singh et al studies.[4] In our study, we observed that height found reduced in size with advancement of age, which are also in line with Singh et al. [4] Duffner et al used mid-sagittal plane for measuring the height, whereas Singh et al used transverse plane and ventrodorsal extension for measuring the 3rd ventricle and we measured the height and width in coronal plane and length in axial plane, so some variations were found in measurements of various studies.[4,10] Study by Aukland et al from Norway also reports width of 3rd ventricle was found greater in male as compared to female and it increases with age.[15] While study conducted by Shrestha et al on Nepalese, showed results contrary to our study that width of 3rd ventricle was found more in females than in males, but they conclude the same increase in width with age.[5] A study from Iraq showed that 3rd ventricle width is age dependent not gender which also support our study for age difference.[16] Our study reveals similar results when compared with Indian and European nations no significant racial difference was found. (17-19) Same is true with study by Hamidu et al of Zaria-Nigeria. [20].

CONCLUSION

Our results suggest length of 3rd ventricle was found greater in females as compared to males while width and height found greater in males than females. However in comparison with age we found that height reduced in size whereas length along with width increased with advancement of age. On comparison with various studies we found with advancement of age, sexual dimorphism is observed in measurements. MRI with quality of 3D and harmless electromagnetic waves is best modality and gives novel and finest images of the ventricles and brain soft tissues.

Author's Contribution:

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Data Analysis:	Tanweer Fatima,
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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

Morphometrical Analysis of Diaphyseal Nutrient Foramina of Adult Human Dry Fibulae

Noman Ullah Wazir[1], Muhammad Haris[2], Najma Baseer[4], Sobia Haris[3], Farah Deeba[3] and Muhammad Jehangir Khan[5]

ABSTRACT

Objective: To investigate and analyze the morphometry of diaphyseal nutrient foramina in adult human dry fibulae.
Study Design: Cross-sectional study
Place and Duration of Study: This study was conducted at the Department of Anatomy, Nowshera Medical College, Nowshera, Pakistan from September, 2021.
Materials and Methods: The materials contained dry fibulae of a total of 20, out of which 12 were of the right side and 8 were left sided. The bone's length and the dimension of the nutrient foramina from the proximal end were determined. The Foramen Index (FI) was computed utilizing the formula such as the length/distance of nutrient foramen (DNF) from proximal end was divided by the total bone's length (TL), and then multiplied by a factor of 100. FI = (DNF/TL) x100.
Results: A single nutrient foramen was found in 13 bones (65%) in the left sided ones and 07 bones (35%) in the right sided fibulae. The left fibula had an average length of 34.6±2.3 cm while the right fibula had a length of 34.9±2.2 cm. On the left side, the FI was 47.5±7.6 while on the right side, it was 50.3±11.5. Type-I foramen was discovered in two (10%) bones, Type-II was found in 15 (75%) bones, and Type-III was found in three (15%) bones in the right fibulae. Whereas, in Left Fibulae, Type-I foramen was not discovered in any of the bone, Type-II was found in 18 (90%), and Type-III was found in two bones (10%).
Conclusion: These findings add to our knowledge of the morphometry of nutrient foramina of the adult human dry fibulae. Now a days, microvascular bone transfer becomes increasingly prevalent, such information about nutrient foramina will be useful to orthopedic and trauma surgeons.

Key Words: Anatomy, diaphyseal foramen, dry fibula, human, morphometry, nutrient foramen.

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INTRODUCTION

The fibula is a long bone on the lateral side of the leg. Aside from the muscles linked to it, it receives its neuro-vascular bundle. The nutrient artery that supplies the fibulae comes from the peroneal artery and spirals around the fibula's neck before descending along the fibula deep to the flexor hallucis longus. It emits a nutrient artery at the center of the fibula, which enters the nutrient foramen and ramifies within the fibula.[1] The increasing end of the bone, which is meant to expand at least twice as quickly as the non-growing end, determines the orientation of the nutrient foramina. As a consequence, the nutrient arteries shift away from the developing terminal of the bone.[2] Nutrient foramina information and details are important in clinical operations such as bone grafting and vascularized bone transplantation which is done microsurgically.[3] Fibula can be transplanted with little problems to repair gaps or faults in bones caused by a variety of reasons. Fibula can be uprooted with its nutrient arteries anastomosed with the vessels near the recipient's bone. Because the transplant is a live bone, it can fuse with the recipient's bone in the same way as regular fracture pieces do.[4] The compensations of the free vascularized fibular flap in removing mandible cancers comprise its capacity to be formed with comparative effortlessness and grafted at the same time tumors are excised, resulting in a decrease in surgery time.[5-7] To progress with the free implant of the vascularized bone, topographical information of the nutrition foramina of the fibula is required.[8] The spreading of nutrient foramina in long bones allows

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surgeons to pick bone section levels to insert the graft lacking injuring the nutrient arteries, thereby conserving diaphyseal vascularization and transplant association.[9] The distribution and exact position of the nutrient foramina in the bone shaft is critical to avoiding injury to the nutrient arteries throughout orthopedic operations such as crack mending, bone grafting, bone surgery, and in medico-legal matters. The current study was aimed to investigate the topographic and morphometric aspect of the diaphyseal nutrient foramina of adult human dry fibulae.

MATERIALS AND METHODS

This cross-sectional study was carried out in the Department of Anatomy, Nowshera Medical College, Nowshera, Pakistan in September, 2021. A total of 20 fibulae of unidentified age and sex were inducted and studied, with 12 right sided and 08 were left sided. Using a magnifying lens, all of the bones were examined for the orientation, position, and number of the nutrient foramina. The existence of a well-marked groove directing to the nutrient foramina and a conspicuous somewhat elevated edge at the canal's beginning helped to identify them. Each bone was put on an osteometric board and its total length was recorded to calculate its length. The measurement was taken between the tip of the fibula's head and the point of the lateral malleolus. The fibula's nutrient foramen was discovered, and the bone was placed on an osteometric board to measure the length between the nutrient foramen and the bone's proximal end. FI was measured using the Hughes formula, which was determined such as the length of the foramen from the proximal end (D) was divided by the complete bone's length (L), and then multiplied by hundred.[10] FI = (DNF/TL) x 100 where DNF=the distance between the bone's proximal end and the nutrient foramen; and TL=total bone length. According to FI, the location of the foramina was classified into three categories;[11] Type-I had a foramen index lower than 33.3, and the foramen was located in the proximal portion of the bone. Type-II had a foramen index ranging from 33.3 to 66.6, with the foramen located in the central part of the bone. Type=III had a foramen index more than 66.6, and the foramen was located in the distal part of the bone. SPSS version 25.0 was employed to enter and analyze data. Descriptive statistics i.e., mean, standard deviation, frequencies and percentages were identified for bone length and length of the nutrient foramen from the proximal end. The foramen index (FI) was also calculated.

RESULTS

Twenty adult human dry fibulae of indefinite age and sex were studied for topographic and morphometric parameters, out of which 12 were right sided and 08 were left sided. Single nutrient foramen was found in 13 bones (65%) in the left sided ones and 07 bones (35%) in the right sided. The left fibula had an average length of 34.6±2.3 cm while the right fibula had a length of 34.9±2.2 cm. On the left side, the FI was 47.5±7.6 while on the right side, it was 50.3±11.5. Type-I foramen was discovered in two (10%) bones, Type-II was found in 15 (75%) bones, and Type-III was found in three (15%) bones in the right fibulae. Whereas, in left fibulae, Type-I foramen was not discovered in any of the bone, Type-II was found in 18 (90%), and Type-III was found in 02 bones (10%).

DISCUSSION

The majority of the life blood to the long bones is carried by the nutrient vessels, which go in through the nutrient foramina. Knowledge of these foramina is critical during surgical operations to protect circulation, particularly for the plastic surgeon doing microvascular bone transfer techniques.[12] The nutritive blood supply must be sustained in free vascular bone grafting to enhance fracture healing. It is required for osteoblast and osteocyte existence, as well as graft curing in the recipient.[13] Several studies have been conducted in different populations to establish the direction, location, and number of the nutrient foramen and foramen index of fibulae, but no such study on topography and morphometry of adult human dry fibulae has ever been conducted in our population. Prashanth et al.[14] discovered that 90.2 percent of fibulae had a single foramen and 9.8 percent did not. For fibulae, the mean foraminal index was 49.2. Sixty percent of the fibulae exhibited nutritional foramen at the third and fifth portions. Pereira et al. researched South Brazilian adults.[15] The fibula's typical foraminal index was 46.1 percent. This study assembled statistics on the people of Southern Brazil, providing cultural data for comparison and maybe assisting in operating practices and radiological image explanation. In Indian population research, the lack of nutrition foramen was identified in 12 (6%) of the fibulae, whereas 86.5 percent (173) of the fibulae held single nutrient foramen, 6.5 percent (13) owned double nutrient foramina, and 1 percent (2) fibula possessed triple foramen.[16] Kumar et al.[17] discovered in research that 30 of the 177 bones had more than one foramen, with four foramina pointing towards the developing end of the bone. Mazengenya P et al.[18] discovered the nutritional foramen immediately proximal to the midpoint in research on Korean populations. Anetai H et al.[19] discovered that in 90% of the cases investigated, there was a single nutrient artery, 6.6 percent had a double nutrient artery, and 3.3 percent had no nutrient artery.

CONCLUSION

Thus, the current findings add to our knowledge of the topography and morphometry of nutrient foramina of the adult human dry fibulae. Now a days, microvascular

bone transfer becomes increasingly prevalent, such information about nutrient foramina will be useful to orthopedic and trauma surgeons.

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 Time as Most Effective Factor in Success of Thrombolysis with Streptokinase in Patients with Acute STEMI During COVID 19 Pandemic

Saeed Ahmed[1], Burhan ul Haq Muhammad Saqib[1], Tahmeena Sarafaraz[4], Shahzeb Saeed[2], Muhammad Shoaib[2] and Asnad[3]

ABSTRACT

Objective: The objective of this study to evaluate time as most effective factor in success of thrombolysis with streptokinase in patients with acute STEMI during covid 19 pandemic.

Study Design: Prospective observational study

Place and Duration of Study: This study was conducted at the Kashmir institute of Cardiology, Mirpur Azad Jammu and Kashmir, from April 2020 to December 2020 for a period of nine months.

Materials and Methods: Patients presenting in emergency department with Acute STEMI were included, patients were analyzed via history, clinical examination and ECG findings of Acute STEMI.

Results: Total of 110 patients were included in study. 80% (88) patients were male and 20%(22) patients were female. Which shows increase in the number of female patients with acute STEMI In this study we have tried to compare ECG based success criterion with international data and our data back in 2016. During the study we found successful thrombolysis around 45% during covid 19 pandemic.

Conclusion: Time from onset of symptoms of Acute STEMI and start of streptokinase treatment was proven to be most effective method to improve the chances of success of streptokinase treatment and reduce mortality in such patients, as regard to my previous study in 2016 in same institute success of thrombolysis was markedly reduced with streptokinase during the covid 19 pandemic using the same treatment parameters.

Key Words: ST-segment elevation myocardial infarction, Streptokinase, time to streptokinase treatment, Covid-19.

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INTRODUCTION

ST segment elevation myocardial infarction is one of the most serious types of acute coronary syndrome that is related with very high mortality if there is delay in treatment.[1]

Decreased mortality in last decade is due to this known factor of delayed treatment causes high mortality has led to formation of ICUs equipped with advanced and early care using strategies like emergency percutaneous coronary inhtervention.[2]

Rupture of atherosclerotic plaque within coronary arteries resulting in exposure of injured vessel wall to coagulating factors in the blood resulting in thrombus formation is one of the most common causes of STEMI.[3] Time is most efficient factor. Starting the streptokinase treatment in less than 30 minutes helps establish the blood flow to the compromised heart muscles. Each Delay of 30 minutes increases the relative risk of 1 year death by approximately 8% [4,5].

Success of thrombolysis clinically is evident with resolution of symptoms of MI, more than 70% resolution of ST segment elevation and by runs of slow VT also called idioventricular rhythm.[6]

ECG is a very quick test to establish diagnosis of ST segment elevation myocardial infarction[7,8].

STEMI is defined as 4th universal definition; ST elevation of more than 0.25mv in leads V2 and V3 in males less than 40 years, ST elevation of more than 0.20mv in males more than 40 years and ST elevation of more than 0.15mv in females is termed as acute STEMI.[9]

The objective of this study is to determine the time as most effective factor in success of thrombolysis with

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streptokinase in patients with acute STEMI during covid 19 pandemic.

MATERIALS AND METHODS

This observational study was conducted in emergency and CCU department of KIC, Mirpur Azad Jammu and Kashmir from April 2020 to December 2020 after approval from hospital ethical committee. Patients of ages 20-85 years with symptoms and ECG changes of acute MI are included in this study. exclusion criterion were ages <20 and >85, previous intracranial hemorrhage, known cerebral vascular lesion, known malignant intracranial neoplasm, suspected aortic dissection, active bleeding, significant close-head or facial trauma in last 3 months, recent surgery within 3 months. Informed verbal consent was taken from all patients. First patient was given Asprin 300mg and clopidogrel 300mg along with enoxaparin 1-2mg/kg once and after this streptokinase was administered in next 1 hour. ECG done at baseline and at 90 minutes was checked for ST resolution.

Statistical Analysis: SPSS for Windows version 20 (SPSS, Inc., Chicago, IL, USA) was employed for all statistical analyses.

RESULTS

Total of 110 patients were included in study. 80% (88) patients were male and 20% (22) patients were female.

Table No.1: Distribution by Gender

	Number of patients	Percentage	Number of patients in 2016	percentage of patient in 2016
Male	88	80%	72	82.8%
Female	22	20%	14	16.1%
Total	110	100%	87	100%

Table No.2: Distribution by Age

	No. of patients	%age	Number of patients in 2016 study	%age of patients in 2016 study
Age 20-39 years	10	9.5%	5	5.6%
Age 40-59 years	45	40%	41	46%
Age 60-70 years	45	40%	38	42.7%
Age 70-85 years	10	9%	5	5.6%
Total	110	100%	89	100%

It shows increase in the number of female patients with acute STEMI In this study we have tried to compare ECG based success criterion with international data and our data back in 2016. During the study we found successful thrombolysis around 45% during Covid 19 pandemic.

Table No.3: Parentage by success of thrombolysis

	No. of Patients in this study	%age in this study	Frequency of patient in 2016 study	%age in 2016 study
Successful	50	45%	49	55%
Failed thrombolysis	60	55%	40	45%
Total	110	100%	87	100

DISCUSSION

Since last century streptokinase has proven to be cheap and effective way to treat STEMI[10-13]. In our study we tried to compare time to treatment with streptokinase success in patient with acute STEMI before covid 19 and during covid 19 pandemic.

In this study we have tried to compare ECG based success criterion with international data and our data back in 2016,

In our study in 2016 we had 87 patient with acute MI, 72 were male and 14 were female which makes it a 82.8% male patients and 16.1% female patients. While in this study we had 110 patient out of which 88 or 80% were male and 22 patients or 20% were females. Which shows increase in the number of female patient with acute STEMI.

Successful thrombolysis was seen in 55% of patient with acute STEMI in 2016 study, while recent study during covid 19 pandemic showed less number of successful thrombolsis around 45%.[14 -17]Percentage of acute STEMI in ages 40-59 years also increased from 40% to 46%. There was also an increase in number of STEMI cases at ages 60-70 years which increase from 38% to 42.7%. while in ages 71 to 85 years number of STEMI had seen a significant drop from 9 to 4.6%.[11,12]A study by fanaroff and Garcia published in JAMA also showed same results, there was increased number of patients with more ischemic time possibly due to late presentation and had more complications. Age distribution of patient compared to our study in 2016[18-21] was also changes, there were more number of young males, number of MI increased in ages 20-39 from 5.6% to 9%.

CONCLUSION

Based on above mention facts, our own data comparison along with comparison with international data. It is clear that Covid 19 has increased the burden of acute STEMI and more patient have ended up with more complications and decreased number of successful thrombolysis in acute STEMI patient during Covid 19 pandemic points towards either late

presentation of patients or possible more clotting issues that are known to be related to covid 19 virus despite same protocol for streptokinase.

Author's Contribution:

Concept & Design of Study:	Saeed Ahmed
Drafting:	Burhan ul Haq Muhammad Saqib, Tahmeena Sarafaraz
Data Analysis:	Shahzeb Saeed, Muhammad Shoaib, Asnad
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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 Dietary Sodium and Potassium Effects on Blood Pressure in Women Mirpur AJK

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ABSTRACT

Objective: The objective of this study to evaluate dietary sodium and potassium effects on blood pressure in women Mirpur AJK.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Department of KIC, Physiology and Biochemistry Mirpur Azad Jammu and Kashmir from January, 2020 to July, 2021 for a period of one and a half year.

Materials and Methods: We select 210 women from Mirpur AJK and their blood pressure was assessed both systolic and diastolic pressure. We take history from women and those women take more sodium as compare potassium in their diet placed in Group A and those women take more potassium as compare to sodium in their diet placed Group B.

Results: Those women whose take sodium more in their diet their blood pressure was higher that as Systolic BP - 24 hours is (139.9 + 9.2 mmHg) and Diastolic BP - 24 hours is 88.6 + 5.9 mmHg, Those women who take Potassium higher as compare to sodium in their diet, their blood pressure is lower which is Systolic BP - 24 hours 123.4 + 6.3(mmHg) and Diastolic BP - 24 hours 80. 9 + 6.5 mmHg.

Conclusion: Sodium salt consumption in diet increased blood pressure with adverse effect in women and potassium salt intake in diet decrease blood pressure in women. There is recommended that women should take potassium containing diet.

Key Words: Dietary Sodium, Dietary Potassium, Blood Pressure

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INTRODUCTION

Sodium is important for fluid balance and cellular homeostasis. Homeostasis defines the role of sodium in fluid matrix" of the body.[1]For homeostasis quantity of sodium is required associated with intake of sodium at optimum level.[2] BP replies to changes in dietary sodium vary widely, foremost to the perception of salt-sensitive (SS) BP.[3,4] Those person who eat sodium per day more than (6.0g) they are at the risk of taking of hypertension.[5,6]

Result showed special effects of dietary sodium on blood pressure have also produced opposing results, while current indication proposes that most BP upsurges are related with sodium consumptions of more sodium.[7] The connection among families and minors is mainly unexamined .[8]Numerous of scientific research designate that cumulative consumption potassium decreases BP in hypertensive grown-ups.[9,10] However, inhabitants-based research has unsuccessful to demonstration such an connotation.[11] In younger populations research showed that potassium effect are limited and restricted.[12] The objective of this study to evaluate effect on blood pressure after intake dietary sodium and potassium in women Mirpur AJK.

