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March 11, 2021 was observed a World Kidney Day globally. Each year the objective of the Kidney Day is to raise awareness about the renal diseases and how keep the kidneys healthy. The theme of the day this year was “Living Well with Kidney Diseases”. The theme focused on educating and raising awareness about effective management of symptoms and the patient empowerment, with the goal of life participation. Pakistan ranks eighth in the list of the countries with increasing rates of renal diseases. Seventeen million people around the country are suffering from different kidney diseases. Chronic Kidney Disease (CKD) is increasing rapidly in Pakistan according to the experts. The reason for the high rise is pointed towards late diagnosis. Other causes include renal stones, and large number of patients suffering from uncontrolled diabetes mellitus and long standing hypertension.

Chronic Kidney Disease (CKD) is a worldwide threat to health, with a global prevalence of 13.4%. Amongst them the patients with end-stage renal disease (ESRD) requiring kidney transplantation are predicted to be between 4.9 and 7.0 million. Chronic debilitating diseases like diabetes mellitus, hypertension and obesity are on top of the list of causes for CKD. Communicable diseases like HIV / AIDS and autoimmune diseases like Systemic Lupus Erythematosus (SLE) also contribute in the etiology. CKD is a high contributor of morbidity and mortality all over the world. It also imposes an economic burden on the country. In a recent systematic review, the prevalence of CKD is 21.2% in Pakistan, of which age- specific prevalence is 43.6% among the elderly (age more than 50 years) and 10.5% among the population who are less than 30 years. However the gender-specific prevalence shows variability in different systemic reviews. In developing countries like ours, one of the drawbacks in estimating the exact prevalence of the disease are the limited and unevenly health facilities between the urban and the rural regions.

As more patients are diagnosed with CKD in Pakistan. Majority of them require immediate dialysis and in a large number the cause of the disease remains mostly speculative. The Pakistan-based clinical database of kidney patients states diabetes mellitus accounts for the etiology of end-stage renal disease in 33% of the population and 44% of the total patients on dialysis are suffering from hepatitis C infection. In a current study about the causes of end-stage renal disease 26.31% patients are idiopathic. Diabetes mellitus and hypertension on top of the list accounts 19.67% and 19.45% respectively. Other etiologies mentioned are lower urinary tract obstruction, stone disease, tubulointerstitial nephritis, polycystic kidney disease, reflux, glomerular diseases and renovascular disease. There is still a very limited data available on the spectrum of kidney diseases leading to end-stage renal disease in our country. Kidney is not just the only organ which is affected, but chronic renal disease leads to a number of other systemic effects which needs management besides treating and saving the kidney. Numerous blood related parameters have been shown to be deranged in CKD and the patients' presents with anemia, leukocyte dysfunctions and coagulopathies.

Pakistan Society of Nephrology utilized the best possible human resources in the country and joined together to take the initiative of preparing database of the kidney patients and the impact of disease. The project started in 2018 to keep proper record of ESRD patients in Pakistan and now it has been shifted from manual recording to an online Pakistan Renal Registry. There is major under detection of early stages of CKD in the developing countries and the shocking fact turned out to be ignorance about have a renal disease in 2.3% individuals in our country. Diabetes mellitus is very common in our country and Pakistan reached fourth position in top ten countries in the world with more than 19.4 million diabetic patients in 2019. Awareness about the renal diseases is the need of the hour. Normal individuals must be educated through print and electronic media, seminars and talks to follow exercise, weight control, consumption of balanced...
diet, stay hydrated, maintain cholesterol levels, avoid unnecessary analgesic use, get annual medical checkups and know their family history of diabetes mellitus and hypertension.  

The preservation of the health is easier than the cure of the disease.

(Photograph by Ali Rizvi)
Prostate cancer is a disease process that affects the older person at a higher rate than other age groups. Intensified screening efforts in recent years have been made to make diagnosis of early-stage disease. Prostate cancer remains the second leading cause of cancer diagnosis worldwide. The diagnostic modalities available for diagnosing & evaluating prostate cancers are digital rectal examination (DRE), prostatic specific antigen (PSA) & Transrectal ultrasound with sextant Transrectal ultrasound guided biopsies, either using 6 core or 12 core technique. The use of Transrectal Power Doppler ultrasound imaging with targeted biopsy technique will improve prostate cancer detection on area of hypervascularity, which suggest biologically aggressive tumors.

Screening of prostate aims to reduce the mortality from prostate cancer. The objective of the study is to determine the diagnostic accuracy of Transrectal Power Doppler ultrasound in diagnosing prostate cancers using histopathology as gold standard.

**Methodology:** Fifty-five (55) patients referred from the outpatient & indoor Department of Urology, Surgery & Oncology Medicine of Jinnah hospital Lahore to Radiology department fulfilling the inclusion criteria whose PSA reports show raised serum prostatic specific antigen level > 6.5 ng/ml with or without abnormal digital rectal examination will be included in this study. An informed consent, with promise of confidentiality, was obtained from them for using their data in research. The demographic information (age) will be collected.

These cases were subjected to Transrectal Power Doppler ultrasound using endocavity probe of 10 MHZ attached to GE Logic Pro Color Doppler machine. The Power Doppler ultrasound of the prostate was done to see any area of hypervascularity in the prostate to make the diagnosis of prostate cancer. All the cases underwent targeted & sextant Transrectal prostate biopsies. Results of the histopathology were taken as gold standard.

**Results:** The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of the Transrectal Power Doppler Ultrasound in diagnosing prostate cancer is 97.1%, 80.0%, 89.4%, 94.1% and 90.9%.

**Conclusion:** Transrectal Power Doppler Ultrasound is a good diagnostic tool to increase the rate of detection of prostate cancers, but cannot completely replace the sextant biopsy technique even with state-of-the-art high frequency Power Doppler imaging. Therefore, at present targeted biopsy should always be accompanied by complete sampling of the gland with sextant biopsies.

**Keywords:** Prostate, Prostatic specific antigen, Transrectal Ultrasound, Digital Rectal Examination, Transrectal Power Doppler Ultrasound, Targeted & Sextant Biopsies.
Screening of prostate cancer has generated considerable debate within medical community. Historically, digital rectal examination has been the principal method of examination of prostate. The advent & refinement of ultrasound technology has provided a new method to examine prostate. Transrectal ultrasound with prostate biopsy, a generally well tolerated outpatient procedure, in conjunction with the development of serum assays for prostatic specific antigen (PSA), most widely used oncological biomarker, has high organ specificity is an excellent tumor marker, has resulted in an impressive change in the manner of diagnosis of prostate cancers.

The current modalities for diagnosing & evaluating prostate cancers are digital rectal examination (DRE), prostatic specific antigen (PSA) & Transrectal ultrasound with sextant biopsies, either using 6 core or 12 core technique. Sextant biopsy included bilateral base, mid-gland and apical samples. On average two core biopsy samples of each of the six sextants, totaling 12 separate samples are obtained.

With increased neovascularity in pathologic specimens of prostate cancers, the use of Transrectal Power Doppler ultrasound imaging with targeted biopsy might be expected to improve prostate cancer detection on area of hypervascularity, which suggest biologically aggressive tumors, can enhance the diagnosis of prostate cancers. Available evidence confirms that combining different ultrasound modalities significantly improves diagnostic performance. With MRI-US fusion image, targeted biopsy of suspicious areas on MRI is possible and fusion image guided biopsy can provide improved detection rate. Prevalence of prostate cancer is 46% in 70-81 years of age.

**METHODOLOGY**

Study Design: Cross sectional Study.

Setting: Department of Diagnostic Radiology, Jinnah Hospital Lahore.

Duration of study: June 2020 to November 2020.

Sample size: The calculated sample size with 90.2% sensitivity, 77.4% specificity, 46.0 % expected prevalence of disease, taking 10% desired precision and 90.0 % confidence level is 55 cases.

Sample technique: Non-probability Purposive sample.

Sample selection:

Inclusion criteria:
1. Male between age of 70-81 years.
2. Patients with raised prostatic specific antigen level (> 6.5 ng/ml).
4. Without abnormal digital rectal examination with prostatic specific antigen level >6.5 ng/ml.

Exclusion criteria:
1. Patients already diagnosed to have prostate cancers (previous history).
2. Patient operated for any prostate pathology (previous history).
3. Patient diagnosed with prostatitis (Dysuria, fever, pain in genital area, lower abdominal pain, pain on erection and ejaculation).
4. Patients diagnosed with urinary tract infections (multiple pus cells on urine complete).

Fifty-five (55) patients referred from the outpatient & indoor Department of Urology, Surgery & Medicine of Jinnah hospital Lahore to Radiology department fulfilling the inclusion criteria whose PSA reports show raised serum prostatic specific antigen level > 6.5 ng/ml with or without abnormal digital rectal examination will be included in this study.

An informed consent, with promise of confidentiality, will be obtained from them for using their data in research. The demographic information (age) will be collected.

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in the prostate to make the diagnosis of prostate cancer.

All the cases underwent targeted & sextant Transrectal prostate biopsies. Results of the histopathology were taken as gold standard.

The collected information was entered into SPSS version 23 and analyzed through its statistical program.

The age, prostatic specific antigen level (> 6.5 ng/ml) and size of lesion are quantitative variables and will be presented as Mean ± SD (standard deviation). The findings of digital rectal examination (normal or abnormal), area of hypervascularity (benign / malignant), location of lesion (peripheral, central & transition zones), size of prostate (normal or enlarged), number of lesions (solitary / multiple), peri-prostatic involvement and calcification are qualitative variables and will be presented as frequency & percentages.

The comparison of Power Doppler ultrasound with histopathology was made to calculate sensitivity, specificity, diagnostic accuracy and predictive values of Power Doppler ultrasound.

RESULTS

The study was conducted in the department of Diagnostic Radiology, Jinnah Hospital Allama Iqbal Medical College Lahore. Total of 55 patients were included in this study.

The cases were the patients presented with raised prostatic specific antigen > 6.5 ng/ml with or without abnormal digital rectal examination. Age group included in this study is 70-81 years.

By distribution of age, the patients between age of 70-75 years were 31 (56.4%) and patients between age of 76-81 years were 24 (43.6%) with Mean ± SD (75.7 ± 3.5 year).

All the cases included in this study were having increased Prostatic Specific Antigen level (PSA) > 6.5 ng/ml with Mean ± SD (55.29 ± 110.02) ng/ml.

By distribution of size of lesion, total lesions between size of 5-10 mm are 10 (18.1%), 11-20 mm are 33 (60%), 21-30 mm lesions are 8 (14.5%) and lesion size between 31-40 mm are 4 (7.2%) with Mean ± SD (16.05 ± 0.675).

Distribution of cases by Digital Rectal Examination (DRE), total of 16 (29.0%) with normal DRE findings and 39 (71.0%) with abnormal DRE findings are noted in this study.

Distribution of cases by area of hypervascularity, diagnosed as malignant on Transrectal Power Doppler Ultrasound were 38 (69.0 %) and cases diagnosed as benign patients on Transrectal Power Doppler Ultrasound on the basis of absent area of hypervascularity were 17 (30.90 %).

By distribution of location of lesions, the lesions located in the Peripheral Zone were 38 (69.0 %), lesions located in the Transitional Zone were 15 (27.3 %) and lesions found in the Central Zone were only 02 (03.7 %).

By distribution of cases by size of prostate (Enlarged / Normal), total cases with enlarged prostate were 54 (98.1%), and cases with prostate size within normal limits were 01 (01.9%).

By distribution of cases by number of lesions, total cases with solitary (single) lesions were 48 (87.3%) and total cases with multiple lesions were 07 (12.7%).

By distribution of cases with peri-prostatic involvement, total cases with periprostatic involvement were 09 (16.3%), and cases with absent peri-prostatic involvement were 46 (83.7%).

By distribution of cases with prostatic calcifications, total cases with prostatic calcifications were 18 (32.7%) and cases with absent prostatic calcifications were 37 (67.3%).

Total cases diagnosed as malignant (Prostatic Carcinoma) on histopathology were 35. Out of 35 cases, total number of cases diagnosed on Targeted biopsy alone were 12 (34.3%), diagnosed on Sextant biopsies alone were 02 (05.7%) and total number of cases diagnosed on both Targeted and Sextant biopsies were 21 (60.0%).

Total cases diagnosed as benign cases on histopathology were 20. Out of 20 cases, 15 (75%) were diagnosed as Benign Prostatic Hyperplasia and 05 (25%) were diagnosed as Prostatitis.

On comparison with Transrectal Power Doppler Ultrasound with histopathology in diagnosing malignancy of prostate out of 55 patients, Transrectal Power Doppler Ultrasound detected 38 patients to be positive for malignancy and 17 patients to be negative for malignancy. On histopathology out of 38 patients, 34 patients were (TP) and 4 patients were (FP), out of 17 patients declared negative (Benign) on Transrectal Power Doppler Ultrasound showed
positive in 01 cases (FN) and true negative in 16 cases (TN).

Sensitivity of Transrectal Power Doppler ultrasound for diagnosis prostate cancers was 97.1%, Specificity of 80.0% and Diagnostic Accuracy was found to be 90.9%.

Positive predictive value of Transrectal Power Doppler Ultrasound for prostatic malignancy was 89.4% and predictive value for negative test was 94.1%.

DISCUSSION

Prostate cancer is a disease process that affects the older person at a higher rate than other age groups & most common neoplasm in men.21, 25, 27, 29 Intensified screening efforts in recent years have been made to make diagnosis of early-stage disease.1 In past; digital rectal examination has been the principal method of examination of prostate.3 The current diagnostic modalities for diagnosing & evaluating prostate cancers are digital rectal examination (DRE), prostatic specific antigen (PSA) & Transrectal ultrasound with sextant Transrectal ultrasound guided biopsies, either using 6 core or 12 core technique.7,9 Deliveliotis C, Manousakas T et al conducted study revealed the sensitivities of TRUS and DRE were 75% and 50%, while specificities were 83 and 100% respectively.15 Hypervascularity in prostate cancer has been demonstrated using Transrectal Colour and Power Doppler ultrasound, and the distribution of Doppler signals provides information in addition to that obtained from the grey-scale image of conventional TRUS. Several studies have evaluated the usefulness of CDUS, and PDUS for detection of prostate cancer and guidance in targeted biopsies.10-13,20,21 Studies have shown that Sonographic contrast / contrast-enhanced Transrectal Ultrasonography (CE-TRUS) & Transrectal real time tissue Elasto-graphy (TRTE) could be used as a complement to significantly improve detection rate of prostate cancer.22,23,24,25,27,30

The present study was conducted to evaluate the usefulness of Transrectal Power Doppler Ultrasound in the diagnosis of prostate cancer especially in patients with raised PSA level more than the age specific levels. Transrectal Power Doppler ultrasound was performed before biopsy using machine GE Logic Pro Color Doppler system with Endorectal Probe of 10 MHZ. The Doppler gain was adjusted to a point below the range at which no background signals were observed.22 Scanning to detect flow was continued for approximately 5 minutes in each patient, and examination consisted of sequences of axial image from apex to base. All the prostate biopsies were done by using Bard Monopty Biopsy Needle 18 gauge with 20 cm length on Transrectal probe with attachment for needle guidance.

In present study all the patients were given Injection Rocaphin 1 gm IV Stat Prior to procedure, subsequently followed by Cap. Cefspan-400mg One OD for five days. In present study all the patients underwent targeted biopsies on the basis of hypervascularity on TR-PDU followed by complete sampling of the prostate by sextant biopsies. Although the positive yield of targeted biopsy in our study was good and 12 (34.3%) cases were diagnosed on targeted biopsy alone, 02(05.7%) cases were diagnosed on sextant biopsies alone and 21(60.0%) prostate cancers were diagnosed on both targeted and sextant biopsies. So on the basis of our results, we conclude that targeted biopsy with Power Doppler imaging cannot completely replace sextant biopsy technique to diagnose prostate cancer even with state of the art high frequency Power Doppler imaging. In the present study the sensitivity of Transrectal Power Doppler Ultrasound is 97.1%, specificity is 80.0%, Positive predictive value is 89.4%, Negative predictive value is 94.1% and Diagnostic Accuracy is 90.9%.

Results of our study are close to the study conducted by Kimura G et al.16 Results of the present study are also quite comparable to study conducted by Remzi M.18 Present study is also comparable to study conducted by Takahashi S.19

However, nothing can be said with certainty, because we also have false positive & false negative reports in our study. There are four false positive and one false negative report in our study. So limitations of the study should be acknowledged. The most common factors which probably resulted in false values are increased vascularity in the dependent portion of prostate, as in our study the Transrectal Power Doppler ultrasound with biopsies done in left lateral decubitus position.26 This is supported by the study conducted by Halpern EJ et al.27

Complications reported in present study are very few Out of 55 patients, only 01(1.8%) patient was hospitalized for septicemia, who has not fully
complied with antibiotic regimen. Only 04(7.27%) patients developed haematuria, required hospitalization, settled in one week.

CONCLUSION

It is concluded from the current study that Transrectal Power Doppler ultrasound is a useful tool for increasing the rate of detection of prostate cancer, however PDU-guided target biopsy alone cannot completely replace sextant biopsy technique for cancer detection because of the existence of PDU-negative cancer. So targeted biopsies on the basis of increased vascularity coupled with sextant biopsies will be the best method for the detection of prostate cancer. Further advances in ultrasound technology may enable the detection of prostate cancer by target biopsy alone and consequently may reduce the number of unnecessary biopsies. Therefore, at present targeted biopsy should always be accompanied by complete sampling of the gland with sextant biopsies.

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Authors Contributions

Conception & Design: Dr. Naeem Ahmad Khan.
Collection & Assembly of data: Dr. Naeem Ahmad Khan, Dr. Tanweer Ahmad.
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Lichen Planus is a chronic inflammatory disorder involving mucosae and the skin affecting 0.5 to 1.99% of the general population. Its exact etiology is unknown but it is believed to result from an autoimmune response in which basal epithelial cells are recognized as foreign because of the change in the antigenicity of their cell surface. The classic clinical presentation of lichen planus lesion is a violaceous, flat-topped papule. Lesions may also have a thin, transparent, and adherent scale. Wickham’s striae, which are defined as fine whitish points or lacy lines, may be seen on the surface of well-developed papules. It has different clinical subtypes based on the morphology of the lesions and the site of involvement. They include classic, hypertrophic, vesiculobullous, actinic, annular, linear, orogenital, follicular, lichen planus pigmentosus and guttate lichen planus.

Lichen planus has been associated with various factors such as anxiety, diabetes, autoimmune diseases, mainly chronic liver disease, intestinal diseases, increased cholesterol, medications, stress, hypertension, infections, contact with dental material and malignancy especially in oral lichen planus. Its association with diabetes mellitus has been reported in patients of diabetes mellitus in various studies. Ahmed et al in 2011 at Karachi, Pakistan found that 6.9% patients of diabetes mellitus had lichen planus. Mohsin et al conducted a similar study on diabetic patients from 2010 to 2012 and found that lichen planus was diagnosed only in 1.8% patients of Type 2 diabetes. A Another study in India, by Timshina et al in 2012 also found that only 1.8% of diabetics developed lichen planus.

Atefi et al in 2012 conducted a study in Iran on patients suffering from lichen planus to observe
frequency of diabetes mellitus and impaired fasting glucose. They evaluated 80 patients with lichen planus, out of which 48 were females and rest were males. The diagnosis of diabetes mellitus and impaired fasting blood glucose was based on the 2007 guidelines of American Diabetes Society. They found that 16 patients (20%) had diabetes mellitus and 14 patients (17.5%) had impaired fasting blood glucose levels. So, total 30 out of 80 patients (37.5%) had impaired glucose metabolism.

Various studies have been done to see the frequency of lichen planus in diabetes mellitus. However, little data is available to determine frequency of diabetes mellitus in patients of lichen planus. The present study was undertaken to explore frequency of diabetes mellitus and impaired glucose tolerance in patients of lichen planus. This will help us to formulate local guidelines for regular screening of diabetes and impaired fasting glucose levels in patients presenting with lichen planus. To the best of our knowledge no local study of this kind could be found during literature search.

**METHODOLOGY**

This was a cross sectional study conducted at Dermatology department unit I, Jinnah Hospital, Lahore for a period of six months from September 2016 to March 2017. A total of 155 patients of both genders, between ages 15-60 years with a clinical diagnosis of lichen planus, and not having any other dermatologic disease were enrolled in the study. Patients taking oral steroids and pregnant patients were excluded from the study. Written informed consent was taken.

The data was collected by researcher herself and entered on a pre designed structured proforma. Demographic data including name, age, gender and duration of lichen planus were all recorded. Patients’ blood sample was drawn after 8 hours of fasting using aseptic technique and sent to lab for detecting HbA1c levels and fasting blood glucose levels.

The lab findings were noted and recorded into the proforma also. All the tests were done from the same laboratory, to eliminate bias and confounding variables were controlled by exclusion. All the collected data was entered and analyzed through SPSS version 20.0.

**RESULTS**

A total of 155 cases fulfilling the inclusion criteria were enrolled in the study.

The ages of the patients ranged from 15 to 60 years with mean of 44.12+7.14 years. Age distribution of the patients showed that majority of the patients was between 41 to 60 years of age, i.e 69.67%. Males were 58.71% (n=91) while 41.29% (n=64) were females. Majority of patients had duration of disease more than 5 years. (Table 1)

Frequency of diabetes mellitus in patients with lichen planus was recorded as 17.42% (n=27), while 22.58% (n=35) had impaired fasting glucose only. (Table 2)

The data was stratified for age, gender and duration of disease. Chi-square test was used, post stratification, with p-value <0.05 considered as significant. This showed that there was no statistically significant difference of results among patients of different age, sex and duration of the disease.

**DISCUSSION**

Lichen Planus is a chronic inflammatory skin disorder with unknown etiology. It is known to be associated with Hepatitis C, vitiligo alopecia areata and diabetes mellitus. In the previous studies, it was found that diabetes mellitus and impaired fasting blood glucose were prevalent in patients of lichen planus. Various studies have been done to see the frequency of lichen planus in diabetes mellitus. However, little data is available to determine the frequency of diabetes mellitus in patients of lichen planus. The present study was planned to explore the frequency of diabetes mellitus and impaired fasting blood glucose in diagnosed patients of lichen planus. That will help us to formulate local guidelines for screening of diabetes mellitus in patients of lichen planus.

| Table 1: Demographic Details of the Patients (n=155) |
|--------------------------|------------------|----------------|
| Age(in years)            | No. of patients  | %              |
| 15-40                    | 47               | 30.33          |
| 41-60                    | 108              | 69.67          |
| Gender                   | No. of patients  | %              |
| Male                     | 91               | 58.71          |
| Female                   | 64               | 41.29          |
| Duration of disease      | No. of patients  | %              |
| 1-5 yrs                  | 19               | 12.3           |
| >5 yrs                   | 136              | 87.7           |
regular screening of diabetes in patients presenting with lichen planus. In our study, mean age of patients was 44.12±7.14 years with 58.71% (n=91) males and 41.29% (n=64) females. Frequency of diabetes mellitus in patients with lichen planus was recorded as 17.42% (n=27), while 22.58% (n=35) had impaired fasting blood glucose. So, total 62 out of 155 patients (40%) had impaired glucose metabolism. When we stratified our data for age, gender and duration of disease it showed that there was no statistically significant difference of results among patients of different age, sex and duration of the disease.

In a similar study conducted in Iran by Atefi et al in 2012, 80 patients with confirmed lichen planus were studied. Their mean age was 52.04 ± 8.88 years and total 30 out of 80 patients (37.5%) had impaired glucose metabolism. These results were comparable to ours.

In another study, done in 2004 in Turkey, to determine the frequency of Hepatitis B, C and diabetes mellitus in patients of lichen planus 41 patients out of 260 (15.7%) were diagnosed as diabetics. However, they did not investigate the blood samples for impaired fasting blood glucose levels.

Previously, many studies have shown variable relationships between diabetes mellitus and lichen planus. Guggenheimer, et al in 2000, reported the incidence rate of 0.5% of oral LP among patients with insulin-dependent diabetes mellitus. In another study in Turkey in 2007, the prevalence of diabetes mellitus in patients with lichen planus was found to be 26.7%. In addition, they found a significant difference between the concentration of HbA1c, fasting blood sugar and insulin resistance in patients with lichen planus and the control group.

Some authors however showed no or little correlation between lichen planus and diabetes mellitus. In 2011, Arshiya S et al, in India, observed diabetes mellitus in only 10% (5 of 50) of their patients with oral lichen planus. They found that the frequency was far less than the expected prevalence. This difference in results can possibly be due to difference in ethnicity, genetic makeup and different criteria used to diagnose diabetes mellitus.

The limitation to our study was that we had no control group to compare our results with. The results of our study are helpful for us to formulate local guidelines for regular screening of diabetes mellitus and impaired fasting glucose levels in patients presenting with lichen planus. This will help in early detection and timely management of diabetes mellitus in patients of lichen planus.

### CONCLUSION

It is concluded that the frequency of diabetes mellitus and impaired fasting glucose in patients with lichen planus presented in dermatology outpatient department of Jinnah hospital, Lahore, is 17.5% (n=27) and 22.58% (n=35) respectively.

### Conflict Of Interest

The authors declare that they have no conflict of interest.

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### Limitations of Study

Our study has smaller sample size.

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FREQUENCY OF DIABETES MELLITUS AND IMPAIRED FASTING GLUCOSE IN PATIENTS WITH LICHEN PLANUS


Abstract

Objective: To compare the functional outcome in terms of post operative mobility for unipolar versus bipolar uncemented hemiarthroplasty in elderly patients with displaced intracapsular femoral neck fractures.

Methodology: One hundred and thirty eight patients fulfilling inclusion and exclusion criteria presenting to orthopedic unit of Jinnah Hospital Lahore with fracture neck of femur were selected for study. After ethical approval from supervisor and written consent from patients, Patients were divided into two groups randomly by lottery method and enrolled for unipolar and bipolar hemiarthroplasty in group A and B respectively. The operative procedures were performed by an experienced team of surgeons of the Orthopedic Department of Jinnah Hospital Lahore under spinal anesthesia and hemiarthroplasties were done through lateral approach. Functional outcome was measured at 12 weeks using Timed up and go test.

Results: As regard to the Functional Outcome, 38 (27.5%) patients had good outcome and 100 (72.5%) patients had bad outcome. Out of Good functional outcome, 10 Patients had undergone Unipolar Hemiarthoplasty and Bipolar Hemiarthoplasty was done in 28 patients. Out of Bad functional outcome, 59 patients had Unipolar Hemiarthoplasty and 41 had Bipolar Hemiarthoplasty (Table-3). Out of 138 patients, 56 (40.6%) were using no walking aid and 82 (59.4%) were using walking aid.

Conclusion: Functional outcome in term of mobility is better in case of bipolar hemiarthroplasty as compared to unipolar hemiarthroplasty.

Key Words: Bipolar hemiarthoplasty, Functional outcome, Intracapsular femoral neck fractures, Timed up and go test, Unipolar hemiarthroplasty.

Hip fracture is a significant health care problem worldwide in elderly population, with an annual incidence of approximately 1.31 million hip fractures in 1990, which is expected to rise to 6.26 million globally by 2050, due to increasing mean age of population worldwide and morbidities associated with elderly patients like osteoporosis and poor cognition. Although both unipolar and bipolar hemiarthroplasty are approved treatment for displaced fracture neck of femur in elderly, the theoretical advantage of bipolar over unipolar prosthesis is the reduction of acetabular erosion due to movement at two poles causing less movement at prosthetic head and acetabulum as compared to unipolar implant.
The most common treatment for displaced fracture neck of femur in elderly is unipolar hemiarthroplasty because it is less expensive. It may prove expensive in case of postoperative complications leading to revision surgeries. In this controversy Bhushan M Sabnis, I J Brenkel in Scotland United Kingdom compared the functional outcome in term of mobility and observed good results of 33% for bipolar and 13% for unipolar hip hemiarthroplasty. Morvin I7 conducted a study on cemented versus cementless hemiarthroplasty in femoral neck fracture in elderly patients and reported that, Cementless hip arthroplasty is an established treatment for femoral neck fracture in pre-injury mobile elderly patients. Cement pressurization raises intramedullary pressure and may lead to fat embolization, resulting in fatal bone cement implantation syndrome, particularly in patients with multiple comorbidities. The cementless stem technique may reduce this mortality risk but it is technically demanding and needs precise planning and execution.

The treatment goals for femoral neck fractures are early return to a satisfactory functional status, minimization of mortality, morbidity and the need for re-operation. The management of intracapsular femoral neck fractures in active elderly patients is controversial. There is no consensus on the treatment of choice with respect to internal fixation, unipolar or bipolar hemiarthroplasty and total hip replacement. However, active elderly patients (aged 70–90 years) with femoral neck fractures have poor results after unipolar hemiarthroplasty owing to increased demands on such hip.

Although the results of the previous studies are promising, but there is still no definitive answer and the treatment norm has not changed. Because this study used the Timed Up and Go test, which was an early clinical indicator of functional outcome in patients with a hip fracture treated with hemiarthroplasty. This study included well-defined group of patients and has the power of a prospective randomized control trial, it offered the definitive answer that would change the norm of treatment.

METHODOLOGY

One hundred and thirty eight patients aged 50yrs or above with Garden type III or IV fracture were selected through non probability purposive sampling technique. Patients were admitted through the emergency department of Jinnah hospital Lahore after initial resuscitation according to ATLS protocol. Patients with undisplaced fracture, preexisting arthritis, predisposition to osteoporosis, ipsilateral femoral shaft fracture, poly-trauma patients and patients who were not independent ambulatory before injury were excluded from study. Ethical approval for this study was taken from supervisor. After informed consent, patients were randomized by lottery method to one of the groups of the study. Patients in Group A were treated by uncemented unipolar (Austin Moore) prosthesis, while Group B patients underwent uncemented bipolar hemiarthroplasty. Prophylactic antibiotics for infection were given preoperatively and postoperatively. Deep vein thrombosis prophylaxis was given to every patient postoperatively. Patients were discharged on third postoperative day and stitches were removed on 14th postoperative day.

The operative procedures were performed by a single selected team of surgeons of the Orthopedic Department of Jinnah Hospital Lahore under spinal anesthesia and hemiarthroplasties were done through lateral approach.

The patients were followed up at three months and their mobility level was assessed by an independent observer by Timed up and go test. The observer was not allowed to look at the file of the patient to know the type of surgery performed. All the information including outcome variables was recorded on a specially designed proforma by the researcher. All the data was entered on SPSS for windows version 10.

Mean and standard deviation was calculated for quantitative variables i.e. age and timed up and go score. Frequencies and percentages were calculated for gender and outcome variables like independent mobility versus dependent mobility. Chi-square test was used to compare outcome variable in both groups. A p-value < 0.05 was considered statistically significant. Effect modifiers like age and sex were controlled by stratification. Chi square test was applied to see significant difference.

RESULTS

Out of 138 patients, 74 (53.6%) were male and remaining 64 (46.4%) were female. Regarding age of the patients, mean age was 65.12 and Standard
Deviation was 8.671. In time up and go score test, 45 (32.6%) patients were able to complete the task in less than 20 sec and the task was completed in more than 20 sec in 93 (67.4%) patients (Table 1).

Out of 138 patients, 56 (40.6%) were not using walking aid and the patients using walking aid were 82 (59.4%) as shown in the (Table-2).

As regard to the functional outcome, 38 (27.5%) had good outcomes and 100 (72.5%) had Bad outcome. Out of good functional outcome, 10 patients have unipolar hemiarthroplasty and 28 have bipolar hemiarthroplasty and out of bad functional outcomes, 59 patients have unipolar hemiarthroplasty and 41 have bipolar hemiarthroplasty.

DISCUSSION

Although surgeons have reached consensus regarding the treatment of undisplaced femoral neck fractures but controversy still persists regarding the management of displaced femoral neck fractures.8 The choice of treatment and outcome assessment in very elderly patients is contentious, because of their limited life expectancy. This makes early satisfaction as important as long-term outcomes.12 With an annual mortality of around 30% and associated substantial impairment of independence and quality of life, the treatment goal for hip fractures is to return to pre-injury mobility status as early as possible.13

The surgical options for hip fractures include internal fixation, hemiarthroplasty, and total hip replacement. Hemiarthroplasty is considered the optimal treatment for elderly patients with displaced femoral neck fractures and produces satisfactory results.14 Nonetheless, for patients who are mobile, socially independent and fit, the treatment is controversial. Internal fixation has a high rate of nonunion and is inferior to hemiarthroplasty. According to the Norwegian hip fracture register, patients treated with hemiarthroplasty had less pain and were more satisfied with the outcome than those treated with internal fixation.15

Hemiarthroplasty using the Austin Moore prosthesis remains a popular choice.16 Bipolar prosthesis enable reduction of acetabular wear and increase in prosthesis life and function.17,18 Compared to unipolar hemiarthroplasty, bipolar hemiarthroplasty confers better19 or similar20 overall outcomes as well as better pain relief and function. It is therefore recommended for active patients.21 Although bipolar prosthesis are more costly, they may be cost-effective in terms of better functional outcome.22 For patients aged 60 to 80 years with displaced femoral neck fractures, bipolar hemiarthroplasty was most commonly used, whereas for those aged ≥80 years, unipolar hemiarthroplasty was more popular.18

Total hip replacement as a primary treatment has also been considered; its results are variable.22,23 The Scottish intercollegiate guidelines and other studies recommended cemented hemiarthroplasty.18,24,25 Cemented bipolar hemiarthroplasty achieves good short and long-term results.18 Uncemented hydroxyapatite coated femoral stems also achieve good long-term prosthesis survival in total hip replacements.26,27 Uncemented hydroxyapatite coated bipolar hemiarthroplasty also achieves good midterm outcomes in elderly patients with femoral neck fractures.28 Outcomes following cemented versus uncemented bipolar hemiarthroplasty are not significantly different (except for shorter operative time and less blood loss in the uncemented group).28 Postoperative mortality is high in elderly patients undergoing surgery for intracapsular femoral neck fractures.26

In our study, patient mobility and mortality were therefore reviewed at the 3-months follow-up. Patients who were able to walk unaided or using one

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Table 3: Functional Outcome

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Table 4: Functional Outcome

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<tr>
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<tr>
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</tr>
<tr>
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<td>Bipolar</td>
<td>41</td>
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<td>Total</td>
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stick before injury were considered active and treated with uncemented bipolar hemiarthroplasty. They were fitter, more mobile and had less co-morbidity and expected to have superior results. Nonetheless, even after adjusting for the preoperative mobility and ASA score, results of bipolar hemiarthroplasty remained better than those of unipolar hemiarthroplasty. Active patients with more demands on their hips, usually have more problems after unipolar hemiarthroplasty in the form of hip pain, increased rate of dislocation, acetabular wear and protrusion.

In patients undergoing bipolar hemiarthroplasty, cardiac diseases, living in a nursing home, chronic pulmonary disease, previous myocardial infarction, pneumonia, high creatinine levels, long operating time and male gender were associated with mortality at 6 months. In our study, specific co-morbidities were not analyzed, but the ASA score encompasses all these and is the important factor determining mortality.

All our patients were operated through the lateral approach with an anterior exposure. Our study was limited by the lack of randomization in treatment, leading to selection bias. Patients treated with bipolar hemiarthroplasty had an obvious better case mix. Total hip replacement was not considered as a treatment option owing to the protocol in our hospital. In our elderly patients with femoral neck fractures who were fit and physically young, uncemented bipolar hemiarthroplasty seemed to achieve better functional outcome.

CONCLUSION

There is no definite cut-off age for unipolar or bipolar hemiarthroplasty. Active patients with more demands on their hips, usually have more problems after unipolar hemiarthroplasty in the form of hip pain, increased rate of dislocation, acetabular wear and protrusion. Functional outcome in term of mobility is better in case of bipolar prosthesis as compared to unipolar prosthesis.

Conflict of Interest: There is no conflict of interest to declare by any author.

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Diabetes mellitus is a chronic disorder which has taken a pandemic form. According to estimates made in 2013 approximately 382 million people are suffering from diabetes mellitus all over the world. The situation in South Asia is alarming where prevalence of DM is expected to increase by 151% between years 2000 to 2030.1-2 One of the most common complications of DM is peripheral neuropathy affecting patients suffering from both type 1 and type 2 DM.3-4 It leads to loss of protective sensation particularly in feet and makes an individual prone to development of ulcers which mostly takes a chronic form and eventually may lead to the amputation of the limb. Although it varies in severity, the overall prevalence of diabetic neuropathy varies around 20% - 30%.4-5 Almost half of the patients suffering from DN ultimately develops the painful form of this diabetic complication.4

The role of vitamin D in musculoskeletal system is a well-known entity. However, over the past decade, its extraskeletal effects has become a huge attraction. There is good evidence that vitamin D plays role in immune and cardiovascular system and even in cancer prevention.5-6 Although there are no

### ABSTRACT

**Background:** Diabetes is a chronic problem present globally with painful diabetic polyneuropathy being one of its most common complications. Various drugs have been used till date to treat this painful condition with variable success rates and many side effects.