MATERIALS AND METHODS

This cross-section study was directed in department of KIC, Physiology and Biochemistry Mirpur Azad Jammu and Kashmir from January 2020 to July 2021 after approval from hospital ethical committee. We select 210 women from Mirpur AJK and their blood pressure was assessed both systolic and diastolic pressure. We take history from women and those women take more sodium as compare potassium in their diet placed in Group A and those women take more potassium as compare to sodium in their diet placed Group B. We check their blood pressure at least six weeks in KIC Mirpur AJK.

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Statistical Analysis: SPSS for Windows version 20 (SPSS, Inc., Chicago, IL, USA) was employed for all statistical analyses.

RESULTS

We select 210 women for sodium and potassium diet from Mirpur AJK and their blood pressure was analyzed. Those women whose take sodium more in their diet their blood pressure was higher that as Systolic BP - 24 hours is (139.9 + 9.2 mmHg) and Diastolic BP - 24 hours is 88.6 + 5.9 mmHg, those women who take Potassium higher as compare to sodium in their diet, their blood pressure is lower which is Systolic BP - 24 hours 123.4 + 6.3(mmHg) and Diastolic BP - 24 hours 80. 9 + 6.5 mmHg. We take blood samples from both groups women and analyzed the samples on micro lab 300 for serum lipid profile. (Cholestol, HDL, LDL, VLDL and Triglyceride). For the study we use kits made of Merck Pvt.

Table No.1: Participant characteristics of women

	(n=105) Dietary sodium	(n=105) Dietary potassium
Age (years)	30.4 ± 6.2	30.7 ± 7.6
Female (%)	70	30
Body weight (Kg)	68.1 ± 11.4	74.4 ± 11.5
BMI (kg/m2)	25.3 ± 2.6	25.4 ± 2.7
SBP sitting (mmHg)	138.9 ± 7.2	135.4 ± 7.3
DBP sitting (mmHg)	84.6 ± 6.7	85. 7 ± 5.7

Table No.2: Ambulatory blood pressure monitoring. Mean values of blood pressure in women

(n=105) Dietary sodium Women	(n=105) Dietary potassium Women
Systolic BP - 24 hours (mmHg)	Systolic BP - 24 hours (mmHg)
139.9 ± 9.2	123.4 ± 6.3
Diastolic BP - 24 hours (mmHg)	Diastolic BP - 24 hours (mmHg
88.6 ± 5.9	80. 9 ± 6.5

Table No.3: Biochemical profile of women

(n=105) Dietary sodium	(n=105) Dietary potassium
Fasting Blood Glucose(mg/dl)	
132.8 ± 4.2	98.4 ± 4.9
Total Cholesterol (mg/dl)	
245. ± 12.8	192.6 ± 30.5
LDL (mg\dl)	
127.8 ± 22.5	116.5± 18.5
HDL (mg\dl)	
57. ± 8.5	42.5 ± 9.2
Triglycerides (mg\dl)	
179.2 ± 32.5	143.3 ± 31.2

DISCUSSION

(Na) was unconnected to blood pressure variations through puberty, although amongst contributors with consumptions (4000mg/d) and more. Numerous research on children and minors have observed blood pressure and sodium intake, counting an previous research that create no strong connotation among girls .[13]Sodium is important for fluid balance and cellular homeostasis. Homeostasis define the role of sodium in fluid matrix" of the body .For homeostasis quantity of sodium is required associated with intake of sodium at optimum level.[2] BP replies to changes in dietary sodium vary widely, foremost to the perception of salt-sensitive (SS) BP. Those person who eat sodium per day more than (6.0g) they are at the risk of taking of hypertension Result showed special effects of dietary sodium on blood pressure have also produced opposing results, while current indication proposes that most BP upsurges are related with sodium consumptions of more sodium .[7] The connection among families and minors is mainly unexamined .[8]Numerous of scientific research designate that cumulative consumption potassium decreases BP in hypertensive grown ups. However, inhabitants-based research has unsuccessful to demonstration such an connotation.[11] In younger populations research showed that potassium effect are limited and restricted. This cross section study was directed in department of KIC, Physiology and Biochemistry Mirpur Azad Jammu and Kashmir from January 2020 to July 2021 after approval from hospital ethical committee. We select 210 women from Mirpur ajk and their blood pressure was assessed both systolic and diastolic pressure. We take history from women and those women take more sodium as compare potassium in their diet placed in Group A and those women take more potassium as compare to sodium in their diet placed Group B. We check their blood pressure at least six weeks in KIC Mirpur AjkConsequences from dissimilar research stages in (NH and NE) Examination result have been mutable.[14,15] Research data across numerous survey stages found that advanced sodium consumptions were related with advanced occurrence of raised Blood pressure.[16] We select 210 women for sodium and potassium diet from Mirpur ajk and their blood pressure was analyzed. Those women whose take sodium more in their diet their blood pressure was higher that as Systolic BP - 24 hours is (139.9 + 9.2 mmHg) and Diastolic BP - 24 hours is 88.6 + 5.9 mmHg, Those women who take Potassium higher as compare to sodium in their diet, their blood pressure is lower which is Systolic BP-24 hours 123.4 + 6.3(mmHg) and Diastolic BP-24 hours 80. 9 + 6.5 mmHg. We take blood samples from both groups women and analyzed the samples on Microlab 300 for serum lipid profile. (Cholestol, HDL, LDL, VLDL and Triglyceride). For

the study we use kits made of Merck Pvt. One research showed that SBP augmented by (0.4mmHg) for each-day upsurge in sodium consumption.[17] The result showed that potassium concentration and intake short and little effect on blood pressure as sodium intake or consumption in diet.[18] In study in boarding schools sodium consumption decrease blood pressure (1.7-m Hg and 1.5-mm Hg) with decrease 15% to 20% sodium consumption.

CONCLUSION

Sodium salt consumption in diet increased blood pressure with adverse effect in women and potassium salt intake in diet decrease blood pressure in women. There is recommended that women should take potassium containing diet.

Author's Contribution:

Concept & Design of Study:	Saeed Ahmed
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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

Vitamin B12 Deficiency in Patients with Type-II Diabetes Mellitus Using Metformin

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ABSTRACT

Objective: To find out the prevalence of vitamin B12 deficiency among the patients with type-II diabetes mellitus using metformin.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Abbasi Institute of Medical Sciences Muzaffarabad. Study was completed in six months duration from July 2021 to December 2021 for a period of six months.

Materials and Methods: All previously diagnosed cases with type-II diabetes mellitus using metformin for more than six months duration was included in this study. Blood level of vitamin B12 was measured in all cases. SPSS-17 software was used for data analysis. P-value <0.05 was taken statistically significant.

Results: Total 200 cases were studied including 127(63.5%) male and 73(36.5%) female cases. 23% diabetic patients using metformin were having vit-B12 deficiency with the blood level <150 pg/ml. age range of the patients was 30-75 years with mean age of 45.7 ± 5.8 years. Smokers were having more incidence of vit-B12 deficiency than non-smokers. Use of multivitamins prevent B-12 deficiency.

Conclusion: Use of metformin in diabetes mellitus is strongly associated with B-12 deficiency, so endocrinologist and physician should evaluate diabetic patients for B-12 deficiency and treat it properly.

Key Words: Diabetes mellitus,Vitamin B12, Metformin

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INTRODUCTION

Diabetes mellitus is defined as an endocrine disorder characterized by impaired metabolism of carbohydrates, fats and proteins.[1] 5-7% of united state population is affected from diabetes mellitus due to unhealthy eating practices and sedentary life style.[2] According to Al Saeed et al about 7.2 million Pakistanis are suffering from diabetes mellitus and its prevalence in urban population is 10.6% as compared to 7.7% in rural population.[3] Metformin from the group of biguanides is the most commonly used drug for type-II diabetes mellitus.[4] Its most common side effect is gastrointestinal disturbance that limit its compliance and efficacy.[5]

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Mostly neglected side effect of this drug is vitamin B-12 deficiency which can cause subacute degeneration of spinal cord.[6] Vitamin B12 deficiency is defined as concentration <150 pmol/L.[7] According to a study conducted by Alvarez et al B12 deficiency was found in 67% of study population.[8] Metformin decreases serum level of B12 by 22-29% as compared to placebo and glyburide.[9] Metformin associated B12 deficiency depends on the dosage and duration of metformin use and age of the patient.[10] Purpose of conducting this study is to highlight the most important side effect of metformin use causing B12 deficiency in diabetic patients that is commonly neglected. This study will help the physicians and endocrinologist to estimate frequency of B12 deficiency in diabetic patients to treat them early and prevent their complications and to consider dosage and duration of metformin in relation to B12 deficiency.

MATERIALS AND METHODS

This is a cross sectional study conducted in Abbasi Institute of Medical Sciences Muzaffarabad. Study was completed in six months duration from July 2021 to December 2021. Ethical approval was taken from the institutional review board and consent was also taken from all the patients for including them in this study. Sample size was calculated using WHO sample size calculator. Our sample size was 200 with 95% level of

significance. Using consecutive sampling technique all previously diagnosed cases with type-II diabetes mellitus using metformin for more than six months duration was included in this study. Blood level of vitamin B12 was measured in all cases. SPSS-17 software was used for data analysis. P-value <0.05 was taken statistically significant. All data was documented on a performa regarding age, gender, medical history, drug duration and dosage and history of peripheral neuropathy. Patients having B12 level <150 pg/ml were labelled as B12 deficiency, those having B12>220pg/ml labelled as having adequate level. Quantitative variables like age, disease duration, metformin dose, serum B12 level were expressed in means and standard deviation while qualitative variables were expressed in percentages and frequencies.

RESULTS

Total 200 cases were enrolled into this study including 127(63.5%) male and 73(36.5%) female cases. 23% diabetic patients using metformin were having vit-B12 deficiency with the blood level <150 pg/ml, 20(10%) cases with 150-220 pg/ml and 134(67%) cases had B12 level >220 pg/ml (Figure-I). age range of the patients was 30-75 years with mean age of 45.7 ± 5.8 years. Smokers were having more incidence of vit-B12 deficiency (19%) than non-smokers. This study showed that longer the disease duration more deficiency of B12 (p<0.001), similarly increased dose of metformin is associated with more deficiency of B12 (p<0.001) (Table-I).

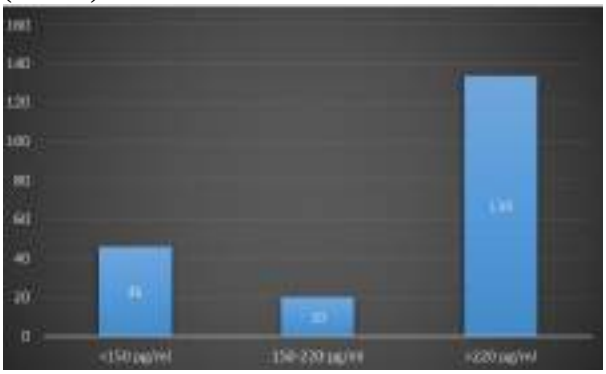

Figure No.1: Vit-B12 values

Table No.1: Baseline characteristics of study group (n=200)

Variables	Mean value
Age (years)	56.52 ± 12.87
Duration of Diabetes mellitus (years)	8.55 ± 4.76
Smoking	38 (19%)
BMI (Mean ± SD)	28.61 ± 3.88
B12 level (Mean ± SD)	457 ± 220
Metformin use	200 (100%)

DISCUSSION

Metformin is a first line of drug therapy in the treatment of type-2 diabetes mellitus.[11] It is taken orally. Its main side effect under study is deficiency of vit-B12. Mechanism by which metformin causes B12 deficiency is not known completely.[12] According to one theory metformin affect intrinsic factor-B12 complex formation hence inhibiting its absorption, but other mechanisms may be involved that are not clear yet.[13] Total 200 cases were enrolled into this study including 127(63.5%) male and 73(36.5%) female cases. 23% diabetic patients using metformin were having vit-B12 deficiency with the blood level <150 pg/ml, 20(10%) cases with 150-220 pg/ml and 134(67%) cases had B12 level >220 pg/ml. A previously conducted study by Lata Kanyal et al reported 31% cases using oral metformin were having B12 deficiency.[14] Elhadd et al stated that metformin dose in inversely proportional to the serum level of B12 with statistical significant p value <0.001.[15] Kim et stated that prevalence of B12 deficiency among the diabetic patients using metformin for more than 12 months was 25.4%. It is close to our study result of 23%.[16] A cross sectional study conducted by Hasan et al in Pakistan stated that B12 deficiency was more among type-2 diabetics using metformin (22.5%) than those not using metformin (7.4%).[17] Zalaket et al concluded that there is strong relation of duration of metformin use and B12 deficiency, hence increased duration more deficiency of B12.[18] Tesega et al reported that Type-2 diabetic patients using metformin for prolong period were having B12 deficiency in 43.7% cases.[19] Dietary habits can also influence serum B12 level which was not considered in this study so that is limitation of our study.[20]

CONCLUSION

This study concluded that prolong use of metformin causes B12 deficiency in significant number of type-2 diabetic patients. It is very important for physicians and endocrinologists to know strong relation of metformin dosage and duration of therapy to predict b12 deficiency and to manage it properly and it is also important for them to differentiate between diabetic neuropathy and B12 deficiency induced neuropathy.

Author's Contribution:

Concept & Design of Study:	Haseeb ul Hassan
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Data Analysis:	Noor-us-Sabahat, Khizra Manzoor, Maryum Saleem Raja
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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 Endocrine Complications in Thalassemia Children Admitted in A Tertiary Care Hospital

Endocrine Complications in Thalassemia Patients

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ABSTRACT

Objective: To determine the frequency of endocrine complications in thalassemic patients requiring repeated blood transfusion admitted in a tertiary care hospital.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Abbas Institute of Medical Sciences Muzaffarabad Azad Kashmir. Duration of study was from July 2021 to December 2021 for a period of six months.

Materials and Methods: Children of age 2-14 years with thalassemia major were included in this study. Venous blood sample (5 ml) was taken from the patients and sent to the institutional laboratory for specific investigations. Data was analyzed using spss-17 software.

Results: Total 180 cases were enrolled into this study including 110(61.1%) male and 70(38.8%) female cases. Mean age of the patients was 7.21 ± 3.54 years. Mean number of blood transfusions per month in this study was 3.32 ± 1.42 while 123 (68.3%) had blood transfusion more than two times per month in this study. Parental consanguinity was found in 130(72.2%) cases. Diabetes mellitus was found in 42(23.3%) and hypothyroidism was found in 28(15.5%) cases.

Conclusion: Significant frequency of endocrine complications was found in thalassemic children in our study. Endocrine complications were associated with age, number of blood transfusions per month, parental consanguinity and duration of disease.

Key Words: Thalassemia, Blood transfusion, Diabetes Mellitus, Endocrinal complications

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INTRODUCTION

According to a report of Thalassemia International Federation prevalence of Beta thalassemia is 200,000 patients all over the world.[1] Lack of proper early diagnosis, genetic counselling and screening, this problem is a big threat for future.[2] In beta thalassemia, there is reduced production of beta subunit of hemoglobin and leading to microcytic hypochromic anemia.[3] On hemoglobin analysis we see nucleated red blood cells in deranged peripheral blood smear and reduced level of hemoglobin-A. Hepato-splenomegaly and anemia are commonly found in patients with thalassemia major usually under two years of age.[4]

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MATERIALS AND METHODS

This is a cross sectional study conducted in Abbas Institute of Medical Sciences Muzaffarabad Azad Kashmir. Study was started in July 2021 and completed after six months in December 2021. Ethical consent was taken from the guardians of all patients and approval was also taken from the institutional review board. Sample size was calculated using WHO sample size formula. Consecutive sampling technique was used for sample selection. Patients with age 2-14 years, confirmed cases of thalassemia major on repeated blood transfusions (at least twice a month) of both genders were included in this study. Beta thalassemia was diagnosed on the basis of fetal hemoglobin level >50% on HB electrophoresis. All data was recorded on a predesigned performa. Venous blood sample (ml) was taken from the patients for specific investigations in the institutional laboratory. These tests were performed by a well-trained pathologist with at least five years of experience after post-graduation. Endocrinal complications were labelled if fasting blood glucose was >126 mg/dl on two different days (diabetes mellitus) and hypothyroidism when free T4 was <0.93 ng/dl. Data was analyzed using SPSS17 software. Means and standard deviation were determined for quantitative variables like age, disease duration, fasting

blood glucose level and free T4 level. Frequency and percentages were determined for qualitative variables like gender, parental consanguinity and residential area. P value < 0.05 was considered statistical significant.

RESULTS

Total 180 cases were studied including 110(61.1%) male and 70(38.8%) female cases. Mean age of the patients was 7.21 ± 3.54 years with age range of 2-14 years.

Table No.1: Characteristics of study cases (n=180)

Characteristics		Frequency (%)
Age (years)	<5	68 (37.8%)
	>5	112 (62.2%)
Gender	Male	110 (61.1%)
	Female	70 (38.8%)
Residential area	Rural	96 (53.3%)
	Urban	84 (46.6%)
Disease duration	<1 years	51 (28.3%)
	>1 years	129 (71.7%)
Number of blood transfusions	< 2 years	57 (31.7%)
	>2 years	123 (68.3%)
Parental consanguinity	Yes	130 (72.2%)
	No	50 (27.7%)
Hypothyroidism	Yes	28 (15.5%)
	No	152 (84.4%)
Diabetes mellitus	Yes	42 (23.3%)
	No	138 (76.6%)

Table No.2: Stratifications of endocrine complications with study variables

Characteristics		Endocrine complications Yes (70) No (110)		P-value
Age (years)	<5 (68)	9	59	0.014
	>5 (112)	61	51	
Gender	Male (110)	43	67	0.112
	Female (70)	27	43	
Residential area	Rural (96)	36	60	0.05
	Urban (84)	34	50	
Disease duration	<1 years (51)	25	25	<0.001
	>1 years (129)	45	84	
Number of blood transfusions per month	< 2 years (57)	14	43	0.003
	>2 years (123)	56	67	
Parental consanguinity	Yes (130)	62	68	<0.001
	No (50)	8	42	

Mean number of blood transfusions per month in this study was 3.32 ± 1.42 while 123 (68.3%) had blood transfusion more than two times per month in this study. Disease duration was <1 year in 51 (28.3%) while >1 year in 129(71.7%). Parental consanguinity was found in 130(72.2%) cases. Diabetes mellitus was found in 42(23.3%) and hypothyroidism was found in 28(15.5%) cases (Table-I).

Endocrine complications have been stratified with regard to the study variables in table-2.

DISCUSSION

Thalassemia is a heterogeneous group of inherited abnormalities of hemoglobin synthesis causing life-threatening anemia requiring repeated blood transfusions. Beta Thalassemia major is a severe form of thalassemia with short life expectancy and severe symptoms. Thalassemia is very common in Asian and Middle Eastern countries.[11] With the advancement of medical field now thalassemia patients have longer life expectancy than the past. In developing or under developed countries it is a major threat for the population and a great burden on the health system to manage these cases. With the passage of time its prevalence is decreasing due to public awareness and counselling of families regarding avoidance of cousin marriages. Its treatment require repeated blood transfusion to manage the anemia and chelation therapy for iron overload and management of endocrinal abnormalities like diabetes mellitus and hypothyroidism.[12] Bone marrow transplantation is an advanced definite treatment but very expensive and suitable for few patients only. According to a study by Hassan et al incidence of beta thalassemia major has decreased from 1:250 to 1:4000 live births.[13] According to Bordbar et al its incidence reduced from 2.3 to 0.82 cases per 1000 live births in a 10 years study duration.[14] Its incidence can be reduced using strategies like screening of population, genetic counselling and termination of affected pregnancies.[15] In our study 110(1.1%) were male and 70(38.8) were female cases. According to Casale M et al 65.7% of their thalassemic cases were male.[16] In our study mean number of blood transfusions per month in this study was 3.32 ± 1.42 while 123 (68.3%) had blood transfusion more than two times per month in this study. Disease duration was <1 year in 51 (28.3%) while >1 year in 129(71.7%). Parental consanguinity was found in 130(72.2%) cases. Diabetes mellitus was found in 42(23.3%) and hypothyroidism was found in 28(15.5%) cases. Previously a study conducted in Malaysia reported mean age of the cases in their study group as 10.8 ±3.44 years.[11] Yassin et al reported mean duration of disease 8.2 ±3.3 years in most of the cases in their study sample. This disease duration is very long as compared to our findings that may be due to increased life expectancy in their country due to advanced medical treatment as compared to our country with limited resources.[18] Previously a study conducted by Sevimli C et al reported diabetes mellitus in 43.8% and hypothyroidism 20% in their study cases.[19] These findings are comparable to our results.

CONCLUSION

In our study very high frequency of endocrine complications were found in thalassemic patients. Factors influencing frequency of endocrine

complications include age, gender, residential status, disease duration and number of blood transfusions per month. Genetic counselling, public awareness and population screening are effective strategies to reduce incidence of this disease.

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 Indications of Cesarean Section in Nulliparous Women Presenting in Labor

Uzma Shoaib[1], Sadaf Saifullah[1], Wajeha Khurshid[2], Sajida Iqbal[3], Atiya Bibi Khan[2] and Iram Sarwar[2]

ABSTRACT

Objective: To study the frequency of indications of cesarean section in nulliparous women presenting in labor.
Study Design: Descriptive case series
Place and Duration of Study: This study was conducted at the Obstetrics and Gynecology of Department, Ayub Teaching Hospital Abbottabad Jan 2019 to Dec 2020 for a period of two years.
Materials and Methods: 238 pregnant nulliparous females. Nonprobability purposive sampling technique. Only pregnant nulliparous females were included in the study. After taking written informed consent from every nulliparous pregnant female coming to labor room, history was taken, clinical examination and laboratory investigations were done. Data related to age, height, weight, BMI, parity and complications was obtained. All the data was subjected to SPSS version 20 for data analysis.
Results: The incidence of Cesarean section was maximum 175 (73.52%) at age group 16-20 years and was minimum 13 (5.46%) at age group 31-40. The incidence of Cesarean section was maximum 130 (54.62%) at height 5 feet and minimum 33 (13.86%) at height 5.5 feet. The incidence of Cesarean section was maximum 105 (44.11%) at weight group 45-60 Ibs and were minimum 33 (13.86%) at weight group 81-105 Pb. The incidence of Cesarean section was maximum 125 (52.52%) at body mass index 26-36 and was minimum 23 (9.66%) at body mass index 37-45. The incidence of Cesarean section was 123 (51.68%) in Lower segment cesarean section and 115 (48.32%) in vaginal delivery.
Conclusion: The rate of cesarean section in nulliparous was found to be 51.68% and this high rate could be explained on the basis of fact that the hospital receives high risk cases referred from other hospitals.

Key Words: Gestation, Pregnancy, Cesarean section, Fetal Distress, Obstructed Labor

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INTRODUCTION

One of the most common and frequently performed operations is incision of uterus to cause delivery of fetus. It carries very small harm to mother as well as fetus[1]. Various operations being done in labor room this one is less fatal[2]. Since Roman times it has been in use. But first evidence of performance of this procedure was available in history in late sixteenth century[3].

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In 2018; twenty one percent of all live born fetuses were through this operation in the whole world. In Brazil, Argentine and the like countries it was maximally performed operations of obstetrics. Chad was a country with least percentage of cesarean section. In India and Pakistan the percentage of births through cesarean section was almost same i.e., 14%[4]. In comparison to Latin America percentage of this operation performance is less in Asia[5]. But in countries like China the percentage of births by cesarean section is raising[6].

This procedure has lowered the occurrence of life threatening risks to both mother and neonates[3]. Although in America, Britain and the like countries percentage of this operation has raised up to twenty one yet no statistical evidence has been seen any further decrease in life threatening risks above fifteen percent of cesarean section operation. Rather increase in percentage of this operation has led to more chances of loss of life of female and neonate in those countries[6-10].

This procedure carries certain risks too. There may be side effects of medicines and physical damages of anesthesia procedure. Chances of getting fatal infections also exist. Hospital admission may be

extended leading to further financial burden. The neonate may also get hospital acquired infection[11,12].

Ayub Teaching Hospital (ATH) Abbottabad is one of the tertiary care hospitals of Khyber Pakhtunkhwa (KPK) that provides health care services not only to the population of whole Hazara Division but some parts of Azad Jamu and Kashmir, Gilgit Baltistan. Like the rest of the country, in the province of KPK the people are not observing family planning and a married couple carries four children on an average. As most of the marriages take place early adulthood so female above 21 years of age usually has a baby with her. Most of couples want to have children above four[13].

MATERIALS AND METHODS

Descriptive case series conducted at Obstetrics and Gynecology of Department. Ayub Teaching Hospital Abbottabad Jan 2019 to Dec 2020.

Sample Size: 238 pregnant nulliparous females.

Sampling Technique: Nonprobability purposive sampling technique.

Selection Criteria:

Inclusion criteria: All Nulliparous women at term (vertex and non-vertex) gestation with any presentation in active phase of spontaneous labor.

Exclusion criteria: All multipara women undergoing elective caesarean section and caesarean hysterectomy will be excluded from the study.

Collection of Data: After taking written informed consent from every nulliparous pregnant female coming to labor room she was enrolled in the study. Every enrolled nulliparous female was examined clinically after taking a thorough history. Laboratory investigations were done. Data was collected with respect to age, weight, parity, height, BMI and previous obstetrics history related to complications. Data was collected by a single person to avoid errors.

Statistical Analysis: All the data was subjected to SPSS version 20 for data analysis. Descriptive data was obtained. Their frequencies and percentage was generated. Tables were formed.

RESULTS

The incidence of Cesarean section was maximum 175 (73.52%) at age group 16-20 years and was minimum 13 (5.46%) at age group 31-40 as shown in table No 1.

The incidence of Cesarean section was maximum 130 (54.62%) at height 5 feet and minimum 33 (13.86%) at height 5.5 feet as shown in table No 2.

Table No 1: Age distribution of participants

Sr No	Age (years)	Cases (238)	age%
1	16-20	175	73.52%
2	21-30	50	21.00%
3	31-40	13	5.46%
Mean	**Standard Deviation**	**Minimum**	**Maximum**
23.92	4.07	16.00	40.00

Table No.2: Height of study participants

Sr. No	Height (Feet)	Cases (238)	age%
1	4.5	75	31.15%
2	5.00	130	54.62%
3	5.5	33	13.86%
Mean	**Standard Deviation**	**Minimum**	**Maximum**
5	0.07	4.5	5.5

The incidence of Cesarean section was maximum 105 (44.11%) at weight group 45-60 Ibs and were minimum 33 (13.86%) at weight group 81-105 Ibs as shown in table no 3.

Table No 3: Weight of study participants

Sr No	Weight (Pbs)	Cases (238)	age%
1	45-60	105	44.11%
2	61-80	100	42.00%
3	81-105	33	13.86%
Mean	**Standard Deviation**	**Minimum**	**Maximum**
64.13	7.14	45	105

Table No 4: Body Mass Index of study participants

Sr No	Body Mass Index	Cases (238)	age%
1	18-25	90	37.81%
2	26-36	125	52.52%
3	37-45	23	9.66%
Mean	**Standard Deviation**	**Minimum**	**Maximum**
26.90	3.19	18.76	45.21

Table No. 5: Frequency of indications of cesarean section

Cephalopelvic Disproportion	Cases (238)	age%
Present	11	4.62%
Absent	227	94.96%
Breech Presentation		
Present	24	10.08%
Absent	214	89.92%
Pre eclampsia		
Present	8	3.36%
Absent	230	96.64%
Eclampsia		
Present	14	5.88%
Absent	224	94.12%
Fetal Distress		
Present	46	19.32%
Absent	192	80.25%
Obstructed Labor		
Present	6	2.52%
Absent	232	97.48%
Placenta Previa		
Present	5	2.10%
Absent	233	97.90%
Twin Pregnancy		
Present	3	1.26%
Absent	235	98.74%

The incidence of Cesarean section was maximum 125 (52.52%) at body mass index 26-36 and was minimum

23 (9.66%) at body mass index 37-45 (table 4). The incidence of Cesarean section was 123 (51.68%) in Lower segment cesarean section and 115 (48.32%) in vaginal delivery as shown in table no 5. Frequency of indications of cesarean section is denoted in table no 5.

DISCUSSION

To incise the uterus to deliver the fetus has been practiced since centuries. In early days dead pregnant female was used to be incised through her uterus to get her baby to be delivered. But with advances in surgery this procedure was adopted to save lives of both mother and infant. Now a days this procedure is being done whether indicated or not. Percentage of babies born by this operation is rising throughout the globe. It is as low as 1.4% in Chad and as high as 55.5% in Brazil. It is done where medically indicated and sometimes on demand of female. In some countries it is practiced to have unethical financial benefits[14,15,16].

In this descriptive case series, 238 nulliparous pregnant females were studied. Their age ranged from 16 to 40 years. Age group ranging from 16 to 20 years experienced cesarean section maximum i.e., 73.52% (175). Age group ranging from 31 to 40 years experienced the least i.e., 13%. These results were in accordance with another study carried out in Ethiopia where the age group where it was performed least was above 30 years[17].

Females with height less than five feet had to experience more cesarean section as compared to females with height more than five feet. Same results were seen in a study brought out in Rwanda[18].

Similarly females with body weight between 45 to 60 pounds went through this procedure maximally i.e., 44.11%. Ladies with body weight ranging from 81 to 105 pounds went through this operation the least i.e., 13.86%. This was in accordance with another study carried out in France [19]. The most common indication of cesarean section in the study population was fetal distress in 47 (19.75%) patients. It was followed by breech presentation in 24 (10.08%) patients, eclampsia in 14 (5.88%), cephalopelvic disproportion in 12 (5.04%), and pre-eclampsia in 8 (3.36%) patients.

Other lesser indications for cesarean section were obstructed labor (6; 2.52%), placenta previa (5; 2.10%), twin pregnancy with one breech (3; 1.26%), 2 (0.84%) cases each of premature rupture of membranes (PROM), IUGR plus vaginal septum and prolonged latent phase of labor (2; 0.84%) and 1 (0.42%) case each of IUGR plus decreased fetal movements, IUGR plus oligohydramnios, oblique lie plus PROM, hydrocephalus, and occipito-anterior position. The researchers reported a cesarean section frequency of 6.2% with a range of 4.15 to 16.8%. . Before delivery hemorrhage and fits before delivery due to hypertension/fits due to hypertension were associated with mother death. Uterine rupture, anterpartum hemorrhage and cord prolapse were associated with early neonatal death[20]. In a study carried out in Karachi it was found that females with previous history of this procedure underwent the cesarean section maximally then delayed labor and non-progression of development of fetus was the least indication[21].

CONCLUSION

The most common indication for cesarean section was found to be fetal distress. It was followed by breech presentation. The least common indication was decreased movements of fetus.

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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

Online Teaching, a Big Challenge for Developing Countries during the Era of Covid 19, A Survey Conducted in Medical Students of Southern Punjab, Pakistan

Mukhtar Hussain[1], M. Ahmad Mukhtar[2], Amna Mukhtar[3], Naila Tariq[2], Aeimen Khalid[2] and Rubina Mukhtar[4]

ABSTRACT

Objective: To find out perception of medical students and scope versus limitations of online teaching in field of medical education during the course of Covid-19 pandemic when schools, colleges and universities were shut down in emergency and online teaching was initiated with intention to fill the stopgap with little to no preparation, inadequate resources and scarce training of teachers

Study Design: Observational study

Place and Duration of Study: This study was conducted at the different medical colleges of southern Punjab from January 2021 to December 2021 for a period of one year.

Materials and Methods: Self designed online questionnaire was circulated among medical students of south Punjab. Response of students was collected, recorded and analyzed for.

Results: Number of total participants was 485. Satisfaction level of students was not optimum being less than 35%. Ground reasons behind were deficiency in pertinent resources and materials, technical problems, lack of favorable home environment for online learning, non-availability of internet facilities to most of students living in remote areas. 68.5 % students rebuffed continuation of online classes with main reason of being unable to learn without one to one classes and to maintain daily routine.

Conclusion: Online teaching is a big challenge for education department especially in highly specialized field of medical education and might lower not the standard of education but also skills and competency of front line soldiers of future. There is utmost need for strategic planning to uplift our online medical education system to strengthen, secure and accomplish our health care system.

Key Words: Online Teaching, COVID-19, Education, Medical Students, Health System

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INTRODUCTION

Covid-19 pandemic is a big challenge of the day for healthcare system worldwide[(1)]. Pandemic emerged from china in 2019 and entrapped most of the countries in whole world [(2,3)]. Pandemic remained inauspicious and badly affected physical and mental health[(4)]. Millions of Covid 19 related deaths have been recorded. Most of the countries especially developing countries got their economy traumatized by pandemic leading to much challenges. Main focus of concern to utilize all available resources is to treat the infected patients, to control its further spread and to get out of economic losses, overwhelming the large adverse effect of pandemic on education system.

Lockdown is implemented by authorities as an emergency protocol in states of pandemics. During lockdown, the public is compelled to stay at home and avoid unnecessary visits at public a place that is another key step as a protective measure. Lockdown has worst effects not only on the economy but also the academic career of students due to closure of teaching universities and postponement of examinations[(5)]. A survey by UNESCO in 2017 showed that 264 million children are not registered in school worldwide[(6-8)]. Covid pandemic worsened the situation due to shut down of educational institution from Montessori to higher education level including all technical or non-technical level of teaching institute for in definite time[(9)].

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Students are the assets of any country who build the nation. Their education is already compromised in developing countries like ours not only because of poor strategic planning and least priority given in financial budgets but lack of public awareness, resources and poverty are other important factor. Lock down and closure of educational institutes further aided to downfall of education level of our students based on shifting of formal education to online. There is no didactical replacement of formal education involving teacher –student direct interaction but in the era of covid-19 and lockdown there was no other option then online distant learning to continue teaching with intention to compensate or to minimize the academic loss of university students especially students of health education[8].

MATERIALS AND METHODS

Self-designed questionnaire Google Performa was designed and distributed online or on whatsapp groups to conduct this observational survey. In addition to Scope and limitations, aptitude of medical students towards online teaching was questioned. Total 485 students both from preclinical and clinical classes responded to questionnaire. Students who willingly filled Performa completely were included while incompletely filled Performa excluded from the study. Response of students was recorded and shifted to spss 24 software for analysis. Response to questioners is shown in Table 01. Percentages and frequencies were applied to demonstrate the demographic data (Table 02).

RESULTS

Most of students were not satisfied with online teaching and preponderance was of clinical students. Majority of students were not in favor of continuation of online classes (Graph 01) based on two major reasons, First was the Most of students have no previous experience of online classes (Graph 02) while a significant majority forming 66% of total from remote areas were not even taught computer or electronic media in schools and even were unaware of computer use (Graph 3&4). Second main reason was the lack of training and practice of teachers for online teaching due to abrupt decisions by authorities to replace classroom teaching by digital teaching being the only solution to fill in the gap.

A considerable number of students (63%) showed casual attitude towards online classes and used to attend classes in bed without fresh up while a very small proportion of students remained disciplined for online classes. Mobile or Tab remained the most popular device used for digital classes (Table 03). Maximum rating that was 71% for digital learning was given to basic subjects that does not need any hands on or practical sessions. Clinical students were more worried for their clinical classes as direct interaction to patients was not possible via online system.

Table No.1: Showing response to Questionnaires

Sr#	Questions	Yes		No		Rare/ to some extent	
		Frequency	%tage	Frequency	%tage	Frequency	%tage
1.	Was computer taught in school?	226	32.8	159	67.2		
2.	Do you use computer for assignments?	348	10	49	71.7	98	18.3
3.	Have you used online teaching system before Covid -19?	82	16.8	333	68.7	70	14.4
4.	Would you like to continue online teaching in future?	153	31.5	332	68.5		
5-	Are you satisfied with online teaching?						