**Objective:** To determine the efficacy of Vitamin D in treating painful diabetic neuropathy along with conventional therapy using pregabalin.

**Methodology:** Hundred diabetic patients recruited in this study were randomly divided into two groups. Patients in group A received only oral pregabalin while the patients in group B were given oral vitamin D in addition to pregabalin. Patients in both groups were followed up at 6 weeks and at 12th week after the start of therapy. Age, gender, duration of diabetes mellitus and pain scores were recorded on a pre designed proforma. Data was analyzed using SPSS 16.

**Results:** Group A had 28 (56%) male patients and 22 (44%) female patients while group B had 20 (40%) male and 30 (60%) female patients (p=0.109). The mean age of patients (p=0.342), type (p=0.534) and duration of DM (p=0.869) was comparable in both groups. The pain score of two groups was not significantly different at zero week (p=0.387). However, significant difference is seen in mean pain scores between two groups at 6 weeks (p=0.000) and at 12 weeks (p=0.000); mean pain score being much lower in group B as compared to group A.

**Conclusion:** Single dose of oral vitamin D combined with pregabalin is significantly more effective for the treatment of painful diabetic neuropathy than pregabalin alone.

**Key Words:** Painful diabetic neuropathy, vitamin D, pregabalin
well-defined cut off values to mark vitamin D deficient levels, yet it is a known fact that many children and adults are deficient in this important vitamin.\textsuperscript{5,7}

Various studies have revealed that Vitamin D plays role in the development of DM. Lower levels of vitamin D increases the risk for the development of DM2 and produces glucose intolerance. Many diabetic patients have lower levels of Vitamin D in their body. Restoring the levels of Vitamin D have shown to improve the glycemic control in diabetics.\textsuperscript{6,8-11} He et al have concluded in their study that Vitamin D deficiency is an independent risk factor for DPN.\textsuperscript{12}

Various drugs with variable success have been used for the treatment of painful DN. These include antidepressants (TCAs and SNRIs), anticonvulsants including pregabalin and opioids. Topical agents like capsaicin, topical nitrates and topical TCAs have also been used. Among these, gabapentic has proven to be most efficacious and safe for the treatment of PDN and is the US FDA approved first line drug along with duloxetine for PDN.\textsuperscript{13-17} However, it must be kept in mind that the key to successful treatment is good glycemic control as uncontrolled diabetes is associated with progression of PDN.\textsuperscript{13,15}

Recent studies have shown that correcting vitamin D levels improve glycemic control in patients with type 2 DM and that single IM inj of Vitamin D or short term oral vitamin D therapy has improved the symptoms of PDN.\textsuperscript{9,10,18,19} However, to my knowledge, no study has yet compared the combined effect vitamin D and conventional therapy for PDN with conventional therapy alone.

**METHODOLOGY**

This study was carried out in the medical outdoor units and pain clinic of Mayo hospital, Lahore from January 2018 to June 2018. A total of 100 patients were recruited in this study after taking the approval of research and ethical committee of the hospital. Both male and female patients having ages between 30 and 70 years with type 1 or type 2 diabetes mellitus were included in the study. Patients who were excluded from the study included patients having renal impairment, having thyroid dysfunction, Subjects already taking vitamin D supplementation, Patients having parathyroid dysfunction or impaired calcium homeostasis, Alcoholics, Patients with HBV, HCV or HIV infections and Pregnant patients.

Informed consent was taken. Patients’ identity was kept confidential. Risks and benefits were explained to the subjects. All subjects were interviewed for demographic information such as name, age and gender. Duration and type of diabetes mellitus was noted. Initial assessment of pain was done using numeric pain scale. Patients were randomly allocated in two groups, A and B. Patients in group A received only oral pregabalin150 mg every night while those in group B were given single dose of oral Vitamin D supplementation, 60, 000 IU along with oral pregabalin150 mg every night. Patients were called for follow up at 6th week and then at 12th week and severity of pain was assessed again in both groups. All this information was collected through anespecially pre-designed Proforma. Data was entered and analyzed through SPSS version 16. Quantitative variables like age, duration of diabetes mellitus and pain scores were presented as mean and standard deviation. The Qualitative variables like gender and types of diabetes mellitus will be presented as frequency and percentages. The mean pain score of two groups was compared using t- test with p value < 0.05 taken as significant.

**RESULTS**

This randomized controlled study was conducted on 100 patients, 50 in each group. The mean age of patients in group A was 52.48 ± 10.326 years while the mean age of patients in group B was 54.48 ± 10.628 years (p=0.342). Group A had 28 (56%) male patients and 22 (44%) female patients while group B had 20 (40%) male and 30 (60%) female patients (p=0.109). There were 20 (40%) patients having type-1 DM and 30 (60%) patients having type-2 DM in group A while group B had 17 (34%) type-1 and 33 (66%) patients having type-2 DM (p=0.534). The duration of DM in patients belonging to group A was 10.60 ± 3.188 years while in group B was 10.50 ± 2.873 years (p=0.869). The mean pain score in two groups at 0, 6 and 12 weeks were as shown in table-1. The pain score of two groups was not significantly different at zero week (p=0.387) however, significant difference is seen in mean pain scores between two groups at 6 weeks (p=0.000) and at 12 weeks (p=0.000); mean pain score being much
lower in group B as compared to group A.

DISCUSSION

Painful diabetic neuropathy is one of those complications of diabetes mellitus which is not uncommon. It adds much misery to the life of a diabetic patient by not only making their quality of life poor but also by adding the financial burdens of the treatment of this much resistant form of pain.

Low levels of vitamin D had been attributed as a risk factor for the development of DM. low levels has been associated with poor glycemic control and development of microvascular complications of DM. He et al in their study including type -2 diabetic patients concluded that vitamin D deficiency is an independent risk for the development of peripheral neuropathy. Kostoglou-Athanassiou et al concluded in their study that low levels of vitamin D are seen in type 2 diabetics and also suggested that supplementing the vitamin D levels may improve the glycemic control.

In our study, administration of single oral dose of vitamin D along with the first line therapy with pregabalin significantly improved the pain scores in patients suffering from painful diabetic neuropathy.

This could be attributed to the improvement of glycemic control which is essential for the successful treatment of PDN.

The results of our study were comparable to the study conducted by Basit et al in which single dose vitamin D supplementation improved the symptoms of painful diabetic neuropathy significantly. However, they supplemented the vitamin D levels intramuscularly in contrast to our study in which we administered vitamin D by oral route. Also, they did not give any drug per se for the treatment of PDN in contrast to our study in which we administered pregabalin to the patients in both groups.

Our results are also comparable to the study conducted by Shehab et al in which vitamin D supplementation improved the neuropathy in type 2 diabetics. However, they didn’t not include type -1 diabetic patients in their study. Also vitamin D was administered on weekly basis for 8 weeks alone and neuropathic status was assessed at the end of 8th week in contrast to our study in which single dose oral supplementation was done at the start of therapy along with pregabalin.

In a case reported by Bell, the severe pain of diabetic neuropathy was considerably relieved in a patient when his vitamin D levels were corrected.

Comparable results are also seen in the study conducted by Ghadiri-Anari et al in which oral vitamin D supplementation improved the symptoms of painful diabetic neuropathy in type-2 diabetics. However, vitamin D was supplemented on weekly basis for 12 weeks before assessing PDN in contrast to our study in which we supplemented oral vitamin D as a single dose. Also, no other drug was administered to control the neuropathic pain while we administered pregabalin to the patients in both study and controlled group.

Few studies has been conducted so far showing the beneficial effect of vitamin D replacement on PDN. Also no study so far, to the best of our knowledge, has been conducted in which drug to counter the neuropathic pain was also administered to the patients suffering from PDN. Hence in this regard our study is first of its kind. However, in our study we did not get the baseline levels of vitamin D in the patients recruited in our study. Getting these levels done might have further clarified the role of vitamin D supplementation for the management of PDN.

CONCLUSION

Single oral dose of Vitamin D is effective in treating painful diabetic neuropathy along with conventional therapy using pregabalin and significantly improves the painful symptoms.

Limitations of the Study

The study was conducted on 100 patients. Study conducted of larger scale are needed to further validate the findings.

Acknowledgments

We, the authors, are grateful to the heads of medical units of Mayo Hospital Lahore, who support and encourage us in the conduct of this study.

Conflicts of Interests

None
ROLE OF VITAMIN D ALONG WITH PREGABALIN FOR THE TREATMENT OF PAINFUL DIABETIC NEUROPATHY

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Contribution of the Authors
Dr. Mohsin Masud: Conduct of the study work, data collection, literature review
Dr. Lala Rukh Bangash: Conduct of the study work, literature review, statistical analysis
Dr. Shaheer Nayyer: Data collection, manuscript editing
Dr. Faridah Suhail: Data collection
Dr. Rizwan: Manuscript editing, data collection
Dr. Anam Fatima Bangash: Data collection, literature review

REFERENCE
ASSOCIATION OF MEAN SERUM MAGNESIUM LEVELS IN PATIENTS HAVING NON-INSULIN DEPENDENT DIABETES MELLITUS ALONG WITH ISCHEMIC HEART DISEASE AT A TERTIARY CARE HOSPITAL OF LAHORE

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Abstract

Background: Magnesium cation serves to prevent oxidative stress in the body and regulates various ion transport channels across cell membrane to achieve normal glycemic levels deficiency. Magnesium deficiency has been linked in diabetes and complications though it is generally corrected by replacement. Individuals with Diabetes mellitus are at 2 to 3 folds increased risk for cardiovascular disease (CVD) relative to those without diabetes.

Objective: Our aim of study was to determine the association between mean serum magnesium levels in patients with diabetes having ischemic heart disease.

Methodology: The study design was of cross-sectional descriptive type conducted on 246 patients of medical ward of Jinnah hospital, Lahore.

Results: Out of 246 cases, 47.56% (n=117) were between 30-50 years of age while 52.44% (n=129) were between 51-70 years of age, mean+sd was calculated as 51.08+9.26 years, 57.72% (n=142) were male and 42.28% (n=104) were females, mean magnesium level was calculated as 0.77+0.12 mmol.

Conclusion: It is concluded that mean serum magnesium levels in patients with diabetes having ischemic heart disease were significantly lower.

Key words: Association, non-Insulin dependent Diabetes, Ischemic heart disease, mean serum magnesium levels.

Magnesium (Mg) ions is an important fourth most abundant cation, necessary for various enzymatic actions at cellular level in humans.1 Serum magnesium levels and incidence of diabetes mellitus goes in an opposite direction. Type 2 diabetes mellitus is now prevailing with increased incidence, especially in the developing world.2,3 Diabetes is associated with increased morbidity and mortality because of micro and macro vascular complications. Deficiency of various cations can happen in diabetes mellitus due to poor absorption as a result of oxidative stress. Diabetes is associated with hypomagnesaemia.4 Because of increased urinary losses of various ions including magnesium therefore reduced serum magnesium levels.5 Low serum magnesium level in diabetes is associated with cardiovascular disease. It has role in the pathogenesis of arteriosclerosis, coro-nary spasm, myocardial function, acute myocardial infarction and ventricular arrhythmias.6,7 Administration of Mg2+ supplementation has a protective impact on diabetics by reducing morbidity and mortality.8 Despite numerous reports linking hypomagnesaemia with chronic diabetic complications, still it has not been the field of interest for
ASSOCIATION OF MEAN SERUM MAGNESIUM LEVELS IN PATIENTS HAVING NON-INSULIN DEPENDENT DIABETES

Clinicians. Local data is scanty which showed variable trend in mean serum magnesium levels in diabetic patients with ischemic heart disease. 73.3% patients had low serum magnesium level, 6.7% had normal level and 20% had high level. The present study may guide if diabetics can be treated with supplemental magnesium with concurrently reduced mean serum magnesium level. It will reduce morbidity and mortality associated with diabetes and cardiovascular diseases.

METHODOLOGY

The current study is cross sectional descriptive type that was conducted at the department of medicine, Jinnah hospital, Lahore over a period of 6 months started from January 2019. Total of 246 patients of both genders with age ranges from 35 to 70 years recruited for the study. These 246 individuals were having non-insulin dependent Diabetes Mellitus diagnosed at least 6 months ago on a fasting blood glucose of more than 126mg/dl and having ischemic heart disease evident by ECG findings of ST-T changes, pathological Q waves within last 1 month at least. Individuals having chronic liver disease as evidenced by ultrasonographic evidence of splenomegaly and coarse liver, estimated GFR less than 60 ml/min, taking diuretics that interfere with magnesium ions absorption, history of acute or chronic diarrhea were excluded from our selection criteria. Informed consent was taken for withdraw of blood specimen of 5ml. for the analysis of glycosylated hemoglobin (HbA1C), serum magnesium levels via a standardized automated analyzer along with serum creatinine, liver ultrasound for liver and spleen size and texture on the day of admission. The data was collected by the researchers, entered in the pre-designed proforms and analyzed via using SPSS 18. Quantitative variables like age, magnesium levels and HbA1c were measured as mean and standard deviation. Qualitative variables like gender, hypertension, smoking, dyslipidemia, nutritional status was recorded as frequency and percentages. Data was stratified for age, gender, BMI, hypertension, smoking, prior treatment for diabetes, HbA1c, dyslipidemia and nutritional status. Post stratification t-test was applied. A p value ≤ 0.05 was considered significant.

Table 1: Demographic & Biochemical Parameters of Patients (n=246)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender No (%)</td>
<td>Male:142 (57.72)</td>
</tr>
<tr>
<td></td>
<td>Female: 104 (42.28)</td>
</tr>
<tr>
<td>Age in years (Mean± SD)</td>
<td>51.08±9.26</td>
</tr>
<tr>
<td>35-50 year (no, %)</td>
<td>117 (47.56)</td>
</tr>
<tr>
<td>50-70 year (no, %)</td>
<td>129 (52.44)</td>
</tr>
<tr>
<td>Serum magnesium mmol (Mean± SD)</td>
<td>0.77±0.12</td>
</tr>
<tr>
<td>HbA1c (%)(Mean± SD)</td>
<td>7.51±0.65</td>
</tr>
<tr>
<td>BMI(Mean± SD)</td>
<td>31.19±3.80</td>
</tr>
</tbody>
</table>

Table 2: Cross tabulation of hypomagnesemia in diabetics and ischemic heart disease with HbA1C levels (n=246)

<table>
<thead>
<tr>
<th>HbA1C %</th>
<th>Hypomagnesemia mmol/l</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.5-8.0</td>
<td>0.76</td>
<td>0.17</td>
</tr>
<tr>
<td>&gt;8.0</td>
<td>0.74</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Figure 1: Presence or Absence of Risk Factors in Addition to Ischemic Heart Disease in Diabetics

RESULTS

246 subjects fulfilling the requirement enrolled in this study. 117 patients (47.56%) were between 35-50 years of age while 129 (52.44%) were between 51-70 years of age, mean±S.D. was calculated as 51.08±9.26 years. Demographics of the variables shown in Table No. 1.

Mean serum magnesium level was calculated as 0.77±0.12 mmol, HbA1c was calculated as 7.51±0.65. Qualitative variables in addition to ischemic heart disease in diabetics were hypertension, smoking history, dyslipidemias and malnourishment shown in figure no 1 at baseline. Presence of these variables is significant. When low serum magnesium levels were stratified according to age and gender there was no strong association with a p value > 0.05. Hypomagnesemia is strongly associated regarding to glycosylated hemoglobin levels p value
was < 0.05 with increased HbA1C values shown in table 2.

**DISCUSSION**

Diabetes mellitus recognized as the most common metabolic disorder associated with mortality and morbidity. Due to oxidative stress and shear of the internal milieu because of hyperglycemia, mortality and morbidity is on the rise. Nutritional deficiencies occur in diabetics as a result of osmotic diuresis because of hyperglycemia and poor absorption because of anti-diabetic drugs. Our study revealed hypomagnesemia in patients having non-insulin dependent Diabetes Mellitus with a recent ischemic heart disease irrespective of the age, gender duration of diabetes. The association between hypomagnesemia and HbA1C was weak as well. These results contrast with two studies in which serum magnesium levels were found to be low in non-diabetic patients: one showed mean serum magnesium levels in diabetics and non-diabetics showing 0.89 ±0.08 vs. 0.91 ±0.07 mmol/l7 and another study that showed mean magnesium was lower among those with known diabetes than those without diabetes 0.79 (range: 0.78-0.81) vs 0.85 (0.84-0.85)mmol/l.4

Diabetes mellitus is the most common metabolic disorder associated with deficiency of serum magnesium levels. Magnesium deficiency can be rarely seen in healthy persons but is prevalent in hospitalized patients about 47%. Administration of magnesium supplementation improves the overall metabolic status and thus may be a useful adjuvant to the classic hypoglycemic agents in the treatment of Type 2 diabetic individuals. Magnesium deficiency has been associated with the development of diabetic retinopathy. The serum Mg levels among the cohort with diabetes is in inverse relation with the retinopathy.13

Local data is scanty however a study showing trend in mean serum magnesium levels in diabetic patients with ischemic heart disease with 73.3% patients had low serum magnesium level, 6.7% had normal level and 20% had high level, but mean level of magnesium was not calculated even with this case. Hypomagnesemia is not associated with age or gender but its strongly associated in diabetics especially with prolonged course of the disease and its significant.14

**CONCLUSION**

Mean serum magnesium levels in patients with diabetes having ischemic heart disease had significantly associated each other and was lower especially with poor glycemic control. Primary findings of low serum magnesium that has been observed in our population which may be validated in the large trials and it is the need of hour whether correction of magnesium deficiency leads to improvement in glycemic control and its complications. It is recommended to get serum magnesium levels of diabetic patients. There are certain limitations of our study as the sample size was not large enough and more parameters need to be addressed in our population to establish true spectrum of the disease.

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Stroke is a medical condition in which poor blood flow to the brain results in cell death. Ischemic Stroke occurs as a result of an obstruction within a blood vessel supplying blood to the brain. It accounts for 87 percent of all stroke cases. Globally deaths and disability due to stroke increased to 11.75% with a significant increase in death and disability in under developed countries and stable statistics of death and disability in developed countries.

That a given area of ischemic brain tissue becomes irreversibly damaged (i.e. infarcted) depends on both the degree and duration of ischemia. Administration of alteplase (IV-tPA) within 3 hours of symptom onset is currently the only FDA approved treatment for acute ischemic stroke and endovascular treatment is available for patients with specific contraindications for IV-tPA, such as having undergone recent surgery. However IV-tPA can be beneficial up to 4.5 hours of symptom onset. Despite the proven efficacy of intravenous tissue plasminogen activator...
(IV tPA) within the first 4.5 hours after the onset of symptoms, only a small proportion of stroke victims receive this medication. The lack of administration of IV tPA is mainly due to the delayed presentation of patients to the emergency department.

Patients who arrive at the emergency room within 3 hours of their first symptoms often have less disability 3 months after a stroke than those who received delayed care. The longer the delay between symptom onset and treatment, the less likely the patient will benefit. Two centers in Pakistan provide the facility of thrombolysis for acute ischemic stroke in Pakistan, a Center in Lahore is now providing endovascular therapy.

It is therefore vital that patients present early to the emergency departments so that they may get greatest benefits of treatment. The rationale of this study is to identify the factors responsible for the delayed presentation (after 4.5 hours of symptom onset) of Ischemic Stroke in tertiary care hospitals, so that they are controlled to achieve presentation in time for reperfusion therapy, saving the ischemic penumbra, decrease hemorrhagic transformations and prevention of aspiration.

**METHODOLOGY**

Study was a retrospective cross sectional study of 133 patients who presented in Emergency Department of Services Hospital Lahore between June and December 2018 with symptoms and radiological findings suggestive of Ischemic Stroke. The patients were selected on basis of Simple Random Sampling technique. Symptoms were identified by Emergency physicians and the CT scans were reported by the radiology department. The time of symptom onset for awake patients was the time on which the symptoms first appeared. For patients who woke up with symptoms the time on onset was the time at which patient went to sleep. Medical residents were recruited as interviewers. Interviewers were taught the procedure of obtaining informed consent, the methods of administering the structured questionnaires and recording the responses. Following case identification, the interviewer was informed and written consent was obtained from all patients who agreed to participate by the interviewer prior to the start of the interview. If patients had communication deficits, a caregiver who resided with the patient was consented and interviewed. The interviewer knew only that the patient had been diagnosed with a stroke and that we wanted to know more about the reasons why participants did or did not delay seeking medical attention. The data collected was analyzed using SPSS for Windows ver. 20.0. Quantitative data was analyzed using means and averages. Age and distance from the health care establishment were the only quantitative variable while history of smoking, diabetes, Ischemic heart disease, obesity were qualitative variables. Single family units, level of education and previous knowledge about stroke were also counted as qualitative variables. During descriptive interpretation of data, continuous variables were expressed as means and standard deviations. T test was used post risk stratification. Values were considered statistically significant if p was <0.05.

**RESULTS**

A total of 133 patients with symptoms and radiological findings of Ischemic Stroke were included in the study, out of these 78 patients (58.6%) were male and 55 patients (41.35%) were female. 35 patients (26.31%) patients presented within the thrombolytic window and 98 patients (73.6%) presented late.

For people who reached before 4.5 hours the average age was 64.4 years, distance to nearest tertiary care hospital was 14.37km, distance to services hospital was 18.83km.

For people who reached after 4 hours the average age was 62.41, distance to nearest tertiary care hospital was 29.95km and distance to services hospital was 52.2km.

29.5% male patients reached within 4.5 hours in contrast to just 21.8% of the females.

69.6% of the patients presenting early had some form of formal education whereas of those who
presented late a lesser number (59.2%) were educated. Surprisingly, a greater percentage of patients who presented after 4.5 hours lived in a joint family setup (73.5%) than those who presented within 4.5 hours (54.3%). 57.1% of patients who arrived within 4.5 hours had attendants who recognized that the symptoms were of stroke while this awareness was present in the attendants of only 33.7% of the patients who presented after 4.5 hours. (fig.1)

Fig.1: Time of Presentation of Stroke Patients and Recognition by Attendants.

A staggering 85.4% of patients who presented within the thrombolysis window presented straight to tertiary care whereas only 53.1% of patients presenting after 4.5 hours came straight to tertiary care and 33.7% of them were referred from secondary care institutes. (Fig.2 and fig.3)

Diabetes was found to be much more prevalent 66% against a global prevalence ranging from 9.5-20%. This shows diabetes is much more prevalent in our set up. This results in atherosclerotic plaques and increased rate of atherosclerosis progression.

Fig. 2:

Ironically only 2 (10%) out the 20 people presenting with recurrent stroke did so in the first 4.5 hours following symptom onset meaning 18(90%) presented late despite having suffered from the same issue before. (Table 1)

Table 1: Table 1 Patients Presenting with Recurrent Stroke within and after 4.5 Hours

<table>
<thead>
<tr>
<th></th>
<th>Presenting before 4.5 hours</th>
<th>Presenting after 4.5 hours</th>
<th>Total Patients Presenting with recurrent stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Patients</td>
<td>2</td>
<td>18</td>
<td>20</td>
</tr>
<tr>
<td>Percentage</td>
<td>10%</td>
<td>90%</td>
<td>100%</td>
</tr>
</tbody>
</table>

DISCUSSION

Considering the demographic characteristics of the patients who presented more male patients presented with ischemic stroke than female patients. A review article mainly covering studies from Western Europe, showed the same results as stroke incidence was 30% higher in men than women.11

Only 26.31% patients presented within 4.5 hours which is almost half of the patients (52%) that present within 4.5 hours in the USA.12 This number needs to be increased considerably by addressing the factors associated with delayed presentation that this study has identified.
FACTORS CONTRIBUTING TO DELAYED PRESENTATION OF ISCHEMIC STROKE

By the results of the study it was identified that patients who presented within the thrombolytic window were situated nearer to services hospital than those who presented later. This is a trend that has been seen in a similar studies done in India and Saudia Arabia. Patients who came straight to tertiary care came earlier. As tPA therapy will be given in tertiary care or specialized stroke units, these units should be spaced out so that the distance that the people have to travel to reach them is less and more people can reach in time.

As the patients who were referred from Primary or Secondary care institutes tended to present later. Ambulance and rescue services protocol should include that patients suspected as having stroke should be taken to tertiary care hospitals/stroke unit directly.

Patients presenting earlier were more educated than those presenting late. Low patient education is a known factor for delayed hospital presentation in general. A general awareness to health related issues will be better and the threshold of people to go to healthcare facilities will be lower in educated people. The curriculum being taught in schools and other institutes should include these topics.

Awareness of the symptoms being those of stroke led to more patients presenting earlier. Multiple studies in Korea agree with this finding. Modifiable risk factors are associated with 90% of strokes in various regions of the world. Various countries have done community education about the symptoms and signs of Stroke, an acronym for which is popularly known as and used in campaigns as FAST. Such a campaign will be of vital importance as it will lead to earlier presentations and better outcomes for stroke. Although 66% of patients had diabetes

They had not been educated about the signs and symptoms of stroke or of any other complication of diabetes.

Patients presenting with recurrent stroke or having had stroke previously came later than those with the first episode. This further confirmed a study from Thailand that concluded that knowledge of stroke in patients with recurrent stroke is insufficient. Although patients who are presenting with recurrent strokes have had doctor and hospital contact before but they are still not aware of the symptoms of stroke or the importance of presenting earlier. In various studies it has been noted that between 16 to 30 percent of patients with stroke have another episode in the next 5 years. Thus it is imperative that patients and attendants are counseled and educated better during first presentation on what to expect and do in recurrent episodes.

Limitations of the Study

A limitation of this study is that it was conducted in a single center during a 6-month period and the sample size is small. Despite this limitation, this study provided background information on the factors associated with delay in presentation of stroke patients in Lahore. In order to overcome this limitation, future studies are needed across several hospitals with stroke centers and a thorough evaluation of all factors mentioned in this study as potential causes for delayed arrival of stroke patients for treatment. Also, a bigger sample size to ascertain the findings of this study is highly suggested.

CONCLUSION

Our study has concluded that patients do present within 4.5 hours of symptom onset to tertiary care hospitals and will be eligible for tPA therapy if this service is started. A majority of patients still present late to hospitals and proper interventions and educational programs should be started to reduce the time to present to proper setup.

Well-spaced out stroke units should be made, reducing distance that patients need to travel to reach site of tPA administration. Education of patients and attendants generally and specifically to the symptoms and features of stroke needs to be done and will help patients come early.

Most vital is to ensure that Doctors and Medical Staff educate stroke patients and their attendants about the risk of recurrent stroke and the importance of presenting early to proper tertiary care/stroke
center if recurrent stroke does happen. Since a lot of patients presenting in the ER with stroke were diabetic, proper health education of diabetics should be done to ensure they recognize both the micro vascular and macro vascular complications of diabetes. Since the patients in our study were relatively younger (62 years) rather than the world average of 65 years and above, valuable years are lost in these patients. We need to have national programs for stroke awareness and surveillance programs should also be employed to look for the efficacy of these programs.

REFERENCES


FACTORS CONTRIBUTING TO DELAYED PRESENTATION OF ISCHEMIC STROKE


“YOU ARE ONLY CONFINED BY THE WALLS YOU BUILD YOURSELF”
COVID-19 (SARS-CoV2) is a newly discovered infectious disease, gradually taking the form of a pandemic which has raised alarms for the health system of whole world. It was first identified in Wuhan city [Hubei Province] of China on 31st December 2019, as pneumonia of unknown origin.

Abstract

Background: COVID 19 is new infectious disease which has been declared a pandemic by WHO on 11th Feb 2020. The pandemic has led to enormous health crisis worldwide. Research about effects of COVID-19 on pregnancy outcome is going everywhere in the world, to have more insight into the subject in a relatively shorter period of time. Previously, research done on similar virus outbreaks like SARS and MERS has shown significant maternal morbidity and mortality.

Objective: This study has been designed to evaluate potential effects of COVID-19 on pregnancy outcome in terms of maternal morbidity and mortality.

Methodology: This is a retrospective observational study carried out for period of 3 months from 8th March to 7th July 2020 at Sir Ganga Ram Hospital, Lahore, at a specially designated health facility for COVID positive pregnant designed by Department of Health, Punjab. 53 women who were tested COVID-19 positive were enrolled in this study after fulfilling inclusion criteria and their demographic details, mode of delivery and outcome in terms of morbidity and mortality was collected on standard investigation forms.

Results: In the present study, the mean age of COVID-19 pregnant women was 28 years ±5.1 SD, mean gravidity was 4 ± 1.8 SD and mean gestational age was 27 ± 3.8 weeks. Out of 53 patients, 41 were referrals and rest of the 12 presented directly. 33% of the patients were primigravida and 67% were multigravida. In current study the most common symptom was fever in 9 patients followed by cough in 7, myalgia in 4, and diarrhea in 2 and shortness of breath in 2 patients. Mode of delivery in the 20 patients was LSCS and 7 patients delivered vaginally. It was found that 47% of the patients had lung involvement. Respiratory distress was faced by the 25% of the patients, whereas 17% needed Ventilatory support. Multi organ failure was seen in 8% of the patients. Maternal mortality of 13 % in pregnant females with COVID-19 was observed.

Conclusion: COVID-19 has significant effects on pregnancy outcome in term of maternal morbidity and mortality

Keywords: Morbidity, Mortality, COVID.
Maternal morbidity and mortality with COVID-19 in a tertiary care hospital of Lahore.

The rationale of carrying out this study is to find out the effects of COVID-19 on pregnant women so that timely prevention and treatment can be planned to reduce maternal morbidity and mortality.

**METHODOLOGY**

It was a retrospective observational study. It was carried out in an especially designed health facility under supervision of Department of Obstetrics and Gynecology with collaboration of anesthesia, medical and pediatric departments of Sir Ganga Ram Hospital, Lahore from 8th March to 7th July 2020. All suspected cases of COVID-19 were admitted in isolation ward and tested for COVID-19 by PCR following WHO guidelines and those with positive report were shifted to COVID ward. Patients were kept in well ventilated rooms with full care and necessary precautions were taken for infection control and safety of health workers. A total of 53 patients with positive tests were included in the study after fulfilling the inclusion criteria. Ethical approval from Institutional review board was taken. Detailed history including personal details, comorbidities especially asthma, cardiac problems, Hypertension, Diabetes Milletus, renal disease and anaemia were noted. Symptomatology at presentation was noted. The time and mode of delivery were noted down. Patients in all trimesters were admitted for further monitoring and management. Their mode of presentation, progression of disease, need for any medical attention and obstetrical intervention noted on standard investigation forms.

Data analysis was done with SPSS version 20. Variables of interest were age, gravidity, gestational age, BMI, symptoms on presentation or any worsening, and maternal outcome in terms of morbidity and mortality. Continuous variables like age, parity, BMI and gestational age were analyzed by simple descriptive statistics like mean and standard deviation while Categorical variables like mode of presentation, clinical presentation, medical disorders, maternal outcome, were expressed as number of cases and percentage.
Inclusion criteria: All COVID positive female pregnant patients whether symptomatic or asymptomatic were included in the study.

Exclusion Criteria: Pregnant females without confirmation of COVID 19, or any suspect case for whom testing could not be performed due to any reason were excluded from the study.

**RESULTS**

Among all 53 patients, the maternal age ranged from 20 to 38 years and most of the pregnant women reported in the 3rd trimester. The overall age, gestational age and gravidity of women is shown in Table No. 1.

It was also found that 33% woman were primigravida, 13% were Gravida 2, 34% woman were gravida 3 & 4 whereas 17% woman were gravida 5 & 6. Among 53 patients one patient had multiple pregnancies.

Out of the 53 patients, 41 patients were referred from nearby hospitals and peripheral areas and rest of the 12 patients presented directly to Sir Ganga Ram Hospital as showed in Figure No. 1.

---

### Table 1: General Information of Woman Affected by COVID-19.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sample Points</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>S.D</th>
<th>C.V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td>53</td>
<td>18</td>
<td>38</td>
<td>28</td>
<td>5.1</td>
<td>18%</td>
</tr>
<tr>
<td>Gravidity (Nos.)</td>
<td>53</td>
<td>1</td>
<td>7</td>
<td>4</td>
<td>1.8</td>
<td>44%</td>
</tr>
<tr>
<td>BMI (kg/m^2)</td>
<td>53</td>
<td>20.1</td>
<td>35.5</td>
<td>27.8</td>
<td>3.8</td>
<td>14%</td>
</tr>
<tr>
<td>Gestational age (week)</td>
<td>53</td>
<td>8</td>
<td>40</td>
<td>24</td>
<td>9.1</td>
<td>38%</td>
</tr>
</tbody>
</table>

---

Anemia was reported in 37% cases, 24% patients had hypertension in pregnancy, 18% were diabetic, 6% had cardiac disease and another 6% had other medical disorders, whereas, other 38% (20) of the patients had no associated medical disorders with pregnancy. The detail of is shown in Fig.2.

**Fig.2:** The co-morbidities of COVID-19 patients during pregnancy.

During history taking of the patients with COVID-19, it was found that 10 woman had no symptoms while remaining 43 woman had different type of COVID related symptoms. It was established that 88% of symptomatic patients had history of fever, followed by persistent dry cough in 33% at admission in hospital. The overall 65% patients were found to have dry cough. It was also found that about 53% patients faced myalgia, 49% loss of sense of smell, diarrhea and vomiting were identified in 19% of cases while 23% had history of flu and shortness of breath. The symptoms of COVID-19 in pregnant women are presented in Table No. 2.

Caesarean section was performed in 20 patients with COVID-19, among these cases 5 women had fetal distress, 3 had previous caesarean section and 1 had premature rupture of membranes. Caesarean
section was performed at term in 90% of the cases and one was done at 35 weeks. The analysis on the basis of mode of delivery was carried out and presented in Figure No. 3 below along with fetal outcome.

In this study there were 5 caesarean sections were done due to fetal distress, among 5 patients, 4 were primigravida and one had previous one caesarean section. Two caesarean sections were performed due to previous one caesarean section at term; one caesarean section was indicated due to previous one caesarean section and diabetes. One caesarean section was performed due to previous one with ruptured membranes at term. There were seven cases of preterm delivery, two cases of miscarriages, one case of septic induced abortion followed by laparotomy leading to Obstetrical Hysterectomy.

Figure No.3: Fetomaternal Outcome

The morbidity due to the COVID-19 in 53 patients were observed which is illustrated in the Table No. 3 below, it was found that 47% of the patients had lung involvement in which 15 patients had mild infiltration and 10 had moderate to severe infiltration. The Respiratory distress was faced by the 25% of the patients, whereas 17% needed Ventilatory support. Multi organ failure and Obstetrical hysterectomy also observed in two patients each. Overall, 13% Mortality rate was observed during the pregnancy as shown Table No # 3.

**DISCUSSION**

Millions of people are getting affected by the outbreak of newly emerging COVID-19 infection globally which is still spreading at great speed, leading to tremendous burden on the resources of our health department. Ours is a country, already running short of health care facilities, with a lesser patient to bed ratio, and high maternal and neonatal mortality rate, so COVID-19 is a great challenge facing Pakistani Government. In all countries affected by COVID-19, research work is being done on pregnant females to observe fetomaternal outcome. Many studies have already been done in our country and others are in the process. So it is imperative to collect the data in the local set up and share it in a concise and practical manner.

SARS CoV-2 has led to a pandemic which has made pregnant population vulnerable to the health crisis never seen in the history before. Keeping in view the fetomaternal susceptibility to this infection, the Health Department of Punjab, has designated a dedicated Obstetrics Ward in Sir Ganga Ram Hospital, Lahore as COVID Obstetrics Ward. COVID positive women from Lahore and periphery were referred to this facility. It was managed by multidisciplinary team of obstetricians, physicians, anesthetists, pediatricians and hospital administration.

In the present study, the mean age of COVID-19 pregnant women was 28 years ±5.1 SD, mean gravidity was 4 ± 1.8 SD and mean gestational age was 27 ± 3.8 weeks. Among them 33% of the patients were primigravida and 80% were multigravida. These findings are similar to a recent study by Chen et al, in which nine diagnosed cases of COVID-19 were reported. In these patients the median age was 31 years, 52% were primigravida and 48% were multigravidas.

In a study done by Chen et al and Wu et al the mean age of patients was 29 and 29.4 years respec-
tively. In a study done by Yan J, Chen, Wang the mean duration of gestation was 38, 37 and 40 weeks respectively. This variation may have occurred due to regional differences.\textsuperscript{10-13}

In current study the most common symptom was fever in 9 patients, followed by cough in 7, myalgia in 4, and diarrhea in 2 and shortness of breath in 2 patients. These results are similar to results of a recent study by Chen et al. who reported nine women diagnosed with COVID-19 in their third trimester of pregnancy. The common symptom was fever in 7, cough in 4, myalgia in 3, and sore throat and malaise each in 2 women. None of the patient required ventilator and there was no mortality. These results are quite in accordance with the current study.\textsuperscript{12}

In the present study, Caesarean section was performed in 20 patients with COVID-19, among these 5 women had fetal distress, 3 had previous caesarean section and 1 had premature rupture of membranes. The Cesarean section rate was found to be 92% and 76% in studies done by Zaighum and Matar respectively. A systemic review conducted on 108 females addressing maternal and perinatal outcome with COVID-19 showed that caesarean section was performed in majority of patients, was mainly due to fetal distress but seven patients ended up in spontaneous vaginal deliveries without any complication.\textsuperscript{14,15}

Whether vaginal delivery increases the risk of transmission is unknown. Further research is warranted to study the risk and to produce guidelines for timing and mode of delivery in patients with COVID-19.\textsuperscript{15}

The morbidity due to the COVID-19 in 53 patients was observed. It was found that 47% of the patients had lung involvement in which 15 patients mild infiltration and\textsuperscript{16} had moderate to severe infiltration. The Respiratory distress was faced by the 25% of the patients, whereas 17% needed Ventilatory support. Multi organ failure was seen in 8 percent of the patients. In a study done by Yan and colleagues, out of 116 cases there were 8 cases (6.9%) of severe pneumonia, all of which required ICU admission. In a study conducted by Matar, 2 patients developed multiorgan failure and one developed ARDS. In a study conducted by Smith, one patient required intensive care and ventilation.\textsuperscript{12,15,16}

Overall, 13% Mortality rate was observed during the pregnancy. The literature review in this regard presents a conflicting data. In studies done by Smith and Zaighum, no maternal mortality was observed whereas three women died in a study conducted by Mei Y and colleagues. One maternal death was observed in study conducted by.\textsuperscript{14,16,17}

To facilitate the understanding of pregnancy in COVID-19, we conducted this study which showed pregnant women were affected in all three trimesters, in varying severity. Hence, the effect of SARS-CoV-2 infection on the mother or fetus in the first or second trimester or in patients with moderate to severe infection is unpredictable. SARS-CoV, MERS coronavirus infection was found to be associated with preterm birth, intrauterine growth restriction, intrauterine death, and neonatal death during pregnancy. Considering that the potential of SARS-CoV-2 to cause severe obstetric and neonatal adverse outcomes is unknown, rigorous screening of suspected cases during pregnancy and judicious use of resources needs attention, Long-term follow-up of confirmed cases and their neonates is needed.\textsuperscript{18,19}

CONCLUSION
All the available data shows that COVID-19 poses a significant risk to pregnant women and morbidity and mortality is increased in pregnant women who are COVID-19 positive.

Strength of the Study: This study was conducted, keeping view the risk imposed by COVID-19 pandemic, which is emerging as a massive health problem, leading to morbidity and mortality in general population. As we are living in a developing country where maternal mortality is still high so this study contained a reasonable number of cases to see the impact of this deadly virus on pregnant females.
Limitations of the Study This study does not show the long term effects of the virus on the mother, as it has been conducted over a period of three months only.

Source of funding None

Conflict of interest None

Future recommendation Further data is needed from multicenter trials over a longer period of time to see the effects of the virus on the pregnancy. Vertical transmission and fetal outcome also needs be studied. The safety of various drugs used in COVID 19 need to be documented.

REFERENCES


On 31st December 2019, a pneumonia of unknown origin from Wuhan was reported to the country office of the World Health Organization (WHO) in China. Fever, dry cough, dyspnea, body aches, and abnormal chest CT were the common clinical manifestations in infected individuals. Less common symptoms reported were headache, hemoptysis, diarrhea, and sputum production. This lower respiratory tract infection was identified as a novel Coronavirus (2019-nCoV), the seventh member of the Coronavirus family. On 11th February 2020, WHO named this disease as "COVID-19," which is the acronym of "Coronavirus disease 2019." International Committee on Taxonomy of Viruses (ICTV), labeled...
this virus as syndrome coro-navirus 2 (SARSCoV-2).\(^4\) The salient characteristics of this new virus are its low pathogenicity and high transmissibility which not only distinguishes this virus from the other viruses of the Corona family like SARS-CoV and MERS-CoV but also boosts its spread. The WHO declared this outbreak a Public Health Emergency of International Concern (PHEIC) on 30th January 2020 due to its spread across 18 countries till that date.\(^1\)

The 2019-nCoV is transmitted through respiratory droplets, aerosols, contact, and fomites. The asymptomatic incubation period is 1-14 days with asymptomatic patients reporting to spread the virus even after 24 days.\(^6\) At present vaccines and antiviral drugs against COVID-19 are in the research phase.

Health care workers in general and dental professionals, in particular, are at high risk of getting the infection and transmitting the infection to the community. Dental professionals are routinely exposed either directly or indirectly to the aerosols and respiratory droplets (which may contain viruses, bacteria) due to the nature of their work. Also, contaminated instruments and surfaces are possible routes of spread of viruses and bacteria. Live 2019-nCoV has also been reported to be found in human saliva, putting dental professionals at a very high risk of contracting the disease.\(^7\) WHO, Centers for Disease Control & Prevention (CDC) and the American Dental Association (ADA) recommended guidelines for the prevention of the COVID-19, based on the previous experience of the respiratory infections like SARS-CoV and MERS-CoV.\(^8\) Proper infection control measures and Personal Protective Equipment (PPE) is of utmost importance for dental professionals, at the same time it is equally important for them to be aware of the disease source, transmission mode, clinical manifestation and prevention methods.

A study of Iranian nurses regarding their knowledge towards COVID-19 concluded just over half of the nurses (56.5%) had good knowledge about the source, transmission, clinical manifestation and prognosis, treatment and mortality rate of COVID-19.\(^11\) A similar study in Vietnam reported good knowledge and positive attitude of HCWs toward COVID-19 with the level of some knowledge and attitude lower than that expected for their position level towards the virus. This study recommended additional educational interventions and campaigns for healthcare workers.\(^12\)

Although in this pandemic, it is recommended by health authorities to avoid all elective dental treatments. Dental professionals can become exposed to the virus while treating dental emergencies in asymptomatic patients, infected with COVID-19. Thus, dental professionals should have a high level of awareness regarding the source, mode of transmission, clinical manifestation, and prognosis of the disease to identify those at risk of developing the disease as well as to avoid the spread of disease in the community.

The objective of this research was to assess the knowledge, attitude and perceptions towards COVID-19, of dental professionals working in the dental teaching hospitals in Rawalpindi and Islamabad. Dental teaching hospitals were chosen as the study setting for the purpose of this research, as in developing countries like Pakistan, most of the patients visit teaching hospitals for their dental problems. These hospitals provide treatment at subsidised charges by junior dentists under the supervision of senior dentists.

**METHODOLOGY**

The study population were dental health care professional (dentist and dental assistants) working in the clinical departments of dental teaching hospitals of Rawalpindi and Islamabad. This was a cross-sectional study conducted in April 2020.

Ethical clearance for the study was sought before the commencement of data collection, and approval was obtained from Institutional Ethics Review board of Pakistan Air Force Hospital, Islamabad (Ref: MS/7429). Participants were made aware of the purpose of the study, their right of voluntary participation and assurance of anonymity provided. As the data collection was undertaken
online in order to adhere to social distancing rules in the current COVID-19 situation, participants were informed that their final submission of the online questionnaire will be considered as informed consent to participate in the study. The written details of these statements were provided at the start of the online questionnaire for all participants.

Data collection was carried out virtually using the online software (All Counted). The software allowed only fully completed forms to be submitted by prompting participants to complete the missing sections before the form could be submitted. A representative from each of the 8 Dental Teaching Hospitals in the Twin cities of Rawalpindi and Islamabad was contacted and invited to participate in the study by sharing the link of the questionnaire in their respective official WhatsApp group. Six representatives agreed to participate and shared the link twice in their respective WhatsApp groups to ensure wide coverage of group members who are active at different times. Data collection took place between 3rd April to 14th April 2020.

Before conducting this study, permission was sought to reuse the questionnaire developed and tested in a study assessing knowledge and attitudes of Health Care Workers (HCWs) towards MERs-CoV, by Assad et al (2020). Modifications were made in the questionnaire according to COVID-19 based on information available at the WHO official page. The prepared questionnaire was then sent to two Community & Preventive Dentistry specialists for their expert opinion regarding the content and structure of the questionnaire. After incorporation of changes suggested by them, the questionnaire was pilot tested on 10 dental professionals by sending them the web link of the questionnaire. Based on their feedback, the final questionnaire formulated was then used for data collection purposes.

At the start of the questionnaire, study title was mentioned followed by a brief description of the purpose of the study, reassurance about anonymity as well as participants’ right of voluntary participation in the study. It was also indicated that the final submission of survey responses would be considered as consent to participate in the study.

The questionnaire consisted of 4 parts. First part comprised demographic details (gender, age, profession, professional experience, source of information, Questions were also asked about infection prevention and control program and policy to prevent transmission of respiratory infection in participants’ institutions (6 items). The second part consisted of 15 items regarding knowledge about COVID 19 (etiology, mode of transmission, symptoms, incubation period, prevention, treatment, consequences, risk groups and prognosis). The third constituted 6 items related to the attitude of health care workers towards COVID-19 with yes/no answers. The last part contained 4 items related to perceptions regarding COVID-19 related knowledge, infection and control measures.

A scoring system was used to assess the knowledge of participants. One point was assigned for each correct answer. The total knowledge scores varied between 0 for no correct answer to 15 for all correct answers. To classify knowledge scores as low, moderate, and high level of knowledge, the total score was converted into percentiles. A score of ≤ 50% was designated as a low level of knowledge, 50% to 75% as moderate and ≥75% as a high level of knowledge. Attitude was assessed through yes/no answers. Total attitude scores ranged from 0 for no correct answer to 6 for all correct answers. The total score was divided at the 75th percentile. A score of ≥ 75% was designated as a positive attitude. The data was analyzed using IBM SPSS v.26 (IBM Corporation). Descriptive analysis was used to describe survey item responses. Percentages were used to describe the categorical variables and mean with standard deviation for continuous variables. Shapiro Wilk test was used to analyse data for normality. As none of the major outcomes followed a normal distribution, the Kruskal Wallis H test was used to determine differences between two or more groups of independent variables on a continuous dependent variable. All differences estimated between variables were considered statistically significant at 5%.
RESULTS

Out of approximately 373 dental professionals in 6 dental teaching hospitals, 202 participated in the study (54.1%). Majority (65.8%) were female and just over half of the participants (57.4%) belonged to the age group 26-37 years. Seventy-six percent (76%) were dentists and 41% were having less than 5 years of professional experience. Social media (63.2%) was the most common source of information regarding COVID-19. Less than half of the participants responded in affirmative when asked about infection prevention and control program as well as policy to prevent transmission of respiratory infection in their respective institutions (45% and 28.7% respectively). Baseline characteristics are presented in detail in table 1.

Majority of the participants (80.2%) possessed sufficient knowledge regarding different aspects of COVID-19. There was a good level of knowledge amongst participants about its viral origin (95.5%), transmission through person to person (92.6%) and common clinical manifestations of the disease such as fever and body aches (97%), and shortness of breath (93.1%), whereas knowledge about less common manifestations like diarrhea & dry cough was poor (41.1 and 44.1% respectively). Positive attitudes of the participants were observed regarding the prevention of transmission of COVID-19 by following standard precautions and isolation measures (92.1%) and utilization of all available information about the virus by all HCWs (95.5%). About three quarters of the participants (74.8%) were worried that their family member(s) may get an infection and 71.3% were ready to avail vaccination against the disease, if available. A generally low level of attitude was observed towards active participation of HCWs in hospital infection control program to reduce spread of infection (64.9%).

Perceptions of dental professionals (Table 4) revealed that just over half of the participants considered themselves to be equipped with sufficient information to protect themselves against COVID-19 (55.9%) and the majority of the participants indicated their perception of a lack of sufficient information available regarding COVID-19 (69.8%). Furthermore, a large majority of participants (77.7%) thought government institutions were not able to control the epidemic in the country and a few even considered (4.5%) themselves to have had been in contact with an infected person.

The results of Kruskal Wallis H test (Table 5) revealed a significant difference between knowledge scores for gender and profession with females and dentists scoring more in the knowledge category (p < 0.001). No significant differences between groups were seen for the attitudes category.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Participants (n=202) No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>69(34.2)</td>
</tr>
<tr>
<td>Female</td>
<td>133(65.8)</td>
</tr>
<tr>
<td><strong>Age Groups(years)</strong></td>
<td></td>
</tr>
<tr>
<td>18-25</td>
<td>58(28.7)</td>
</tr>
<tr>
<td>26-37</td>
<td>116(57.4)</td>
</tr>
<tr>
<td>38-49</td>
<td>27(12.6)</td>
</tr>
<tr>
<td>50-60</td>
<td>0</td>
</tr>
<tr>
<td>≥ 61</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td><strong>Profession</strong></td>
<td></td>
</tr>
<tr>
<td>Dentist</td>
<td>155(76.7)</td>
</tr>
<tr>
<td>Dental Assistants</td>
<td>47(23.3)</td>
</tr>
<tr>
<td><strong>Years of experience</strong></td>
<td></td>
</tr>
<tr>
<td>&gt;5 years</td>
<td>84(41.6)</td>
</tr>
<tr>
<td>5-10 years</td>
<td>75(37.1)</td>
</tr>
<tr>
<td>&lt;10 years</td>
<td>43(21.3)</td>
</tr>
<tr>
<td><strong>Is there any infection prevention and control program in your institute?</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>91(45)</td>
</tr>
<tr>
<td>No</td>
<td>87(43.1)</td>
</tr>
<tr>
<td>Unknown</td>
<td>24 (11.9)</td>
</tr>
<tr>
<td><strong>Is there a policy in your hospital to prevent transmission of respiratory infection?</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>58(28.7)</td>
</tr>
<tr>
<td>No</td>
<td>114(56.4)</td>
</tr>
<tr>
<td>Unknown</td>
<td>30 (14.9)</td>
</tr>
<tr>
<td><strong>Where did you get most of information regarding COVID-19?</strong></td>
<td></td>
</tr>
<tr>
<td>Paper sources</td>
<td>12 (6.0)</td>
</tr>
<tr>
<td>Health authorities</td>
<td>42 (20.9)</td>
</tr>
<tr>
<td>Social media</td>
<td>127 (63.2)</td>
</tr>
<tr>
<td>Television</td>
<td>15 (7.5)</td>
</tr>
<tr>
<td>Others (Institutes)</td>
<td>5 (2.5)</td>
</tr>
</tbody>
</table>
DISCUSSION

This study was an attempt to assess the knowledge, attitudes & perceptions of dental professionals regarding COVID-19. Sufficient knowledge of the participants was observed in this study. However, the findings for attitudes domain showed lower results.

Since the outbreak of COVID 19 pandemic, researches all around the world are conducting research regarding knowledge, attitudes & perceptions of HCWs and general public towards the disease. To the best of our knowledge, no such study had been conducted in Pakistan to assess knowledge, attitudes, and perceptions of dental professionals.

**Table 2:** Knowledge of Dental Professionals Regarding COVID-19 (n=202)

<table>
<thead>
<tr>
<th>Question (Correct answer)</th>
<th>Correct answer No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>COVID 19 is a viral infection (yes)</td>
<td>193 (95.5)</td>
</tr>
<tr>
<td>COVID-19 is transmitted by close contact with the infected person (yes)</td>
<td>187 (92.6)</td>
</tr>
<tr>
<td><strong>Major Symptoms of COVID-19</strong></td>
<td></td>
</tr>
<tr>
<td>Fever and body aches (yes)</td>
<td>196 (97)</td>
</tr>
<tr>
<td>Shortness of breath (yes)</td>
<td>188 (93.1)</td>
</tr>
<tr>
<td>Cough with sputum (no)</td>
<td>83 (41.1)</td>
</tr>
<tr>
<td><strong>Minor Symptom</strong></td>
<td></td>
</tr>
<tr>
<td>Diarrhea (yes)</td>
<td>89 (44.1)</td>
</tr>
<tr>
<td>The incubation period is 5-14 days (yes)</td>
<td>173 (85.6)</td>
</tr>
<tr>
<td>There is a relation between animal and COVID-19 (yes)</td>
<td>143 (70.8)</td>
</tr>
<tr>
<td>Travelling history of the last 2 weeks important (yes)</td>
<td>149 (73.8)</td>
</tr>
<tr>
<td>COVID-19 vaccine is available (no)</td>
<td>178 (88.1)</td>
</tr>
<tr>
<td>An effective treatment to eliminate COVID-19 present (no)</td>
<td>164 (81.2)</td>
</tr>
<tr>
<td>Washing hands with soap and water, and using face masks can help in the prevention of disease transmission (yes)</td>
<td>175 (86.6)</td>
</tr>
<tr>
<td>People with chronic illnesses more susceptible to complications resulting from COVID-19 (yes)</td>
<td>182 (90.1)</td>
</tr>
<tr>
<td>Healthcare workers are at a higher risk of infection (yes)</td>
<td>182 (90.1)</td>
</tr>
<tr>
<td>Infection by COVID-19 lead to death in all patients (no)</td>
<td>174 (86.1)</td>
</tr>
<tr>
<td><strong>Level of knowledge regarding COVID-19</strong></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>162 (80.2)</td>
</tr>
<tr>
<td>Moderate</td>
<td>37 (18.3)</td>
</tr>
<tr>
<td>Low</td>
<td>3 (1.5)</td>
</tr>
</tbody>
</table>

**Table 3:** Attitude of Dental Professionals Towards COVID-19 (n=202)

<table>
<thead>
<tr>
<th>Item (correct answer)</th>
<th>Response No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are you worried one of your family members may get an infection? (yes)</td>
<td>151 (74.8)</td>
</tr>
<tr>
<td>Transmission of COVID-19 can be prevented by using standard and isolation precautions given by CDC, WHO? (yes)</td>
<td>186 (92.1)</td>
</tr>
<tr>
<td>Prevalence of COVID-19 can be reduced by active participation of health care workers in hospital infection control program? (yes)</td>
<td>131 (64.9)</td>
</tr>
<tr>
<td>If a COVID-19 vaccine were available, would you have it? (yes)</td>
<td>144 (71.3)</td>
</tr>
<tr>
<td>Intensive treatment should be given to diagnosed patients? (no)</td>
<td>111 (55.0)</td>
</tr>
<tr>
<td>Health care workers must avail themselves of all the information about the virus? (yes)</td>
<td>193 (95.5)</td>
</tr>
<tr>
<td><strong>Level of attitude towards COVID-19</strong></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>178 (88.1)</td>
</tr>
<tr>
<td>Low</td>
<td>24 (11.9)</td>
</tr>
</tbody>
</table>

**Table 4:** Perceptions of Dental Professionals Towards COVID-19 (n=202)

<table>
<thead>
<tr>
<th>Item</th>
<th>Response No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you think you have enough information to protect yourself from this infectious disease?</td>
<td>113 (55.9) Yes: 68 (33.7) No: 21 (10.4)</td>
</tr>
<tr>
<td>Is the available information about COVID-19 in our society sufficient?</td>
<td>61 (30.2) Yes: 141 (69.8) No: 21 (10.4)</td>
</tr>
<tr>
<td>Did you have contact with anyone who has suffered from Corona?</td>
<td>9 (4.5) Yes: 160 (79.2) No: 33 (16.3)</td>
</tr>
<tr>
<td>Are the government institutions able to control the epidemic?</td>
<td>45 (22.3) Yes: 157 (77.7) No: 21 (10.4)</td>
</tr>
</tbody>
</table>

**Table 5:** Distribution of knowledge and Attitude Scores of Dental Professionals (n = 202)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Knowledge Mean (SD)</th>
<th>Test statistic</th>
<th>Attitude Mean (SD)</th>
<th>Test statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>11.57(2.07)</td>
<td>11.97**</td>
<td>4.51 (0.95)</td>
<td>0.026</td>
</tr>
<tr>
<td>Female</td>
<td>12.47(2.30)</td>
<td>4.55 (0.95)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Profession</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dentist</td>
<td>12.50(2.33)</td>
<td>25.41**</td>
<td>4.54 (0.95)</td>
<td>0.046</td>
</tr>
<tr>
<td>Dental Assistants</td>
<td>11.02(1.87)</td>
<td>4.51 (0.95)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age groups</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-25</td>
<td>11.81(1.96)</td>
<td>7.11</td>
<td>4.60 (1.01)</td>
<td>7.50</td>
</tr>
<tr>
<td>26-37</td>
<td>12.34(2.19)</td>
<td>4.44 (0.86)</td>
<td>4.78 (1.15)</td>
<td></td>
</tr>
<tr>
<td>38-49</td>
<td>12.04(3.03)</td>
<td>5.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 61</td>
<td>15.00</td>
<td>4.49 (1.16)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Years of experience</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 5 years</td>
<td>12.11(2.04)</td>
<td>1.06</td>
<td>4.56 (0.87)</td>
<td>0.157</td>
</tr>
<tr>
<td>5-10 years</td>
<td>12.28(2.09)</td>
<td>4.53 (0.91)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 10 years</td>
<td>12.05(2.92)</td>
<td>4.49 (1.16)</td>
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**significant at ≤ 0.001, test statistic: Kruskal Wallis test**
regarding the COVID-19 pandemic. Also, at the time of writing the discussion, it was noted that the literature on this topic is rapidly growing around the world.

As far as knowledge of dental professionals is concerned, our results are in close agreement with those of Giao and colleagues who found sufficient knowledge of HCWs (88.4%) in Vietnam towards COVID-19. However, participants in our study scored higher for the following variables: mode of transmission (92.6% vs. 67%), common clinical symptoms (97% vs. 72.8%), incubation period (85.6% vs. 65.8%), presence of effective treatment to eliminate the disease (81.2% vs. 58.4%) and patients with chronic illness at a higher risk (90.1% vs. 79.2%). Far better knowledge of prevention of disease transmission by washing hands with soap and water, and using face masks were reported in their participants as compared to dental professionals in our study (98.2% vs. 86.1%).

Washing hands with soap and water and using face masks are important measures to prevent the spread of infection with 86.1% dental professionals knowing this. Study on health workers around the world showed that 87% of their participants felt that hands washing with soap and water could help in prevention of COVID-19 transmission.

A similar study assessing knowledge and anxiety level of Iranian nurses revealed that 58% have sufficient knowledge towards COVID-19. Knowledge of nurses regarding common symptoms, prevention and incubation period was less as compared to dental professionals in our study (47% vs. 97%, 68.2% vs. 86.1%, 20% vs. 85.6% respectively). This difference in results of knowledge variables can be attributed to the fact that these studies were conducted ahead of our study, very early during the outbreak of the COVID-19 pandemic and knowledge and awareness regarding the disease is definitely increasing with time and with the emergence of new cases.

Another study conducted on healthcare workers in China regarding attitudes and knowledge related to COVID-19 reported that 89% of their participants had adequate knowledge, which is in line with our findings. Furthermore, the authors report that substantial knowledge among healthcare workers was linked with higher confidence in defeating the condition.

The was general consensus regarding prevention of COVID-19 transmission, with 92% participants showing positive attitudes towards using WHO, CDC standards and isolation precautions, quite similar to findings of a study on Jordanian dentists (97.8%) regarding COVID-19 cross infection control. Furthermore, a majority of the participants’ (74.8%) showed concern about contracting the virus and passing it on to family members, which was very similar to figure (79.8%) in a study conducted on healthcare workers in Vietnam.

Social media was reported as a leading source of information about COVID-19. This was in agreement with studies on HCWs in Iran and Vietnam. These results show that HCWs all around the globe are more inclined to gain knowledge from social media. Knowledge level towards MERS-CoV of Saudi HCWs showed the Ministry of Health website as the main source of information. This difference can be due to a dynamic website of Saudi Health Ministry in terms of updating new information. Health authorities, and mass media in Pakistan should pay more attention to changing their way of information delivery in order to make these media more attractive for people.

Despite sufficient knowledge and good level of attitude possessed by dental professionals, their perceptions regarding COVID-19 spread and control were not very encouraging. This was in contrast to the results obtained from other studies such as the one conducted in Vietnam, and a web-based study conducted on health workers around the world, regarding knowledge and perceptions related to COVID-19, which reported 78% of healthcare workers had positive perceptions.

Results of a study related to Knowledge, Attitudes and Practices (KAP) regarding COVID-19 in
Peruvian population showed that 76.9% of their participants perceived their authorities were not prepared to face the disease, and 62.7% believed that response of their authorities was not effective.” This is very similar to the results seen in our study. There was lack of confidence amongst dental professionals regarding the capability of government institutions to control this pandemic (77.7%). This can be attributed to limited resources as well as a lack of experience of government in managing natural disasters or a pandemic. Political attachment can be another possible reason for this low perception of government’s ability to control the epidemic. This is evident by 69.8% of participants who considered amount of information available about COVID-19 in our society to be insufficient. These significant findings are a call for government as well as health authorities to play an active and effective role in delivering information and improving strategies to deal with this gravid situation.

Although there are no validated questionnaires available for analysis of knowledge, attitudes, and perceptions regarding the Novel Coronavirus, we attempted to use a questionnaire that was pretested for a similar disease epidemic (MERs-CoV). Furthermore, after modifications in the questionnaire, related to COVID-19, we sought expert opinion, and pilot tested it to ensure it worked well to capture dental professionals’ attributes regarding COVID-19 pandemic, in our setting. In addition, the link for the questionnaire was shared twice in each group to ensure wide coverage of participants who are active at different times.

Limitations of the study

The study is not without limitations. In order to generate rapid information and in accordance with social distancing measures, this study was conducted virtually using a convenience sample, which limits the generalizability of results. Nevertheless, it provides a useful insight for the improvement of infection control measures and their implementation in dental teaching hospitals of Pakistan.

CONCLUSION

In conclusion, the dental professionals possessed good level of knowledge regarding COVID-19 and showed positive attitudes towards prevention of spread of the virus. However, the low perceptions regarding the capability of government hospitals to control the spread of the pandemic emphasize the need for substantial efforts required through educational campaigns, focusing more on precautionary and infection control measures to protect health care workers as well as patients from COVID-19 infection.

Conflicts of Interest

The authors declare no conflicts of interest.

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KNOWLEDGE, ATTITUDE AND PERCEPTIONS TOWARDS COVID-19 AMONGST DENTAL PROFESSIONALS


SURGICAL OUTCOME OF BI-CONDYLAN FRATURES OF PROXIMAL TIBIA

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Abstract

Background: Tibial plateau fractures results either from high energy motor vehicle accidents or as a result of axial loading such as fall from height and other sources of trauma with high energy mechanism in young or as a result of low energy trauma in case of old population and patient with osteoporotic bones.

Objectives: To evaluate the functional outcome of operative stabilization of lateral and medial condyles of tibia with locked plating with or without additional screws from the medial side.

Methodology: 40 patients with proximal tibial fractures involving both the condyles admitted through emergency department of services hospital were included in this study. A written consent and permission from the hospital ethical committee was obtained. Each patient was operated with a locked lateral plate. After open reduction and internal fixation (ORIF) surgery above knee back slab was applied to each patient and quadriceps and hamstrings isometric exercise was started. The patients were discharged from the hospital on an average of 3 to 7 days. All patients were followed at first, second, third, fourth and sixth week and thereafter at fourth and six months and finally at 1 year, clinically and radiologically using Rasmussen functional and anatomical score.

Results: 75.0% of subjects were males and 25.0% were females. 70.0% of patient were between 25-40 years of age. While 25.0% were 40-60 years and 5.0% were 68-70 years. 80.0% of the fractures united in 12 to 16 weeks 12.5% patients union achieved at fifth month and in 7.5% patients union occurred at sixth month. 7.5% patients developed infection.

Conclusion: It is concluded from our study that ORIF with single locked compression plating seems to be a good implant for bi-condylar proximal tibial fractures. It resulted in excellent functional and anatomical outcomes.

Keywords: External fixation, internal fixation, locking plate, tibial plateau fractures

Tibia Plateau comprises of medial and lateral tibial condyles also called as medial and lateral tibial plateau. Medial condyle is thicker and bears sixty percent of knee joint weight. It is concave in shape and located slightly more distally than the lateral tibial condyle. Lateral tibial condyle is convex in shape, thinner, weaker and more proximal than the medial condyle. It is separated from the medial condyle by intercondylar eminence. Tibial plateau fractures results either from high energy motor vehicle accidents or as a result of axial loading such as fall from height and other sources of trauma with high energy mechanism in young’s or as a result of low energy trauma in case of old population or patient with osteoporotic bones. Males are more common sufferer than females. Tibia plateau fractures results in a wide spectrum of injuries with varying challenges to the orthopedic consultant on presentation. Bi-condylar fractures of tibia involve


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SURGICAL OUTCOME OF BI-CONDYLAR FRACTURES OF PROXIMAL TIBIA

the medial and lateral weight bearing portion of proximal tibia. The prognosis of injury pattern depends upon the particular configuration and geometry of these fractures. It comprises 1% of all fractures. These fractures are associated with articular surface incongruity, varus and valgus malalignments, ligamentous injury, meniscal injuries and neurovascular injuries. Careful review of the literature indicates that health of articular cartilage, presence of meniscus, overall alignment of tibia and mediolateral stability is of equal importance. When these fractures are associated with open wounds, especially the fractures that require soft tissue envelopes have been associated with major wound complications. With extensive surgical exposure of proximal tibial fractures the chances of infection cannot be negated. Because of the above mentioned fractures the functional outcome of these fractures is variable. For patients whose jobs require high degree of mobility, tibial plateau fractures significantly delay the return to original job. Most patients need extensive rehabilitation programs to regain the knee range of motion and muscle strength. Although with extensive rehabilitation program, the outcome is good but return to the sports in case of competitive athletes may be delayed for months.3,16,17 Ideal management of these fractures is controversial and still there is no consensus on either of the best method of fixation.3 A lot of surgical techniques are available to fix the bi-condylar fractures of tibia. These includes bi-column fixation with buttress plates, arthroscopic assisted reduction8 and elevation with support using calcium phosphate and percutaneous screw fixation, balloon tibioplasty and external fixation using the ilizarov technique.3,13 Moreover these fractures can also be fixed with intramedullary nailing with compression bolts. Recent development of locked plating and minimally invasive technique has improved the clinical outcome of these fractures. These fractures can also be fixed with posteroomedial buttress plate support for generally less involved medial condyle and elevation and supporting the lateral column with locked plate fixation of lateral tibial condyle. Single locked plating through anterolateral approach has also been used.18 This minimal invasive locking plate osteosynthesis provides an alternative to intramedullary devices, external fixation and conventional plate reconstruction.14 It provides the precise and stable fixation in intra articular fractures. Complication rate especially skin and ligamentous damage is less with locked plating. It provides the balance between mechanical and biological tradeoffs.5

Bi-condylar fractures can be stabilized with single locked plating4 or double plating. Clinical and biomechanical data support both of these modes of surgical options. Double plating requires two separate incisions, extensive surgical exposure, more periosteal stripping, wound problems, non-union and delayed union even in expert surgical hand. Locked plating applied unilaterally is a reasonable option for bi-condylar fracture of tibia.11 It carries the decreased morbidity to the patients with proximal tibial fractures.

METHODOLOGY

This prospective study was conducted at Department of Orthopaedic Surgery, Services hospital, Lahore from December 2018 to December 2019. A total number of 40 patients having bi-condylar fractures of proximal tibia were included in the study. All patients were admitted through emergency department of this hospital. Patients with severe co morbidities and poly-trauma patients were excluded from the study. On admission data was recorded and detailed history and clinical examination was performed. All patients were resuscitated according to ATLS protocols. Informed written consent was taken from each patient. The baselines investigations and X-ray of the knee joints AP, Lateral and oblique views were done. For assessment of postero-lateral and posteromedial fragments, CT scan of knee joint was done for each patient. For ligamentous injury assessment, MRI was done if it is required. After fitness of patient for anesthesia, the fracture was fixed with single locked compression plate with anteromedial or anterolateral incision. After surgery the back slab was
applied. Post operatively each patient was managed with analgesia and antibiotics. IV antibiotics were continued for 3 to 7 days. The patients were discharged in 4 to 7 days post operatively. Each patient was followed clinically and radiologically at 1\textsuperscript{st}, 2\textsuperscript{nd} and 6\textsuperscript{th} week and thereafter at 3\textsuperscript{rd} and 6\textsuperscript{th} month and then at 1 year. Rasmussen functional and anatomical score was used to assess the functional and radiological outcome of these fractures.

RESULTS

This prospective study included 40 patients, out of which there were 75.0\% males and 25.5\% females. 70.0\% of patient were between 25-40 years of age. While 25.0\% were 40-60 years and 5.0\% were 68-70 years. Right knee was involved in 62.5\% patients, while the left knee was involve in 37.5\% patients. Mode of injury was road traffic accidents in 8.5\% patients, while in 12.5\% patients it was fall from height, and in rest of 5.0\% patients it was slip and fall. 35 patients sustained closed fractures, while 5 patients had open fractures. 80.0\% of the fractures united in 12 to 16 weeks 12.5\% patients union achieved at fifth month and in 7.5\% patients union occurred at sixth month. 7.5\% patients developed infection. The infection was superficial and it was managed conservatively with IV antibiotics and ASD. All these patients recovered after 5 days. The mean functional Rasmussen score at 6 month follow up was (26.30 ± 1.54 SD) with a range of (25-29) with significant p value (p value <0.001) functional Rasmussen at last follow up (1 year) was (28.33 ± 1.56) ranged between (26-30) with significant p value (p value <0.001). The mean anatomical Rasmussen score at 6 month follow up was (16.12 ± 1.52) with a range of (16-18) and at last follow up (1 year) the mean anatomical Rasmussen score was (16.57 ± 1.38) ranged from (16-18) with insignificant p value (p value <0.096).

DISCUSSION

Proximal tibial fractures are associated with spectrum of ligamentous, meniscal and bony injuries that can result into significant morbidities. The treatment is always challenging to the orthopaedic consultant because of significant joint incongruity, displacement and excessive soft tissue damage. The aim of surgery is to maintain the joint congruity, limb length difference, stability of the knee joint, restoration of the varus and valgus, mal-alignment and overall improvement of the knee joint movements. When the non-operative treatment is opted there is inadequate reduction of articular surface and limb length discrepancy.

Majority of patients in our study were young males as the young persons are more exposed to trauma as compared to old population. But the gender didn’t affect the outcomes in our patients. Study of Reddy et al.\textsuperscript{1} also shows that males are more
sufferer than females. Similarly the modes of injury in most of our patients were road traffic accident followed by fall from height and then slip and fall.

Studies also have shown that road traffic accident is the predominant cause of trauma. Moreover right knee joint was involved more than the left knee joint. This finding is comparable to our study. However whether right or left side was involved, it had no effect in the functional outcome of the patient.

In our study 35 patients got closed SCHATZKER type 4 fracture while rest of 5 patients got open fracture. Out of 5 patients who got infection, 2 required the debridement procedures and IV antibiotics. The average wait interval in our patients after admission and surgery was 4 to 7 days. It was more for open fractures (9 days). Only one patient had 110 degree flexion after the surgery, which didn’t improve with physiotherapy, reason being that this patient had open fractures.

Loss of articular reduction up to 3mm was observed in 2 of our patients. It was due to screw loosening in the osteoporotic bone, but it didn’t affect the functional recovery. The locking plate provides angular stability. Study of Gosling et al. 4 also shows that locked plating applied unilaterally is a reasonable approach for fixation of bi-condylar fractures of tibia. In his study Raza et al. 5 chooses locking plate as improved outcome regarding the angular stability. In most of our patients 32 (80%) fracture united in 12-16 weeks, and these patients had excellent results regarding fracture union and range of motion. Where there is slight delay in the union (20% patients), the results were good.

Excellent functional and radiological outcomes by using single locking plate with MIPPO technique indicate that it is a good treatment option for bi-condylar tibial plateau fractures. Although technique is demanding, this procedure provides reliable stability. The pot-op complications can be decreased by proper timing of surgery, avoiding the dissection of comminuted bone fragments and with good periosteal and soft tissue dissection. Medial fragment fixation requires the multiple locking screws for fixation primarily in the coronal plane.

Limitations of Study

Our study included the small number of patients. Moreover it was done only on the patients having bi condylar fractures of tibia. It did not include the other proximal tibial fractures. It is recommended that it should be conducted on large number of patients.

CONCLUSIONS

It is concluded from our study that ORIF with single locked compression plating seems to be a good implant for bi-condylar proximal tibial fractures. It resulted in excellent functional and anatomical outcomes.

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No funds were received from any government or private organization for this study.

Conflict of Interest

The authors declare that they have no conflict of interest.

Ethical Approval

This study was approved by institutional review board Services Hospital Lahore.

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Fungal sinusitis refers to a spectrum of conditions that is caused by fungal infection of nose and paranasal sinuses. This is a rapidly progressive disease that is usually seen among patients with diabetes mellitus and immunocompromised patients. Rhinosinusitis may involve paranasal sinuses unilaterally or bilaterally.