Table No.2: Showing Demographic features n=485

Demographic Feature	Frequency	%tage
Gender		
Females	274	56.5
Male	211	43.5
Total	485	100
Age		
<20	50	61
>20	189	39
Total	485	100
Study year		
Preclinical (1st + 2nd year)	213	36.9
Clinical (3rd + 4th +5th Year)	141	24.4
Total	485	100

Table No.3: Devices used for online teaching

Sr #	Device	Number of students used	Percentage
1-	PC	9	1.9
2-	Laptop	52	10.7
3-	Mobile/Tab	384	79.2
4-	opertunistic	40	8.2
	Total	485	100

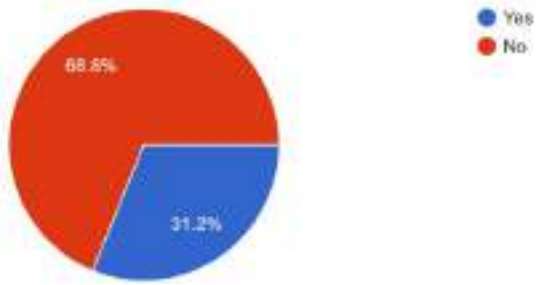

Figure No.1: Would you to prefer to contine with online teaching? – 481 response

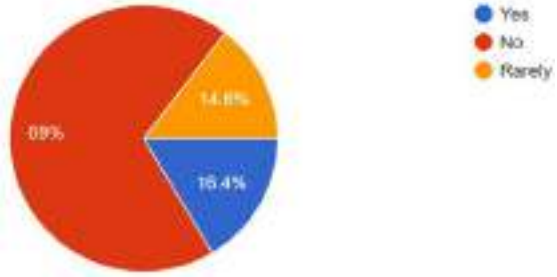

Figure No.2: Have you used online teaching and coaching systems BEFORE covid-19 lockdown? -– 481 response

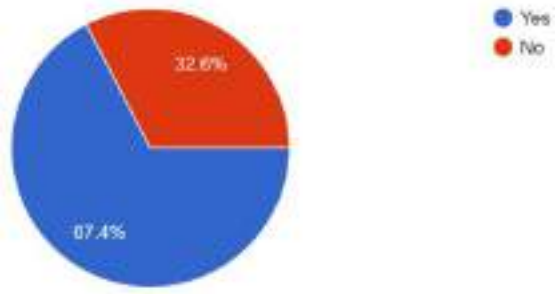

Figure No.3: Were you taught computer in school? - – 484 response

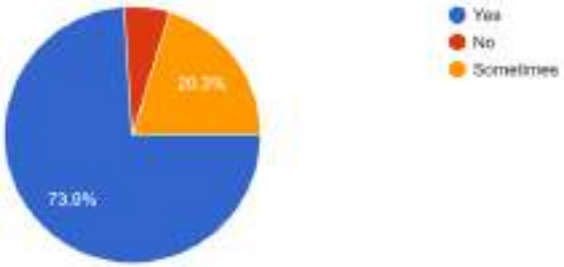

Figure No.4 Do you use computers/mobiles for your assignments? - – 484 response

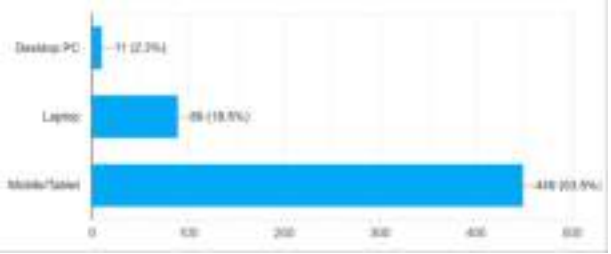

Figure No.5: What device you use for online learning purposes? – 480 response

DISCUSSION

Covid 19 is a highly infective disease presenting with Pneumonia like picture, caused by corona virus. It's a communicable disease that has proven transmission via animals and direct contact with infected human via touching, coughing and sneezing[2,10]. There is no definitive treatment protocols rather supportive treatment is the only elucidation for infected patients. Prevention is foremost affective in controlling this pandemic and is being exercised worldwide[4,11,12]. Thus the prime focus is to control its spread. Isolation and quarantine of infected patients are major measure to control the spread of infection. Use of face mask, frequent hand wash, Social distancing and to stay at home or self-quarantine are the key measures to prevent its spread[2,4,13].

It is imperative to stay at home to implement social distancing and to put this deadly disease behind bar. Different studies have shown significant impact of indoor confinement on mental stress and anxiety levels[4,14]. It is far much damaging for university students to stay home free of assignments. Lock down and shutting schools, colleges and universities was the only option to protect our children from deadly pandemic of Covid-19[15]. Temporary closer of educational institutes was decided by number of increasing countries including Pakistan.

In this epoch, online teaching or learning is the best possible solution to keep students busy on one end and to minimize their academic loss on the other end[14].

Although COVID 19 is a global issue and affected whole world but is more challenging in developing countries because of strain on already compromised health department and poor to negligible utilization of electronic media in education system. There was a great lapse of prerequisites for online teaching in our education department. Department was neither equipped nor up for it. Neither teachers nor students were proficient or having aptitude for online teaching[16]. All these together intensely affected our education quality especially that of medicine. Medical students are highly precious to be future frontline soldiers against these types of disasters[2]. A paramount concern is indispensable to scrutinize and rectify the short falls of online teachings.

Covid crisis forced the shifting of formal classroom education to distant learning that was taken as non-formal earlier. Seminars shifted to webinar and personnel meetings shifted to virtual ones[17]. A study by Lederman shows that both students and teachers are in a situation to face and pass this unwilling process of distant teaching and learning[6]. No other stopgap is on record to compensate the huge academic loss especially in field of medicine that is highly noteworthy. Medical education needs face to face classes and physical clinical training that was suspended during eve of

COVID for the sake of physical health of medical students who have always been at high risk of exposure to communicable diseases due to direct interaction with patients during wards classes. Abrupt decision of authorities to shift to online classes in the wake of their time and academic loss initially created lot of problems on both sides. Students were neither use to nor aware of this genre. Similarly teachers especially of our country being under developed country were not prepared for online classes. Lack of preliminary or rudimentary teachers' trainings reverberated in hassles of preparing for online lectures and presentations. More over infrastructure and resources for online classes were insufficient too. In sum, total forced students to continue learning at odds with their satisfactory level compromising the quality of education.

Online teaching has its own cons and pros. Multiple advantages include absent physical boundaries and convenient for students to learn in their comfort zone. Nevertheless it has its own challenges, even as one to one interaction being the best form of communication is usually best perceived in comparison to remote classes.

One study conducted by Graham & Pasi aided the stumbling blocks of online teaching and elaborated how prompt decision of school closure left no time for strategic planning and planned transition to remote learning. Examination oriented syllabi remained no longer fit for purpose as all exams and test were held up. Most of students bump into anxiety of uncertainty for their academic year progress in university[18]. Not only might this but slowed down the exam progress especially of those students who find no access to technology or befitting learning environment at home. In a nut shell, this pandemic has transformed centuries old face to face learning and teacher student relationship to that is technology driven one. Many factors including complexity, technical issues, insufficient infrastructure to consolidate a new medium are coupled with Stumbling blocks to assimilate multimedia based distant learning[19].

CONCLUSION

During the era of Covid-19, Unplanned and unanticipated execution of online teaching on hit or miss basis in contemplation of keeping students at home concerning their health has been a big challenge for under developed countries like ours with skimpy infrastructure for said purpose. This is a matter in question demanding instant and efficacious measures for tactic plans to minimize the decline in education, trainings and skills levels of medical students that might lead to downturn of our health care system.

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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

To Determine Frequency of Low Birth Weight in Pregnancies with Hyper-Uricemia and Pre-Eclampsia

Saliha Ghias Ud Din[1], Wajiha Shadab[2], Ayesha Mobeen[2], Sadaf Afzal[2], Farah Javed[2] and Mavra Tufail[2]

ABSTRACT

Objective: To determine frequency of low birth weight in pregnancies complicated with Hyper-uricemia and Pre-eclampsia.

Study Design: Descriptive Cross-Sectional study

Place and Duration of Study: This study was conducted at the Department of Obstetrics and Gynecology, Islamic International Medical College Trust, Railway Teaching Hospital, Rawalpindi from September 2014 to March 2015.

Materials and Methods: 80 singleton term pregnant women with preeclampsia and hyperuricemia delivered either by vaginal delivery or caesarian section were included in the study. Non-probability consecutive sampling technique was used. Study group had blood pressure >140/90 mmHg on at least two distinct time 4 hours apart and proteinuria of >300 mg /24 hours measured by urine dipstick method. Fetal weight was measured 10 minutes after delivery of baby. One sample t-test was applied to find out any significant difference regarding the low birth weight in study population. Association of low birth weight with gestational age, parity type, age groups and serum uric acid level was also assessed by applying chi square test.

Results: Mean of age of the subjects was calculated as 26.86 $\pm$4.525 years. Mean birth weight of the neonates was calculated to be 2.382 $\pm$ 0.298 kg. 60 (75%) neonates had birth weight less than 2.5 kg and 20 (25%) neonates had birth weight 2.5 kg or more with the p value of 0.043 indicating a statistically meaningful difference.

Conclusion: Frequency of babies with low birth weight increases in pregnancies that are complicated with hyperuricemia and pre-eclampsia as 75% neonates reported low birth weight.

Key Words: Hyperuricemia, pregnancy induced hypertension, Frequency, Low birth weight

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INTRODUCTION

Pre-eclampsia accounts for about three to five percent of all the pregnancies[(1)]. It is second most important cause of maternal mortality and responsible for increase in preterm birth, perinatal mortality and around 30% low birth weight newborns[(2)]. Obesity, anemia, and chronic hypertension are notable risk factors for pre-eclampsia.[(3)]

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Pre-eclampsia mainly occurs because of placental dysfunction, and it comprises of vasospasm, endothelial dysfunction, thrombosis of placenta and defective trophoblastic invasion[(4)]. Pre-eclampsia can also result in decreased liquor and non-reactive cardiotocography and bad biophysical profile in the fetus[(5)].

Raised serum uric acid level in first twelve weeks of pregnancy is linked with development of preeclampsia later[(6)]. Increased uric acid level results in oxidative stress that results in reduced uterine contractility and altered vascular relaxation[(7)].Proteinuria is the clinical manifestation which is used to diagnose the disorder[(8)]. Women with pre-eclampsia and raised uric acid levels have high incidence of preterm delivery resulting in increased neonatal intensive care unit admissions. This can be due to low birth weight, hypoglycemia, jaundice, hypoxia, respiratory difficulties, neonatal sepsis and prematurity[(9)]. Proposed etiologies for raised uric acid are altered kidney function, excessive tissue degradation and acidosis[(9)]. In non-pregnant population, raised uric acid is regarded risk factor in causing raised blood pressure, cardiovascular disease and kidney disease[(10)].

According to the study by Kang, in women with pre-eclampsia raised uric acid not only indicates disease

severity but is also involved directly in the pathogenesis of the disorder[11]. Hyperuricemia (>4.5 mg/dL) is the first biomarker seen in the laboratory tests providing early evidence of disease at 20 or less gestational weeks. Hyperuricemia has also demonstrated its usefulness to predict maternal and fetal complications and disease sequelae at a later age for both mother and baby[12].

Neonatal outcome depends primarily on weight at birth[13]. Low birth weight causes significant burden on health services. It can lead to diseases like diabetes, hypertension, obesity, and heart diseases in adulthood leading to profound impact on the society's burden of disease and finances[14]. Serum uric acid has a strong relation with low birth weight in pre-eclamptic women[15]. There is insufficient research data regarding the neonatal outcomes in hyperuricemia and pre-eclampsia complicated pregnancies. This study aimed to assess the occurrence of low birth weight among pregnancies complicated with hyperuricemia and pre-eclampsia. Results of the present study contributed to guiding the obstetrician to recognize the adverse outcomes of the synergistic effect of hyperuricemia and pre-eclampsia and make decision to improve both maternal and fetal outcome.

MATERIALS AND METHODS

A descriptive cross-sectional study was performed in the of Gynecology & Obstetrics department of Islamic International Medical Complex Trust, Railway Teaching Hospital, Rawalpindi from 29th September 2014 to 29th March 2015. Study was conducted with the consent of hospital ethical committee. A total sample of 80 patients was estimated utilizing World Health Organization sample size calculator. Non-probability consecutive sampling technique was used. Singleton, cephalic, term (37>/= completed week) with preeclampsia and hyperuricemia delivered either by spontaneous vaginal delivery or caesarian section were included in the study. All other causes of low-birth-weight babies like anomalous babies, all high-risk pregnancies like diabetes mellitus, multiple gestations, coagulation disorder, moderate to severe anemia and patients taking hyperuricemic drugs like thiazide diuretic, pyrazinamide were not included in the study.

Verbal consent had been taken from the subjects. Study group had blood pressure >140/90 mmHg on two distinct occasions 4 hours apart and proteinuria of >300 mg /24 hour measured by urine dipstick method. Fetal weight was measured 10 minutes after delivery of baby. Serum uric acid was measured by consultant hematologist in Railway Hospital Rawalpindi.

The collected data was entered in SPSS version 20. Descriptive analysis was done for age, uric acid, gestational age, and birth weight. Qualitative variables like low birth weight, parity, were featured as frequencies and percentages. One sample t-test was applied to find out any significant difference regarding the low birth weight in study population. Association of low birth weight with gestational age, parity type, age groups and serum uric acid level was also assessed by applying chi square test. A p-value of ≤ 0.05 was deemed as significant with 95% confidence interval.

RESULTS

80 pregnant women achieving the inclusion and exclusion criteria were registered after informed consent. Mean age of the patients was 26.86 $\pm$ 4.53 years. 29 (36.2%) patients were ranging from 18 to 24 years, 28 (35%) ranged from 25 to 29 years and 23 (28.8%) patients were 30 years or more. Gestational age of the subjects was recorded to be 38.50 $\pm$ 0.35 weeks. Levels of serum uric acid were observed to be 5.38 $\pm$ 0.76 mg/dl. Mean birth weight was calculated to be 2.38 $\pm$ 0.29 kg. 35 (43.8%) females were primigravida, 20 (25%) were para 1 and 25 (31.2%) were para 2 and more.

Regarding frequency of low-birth-weight babies in pregnancies complicated with hyperuricemia and pre-eclampsia, 60 (75%) neonates had birth weight less than 2.5 kg and 20 (25%) neonates had birth weight 2.5 kg or more with the p value of 0.043 indicating a statistically significant difference.

TableNo.1: Association of low birth weight with gestational age, parity type, age groups and serum uric acid levels by applying chi sq test

Factors	Birth Weight		p-value
	Birth weight less than 2.5 kg n=60	Birth weight 2.5 kg or more n=20	
Gestational Age (Weeks)			
less or equal to 38.5 weeks	43 (71.6%)	11 (55%)	0.168
more than 38.5 weeks	17(28.3%)	09 (45%)	
Parity Type			
Primigravida	28 (46.6%)	07 (35%)	0.104
Para 1	17 (28.3%)	03 (15%)	
Para 2 or more	15 (25%)	10 (50%)	
Patients Age (Years)			
18 - 24 years	22 (36.6%)	07 (35%)	0.754
25 - 29 years	22 (36.6%)	06 (30%)	
30 years or more	16 (26.6%)	07 (35%)	
Serum Uric Acid Level (mg/dl)			
less or equal to 5.5	43 (71.6%)	16 (80%)	0.463
more than 5.5	17 (28.3%)	04 (20%)	

In our study 59 (73.8%) women whose uric acid levels was up to 5.5 mg/dl had 43 (71.6%) babies with low birth weight and 21 (26.2%) women with uric acid

more than 5.5 mg/dl had 17 (28.3%) babies with low birth weight. Similarly, according to the gestational age, 54 (67.5%) neonates had gestational age less or equal to 38.5 weeks and 26 (32.5%) neonates had gestational age of more than 38.5 weeks.

Association of low birth weight was also evaluated with respect to gestational age, parity type, age groups and serum uric acid level as shown in Table-1. There was not any statistically substantial difference found with any of the variables under investigation showing no significant association. Thus, low birth weight of the babies is not corelated with gestational age, parity type, age groups and serum uric acid level.

DISCUSSION

Recently the effectiveness of hyperuricemia has been highlighted not only as a biomarker of preeclampsia but also as a predictor of undesirable fetal and maternal outcomes. The present study shows that finding maternal hyperuricemia nearby delivery is related to adverse maternal and fetal outcomes. Gestational hypertension with the occurrence of hyperuricemia increases the fetal risk as suggested in a study conducted by Hawkin et al[16]. Earlier studies have also indicated a relationship among hyperuricemia and adverse obstetric outcome in hypertensive pregnancy[17][18][19]. Results of our study also strengthen this relationship and it is shown that women with hypertension in pregnancy along with high uric acid results in low-birth-weight babies. Hyperuricemia in women with preeclampsia results in renal disease in mothers and preterm births.

In the present study 59 women whose uric acid level was up to 5.5 mg/dl had a more babies 43 (72.8%) with low birth weight, compared to the women with uric acid above 5.5 mg/dl (n = 17, 28.3%). However, this variation was not significant (p = 0.463). This demonstrated that as the level of serum uric acid increases the incidence of low-birth-weight increases. D' Anna et al, 2000 and Feig et al. 2004 present similar results[20][21].They demonstrated significant relationship among hyperuricemia and fetuses with low birth weight. Another study conducted by Devia et al also revealed similar trend[22]. This tendency of raised uric acid leading to poor outcome as concerned to fetus implies that most likely it's causing growth restriction and the outcome is manifested as low birth weight.

There is a debate concerning whether uric acid is only a biomarker of disease or direct contributory in evolution of preeclampsia and fetal growth restriction [23]. While the exact origin of raised uric acid in preeclampsia is not exactly known decreased renal clearance has been suggested as a plausible cause in studies[24]. This tendency of decrease in clearance of urate generated by the infusing vasoconstrictors like norepinephrine and raised blood uric acid level and decrease clearance detected in glomerulonephritis might imply that the uric acid could become an early indicator of preeclampsia[25]. Beside decreased clearance of uric acid by kidneys increased production by placenta because of ischemia is also seen. Elevated levels of metabolites of purine have been detected in fetuses exposed to hypoxia[26] which enters maternal circulation where they are degraded by maternal xanthine oxidase in preeclampsia. This mechanism explains the link between the raised uric acid levels and restricted fetal growth. Proactive role for uric acid in the evolution of pre-eclampsia has been proposed[27]. The consequent poor fetal outcome in patients with high levels of uric acid implies that it causes growth restriction, reflected as low birth weight[6].

From these findings it can be presumed that adverse fetal consequences in pre-eclampsia, may be the result of hyperuricemia associated with pre-eclampsia. Put differently in pre-eclampsia, the higher the levels of uric acid the higher the chances of adverse fetal effects. Thus, serum uric acid assessment can serve as a good prognostic tool in identifying the gravity of the disease and accordingly decide the time of delivery to ensure safety both for mother and the fetus. Pakistan is a developing country and cannot afford high health budget. Results of this study will guide the obstetrician in recognizing the burden of this disease.

CONCLUSION

Raised uric acid level associated with pre-eclampsia is a significant risk factor for poor fetal outcome. Frequency of babies with low birth weight increases in pregnancies that are complicated with hyperuricemia and pre-eclampsia as 75% neonates reported low birth weight.

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Original Article

Clinical Reasoning And Problem-Solving Skills

Creating High Cognitive Level MCQS will Drive Students to Clinical Reasoning? A Case Study

Imtiaz Uddin[1], Halima Sadia[2], Mehreen Lajber[1], Husnain[2] and Somia Afzal[2]

ABSTRACT

Objective: To develop clinical reasoning and problem-solving skills, medical students must be assessed at a high level of cognition according to Bloom's taxonomy. MCQs are the most employed assessment tools in medical education.

Study Design: Quantitative cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Pharmacology, Bacha Khan Medical College Mardan from 2016 to 2019.

Materials and Methods: A quantitative cross-sectional study has been performed using 250 MCQs in the final assessment exam of Bacha Khan Medical College Mardan. Each MCQ was analysed separately by five independent assessors to score it according to modified Bloom's Taxonomy. Three students also analysed each MCQ for the level of cognition. Inter-rater reliability was determined both for students and faculty. Item Analysis for MCQs was also performed.

Results: The findings showed that for high-level MCQs, inter-rater reliability between faculty was in a good range of 0.78 while between faculty and students were low as 0.27. It was also found that most high-level MCQs were in the poor discriminative index.

Conclusion: Low inter-rater reliability between students and faculty shows that faculty may create an MCQ at a high level, but the students' approach towards it may be lower order. Along with improving the assessment standards, it is also necessary to explore other factors, especially the teaching strategies to foster high-level critical thinking and clinical reasoning in medical students.

Key Words: Clinical reasoning, MCQs, Item analysis

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INTRODUCTION

Medical students must attain learning at a high level of cognition to develop clinical reasoning, critical thinking, and problem-solving skills. These competencies are essential for clinical practice[1]. It is now greatly emphasized that these competencies should develop in preclinical years. The development of these competencies requires proper instructional strategies and an assessment system. Bloom's taxonomy is the most important framework from which the educators have taken help in designing instructional strategies and assessment at a high level of cognition[2].

The modified Blooms taxonomy having three tires is most commonly applied for this purpose due to more inter-rater reliability, especially in designing ssessments[3].

In medical education, the most commonly used tool for assessment is the MCQs. With proper training, it is possible to construct MCQs that assess a high level of cognition[4]. MCQs at a high level can also be generated through software'[5]. The validity of MCQs to test the higher level of cognition has been established through various studies[4]. A significant correlation has also been found between MCQs at a high level and other assessment tools as for as student assessment score is concern[6]. MCQs created at a high level of cognition have a strong test effect[7]. It has been found that students who pass through the assessment system have a more significant percentage of MCQs of high cognition prefer deep learning. Due to a more significant percentage of low-level MCQs in examinations, it has been assumed that medical students have resorted to superficial level learning[8]. However, in most pre-clerkship medical exams, a meager percentage of high-level MCQs have been found[9]. Even in most clinical subject exams, the MCQs are of recall level with significantly less percentage in a higher level of cognition[10].

It can be inferred from these findings that if MCQs are created by faculty to be categorized as high level, the

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student will also approach them in the same order. However, some of the recent studies are in contrast with this concept. Some studies have found statistical differences in the perspective of faculty and students and among the students for low and high-level MCQs[11].Low performers with less confidence may put an MCQ in higher-order, categorized as low order by faculty. Similarly, higher performers may assign a higher-order MCQ to lower-order due to cueing and pattern recognition[12]. It has been suggested that one of the main factors for students to approach an MCQ for a level of cognition is the instructional strategy. Students taught a particular course content at a higher level will approach the relevant MCQ in that particular order and vice versa [13] However, one of the previous studies showed no significant difference in scores of two cohorts, undergone conceptualized and route learning[14]. So, the most important aspect related to the MCQs level of cognition is whether the perspective of faculty (MCQs creators) and students (examinees) is the same for a higher level. Do the students approach the MCQs designated by faculty at a higher level in the same order? What is the validity of higher-order MCQs based on item analysis if the students are taught through instructional strategies that foster only low-level cognition?

This study has been performed to find the interrater reliability of high cognitive level MCQS between faculty and students. High-level MCQs are also evaluated for their validity in terms of difficulty Index and discrimination index. Their difficulty has also been compared with low-level MCQs**.**

MATERIALS AND METHODS

A quantitative, cross-sectional descriptive design was used to conduct the study. All the MCQs from the final exams of Bacha Khan Medical College Mardan from 2016 to 2019 in Pharmacology were included in the study. The total number of MCQs was 250. According to Modified Blooms Taxonomy, each MCQ was analyzed separately by five independent assessors (Faculty members) against preformed criteria to score it as level I, level II or level III of the cognitive domain. Three students also analyzed each MCQ at level II and Level III for the level of cognition. The students who were selected were high performers. Inter-rater reliability was determined both for students and faculty. Item Analysis was also performed to determine the discriminative Index and Item difficulty index. Table 1 shows the Proforma of MCQs evaluation for scoring the level of cognition according to Bloom's Taxonomy[15].

RESULTS

The findings showed that most MCQs were at the C1 level with no MCQs in C3level. MCQs in C2 level in 2016,17 18 19 were 8% 20% 10% and 6% respectively. For high-level MCQs, inter-rater reliability between faculty was in the good range of 0.78, while between faculty and students were low as 0.27.

Table No.1: Proforma of MCQs evaluation for scoring the level of cognition according to Blooms Taxonomy

Question No.	Blooms Taxonomy
	Level I Knowledge (recall of information including direct questions asking to check the factual recall, containing words like enumerate list.)
	Level II Application (ability to interpret data; questions including lab data or containing words like analyse)
	Level III Problem–solving (Use knowledge and understanding in new circumstances, including scenario-based questions containing case description and lab data asking students to initially make a diagnosis and then suggest the subsequent appropriate investigation; management modalities and counsel*ling.*

The mean difficulty level for C1 level MCQ was 0.37±.04 while that for C2 was 0.23. ± .01 .C2 level MCQs were significantly more complex than C1 level. Evaluating the quality of C2, it was found that most MCQs were in poor discriminative index with a mean value of 0.31±.02

DISCUSSION

In this study, inter-rater reliability for high-level MCQs among the faculty was high, while low between students and faculty. This is in accordance with the previous study[11].In one of the studies, it was found that students approach the level of cognition for particular MCQs depending on their competency. Those students who are well performers approach the MCQs directly by recognising various patterns, while low performers approach it as high level by analytic thinking and problem solving[12]. In another study, it was found that the faculty may assign an MCQ as high order may be approached by the students as low order while an MCQ assigned by faculty as low order may be approached as high order by the students due to various factors of pattern recognition, cueing and most importantly their learning methods[13].

The result of this study showed that high-level MCQs were more challenging in comparison to low-level MCQs. Previous studies in various fields have shown the same findings[16,17,2]. It can be concluded from this finding that as high-level MCQs involve high-level critical thinking, so they require more effort in solving, as evident from their high difficulty index

The most exciting finding of this study shows that the mean Discriminative Index of the MCQs in the C2 level

is in the poor range. This means that high cognition level MCQs are not performing well. A previous mega study conducted in non-medical subjects showed similar results. That study showed C1 level MCQs having a better discriminative index[17]. In contrast, another study found higher level MCQs to have better discriminative indices than low-level MCQs [16]. So, the high cognitive level as designated by the faculty cannot be alone taken as the sole factor for the validity of MCQs.

In conclusion, it can be stated that faculty may create an MCQ at a high level, but the student's approach towards it may be in the lower order. This factor affects the validity of high-level MCQs, as evident by the poor Discrimination index. Along with improving the assessment standards, it is also necessary to explore other factors, especially the teaching strategies to foster high-level critical thinking and clinical reasoning in medical students.

CONCLUSION

Low inter-rater reliability between students and faculty shows that faculty may create an MCQ at a high level, but the students' approach towards it may be lower order. Along with improving the assessment standards, it is also necessary to explore other factors, especially the teaching strategies to foster high-level critical thinking and clinical reasoning in medical students.

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Original Article

Comparison of Efficacy of Foleys Catheter with Prostaglandin E2 Gel for Induction of Labor in Women with Previous One Caesarean Section for Non-Recurrent Cause

Laila Zeb, Tanveer Shafqat and Nosheen Akhtar

ABSTRACT

Objective: To compare the efficacy of Foley's Catheter versus Prostaglandin E 2 GEL for IOL in women with previous one Caesarean Section for a non-recurrent cause.

Study Design: Randomized controlled trial study

Place and Duration of Study: This study was conducted at the in Gynae B unit MTI, LRH, Peshawar from 4th December 2019 to 3rd June 2020.

Materials and Methods: Ninety (90) women undergoing IOL at term pregnancy with previous one cesarean section for non-recurrent causes were included. They were grouped randomly as group A (Foley catheter group) & group B (prostaglandin E2 (PGE2) gel group) by using the lottery method. Patients in both groups were analyzed for successful induction, induction delivery interval, and complications like hyper stimulation, fetal distress, and scar dehiscence. Data was entered in a structured proforma and analyzed using SPSS version 19.

Results: Mean age of women in group A was 28.68 ± 3.26 years and mean gestational age was 38.62 ±1.26 weeks. In group B mean age was 27.577± 3.07 years and mean gestational age was 38.777±1.49 weeks. The delivery interval after induction was16.04 hrs. in group A and 20.84 hrs. in group B. In group A, the delivery within 24 hours was seen in ales (89%) women who were > 39 weeks pregnant. Delivery within 24 hours was seen in 36(80%) patients in group A as compared to 22(48.9%) in Group B (P 0.002).

Conclusion: In this study, both the methods of induction in the women with a previous cesarean section were safe and effective. The cervical ripening effect of the Foley catheter was as good as that of the Prostaglandin E2 gel.

Key Words: Foley catheter, Induction of labor. Prostaglandins E2 gel.

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INTRODUCTION

Obstetricians are reluctant to give Trial of Labor to women who have had a previous cesarean section because there is a risk of uterine rupture, which might pose a threat to the mother and the fetus, as well as the possibility of subsequent litigation.[1,2] Although the trial of labor is safe, but it is not without risk and should be done with caution[3]. According to studies on vaginal birth after cesarean section, 60–80 percent of women who are allowed to labor after a previous cesarean section would deliver vaginally.

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The majority of studies on prostaglandin E2 gel (PGE2) induction have been conducted on women with simple obstetric histories, and there has been little research on the outcome and safety of vaginal prostaglandin for labor induction in individuals who have undergone previous caesarean section. The American College of Obstetricians and Gynecologists (ACOG) is not recommending the use of prostaglandins for labour induction.[4] However Prostaglandins are recommended by the Royal College of Obstetricians and Gynecologists even in situations of a trial of labor in women with previous cesarean section. [5-6]

In vaginal births with a history of Cesarean section, uterine rupture is a well-known but uncommon complication. In women with previous one CS, the incidence of uterine rupture was 0.5–0.9 percent, compared to 0.2 percent in women who have never had a CS. [7]Although in women with a previous CS the overall incidence of UR is low. Among women attempting vaginal birth after a previous cesarean section, labour is induced in 18%-27%. Previous studies have shown that 60%-80% of women with one previous cesarean section will deliver vaginally if a trial of labor is allowed, even when induced. [8]

Pharmacological agent (such as prostaglandins (PGE), oxytocin, estrogens, mifepristone) and non-pharmacological techniques (such as a transcervical Foley catheter, bougies and fore waters amniotomy) are used to ripen the unfavorable cervices.[9] The intracervical Foleys balloon catheter for cervical softening is gaining popularity for IOL in previous scars, with results comparable to pharmacological agents.[10,11] Prostaglandins given externally promote cervical ripening and expedite the delivery , but these also increase uterine hyper stimulation and lead to an abnormal fetal heart rate changes. In addition to maternal issues, uterine rupture can result in neonatal morbidity and stillbirth.[12] So, in women who have had a previous cesarean section, a cautious strategy for labor induction may be used.

MATERIALS AND METHODS

This Randomized controlled trial was conducted in Department of Obstetrics and Gynecology "B" Unit; Lady Reading Hospital Peshawar from 4th December 2019 to 3rd June 2020.Aproval was taken from hospital Ethical board. Sample size was 90 i.e. 45 in each group. P1 success of Foley catheter for labor induction being 84% & P2 success of Prostaglandin E2 for induction of labor being 50 % based on previous study. Significance level was 5% and power was 80% under WHO sample size calculation formula.

Sampling technique was Consecutive non-probability sampling. Inclusion criteria included women aged 18 to 35 years with previous one cesarean section for non-recurrent causes, Gestational age of ≥ 37 weeks assessed by early ultrasound, Singleton pregnancies with a cephalic presentation and Bishop's score of ≤ 6 were included. Women with controlled gestational diabetes mellitus and mild pregnancy induced hypertension were also included. While patients with previous one classical caesarean section, relative cephalopelvic disproportion, polyhydramnios, placenta previa, estimated fetal weight > 4.2 kg and positive scar tenderness were excluded. All women admitted to Department of Obstetrics and Gynecology "B" unit, Lady Reading Hospital Peshawar were included in the study that fulfilled the inclusion criteria. A written informed consent was taken from them for including them in the study. A detailed history, examination and investigations were done. A CTG was done before starting IOL. They were grouped randomly as group A (Foley catheter group) & group B (prostaglandin E2 (PGE2) gel group) by using lottery method. In group A, a 16-18 French Foley catheter with a 30-40ml balloon was inserted into the endocervical canal and the balloon was inflated with 30-40ml of sterile water to ripen the cervix under aseptic conditions. The catheter was strapped to the thigh with gentle traction. The catheter was checked for its position and the traction at 4-6 hours intervals. The time limit for catheter was 24 hours if it was not expelled spontaneously and whether the modified Bishop's score had improved or spontaneous rupture of the membranes had occurred. Patient was put on I/V antibiotics. In group B 0.5 mg Dinoprostone PGE2 gel was used. The next dose was repeated at 6 hours if the Bishop's score ≤ 6. In both groups if bishop score was improved then artificial Rupture of the Membranes (ARM) was done, followed by the starting with an intravenous oxytocin infusion of 2.5 units of oxytocin in 500ml of 5% dextrose at 10 drops/minute. The dose was increased at 10 drops/minute interval up to a maximum of 60 drops/ minute, or till the desired uterine contractions achieved. Meanwhile all the women in both groups were monitored for scar tenderness. Pulse was recorded after every 15-30 minutes in active stage of labour. Fetal wellbeing was checked by intermittent auscultation and one hourly Cardiotocography (CTG). Labour progress was monitored on Partogram. In case of failure to deliver within 24 hours or complication like fetal distress, uterine rupture, scar dehiscence, Category I cesarean section was done. All the information obtained including demographic details was entered in predesigned proforma. Statiscal analysis was done in SPSS 19. Mean and standard deviation were calculated for numeric variables like maternal age, gestational age, modified Bishop Score at induction and after 12 hours of induction, delivery interval after induction and parity in both groups.

Frequency and percentages were calculated for both groups for categorical factors such as delivery within 24 hours after induction. Successful induction was stratified by maternal age, gestational age, parity, and the modified Bishop Score at the time of induction in both groups. The Chi-square test was performed to evaluate outcomes in both groups after stratification, with a p-value ≤0.05 deemed significant.

RESULTS

Table No.1: Demographics of Both Groups (mean values)

Demographics	Group A (N=45)	Group B (N=45)
Patients' mean age in years	28.68± 3.26	27.57±3.07
Patients' mean gestational age in weeks	38.62 ±1.26	38.77±1.49
Score of Bishop Scale (at induction)	3.62 ±1.46	3.35 ±1.43
Bishop score after 12 hours of induction	8.62 ±1.91	6.86 ±2.41
Delivery interval after induction(hours)	16.04 ±5.89	20.84 ±6.60
Parity	1.64±1.02	1.57 ±1.01

The demographics of Group A and B are given in Table 1. The two groups were almost similar in maternal age, gestational age, and Bishop score at the time of induction, but differed in the Bishop score after 12 hours of induction (8.62 versus 6.86) and in the delivery interval after induction considerably.

In Table 2, the A and B groups were further divided based on induction to the delivery interval. Delivery within 24 hrs. (P-value of 0.005), occurred in the 18-27-year age group.

Table No.2: Induction delivery interval in different age groups

Age Range	Groups	Delivery within 24 hours		P-value
		YES	NO	
18-27 Years	A	16 (84.2%)	31 (5.8%)	0.005 (signi-ficant result)
	B	11 (42.3%)	15 (57.7%)	
28-35 Years	A	20 (76.9%)	6 (23.1%)	0.173
	B	11 (57.9%)	8 (42.1%)	

Table 3 Shows the delivery intervals in two gestational age groups. In group A, the delivery within 24 hours was seen in the maximum number of females (89%) that were greater than 39 weeks pregnant. There existed a significant difference (p-value: 0.008) between two groups A and B, with a gestational age of 37-39 weeks.

Table No.3: Delivery Interval with Respect to Gestational Age

Gestational age	Groups	Delivery within 24 hours		P-value
		Yes	No	
37-39 weeks	A	28 (77.8%)	8 (22.2%)	0.008 (signi ficant result)
	B	16 (47.1%)	18 (52.9%)	
>39weeks	A	8 (88.9%)	1 (11.1%)	0.095
	B	6 (54.5%)	5 (45.5%)	

A significant number (78%) of women in group A with parity between 1-3, delivered in 24 hours (p value= 0.008). While, in another category (parity >3), 100% females of group A had delivery within 24 hours. 95.2% of women in group A with Modified Bishop Score of 0-3, delivered within 24 hours, and 4.8% delivered after 24 hours with significant difference (p-value 0.000). 66.7% of Group A and 100% of Group B females with Modified Bishop Score of 4-6, delivered within 24 hours, with a significant result (p-value= 0.005).

Table 4 shows, 80% of Group A females delivered within 24 hours, while females of Group B delivered almost equally before 24 hours (48.9%), and after 24 hours (51.1%). There existed a significant difference (p-value: 0.002) between groups A and B for delivery time within 24 hours.