Fungal sinusitis is not a rare disease now a day (incidence ranges from 4.4 % to 6.7% worldwide). In countries like Sudan, Saudi Arabia and southwestern states of USA, and in northern parts of India, this disease is endemic and its prevalence is increasing day by day.

Fungi are found mainly in air, dust, soil, plants, and decaying organic matter. They adhere to dust particles and are inhaled and deposited on the nasal and paranasal sinus mucosa. The warm, moist environment of the upper respiratory tract is an ideal environment for the proliferation of these organisms. Studies have shown the evidence of presence of fungal infection among patients with rhinosinusitis.

Various other risk factors and medical condi-
tions have been associated with this fungal sinusitis like atopy in allergic fungal sinusitis and diabetic ketoacidosis in mucedary mycosis, malignant diseases and corticosteroid or immunosuppressant therapy etc. Fungal sinusitis may be divided in two diagnostic categories: non-invasive form (fungal ball and allergic fungal sinusitis) and invasive form (acute invasive, granulomatous invasive and chronic invasive fungal sinusitis). Mucor, Rhizopus, Rhizomucor, Absidia, and other Mucorales fungi that belong to the division Zygomycota, or Aspergillus species that belong to the division Ascomycota, may be responsible for the disease. These organisms are found saprophytically in decomposed substances, soil and fruits, and in the throats, nasal cavities, and feces of healthy individuals; but they may become pathogenic in immunocompromised patients and in patients with uncontrolled DM. Aspergillus Fumigatus is the most common organism found in both forms of fungal sinusitis.

Invasive fungal sinusitis has always been a diagnostic and therapeutic challenge for the otorhinologist due to its high mortality (up to 50% with treatment and it was up to 90% without treatment), morbidity, and resistance to treatment.

The clinical presentations of fungal rhinosinusitis included nasal stuffiness (27.9%), nasal discharge (27.9%), facial pain (27.9%), fever (24.3%) and headache (19.8%). One-fifth of cases had an underlying hematologic malignancy. Invasive fungal rhinosinusitis was significantly associated with hematologic malignancy and neutropenia.

Establishing a diagnosis and start appropriate treatment is essential for the management of the patients with fungal sinusitis. However, establishing a diagnosis is difficult as patients are usually immunocompromised as a result of diabetes mellitus, systemic chemotherapy, organ transplant or long-term systemic use of steroids.

Radiologic findings vary from non-specific mucosal thickening to an opacified sinus with calcification and bone erosion or destruction. On MRI signal hypointensity is distinctive feature of fungal infection, either low Signal on T1 and T2 when there is fibrosis, or a total absence of signal on all sequences due to paramagnetic effect of heavy metals present in fungal ball. MRI plays vital role in diagnostic evaluation of patient with fulminating aggressive fungal infection because of its ability to identify spread of infection from turbinates to sinuses, orbits, intracranial cavity and can differentiate between benign infections, neoplasm and hemorrhage; though Gold standard for fungal infections is histopathology.

In a study by Groppo, et al, which was conducted on 17 immunocompromised patients with suspected fungal sinusitis, MRI showed sensitivity of 85%, specificity 83%, positive predictive value of 93% and negative predictive value 71% (keeping the histopathology as gold standard).

Routinely, CT scan of paranasal sinuses is advocated for detection of fungal sinusitis, which highlights the disease as opacification, and thickening of nasal mucosa or infiltration to the lateral wall. These same very findings can also be depicted with MRI. MRI has the advantage of being non-invasive and free of radiations which can be hazardous to our patients, who already may be immunocompromised. Moreover, the studies which have depicted the diagnostic accuracy of MRI are scanty and are done on small patient population. So, I want to determine the diagnostic accuracy of the MRI. The results of this study will help our patients by offering a better modality which may be less hazardous to our patients.

**METHODOLOGY**

It was a Cross sectional survey. The study was conducted at Department of Radiology, Allama Iqbal Medical College/ Jinnah Hospital, Lahore. The calculated sample size is 60 cases with 95% confidence level, 14% margin of error and taking expected percentage of fungal sinusitis i.e., 42%,
with 85% sensitivity, 83% specificity of MRI in the diagnosis of fungal sinusitis by taking histopathology as gold standard. Study was conducted from February 2020 to July 2020, using Non-probability purposive sampling.

Inclusion Criteria
- Gender: both male and female
- Age: 20-60 years
- Patients referred from ENT with strong clinical suspicion of fungal sinusitis.

Exclusion Criteria
- Contraindications to MRI i.e., history of metallic stents, or denture, or pace makers
- Patients refusing from sinunasal endoscopy or MRI
- Patients already having surgery for sinunasal pathology

Sixty cases fulfilling inclusion criteria in outdoor and indoor Departments of Jinnah Hospital, Lahore with suspicion of fungal sinusitis were enrolled for the study. An informed consent was taken from patients by explaining the purpose, procedure, benefits or hazards of the investigation. Axial, coronal and sagittal images of paranasal sinuses of selected cases were performed on Philips 1.5 tesla using superconducted magnet MRI machine. Signal hypointensity both on T1 and T2 weighted images was primary criteria for diagnosing fungal infection. The MRI findings were later confirmed by sinunasal endo-scopy and histopathology taking as gold standard.

RESULTS

The total number of patients included in the study was 60 (including both males and females).

The mean age of the patients included in the study was 29.56 ± 6.18 years [range 20 – 45]. There were 15 (25%) patients of age range of 20 – 30 years, 19 (31.7%) patients of age range of 31 – 40 years, 17 (23.3 %) patient of age range of 41 – 50 years, 9 (15%) patients of age range of 51 – 60 years.

Patients were also distributed according to sex.

There were 34 (56.7%) male patients in the study, while 26 (43.3%) patients were female. Male to female ratio was 1:3.

Out of 60 patients included in the study, the fungal sinusitis on MRI was detected to be positive in 41 patients. Of these, 39 were proved on histopathology, so were labeled as true positive, while rest of the two patients were labeled as false positive. Histopathology was negative in total 19 patients. Out of these 5 were positive on histopathology (false positive) and 14 were also seen negative on histopathology (true negative).

The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of MRI for diagnosis of fungal sinusitis was 88.6%, 87.5%, 95.1%, 73.7% and 88.3%, respectively.

DISCUSSION

In our study, the mean age of the patients was 29.56 ± 6.18 years. The mean age in a study by Baloch ZA,24 was 27.3 +/- 12.98 years ranging from 9 to 64 years. Eighty percent of the patients were below fifty years of age. The results of both studies are close to the result described by Thahim K, et al,16 that was 20.75 years and Mian MY, et al,26 which was 24 years. All patients in study by Zakirullah, et al,26 most of the patients were young with a mean age at presentation 20 years and 83% were in 2nd and 3rd decade of life which is also comparable to that in our study i.e. approximately 72.7% patients were in 2nd and 3rd decade of life.

Regarding the gender distribution in patients included in our study, there was a female preponderance with 56.7% female and 43.3% male. This female predilection was also observed in study by Baloch ZA, et al,24 who observed that there were 26.3% male and 73.7% females in their study. Danyal R, et al,27 and Krishnan S, et al,28 also found female predilection. But Mian MY, et al,28 and Thamim K, et al,16 found male preponderance with ratio of 3:1 and 7:3. However, in a review of patients at UT Southwestern, in children, male dominated (M/F ratio 2.1:1; average age=13 year) and in adults
females dominated (M/F ratio 1:1.4; average age 36 year).  

The sensitivity of MRI for detection of fungal sinusitis was 88.6%, which is high. A high sensitivity is particularly important when choosing a modality for screening immunocompromised patients with sinus and facial signs and symptoms, since missing a diagnosis may delay in initiation of the treatment and may result in poor outcome. This higher sensitivity of MRI has also been confirmed by Groppo et al.  

The specificity of MRI in detection of fungal sinusitis was also high i.e. 87.5%. A high specificity of MRI (83%) was also observed by Groppo et al. This high specificity also proves that it can also depict the true negative cases as well. This makes it a useful investigation for establishing the diagnosis.  

The sensitivity and specificity of CT scan and MRI in detection of inflammatory condition of sinuses was also tested in another study by Fawaz AS, et al and it was observed that the sensitivity of CT and MRI in diagnosing inflammatory lesions was 95% versus 61%.  

The positive predictive value of MRI was also very high i.e., 95.1% while a low negative predictive value of 73.7% was observed in our study. The positive predictive value of 93% and negative predictive value 71% were also observed by Groppo et al.  

The diagnostic accuracy found in our study was high i.e., 88.3% which makes it a reliable test for investigating the fungal sinusitis disease.  

In our study, the low signal hypointensity (which is distinctive feature of fungal infection) was used to define the fungal sinusitis. Several factors might decrease the signal intensity in a T2 weighted image, including the presence of calcium, air or ferromagnetic elements. Moreover, the presence of iron and managanese in quantities significantly greater than those seen in bacterially infected mucus might even better explain the sharp decrease in signal activity seen on T2 weighted MR images of fungal concretions.  

MRI allows visualization and differentiation of the soft-tissue structures of the paranasal sinuses and the adjacent orbital and intracranial cavities. MRI with gadolinium contrast is used to evaluate sinusosal, intracranial or orbital complications of rhinosinusitis.  

There are few limitations of the study. This was a single center study with a limited population size. All the reports were interpreted by single expert radiologist. The interobserver variation in reporting may also affect the diagnostic accuracy.  

CONCLUSION  

The study concludes that MRI for diagnosis of fungal sinusitis has shown a high sensitivity, specificity and diagnostic accuracy. So, it can be considered a reliable investigation among patients suspected with fungal sinusitis. It is suggested that MRI should be preferred over CT scan for diagnosis of fungal sinusitis as it is free of radiation and is non-invasive whenever it is available.  

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Limitation of study None  

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Conflict of Interest The idea presented in this article is solely of the authors and is in no direct conflict to any individual or institution.  

Authors Contributions  

Conception & Design: Dr Fatima Iqbal & Dr Naeem Ahmad Khan.  

Collection & Assembly of data: Dr. Fatima Iqbal, Dr. Naeem Ahmad Khan, Dr Tanweer Ahmad.  

Literature Review & Critical Revision of the article for important intellectual content: Dr Tanweer Ahmad & Dr. Basma Khan.  

Final approval of the article: Dr Aamer Nadeem Chaudhary.
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Abstract

Objective: To compare the efficacy of two intravenous fluid regimens of ringer lactate on prevention of postoperative nausea and vomiting in laparoscopic cholecystectomy.

Methodology: The study was conducted after the approval of hospital ethical committee. Patients between 18-60 years of age, belonging to ASA Grade I-II and undergoing elective laparoscopic cholecystectomy were included. All patients kept nil per orally from 2300 hr on night before surgery and premedicated with tablet diazepam 0.2 mg/kg in the night and on the morning of surgery. In the operation theatre, an 18-G IV cannula inserted and monitoring for heart rate, blood pressure, ECG, end-tidal CO2 and SpO2 was initiated. The patients were randomly allocated to one of the two groups using computer-generated random table. Thereafter, intravenous fluids were administered to the patients over a period of 15 min prior to the induction of anesthesia in accordance with the groups i.e. Group A: Ringer lactate 4-ml/kg body weight and Group B: Ringer lactate 10-ml/kg body weight. Anesthesia was induced only after infusing full amount of calculated intravenous fluid. Blinded observer made all the observations in the post-operative period. The VAS sores for PONV recorded postoperatively at 0, 1 and 4 hour, and then 4 hourly for 24 hours. Final outcome measured at 24 hours. Injection ondansetron 4 mg IV used as rescue antiemetic whenever VAS scores (for PONV) becomes > 5 or the patient vomits. All the obtained data was recorded on the structured proforma.

Results: The mean age in group “A” was 37.9 years ± 5.4 SD years and in group “B” was 38.2 years ± 7.7 SD. The independent t-test was applied and p-value resulted in p = 0.06 proving that there was no significant difference in mean age between two groups. In group A, treatment was found to be efficacious (as per our operational definition) in 30.0% (n=9) of patients, while in group B it was efficacious in 70.0% (n=21) of patients. P-value (chi-square) was 0.002 (< 0.05), implies that treatment was significantly more efficacious in group B (Ringer lactate 10 ml/kg).

Conclusion: Pre-treatment with higher volumes of crystalloid solution (ringer lactate 10ml/kg versus 4ml/kg) prior to anesthesia results in better prevention of postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy.

Keywords: Pretreatment, Preload, Fluid, PONV, Laparoscopic cholecystectomy, Laparoscopy associated PONV, Ringer Lactate, Hartmann’s Solution

Nothing by mouth preoperative period may lead to 10 to 12 hours in our set ups especially in surgeries that are planned for morning due to overnight fasting. These periods leading to hypovolemia may exacerbates postoperative nausea and vomiting (PONV)\(^1\). However, data on the efficacy of supplemental intravenous fluids for PONV prophylaxis are conflicting\(^2\). The incidence of post operative nausea and vomiting (PONV) following ambulatory surger-
COMPARISON OF EFFICACY OF TWO INTRAVENOUS FLUID REGIMENS OF RINGER LACTATE

ry is 40%–60% and ambulatory patients undergoing laparoscopic surgery are at particularly high risk. PONV continues to occur despite pharmacological prophylaxis in high risk patients. PONV can cause delays in meeting discharge criteria both from the recovery room to ward and from the day ward to home. PONV causes patient discomfort and can cause unanticipated overnight hospital admission which results in increased economic costs\(^3\). PONV control is a strong patient priority and there is a strong association between PONV and patient dissatisfaction with their anaesthesia care. The routine use of antiemetics remains controversial as their efficacy is limited in patients with low risk profiles\(^6\). This prospective, randomized, blinded study is designed to determine if administration of 4 ml/kg of crystalloid solution reduces post-operative nausea and vomiting in patients undergoing laparoscopic surgery as compared to 10ml/kg of crystalloid solution. Hartmann’s Solution is also called Ringer Lactate contains: sodium 131 mmol litre\(^{-1}\), potassium 5 mmol litre\(^{-1}\), calcium 2 mmol litre\(^{-1}\), chloride 111 mmol litre\(^{-1}\) and lactate 29 mmol per litre. According to the study performed by Bhukal I et al in 2012 in India the incidence of PONV in patients receiving 4 ml/kg of crystalloid was 72.5 % as compared to 30% in patients receiving 10ml/kg of crystalloid\(^9\). Both the concentrations are in practice but literature showed good efficacy in controlling PONV with 10ml/kg /hour of crystalloid. If result of our study showed it better then we can change our management protocols accordingly for decreasing morbidity of our patients.

METHODOLOGY

This was a randomized controlled trial. Study was conducted at General Operation theatre, Sandeman Provisional Hospital, Quetta. Six months after the approval of synopsis. (01.01.2018 to 30.06.2018). Sample size of 60 cases; 30 cases in each group is calculated with 95% confidence level, 80% power of test and taking frequency of PONV 72.5% in 4ml/kg group and 30% in 10ml/kg group. Sampling Technique: Non-probability, purposive sampling.

Inclusion Criteria:
1. Both genders
2. Age between 18 to 60 years.
3. ASA grade 1 and 2 undergoing laparoscopic cholecystectomy
4. Non Smoker i.e. Never smoked in life

Exclusion Criteria:
The following cases were excluded from study because these cases act as confounders and interfere with results, thus producing bias in the study. These are:
1. Those with established gastrointestinal disease
2. Patients who develop intraoperative hypotension (mean blood pressure less than 60) or excessive blood loss (more than 500ml)
3. Cholecystectomy lasting for more than 2 hours
4. Patients taking antiemetic drugs or history of motion sickness
5. Patients known with renal disease such Serum creatinine above 1.2 mg/dl

The study was conducted after the approval of hospital ethical committee. Patients between 18-60 years of age, belonging to ASA Grade I-II and undergoing elective laparoscopic cholecystectomy were included. Written informed consent was taken from all the patients prior to their inclusion. During pre-operative visit all patients were familiarized with visual analogue scale (VAS) of 0-10cm for post-operative nausea and vomiting (PONV). On this scale, score 0 mean no nausea while score 10 means worst imaginable nausea. Occurrence of vomiting scored as 10. All patients kept nil per orally from 2300 hr on night before surgery and premedicated with tablet diazepam 0.2 mg/kg in the night and on the morning of surgery. In the operation theatre, an 18-G IV cannula inserted and monitoring for heart rate, blood pressure, ECG, end-tidal CO\(_2\) and SpO\(_2\) was initiated. The patients were randomly allocated to one of the two groups using computer-generated random table. Thereafter, intravenous fluids were
administered to the patients over a period of 15 min prior to the induction of anesthesia in accordance with the groups, as shown below:

Group A: Ringer lactate 4-ml/kg body weight
Group B: Ringer lactate 10-ml/kg body weight

The observer was present in the operation theatre at the time of preloading or during conduct of the case under general anesthesia. Anesthesia was induced only after infusing full amount of calculated intravenous fluid. Intravenous fluids were continued in the form of Ringer’s lactate (2 ml/kg/h) for 24 hr post-operatively. Blinded observer made all the observations in the post-operative period. The VAS sores for PONV recorded postoperatively at 0, 1 and 4 hr, and then 4 hourly for 24 hrs. Final outcome measured at 24 hours. Injection ondansetron 4 mg IV used as rescue antiemetic whenever VAS scores (for PONV) becomes > 5 or the patient vomits. All the obtained data was recorded on the structured proforma. Data was entered and analyzed in SPSS version 20. For qualitative variables like gender, ASA, efficacy (nausea, vomiting) measured as frequency and percentages. Quantitative variables like age are measured as mean or standard deviation. Chi-square test was applied to compare efficacy between two groups. P value less than or equal to 0.05 considered significant. Stratification with respect to age, gender, and ASA status was done. Post stratification Chi-square test was applied.

RESULTS

All the enrolled 60 patients completed the study from 01.07.2019 to 31.12.2019 making the study period 6 months. Patients were divided into two group i.e.” A” and “B”.

The mean age in group “A” was 37.9 years ± 5.4 SD years and in group “B” was 38.2 years ± 7.7 SD. The independent t-test was applied and p-value resulted in p=0.06 proving that there was no significant difference in mean age between two groups.

In group A (4 ml/kg), treatment was found to be efficacious (as per our operational definition) in 30.0% (n=9) of patients, while in group B (10 ml/kg) it was efficacious in 70.0% (n=21) of patients. P-value (chi-square) was 0.002 (< 0.05), implies that treatment was significantly more efficacious in group B (Ringer lactate 10 ml/kg).

Gender distribution of the patients showed that in both groups most of the patients were female. All the data is summarized in Table 1. Distribution of Age, Gender and ASA are given in Table 2 and 3.

After applying chi square test, it was found that there was no significant difference in gender distribution for two groups.

After applying chi square test, it was found that there was significant difference in two groups for the frequency of PONV ( p= 0.02) Hence proving that 10ml/kg ringer lactate is superior in controlling PONV better than 4ml/kg ringer lactate.

After applying chi square test, it was found that male responded to 4ml/kg ringer lactate while female responded well to 10ml/kg

After applying chi square test, it was found that there was significant difference in patients who were less than 40 year old and there was no significant difference in 40 and above class for the frequency of PONV.

DISCUSSION

Postoperative nausea and vomiting (PONV) are distressing and frequent adverse events of anesthesia
and surgery. These symptoms predispose to aspiration of gastric contents, increased intraocular pressure, psychological distress, and delayed recovery and discharge times. PONV can lead to delayed post-anesthesia care unit (PACU) recovery room discharge and unanticipated hospital admission, thereby increasing medical costs. Numerous antiemetics have been studied for the prevention and treatment of PONV following surgeries under general anesthesia. These drugs include butyrophenones (e.g., droperidol), benzamides (e.g., metoclopramide), antihistamines (e.g., dimenhydrinate), corticosteroids (e.g., dexamethasone), propofol, oxygen, and serotonin receptor antagonists (e.g., ondansetron).

Most of published trials indicate improved prophylaxis against PONV by avoiding risk factors and/or by using effective antiemetic therapy in patients scheduled for surgery. Traditional antiemetics (droperidol, metoclopramide, and alizapride), non-traditional antiemetics (propofol and dexamethasone), and serotonin receptor antagonists (ondansetron, granisetron, tropisetron, dolasetron, and ramosetron) have been studied for the prevention of PONV.

Serotonin receptor antagonists are more effective than traditional antiemetics. Aprepitant a neurokinin-1 receptor antagonist is newer drug which has even proven better than serotonin receptor antagonists. Combination antiemetic therapy with granisetron plus droperidol or granisetron plus dextromethasone is highly effective in preventing PONV.

Rationale of current study was to gather data on two different volumes of crystalloid solution (ringer lactate 4 ml/kg and 10 ml/kg) for prevention of PONV in our settings. Our main aim was to compare the efficacy of preloading with different volumes of crystalloids (10ml/kg versus 4ml/kg) on prevention of PONV. All patients were randomized to two groups. Group A received Ringer lactate 4-ml/kg and Group B received Ringer lactate 10-ml/kg 15 minutes prior to the induction of anesthesia. Our results showed that In group A, treatment was found to be efficacious in 30.0% (n = 9) of patients versus 70.0% (n=21) in group B (P < 0.05). Stratification with respect to age, gender and ASA grades showed treatment was more efficacious in group A in younger age group (<40 years), in both genders and in both ASA grades (P<0.05).

Our results are in concordance with the results already published on the subject. Chaudhary S, et al in their prospective randomized clinical trial aimed to study the effects of pre-operative intravenous fluid supplementation, either crystalloids or colloids, on PONV(11). They enrolled 60 female patients undergoing elective open cholecystectomy and randomly allocated them to three equal groups A, B and C. All patients received preoperative fluid supplementation. Group A patients received 2 ml/kg Ringer lactate iv (intravenously) and served as control, Group B patients received 4 ml/kg Ringer lactate iv whereas Group C patients received 12 ml/kg of 4.5 per cent hydroxyethylstarch (Hextend) iv. All patients underwent cholecystectomy under standard anesthesia technique with intraoperative fluid replacement by Ringer’s lactate (6 ml/kg/h). An independent blinded observer assessed PONV during first 24 h following surgery using visual analogue scale (VAS) score (0=no nausea, 10=worst imaginable nausea or vomiting). Rescue antiemetic was given whenever VAS was > 5. Their results showed

### Table 3: Stratification Of Ponv According To Gender

<table>
<thead>
<tr>
<th>GENDER</th>
<th>GROUP A (Ringer Lactate 4 ml/kg)</th>
<th>GROUP B (Ringer Lactate 10 ml/kg)</th>
<th>P-value Chi-square</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>YES 5</td>
<td>10</td>
<td>0.022</td>
</tr>
<tr>
<td></td>
<td>NO 8</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>YES 4</td>
<td>7</td>
<td>0.025</td>
</tr>
<tr>
<td></td>
<td>NO 13</td>
<td>18</td>
<td></td>
</tr>
</tbody>
</table>

### Table 4: Stratification Of Ponv According To Age

<table>
<thead>
<tr>
<th>AGE-GROUPS</th>
<th>GROUP A (RINGER LACTATE 4 ml/kg)</th>
<th>GROUP B (RINGER LACTATE 10 ml/kg)</th>
<th>P-value Chi-square</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 40 years</td>
<td>YES 7</td>
<td>11</td>
<td>0.018</td>
</tr>
<tr>
<td></td>
<td>NO 16</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>40 and above</td>
<td>YES 2</td>
<td>10</td>
<td>0.061</td>
</tr>
<tr>
<td></td>
<td>NO 5</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>
that VAS scores in Groups B and C patients were less than that of Group A patients at all time intervals post-operatively and became significantly different at 4 h post-operatively. The VAS scores of Groups B and C patients were comparable throughout. A significantly large number (90%) of Group A patients required rescue antiemetic as compared to 50 and 55 per cent patients in Group B and Group C, respectively. Authors concluded that pre-operative intravenous fluid supplementation using crystalloids and colloids results in significantly decreased incidence of PONV. Both, crystalloids as well as colloids were found to be equally effective in preventing PONV.

Apfel CC, et al in their review analysis performed a literature search using CENTRAL, MEDLINE, EMBASE, CINAHL, and Web of Science. They included prospective randomized controlled trials that reported PONV event rates in patients receiving supplemental i.v. crystalloids or a conservative fluid regimen after elective surgery under general anesthesia. Studies were evaluated with regard to random sequence generation, allocation concealment, blinding of participants, personnel, and outcome assessment, incomplete outcome data, and selective reporting. They identified 15 trials (n=787 crystalloids; n=783 conservative fluids). Their analysis showed that compared with conservative fluids, i.v. crystalloids reduced the risk of early postoperative nausea (PON) (relative risk 0.73, 95% confidence interval 0.59-0.89; P=0.003), late PON (0.41, 0.22-0.76; P=0.004), and overall PON (0.66, 0.46-0.95; P=0.02). However, they found that I.V. crystalloids did not reduce the risk of early postoperative vomiting (POV) (0.66, 0.37-1.16; P=0.16) or late POV (0.52, 0.25-1.11; P=0.09), but did reduce overall POV (0.48, 0.29-0.79; P=0.004). They concluded that supplemental i.v. crystalloids were associated with a lower incidence of several PONV outcomes.

McCaul C, et al aimed to examine the effects of intravenous compound sodium lactate (CSL) with and without caloric supplementation with dextrose on nausea, vomiting and pain following general anesthesia for laparoscopy. They compared I/V fluid loading with and without supplementary dextrose for the prevention of postoperative nausea and vomiting (PONV). They enrolled 120 ASA-I female patients undergoing elective gynecological laparoscopy and randomized them to one of three groups, and received either: (a) CSL 1.5 mL.kg(-1) per hour fasting duration; (b) CSL, 1.5 mL.kg(-1) per hour fasting duration with 0.5 g.kg(-1) dextrose added in 50% formulation (CSL/dextrose); or (c) no iv fluid (control). Their results showed that compared with control the percentage of patients who had no PONV within 24 hr of anesthesia in the CSL and CSL/dextrose groups was 78% vs 83% and 71%, P=0.81 and P=0.683 respectively. They concluded that administration of dextrose is associated with nausea, increased opioid requirement and late thirst after elective gynecological laparoscopy and I/V fluids did not decrease PONV.

The limitations in our study was that we did not classify the PONV as early or late i.e. first postoperative 6 hours and then 6 to 24 hours of postoperative period. By classifying PONV, we would have gotten a better picture for understanding the time frame at which most patients are prone to develop PONV.

In summary, PONV is a frequent complication and may be a reason for increased morbidity and cost of treatment. Following elective surgery, it is believed to result from gut ischemia consequent to hypovolemia from overnight fasting. The etiology and consequences of PONV are complex and multifactorial, with patient-, medical- and surgery-related factors. A thorough understanding of these factors, as well as the neuropharmacology of multiple emetic receptors [dopaminergic, muscarinic, cholinergic, opioid, histamine, serotonin (5-hydroxy-tryptamine; 5-HT)] and physiology [cranial nerves VIII (acoustic-vestibular), IX (glossopharyngeal) and X (vagus), gastrointestinal reflex] relating to PONV are necessary to most effectively manage PONV. Adequate intravenous hydration and adequate pain control proved to be effective in reducing the incidence of PONV.
CONCLUSION

Pre-treatment with higher volumes of crystalloid solution (ringer lactate 10ml/kg versus 4ml/kg) prior to anesthesia results in better prevention of postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy. Further large-scale studies are needed before recommending it in routine clinical use.

REFERENCES

The spleen is a delicate, fist-sized organ under your left rib cage near your stomach. Blunt abdominal trauma is one of the leading causes of death and splenic injuries are one of the common culprits. Ultrasonography is the commonly used imaging method as it is cheap and widely available. However, CT scan is considered as the radiological gold standard.¹

A ruptured spleen is an emergency medical condition that occurs when the capsule-like covering of the spleen breaks open, pouring blood into your abdominal area.² One study has reported the frequency of splenic injuries was 26% among patients with blunt abdominal injuries.³ Missed splenic injury is the most common cause of preventable death after abdominal trauma. As clinical presentation varies widely awareness of spectrum of presentations and their relative importance is vital for diagnosing and managing splenic injuries successfully.⁴,¹⁸,¹⁹

Evaluating patients who have sustained blunt abdominal trauma remain one of the most challenging and resource intensive aspects of acute trauma care. Ultrasonography (USG) meets all these mea-
sures. Including this, USG can also be performed on pregnant patients, on patients with clotting disorders, and on patients with prior laparotomies and above all during trauma resuscitation without interfering with the therapeutic measures.\(^5\)

An initial prospective investigation has demonstrated screening USG to have a specificity of 96% and an overall accuracy of 96% in the detection of intra-abdominal injury.\(^6\) One study reported that the sensitivity, and specificity of US detection of splenic injuries were 73%, and 100% respectively when compared with CT.\(^7\) But another study reported that the sensitivity, and specificity of US detection of splenic injuries were 82.5%, and 96.36% respectively when compared with CT.\(^8\) One more study showed that USG correctly had a sensitivity of 80% (95% CI: 44%-98%) and a specificity of 99% (95% CI: 95%-100%) for detection of splenic injuries taking CT as gold standard.\(^9\)

Rationale of this study is to assess the diagnostic accuracy of USG in diagnosis of splenic injuries taking CT as gold standard. Literature has reported that USG is a reliable tool for detection of splenic injuries and can be a reliable replacement of CT scan. CT scan is an invasive method and usually required contrast medium which has hazardous effects on kidney. Moreover, CT scan in not readily available in every setting, particularly, in peripheral areas. The literature showed that USG can replace CT scan. But controversial evidence has been noticed in literature. So, we conducted this study to confirm the diagnostic accuracy of USG in local setting. This will help to improve our practice, local guidelines and will help to replace invasive procedures.

**METHODOLOGY**

It was a cross-sectional study at Department of Radiology, Jinnah Hospital, Lahore. Duration of Study (January 2020 to November 2020). Sample size of 150 patients were calculated with 95% confidence level and taking expected percentage of splenic injury i.e., 26% (2) and sensitivity of USG i.e., 82.5% (7) with 10% margin of error and specificity of USG i.e., 96.36% (7) with 3% margin of error taking CT as gold standard. Sampling Technique was Non-Probability, convenient sampling. Inclusion Criteria: Patient of age 16-75 years of either gender presenting with blunt abdominal injury due to accident and undergoing CT scan for diagnosis of internal injuries. Exclusion criteria: Patients if the CT were interrupted or not completed (on medical record). Patients with pacemaker or metal clip in brain (on history).

One Hundred and fifty patients who fulfill inclusion and exclusion criteria were included in the study referred to Department of Radiology, Jinnah Hospital Lahore. Informed consent was obtained from each patient. Demographic details (name, age, gender, cause of trauma) were recorded. Then patients were scanned with ultrasound doppler machine of GE LOGIC 5 PRO using 3.5 to 7.0 MHz convex probe. The scans were done by a Radiologists. Patients were labeled as positive or negative. Then CT scans with IV contrast of these patients were performed on PHILIPS Mx 16 EVO. The CT scans were reported by a consultant Radiologist. Reports were followed and patients were labeled as positive or negative. All the information was recorded on a pre-designed Proforma.

Data was entered and analyzed in SPSS version 22. Quantitative data like age was presented as mean and standard deviation. Qualitative data like gender, cause of injury and splenic injury (on USG and CT scan) was presented as frequency and percentage. Data was stratified for age, gender and cause of injury.

**RESULTS**

In this study total 150 cases were enrolled. The mean age of the patients was 44.24±17.58 years with minimum and maximum ages of 17 & 75 years respectively.

In this study 123 (82%) patients were male and 27 (18%) patients were females. Male to female ratio of the patients was 4.5:1.
According to this study splenic injury caused by accident among 122 (81.3%) patients and injury due to fight/blow was noted in 28 (18.7%) patients.

The USG diagnosed positive splenic injury in 83 (55.3%) patients and USG diagnosed negative splenic injury in 67 (44.7%) patients.

The CT diagnosed positive splenic injury in 79 (52.67%) patients and CT diagnosed negative splenic injury in 71 (47.33%) patients.

According to this study the sensitivity, specificity, PPV, NPV and diagnostic accuracy of USG for diagnosing splenic injury was 94.94%, 88.73%, 90.36%, 94.03% & 92% taking CT as gold standard. The study results showed that in patients with age ≤ 50 years the sensitivity, specificity and diagnostic accuracy of USG for diagnosing splenic injury was 91.11%, 86.96% and 89.01% respectively taking CT as gold standard. Similarly, in patients with age > 50 years the sensitivity, specificity and diagnostic accuracy of USG for diagnosing splenic injury was 100%, 92% and 96.61% respectively.

The study results showed that in male patients the sensitivity, specificity and diagnostic accuracy of USG for diagnosing splenic injury was 97.01%, 92.86% and 95.12% respectively. Similarly, in female patients the sensitivity, specificity and diagnostic accuracy of USG for diagnosing splenic injury was 83.33%, 73.33% and 77.78% respectively taking CT as gold standard.

The study results showed that in patients with accidental cause of injury the sensitivity, specificity and diagnostic accuracy of USG for diagnosing splenic injury was 93.55%, 88.33% and 90.98% respectively. Similarly, in patients with cause of injury due to fight/blow the sensitivity, specificity and diagnostic accuracy of USG for diagnosing splenic injury was 100%, 90.91% and 96.43% respectively.

DISCUSSION

The incidence of splenic trauma has decreased presumably following the introduction of strict traffic rules and the mandatory wearing of seat belts. Availability of modern imaging techniques including CT scan and USG have greatly improved defining the extent of the splenic injury, active bleeding and other visceral damage in the traumatized patient. In this study the sensitivity, specificity, PPV, NPV and diagnostic accuracy of USG for diagnosing splenic injury was 94.94%, 88.73%, 90.36%, 94.03% & 92% taking CT as gold standard. Some of the studies are discussed below showing their results as.

One study reported that the sensitivity, and specificity of US detection of splenic injuries were 73%, and 100% respectively when compared with CT. One more study showed that USG correctly had a sensitivity of 80% (95% CI: 44%-98%) and a specificity of 99% (95% CI: 95%-100%) for detection of splenic injuries taking CT as gold standard.

A study by S Sinha et al documented that non-operative management of blunt splenic trauma in adults can be performed with an acceptable outcome. Although CT is classed as the ‘gold standard’, initial imaging for detection and evaluation of blunt splenic injury, USG can play a major role in follow-up imaging and potentially avoids major radiation exposure. Based on the reviewed literature, routine imaging follow-up CT scans may not be indicated in asymptomatic patients with lower grade blunt splenic or hepatic injuries. Contrast-enhanced ultrasound is a promising alternative imaging modality for the follow-up of these patients. CEUS is a promising imaging modality that can detect most abdominal solid organ injuries in children while eliminating exposure to ionizing radiation. Blunt abdominal trauma is a common problem in children. Computed tomography (CT) is the gold standard for imaging in pediatric blunt abdominal trauma, however up to 50% of CTs are normal and CT carries a risk of radiation-induced cancer. Nuclear scans can be used to assess splenic injury in trauma patients in rare cases.
An initial prospective investigation has demonstrated screening USG to have a specificity of 96% and an overall accuracy of 96% in the detection of intra-abdominal injury.

Doody O et al showed that although CT remains the gold standard in blunt abdominal trauma, US continues to play an important role in assessing the traumatized spleen.

The USG evaluations of 371 patients demonstrated that in 65 patients with significant injuries, USG detected 53, that is, had an 81.5% sensitivity and 99.7% specificity. They conclude that USG should be the primary adjuvant instrument for the evaluation of injured patients because it is rapid, accurate, and is potentially cost-effective shown by Rozycki et al in their study.

One more study by Richards et al revealed in their study results that sensitivity of US for detection of Blunt splenic injury was 69%, but was 86% for grade III or higher injuries. USG is most sensitive for the detection of grade III or higher Blunt splenic injury based on the presence of haemoperitoneum. USG may also identify Blunt splenic injury on the basis of parenchymal abnormality, with a diffuse heterogeneous pattern most commonly encountered. Sonographic evaluation for both free fluid and parenchymal injury improves sensitivity of US.

Another study reported that the sensitivity, and specificity of US detection of splenic injuries were 82.5%, and 96.36% respectively when compared with CT.

McGahan et al showed the sensitivity of USG in detecting free fluid in abdominal trauma patients was 63%, specificity was 95%, and accuracy was 85%. The positive predictive value of USG in identifying fluid correlated with CT, or operation was 86% and negative predictive value was 85%.

CONCLUSION

This study showed that the USG in diagnosis of splenic injuries is very useful diagnostic tool with higher value of diagnostic accuracy taking CT as gold standard. Therefore, it can be used in centers with confidence where CT is not available.

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Limitation of Study Ultrasound was performed by Radiologists having variable experience.

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Conflict of Interest The idea presented in this article is solely of the authors and is in no direct conflict to any individual or institution.

Authors Contributions

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Literature Review & Critical Revision of the article for important intellectual content: Dr. Tanweer Ahmad, Dr. Basma Khan.