Table No.4: Comparison of Delivery within 24 Hours in Both Groups

Delivery within 24 hours	A	B	P-value
Yes	36(80%)	22(48.9%)	0.002 (significant result)
No	9(20%)	23(51.1%)	
Total	45(100%)	45(100%)	

DISCUSSION

Inducing labor in women who have had a previous cesarean section increases the risk of uterine rupture, especially when prostaglandins are used.[13] Balloon catheters have been shown to be effective and safe in women who have had a previous caesarean section, with vaginal birth rates ranging from 55.7 % to 71% and uterine rupture rates ranging from 0.3 percent to 1.6 percent. Some studies discourage the use of prostaglandins for cervical ripening and instead recommend using a balloon catheter.[14] Geeta P et al observed that using Prostaglandin E2 vaginal gel is both safe and effective, resulting in a successful vaginal delivery without a risk of scar rupture.[15]

In our study, the Foley catheter and the PGE2 gel had similar effects on cervical ripening in women with previous one lower segment cesarean section, which is comparable to Jhakar S et al.[16]. There are various advantages of the Foley catheter over prostaglandin E2 gel, including a lower cost, a shorter induction delivery interval, a greater rate of VBAC, and decreased risk of uterine hyper tonicity or tachysystole.

According to Masood A's study Foley catheter induction was associated with the lowest rupture rate in the induced group, which was comparable to the results in the spontaneous trial of the labor group. [17] In the large MEDICS research [18], the use of prostaglandins to induce labor was linked with a negligible increase in the risk of uterine rupture when compared to mechanical methods of induction. According to a randomized control trial done by the PROBAAT study group, the results of labour induction with a Foley catheter was similar to the induction of labour with the Prostaglandin E2 gel, with fewer maternal and neonatal side effects.[19]

The use of a Foley catheter over prostaglandins was preferred in this study because the method more closely matched the physiology of labor onset, resulting in a lesser risk of hyper stimulation, fetal heart rate abnormalities, and postpartum hemorrhage. Multiple techniques for IOL in the previous scar were evaluated

in a large database systematic analysis by West HM et al, and found equivalent outcomes in terms of safety and effectiveness of induction of labor using Prostaglandins and Foleys catheter.[20] In terms of delivery within 24 hours of IOL in both groups, the results of our study are comparable to Zhu et al's meta-analysis.[21] The effectiveness and safety of Foleys balloon catheter and prostaglandin E 2gel for IOL were compared in an Indian study by Ziyauddin F et al., who discovered that the Foleys catheter group had a slightly shorter induction to delivery time. In neither group, scar dehiscence was detected.[22] Furthermore, the Foleys catheter group had a shorter time from induction to delivery and no incidences of scar dehiscence.

CONCLUSION

Both techniques of induction were shown to be safe, simple, and effective in women with previous cesarean section in this research. The Foley catheter has several advantages over the prostaglandin E2 gel, such as lower costs, reversibility, and a lower risk of systemic and serious side effects such as uterine hyper stimulation and rupture, as well as significant cervical ripening and dilatation and a shorter induction to delivery interval.

Author's Contribution:

Concept & Design of Study:	Laila Zeb
Drafting:	Tanveer Shafqat
Data Analysis:	Laila Zeb, Nosheen Akhtar
Revisiting Critically:	Tanveer Shafqat
Final Approval of version:	Tanveer Shafqat, Laila Zeb

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

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Original Article

Frequency and Outcome of Cardiovascular Disease in Pregnant Women Presenting with Shortness of Breath in Low Resource Setup

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ABSTRACT

Objective: To determine the frequency and causes of cardiac disease in pregnant women presenting to obstetric unit and to assess the associated maternal and fetal outcome in cardiac patients.

Study Design: Descriptive Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Obetet and Gynae, Civil Hospital Karachi from June, 2020 to Dec, 2020 for a period of six months.

Materials and Methods: Pregnant women between 18-40 years of any gestational age and parity presenting to antenatal clinic or emergency with complain of shortness of breath and/or palpitation were included in the study. Patients with hyperthyroidism and asthma were excluded .History pertinent to cardiovascular disease was taken followed by examination. Selected patients were seen by a consultant cardiologist and an echocardiography was performed. Patients diagnosed with cardiac disease were identified, treated in collaboration with cardiologist. Maternal and fetal outcome was noted. All data was analyzed for descriptive statistics.

Results: A total of 252 pregnant women presenting with shortness of breath and/or palpitation were included in the study. Mean age of women was 31 years and mean gestational age was 35 years . Majority of patients were un booked(77.8% n=14) and multipara (50%n=9) A total of 18 (7%)women were diagnosed as cardiac disease in pregnancy. The most common cause was valvular heart disease observed in 61.1 %(n=11) followed by cardiomyopathy in 27.7% (n=5) Congenital heart disease and ischaemic heart disease were diagnosed in 5.6% each (n=1). Mitral stenosis and regurgitation were common valvular lesions. ICU admission and ventilator support was required in 77.8% (n=14) and 55.6% (n=10) women respectively. Mortality rate was 11.1%(n=2) .Adverse fetal outcome included IUD in 22.2%(n=4) ,low birth weight16.7%(n=3),preterm birth 44.4%(n=8) and NND 5.6%(n=1).

Conclusion: Cardiac disease in pregnancy is associated with significant maternal and perinatal morbidity and mortality

Key Words: Valvular Heart Disease (VHD)- Cardiomyopathy (CMP)–Congenital heart disease (CHD)-Iscaemic heart disease (IHD)

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INTRODUCTION

Cardiac disease is the most important cause of indirect maternal deaths during pregnancy and puerperium accounting for about 10% maternal mortality.

Cardiac disease complicates 1-4% of pregnancies and accounts for 10=15% mortality[1]. Congenital heart defects are observed as most frequent cause of cardiac disease in pregnancy in developed countries whereas rheumatic heart disease is more common world -wide. In general stenotic valvular lesions are tolerated less than regurgitant lesions due to limited cardiac output and peripheral vasodilation. Valvular heart disease (VHD) may first time be presented and diagnosed during pregnancy due to hemodynamic changes occurring in pregnancy. The number of women in childbearing age with cardiac disease is rising due to better diagnostic tools and care during childhood[2]. Cardiac disease in pregnancy poses a challenge to obstetricians and needs specific care by multidisciplinary team including obstetrician, cardiologist and anaesthetist. Studies have shown that cardiac disease in pregnancy is associated with chances of adverse maternal and fetal outcome[3,4]. Shortness of breath and palpitations are very common and are mostly due to physiological changes associated with pregnancy

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or anaemia but these symptoms could be due to underlying cardiac disease[5]. Therefore it is important to evaluate these patients carefully and seek advice from cardiac consultants when required. Maternal mortality can be reduced with early diagnosis and treatment of cardiac disease.

The aim of this study was to identify pregnant women with cardiac disease and to manage them in collaboration with cardiologist and observe the maternal and fetal outcome associated with cardiac disease in pregnancy. This will help to estimate the magnitude of this problem in our local population and we would be able to suggest some recommendations in our routine obstetrics for management of pregnant women with cardiac disease which will help to reduce maternal and fetal complications in future.

MATERIALS AND METHODS

This was a cross sectional study conducted from June to December 2020 at the department of obstetrics & gynaecology Civil Hospital Karachi which is a tertiary care centre. A total of 252 pregnant women between 18- 40 years of any parity and gestational age presenting to obstetric antenatal care clinic and emergency department with shortness of breath and / or palpitations were included in the study. Patients referred from primary and secondary care with suspicion of cardiac disease were also included in this study. Patients with history of hyperthyroidism and respiratory problems were excluded. Focused history pertinent to cardiovascular symptoms like severity of dysponea, orthopnea, cyanosis, chest pain and excessive weight gain was taken. This was followed by general physical examination to check blood pressure, pulse, respiratory rate, edema, chest auscultation for crepitation and cardio-vascular examination for presence of murmur. Obstetric examination included symphysio-fudal height, amount of liquor, fetal heart sound auscultation and expected fetal weight. All patients with provisional diagnosis of cardiac disease were seen by a consultant cardiologist and undergone ECG and transthoracic echocardiography at our cardiology department. Patients diagnosed with cardiac disease were mutually managed by consultant obstetrician, cardiologist and anesthetist. All observations were noted on a proforma. Maternal and fetal complications as well as mode of delivery were also recorded. Maternal outcome measures included New York Heart Association (NYHA) class, cardiac failure, atrial fibrillation, ICU admission, need of ventilatory support and mortality. Fetal outcome measures were prematurity, low birth weight, intrauterine fetal death and neonatal death. All data was entered on SPSS 20 and analyzed for descriptive statistics. Categorical data was described as frequency and percentages and continuous data as mean and standard deviation.

RESULTS

The study included 252 pregnant women between 18-40 years presenting with shortness of breath and /or palpitations. In these women 18 (7.14%) were diagnosed as cardiac disease in pregnancy. The mean age of patient was 31 years and mean gestational age was 35 years. Majority of patients n=14(77.8%) were un-booked including 5 referrals. Multiparty was observed in 9(50%) women while 6(33.7%) were grand multipara and 3 (16.8%) women were primigravida. The most common diagnosis was valvular heart disease 61.1% (n=11) followed by cardiomyopathy 27.7% (n=5) and both the congenital heart disease and ischaemic heart disease were diagnosed in 5.6% (n=1) women. In patients with VHD the mitral stenosis 27.7% (n=5) was most common including two patients with prosthetic heart valves followed by mitral regurgitation in 22.2% (n=4), aortic and tricuspid regurgitation in 5.6% (n=1) cases. In this study 33.3% (n=6) women were hypertensive and 11.2% (n=2) developed pulmonary oedema. Accordinng to NYHA Classification 38.9% (n=7) presented with symptoms of class III, 33.3% (n=6) class II and 27.7% (n=5) class IV. Echocardiography showed ejection fraction less than 30 in 22.2% (n=4) whereas ejection fraction between 30-40% and > 40% was observed in 38.9% (n=7) women. Demographic and clinical features are described in table 1.

Table No.1: Characteristics of pregnant women with cardiac disease

Demographics	
Age mean (SD)	31 years ± 4.12
Gestational age mean(SD)	35 weeks ± 3.13
Primi n(%)	3 (16.7%)
Multipara n(%)	9 (50%)
Grand multipara n(%)	6 (33.3%)
Diagnosis n(%)	
Valvular Heart Disease	11 (61.1%)
Cardiomyopathy	5 (27.7%)
Congenital Heart Disease	1(5.6%)
Ischaemic Heart Disease	1(5.6%)
NHY Classification n(%)	
Class II	6(33.3%)
Class III	7(38.9%
Class IV	5(27.7%
Ejection fraction n(%)	
< 30%	5(27.7%)
30- 40%	8 (44.4%)
>40%	5 (27.7%)

Cardiac failure, and atrial fibrillation were encountered in 16.8 (n=3) and 11.2% (n=2) women respectively. Pulmonary hypertension was diagnosed in 11.2% (n=2). ICU admission was required in 77.8% (n=14) women with cardiac disease and ventilator support was needed in 55.6% (n=10) women. Maternal mortality

encountered in 11.2% (n=2) which included cases of severe mitral stenosis and cardiomyopathy. Perinatal outcome was good in 55.6% (n=10) women. Adverse perinatal outcome included preterm birth 44.4% (n=8), low birth weight 50% (n=9) stillbirth in 22.2% (n=4) and neonatal death in 5.6%(n=1) women. Maternal and perinatal outcome is represented in table 2.

Table No.2: Adverse Maternal and fetal outcome

Complication	Frequency	Percentage
Cardiac failure	3	16.8%,
pulmonary artery hypertension	2	11.2%
Arrhythmia	2	11.2%
Caesarean delivery	9	50%
ICU admission	14	77.8%
ventilatory support	10	55.6%
Intrauterine death	4	22.2%
Neonatal death	1	5.6%
Preterm birth	8	44.4%
Low birth weight		

DISCUSSION

Cardiac disease in pregnancy is one of the most significant causes of maternal morbidity and mortality[6]. Cardiac disease may be a pre- existing condition already diagnosed prior to the pregnancy or may be first time diagnosed during pregnancy as a result of physiological changes of pregnancy which makes the disease symptomatic. Cardiac disease seen in pregnancy includes congenital heart disease, valvular heart disease, cardiomyopathy, pulmonary artery hypertension and ischaemic heart disease.

In a study by silverside CK the most cardiac complications were observed in antepartum period followed by postpartum period and less were observed in post-partum period co relating with our study[7]. Our 61% patients were antepartum, 33% intrapartum and 16% presented after delivery. Most of patients (80 %) were un-booked including 5 referrals from primary and secondary care services. Rheumatic heart disease is almost eradicated in developed countries, however it still exists in low resource countries like Pakistan. The highest prevalence of RHD is reported in India, Pakistan, Indonesia, China and Congo[7]. Studies have shown that RHD accounts for majority of cases of cardiac disease in developing countries[8,9,10]. In a systemic review conducted at south africa it was reported that valvular heart disease was most common in antenatal cardiac patients and they found 71-84% cases of mitral stenosis ,mitral regurgitation and prior mitral valve repair[11]. In this study we also found rheumatic heart disease as the most common cardiac disease identified in 61.1% women followed by cardiomyopathy in 27.7%, whereas congenital heart disease and ishaemic heart disease were less common as both were found in 5.6% cases. The most common valvular lesion in this study was mitral stenosis followed by mitral regurgitation comprising about 80% of VHD cases, while others included tricuspid and aortic regurgitation. Physiological changes in pregnancy like increase in stroke volume, cardiac output and heart rate are poorly tolerated by patient with severe valvular stenosis and thus women may first time present with symptoms of cardiac de-compensation in pregnancy which may result in adverse maternal and fetal outcome. In a local study CMP was found to be more common seen in 42.9% followed by VHD (22.1%).[12] Women with mechanical prosthesis are at high risk of complications during pregnancy and are advised for early referral a tertiary care Centre[13]. In this study two patients were referred due to mechanical heart valves both were symptomatic and treated in collaboration with cardiologist. Diao M in their study found significant association of severity of cardiac disease with New York Heart Association (NYHA) class[14]. In this study 28% (n=5) women presented with NYHA class IV whereas NYHA class III and II were observed in 39% (n=7) and 33% (n= 6) women respectively.

Women with VHD have a high rate of deterioration during pregnancy and increased morbidity due to cardiac failure and arrhythmias which results in hospitalization and need for treatment[15]. In a local study congestive cardiac failure was found in 20% cases whereas infective endocarditis and thromboembolism were seen in 2% cases[16]. In our study we found cardiac failure in 16.8%, pulmonary artery hypertension and arrhythmia in 11.2% women diagnosed with cardiac disease. Other morbidities included ICU admission and ventilator support required in 77.8% and 55.6% respectively. Cardiac disease in pregnancy is the most common indirect cause of maternal deaths world-wide. Specially, in developing countries it is associated with high rates of adverse maternal outcome[17]. Hameed et al in their study found maternal death rates of 2% in women presenting with valvular heart disease[18]. A local study also found high mortality in women with cardiac disease in pregnancy[19]. In this study two maternal deaths were encountered (11.2%). One patient presented with cardiomyopathy while the other was a case of severe mitral stenosis with severe pulmonary artery hypertension.

Assessment of neonatal risks in women with cardiac disease is not extensively studied specially in low resource countries like Pakistan but it is very important for assessment and decision making for further management. The most common complications are prematurity, fetal growth restriction and perinatal death[20]. A study conducted in Pakistan by Aamir also found association of cardiac disease with preterm birth, low birth weight, neonatal (.6%) and maternal mortality (12%). In this study perinatal outcome was good in 55.5% women with cardiac disease. Whereas adverse

perinatal outcome included intrauterine death (22.2%), low birth weight (16.6%) and neonatal death (5.6%) in these women. Timely diagnosis of cardiac disease before planning a pregnancy and prompt treatment prior to pregnancy is likely to reduce neaonatal and maternal complications.

CONCLUSION

Pregnancy with cardiac disease is associated with significant risk of maternal morbidity and mortality and adverse perinatal outcome. Though majority of patients tolerate pregnancy well , timely referral to a tertiary care is very important for management of these patients by a multidisciplinary team .Diagnosis and treatment of cardiac disease before pregnancy may reduce the risk of maternal and perinatal complications. The study concluded that NYHA CLASS> II ,pulmonary hypertension and ejection fraction < 30% is associated with poor maternal outcome.

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Original Article

Correlation of Local Recurrence in Oral Squamous Cell Carcinoma with Tumour Size, Resection Margins and Delay in Post-Operative Adjuvant Radiation

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ABSTRACT

Objective: To correlate local recurrence in oral squamous cell carcinoma with tumour size, safe margin resection and delay in post-operative adjuvant radiotherapy.

Study Design: Cohort study.

Place and Duration of Study: This study was conducted at the ENT Department, Jinnah Medical College Hospital, Karachi between November 2017 and December 2021.

Materials and Methods: All patients presented with resectable squamous cell carcinoma of oral cavity were included in the study. These were followed-up with minimum period of two years for disease recurrence at the primary site.

Results: Total 116 patients were included in the study, out of which 29(25%) were females and 87(75%) were males with mean age of 48.8 ± 8.2 years. Most common site was buccal mucosa 64(55.1%) and moderately differentiated carcinoma on histopathology 96(82.8%). Local recurrence rate was 0% in T1, 8.6% in T2, 19.1% in T3 and 40.0% in T4 lesions (p-value = 0.001), 1.6% where safe margin is > 10 mm, 34.7% where margins are between 1 to 5 mm and 100% where < 1 mm (p-value = 0.002). Similarly recurrence rate was 5.5% when adjuvant radiation started within 1 month, 4.8% when started between 1 to 3 months, 30.4% when between 3 to 6 months and 78.5% when started > 6months after primary surgery (p-value = 0.001).

Conclusion: There are higher local recurrence rate in patient presenting with advanced T-stage disease, less distance of tumour from the resected margins and delay in initiation of post-operative adjuvant radiation therapy.

Key Words: Oral carcinoma, Tumour recurrence, Adjuvant Radiotherapy, Oral tumours, Local recurrence.

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INTRODUCTION

Squamous cell carcinoma of the oral cavity is the commonest malignancy in head and neck region.[1,2] As estimated in 2018, global deaths per year due to oral carcinoma are around 177,000.[3] This condition is much more prevalent in sub-continent specially in Karachi due to addictions such as pan, chaliya and gutka. According to the Karachi cancer registry, it is the second commonest malignancy in both genders.[4] Surgery is the preferred modality of treatment with adjuvant chemo-radiation in advance disease. Despite many advancement in its management, overall survival rate has not changed significantly over last 20 years.[5] Loco-regional recurrence is common despite of the new treatment modalities. Loco-regional recurrence is a significant fate-deciding feature for patients of oral carcinoma and we face this challenge every day. Tumour stage, size, histopathological feature, delays in adjuvant chemo-radiation and safe margin resection plays important part in deciding patient's fate.