Final approval of the article: Dr. Naeem Ahmad Khan

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The meniscus is triangular cartilage that lies between the femur and tibia in the knee. There are two menisci, one on the medial side of the knee joint, one on the lateral side of the knee joint. The primary function of the meniscus is to assist with distributing compressive forces during dynamic knee joint movements and static loading to decrease impact on bone. In addition, the menisci also play important roles in knee joint lubrication, proprioception and serve as secondary joint stabilizers.

The reported prevalence of meniscal injury is 58% among knee injuries. Being common and typical in sports activities, road traffic accidents and domestic falls, especially troublesome for young...
patients. It has significant financial implications and is one of the major causes of physical disability.\(^{5}\) Orthopedic surgeons commonly examine patients with knee joint pain; however, precisely diagnosing an intra-articular cause of pain is difficult. MRI of the knee is used to diagnose disorders of the knee joint because the high soft tissue resolution allows precise imaging of intra-articular structures.\(^{6,7}\) Magnetic Resonance Imaging (MRI) has now established itself as fast and non-invasive imaging alternative complementing physical examination in the evaluation of injuries of the knee. Although conventional radiography and computed tomography (CT) are frequently used for detection of osseous injuries of the knee, MRI with its much better soft tissue contrast remains the main imaging modality of excellence for accurately depicting abnormalities of articular cartilage and soft tissue injuries of tendons, ligaments, and the menisci.\(^{4}\) MR imaging remains a reliable tool for assessing meniscus tears and cartilage defects preoperatively.\(^{16}\) MRI continues to be the imaging modality of choice, and surgical management is the mainstay of treatment for meniscal tears.\(^{17}\)

According to recent literature research the sensitivity, specificity and diagnostic accuracy of MRI for lateral meniscus injury is 65%, 88.46% and 81.94% respectively.\(^{7}\) While another study reported sensitivity and specificity of MRI as 100% and 75%.\(^{6}\) Respectively recent study published in 2015 on Saudi population reported sensitivity and specificity as 85.7% and 95% with diagnostic accuracy as 92.5%.\(^{8}\) A local study reported diagnostic accuracy of MRI for lateral meniscus was sensitivity 87% and specificity of 88%.\(^{9}\)

In Pakistan there is wide range of reported sensitivity (65%\(^{7}\)-100%\(^{6}\)) and specificity (75%\(^{8}\) – 95%\(^{6}\)). We expect high diagnostic accuracy of this non-invasive procedure (MRI) for diagnosis of lateral meniscus injury for orthopedic surgeons, to encourage & to alter their practice of invasive procedure (arthroscopy) for better diagnosis and to avoid unnecessary diagnostic arthroscopies in patients with lateral meniscus injury in future.

**METHODOLOGY**

This cross-sectional study was done at Department of Diagnostic Radiology, Jinnah Hospital Lahore. Study was completed in six months (April 2020 to September 2020). Using non probability consecutive sampling, data was collected from 106 patients, the sample size is calculated using expected diagnostic accuracy of MRI for lateral meniscus as sensitivity 87% and specificity of 88%.\(^{9}\) We used expected prevalence of meniscus injury among all knee joint injuries as 58%\(^{4}\) and used 8% margin of error for sensitivity and 8% margin of error for specificity and 95% confidence level. Patients regardless of gender with age 18-80 years with severe knee joint pain and locking, referred for diagnostic evaluation were included. Patients with joint disease, e.g. rheumatoid arthritis (as assessed on digital X-Rays) and previous knee operations (on medical record) were excluded. All 106 patients meeting inclusion criteria & presenting with clinical suspicion of lateral meniscus injury referred by orthopedic surgeons from Outdoor, Indoor and Emergency Departments of Jinnah Hospital Lahore were included in this study. Informed consent for magnetic resonance imaging and arthroscopy from all the patients were taken before study. Data about age, gender, body weight, height and BMI were recorded on structured questionnaire. All data was entered and analyzed using SPSS version 22. Mean ± S.D was used for quantitative data such as age and BMI of patients. Frequency and percentages were used for qualitative data such as gender, signs & symptoms.

**RESULTS**

The mean age of patients in this study was 49.75 ± 18.47 with age range of 18 and 80 years. There were 38 (35.85%) cases with 18-40 years of age and 68 (64.15%) were 41-80 years of age. There were 66 (62.26%) male and 40 (37.74%) female cases. The mean weight, height and BMI were 77.64 ± 10.95 kg, 1.68 ± 0.07 and 29.02 ± 2.19. There were 47 (44.34
%) obese and 59 (55.566%) were non-obese. On arthroscopy lateral meniscus injury was diagnosed in 83 (78.30%) of the cases while in 23 (21.70%) the diagnosis was negative. On MRI the diagnosis was positive in 82 (77.36%) of the cases while in 24 (22.64%) cases the findings were negative. On comparing diagnosis on both MRI and Arthroscopy we found Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value and Diagnostic Accuracy was 96.39%, 91.3%, 97.56%, 87.5% and 95.28%.

DISCUSSION

Understanding of the meniscus has changed considerably since last century. In 1887, Sutton described the meniscus as the functionless remains of a leg muscle. Not until 1948 did Fairbanks appreciate that "meniscectomy is not wholly innocuous," in his classic report of post meniscectomy radiographic changes. Research and knowledge of the meniscus has continued since then. The critical importance of the meniscus of the knee joint is now understood. A study was done on 70 patients ranging in age between 22 and 59 years (41 men and 29 women). Another study took total number of patients consisting of 30 men and 24 women with age ranging from 19-59 years. (Mean age: 30.4 years). In this study we took 106 patients aged 18-80 years with higher male predominance. We found mean age of patients in this study 49.75 ± 18.47 with age range of 18 and 80 years. There were 66 (62.26 %) male and 40 (37.74%) female cases. The gender distribution as according to above study but mean age is different.

History taking regarding mechanism of knee injury gives a vital clue to the internal derangements of knee joint. Hyperextension with an audible pop suggests a likely diagnosis of anterior cruciate ligament (ACL) tear. Direct blow to the knee if sideways would point toward collateral ligament injury and if in the front would indicate cruciate ligament injury. Although clinical examination is most important for the diagnosis of ligament injury, painful stress exami-
reliably identify lateral meniscus injury of knee is much higher as was previously thought. Multiplanar imaging capabilities, cost benefit, and non-invasiveness make MRI an important diagnostic modality.

**CONCLUSION**

Through the findings of this study we conclude high diagnostic accuracy of MRI as compared to arthroscopy. In future this non-invasive procedure (MRI) can be adopted for quick and accurate method to diagnose lateral meniscus injury.

**Acknowledgment** The authors thanks all the participants who took time out for this study and provided statistical, technical and intellectual support.

**Limitation of Study** The Arthroscopies were performed by Orthopedic surgeons having variable surgical experience.

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**Conflict of Interest** The idea presented in this article is solely of the authors and is in no direct conflict to any individual or institution.

**Authors Contributions**
Conception & Design: Dr Tanweer Ahmad, Dr Basma Khan.
Collection & Assembly of data: Dr. Fatima Iqbal, Dr. Ayesha Ashfaq, Dr. Mahwash Shoaib.
Literature Review & Critical Revision of the article for important intellectual content: Dr Naeem Ahmad Khan & Dr Tanweer Ahmad.
Final approval of the article: Dr Tanweer Ahmad.

**REFERENCES**


EFFECT OF 3 IU OF OXYTOCIN ON UTERINE CONTRACTION AND HAEMODYNAMICS DURING ELECTIVE CESAREAN SECTION IN SPINAL ANESTHESIA

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Abstract

Background: Caesarean section is among the most commonly done operative procedure in females around the globe. Surgical complications include bleeding, reduction in number of red blood cells, dangers associated with blood transfusions, surgical removal of uterus and in most serious cases, end of life of patient. Oxytocin is the drug that is usually used to enhance uterine tone. It is employed in various doses and at distinct timings.

Objectives: The objectives of the study are to know the effect of three units of oxytocin on the contraction of uterus and haemodynamics during planned surgery (cesarean section) under regional (spinal) anesthesia, to study the effect of five units of oxytocin on contraction of uterus and haemodynamics during planned surgery under regional anesthesia and to compare the two doses of oxytocin (3 IU & 5 IU) on contraction of uterus and haemodynamics during planned surgery employing regional anesthesia.

Methodology: It was randomized control trial study in which 200 patients visiting Department of Anesthesiology/ ICU, Lahore General Hospital, Lahore/Postgraduate Medical Institute, Lahore were included. The patients were randomly divided into 2 groups by draw method (Group-1 was controlled and Group-B was experimental). The data was entered and analyzed using SPSS version 20.0. Chi-square test was used to compare the efficacy of oxytocin.

Results: Mean age in group 1 was 25.19 years with SD + 3.58 while mean age was 24.50 in group 2 with SD +3.62. Regarding tone of uterus, incomplete contraction was observed in four out of hundred (4.0%) cases in group one, and in group two partial contraction was seen in six out of hundred cases (6.0%).

Conclusion: Study concluded that in elective caesarean section under spinal anesthesia three units (bolus) dose of oxytocin is quiet enough to produce sufficient contraction of uterus.

Key Words: Oxytocin, Uterine contraction, cesarean section, spinal anesthesia

Caesarean surgery is the frequently done procedure among females. The incidence of these surgeries have risen to twenty percent to thirty percent in most advanced regions of the world, almost forty percent in China, and about seventy percent in few regions of Latin American (Martin et al., 2007). Bleeding, deficiency of RBCs, dangers of blood transfusion, surgical removal of uterus and the demise of mother are the adverse effects of Caesarean surgery. Life threatening bleeding is the most important reason cause of death of mother around the globe. It is in most of the cases caused by lack of tone of uterus (Sheehan et al., 2011). Oxytocin is the frequently employed drug for maintaining uterine tone. It is given in various doses and intervals (Kiran et al., 2013).

Though it is used as a precautionary medicine
yet oxytocin has been related to remarkable incidence of adverse effects affecting mothers health and her death (Cooper, Lewis & Neilson, 2002). It may also cause serious consequences in fetus including low supply of oxygen to the fetal tissues, increased movement of uterine muscles which may result in its disruption (Langesaeter et al., 2009). As an I/V bolus dose, it can result in little drop of blood pressure (both systolic and diastolic), reflexively rise of heart rate, chest pain and an increased output from the heart. It depends on how much dose was given to the patient (Connell & Mahomed, 2009; Jonsson et al., 2010; Tsima, Madzimbamuto & Mash, 2013).

Notable harmful consequences may result in mother, fetus and the new born baby with the utilization of oxytocin (Tsen & Balki, 2010).

Present studies have concluded that a single dose of three to five units of oxytocin is adequate balancing the danger of harmful episodes with the advantage of stopping bleeding in frequent patients (Carvalho et al., 2004; Balki et al., 2006; Sartain et al., 2008; Butwick et al., 2010; Tsima, Madzimbamuto & Mash, 2013).

Though it is accepted that oxytocin plays an important role in controlling bleeding after vaginal delivery yet very few observation has been done to its significance in C. section (Elbourne et al., 2001). Oxytocin is as important in Caesarean section as is beneficial in vaginal delivery (Lokugamage et al., 2001; Munn et al., 2001).

The Royal College of Obstetricians and Gynaecologists (UK) approves a slow I/V bolus dose of five units oxytocin following the delivery of baby by caesarean surgery (Sheehan et al., 2011). This dosage has been established according to the principles of managing 3rd stage of labor actively (Cotter, Ness & Tolosa, 2001; Begley et al., 2010). It is a frequent implementation in nearly all regions of Europe and Australia (Mockler, Murphy & Wallace, 2010). However many studies have revealed the truth that smaller doses of oxytocin can prove to be potent as compared to those advocated by the recent guidelines (Cooper, Lewis & Neilson, 2002; Carvalho et al., 2004; Balki et al., 2006; Sartain et al., 2008; Butwick et al., 2010). Currently a very little dose of 0.35 units has been observed to be the minimal potent dose for ninth percent of patients (ED90) for planned C. section (Carvalho et al., 2004). In year 2008 a questionnaire of three hundred and sixty five obstetricians and anesthetists was done in UK. It was found that nearly all of them employed an initial ‘slow bolus’ of at least five units (Wedisinghe, Macleod & Murphy, 2008), a occasionally infusion of oxytocin was used in some cases, usually ten units/hour (Sartain et al., 2008).

Butwick and colleagues (2010) carried out a research study to estimate the minimum effective lowest possible dose of oxytocin for adequate contraction of uterine muscles during caesarean section. Seventy five patients undergoing elective section under subarachnoid block were randomly given oxytocin (0.5, 1, 3, & 5 units) or placebo. A blinded obstetrician estimated contraction of uterine muscles as either sufficient or not adequate. Smallest possible adequate oxytocin doses were examined ED (50) and ED (95). Harmful effect like fall in blood pressure was also noted. Score of uterine contraction was considerably lower in patients receiving 0 unit oxytocin at 2 and 3 minutes compared with and 5 units of oxytocin. The higher incidence of blood pressure fall was much higher after 5 IU of oxytocin VS 0 units at 1 minute (47% VS 7%). So it is not recommended in elective C - section to use 05 IU of oxytocin to achieve satisfactory uterine contraction with low doses (0.5, 3 IU) of oxytocin (Butwick et al., 2010). So scoring showed that these effects were least in those cases who received zero units of oxytocin at interval of two and three minutes contrary to those with three and five intravenous units of oxytocin versus zero units at one minute (47% VS 7%).

Therefore the routine use of 05 IU of oxytocin during elective US C-section is not recommended as sufficient. Because adequate uterine muscles contraction can be achieved by using lower doses (0.5 – 3 IU) of oxytocin (Butwick et al., 2010).
METHODOLOGY

It was randomized control trial study in which 200 patients visiting Department of Anesthesiology/ICU, Lahore General Hospital, Lahore/Postgraduate Medical Institute, Lahore were included. Non probability purposive sampling was used. The patients were randomly divided into 2 groups by draw method (Group-1 was controlled and Group-B was experimental). The data was entered and analyzed using SPSS version 20.0. Quantitative variables like age, drop in blood pressure and heart rate were presented by means of mean and SD. Chi-square test was used to compare the efficacy of oxytocin. P-value ≤ 0.05 was considered as significant. Independent T sample test was used to compare the means of heart rate and blood pressures of both groups. An informed consent was taken from each patient.

RESULTS

Result shows that mean age in group 1 was 25.19 years with SD + 3.58 while mean age was 24.50 in group 2 with SD +3.62.

Table 1: Distribution of Patients by Age

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Group-1</th>
<th>Group-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>18</td>
<td>3 (3.0%)</td>
<td>2 (2.0%)</td>
</tr>
<tr>
<td>19</td>
<td>2 (2.0%)</td>
<td>3 (3.0%)</td>
</tr>
<tr>
<td>20</td>
<td>13 (13.0%)</td>
<td>12 (12.0%)</td>
</tr>
<tr>
<td>21</td>
<td>0 (0.0%)</td>
<td>2 (2.0%)</td>
</tr>
<tr>
<td>22</td>
<td>7 (7.0%)</td>
<td>11 (11.0%)</td>
</tr>
<tr>
<td>23</td>
<td>1 (1.0%)</td>
<td>8 (8.0%)</td>
</tr>
<tr>
<td>24</td>
<td>11 (11.0%)</td>
<td>11 (11.0%)</td>
</tr>
<tr>
<td>25</td>
<td>23 (23.0%)</td>
<td>24 (24.0%)</td>
</tr>
<tr>
<td>26</td>
<td>4 (4.0%)</td>
<td>6 (6.0%)</td>
</tr>
<tr>
<td>27</td>
<td>6 (6.0%)</td>
<td>3 (3.0%)</td>
</tr>
<tr>
<td>28</td>
<td>7 (7.0%)</td>
<td>5 (5.0%)</td>
</tr>
<tr>
<td>29</td>
<td>1 (1.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>30</td>
<td>22 (22.0%)</td>
<td>8 (8.0%)</td>
</tr>
<tr>
<td>31</td>
<td>0 (0.0%)</td>
<td>1 (1.0%)</td>
</tr>
<tr>
<td>32</td>
<td>0 (0.0%)</td>
<td>1 (1.0%)</td>
</tr>
<tr>
<td>35</td>
<td>0 (0.0%)</td>
<td>3 (3.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>100 (100.0%)</td>
<td>100 (100.0%)</td>
</tr>
</tbody>
</table>

Regarding tone of uterus, incomplete contraction was observed four out of hundred (4.0%) cases in group one, and in group two partial contraction was seen in six out of hundred cases (6.0%).

Chi-Square test was used for comparing the efficacy between two groups, p value was computed to be 0.516, leading to the conclusion that no statistically remarkable difference was found in the potency.

DISCUSSION

During study it was found that in elective caesarean section employing regional (spinal) anesthesia, three units bolus dose of oxytocin was enough for adequate uterine contraction with significantly low incidence of fall of blood pressure (hypotension) and increased heart rate (tachycardia) as compared to five units of oxytocin. Fall in mean BP was more in group one (5 units oxytocin) compared to group two (3 units oxytocin). Likewise mean heart rate was also more in group one than in group two.

In 200 research study, Connell & Mahomed showed that when oxytocin is given as an intravenous bolus dose, brief episode of hypotension (drop in both systolic and diastolic blood pressure) increa-
EFFECT OF 3 IU OF OXYTOCIN ON UTERINE CONTRACTION AND HAEMODYNAMICS

sed heart rate, chest discomfort and an increase in cardiac output results, depending upon the dose (Connell & Mahomed, 2009).

The danger of adverse effects of oxytocin during childbirth has resulted in a discussion about the correct dose of the drug. In 2004, a research study was done by Carvalho. He observed that the most favorable intravenous dose of oxytocin balancing the danger of side effects with the advantage of preventing post-op (caesarean section) bleeding (hemorrhage), is 3–5 IU following the delivery of the baby (as a single prophylactic dose for all cases) (Carvalho et al., 2004).

In consistent with our study, a study done by Balki in year 2006 showed that the regular use of five units of oxytocin during elective Caesarean surgery can no longer be endorsed because adequate contractions of uterus may be produced by smaller doses of oxytocin (0.5-3 units) (Balki et al., 2006).

The guidelines of the Royal College of Obstetricians and Gynaecologists (UK) on caesarean section advocate for a slow intravenous bolus dose of five units of oxytocin following birth of the baby (Sheehan et al., 2011).

Some other studies also favor for use of even lower doses of oxytocin than those endorsed by current guidelines. Cooper and coworkers in their study revealed that minimum effective bolus of oxytocin may be as low as 0.35 units for ninety percent of patients (ED 90) in elective surgeries (C Section) (Cooper, Lewis & Neilson, 2002).

However contrary to this, many practitioners disagree about the above mentioned recommended dose of oxytocin. Wedisinghe, MacLeod and Murphy (2008) carried out a review of 365 obstetricians and anesthetists in UK. This review gave the perspective that almost all of them gave an initial ‘slow bolus’ of at least five units followed by oxytocin infusion at the rate of ten units per hour.

Likewise, Lohit and Slater (2010) declared after a research that twenty percent of patients receiving 0.5 and one unit required additional doses of oxytocin. Even thirteen percent of the patients receiving five units required further doses of oxytocin. So, even five units of oxytocin were not enough in many patients. Bhattacharya and colleagues (2013) compared systemic (haemodynamics) and uterotonic effects of same doses (3 units) of oxytocin given to the patients as bolus versus intravenous infusion. They found that bolus dose of oxytocin (3 units I/V over 15 sec) and infusion of oxytocin (I/V infusion over 5 minutes) had similar effects on uterus. However bolus doses of the drug resulted in more adverse effects.

A study was performed by Butwick and colleagues (2010) to establish the lowest adequate dose (bolus) of oxytocin for sufficient contractions and tone of uterus (UT) during elective surgery (Caesarean Section). Seventy-five patients going through planned Caesarean section with spinal anesthesia received oxytocin (0.5, 1, 3, 5 units) or placebo. Oxytocin induced side-effects (including hypotension) were noted in record. Study showed that regular use of 5 units oxytocin during elective C Section can no longer be endorsed as suitable. Tone of uterus can be achieved with small doses of oxytocin (0.5-3 units). While the two doses of oxytocin (3 IU and 5 IU) are compared, study found that three units of oxytocin adequately lead to sufficient contraction of uterus.

Although most of the studies are in accordance with our results that instead of five units, three units of oxytocin achieved adequate uterine contraction, yet we will recommend more studies to establish a final opinion.

CONCLUSION

Study concluded that in elective caesarean section under spinal anesthesia three units (bolus) dose of oxytocin was quiet enough to produce sufficient contraction of uterus. It was related to notably lesser incidence of hypotension and increased heart rate (tachycardia), in comparison to five units of oxytocin.
REFERENCES


Abstract

Objective: The objective of this study was to determine the frequency of different clinical patterns of melasma in males.

Methodology: 130 patients of melasma, fulfilling the inclusion criteria, were selected after taking a written informed consent from the patient. Relevant history was asked and examination was done and recorded on a predesigned standardized proforma. In clinical examination, face of each patient was examined in good light with naked eye and with the help of magnifying glass (x3) to assess lesion details adequately. MASI score was calculated. Each patient was examined with Wood’s lamp (365nm) in a dark room to assess whether the melasma becomes more prominent (epidermal), remains the same (dermal) or shows mixed features (mixed). The pattern of melasma was noted with naked eye and with the help of magnifying glass whether its centrofacial, malar, mandibular (as per operational definition). Confidentiality of the data was ensured.

Results: The minimum MASI score was 6 and maximum was 24 with mean and standard deviation was 16.66 ± 5.48. Wood’s lamp examination showed that 51.5% patients had epidermal type of melasma, 38.5% patients had dermal and 10% patients had mixed type of melasma. Regarding the clinical patterns, 66.2% of the patients had malar distribution while centrofacial pattern was seen in 33.8 and no patient with mandibular pattern of melasma was observed.

Conclusion: Malar pattern was predominant, seen in 66.2% of the patients, followed by centrofacial pattern in 33.8% patients, and no patient of mandibular pattern was seen.

Key Words: Melasma, males, malar, centrofacial

Melasma is an acquired hypopigmentary disorder characterized by the development of blotchy, light-to-dark brown macules distributed symmetrically on sun exposed parts of the body. Melasma is a common dermatological problem in this part of the world in both the sexes. It does not cause physical limitation but it does cause a significant psychological impact on patients. It most commonly involves upper lips, checks and forehead, predominantly women with Fitzpatrick skin types IV to VI, especially those living in areas of intense ultraviolet radiation. It is more common in adult women of childbearing age and men account for only 10% of the cases.1

Although less common but men are also seen to be affected by this condition. Virtually all demographic studies have sampled predominantly female patients. Men make up a comparative minority of those afflicted with melasma. As a result, investigative work in determining the unique characteristics of melasma in men has lagged behind similar studies in female patients. Melasma in men is a poorly studied subject also in our country. The objective of this study was to determine the frequency of diffe-
FREQUENCY OF DIFFERENT CLINICAL PATTERNS OF MELASMA IN MALES

rent clinical patterns with which melasma presents in the male population of this region.

METHODOLOGY

It was a descriptive cross sectional study. 130 male patients of melasma presenting to Dermatology OPD of Jinnah Hospital, Lahore and fulfilling the inclusion criteria were selected after taking a written informed consent from the patient. Relevant history was asked and examination was done and recorded on a predesigned standardized pro forma. In clinical examination, face of each patient was examined in good light with naked eye and with the help of magnifying glass (x3) to assess lesion details adequately. MASI score was calculated.

Each patient was examined with Wood’s lamp (365nm) in a dark room to assess whether the melasma became more prominent (epidermal), remains the same (dermal) or shows mixed features (mixed).

The pattern of melasma was noted with naked eye with the help of magnifying glass whether its centrofacial, malar, mandibular (as per operational definition).

All the findings were recorded in a predesigned pro forma. All the findings were recorded and collected by the researcher herself.

Data was analyzed using SPSS 20. Quantitative variables (i.e. age, duration, MASI score) were presented by using mean, +/- standard deviation. Qualitative variables (i.e. Fitzpatrick skin type, type of melasma under Woods lamp, clinical pattern of melasma (centrofacial pattern, malar pattern, mandibular pattern) were presented by using frequency tables, percentages and appropriate graphs where applicable. Data was stratified for age, family history of melasma, history of outdoor working, type of melasma and baseline MASI score. Chi-square test was used post stratification with p-value < 0.05 considered as significant.

RESULTS

Of a total of 130 patients, it was observed that the minimum age was 18 years and maximum age was 40 years with mean and standard deviation 29.65 ± 5.79 years. The majority of the patients were between 25 and 30 years of age. In 52.3% of the patients family history of melasma was positive and negative in 47.7% of the patients. Regarding occupation, 56.9% were outdoor workers whereas 43.1% were indoor workers. When calculated, the minimum MASI score was 6 and maximum was 24 with mean and standard deviation was 16.66 ± 5.48. Wood’s lamp examination showed that 51.5% patients had epidermal type of melasma, 38.5% patients had dermal and 10% patients had mixed type of melasma [Figure 1]. Regarding the clinical patterns, 66.2% of the patients had malar distribution while centrofacial pattern was seen in 33.8 and no patient with mandibular pattern of melasma was observed. [Figure 2]

DISCUSSION

Melasma is a common dermatological problem in this part of the world in both the sexes. It does not cause physical limitation but it does cause a significant psychological impact on patients. Virtually all demographic studies have sampled predominantly...
female patients, reflecting the fact that melasma is generally considered a disease of this gender. Men make up a comparative minority of those afflicted with melasma. As a result, investigative work in determining the unique characteristics of melasma in men has lagged behind similar studies in female patients.

Melasma in men is a poorly studied subject also in our country. To date no local study has been conducted to determine the frequency of different clinical patterns of melasma in males. Therefore, this study is planned to see the patterns with which this cutaneous problem manifests in males in our population.

The objective of the present research was to determine the frequency of different clinical patterns of melasma in males. In this regard the present descriptive cross sectional study was conducted at Dermatology Outpatient Department, Jinnah hospital Lahore. So one hundred and thirty patients diagnosed to have melasma were included by fulfilling the inclusion and exclusion criteria by using non probability consecutive sampling.

The mean age in this study was 29.7 which is slightly less than found in other studies. There were 52.3% patients having melasma in family history and 56.9% patients were outdoor workers. This was in concordance with the study conducted by Sarkar et al in which almost 40% of the patients had family history of melasma and 58.5% of the male melasma patients were outdoor workers. There were 51.5% patients having epidermal melasma under wood’s lamp, 38.5% patients having dermal melasma and 10% patients having mixed melasma. Epidermal type has also been reported in the previous studies to be the commonest type amongst males.

With regards to the clinical patterns, malar pattern was predominant, seen in 66.2% of the patients, followed by centrofacial pattern in 33.8% patients. This predominance of malar pattern of melasma amongst males has been observed in previous studies also. However, in contrast to these studies, no patient with mandibular pattern of melasma was observed in our study. Mandibular pattern, indeed, has been described as a rare pattern and in some studies declared to be clinically and histopathologically different entity than other types of melasma.

On comparing the results of this study with studies observing the clinical patterns of melasma in females, there is definite predominance of malar pattern in males as compares to the centrofacial pattern observed in females. Also on Wood’s lamp examination, epidermal type is more common in males. This also suggests that melasma in males would be more responsive to treatment as epidermal type is more amenable to melasma directed therapies.

This study shows that the clinical patterns of melasma in males in this population is predominantly the same as in other parts of the world especially India, probably because of climatic, occupational and racial similarities. However mandibular pattern was not observed in our study, suggesting some other factors playing their role like ethnicity, geographical variations etc. Therapeutically, male melasma would be better responsive to treatment as majority of the males had epidermal type on Wood’s lamp examination in our study, which too was in concordance with previous literature. However this needs further studies and research to compare the response of melasma directed treatment in males and females.

There were certain limitations of our study. Other than statistical limitation of a small sample size, the only etiological and/or exacerbating factors of melasma addressed were family history and outdoor exposure (sunlight exposure), both of which showed to be playing a significant role. However other risk factors like use of cosmetics, hormonal derangements, drugs etc were not ruled out. Third, this study was too population specific and cannot be applied to male population in other parts of the country, for which further studies can be carried out.

**CONCLUSION**

Amongst the clinical patterns, malar pattern
FREQUENCY OF DIFFERENT CLINICAL PATTERNS OF MELASMA IN MALES

Table 1: Stratification with Respect to Type of Melasma under Woods Lamp (n = 130)

<table>
<thead>
<tr>
<th>Type of melasma</th>
<th>Clinical patterns</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Centrofacial</td>
<td>Malar</td>
<td></td>
</tr>
<tr>
<td>Epidermal</td>
<td>21</td>
<td>46</td>
<td>67</td>
</tr>
<tr>
<td>Dermal</td>
<td>16</td>
<td>34</td>
<td>50</td>
</tr>
<tr>
<td>Mixed</td>
<td>7</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td>44</td>
<td>86</td>
<td>130</td>
</tr>
</tbody>
</table>

was predominant, seen in 66.2% of the patients, followed by centrofacial pattern in 33.8% patients, and no patient of mandibular pattern was seen.

Limitations of Study

Other than statistical limitation of a small sample size, the only etiological and/or exacerbating factors of melasma addressed were family history and outdoor exposure (sunlight exposure), both of which showed to be playing a significant role. However, other risk factors like use of cosmetics, hormonal derangements, drugs etc. were not ruled out. Third, this study was too population specific and cannot be applied to male population in other parts of the country, for which further studies can be carried out.

Conflict of interest There was no conflict of interests in this study.

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Contribution of the authors Each author acknowledges that she has contributed substantially to the work described in the manuscript and its preparation.

REFERENCES

Normal pregnancy is a state of altered metabolism which are crucial for further proliferation and development of fetus. Changes in maternal metabo-lism due to the effect of certain hormones and meta-bolic factors lead to decreased insulin sensitivity in peripheral tissue. This altered mechanism of insulin resistance (IR) is beneficial to accelerate the nutrient supply to the growing fetus as well as it helps to meet maternal metabolic requirements. Although these metabolic changes are physiological; further impairment of this phenomenon may lead to the development of gestational diabetes mellitus. Normal pregnancy is diabetogenic condition in which there is mild fasting hypoglycemia and postprandial hyperglycemia. Prevalence of gestational diabetes mellitus (GDM) is increasing day by day and currently it is about 2–10% of all normal pregnancies. This metabolic disease is a causative agent for maternal as well as fetal morbidities such as pregnancy-induced
hypertension, abdominal delivery and fetal anomalies. Special attention should be given to overweight and obese women even without GDM to minimize the perinatal complications during pregnancy. Furthermore, glucose tolerance and insulin sensitivity status in overweight females and females with GDM during pregnancy should be taken in account. Insulin sensitivity in pregnancy can be interpreted as euglycemic status achieved at the cost of hyperinsulinemia of pregnancy. Gestational insulin resistance is said to be a cofactor in insulin-desensitizing effects of various hormones during normal pregnancy. Placental growth hormone and more marked maternal adiposity play a key role in it. Body mass index (BMI) in the females prior to pregnancy state and weight gain during pregnancy are positively linked with insulin resistance, thus obesity plays a crucial role in occurrence of insulin resistance and gestational diabetes mellitus. There is much more fat deposition in early pregnancy and an increased fat mobilization in advanced pregnancy stages.

Obesity is said to be a global epidemic of today’s world. Worldwide prevalence of obesity and overweight manifests about 60%, and this condition has altered the entire scenario of the pregnancy phenotype and morphology. With pre-pregnancy obesity and overweight; there is already chances of enhanced IR and, when compounded by pregnancy-induced IR, the intrauterine environment is thus characterized by major metabolic derangements along with inflammation and oxidative stress. When there is low physical activity and excessive weight gain in pregnancy, the metabolomic and microbiome status of pregnant mothers is also impaired which further creates the features of metabolic syndrome.

With the advancement of age, levels of overweight and obesity are markedly increased especially for women in developing countries. Studies have described that obese women prior to pregnancy; have more chances to gain excessive weight during gestational period. Pregnancy is characterized by multiple physiological changes along with fat and weight gain as well as the insulin resistance. Altered state of adipose tissue structures and its function during pregnancy as well as factors responsible for insulin resistance in pregnancy are not completely clear. We sought to find out body weight related gestational insulin resistance in lighter weight and heavier weight pregnant women. Further more comparison of insulin levels of pregnant women to non-pregnant controls was also performed.

**METHODOLOGY**

It was a comparative cross-sectional hospital based study. This study was conducted at Jinnah Postgraduate Hospital Lahore which is second largest teaching hospital of Punjab. The study was carried out at the antenatal clinic of Gynae and Obstetrics OPD. The duration of study for sampling at the hospital was two month and study was performed in March 2019. The sample size of the study was 90 women, 65 pregnant subjects and 25 non-pregnant healthy controls which were further divided into two weight groups; less than sixty kg of weight and equal to & more than sixty kg of weight. Pregnant women were assigned to groups according to weight, less than 60 kg (Group 1; n=39) and equal to & more than 60 kg (Group 3; n=26). Same two groups of non-pregnant control subjects, according to weight, less than 60 kg (Group 2; n=11) and more than 60 kg (Group 4; n=14). Ethical approval was taken from the Ethical Review Committee, Principal of Allama Iqbal Medical College and Head of Gynae Department. Informed verbal consent of all the subjects was taken. Participants as subjects/cases were pregnant and attending antenatal clinic in their first and second trimester while the subjects as control were non-pregnant women visiting as attendants of patients or for minor ailments to Gynae OPD clinic. Participants with adequate health were included. Women with doubtful pregnancy and with recent or chronic conditions that could affect or interfere with target markers were excluded. Preg-
nant women in their third trimester and unwilling women also excluded.

Maintaining the standard venipuncture technique, 5ml blood was taken into yellow top gel test tubes during the first and second trimester. Immediately after taking the blood, glucose level was checked by the use of Glucometer and entered in the corresponding column. These samples were allowed to freely clot, spun at 3000 rpm for 15 minutes and then serum stored at -80°C in appropriate tubes until analysis was done. The frozen serum samples were removed from the freezer and allowed to thaw at room temperature before being analyzed for insulin by ELIZA kit, according to manufacturer’s instructions and protocol. Results were expressed as mean + standard error of mean (S.E.M) Statistical analysis was performed using Graph Pad prism 5 for Windows. Frequencies and percentages were calculated and data was presented in tables and figures. Normal distribution of the variances was tested. Student t-test (unpaired t test) was used to compare the significance of the difference in the mean values of any two groups. Statistically significant P value was considered as less than 0.05.

RESULTS

In a random study, glycemia and insulinemia were studied in the pregnant females and also in non-pregnant females as controls. In pregnant women of both weight groups of less than 60 kg and more than 60 kg collectively, mean insulin level was 41.68 + 0.8658mIU/L. In the controls the values were 24.86+1.426mIU/L. In pregnant subjects insulinemia was about 67% greater as compare to the controls. The values had been highly significantly different in both the comparing groups (p<0.0001). Thus there has been comparatively hyperinsulinemia in the pregnancy in the subjects with less than 60 Kg body weight as compared to non-pregnant controls.

Weight = &>60 Kg of cases and controls: In pregnant women with the body weight = &>60kg insulin level was 43.47+1.507 mIU/L and in non-pregnant controls with the body weight >60kg insulin level was 23.97+1.768mIU/L. In the pregnancy insulinemia was about 82% greater as compare to the controls. The values had been highly significantly different statistically in the comparing groups (p<0.0001).Thus there has been also marked hyperinsulinemia in the pregnancy in the subjects with body weights above 60 Kg comparing to their control groups.

Comparison of Insulin Levels in lighter and heavier pregnant subjects: In the comparison of the pregnancy related hyperinsulinemia in relation to body weight, it has been observed that in the subjects with greater body weight, the hyperinsulinemia has been observed almost 3% intensive than the subjects of comparatively lighter body weight and result is statistically non-significant.

In pregnant women both gestational groups of 4 to 8 and 9 to 14 weeks of gestation collectively, mean glucose level was 104.6 + 2.082 mg/dl. In non-pregnant control the values were 110.5+2.430mg/dl. In early pregnancy glycemia was about 5.4% lesser as compare to the controls. The values had been not significantly different in both the comparing groups (p: 0.1136). Thus there has been comparatively lower glycemia in the phases of the pregnancy studied as compared to the non-pregnant state.

Weight Related Comparisons (Table 2 and Fig. 2)
Weight < 60 Kg of cases ant controls: In pregnant women with the body weight <60 kg insulin level was 40.36+1.031 mIU/L and in non-pregnant controls with the body weight <60 kg, insulin level was 26.01+2.383mIU/L. In the pregnancy groups, insulinemia was about 55% greater as compare to the controls. The values had been highly significantly different statistically in the comparing groups (p<0.0001).Thus there has been comparatively hyperinsulinemia in the pregnancy in the subjects with less than 60 Kg body weight as compared to non-pregnant controls.
women with the body weight <60 kg, glucose level was 106.1±2.903mg/dl and in non-pregnant controls with the body weight <60 kg glucose level was 109.9±4.445mg/dl. In studied phases of pregnancy glycemia was about 3.5% lower as compare to the controls. The values had not been statistically significant in both the comparing groups (p: 0.5237). Thus there has been comparatively no difference in glycemia in the pregnancy in the subjects with 60 kg and less body weight when compared to the respective controls.

Comparison of Glucose Levels in lighter and heavier pregnant subjects: In the comparison of the pregnancy related glycemia in relation to body weight it has been observed that in both categories of the weight subjects, glycemia had been observed lower than the respective non-pregnant controls. The heavier body weight pregnant group showed better lowering of the glycemia (p=0.08) than lighter weight group with their respective control comparisons (p=0.52).

DISCUSSION

The adaptations of the gestation are necessary ingredients for the successful outcome of the pregnancy. The emergence of placenta during the pregnancy is the source of several adaptations with the productions of several substances, the prominent are the hormone. The studies have reported about increased insulin clearance in this phase that indicates the increase production of insulin. The mild insulin insensitivity is characteristic feature of pregnancy because of the enhanced fetal demand for glucose. However the dual role of insulin in the pregnancy through the adaptations of reduced

**Table 1**: Average insulinemia Mean + SEM in two category of comparatively lighter and heavier weight pregnant and non-pregnant control subjects.

<table>
<thead>
<tr>
<th>Grp. No</th>
<th>Weight Group</th>
<th>N</th>
<th>Status</th>
<th>Mean±SEM mIU/L</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both weight Groups</td>
<td>65</td>
<td>Pregnant Cases</td>
<td>41.68±0.8658</td>
<td>p&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Both weight Groups</td>
<td>25</td>
<td>Non-Pregnant Controls</td>
<td>24.86±1.426</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 &lt;60 Kg</td>
<td>39</td>
<td>Pregnant</td>
<td>40.36±1.031</td>
<td>&lt;0.0001 Comparison b/w Group 1 &amp; 2</td>
<td></td>
</tr>
<tr>
<td>2 &lt;60 kg</td>
<td>11</td>
<td>Non-pregnant</td>
<td>26.01±2.383</td>
<td>p&gt;0.001 Comparison b/w Group 2 &amp; 4</td>
<td></td>
</tr>
<tr>
<td>3 =&amp;&gt;60 Kg</td>
<td>26</td>
<td>Pregnant</td>
<td>43.47±1.507</td>
<td>P=0.824 Comparison b/w Group 1 &amp; 3</td>
<td></td>
</tr>
<tr>
<td>4 =&amp;&gt;60 Kg</td>
<td>14</td>
<td>Non pregnant</td>
<td>23.97±1.768</td>
<td>&lt;0.0001 Comparison b/w Group 3 &amp; 4</td>
<td></td>
</tr>
</tbody>
</table>
insulin insensitivity otherwise referred as insulin resistance. Generally Insulin resistance is known as a major cause of type 2 diabetes mellitus and leads to the development of metabolic disorders such as hypertension and impaired lipid profile along with obesity and visceral adiposity. Obesity is generally negatively associated with insulin sensitivity status of the individuals. It is considered that elevated levels of free fatty acids as in case of adiposity of obesity; impair the insulin-signaling pathways and cause insulin resistance. Insulin resistance and beta-cell defects of pancreas together, lead to impaired insulin secretion in response to glucose. Subsequently there is occurrence of impaired glucose tolerance, hyperglycemic state, GDM and type 2 diabetes mellitus.

Recently a different mechanism is understood on insulin resistance and shown to be the results of energy surplus in the cells. It is proposed that these surplus energy signals are mediated in the cells by adenosine triphosphate ATP and adenosine monophosphate-activated protein kinase (AMPK) signaling pathways. It is evident that insulin sensitizing medicines decrease the ATP production in the mitochondria of cells; this finding also favors the above theory. Another evidence is that weight loss; restricted calories diet and exercise diminish the ATP in insulin sensitive cells, thus enhance the insulin sensitivity or lower the insulin resistance. This new theory justifies the cellular and molecular mechanism of insulin resistance in obesity and lipodystrophy.

The present study demonstrates that there is overall hyperinsulinemia in the pregnant subjects irrespective of other factors such as weight. In the comparison of the pregnancy related insulin levels in relation to body weight it has been observed that in the subjects with greater body weight at least 60 Kg and above, the hyperinsulinemia has been observed almost 3% intensive than the subjects of comparatively lighter body weight at least below 60 Kg body weight. There is possibility of greater fat contributing to the weight, incurs intensive insulin resistance, although a minor difference. The prevalence of combined mechanisms of type 2 diabetes and specifically understood for pregnancy, cannot be ruled out.

In the pregnancy groups, glycemia was about 5.4% lesser as compare to the non-pregnant controls.

Table 2: Average glycemia Mean + SEM in two category of comparatively lighter and heavier weight pregnant and non-pregnant control subjects.

<table>
<thead>
<tr>
<th>Grp. No</th>
<th>Weight Grp.</th>
<th>N</th>
<th>Status</th>
<th>Mean ± SEM mg/dl</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both weight Groups</td>
<td>65</td>
<td>Pregnant Cases</td>
<td>104.6 ± 2.082</td>
<td>P=0.1136</td>
<td></td>
</tr>
<tr>
<td>Both weight Groups</td>
<td>25</td>
<td>Non-Pregnant Controls</td>
<td>10.5±2.430</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>&lt;60 Kg</td>
<td>39</td>
<td>Pregnant</td>
<td>106.1±2.903</td>
<td>0.5237 Comparison b/w Group 1 and 2</td>
</tr>
<tr>
<td>2</td>
<td>&lt;60 Kg</td>
<td>11</td>
<td>Non-pregnant</td>
<td>109.9 ± 4.445</td>
<td>0.5476 Comparison b/w Group 1 and 3</td>
</tr>
<tr>
<td>3</td>
<td>&gt;60 Kg</td>
<td>26</td>
<td>Pregnant</td>
<td>103.5 ± 2.727</td>
<td>0.0868 Comparison b/w Group 3 and 4</td>
</tr>
<tr>
<td>4</td>
<td>&gt;60 Kg</td>
<td>14</td>
<td>Non-pregnant</td>
<td>111±2.738</td>
<td></td>
</tr>
</tbody>
</table>

Subjects. Statistically Non-Significant Difference.
The values had been not significantly different in both the comparing groups. The heavier body weight pregnant group showed better lowering (p=0.08) of the glycemia than lighter weight group with their respective control comparisons. It may be correlated to insulin responses to the weight variations in the early pregnancy mothers. In heavier weight subjects, there had been observed intensive hyperinsulinemia than the lighter weight mothers. The greater insulinemia in the heavier weight mothers is probably responsible for almost significant lowering of glycemia.

Greater body mass index especially fat mass accelerates the development of gestational insulin resistance.\(^27\) If there is more hypertrophy of the adipose tissue rather than hyperplasia in advanced stages of pregnancy, there may be even much pronounced insulin resistance.\(^28\) The underlying mechanism of gestational insulin resistance and its correlation with very large fat cells and greater magnitude of adiposity, is likely to be multifactorial.\(^29,30\)

CONCLUSION

The adaptations of the gestation are necessary ingredients for the successful outcome of the pregnancy for the mother as well as the growing fetus. In present study, the highly significant increase in insulin levels in both weight groups of pregnancy as compare to non-pregnant state of local populations has been observed. Furthermore, it has been concluded that there is almost 3% intensive hyperinsulinemia in the pregnant subjects with greater body weight than the subjects of comparatively lighter body weight. There is possibility of greater fat contributing to the weight incurs intensive insulin resistance. Adipose tissue hypertrophy and large size of adipocytes as in overweight and obese women, promote gestational insulin resistance.

Recommendations

It is recommended that study should be performed on a large number of subjects with proper matching of the groups on the basis of weight and obesity. Further larger studies are strongly suggested on the objectives studied and discussed.

Authors’ Contributions

Dr. Shazia Ramzan designed the initial study, searched related literature, collected data and conducted the study. Dr. Afifa Mahmood designed the initial draft of manuscript. Dr. Zaheer Iqbal worked on literature search, reviewed and finalized results and discussion. Dr. Syedda Amina Rizvi reviewed the literature, and contributed to the discussion. Dr. Foquia Tasser Hunan and Dr. Amir Shoaib reviewed the study outcomes and conclusion and made corrections too. All authors contributed to the final manuscript.

Conflict of Interest

None

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Kindness is free
The concept of organ donation has been gaining popularity among the general populace ever since it was realized that donating organs can be life-saving in treating many chronically fatal diseases. First introduced in 1954, the procedure of harvesting and allogenic transplantation has been perfected over the decades, leading to substantial improvement in the life of patients who have undergone the procedure.

The rates of voluntary organ donation from the public have grown over time, but there is still a grave shortage of organs. In 2018, there were about 36,000 organ transplants in the U.S. Still, over 113,000 patients are on the waiting list. Even though the gap is large, more and more people are voluntarily regis-
tering themselves to donate organs after their death\(^1\) in well-developed countries. Still, third-world countries like India and Pakistan are much worse as the number of such voluntary donors is next to nothing.

There are many legislative, ethical, cultural, and personal barriers that result in such low numbers of people donating in third world countries\(^2\). The most crucial factor affecting organ donation is the lack of awareness about the concept. That is why first world countries like Spain boast an impressive organ donation rate of 43.4 per million organ donations (highest in the world), but in third world countries like India, the rate drops to 0.8 per million\(^3\).

As medical personnel are most likely to come in contact with patients who need transplants, their knowledge and attitudes regarding organ donation can be decisive factors in creating a favorable environment for potential donors. Medical students are a particular group that can create better awareness of the whole transplant procedure as future doctors. Although most medical students favor organ transplantation, only about one-third of them know about the technicalities and procedure\(^4\). In the recent past, other such studies have been conducted in Saudi Arabia, Poland, Spain, and Iran\(^5\). An assessment of the current awareness levels and attitudes of the medical students in Pakistan towards organ donation would help in the planning of programs that can guide the medical students better in the future.

**METHODOLOGY**

This cross-sectional survey was conducted in the final year of MBBS students of Allama Iqbal Medical College, Lahore, to assess organ donation’s knowledge and attitudes from August 2019 to September 2019. Inclusion criteria comprised all the medical students from the final year of MBBS studying in AIMC. We excluded all the students who were not a part of the medical program and those who were not in the final year. Out of 320 final year medical students, we could not reach 22 students because of unavailability, and 30 students did not return the questionnaire. 268 participants were included in the study. The research team designed a questionnaire by modifying a previously developed questionnaire to assess medical students' knowledge and attitudes. There were 12 questions in the knowledge part and 32 in the attitude part. The questionnaires used close-ended, dichotomous, multiple-choice, and Likert scale format questions to evaluate the subjects. The questionnaires were given to the respondents and collected back after anonymous completion. We analyzed the data using IBM SPSS ver: 23 and was presented as frequency and percentages.

**RESULTS**

The study included 268 students, out of which 92 (34.3%) were males, and 176 (65.7%) were females. The mean age was 22.7 (± 2.3) years. All the participants were Muslims by religion. All the participants were aware of the term “organ donation.” 246 (91.8%) of the students believed organ donation is harvesting tissues, blood, and organs from both alive and dead donors. Only 28 (10.4%) believed blood donation to be organ donation. Students were then asked if they knew which organs can be donated. There was a higher level of awareness regarding the donation of the liver, kidney, heart, blood, eyes, and bone marrow (>50%). Most of the respondents were unaware that skin, intestines, pancreas, bone, and lungs (<50%) can be donated (Table 1).

<table>
<thead>
<tr>
<th>Organ</th>
<th>Can be donated</th>
<th>Cannot be donated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>214 (79.9%)</td>
<td>54 (20.1%)</td>
</tr>
<tr>
<td>Heart</td>
<td>168 (62.7%)</td>
<td>100 (37.3%)</td>
</tr>
<tr>
<td>Liver</td>
<td>206 (76.9%)</td>
<td>62 (23.1%)</td>
</tr>
<tr>
<td>Lungs</td>
<td>106 (39.6%)</td>
<td>162 (60.4%)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>20 (7.5%)</td>
<td>248 (92.5%)</td>
</tr>
<tr>
<td>Intestines</td>
<td>16 (6%)</td>
<td>252 (94%)</td>
</tr>
<tr>
<td>Blood</td>
<td>260 (97%)</td>
<td>8 (2.9%)</td>
</tr>
<tr>
<td>Bone marrow</td>
<td>176 (65.7%)</td>
<td>92 (34.3%)</td>
</tr>
<tr>
<td>Bone</td>
<td>34 (12.7%)</td>
<td>234 (87.3%)</td>
</tr>
<tr>
<td>Skin</td>
<td>96 (35.8%)</td>
<td>172 (64.2%)</td>
</tr>
<tr>
<td>Cornea</td>
<td>176 (65.7%)</td>
<td>92 (34.3%)</td>
</tr>
</tbody>
</table>

Table 1: Knowledge Regarding which Organs can and cannot be Donated
When asked if the participants knew about the existence of the Human Organ Transplant Authority (HOTA) of Pakistan, a federal organization that enrolls live/deceased donors and issues transplant license, only 120 (44.8%) responded in affirmative. The mean of correct answers regarding the policies of HOTA was 59.7% (Table 2).

Most of the respondents (76.9%) knew that a person can donate a part of his liver, but only 12.7% believed that undergoing such a procedure can be detrimental to their health. Similarly, 79.9% thought that they can donate one of their kidneys, but only 27 (10%) of the participants knew that donating a kidney is not entirely safe.

Regarding the harvest of donor organs, 26.1% (70) answered correctly when asked if an organ can be recovered from a dying person after cardiac or brain death or both. Details of answers to questions regarding HLA cross typing, consent of the donor, organ transplant duration, immunosuppression, and long-term follow-up are given in Table 2. The mean correct score was 54%.

Two hundred and sixteen (80.6%) respondents believed that it is important to tell family and friends about their wish to donate organs after death. Even though 82.8% (n=222) of the participants either ‘agreed’ or ‘strong-ly agreed’ that organ donation should be promoted in Pakistan and 94% (n=252) believed that donating organs can save someone’s life, only 29.9% (n=80) were comfortable to donate their organs. 212 (79.1%) of the participants were ready to accept donated organs for themselves in case of a need.

Regarding concerns about the organ donation process, 178 (66.4%) of the participants reported that organs' illegal buying and selling as their biggest concern. 82(30.6%) felt that organ donation would be against their religion, 66(24.6%) believed that they would be prematurely diagnosed as brain dead if they agreed to be organ donors, and 58(21.6%) said that the hospital staff would not work hard enough to save their life if they were organ donors.

More than half of the participants (53%, n=142) believed that the residents of Pakistan should be automatically placed on a national register to donate organs, with a choice to cancel the registration after the age of 18. Regarding religion, 44.8% (n=120) thought that their faith allowed organ donation, and 61.9% (n=166) felt that God would reward such an act. The attitudes of participants regarding different mitigating factors such as family support, availability of information are detailed in Table 4. 20 responses were recorded on a five-point Likert scale with the following response options: 1 = Strongly Agree, 2 = Agree, 3 = Neither Agree nor Disagree, 4 = Disagree, 5 = Strongly Disagree.

### Table 2: Knowledge Regarding the Process and Policy of Organ Donation

<table>
<thead>
<tr>
<th>Organ donation process</th>
<th>Yes</th>
<th>No</th>
<th>Don’t know</th>
</tr>
</thead>
<tbody>
<tr>
<td>HLA typing is necessary for even for corneal transplant</td>
<td>106 (38.1 %)</td>
<td>60 (22.4 %)</td>
<td>102 (38.1%)</td>
</tr>
<tr>
<td>The donor must give consent to harvest his organs before dying</td>
<td>164 (61.2%)</td>
<td>34 (12.7%)</td>
<td>70 (26.1%)</td>
</tr>
<tr>
<td>Harvested organs like liver and heart must be transplanted immediately as they cannot survive for long outside the body</td>
<td>164 (61.2%)</td>
<td>28 (10.4%)</td>
<td>76 (28.4%)</td>
</tr>
<tr>
<td>The recipient must be put on long term immunosuppressive therapy for kidney transplant</td>
<td>168 (62.7%)</td>
<td>32 (11.9%)</td>
<td>68 (25.4%)</td>
</tr>
<tr>
<td>The recipient and living donors require long term follow up after the procedure</td>
<td>168 (62.7%)</td>
<td>26 (9.7%)</td>
<td>74 (27.6%)</td>
</tr>
<tr>
<td>Policy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prohibits any buying or selling of organs</td>
<td>80 (66.6%)</td>
<td>40 (33.4%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Provides access to transplant facility for all nationalities equally</td>
<td>66 (55%)</td>
<td>54 (45%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Gives donated organs from deceased donors to the first person on the waiting list regardless of nationality</td>
<td>71 (59.1%)</td>
<td>49 (40.3%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Puts no pressure on the deceases donor family or living donor to donate</td>
<td>72 (60%)</td>
<td>48 (39.6%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>All Live donors are provided with health insurance for life</td>
<td>44 (36.6%)</td>
<td>76 (63.4%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>All families of the deceased will receive social support if they need it</td>
<td>54 (45%)</td>
<td>66 (54.5%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>
KNOWLEDGE AND ATTITUDES OF FINAL YEAR MEDICAL STUDENTS REGARDING ORGAN DONATION

DISCUSSION

The numbers of patients on the transplant lists are increasing day by day, and the gap between demand and supply is vast. Therefore, much emphasis is placed on raising awareness regarding organ donation to decrease morbidity and mortality of critically ill patients. Medical professionals' knowledge and attitudes are of the utmost importance because they are directly involved in the process of education and counseling of potential donors. This study's focus was on the final year medical students, as they would soon start their practice and come across many patients who could be convinced to donate their organs, saving many lives.

Regarding the final year students' knowledge, most (n=246, 91.8%) knew the correct definition of the term “organ donation.” However, only 28 (10.4%) participants answered correctly when asked if donating blood was equal to organ donation. Awareness regarding the type of organs that can be donated varied highly. Over 50% stated that liver, kidney, heart, blood, eyes, and bone marrow. However, very few knew that skin, intestines, pancreas, bone, and lungs can also be donated. These results were similar to the studies conducted by Vincent et al. and Sahin and Abbasoglu, which found that the students knew that kidneys, cornea, eyes, and heart can be donated. Still, the knowledge about other organs was lacking.

### Table 3: Attitudes Regarding Organ Donation

<table>
<thead>
<tr>
<th>Attitude</th>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Neither Agree nor Disagree</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organ donation is a good thing and should be promoted in Pakistan</td>
<td>116 (43.3%)</td>
<td>106</td>
<td>36 (13.4%)</td>
<td>4 (1.5%)</td>
<td>6 (2.2%)</td>
</tr>
<tr>
<td>Registering as organ donor could save somebody’s life</td>
<td>148 (55.2%)</td>
<td>104</td>
<td>0 (0%)</td>
<td>14 (5.2%)</td>
<td>2 (0.7%)</td>
</tr>
<tr>
<td>Donor register of Pakistan, with the ability to refuse if they wish</td>
<td>40 (14.9%)</td>
<td>102</td>
<td>66 (24.6%)</td>
<td>40 (14.9%)</td>
<td>2 (0.7%)</td>
</tr>
<tr>
<td>I think my donation whether living or after death is going to impact my life after death in a good way</td>
<td>74 (27.6%)</td>
<td>94 (35.1%)</td>
<td>68 (25.4%)</td>
<td>22 (8.2%)</td>
<td>10 (3.7%)</td>
</tr>
<tr>
<td>Organ donation is an act which will be rewarded by God</td>
<td>72 (26.9%)</td>
<td>94 (35.1%)</td>
<td>92 (34.3%)</td>
<td>6 (2.2%)</td>
<td>4 (1.5%)</td>
</tr>
<tr>
<td>Organ retrieval process after death may cause body disfigurement</td>
<td>14 (5.2%)</td>
<td>102 (38.1%)</td>
<td>68 (25.4%)</td>
<td>68 (25.4%)</td>
<td>16 (6.0 %)</td>
</tr>
<tr>
<td>Organ donation will increase if social support is provided to family (of the deceased), regardless of whether they donate or not</td>
<td>72 (26.9%)</td>
<td>114 (42.5%)</td>
<td>56 (20.9%)</td>
<td>24 (9.0%)</td>
<td>2 (0.7%)</td>
</tr>
<tr>
<td>You don’t find many opportunities to register as organ donor in Pakistan</td>
<td>64 (23.9%)</td>
<td>112 (41.8%)</td>
<td>70 (26.1%)</td>
<td>22 (8.2%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>While registering for organ donation, you may not get answer for all your questions</td>
<td>44 (16.4%)</td>
<td>148 (55.2%)</td>
<td>58 (21.6%)</td>
<td>16 (6.0%)</td>
<td>2 (0.7%)</td>
</tr>
<tr>
<td>You are not healthy to donate</td>
<td>26 (9.7%)</td>
<td>64 (23.9%)</td>
<td>96 (35.8%)</td>
<td>66 (24.6%)</td>
<td>16 (6.0%)</td>
</tr>
<tr>
<td>Your age is not fit for donating your organ</td>
<td>22 (8.2%)</td>
<td>46 (17.2%)</td>
<td>82 (30.6%)</td>
<td>94 (35.1%)</td>
<td>24 (9.0%)</td>
</tr>
<tr>
<td>Operation procedure for procuring organs is discouraging</td>
<td>28 (10.4%)</td>
<td>90 (33.6%)</td>
<td>92 (34.3%)</td>
<td>52 (19.4%)</td>
<td>6 (2.2%)</td>
</tr>
<tr>
<td>You are worried that organ donation might leave you weak and disabled</td>
<td>28 (10.4%)</td>
<td>122 (45.5%)</td>
<td>66 (24.6%)</td>
<td>48 (17.9%)</td>
<td>4 (1.5%)</td>
</tr>
<tr>
<td>I don’t trust the health care system in Pakistan and it is better to go abroad for organ donation and organ transplantation</td>
<td>74 (27.6%)</td>
<td>92 (34.3%)</td>
<td>58 (21.6%)</td>
<td>36 (13.4%)</td>
<td>8 (3.0%)</td>
</tr>
<tr>
<td>Emotions of your family members while organ are being taken make you feel concerned</td>
<td>52 (19.4%)</td>
<td>134 (50.0%)</td>
<td>58 (21.6%)</td>
<td>22 (8.2%)</td>
<td>2 (0.7%)</td>
</tr>
<tr>
<td>Would you accept an organ or body tissue from a donor if it was needed to maintain your own life?</td>
<td>70 (26.1%)</td>
<td>142 (53.0%)</td>
<td>44 (16.4%)</td>
<td>2 (0.7%)</td>
<td>10 (3.7%)</td>
</tr>
</tbody>
</table>

**I would be more likely to donate:**

<table>
<thead>
<tr>
<th>Reason</th>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Neither Agree nor Disagree</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>If I knew that my family would have no objection to allowing donation of my organs at the time of my death</td>
<td>38 (14.2%)</td>
<td>108 (40.3%)</td>
<td>74 (27.6%)</td>
<td>38 (14.2%)</td>
<td>10 (3.7%)</td>
</tr>
<tr>
<td>If I knew more about what is organ transplant and how it is done</td>
<td>58 (21.6%)</td>
<td>124 (46.3%)</td>
<td>50 (18.7%)</td>
<td>32 (11.9%)</td>
<td>4 (1.5%)</td>
</tr>
<tr>
<td>If more information was available about the viewpoint of my religion with regard to organ donation</td>
<td>100 (37.3%)</td>
<td>124 (46.3%)</td>
<td>22 (8.2%)</td>
<td>18 (6.7%)</td>
<td>4 (1.5%)</td>
</tr>
<tr>
<td>If I knew where I could register</td>
<td>50 (18.7%)</td>
<td>118 (44.0%)</td>
<td>64 (23.9%)</td>
<td>26 (9.7%)</td>
<td>10 (3.7%)</td>
</tr>
</tbody>
</table>
Even though there is only one federal organization dealing with the enrolment of organ donors and its legislations in Pakistan, only 60 (44.8%) of the participants knew about the existence of the Human Organ Transplant Authority (HOTA). The number of students who had the right knowledge about the policies of HOTA was even fewer. These statistics are slightly better than other such researches conducted to find the awareness of specific organ donation process, but the overall numbers are not satisfactory at all.8,9,11,12

Very few participants (26.1%) had clear concepts about organ harvest both after cardiac and brain death. Similarly, most of the participants knew that people can donate their liver (76.9%) and kidneys (79.9%) before death but did not know if the donation process can harm the donor (12.7% and 10.07%, respectively). Technical questions about HLA typing, the need for immunosuppression, duration of follow-up, and others yielded varied answers with a mean score of 57.1%. The knowledge scores were comparable with the studies conducted by Tagizadieh et al.8 and Poreddi et al.12

As for the attitudes towards Organ Donation and Transplantation (ODT), even though most participants believed that organ donation should be promoted further as it can save lives, very few were ready to donate their organs. However, almost 80% would accept a donated organ if they needed it for themselves. This attitude indicates the fear and stigma associated with ODT, despite the knowledge of its benefits. These results are in contrast to studies conducted in Poland (96.4%).6,9,12

The leading concerns for the poor attitude towards registering as an organ donor include illegal trade of organs 66.4%, prohibition by religion 30.6%, carelessness of doctors and hospital staff in dealing with registered donors (24.6%). Rydzewska et al., Sahin and Abbasoglu10, and Atamanuk et al.13 reported similar concerns in their studies.

Over 60% of the participants stated that they would be more willing to donate if they had more information about the organ donation process, if they were clear about the organ donation rules by their religion, and if they knew where they could register. Considering the lack of knowledge of final year medical students regarding the technical details and rules of ODT set by law and religion, the abysmal numbers of donated organs by the general population in Pakistan is understandable.

CONCLUSION

Final year medical students possess poor knowledge and attitudes regarding organ donation. We need a robust awareness campaign at the university level, so the newly graduated doctors can educate the public and ward off stigmas regarding ODT when they join the clinical practice.

Acknowledgments

We are grateful to the Department of Community Medicine for supervising this research and final year medical students for cooperating during data collection for this research. We would also like to appreciate the hospital ethical review board of Jinnah Hospital Lahore for the opportunity for data collection.

Limitations of the study There are a few limitations to our research. The study used a cross-sectional design, and because of this, we could not establish causation between study variables used in our research. We can also not generalize the knowledge and general attitude towards organ donation to the lower merited medical colleges in other parts of Pakistan. Another drawback of this study was the small sample size. All the knowledge questions were close-ended questions, which could have led to some participants guessing the right option and resulted in a false representation of students' knowledge.

Conflicts of interests None
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Authors contributions

Following participants contributed in research
1. Dr. Muneeb Ahmad, M.B.B.S. Department of Community Medicine AIMC/JHL
2. Dr. Fatima Tahir, M.B.B.S. Department of
KNOWLEDGE AND ATTITUDES OF FINAL YEAR MEDICAL STUDENTS REGARDING ORGAN DONATION

Community Medicine AIMC/JHL

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Otalgia is defined as ear pain. This simple definition for this common problem however does not do justice to the complexity of the issue and to the nuisance that this pain can be. The pain can range from a mild inconvenience to debilitating and this is the reason why earache can be an ENT emergency at times. Earaches can be primary with causes originating in the ear and referred pain that is felt in the ear but stemming from some other area as the ear has a rich nerve supply from multiple different nerves which further innervate multiple other structures, pathology of which can be referred to the ear.

Primary otalgia (that which stems from pathology within the ear) can be due to a variety of pathologies, including many of inflammatory, traumatic and neoplastic etiologies. These include pathologies such as otitis media (most common), otitis externa, foreign bodies, barotrauma, Ramsay Hunt synd-
Referred otalgia and the multiple areas from which this pain can be referred from makes localizing the origin of otalgia a particularly intriguing process. Pain can be referred from the neck, throat, jaw, nose and sinuses, teeth and mouth. Late diagnosis of otalgia of the referred kind can lead to irreversible consequences. Undetected progression of pathology affecting the areas from which pain can be referred from can be very detrimental. Indeed, lethal conditions such as carcinoma of the tongue can cause pain in the ear with dire, possibly fatal results if not promptly managed.

Quality of life among patients with otalgia can be adversely affected with sleep disorders, headaches, fatigue amongst the detriments associated with otalgia. Earaches can affect mental health and may have such an adverse effect that they cause the patient to seek psychiatric help. Otalgia can affect different age groups, children suffering from primary otalgia and adults most often are afflicted with referred otalgia.

By gauging the patient’s knowledge of earaches, medical professionals can more appropriately mold their approach to counselling the patient regarding their problem, tackling issues which patients might not have adequate knowledge of or which are more pertinent to alleviating the patient’s condition and distress. The patient’s perception of an illness is one of the key determining factors of how they will comply with the treatment. By assessing the patient’s knowledge and understanding which areas need to be classified or explained in more detail, the patient’s perception of his own condition may be altered in a positive way which may ultimately aid them into becoming healthy once again. For this reason, we have put together this article in order to give health professionals adequate insight into the extent of patient’s knowledge regarding otalgia.

The objective of the study was to assess the knowledge of earache amongst the general population of Lahore.

**METHODOLOGY**

Questionnaires of the research topic were provided to individuals that met the inclusion criteria. The questionnaires were distributed both online and manually. The data from 256 questionnaires was compiled, statistical data tabulated and finalized. Common trends and patterns were found and written. All the data collected was entered in SPSS (Statistical Package for the Social Sciences) version (22). The qualitative variables were presented as frequency and percentage and the quantitative variables were presented as mean and standard deviation. The independent variable was cross tabulated with the dependent variable (x) and any association was found using chi square test of significance. A p value of <or=0.05 was taken as statistically significant.

**RESULTS**

The study was conducted amongst 256 individuals, all of whom were not employed as medical professionals. Of these individuals, 161(62.9%) stated that they have previously experienced an earache whilst 92(35.9%) answered this question incorrectly. Otalgia can cause agonizing pain, however, on inquiring of the maximum intensity of pain that
can result from earaches few 48(18.8%) were aware that the pain can be very severe, 102(39.8%) respondents thought the pain could maximally be severe, 52(20.3%) respondents that it could be moderate at most and 54(21.1%) individuals believed that earache could not be more than mild pain.

105(41.0%) individuals were aware that none of the mentioned home remedies were advisable, 94(36.7%) thought using warm oil was acceptable, 41(16.0%) chose the use of cotton buds to clean the ears whilst 16(6.25%) were under the impression that the use of garlic or garlic juice is beneficial.

Of the respondents, 103(40.2%) were aware that the first aid measure allowing temporary relief of pain before visiting the doctor was the use of over the counter pain medication, 93(36.3%) opted to use oil, 54(21.1%) selected the use of cotton buds and 6(2.3%) chose sponging.

143 (55.9%) were aware that ringing in the ears, hearing loss and loss of balance could all be possible symptoms accompanying earache. 113(44.1%) individuals were unable to give the correct response. 160(62.5%) individuals were aware of this whilst 96(37.5%) respondents failed to give the appropriate response. 11(4.3%) respondents were able to select the correct options. The remaining individuals were not able to identify all of these options. (78(30.5%)

Less than half of the respondents (78-30.5%) knew that earaches could be a symptom of potentially life-threatening diseases. 27(10.5%) people were aware that uncontrolled diabetes could lead to earaches despite diabetes being a very common disease.

**DISCUSSION**

In order to effectively deal with any medical issue, the population should have a basic understanding of what the problem is, why they are experiencing it and at the very least rudimentary comprehension of how to deal with the problem in the initial phase (in particular knowing when they should seek the aid of a medical professional). It is ‘knowledge’ of these aspects that we particularly emphasize in our article. There is a great paucity of literature focused on this specific area of interest and in a broader view in any literature focused on gauging knowledge of otalgia, regardless of the population. As such, it is an arduous task to support our findings with data from other studies on this topic as it simply does not exist. However, we were able to find several studies that support the validity, accuracy and relevance of the questions put forward to the study population and so are highlighting them here.

Ear ache is a common condition and frequent cause of visits to primary care physicians.17,18 Adegbiji et al.9 reported prevalence data of 36.2% (i.e. 947 out of 2616), although not strictly prevalence data 62.9% of individuals in our study reported that they have experienced an earache during their lifetime, further highlighting how common this

**Table 1:**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Correct response</th>
<th>Incorrect response</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Frequency</td>
<td>Percentage</td>
</tr>
<tr>
<td>Is it advisable to clean ears regularly with cotton buds/ Q tips/ hairpins?</td>
<td>114</td>
<td>44.5</td>
</tr>
<tr>
<td>Can diseases of other areas cause pain in the ear i.e referred pain?</td>
<td>175</td>
<td>31.6</td>
</tr>
<tr>
<td>If yes, which areas can the pain be referred from? Pick the correct answer(s)?</td>
<td>0</td>
<td>100.0</td>
</tr>
<tr>
<td>Can earaches be severe enough to be dealt as an emergency?</td>
<td>143</td>
<td>44.1</td>
</tr>
<tr>
<td>What is the maximum intensity of pain that earaches can cause?</td>
<td>48</td>
<td>81.3</td>
</tr>
<tr>
<td>Which home remedies are recommended for earaches?</td>
<td>105</td>
<td>59.0</td>
</tr>
<tr>
<td>What first aid measures can be used at home before consulting a doctor in order to achieve temporary relief of pain?</td>
<td>103</td>
<td>59.8</td>
</tr>
<tr>
<td>What other symptoms/features can occur with earaches?</td>
<td>143</td>
<td>44.1</td>
</tr>
<tr>
<td>How can earaches affect quality of life?</td>
<td>160</td>
<td>37.5</td>
</tr>
<tr>
<td>When should you consult a doctor for earache? Select the right option(s)</td>
<td>11</td>
<td>95.7</td>
</tr>
<tr>
<td>Can earache be the presenting symptom of life-threatening diseases?</td>
<td>78</td>
<td>69.5</td>
</tr>
<tr>
<td>Which of the following diseases can lead to ear ache if not properly treated?</td>
<td>27</td>
<td>89.5</td>
</tr>
</tbody>
</table>
KNOWLEDGE OF OTALGIA (EARACHE) AMONGST THE POPULATION OF LAHORE

problem really is.

Use of cotton buds to clean the ears can be very detrimental leading to otitis externa and foreign body retention, both important causes of earache 20. It has been repeatedly found that right ear otalgia is more frequent than both left ear otalgia and bilateral otalgia 21,22,23 which can be easily explained as most of the world’s population is right-handed and therefore cleans the right ear more. Furthermore, a studied conducted amongst the pediatric population of the US 24 showed that 26338 children were treated for cotton tip applicator related injury in ER, which they state is actually an underestimation. This again emphasizes the role of the use of cotton buds as a major cause of otalgia. 55.1% of the individuals in our study were not aware that it is not advisable to clean the ears regularly with cotton tip applicators. Other studies also report finding this misconception in the tested sample. 25,26,27

A larger number of individuals (68.4%) were aware that pain can be referred from other parts of the body to the ear. Indeed, in a study of 500 visiting the ENT clinic 58 presented with primary otalgia and 28 with secondary. 28 Another research 19 reported that 32.63% of the total cases of otalgia were cases of secondary otalgia. Another study found 12.2% of patients of otalgia had pain referred from other areas. Toothaches and TM joint pathology were reported to be frequent causes of referred otalgia.

Earaches can cause excruciating pain and can present as an emergency. One study focusing on earaches due to swimming in the US estimated that earaches due to swimming alone caused 39900 ER visits. In a study conducted in Nigeria, 19 34.7% earaches were severe enough to warrant presentation to the ER.

On inquiring of the remedies used prior to presentation to the ENT department, one research 19 found that 49.8% of individuals used over the counter medication, 24.6% used herbal medication, 17.8% used prescribed medication and 7.7% took no treatment. We similarly found that 40.2% respondents in our study were aware that over the counter pain medication could be used for temporary pain relief prior to presentation to the ENT department.

A multitude of symptoms can accompany otalgia, some common ones being tinnitus, vertigo and hearing loss. The literature is replete with examples of this, with many articles giving a number of symptoms 14,17,19,28,29,30 associated with otalgia and emphasizing mention of these symptoms during history taking. 31 55.9% individuals were able to correctly identify the symptoms that could be associated with earache.