The histopathological grading and tumour free margins of the resection are other prognostic factors.[6] Numerous histopathological schemes are available for grading of carcinoma, but none is satisfactory to predict prognosis in these tumours.[7] Tumour free surgical margins is also considered imperative to predict overall long term prognosis and recurrence rate.[8,9] A safe margin of 5 mm or more is associated with enhanced local recurrence control and disease free survival.[10] Safe margin is not only significant for recurrence and survival, rather it is

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also very pertinent for making decision regarding post-operative adjuvant radiotherapy and chemotherapy. It is very important for decreasing both local as well as regional recurrence of the disease.

This is a cohort study where we had followed up patients of oral carcinoma for local recurrence and to correlate it with primary tumour size, safety margin on resection in final histopathology and delay in initiation of post-operative adjuvant radiation therapy due to any reason.

MATERIALS AND METHODS

This was a cohort study conducted at the department of Otorhinolaryngology, Jinnah Medical College Hospital (JMCH), Korangi, Karachi. This study was started in November 2017 and patients were followed up till December 2021. Prior ethical review committee (ERC) approval from JMCH was taken before the start of this study. Written consent was also taken from all the patients included in the study. Inclusion criterion was all patients of oral squamous cell carcinoma operated at JMCH and underwent surgery as the primary treatment with or without adjuvant radiotherapy and followed up regularly for local recurrence. Exclusion criterion were patients who lost for follow-up, who had not given written consent for inclusion in this study, where data like safety margin resection was not available on final histopathology and where there was nodal recurrence after surgery. All the demographic and relevant data was entered on a pre-designed proforma. These patients were followed up regularly in OPDs and on phone calls for local recurrence for a minimum period of 2 years (till January 2022). Patients underwent primary surgery with neck dissection and post-operative adjuvant radiation therapy when required. Patients at clinical stage I-II were treated with surgery, if there were adverse features on final histopathology then adjuvant radiation therapy was given. Patients with stages III-IV underwent surgery first followed by postoperative radiotherapy. Primary resection of the tumour was done with taking care to have at least 10 mm tumour free margins where possible. Larger defects were repaired with different local, regional or free flaps. For clinical N_0 cases, ipsilateral selective neck dissection was done from level I to III. In cases where nodal metastasis was present (cN+), ipsilateral or bilateral radical/modified radical neck dissection was performed. SPSS 20.0 was used for statistical analysis. Chi-square or Fisher's exact test were used for different categorical parameters and p-value of <0.05 was considered significant.

RESULTS

There were a total of 116 patients included in this study having minimum age of 24 years to maximum age of 84 years, with a median age of 48.8 ± 8.2 years (table 1). There were 87 males and 29 females with a ratio of 3:1. Buccal carcinoma was the most common site (55.1%), followed by tongue carcinoma (27.5%). Other site of carcinoma are shown in table 2. Of the 116 cases, 12 were well differentiated, 96 cases were moderately differentiated and 8 patients were poorly differentiated squamous cell carcinoma. Wide local excision of tumour with unilateral neck dissection was done in 107 cases and bilateral neck dissection was done in 9 cases.

Table No.1: Basic demography

Total number of patients N =		116
Gender	Male	87 (75%)
	Female	29 (25%)
	Male to Female ratio	3:1
Age	Minimum age (in years)	24
	Maximum age (in years)	84
	Mean Age (in years)	48.8 ± 8.2
Local Recurrence	Positive	25 (21.5%)
	Negative	91 (78.5%)
Neck Dissection	Unilateral	107 (92.2%)
	Bilateral	9 (7.8%)
Cell differentiation on Histopathology	Well Differentiated	12 (10.3%)
	Moderately Differentiated	96 (82.8%)
	Poorly Differentiated	8 (6.9%)

Fig 1 shows the correlation between the primary tumour size (T stage) with the recurrence. In early T1 lesions out of total 11 cases, no recurrence occurred in any patient (0%), in T2 lesion out of 23 cases, recurrence was present in 2 (8.6%), in T3 out of 47 cases, recurrence occurred in 9 (19.1%) while in T4 lesion out of total 35 cases, recurrence was positive in 14 patients (40%),. So there was a definite increase in recurrence rate with the increase in primary T stage (p-value = 0.001). Fig 2 depicts the correlation between the safety margin on resection with the recurrence rate. In those patients where the tumour was reaching upto the resected margin (< 1 mm.), out of total 8 cases, recurrence occurred in all patients (100%), in cases where the tumour margins were close to resected margin (> 1 mm to < 5mm.), out of total 46 cases, recurrence occurred in 16 (34.7%) while in cases where tumour margins are distinct/far from resected margin (> 10 mm) out of total 62 patients, recurrence was positive in only 1 case (1.6%). So There was again positive correlation of recurrence with the safety margin resection (p-value = 0.002).

Post-operative radiation therapy was given in 82 cases out of total 116 cases. Out of these 82 cases, 18 patients received radiotherapy within 1 month after surgery, 27 received between 1 to 3 months, 23 received between 3 to 6 months and 14 received after 6 months of surgery.

Table No.2: Site of lesions, T staging and tumour margins

Site	Total No. of cases N (%)	T staging				Tumour margin on histopathology		
		T1	T2	T3	T4	Involved (< 1 mm)	Close (1 - < 5 mm)	Distinct (> 5 mm)
Buccal mucosa alone	64 (55.1%)	4	12	28	20	1	19	44
Tongue	32 (27.5%)	6	7	9	10	2	14	16
Buccal mucosa + Upper alveolar margin	1 (0.86%)	1	0	0	1	0	1	0
Buccal mucosa + Lower alveolar margin	10 (8.6%)	0	0	6	4	4	6	0
Hard Palate	4 (3.4%)	0	3	1	0	0	3	1
Buccal mucosa + Retromolar trigone	3 (2.5%)	0	0	2	1	1	2	0
Lip	2 (1.7%)	1	1	0	0	0	1	1
Total	116(100%)	11	23	47	35	8	46	62

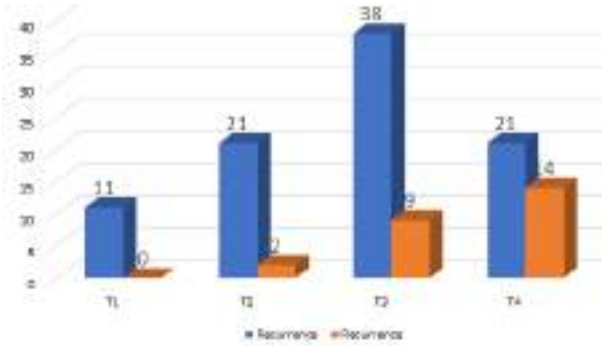

Figure No.1: Correlation of Tumour size (T staging) with recurrence

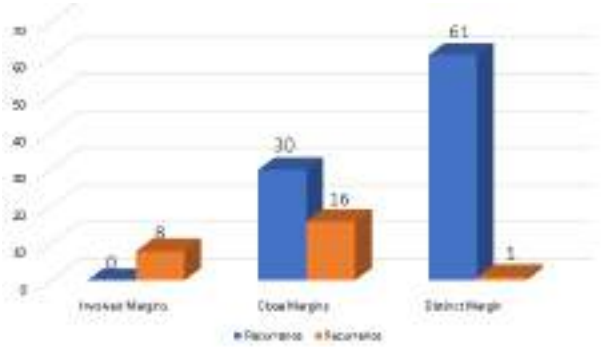

Figure No. 2: Correlation of Tumour margin on histopathology with Recurrence

Fig 3 represents the correlation of delay in post-operative radiation therapy with the recurrence rate. In patients who received radiotherapy within 1 month, out of 18 only 1 patients had recurrence (5.5%), those who received between 1 to 3 months, out of 27, 4 had recurrence (14.8%), those who had radiotherapy between 3 to 6 months, out 23, 7 had recurrence (30.4%) and those who had radiotherapy after 6 months, out of 14, 11 had recurrence (78.5%). Again there is a definite positive correlation of recurrence with delay in post-operative radiotherapy (p-value = 0.001). The recurrence time varied from 2 months to 60 months with median survival time of 12.09 ± 1.2 months and most of the recurrences were noted within first 12 months.

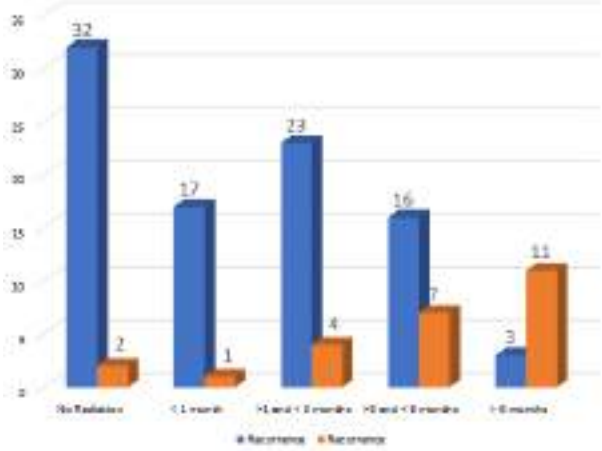

Figure No. 3: Correlation of Delay in post-operative Radiotherapy with Recurrence

DISCUSSION

Carcinoma of the oral cavity has a very high global burden, having approximately 275,000 new patients every year.[11] It ranks second among all malignancies in countries like Pakistan and India.[12] Different variables are used to calculate loco-regional recurrence and thus overall prognosis in oral carcinoma. It usually comprises of TNM staging, histological differentiation of cells and sometimes different sub-sites in the oral cavity. The final outcome in oral carcinoma is mainly affected by the clinical staging at time of presentation. More tumour mass is related with high metastasis in the nodes, greater loco-regional recurrence and thus overall bad prognosis.[13] The currently used 'TNM' staging narrates very well in oral carcinoma regarding overall prognosis and patient's survival. Less is the clinical T-stage, better is the prognosis and thus treatment is less complicated and more succesful.[14] Our study also supports the similar finding where recurrence rate increased from 0% to 40% in T1 to T4 lesions.

Another significant factor for prognosis and recurrence in oral squamous cell carcinoma, is the distance of tumour from the resected margin. It is considered as the utmost significant prognostic factor even if it is measured independently with other factors.[15,16] The decision for safe margin is made by the surgeons during operation by considering the site and extent of the primary tumour and bearing in mind how to reconstruct the defect after excision.[17] A negative margin is defined as the resected tissue does not contain any tumour cells within a zone of 10 mm all around the tumour while the close margin is defined as the resected tissue is free of tumour cells for at least 5 mm zone.[18] If the tumour cells are present in any of the excised margin, it is called as positive. The excised margins are also considered as positive even if the margins has only dysplastic changes or carcinoma in-situ.[19] Many other studies have also shown distance of the tumour from the resected margin has no importance as far as the margins are tumour free. They consider that close margin (< 5mm) is comparable to clear margin (> 10 mm) and it has same value for recurrence.[20] Thus according to these studies, presence of close margin is not used for decision making regarding post-operative adjuvant radiotherapy or chemotherapy.

Different studies had mentioned different cut-off values for close margins in oral carcinoma ranging from 1 mm to 7 mm. A study by Tasche et al showed that only significant margin involvement for recurrence is important if it is less than 1 mm.[21] While a study by Zanoni et al showed that recurrence rate is higher only if the resected margins for tumour is < 2.2 mm.[22] In our study, there was a definitive difference in the recurrence rate between the group having positive margins (< 1 mm.), close margins (1 to < 5 mm.) and distinct margins (> 10 mm.).

In our region, there is one problem of delay in timely post-operative adjuvant radiation therapy because of so many reasons. It could be financial as patient is not able to afford high cost, lack of education in patients/their attendant considering radiotherapy as hazardous, poor post-operative wound healing and poor nutritional status of the patient so not fit to receive radiotherapy and over-burden on radiotherapy departments especially in public sector institutions having long waiting list. Delay in initiation of adjuvant radiotherapy is defined as start of radiotherapy more than 6 weeks after the primary surgery. This delay in adjuvant radiotherapy is one of the important reason for higher recurrence rate both at the primary site and in cervical nodes.[23] Our study also shows the similar results with much higher recurrence of 78.5% when there is delay for more than 6 months versus only 5.5% when radiotherapy was initiated within one month after surgery. The most important cause for delay in our study was found to long waiting list in radiotherapy departments.

To conclude, oral carcinoma is one of the most common malignancy in Pakistan. We have studied the correlation of local recurrence with the primary tumour size (T-stage), safe margin on resection and delay in post-operative adjuvant radiotherapy. The limitation of this study is that it was conducted in only one center with limited number of patients. More studies with multicenter involvement and higher number of patients are required further to investigate these prognostic factors for the recurrence of oral carcinoma in our region.

CONCLUSION

Local recurrence after primary surgery is a dilemma for surgeon, patient and family. There are increased chances of recurrence in patient presenting with advanced T-stage disease, less distance of tumour from the resected margins and delay in initiation of post-operative adjuvant radiation therapy.

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Review Article

Challenges in Achieving The Health-related Millennium Development Goals

Success and Challenges in Achieving The Health-related Millennium Development Goals (MDG 4, 5 & 6) in Developing Countries—A Lesson for Sustainable Development Goals: A Systematic Review

Hafsa Shaikh[1], Naeema Asghar[2], Farhat Jafri[3], Fareedah Islam[4], Nusrat Ali[5] and Adil Ramzan[5]

ABSTRACT

Objective: To assess challenges and success in attaining the health related Millennium Development Goals (MDG 4, 5 & 6) in developing countries.

Study Design: A systematic review

Place and Duration of Study: This study was conducted at the Agha Khan University from April to September 2018.

Materials and Methods: Systematic search for published literature using search term Challenges, Successes, Achieving, Health related MDGs and Developing countries. Data bases like Pub-Med, Science direct and Google Scholars were used to search the studies. Eligibility criteria were set to select the article for review. Filters for article type, free full text, years of publication were applied for more focused review.

Results: Systematic review finding revealed that weak governance, lack of strategic leadership, financial constraints and low budget allocation and lack of human resource for health capacity were identified as the most documented challenges. Among successes it includes multi-sectoral approach, increased health service package, increased health service coverage, and poverty reduction strategies.

Conclusion: Systematic review findings present a complex picture of progress towards health related MDGs. Results clearly indicate that reducing maternal and child health related indicators are merely not a technical process but interplay of several non-health determinants including poverty, socioeconomic disparities, health inequities along with leadership and governance.

Key Words: Millennium Development Goals, Sustainable Development Goals, Health outcomes

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INTRODUCTION

In 2000, 189 heads of state adopted the UN Millennium Declaration and endorsed a framework for development.

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The declaration established eight Millennium Development Goals (MDGs) and twenty-one set quantifiable targets for 2015. MDGs identified a number of indicators for monitoring progress, several of which relate directly to health[1,2].

Most aid agencies and civil society organizations reoriented their work towards the achievement of the Millennium Development Goals (MDGs)[3]. The MDGs were associated with increased access to resources from development partners. Low-income countries, tied their development plans to the MDGs which provided good incentives for translating and operationalizing them[4].

There is evidence stating remarkable progress towards achieving the MDGs[5]. According to the UN MDGs Report 2012, child mortality has been steadily decreasing globally and immunization rates are over 90% in almost two-thirds of all countries[6]. Professional assistance during childbirth has improved from 55% in 1990 to 65% in 2010[7].

However, progress across all MDGs has been limited and uneven across countries, particularly in African and Asian continent. Three of eight MDGs were health

goals: Goal 4 (reduce child mortality), Goal 5 (improve maternal health) and Goal 6 (combat HIV/AIDS, malaria and other diseases)[8]. According to the World Health Organization (WHO) report 2015, some countries have made impressive gains in achieving health-related targets[9].

The MDGs were expired in 2015 and a new set of Sustainable Development Goals (SDGs) were developed and fit into a global development framework beyond 2015 which were signed on 25th September, 2015 which included a set of 17 SDGs.[10,11]

To achieve sustainable development, the Agenda 2030 underlines the fundamental importance of reliable, timely and disaggregated data and statistics. These are indispensable to analyze development challenges; measure progress and make evidence decisions[12].

MATERIALS AND METHODS

This study included published Primary and Secondary literature from Jan, 2014 to December, 2021 on success and challenges in attaining health related MGDS. The international electronic databases like Pub Med, Science direct as well as Google Scholar were used using detailed search strategy in consultation with second reviewer. Cross referencing of systematic reviews was also undertaken to identify relevant articles using manual search. The search terms were grouped into major concepts of Success, Challenges, achieving, Millennium Development Goals, and Developing Countries. In order to make uniform search terms, the Medical Subject Headings (MeSH) were also utilized wherever applicable. Besides, bullion operators "AND" and "OR" were also used.

The inclusion criteria was 1) Articles clearly states successes and challenges in achieving Health related MDGs; 2) Studies conducted in LMICs; 3) Literature reviews, Commentaries, Policy paper, Special Issues and Opinion paper. Economic evaluation and any experimental studies such as RCTs or clinical trials or study discussed the policies and reforms carried out by government in attaining the MDGs were excluded. Language limitations were imposed, due to resource constraints and studies were only considered if an abstract and full article existed.

There were two reviewers involved in selection of studies for systematic review. The resulting studies were first screened by titles, followed by abstract and full text to eliminate studies not meeting criteria. After screening, total twenty-four (n=24) articles were available for review. Finally, the information extracted from 24 available studies was documented in self-design extraction form.

RESULTS

Conceptual framework detail is shown in Figure 1 and Figure 2 depicts the consort diagram for study selection process.

Out of twenty-four studies, five were based on Commentary (n=05) and eleven (n=11) have used secondary review as a methodology that includes, Literature review, secondary analysis, and simple non-systematic reviews. Where others include Cross-sectional study (n=1), Policy Paper (n=1), Special Issue (n=1), Case study (n=1), Narrative Review (n=1) and Survey (n=1). However, two (n=2) studies have not mentioned any study design.

1. Leadership and Governance: Around 62.5% have identified challenges specific to leadership and Governance and 58.8% studies have evident leadership and governance related matter as one of the major success factors. It was noted that strong political will and commitment, multi-sectoral approach, effective and integrated strategic planning, health reforms initiatives, policy alignment with global targets[21,31,36], harmonization of legal and policy framework[22], decentralized governance structure[22,33], strengthening of leadership capacities[37], improved accountability[33] and improved coordination &collaboration[23,38] with national & regional partners as booster in attaining MDGs.

2. Healthcare financing: Around 41.6% studies have identified challenges under area of healthcare financing, whereas five 20.8% studies have documented success linked with Health care financing. The key financing challenge include low budgetary allocation to health along with reliance on external funding assistance, inappropriate allocation of funds-- more money spend on tertiary care than primary care[39], lack of financial resource for data collection[35], high cost of health care[21].To counter this healthcare financing issue, few countries have increased allocation of funds by focusing on basic essential service package as identified in countdown countries study[39]. Other financing mechanism that would result in attaining health related goal includes performance-based financing and health insurance mechanism[34].

3. Health work force: In 37.5% studies challenges related to health work force were highlighted. The most common challenge was shortage of workforce and lack of human resource capacity. Other challenges include Lack of employment opportunities, lack of coordination among different health cadres, lack of involvement of public health professional in planning and decision making[30], lack of adherence to standards.

Only 20.8% have identified success linked with health workforce[33,33,36]. Other success studies evident involvement of public health professional in decision making[30], adequate provision of skilled workforce[38] and introduction of emergency human resource plan[25].

4. Health Information System: Health information system related challenges were identified in 29.1% studies which include inadequate and unreliable data system and, inconsistency and lack of data report. Only three 12.5% studies have identified measures that would contributed in attaining MDGs linked with

healthy information system include good data Surveillance system, infrastructure of health network system[23], strengthening of health information management system[36] and institutionalization of deaths audits[33].

5. Access to essential medicines, commodities and infrastructure: Around 54.1% studies have identified challenges in this area. The most frequently reported challenges include lack of access to primary health care and basic health package, Lack of material resources and commodities, poor health infrastructure.

As far as measures that had contributed in attaining goals have been identified by eight (33.3%) studies, most observed findings include increase in health service coverage[29-31,33,34], provision of integrated basic health service package for mothers and children[18,31,34,35], strengthening the pharmaceuticals companies to ensure availability of medicines and medical supplies[18] and improving the health infrastructure[31].

6. Health Service Delivery: Total ten (41.6%) studies had identified challenges pertaining to this domain. The most distinct challenge includes poor quality of health service followed by inadequate utilization of health services and lack of service ranges/ integrated care.

The 12.5% studies had documented actions that turned into success in achieving few of the health related MDG targets include resource extension for health-related programs[25,33], improved quality of care provision[26,36] and strengthening referral and coordination mechanism[36].

1. Contextual Factors, including non-health systems determinants: Contextual factors including non-health systems determinant turned out as a major challenge for developing countries. Around 79.1% studies has emphasized challenges linked with non-health related determinants. The most pronounced challenge was poverty followed by health inequities (n=8), cultural barriers (n=7), environmental factors and socio-economic inequities (n=3). Other non-health determinants include lack of community engagement and participation, lack of female education, poor household knowledge, violation of human rights, violence against women, insecurity, poor water and sanitation facilities, inadequate transportation and uncontrolled population.

Whereas 37.5% studies found that non-health determinants have also greatly contributed in overall attainment of MDGs including health. The studies have identified that poverty reduction approach, improving health equity can improve health related MDGs. Remaining success factors included women empowerment, community engagement, environment management measures and Political stability.

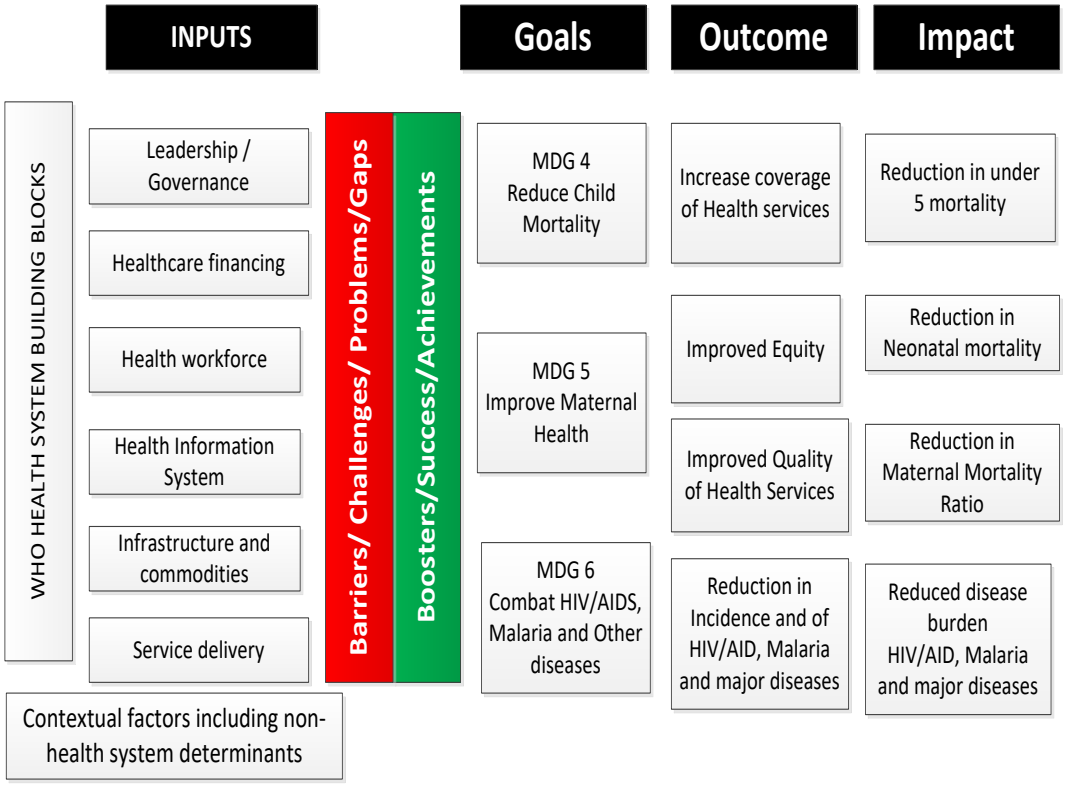

Figure No.1: Conceptual Framework

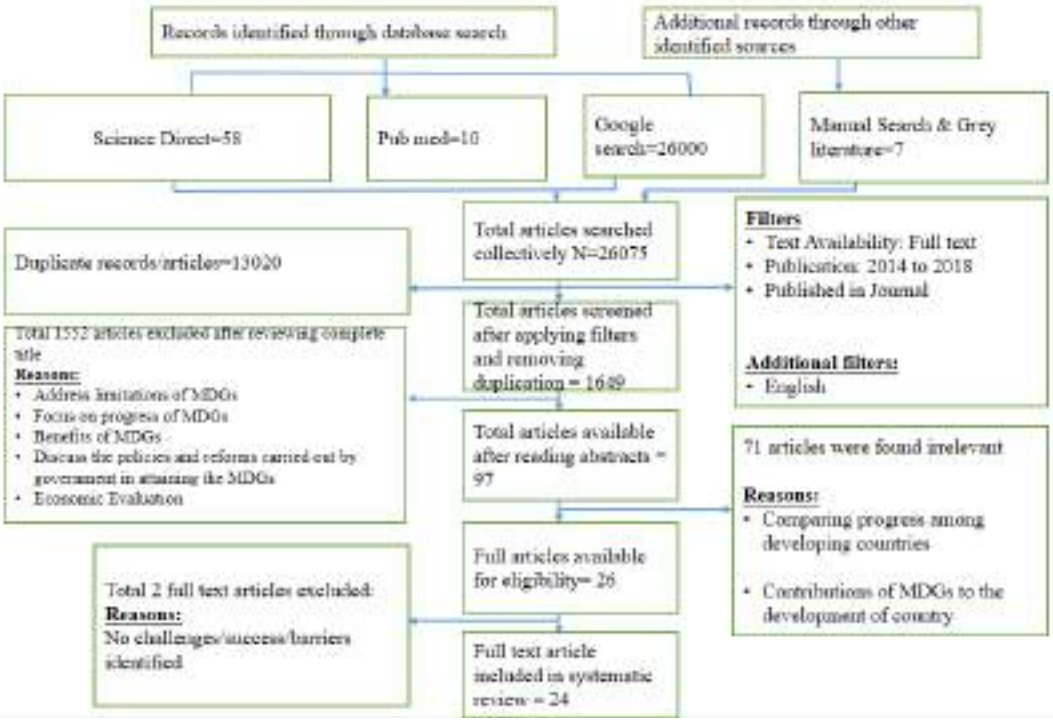

Figure No.2: Consort Diagram for Study Selection

DISCUSSION

This systematic review has focused on challenges and successes that will allow us to understand the reasons behind achieving health linked MDGs in developing countries.

Systematic review findings revealed that weak governance, lack of strategic leadership, financial constraints, shortage of skilled workforce, poor access to primary health care, health inequities and poverty were the major challenges developing countries have faced in not attaining health goals.

Vietnam has achieved MDG 4 & 5, partially due to strong political will and ownership of government in support of MDGs by aligning policies into global target. Other possible reasons of weak governance highlighted by other studies are lack of political commitment and accountability and poor accountability and responsiveness[14,16,23].

One of the success factors in achieving health related goals by fast contract countries was catalytic strategies for leadership, partnership and better accountability that has improved the governance capacity and structure[35]. Leadership, commitment and responsiveness has allowed Cambodia and Bangladesh to achieve MDG 6[30].

Another major challenge identified was financial constraints due to lack of funding for health expenditure and low budgetary allocation specifically for MDGs activities[14,18,23,27,29,30,38,39]. Developing countries have other obligations to meet with very scarce resources, sinking funds in meeting MDGs would be challenging for Nigeria to allocate for health-related task[14]. Inappropriate financing is another challenge. In Pakistan; major chunk of health budget was allocated to tertiary care rather than primary care[39].

To better address the financial challenges, countries have adopted several strategies; among such strategy performance-based financing has been introduced in Rwanda[34]. Other countries have adopted multi-sectoral strategy to pool all the resources and developed a unified and integrated plan of action to avoid duplication and financial losses[34]. Similar approach has been adopted by Peru[18]. Moreover systematic review findings also highlighted that provision of basic service package improved significantly by shifting the financing gear from curative to preventive care[18,31,34,35].

Systematic review findings also explored accessibility issue for primary health care services, multiple studies have identified poor infrastructure[17,26,31,39], lack of material resources and commodities[18,26,27,31,33] as its cause. Such issues lead to poor quality of service delivery, lack of utilization of health services as identified by study on infant and child mortality status of Bangladesh[31]. To fix this issue Ethiopia and Nicaraguanunder health sector development plan increased access to medicines and supplies by strengthening of Pharmaceuticals and medical supplies in priority areas and also resource extension for health programs[18]. Afghanistan dealt with this issue differently and shifted from vertical interventions (EPI) to more integrated approaches to RMNCH services to ensure accessibility to basic health package[18].

Under contextual factor, poverty and health inequities were the major barrier as they have undermined the

overall progress and remained major reason of failure for not achieving health MDGs. The studies conducted in Vietnam and Pakistan concluded that health inequities and inequalities resulting from differential impacts of socioeconomic determinants on geographic regions and between socioeconomic groups pose major challenge[15].

Countries that have achieved health related MDGs have focused on poverty reduction approach with special focus to marginalized group of population. Policy efforts made by Vietnam aimed at closing gaps in health between different socioeconomic groups and have achieved MDG 4 & 5[15]. Peru and Rwanda has successfully implemented pro-poor and targeted health strategy in childhood immunization thus have increased equity in health outcome[18] and would helped in achieving all three-health related MDGs.

CONCLUSION

The findings present a complex picture of progress towards health related MDGs. Results clearly indicate that reducing maternal and child health related indicators are merely not a technical process but interplay of several non-health determinants including poverty, socioeconomic disparities, health inequities along with leadership and governance.

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Case Report

Dilemma in Diagnosis of Parotid Gland Swelling: A Case Report of Pilomatrix Carcinoma Involving Parotid Gland

Jehan Alam[1], Raja Muhammad Daniyal[1], Tariq Mahmood[2], Sumaira Babar[2] and Ambreen Mahboob[1]

ABSTRACT

Pilomatrix carcinoma mostly occurs in the head & neck region and upper and lower extremities are also known sites of pilomatrix carcinoma. It is usually misdiagnosed as other benign tumors and leads to inadequate treatment planning which eventually results in recurrence as in our case. We present this case due to its relative rarity, to raise awareness about its clinical features, diagnosis and treatment. A male patients with age 27 years old presented to our OPD with complains of recurrent swelling in right infra auricular region. It was diagnosed as keratinizing squamous cell carcinoma. Primarily diagnosed with the help of FNAC, CT scan and finally with excisional biopsy of the mass.

Key Words: Pilomatrix Carcinoma, Parotid Gland, Malignant Pilomatrixoma, Tumor

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INTRODUCTION

Pilomatrix carcinoma most commonly occurs in the head & neck region and back especially in sun damaged skin[1]. However upper and lower extremities are also known sites of pilomatrix carcinoma. This neoplasm is dermo-hypodermic in nature and is mostly known among dermatopathologists and dermatologists[2]. Due it's relative rarity in the parotid gland Oral & Maxillofacial Surgeons usually do not consider it in the differential diagnosis and misdiagnosed as other benign tumors (cysts, adnexal tumor, granulomatous inflammation) or as malignant tumor such as (SCC, small round blue cell tumor, malignant skin appendages).

Pilomatrix carcinoma is a malignant variant of pilomatrixoma also known as malignant pilomatricoma, metrical carcinoma and calcifying epitheliocarcinoma[3]. It is a low grade malignant lesion which is locally aggressive with low metastatic potential.

Common presentation is a hard slow growing subcutaneous mass associated with pain and inflammation. It frequently appears as single nodule and it varies between 1-1.5cm in size[4]. Due to the small number of cases optimal treatment has not been established. Most publications advocate wide local excision with adequate margins varying between 5mm -2 cm. The role of postsurgical radiotherapy and chemotherapy has not been established.

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CASE REPORT

A 27 year old male presented to our OPD with complains of recurrent swelling in right infra auricular region. Patient provided written informed consent for the use of his images and publication for this case. According to the patient the swelling first appeared 8 months back for which FNAC was done and showed lymphoepithelial lesion. He underwent excisional biopsy of the mass 3 months back. Specimen was well defined and lobulated measuring 4.0 x 2.0 x 1.0 cm and grayish white in colour. On cut section the surface was homogenous with flecks of white. It was diagnosed as keratinizing squamous cell carcinoma. After the biopsy he started noticing recurrence of the swelling which was progressively increasing in size, not associated with pain or fever. We advised CT scan face with contrast which showed a complex soft tissue density enhancing mass in the parotid gland measuring about 1.9 x 1.1cm. PET CT scan was advised for detection of distant metastasis. It showed peri lesional fat stranding and overlying skin thickening. Findings were consistent with recurrent disease in the surgical bed. Therefore patient was planned for wide local excision with ipsilateral neck dissection upto level IV, followed by primary closure with rotational advancement flap (Figure 1). Patient had no complication other than early postoperative pain. Postoperative radiotherapy was

advised but patient refused. PET CT scan was repeated after 7 months for detection of metastasis which is rare but could be fatal. On PET CT scan there was no metastasis and surgical bed was disease free (figure: 2). Patient is on regular clinical follow up and no local recurrence or metastasis has been observed in 2.5 years.

Figure No.1: Wide local excision of a tumor along with neck dissection

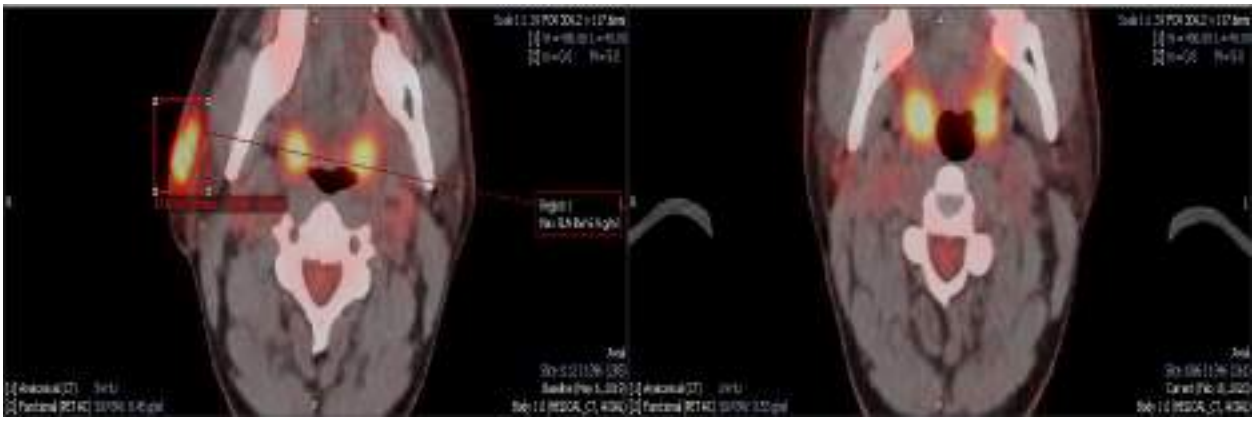

Figure No.2: Comparison of preoperative and postoperative PET CT scan

DISCUSSION

As misdiagnosis of pilomatrix carcinoma is common due to its atypical presentation and leads to inadequate treatment planning which eventually results in recurrence as in our case. Pilomatrix carcinoma can occur as a solitary nodular lesion or as transformation of long standing pilomatricoma[5]. It is more common in males than females with a ratio of 3:1 and more common in head and neck region especially sun exposed skin[6]. Investigations include FNAC which is not useful in distinguishing it from other tumors as it shows only malignancy in aspirated cells. There is no clear radiological criteria of pilomatrix carcinoma. However, CT and MRI can be useful in determining the extent of the lesion, bony invasion as well as nodal metastasis. PET-CT is recommended to rule out distant metastasis, which is rare but cases of lung metastasis have been reported. Most histopathologists are challenged in diagnosing this tumor as there is no clear histological criteria in distinguishing this entity from other tumors. However, some histological findings could help in diagnosis such as increased mitotic rate, prominent nucleoli and cellular pleomorphism. These findings were also noticed in our case. Other characteristic features of pilomatrix carcinoma are epithelial islands of basaloid cells, ghost cells or shadow cells, deposits of basophilic calcium, infiltration of skin and soft tissue, central necrosis and invasion of the blood and lymphatic vessels. Some immunohistochemical markers such as Ki-67 expression in the peripheral portion indicate that tumor has high proliferation rate and is invasive. Recommended surgical treatment for is wide local

excision with safe margins of (0.5-2cm). Role of radiotherapy is yet to be established. In our case patient remained tumor free for more than 2 years without radiotherapy. There is no effective chemotherapy accepted for control of local growth. For surveillance of local recurrence regular physical examination is recommended. Ultrasound, MRI and PET-CT scan could be used. Biopsy could be performed to analyze recurrent mass.

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