Quality of life can be starkly impacted by earaches. A study conducted in Nigeria 19 showed 65.7% patients reported sleep disturbances, 54.5% missed work, 49.7% decline in social functioning. Another study focusing on otalgia in swimmers noted 24% patients had missed activity with a median of 2 days of activity impacted by earache. 24

Earaches can be more than a mere inconvenience and can be a symptom of underlying potentially life-threatening conditions such as carcinoma of different regions. 19,32,33,34,35 A case was reported in which otalgia was the presenting symptom of nasopharyngeal carcinoma. 36 33% of patients of carcinoma of the base of the tongue had otalgia in one study. 13 Another study reported that 6% of the cases of referred otalgia were due to pharyngeal carcinoma. 36 Metastasis from far of regions can be a cause of earaches, as is exemplified in a study by Dally. 37

Diabetes has emerged as a major disease of the masses in the post-industrial era with both lower income countries and more affluent nations being afflicted with the illness and its myriad of complications. Amongst its complications, necrotizing| malignant otitis externa is a cause of extreme pain in the ear. 31 Diabetes is an important point in history taking in a patient with otalgia 29 and should always be considered in diabetics with severe ear pain. 31

CONCLUSION

Overall, the results were promising showing that most individuals had good knowledge of otal-
Knowledge in certain areas, however, such as when a patient of otalgia should go to the doctor or the places from which otalgia can referred from and whether or not otalgia can be a symptom of potentially life-threatening illness was poor.

**Recommendations**

The authors suggest the use of published works, televised educational programs and the utilization of mass media platforms such as the internet to promote education of the matters pertaining to the knowledge of earache such as to enhance knowledge and remove possible misconceptions.

**Limitations**

Our study does admittedly suffer from some limitations. The sample size is relatively small and convenience sampling may slightly influence the results.

**Conflicts of Interest**

The authors declare there is no conflict of interests.

**Funding Sources**

The authors declare that they did not receive any funding from any institution.

**Contributions of the authors**

- Conception or design of the work: Dr Syed Ahmed Shahzaeem Hussain, Dr Syed Ahmed Shahzain Hussain
- Data collection: Dr Syed Ahmed Shahzaeem Hussain, Dr Syed Ahmed Shahzain Hussain, Dr Syed Muzahir Hussain,
- Data analysis and interpretation: Dr Syed Ahmed Shahzaeem Hussain
- Drafting the article: Dr Syed Ahmed Shahzaeem Hussain
- Critical revision of the article: Dr Syed Muzahir Hussain, Dr Syed Ahmed Shahzaeem Hussain
- Final approval of the version to be published: Dr Syed Muzahir Hussain, Dr Syed Ahmed Shahzaeem Hussain

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Chronic pain always come with a number of complications including stress, depressed mood, poor sleep quality, insomnia and fatigue. Multiple studies have tried to explore the complex relationship among pain, stress and poor sleep quality. It has been seen that pain itself causes poor sleep quality. Poor sleep results in stress, depressed mood, insomnia, and fatigue causing the pain to worsen. Good control of pain resulted in decreased stress and improved sleep quality. Improving the sleep quality on the other hand causes reduction in pain scores. Adding to complexity, Sleep disturbances have also been associated to chronic use of opioids.

Melatonin is a hormone produced mainly in the pineal gland and some peripheral tissues which controls the circadian rhythm. Recent studies suggest that Melatonin has hypnotic, anti oxidative, anticonvulsant, antinociceptive and analgesic properties. Literature suggest that use of melatonin not only improves the quality of pain but also reduced the pain intensity and total analgesic consumptions in chronic pain patients. Melatonin has been used for a variety of chronic pain conditions like fibromyalgia,

**Abstract**

**Objective:** To compare the effects of melatonin and midazolam as anxiolytic and sedative to improve the quality of sleep and life in patients with chronic pain. It was a randomized control trial conducted at the Department of Anesthesia and Pain Management, Gujranwala medical college, Gujranwala from May to October 2019.

**Methodology:** 50 patients with chronic pain as per operational definition were randomly allocated either in Group A or B. Patients were asked to rate the quality of their sleep during the disease period to assess the baseline sleep quality. Patients in group A were prescribed Tablet melatonin 3 mg orally at night while patients in Group B were prescribed Tablet Midazolam 7.5 mg orally at night along with the other pain medication required. Patients were followed up at 1 week and at 2 weeks from the first day of the drug. Patients were asked to rate the quality of sleep as per operational definitions & for any additional side effects they observed after taking the drug. Any change from baseline sleep quality or adverse effects were noted. The whole information was collected through performa.

**Result:** Quality of sleep was improved in 22 patients of group-A and in 20 patients of group-B.

**Conclusion:** Both melatonin and midazolam are effective in improving the quality of sleep in patients with chronic pain, in all age groups and genders.

**Keywords:** Melatonin; Midazolam; Sleep quality; Chronic Pain; Analgesia.
migraine, tension headache, cluster headache, backache, irritable bowel syndrome, rheumatoid arthritis and critical care with a varying degree of success and effects. Its has also been studied as a premedication anxiolytic in comparison to midazolam, giving contradictory results. Some advocates melatonin is better to use while others say it is of no use in reducing anxiety. An extensive data search was made and we could not find a study comparing the effects of melatonin and midazolam in chronic pain patients. So we designed this study with the aim to compare melatonin and midazolam in improving the quality of sleep in chronic pain patients. Melatonin may prove a better alternative to midazolam and other benzodiazepines in chronic pain management due to its sedative, anticonvulsive and antinociceptive effects.

**METHODOLOGY**

The randomized control trial was conducted in Department of Anaesthesiology, DHQ teaching Hospital, Gujranwala medical college, Gujranwala from May to October 2019 with a sample size of 50 patients (25 in each group). Non probability consecutive sampling method was used for the selection of sample. Patients aged 12-70 years, of both genders, with chronic pain of any body part for at least 12 months duration were included in this study. Patients with known allergy to study drugs (melatonin or midazolam); with diagnosed psychiatric disorders; or with a history of benzodiazepines or melatonin use for more than 1 week were excluded from this study.

After ethical approval by local research and ethic committee, 50 patients fulfilling the criteria were enrolled in this study from outpatient department. After an informed consent, Patients were allocated randomly using random number table to one of the two groups comprising 25 patient each. (Group A: Melatonin and Group B: Midazolam).

After taking a detailed history and physical examination diagnosis of chronic pain was established as per operational definition. Medical record was carefully reviewed to check the current medication and the problems. Patients were asked to rate the quality of their sleep during the disease period into one of following four categories.

1. Excellent. There was no interruption in at least 6 hours of sound sleep and patient woke in the morning quite fresh.
2. Good. There was a little interruption during 6 hours of sound sleep. Patient did wake up during night once or twice or the patient was not feeling fresh in the morning.
3. Bad. Patient had to wake up 3 times or more during the 6 hours of sleep.
4. Very Bad. Patient was unable to sleep and was awake most of the night.

Baseline Sleep category 1, 2, 3 or 4 was noted and the study drugs were prescribed. Patients in group A were prescribed Tablet melatonin 3mg orally at night while patients in Group B were prescribed Tablet Midazolam 7.5 mg orally at night along with the other pain medication required. Patients were followed up at 1 week and at 2 weeks from the first day of the drug. Patients were asked to rate the quality of sleep as per operational definitions. Any change in the sleep category was noted. Improvement in sleep quality was marked ‘Yes’, when there was at least 1 step improvement in baseline sleep category at 1 or 2 weeks. Patients were asked for any additional side effects they observed after taking the drug and the response was noted. The drug was either continued if good or changed if found not satisfactory. The whole information was collected using specially designed Performa. All the collected information was entered and analyzed using IBM SPSS version 23.0. The age of the patients were presented by calculating mean and standard deviation. Gender and Improvement in sleep quality was presented by calculating frequency and percentage. Improvement in sleep quality between the two groups was compared using chi square test. P ≤0.05 was considered as significant. Data was stratified for age and gender. Post-stratification, independent sample t-test was applied to check the effect of effect modifiers and p-value ≤ 0.05 was
RESULTS

In this study 50 patients were enrolled and randomly divided equally into 2 groups. Average age of patients was 40.22 ± 12.32 years. Minimum and maximum age of patients was 17 and 66 years. In group B and D average age of patients was 39.73 ± 13.87 and 40.70 ± 10.78 years respectively. Minimum and maximum age in group B patients was 17 and 66 years while in group D minimum and maximum age of patients was 23 and 63 years respectively. (Table 1) 31 patients were male and 29 were female in total. In group-B 17 patients were male and 13 females. In group-D, there were 14 male and 16 female patients. (Table 2) 27 patients were ASA I and 33 were ASA II. In group B 15 were ASA I and 15 were ASA II whereas in Group D ASA I and II were 12 and 18 respectively. (Table 3) Mean duration of analgesia was 266 ± 41.12 minutes in both groups. It was 234.2 ± 25.3 minutes in Group B and 297.8 ± 26.7 minutes in Group D respectively (p<0.0001). (Table 4) Data was stratified for age, gender, and ASA status. Post-stratification analysis didnt reveal any significant results.

DISCUSSION

Melatonin is available as over the counter drug in many parts of the world. In Pakistan it is available as 2, 3 and 5 milligram tablets for oral use. It is mostly known by medical professionals and public as a sleep hormone with minimum or no side effects. Many studies favor the use of melatonin both for the initiation and maintenance of sleep. The hypnotic effects of melatonin are considered as an essential part of its physiological role. In healthy volunteers Melatonin improved sleep onset, duration and quality. Melatonin is neurohormone which exerts its hypnotic effects through the activation of specific melatonin receptors; the MT1 and MT2 receptors. It suppresses normal neuronal activity of brain to the regulate the sleep. Evidence suggest that melatonin also modulate the GABA receptor in central nervous system to produce hypnosis and sleep. Normal physiological secretion of melatonin are at peak levels in the evening when the body is at the lowest point in rhythms of core body temperature, alertness, mental performance and many metabolic functions and with maximum sleep propensity. Melatonin differ from midazolam and other benzodiazipines as it exert its hypnotic effect by using the diurnal rhythm variation in alertness. The sleep inducing effect of melatonin is very mild when compared to midazolam. Moreover, melatonin produces no hangover effects on the day following its intake. Melatonin and its analogs lack negative effects like addiction, dependence as compared to benzodiazipines. We have found in this study that both melatonin and midazolam effectively improved the sleep quality in patients with chronic pain. The number of patients with improved sleep quality was high in melatonin group but it could not
be proved superior statistically. Previous data in this subject is very limited and more researches with a greater sample size are required to produce statistically significant results.

In experimental studies, melatonin is proved as potent analgesic specially in high doses. The physiological mechanism behind its analgesic effect has not been clarified. The effects may be linked to Gi-coupled melatonin receptors, to Gi-coupled opioid μ receptors or GABA-B receptors. The exact site of action of melatonin to produce analgesia is not clear yet. Possibly, it augments GABA-ergic systems and morphine anti-nociception, enhancing GABA-induced currents and inhibiting glycine effects. Melatonin may enhance the levels of β-endorphins and the anti-nociception induced by delta opioid receptor agonists and could activate MT2 melatonin receptors in the dorsal horn of the spinal cord. Melatonin is involved in the modulation of nociceptive transmission. Intrathecally administered melatonin is active against the formalin and thermal-induced nociception at the spinal level in rats. These findings may prove melatonin as a better alternative to midazolam and other benzodiazepines, as melatonin may provide some analgesia in addition to hypnosis whereas benzodiazepines lacks any analgesic effects. However the analgesic dose of melatonin is yet undefined. It has been associated with the relief of pain in patients with extensive tissue injuries. Melatonin has analgesic benefits in patients with chronic pain – fibromyalgia, inflammatory bowel syndrome, migraine, tension headache, cluster headache and even rheumatoid arthritis. Disturbances in melatonin secretion have been proposed to be part of the pathophysiology leading to fibromyalgia. Melatonin when given in doses of 3 mg orally for 4 weeks, 30 minutes before sleeping time, significantly improved sleep quality and resulted in significantly fewer painful trigger points. Melatonin alleviates abdominal pain in patients with inflammatory bowel syndrome (IBS). Melatonin 3 mg for 2 weeks attenuated abdominal pain and bloating and reduced rectal pain sensitivity in patients with IBS. The urinary melatonin concentration was found to be low in subjects suffering from migraine and trials have shown that melatonin may have both therapeutic and prophylactic benefit in patients suffering from migraine headaches. Melatonin even reduces tactile allostynia in neuropathic rats after intrathecal and oral administration. All these studies favor the use of melatonin in chronic pain patients as it has the clear potential to provide analgesia as well as hypnosis. In this study we could not measure the analgesic effects of melatonin. This was one of the shortcomings of this study which need to be addressed in future research. A large sample size will be required, as mentioned above, to produce statistically significant results. We kept this study as simple as possible using a subjective scale to measure the sleep quality. Due to the simple study design, we could not quantify the improvement in sleep quality. Use of a standardized scale for sleep quality measurement like Pittsburgh sleep quality index (PSQI) with cognitive and behavioral assessment tools will produce better quantitative results.

CONCLUSION

Both Melatonin and Midazolam may be used effectively to improve the quality of sleep in chronic pain conditions. Melatonin may be a better choice due to its analgesic potential in addition to hypnosis. Further studies are required to find its optimal dose for a combination of analgesia and hypnosis.

REFERENCES

3. Evans S, Dijias V, Laura C., Lonnie K., Jennie C.I. Sleep Quality, Affect, Pain, and Disability in Children With Chronic Pain: Is Affect a Mediator or


In a healthcare system, a serious patient usually has his first contact with the emergency medical services (EMS). Depending on the perplexity of situation, EMS encounters difficulties in handling of serious patients. The factors of high co-morbidity and multiple pathologies demand immediate clinical decision making by EMS. This asserts least use of diagnostic tools. In such a situation, early warning scores (EWS) can be helpful in assessing the deteriorating state of the patients. Moreover, serious adverse events can be avoided by the use of clinical observations combined with physiological variables. Various EWS have been proposed including Vital Early Warning Score (ViEWS), Modified Early Warning Score and National Early Warning Score (NEWS). The National Early Warning Score (NEWS) was developed by Royal College of Physicians and the National Health Service in UK, in 2012. NEWS is under use on international basis. It has already received wide acceptance due to its applicability in diverse conditions. According to literature, individuals who counter adverse events in clinical wards show physiological deterioration few hours before the occurrence of the event. Thus, such adverse events are assumed to be predictable. Consequently, these events can be prevented by EMS through early recognition and proper management.

The National Early Warning Score (NEWS) was developed by Royal College of Physicians and the National Health Service in UK, in 2012. NEWS is under use on international basis. It has already received wide acceptance due to its applicability in diverse conditions. According to literature, individuals who counter adverse events in clinical wards show physiological deterioration few hours before the occurrence of the event. Thus, such adverse events are assumed to be predictable. Consequently, these events can be prevented by EMS through early recognition and proper management.

NEWS is a ‘track and trigger’ system that helps in identification of individuals with physiological...
abnormalities. It helps in frequent monitoring of vital signs in a fast and effective manner. Although the impact of standardized use of NEWS is under consideration, it is obvious that early diagnosis of high-risk patients can surely improve prognosis. As pre-hospital situation comprises of limited diagnostic tools, any system that helps healthcare workers in understanding patient’s condition and making timely decisions should be beneficial for the patient. Consequently, it is important to evaluate the efficacy of such systems for aiding healthcare professionals in timely and efficient clinical decision-making.

Few research workers have assessed and evaluated the use of NEWS inside the hospital and also at pre-hospital level. The present study was conducted to evaluate the role of tocilizumab in improving NEWS score of patients.

**METHODOLOGY**

The study was conducted from Nov 2019 to March 2020 at Mayo Hospital, Lahore. Patients with age more than 65 years were included in the study. These patients were admitted as with a suspected diagnosis of COVID-19. The NEWS score in each patient was calculated after collecting consent form. The study comprised of two groups, each with 30 patients. Group A received intravenous (IV) corticosteroids (CS) only, whereas, group B was given tocilizumab (TCB) along CS as part of immunomodulatory therapy.

All patients were admitted in the hospital. The day of administering first dose of respective agents was considered as day 0. The patients were followed-up until discharge and NEWS score was calculated again for comparison. The demographics such as age, gender, residential area of patients were noted. Moreover, co-morbidities, symptoms, laboratory values, radiological features and vital signs were recorded from day 0 for each patient. Treatment relevant negative events, use of anti-viral therapy and outcomes were also noted. For assessment of respiratory function, pulse oximetry oxygen saturation/fraction of inspired oxygen ratio (SpO2/FiO2) was used. Changes in clinical status were calculated on the basis of six-point scale that comprised of 1-Discharge, 2-Hospital admission with no supplemental oxygen, 3- Hospital admission with low-flow supplemental oxygen, 4- Hospital admission with high flow supplemental oxygen, 5-Hospital admission with invasive mechanical ventilation (IMV) 6-Death.

The data was presented as frequencies and percentages or means and standard deviations. SPSS v.23 was used for statistical analysis.

**RESULTS**

60 patients with age more than 65 years were

<table>
<thead>
<tr>
<th>Table 1: Demographic Characteristics of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristics</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Age (years) (mean ± SD)</td>
</tr>
<tr>
<td>Gender</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Co-morbidities</td>
</tr>
<tr>
<td>Obesity</td>
</tr>
<tr>
<td>Chronic lung disease</td>
</tr>
<tr>
<td>Chronic heart disease</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Malignancy</td>
</tr>
<tr>
<td>End-stage renal disease</td>
</tr>
<tr>
<td>Dementia</td>
</tr>
<tr>
<td>Lower limb peripheral arterial disease</td>
</tr>
<tr>
<td>Solid organ transplantation</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
</tr>
<tr>
<td>Chronic liver disease</td>
</tr>
<tr>
<td>Charlson co-morbidity index</td>
</tr>
<tr>
<td>Previous systematic corticosteroid therapy</td>
</tr>
<tr>
<td>Smoking</td>
</tr>
<tr>
<td>Symptoms</td>
</tr>
<tr>
<td>Cough</td>
</tr>
<tr>
<td>Fever</td>
</tr>
<tr>
<td>Dyspnea</td>
</tr>
<tr>
<td>Diarrhea</td>
</tr>
<tr>
<td>Myalgia</td>
</tr>
<tr>
<td>Expectoration</td>
</tr>
<tr>
<td>Impaired consciousness</td>
</tr>
</tbody>
</table>
included in the study who were admitted with the suspected diagnosis of COVID-19 infection. The NEWS score was calculated for each patient before admission to the hospital. Patients were divided into 2 groups, A and B, each comprising of 30 patients. Patients in group A received systemic corticosteroids and the ones in group B received sequential treatment with TCZ with a median interval of 1 day.

The demographics of patients are shown in the Table 1. The mean age of patients was 71.3 ± 6.3 years with 42(70%) males and 18(30%) females. The most prominent co-morbidities observed were diabetes mellitus (n=36; 60%) and chronic heart disease (n=25; 41.66%). Fever (n=30; 50%), and cough (n=19; 31.66%) were most prevalent symptoms. Significant difference was present between groups in terms of age, Charlson co-morbidity index and previous systematic corticosteroid therapy.

The vital signs, laboratory test values and chest x-ray findings are shown in Table 2 for both the groups. The groups showed significant difference in terms of $\text{SpO}_2/ \text{FiO}_2$ ratio, Leucocytes x 10⁹ cells, LDH and unilateral alveolar infiltrate findings.

Table 3 shows NEWS values for Group A and Group B, recorded at day 0 and 14 respectively. The mean value for NEWS score for group A was 8.83 whereas group B had a score of 9.43 at day 0. At day 14, the NEWS score for group A dropped to 6.53 whereas in group B score was reduced to 4.86. Significant drop in NEWS score was quite evident in

<table>
<thead>
<tr>
<th>SR. NO.</th>
<th>Group A</th>
<th>Group B</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>NEWS at day 0</td>
<td>NEWS at day 14</td>
<td>NEWS at day 0</td>
<td>NEWS at day 14</td>
<td></td>
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<tr>
<td>1</td>
<td>8</td>
<td>6</td>
<td>7</td>
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<td>28</td>
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<td>29</td>
<td>11</td>
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<tr>
<td>30</td>
<td>10</td>
<td>6</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Mean</td>
<td>8.83</td>
<td>6.53</td>
<td>9.43</td>
<td>4.86</td>
</tr>
</tbody>
</table>

p value (within group) | 0.02 | 0.01 |

p value (between groups) | <0.001 |
ROLE OF TOCILIZUMAB (TCZ) IN IMPROVING NATIONAL EARLY WARNING SCORE (NEWS) IN COVID-19 PATIENTS

Group B. Although both groups showed statistically significant difference between NEWS scores recorded at day 0 and day 14, the difference in NEWS score for group B was more than that of group A. Moreover, this difference of NEWS score between the two groups was found to be statistically significant (p<0.05).

DISCUSSION

The destruction in the healthcare system caused by the pandemic of COVID-19 is no more a secret. The mortality caused by coronavirus disease has alarmed researchers and health care workers all over the world. There has been a dire need to make timely clinical decisions. In such a scenario, the role of NEWS score needs to be evaluated. The present study is an effort towards understanding role of TCZ in reducing NEWS score in pre-hospital situation of COVID-19 patients.

The present study compared improvement in NEWS score for patients undertaking corticosteroids and TCZ as immunotherapy. The findings of present study signify that the NEWS score can be reduced drastically in COVID-19 patients by administration of TCZ immunotherapy. Due to old age of patients, the risk of treatment associated adverse events was higher. However, no significant bacterial or fungal complications occurred in TCZ group during the study.

The previous research work has supported the use of systemic corticosteroids for reducing mortality in COVID-19 patients. However, the use of other medicines is still under debate. One of the most researched medicines is TCZ. Hazbun et al promoted the use of TCZ among patients undergoing mechanical ventilation. Ramiro et al performed two-step approach which included use of high dose methylprednisolone and TCZ in Covid-19 Patients. By comparing the experimental group to the control group, it was concluded that two step approach can improve respiratory recovery. Moreover, the in-hospital mortality and likelihood of invasive mechanical ventilation were reduced. However, Rodriguez-Bano et al claimed that there is no difference on the basis of risk of death or intubation in patients treated with TCZ. Somers et al studied the impact of using TCZ among mechanically ventilated COVID-19 patients. Although decrease in death rate was evident, the occurrence rate of superinfection was higher. However, the study promoted the use of TCZ amongst COVID-19 patients. In this cohort study of mechanically ventilated COVID-19 patients, tocilizumab was associated with a decreased likelihood of death despite higher superinfection occurrence. Randomized controlled trials are needed to confirm these findings.

The research work of López-Medrano et al supports the findings of our study. It compared the efficacy of TCZ with corticosteroids and found that 14-day mortality and 28-day mortality was better in TCZ group along with improvement in clinical manifestations. However, the secondary infection rate was found to be the same in both the groups. This study highly recommended the use of TCZ along with corticosteroids as is the case in our study.

CONCLUSION

The use of NEWS for assessing clinical condition of patients is well-established. TCZ for improving condition of COVID-19 patients is highly acknowledged. And TCZ can be used to improve NEWS score among COVID-19 patients. Further randomized controlled trials should be done to further evaluate our finding.

REFERENCES


Listeriosis, a food borne disease caused by a Gram-positive rod called Listeria. The bacterium can grow over a wide temperature range from 0-45 degree centigrade. Most of the bacteria do not grow well when temperature falls below 4°C, while Listeria can grow at refrigerating temperatures and it grows very well at -1.5 to -45°C. The dairy items are a good source of Listeria. In the 1st documented reports about fatal listeriosis cow’s milk was the source. Since the 1st documentation of food borne Listeriosis in 1981, many food borne outbreaks of L. monocytogenes have been reported all over the world. Listerialosis, may be non-invasive, can present as gastroenteritis. However invasive human listeriosis can be fatal and can manifest as menin-
goencephalitis, septicemia, still births, premature births, abortions.\textsuperscript{5} Mortality rate is 20-30 \% in early onset listeriosis, in high risk groups such as pregnant women, neonates, children, elderly and adults with underlying disease (AIDS, cancer, chronic hepatic disorder, diabetes, transplant patients, patients undergoing dialysis)\textsuperscript{6}.

Sufficient data regarding the occurrence of listeriosis and its antibiotic sensitivity pattern is not available in South East Asian countries. Moreover, the incidence of Listeria especially in boiled milk has not been studied well. In Pakistan few studies have been conducted regarding occurrence of Listeria in food. In a study conducted in Faisalabad the occurrence of Listeria monocytogenes in milk taken from various markets was studied.\textsuperscript{16}

The present study was designed to determine the presence of Listeria in boiled refrigerated milk samples and to see their antibiotic susceptibility pattern.

**METHODOLOGY**

This cross-sectional study was done in Microbiology section, Department of Pathology KEMU, Lahore, from November 2016-April 2017. Randomized, non-probability purposive sampling technique was used. Eighty samples of 25 ml of buffalo milk were taken by using 90\% Confidence level, 5\% margin of error and by taking expected percentage of Listeria in Buffalo milk as 8\%\textsuperscript{7} by using the following formula:

\[
n = \frac{Z_{\alpha/2}^2 \cdot P(1-P)}{d^2}
\]

The samples were taken directly from buffalo under direct supervision. The following inclusion and exclusion criteria were used.

**Inclusion criteria**

1. Buffalo milk boiled for 10 minutes
2. Refrigerated milk for 3 days from domestic and commercial refrigerators.

**Exclusion criteria**

1. Any milk other than buffalo milk.
2. Raw, non-refrigerated or frozen milk.

Forty samples were refrigerated in domestic refrigerators and 40 samples were kept in commercial ones after boiling. The samples were kept for three days at 2-8°C to see the growth of bacteria at refrigerating temperatures.

Samples were processed in Microbiology laboratory, Department of Pathology, on the same day after collection. The culture and sensitivity testing along with Gram staining and the required biochemical testing was performed by following the standard techniques described by Clinical laboratory standards institute (CLSI).\textsuperscript{9} Each sample was inoculated onto the Listeria selective Oxford agar (Oxoid) and incubated at 35 °C for 48 h.\textsuperscript{8}

Isolation techniques used for Listeria separation from milk were the techniques recommended by the International Organization for Standardization and the French association for standardization.\textsuperscript{9} The colony characteristics like size, color, shape, margin, and elevation were assessed by examining for typical Listeria colonies. Gram staining was done. Biochemical Identification was done by catalase test, oxidase, Indole test, Methyl red and motility test.

The standard Kirby Bauer disk diffusion method on Mueller–Hinton agar was used for the antimicrobial susceptibility according to the standard reference procedure of the Clinical Laboratory Standards Institute (CLSI).\textsuperscript{10} The bacteria isolated were tested for their susceptibility to the following antimicrobial drugs: Gentamicin (10 µg), Ampicillin (10 µg), Imipenem (10 µg), Amoxicillin-clavulanic acid (30 µg), Ciprofloxacin (5 µg), Ceftriaxone (30 µg), Chloramphenicol (10 µg), Nalidixic acid (30 µg), Trimethoprim-Sulfamethoxazole (1.25/23.75 µg), and Tetracycline (30 µg). The results were interpreted after 24 hours of incubation. The zone diameter for each antibiotic was translated into susceptible and resistant categories according to the interpretation table given by CLSI.\textsuperscript{11,12}

Data entry and analysis was done by using SPSS 23 version. Qualitative data (milk samples from domestic and commercial refrigerators, presence of Listeria,) was presented by using frequency
tables and percentages. Comparison of contamination in milk from domestic and commercial refrigerators was done by using Fisher exact test, P-value<0.05 was taken as significant.

RESULTS

Total 80 milk samples 40 kept in Domestic & 40 in commercial refrigerators were studied. Listeria was isolated in 3 (4%) out of 80 samples. While remaining 77 (96%) of the samples showed no growth. Out of three positive samples, one was from domestic and the other 2 samples were from commercial refrigerators. However no statistically significant association was seen of Listeria in terms of domestic and commercial refrigeration of milk. i.e., p-value>0.999. (Table-1)

Antibiotic susceptibility pattern of Listeria monocytogenes was also determined for various antibiotics. The antibiotic susceptibility pattern of positive samples from both domestic and commercial sources was the same. (Table-2)

DISCUSSION

Results of present study are in accordance with many past studies; conversely, it is also contrary to some previous studies. In our study we found 3(4%) samples positive for Listeria monocytogenes while Shantha et al in her short communication reported the occurrence of Listeria in the milk samples as 0.76%. The occurrence of Listeria monocytogenes in milk taken from various markets was determined in conducted in Faisalabad. According to this study 9 (2.25%) samples showed presence of Listeria monocytogenes and 30 (7.5%) showed Listeria spp. An Iranian study showed that 1.6% of the investigated milk samples were positive for L. monocytogenes. 15 Rahimi et al determined Listeria species prevalence in ovine, bovine, camel, capri and buffalo milk in Iran. According to their study, the highest occurrence of Listeria was in buffalo milk (11.8%). raw bovine milk showed 10.6%, raw ovine milk was 7.1%, and raw caprine milk showed 4.2% samples positive.

Conversely, one study from Portugal showed 16.7% of L. monocytogenes was isolated from milk samples refrigerated commercially.

In a study conducted by Sanlibaba et al., it was shown that out of 51 isolates from milk, 13 (25.49%) isolates were verified as L.monocytogenes. L. monocytogenes was isolated from milk and curd milk in Algeria. Prevalence of L. monocytogenes was reported to be 2.61% from farm milk samples, 7.5% from tanker milk and 0.5% from curd milk. L.monocytogenes was isolated from 36% of all the studied samples (58 percent of market raw milk, 36% of Bulk tank milk, 28% of Damietta cheese and 24% of Kareish cheese) in a study conducted by AL-Ashmawy et al from Egypt. The occurrence of Listeria spp. was found in milk samples of bovine origin (16.2%) by A. AL-Mariri from

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**Table 1:** Contamination of Listeria species in domestically and commercially refrigerated buffalo milk

<table>
<thead>
<tr>
<th>Listeria</th>
<th>Domestic</th>
<th>Commercial</th>
<th>Total</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>1(2.5%)</td>
<td>2(5%)</td>
<td>3</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Negative</td>
<td>39(97.5%)</td>
<td>38(95%)</td>
<td>77</td>
<td></td>
</tr>
</tbody>
</table>

Total 80  

Note: (*): Fisher Exact test was applied. This test is employed when sample sizes are small, but it is valid for all sample sizes. It is used to examine the significance of the association between the two kinds of categorical data.

**Table 2:** Antibiotic Resistance Pattern for Positive Samples of Milk for Listeria Species in Domestically and Commercially Refrigerated Buffalo Milk

<table>
<thead>
<tr>
<th>Sn</th>
<th>Antibiotics</th>
<th>Commercial Sample 1</th>
<th>Commercial Sample 2</th>
<th>Commercial Sample 3</th>
<th>Domestic Sample 1</th>
<th>Domestic Sample 2</th>
<th>Domestic Sample 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Gentamicin</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Ampicillin</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Imipenem</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td></td>
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</tr>
<tr>
<td>4.</td>
<td>Amoxicillin-clavulanic acid</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>5.</td>
<td>Ciprofloxacin</td>
<td>R</td>
<td>S</td>
<td>IS</td>
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<tr>
<td>6.</td>
<td>Ceftriaxone</td>
<td>R</td>
<td>R</td>
<td>R</td>
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<tr>
<td>7.</td>
<td>Chloramphenicol</td>
<td>S</td>
<td>S</td>
<td>IS</td>
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</tr>
<tr>
<td>8.</td>
<td>Nalidixic Acid</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td></td>
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</tr>
<tr>
<td>9.</td>
<td>Trimethoprim-sulfa meth oxazole</td>
<td>S</td>
<td>S</td>
<td>S</td>
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<tr>
<td>10.</td>
<td>Tetracycline</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Deepti N. Nayak from India reported that according to the type of milk, 12% (3/25) cow milk and 20% (5/25) buffalo milk samples contained Listeria spp. The probable justification for this divergence and incongruity could be due to the difference in isolation and culturing techniques, difference in study designs and difference in sample sources in different studies compared to our study.

Sambyal et al in his study reported that all Listeria isolates showed susceptibility to Ampicillin, Erythromycin, Amoxicillin Sulbactam, Levofloxacin, Enrofloxacin, Gentamicin and multidrug resistant to Cefixime, Amikacin, Cephalexin, Cefuroxime and Clindamycin. The susceptibility pattern of our study is similar to that of reported by Sambyal et al. Jamali et al in his study showed that the Listeria isolates were resistant to tetracycline (49.4%) and penicillin G (43.4%) but remained susceptible to gentamicin, vancomycin and rifampicin. In our study Listeria contaminated samples from both commercial and domestic sources showed resistance for tetracycline and gentamicin.

CONCLUSION
The present study concludes low occurrence of L. monocytogenes in boiled refrigerated milk indicating that properly boiled and refrigerated milk decreases the chances of listeria growth and subsequent risk of listeriosis. The antibiotic susceptibility testing showed Listeria monocytogenes is sensitive to number of available antibiotics providing a good choice of antibiotics to the physicians for the treatment of listeriosis.

Limitation of Study
This study showed low occurrence of Listeria in boiled refrigerated milk probably due to small sample size. With large sample size and longer duration of refrigeration, it can be further confirmed that whether its true low prevalence of Listeria or not.

Acknowledgments
The contribution of King Edward Medical University, Lahore is acknowledged in all aspects starting from supervisor, funds provision, statistical help and all other support staff help is acknowledged with gratitude.

Funding sources
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Conflict of interest
None

REFERENCES


Parasitic infestation, most prevalent in rural and urban communities in developing countries especially in tropical regions is a major public health issue globally causing significant morbidity especially anemia.\(^1\) There is a high morbidity and mortality rate due to these helminthic infections in children cause among developing countries.\(^2\)\(^3\) Due to mildly humid and warm climate with heavy rains in these tropical regions the helminthes parasites have a favorable breeding grounds especially gastrointestinal helminthic infestation flourish in humid temperature were high humidity and poor sanitation and dirty potable water along with overcrowding play important role.\(^2\)\(^4\) Major risk factors for parasitic infections are a large family size, overcrowding, poor environmental sanitation, low quality drinking water, low level of education and lack of health educational programmes.\(^4\)

There are around 3.5 billion people worldwide are suffering from parasitic infestations and almost 450 million constitutes morbidity and mortality.
with majority being children among them. The prevalence of parasitic intestinal infestation geographically including south east Asian region. School and preschool children are at greater risk of Ascaris lumbricoides. Ankylostoma duodenale is more prevalent in the South East Asia region, the Indian subcontinent, North and Central America and different regions of Europe.2,3,5 Parasitic infections are still a public health hazard even in developed countries like USA and UK.7 WHO estimate prevalence of Ascaris lumbricoides around 800-1000 million and 700-900 million cases of Trichuris trichiura worldwide with helminthes with transmission by soil more prevalent affecting almost 1/6th of the global population. Infection with Hookworm is a leading cause of iron deficiency anemia due to intestinal blood loss.a Ascaris lumbricoides infestation present as gastrointestinal obstruction and perforation and leading cause of death. Trichuris trichiura infection among children causes physical and mental retardation along with anemia while infection with both round and whip worms is major cause of protein energy malnutrition among children.7 These infestations with helminthes impairs cognitions and hinders learning abilities of the children and anemia is most significant findings among these cases with intestinal parasites. Several studies have shown a significant association between anemia and intestinal helminthes among pre-school and school going children. Beside this these Intestinal helminthes infections makes children more vulnerable to communicable diseases.3,5,9 The rationale of this study on various intestinal helminth infestation presenting in our tertiary care hospitals is a pre-requisite not only for delineating guidelines and formulate control strategies but also evaluate risk of vulnerable communities.

The objectives of the study was to assess the frequency and type of helminthes infestation among children up to 12 years of age presenting in tertiary care hospitals

**METHODOLOGY**

A cross sectional study was performed at Mayo, children and Ittefaq hospitals of Lahore. A total of 250 stool and blood samples of children upto 12 years of age were taken and examined. After collecting the demographic information the stool samples were inspected by the direct smear and flotation methods. A consultant microbiologist identified helminthes eggs on morphological characteristics. Hematology analyzer (Sysmex KX-21N) was used to assess hemoglobin level of children. Grading of anemia was done according to the WHO guidelines.

**RESULTS**

Of the total 250 stool samples from children examined from different hospitals of Lahore. 29 (11.6%) samples were found infective. Out of these 29 samples tested, 8 (27.6%) were of Hymenolepis nana, 6 (20.7%) were of tenia saginata, 13 (44.8%) were of Ascaris lumbricoides and 2 (6.9%) were of ancylostoma duodenale. (Table no:1). High positivity rate of sample were between 7-8 years of 16.3% and 11–12 years of 17.5%. (Table no:2). 64.4% of sample were from Mayo hospital Lahore. (Table no: 3).

**DISCUSSION**

This study evaluated intestinal helminthes infestations among children presenting in pediatric ward in tertiary care hospital. The stool samples were examined for intestinal parasites by direct microscopic and floatation techniques similarly by study done by Sehgal et al, (2010).10

Our study findings showed that intestinal helminthic infestations among children presenting
to main tertiary care hospitals in Lahore were mainly water borne infestation and major contributing factor is a poor sanitary conditions in homes. Our study found out the prevalence of intestinal parasitic infec-
tions of 11.6%, similar to the prevalence rate of 8.4% in a study by Aly and Mustafa, (2010). Legesse and Erko in their study showed 83.8% had one or more parasites. Prevalence of hookworm was the highest 60.2%, 21.2%, Trichuris trichuria 14.7%, Taenia spp. 13.9%, Entamoeba histolytica 12.7%, Ascaris lumbricoides 6.2%, and Strongyloides stercoralis of 5.8%. Fernandez et al, (2002), examined stool samples both in rural and urban areas, found an overall prevalence of intestinal parasites was 91%. Ascaris lumbricoides was the most common helminthic parasite detected (52.8%) followed by Trichuris trichura (45.6%), Ankylostoma duodenale (37.6%), Strongyloides stercoralis (3.2%) in rural settng.

Table 2: Prevalence of Helminth Infections in Children According to Age and Gender

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Sample Examined</th>
<th>Sample infected Freq. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-3</td>
<td>Male</td>
<td>16</td>
<td>1 (6.25%)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>14</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>3-4</td>
<td>Male</td>
<td>20</td>
<td>2 (10.0%)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>16</td>
<td>1 (6.3%)</td>
</tr>
<tr>
<td>5-6</td>
<td>Male</td>
<td>29</td>
<td>4 (13.8%)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>20</td>
<td>2 (10.0%)</td>
</tr>
<tr>
<td>7-8</td>
<td>Male</td>
<td>17</td>
<td>5 (29.4%)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>26</td>
<td>2 (7.7%)</td>
</tr>
<tr>
<td>9-10</td>
<td>Male</td>
<td>25</td>
<td>4 (16.0%)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>27</td>
<td>1 (3.7%)</td>
</tr>
<tr>
<td>11-12</td>
<td>Male</td>
<td>29</td>
<td>4 (13.8%)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>11</td>
<td>3 (27.3%)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>250</td>
<td>29 (11.6%)</td>
</tr>
</tbody>
</table>

Table 3: Prevalence of Helminth Infections Presented in Children in Different Hospitals of Lahore

<table>
<thead>
<tr>
<th>Name of Hospital</th>
<th>Sample Examined</th>
<th>H. nana Freq. (%)</th>
<th>T. saginata Freq. (%)</th>
<th>A. lumbricoides Freq. (%)</th>
<th>A. duodenale Freq. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mayo Hospital</td>
<td>161</td>
<td>7 (28.0%)</td>
<td>5 (20.0%)</td>
<td>12 (48.0%)</td>
<td>1 (4.0%)</td>
</tr>
<tr>
<td>Ittefaq Hospital</td>
<td>54</td>
<td>1 (1.9%)</td>
<td>0 (0.0%)</td>
<td>1 (100.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Children Hospital</td>
<td>35</td>
<td>3 (8.6%)</td>
<td>1 (33.3)</td>
<td>0 (0.0%)</td>
<td>1 (33.3%)</td>
</tr>
<tr>
<td>Total</td>
<td>250</td>
<td>8 (27.6%)</td>
<td>6 (20.7%)</td>
<td>13 (44.8%)</td>
<td>2 (6.9%)</td>
</tr>
</tbody>
</table>

is in accordann and a 40% infestation with Ascaris lumbricoides. Our study showed a pre-va-lence of Ankylostoma duodenale of 6.9% and prevention of these helminthes infestation depend on promotion of solid and liquid waste disposal, a clean potable water supply and wearing of shoes at all times by children during play are recommended. 

CONCLUSION

Infectivity rate among children is low for para-sitic infestation but tenia saginata has a high infes-
tation rate among other parasites.

Acknowledgments

We are grateful for department of Pathology, microbiology section of Mayo Hospital, Children Hospital and Ittefac Hospital for processing samples collected by the researchers. We would like to appreciate hospital ethical review board of above men-tioned hospitals for providing us opportunity for data collection and sampling.

Limitations of the study

There are a few limitations or constraints in our research. The data was obtained from three pediatric units of tertiary care hospitals results cannot be generalized to popu-
lation. The study used cross-sectional design of study and because of this we were not able to esta-
lish causation between study variables used in our research. Another drawback of this study was small sample size.

Conflicts of interests

None

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Authors contributions

Following participants r contributed in research

Dr. Sharjeel Akhtar: Principal investigator, data collection and discussion writing

Dr. Fareed Ahmad: Afzal Co-investigator, data collection and discussion writing
FREQUENCY OF INTESTINAL HELMINTHES INFESTATIONS AMONG CHILDREN PRESENTING IN PEDIATRIC WARD

collection and discussion writing

Dr. Mamoon Akbar Qureshi: Data analysis and report writing

REFERENCES

Acne is a chronic inflammatory disease of the pilosebaceous glands which affects almost 80% of the population at some point in their lives. It presents with formation of comedones, papules, pustules and nodules. Lesions appear mostly on the face, but can also involve neck, chest, upper parts of back, and shoulders. It is influenced by four main factors which are increased sebum production, hypercor-
questionnaire which was first published in 1994. The DLQI is designed to measure the health-related quality of life of adult patients suffering from a skin disease. It contains ten questions which measure the impact of skin disease on different domains of life of an affected person.

The effect of acne on the quality of life has been studied both internationally and locally. According to a study conducted in Iran in 2011, the effect of acne severity on quality of life was small/none in 48.2% of patients, moderate in 33.6%, very large in 16.8% and extremely large in 1.4% of patients, with \( r = 0.32 \). Another study conducted in Saudi Arabia in 2010 showed no correlation between acne severity and quality of life \( (r = 0.145) \). Study conducted by Vilar et al. in Brazil in 2014 also showed weak correlation with \( r = 0.197 \).

The present study was planned to evaluate the relationship between acne severity and its impact on quality of life in our population. In a disease like acne whose treatment requires greater patient compliance, the effect on quality of life needs to be ascertained early on. Patients’ perception of the disease thus might be an important consideration in the evaluation and treatment of acne vulgaris, leading to better patient care.

**METHODOLOGY**

This was a cross-sectional study conducted at Dermatology department unit I, Jinnah hospital, Lahore from June 2018 to December 2018. A total of 200 patients with a diagnosis of acne vulgaris, of both genders, with ages between 16 and 40 years, and not having any systemic, dermatologic or psychological comorbidity were enrolled in the study. Verbal informed consent was taken. Global Acne Grading System (GAGS) was used to measure the severity of acne.

The data was collected on a structured proforma, recording demographic data i.e. age, gender, and educational status, duration of acne, GAGS score and DLQI score.

Quality of life (QOL) was measured by a valid, Urdu translated version of dermatology life quality index (DLQI). This Index is a general questionnaire which contains 10 questions involving 6 sections: symptoms and feelings, daily activities, leisure, work and school, personal relationships and treatment. Each question has four options, with answers having maximum score of 3 and minimum of 0. The total score of DLQI is between 0 and 30 and the higher the score, the more QOL is impaired.

All the collected data was entered and analyzed through SPSS version 20.0.

**RESULTS**

The mean age of patients was 23.37±4.63 years. Majority \( (n=156, 78.0\%) \) of the patients were aged between 16-28 years. There were 68 (34.0%) male and 132 (66.0%) female patients with a male to female ratio of 1:1.9. The duration of disease ranged from 1 year to 8 years with a mean of 4.13±1.60 years. The educational status of the patients showed that majority \( (n=80, 40.0\%) \) were educated up to matriculation, while only 7.5% \( (n=15) \) and 7.0% \( (n=14) \) were graduates and post-graduates respectively. (Fig 1).

Regarding the severity of the disease, it was seen that 66 (33.0%) patients had moderate while 59 (29.5%) patients had severe acne. Mild and very severe acne was observed in 19.0% and 18.5% of the patients respectively. (Fig 2, 3, 4.)

The DLQI scores ranged from 2 to 23 with a mean of 10.34±6.05. It was seen that 73 (36.5%) patients reported very large effect of acne on quality of life followed by 60 (30.0%) patients who reported moderate effect. Fifty five (27.5%) patients reported small while 12 (6.0%) reported extremely large effect of acne on quality of life (Table 1). It was observed that the greater the severity of acne, the greater was the effect on quality of life. In patients having small effect on quality of life, 94.5% had mild or moderate acne. In patients having extremely large effect on quality of life, 91.6% had severe or very severe acne. (Table 1) When correlated, there was significantly strong positive correlation between the severity of acne and DLQI score across all ages, genders, duration of disease and educational
DISCUSSION

Dermatological diseases have a greater psychosocial impact as compared to other systemic diseases. Significant psychological and social distress may cause depression, anxiety and fear of stigmatization. It can also affect patients' occupational lives. Diseases that involve exposed areas of body and especially during certain periods of life are more likely to adversely impair quality of life. Acne vulgaris is one such disease as it involves facial area and is usually seen during period of adolescence. Several studies have shown that quality of life in patients with acne vulgaris was adversely affected, compared to normal population\(^{[2,4,5]}\). However, there was little local published data which necessitated the present study.

The objective of this study was to determine the correlation between acne severity and quality of life using dermatology life quality index (DLQI). It was a cross-sectional study over a period of 6 months. This study involved 200 patients of both genders aged between 16-40 years with a mean age of 23.37±4.63 years and a male to female ratio of 1:1.9. Takahashi et al. (2006) in a similar study among Japanese patients of acne vulgaris observed mean age of 24.8±7.4 years with much higher female predominance\(^{[10]}\) (1:3.4). Safizadeh et al. (2011) observed mean age of 22.05±4.38 years with male to female ratio of 1:4.6 among Irani patients.\(^{[2]}\)

Table 1: Frequency Table for Effect of Acne on Quality of Life \(n=200\)

<table>
<thead>
<tr>
<th>Effect of Acne on Quality of Life (DLQI Score)</th>
<th>Mild</th>
<th>Moderate</th>
<th>Very Severe</th>
<th>Frequency n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small (2-5)</td>
<td>24</td>
<td>28</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Moderate (6-10)</td>
<td>4</td>
<td>25</td>
<td>22</td>
<td>9</td>
</tr>
<tr>
<td>Very Large (11-20)</td>
<td>9</td>
<td>10</td>
<td>34</td>
<td>20</td>
</tr>
<tr>
<td>Extremely Large (21-30)</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>37</td>
<td>64</td>
<td>62</td>
<td>37</td>
</tr>
</tbody>
</table>

Table 2: Correlation between Severity of Acne and DLQI Score across age groups, gender and duration of disease \(n=200\)

<table>
<thead>
<tr>
<th></th>
<th>Mild ((n=38))</th>
<th>Moderate ((n=66))</th>
<th>Severe ((n=59))</th>
<th>Very Severe ((n=37))</th>
<th>Spearman's Correlation</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean DLQI Score</td>
<td>6.32±5.11</td>
<td>7.92±5.41</td>
<td>12.63±4.51</td>
<td>15.11±5.52</td>
<td>0.555**</td>
<td>0.000</td>
</tr>
<tr>
<td>Age Groups</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16-28 years ((n=156))</td>
<td>6.50±5.24</td>
<td>7.58±5.29</td>
<td>12.70±4.18</td>
<td>15.11±5.37</td>
<td>0.558**</td>
<td>0.000</td>
</tr>
<tr>
<td>29-40 years ((n=44))</td>
<td>5.63±4.84</td>
<td>9.21±5.85</td>
<td>12.33±5.84</td>
<td>15.10±6.23</td>
<td>0.552**</td>
<td>0.000</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male ((n=68))</td>
<td>6.90±4.54</td>
<td>7.63±5.32</td>
<td>12.73±4.34</td>
<td>15.38±5.32</td>
<td>0.534**</td>
<td>0.000</td>
</tr>
<tr>
<td>Female ((n=132))</td>
<td>5.67±5.74</td>
<td>8.10±5.52</td>
<td>12.60±4.59</td>
<td>14.96±5.74</td>
<td>0.540**</td>
<td>0.000</td>
</tr>
<tr>
<td>Duration of Disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-4 years ((n=119))</td>
<td>7.19±5.85</td>
<td>7.83±5.61</td>
<td>13.35±4.65</td>
<td>16.16±4.35</td>
<td>0.556**</td>
<td>0.000</td>
</tr>
<tr>
<td>5-8 years ((n=81))</td>
<td>5.24±3.93</td>
<td>8.08±5.16</td>
<td>11.41±4.07</td>
<td>14.00±6.48</td>
<td>0.550**</td>
<td>0.000</td>
</tr>
</tbody>
</table>

**. Correlation is significant at the 0.01 level (2-tailed).
The DLQI Score in our study population ranged from 2 to 23 with a mean of 10.34±6.05. When correlated, there was significantly strong positive correlation between the severity of acne and DLQI score ($\rho=0.555$, $p=0.000$). The mean DLQI score was found to be higher in our patients (10.34) when compared to Durai et al (6.9). The reason could be due to differences in ethnicity and wider age range of our patients. However they reported a similar correlation between disease severity and DLQI score ($r=0.3034$; $p=0.003$) [12]. Takahashi et al. (2006) also observed significantly strong positive correlation ($r=0.91$; $p<0.05$) between severity of disease and DLQI score [10]. Similar correlation was observed by Safizadeh et al. (2011) between disease severity and DLQI score ($r=0.315$; $p=0.01$) [2].

Kokandi et al. in 2010 however did not observe any significant correlation between disease severity and DLQI score ($r=0.145$, $p=0.127$) [4]. Ilgen et al. (2005) in a previous report also documented that there was no correlation between disease severity and DLQI score. Similarly Yap et al. (2012) reported very poor correlation between disease severity and DLQI score ($r=0.27$; $p=0.001$) in Malaysia [11]. This can be due to the limited sample size of these studies as well as selection bias as only female students were included by Kokandi et al. [4]. Ilgen et al. also included limited number of patients (n=108) with younger age (range 16-29 years) [8].

Duration of disease and educational status were not recorded in most of these studies, which is a point unique to this study. In our study, majority of the patients (59.5%) had the disease for 1-4 years. Chronic disease generally has a greater impact on the quality of life of the patient. However, there was no statistically significant difference in the DLQI between patients with varying duration of disease observed in our study. We also recorded the educational status of the patients. Education level also is thought to affect the disease related quality of life of patients, as the higher the education, the better the patient is able to cope with the effects of disease and tolerance of the treatment. However, in our study it was seen that DLQI was positively associated with disease severity only, regardless of the educational status of the patients.

The present study has found significantly strong positive correlation between severity of acne and DLQI score. This suggests that patients presenting with severe disease should be assessed by DQLI score to detect impairment of quality of life early on. Furthermore, optimal measures should be taken to improve the quality of life among such patients not only by pharmacologic treatment of disease but helping the patient better cope with the psychological and social effects of disease. For this a multidisciplinary approach including help from psychiatrists, psychologists, and other mental health professionals can be sought if required.

Limitations of our study are that only patients visiting our outpatient department were included. The translated DLQI questionnaire which was used measured impaired quality of life only. Depression, anxiety and other psychological problems need to be diagnosed by specialized tools as well as psychiatric consultations. Also these patients were not followed up to see if DLQI improves after effective treatment.

CONCLUSION

In the present study, significantly strong positive correlation was found between severity of acne and DLQI score regardless of patient’s age, gender, educational status and duration of disease. Physicians need to be aware of the psychosocial implications of acne so that early diagnosis and prompt treatment can be started.

Limitation of study

Limitation of this study is that only patients presenting to our outpatient department were included.

Acknowledgements

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Conflict of Interest

The authors declare they have no conflict of interest.
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Stigma is defined as a mark of embarrassment, shame or dissatisfaction resulting in forbiddance, differentiation and omission of a person from being involved in various areas in the society. Social stigma related to mental illnesses is an important on-going issue being seen all around the world especially because of its increased prevalence in medical students. Such social stigmas can be divided into 1) perceived public stigma (society’s beliefs about mental illness), 2) personal stigma, (person’s opinion about mental illnesses) and 3) self-stigma (Individual’s opinion and belief on his/her own mental illness).

Approximately 1 in 4 Americans believe that psychiatric medications are damaging to the body and about 1 in 3 believe that these medications affect with one’s daily routine. Medical students and doctors in general are unwilling to seek advice because of the fears related with secrecy and stigma associated with mental illness and not because of psychiatric medication. In a study conducted in Canada, Kassam el Al, which compared different professional groups including medical students, physicians and psychiatric nurses, it was found out that they had more stigmatizing attitudes as compared to other people.

Pakistan has inadequate resources in health

SOCIAL STIGMAS RELATED TO MENTAL ILLNESSES IN MEDICAL STUDENTS OF ALLAMA IQBAL MEDICAL COLLEGE, LAHORE

Muneeza Arshad,1 Maryam Ejaz,2 Meerub Sohail,3 Nabeela Sarwar,4 Noor-ul-Huda Niazi,5 Naheed Pirzada6

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Abstract

Objective: The study was conducted to find the knowledge, attitude and perception regarding social stigmas related to mental illnesses particularly among the medical students of Allama Iqbal Medical College (AIMC).

Methodology: A cross-sectional study, conducted at Allama Iqbal Medical College, Lahore for one month via structured questionnaires distributed among the medical students of AIMC. The data was entered and analyzed by using SPSS version 17.0

Results: A total of 250 samples, all medical students were evaluated. Majority of the medical students 221(88.4%) out of 250 respondents knew about social stigmas related to mental illnesses. According to 103(43.02%) and 100(40.00%) respondents, social stigmas and lack of awareness hinders psychiatric patients from seeking help, respectively. Even with good knowledge about social stigmas and positive attitude towards mentally ill, medical students are reluctant to seek advice for themselves when suffering.

Conclusion: Majority of the medical students of AIMC were well aware of such stigmas. However, they had less help seeking behavior for their own mental issues which highlights the need to investigate the causes for this hindrance. More should be done for raising awareness and directing mass population to get treatment for any mental illness to curb the long-term effects of social stigmas.

Key Words: social stigmas, mental illnesses, medical students

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Acceptance Date: 22-03-2021
sector with a few number of psychiatrists. Moreover, Pakistanis have strong belief in black magic, evil eye and possession by evil spirits (demons). And whenever a person suffers from a mental illness, the very first thought that arises in these people is that the person is either possessed by a Jinn or is under an influence of a black magic. This social stigma makes it further worse for people to seek psychiatric help.

The high prevalence of depression worldwide in youth and the undergraduate medical students, highlights the need to investigate their help-seeking behavior and factors that may act as barrier to their help seeking. The objective of our study is to explore the knowledge, attitude and practice of students of Allama Iqbal Medical College towards social stigmas and their association with mental illnesses. The objective of the study was to assess the association of social stigmas related to mental illnesses, their Knowledge, Attitude and Perception in the medical students of AIMC.

METHODOLOGY
Study Design:
Descriptive cross-sectional study

Study Setting:
Allama Iqbal Medical College, a public school of medicine, nursing and allied health sciences located in Lahore, Punjab, Pakistan. It is affiliated with Jinnah Hospital, Lahore.

Duration of Study:
One month (April 2018-May 2018)

Sample Size:
250 medical students

Sampling Technique:
Non-probability–Purposive Sampling Technique

Sample Selection:
Inclusion Criteria: Students enrolled in MBBS program who agreed to participate in the study.
Exclusion Criteria: Non-compliant and non-cooperative students of MBBS program.

Data Collection and Analysis Procedure:
Individual consent was obtained orally before the questionnaires were given, ensuring confidentiality. Socio-demographic information which includes age, education, socioeconomic status and other relevant information was collected by using a structured questionnaire. The data was entered and analyzed by using SPSS version 17.0 statistical software. Using the same software, results were drawn using frequency and percentage with the help of simple tables, pie chart and bar graphs.

RESULTS
A total of 250 medical students filled the questionnaire reasonably out of the 265 questionnaires being distributed making the response rate 94.3%.

The sociodemographic characteristics of the respondents showed that 46(18.4%) respondents were the medical students of 1st year, 53(21.2%), 47(18.8%), 56(22.4%) and 48(19.2%) were from 2nd year, 3rd year, 4th year and final year respectively based on the filled questionnaires received. There were 101(40.4%) respondents who fell in the category of age less than or equal to 20 and 149(59.6%) in the category of age greater than 20 years. Female respondents were 132(52.8%) and males were 118(47.2%).

Study revealed that majority of the medical students 221(88.4%) out of 250 knew about social stigmas related to mental illnesses and 222(88.8%) had seen at least someone suffering from mental illness. The significant finding as summarized in table 1 was that even though majority of students considered it like any other illness still 190(76.0%) respondents believed that mentally ill people are more likely to harm others than normal people.

Regarding attitude of the medical students towards social stigmas as summarized in table 2, most of the medical students 108(43.20%) think social stigma as a barrier in seeking help by patients. Aside from social stigma, “lack of awareness” is the second major reason behind hindrance in help seeking behavior as thought by 100(40%) students. On the other hand, 11(4.40%) students believe financial problems are the cause while 24(9.60%) students
picked all the causes, a reason of hindrance and 7(2.80%) thought that there are some other causes behind the hindrance.

When medical students were asked about the possible causes of mental illnesses, their responses were that out of 250, 147(59.27%) considered chemical imbalances and 13(5.24%) believed possession by evil spirits, is the cause of mental illness. 4(1.61%) said that both chemical imbalances and possession by evil spirits is the cause, while 7(2.8%) considered mental illness as a punishment from God. According to large number of people 77(31.05%), none of the causes state dare the basis of mental illness.

According to the respondents, such stigmas could be overcome by awareness 67(26.8%) social support 71(28.4%), self-motivation 38(15.2%), positive attitude from senior doctors 28(11.2%), awareness/social support/ self-motivation all 42(16.8%) or nothing would help them 4 (1.6%) as these are deeply rooted and collective effort is needed for this purpose to curb their effects.

### Table 1: Knowledge of Students Regarding Social Stigmas and Mental Illnesses

<table>
<thead>
<tr>
<th>Finding term, psychological disorder embarrassing?</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>151</td>
<td>60.4</td>
</tr>
<tr>
<td>Yes</td>
<td>99</td>
<td>39.6</td>
</tr>
<tr>
<td>Total</td>
<td>250</td>
<td>100.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Helping your peers seeking support when ill?</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>32</td>
<td>12.8</td>
</tr>
<tr>
<td>Yes</td>
<td>218</td>
<td>87.2</td>
</tr>
<tr>
<td>Total</td>
<td>250</td>
<td>100.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Willing to:</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study or work with someone with mental illness</td>
<td>55</td>
<td>22.0</td>
</tr>
<tr>
<td>Befriend mentally ill people</td>
<td>133</td>
<td>53.2</td>
</tr>
<tr>
<td>Marry a mentally ill person</td>
<td>10</td>
<td>4.0</td>
</tr>
<tr>
<td>No connection with mentally ill people</td>
<td>26</td>
<td>10.4</td>
</tr>
<tr>
<td>Befriend, study or work with someone with mental illness</td>
<td>26</td>
<td>10.4</td>
</tr>
<tr>
<td>Total</td>
<td>250</td>
<td>100.0</td>
</tr>
</tbody>
</table>

### Table 2: Attitude of Students Towards Social Stigmas Regarding Mental Illnesses

<table>
<thead>
<tr>
<th>Helping your peers seeking support when ill?</th>
<th>Frequency</th>
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</tr>
<tr>
<td>Total</td>
<td>250</td>
<td>100.0</td>
</tr>
</tbody>
</table>

### Figure 1: Reasons behind the hinderance in seeking help among psychiatric patients

### DISCUSSION

Mental illness is the cause of high morbidity and mortality around the world and carries a significant stigma. Social Stigma associated with mental illnesses is a prevalent phenomenon that has a negative influence on people with mental illnesses. Hence, not only does the mental illness itself makes their life harder but also the social stigma associated with them by the society. Knowing how social...
stigmas related to mental illnesses affect our society through various ways is essential to properly cure and eradicate these illnesses from our society. This was a KAP study conducted to understand knowledge, attitude and perception of such stigmas related to mental illnesses in medical students of AIMC.

In this study, majority of the medical students (88%) knew about social stigmas and 57% medical students considered mental illnesses like other body illnesses yet 76% of the medical students believed that mentally ill patients are more likely to harm others than normal people, indicating how much dominant Social stigmas are in our society. According to Elliot and colleagues, social stigmas related to mental illnesses socially prohibits a mentally ill by the Society. They are perceived as embarrassment and danger which leads to their elimination from the society (Elliott et al., 1982). A related study in Sri Lanka showed that stigma is a highly complicated and complex concept.

Medical Students who were embarrassed by the term ‘psychological disorder’ were 39.6% and only 4% would be willing to marry someone with a mental disorder. In a related cross-sectional study conducted in Singapore concluded that one-fifth of the students wouldn’t want to have someone with a mental illness. This indicated the attitudes of the people towards social stigmas and people with mental illnesses and how such people are ignored most of the times. This is further convinced in our study by 40% of the students who believed that ‘lack of awareness’ is what hinders psychiatric patients from seeking help. Thus, it can be concluded that the society put forth a mixture of damaging attitudes, unawareness and discernment towards mentally ill people.

Depression is another mental illness that occurs in many people around the world. Regardless of the belief that doctors should be ‘invincible’, mental problems are predominant in them. In a related research, 30% of the medical students might suffer from depression. So, we considered asking medical students about their personal experience of any mental illness or depression. It is seen that doctors and medical students rarely seek psychiatric help when they suffer from mental illnesses and only present themselves to psychiatrists when things go out of hand.

Most of them do not seek medical help because depression is perceived as a stigmatizing illness which also leads to self-stigma. In our study, 53.2% of the medical students suffered from depression and only 36.09% of them sought psychiatric help. And those who didn’t seek help, showed reluctance due to social stigmas (almost 16%) and due to psychiatric help’s insignificance (48%), showing how much a mark of disgrace mental illnesses are considered.

Moreover, presence of social stigmas related to mental illnesses was also found associated with socioeconomic status as 86% of the Medical Students belonged to Middle Class.

According to our research, almost 77% medical students believed that further treatment may be required for a mental illness once treated already. Hence, trusting that mental illnesses are curable is as having only few stigmas related to mental illnesses.

Social stigmas related to mental illnesses in medical students could be overcome by awareness as voted by 26.8% students, by self-motivation as voted by 15.2% students and mainly by social support as voted by 28.4% Students. It is noted that reliable adults are recognized as main helpers in help-seeking process and the choice of informal help may be a better option than psychiatrists.

Overall in our study, we found out that majority of medical students have positive attitudes and are aware of social stigmas surrounding mental illnesses.

LIMITATIONS

• Confinement of research to a small geographical area i.e. Allama Iqbal Medical College, so it led to limitation of sample population and arousal of inaccuracy.
The time limit of one month might have led to the degree of inadequacy of the study.

CONCLUSION

The majority of medical students of AIMC were well aware of the social stigmas related to mental illnesses. Most of them had positive attitudes towards such patients. However, they had less help seeking behavior if the issue was about their own mental health. So more should be done in respect to the awareness of social stigmas related to mental illnesses, importance of seeing a psychiatrist and receiving treatment for any mental illness to reduce the mass effect of stigmas on general population considering the fact that they have a detrimental effect on health care providers too.

REFERENCES


ROLE OF MISOPROSTOL AND MEFANEMIC ACID IN THE MANAGEMENT OF MENORRHAGIA

Aalia Tayyba,¹ Minaam Farooq,² Muhammad Ehsan,³ Muhammad Ayyan,⁴ Mukarram Farooq,⁵ Uswah Ilyas⁶

Abstract

Objective: To find out the efficacy of Misoprostol and Mefenamic acid in the management of menorrhagia and associated dysmenorrhea.

Methodology: The study was conducted at Kishwar Fazal Teaching Hospital, Sheikhupura and Fatima Memorial Hospital Lahore, from April 2018 to August 2019. 120 patients belonging to age group of 20 to 40 years are included in the study. The patients are randomly divided in two groups, group A and group B. Group A received misoprostol 200 microgram three times a day and Group B received Mefenamic acid 500 mg three times a day during first four days of periods for 3 consecutive menstrual cycles. Duration of cycle, bleeding pattern and volume of blood loss was assessed according to the pictorial blood assessment chart (PBAC), hemoglobin, hematocrit and number of pads used were taken into account. Side effects caused by both drugs were also noted. All data analyses were performed using Statistical Package for the Social Sciences (SPSS) software, version 26. T-test and chi-square test were performed. p value < 0.05 is significant.

Results: The study showed that blood loss volume in menstruation per day in mfenamic acid group was 120.60 ± 20 mL before treatment which decreased to 50.70 ± 26.91 ml after treatment (p=0.002). Misoprostol group reduced menstrual blood loss from 137.57 ± 36.90 ml per day to 51.60 ± 34.18ml (p=0.003). Duration of menstrual blood loss in group A was 9.20 ± 3.10 which was reduced to 7.20 ± 2.09 days after treatment (p=0.001) while in group B, menstrual period decreased from 8.35 ± 3.10 to 7.21 ± 3.15 days (p=0.002). The number of pads used by patients in mfenamic acid group before treatment were 21.18 ± 10.12 but after treatment, number noted was 13.23 ± 4.10 (p=0.003). In Misoprostol group, decrease in usage of pads was from 18.52 ± 4.16 to 13.76 ± 4.20 (p=0.001). Dysmenorrhea is not reduced significantly in misoprostol group (p= >0.05) but patients getting mfenamic acid showed marked improvement in lower abdominal discomfort and pain.( p= <0.05).

Conclusion: Both groups cause reduction in menstrual blood loss. Mefenamic acid is more effective in improvement of associated dysmenorrhea.

Key Words: Menorrhagia, Misoprostol, Mefenamic acid, Menstrual blood loss, Milliliters (ml), Pictorial Blood loss Assessment Chart (PBAC)
ROLE OF MISOPROSTOL AND MEFANEMIC ACID IN THE MANAGEMENT OF MENORRHAGIA

Anatomical abnormalities, infections, drugs, pregnancy complications, hematological disorders, medical and endocrine disorders, malignancy and obesity. Menorrhagia is a heavy but regular menstrual blood loss of more than 80 ml blood per vaginum in a normal menstrual cycle.\(^3\)\(^4\) Objective assessment of menstrual blood loss by alkaline haematin method is the best one, but it needs specialized and time-consuming techniques that are not available in routine. So, Higgham et al devised PBAC (Pictorial Blood loss Assessment Chart) which is used for objective assessment of blood loss. It is easy to use and has an important role in monitoring the treatment of menorrhagia. The specificity and sensitivity of pictorial score of 100 or more for diagnosis of menorrhagia is more than 80%.\(^1\)\(^3\) Once baseline score is established, the effectiveness of treatment is monitored by a decrease in score. Many studies have been reported.\(^4\)\(^5\) The causes of menorrhagia (heavy bleeding) are intrauterine and extrauterine. It may occur in the women without any pelvic pathology or medical disorder. If there is no pathological reason, then it may be due to a disorder of endometrial tissue. It is seen in different studies that an alteration in endometrial prostaglandin balance and increased endometrial fibrinolysis cause menorrhagia.\(^6\) Different treatment modalities are available like hormonal, non-hormonal and surgical. Among non-hormonal therapy, Antifibrinolytic agents and anti-prostaglandins are most commonly used for increased menstrual blood loss. Progestrone, oral contraceptive pills, levonorgestrel releasing intrauterine system are frequently used hormonal drugs.\(^7\) Prostaglandins increase bleeding by increasing vascular permeability and preventing platelets’ activity. So, prostaglandin synthetase inhibitors are used to decrease blood loss.\(^4\) Misoprostol is a strong uteronic agent and has a strong vasoconstrictive effect on uterine arteries but only a few studies are available on the role of misoprostol in menorrhagia.\(^10\)\(^11\) So, in this study the aim is to compare the efficacy and side effects of Misoprostol and Mefenamic acid in the treatment of heavy menstrual blood loss and dysmenorrhea.

METHODOLOGY

A total of 120 patients between the age of 20 to 40 years were included in the study and were randomly divided into 2 groups, A and B. Group A was given Misoprostol and Group B Mefenamic acid. Complete history was taken and physical examination was done. Patients with history of irregular menstrual cycle, intermenstrual and postcoital bleeding, any pelvic pathology, hepatic, cardiac, renal, metabolic, haematological, and vascular disorder were not included in the study. Transvaginal ultrasonography was done to rule out any pelvic pathology. Blood sugar level (BSL), Complete blood count (CBC), blood urea nitrogen (BUN), creatinine (Cr), thyroid stimulating hormone (TSH), bleeding time (BT), clotting time (CT), prothrombin time (PT), activated partial thromboplastin time (APTT), serum glutamic oxaloacetic acid transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT) were carried out to rule out other causes of bleeding. Women between age group of 20 to 40 years with complaint of menorrhagia were evaluated, menstrual blood loss was then assessed by PBAC (Pictorial Blood Assessment Chart). Patients with PBAC score of more than 100, normal pelvic examination and normal cervical cytology were selected for the study. Menstrual blood loss was assessed in one pre-treatment cycle by PBAC. A total of 120 patients were included in the study and randomly divided into 2 groups, A and B. Group A was given Misoprostol 200 microgram 3 times/day for first 4 days of menstrual cycle. 500 mg mefenamic acid 3 times/day was given to the patients in group B. The duration of drug intake was same in two groups and treatment continued for 3 cycles. Data was collected and analyzed with (SPSS) software, version 26. T-test and chi-square test were performed.

RESULTS

In the study 120 Patients divided in two groups A and B. Regarding demographic features i.e age,
parity, body mass index and endometrial thickness, there were no significant differences between the 2 groups.

The number of pads used by patients in group A (misoprostol gp) before treatment were 18.52 ± 4.16 and reduced to 13.76 ± 4.20 (p=0.001) and in group B (Mefenamic acid), this reduction is from 21.18 ± 10.12 to 13.23 ± 4.10 (0.001). The duration of menstrual blood loss in group A was 9.20 ± 3.10 which was decreased to 7.21 ± 3.15 days (p=0.001) while in group B, this alteration was 8.35 ± 3.10 to 7.21 ± 3.25 days (p=0.002). The volume of menstrual blood loss in misoprostol group (A) was 137.57 ± 36.80 ml/day before giving medicine and reduced to 51.60 ± 32.18 ml/day (p=0.003) and in mefenamic acid group (B), the reduction in blood loss was from 120 ± 20ml/day to 50.70 ± 26.91 ml (p=0.02). The improvement in dysmenorrhea in women of group A was from 6.60 ± 2.72 to 4.56 ± 2.34 after treatment (p=0.001). It seems that misoprostol could not reduce the severity of dysmenorrhea significantly. But the two agents acted effectively in reducing the duration of the menstrual blood loss and lowering the number of used pads.

Table 1: Demographic Features of Participants

<table>
<thead>
<tr>
<th>Demographic features</th>
<th>Misoprostol group (A)</th>
<th>Mefenamic acid group (B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>32 to 39 years</td>
<td>33 to 38 years</td>
</tr>
<tr>
<td>Parity</td>
<td>P2 to p4</td>
<td>P2 to p5</td>
</tr>
<tr>
<td>Body mass index kg/m2</td>
<td>28 to 32</td>
<td>27 to 33</td>
</tr>
<tr>
<td>Endometrial thickness</td>
<td>12 to 14 mm</td>
<td>10 to 14 mm</td>
</tr>
</tbody>
</table>

The frequency of getting fever was more in group A and nausea, vomiting were more in group B and there was no difference regarding other side effects.

Table 2: Comparison of Blood Loss Between 2 Groups:

<table>
<thead>
<tr>
<th>Methods Of Blood Loss Assessment</th>
<th>Misoprostol Group A</th>
<th>Mefenamic Acid Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of pads used before t/m</td>
<td>18.52 ± 4.16</td>
<td>21.18 ± 10.12</td>
</tr>
<tr>
<td>No. of pads used after t/m</td>
<td>13.76 ± 4.20</td>
<td>13.23 ± 4.10</td>
</tr>
<tr>
<td>Duration of blood loss before t/m (days)</td>
<td>9.20 ± 3.10</td>
<td>8.35 ± 3.10</td>
</tr>
<tr>
<td>Duration of blood loss after t/m</td>
<td>7.21 ± 3.15</td>
<td>7.21 ± 3.25</td>
</tr>
<tr>
<td>Volume of blood loss before t/m (ml)</td>
<td>137.57 ± 36.80</td>
<td>120 ± 20</td>
</tr>
<tr>
<td>Volume of blood loss after t/m</td>
<td>51.60 ± 32.18</td>
<td>50.70 ± 26.91</td>
</tr>
<tr>
<td>Dysmenorrhea before t/m</td>
<td>6.60 ± 2.72</td>
<td>7.72 ± 2.90</td>
</tr>
<tr>
<td>Dysmenorrhea after t/m</td>
<td>5.35 ± 2.69</td>
<td>3.56 ± 2.34</td>
</tr>
</tbody>
</table>

Table 3: Comparison of Haemoglobin (hb) and Haematocrit (hct ) Between 2 Groups:

<table>
<thead>
<tr>
<th>Hb and Hct before and after treatment</th>
<th>Misoprostol Group</th>
<th>p-value</th>
<th>Mefenamic Acid Group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb(before)</td>
<td>10.06g/dl</td>
<td>0.443</td>
<td>10.04g/dl</td>
<td>0.433</td>
</tr>
<tr>
<td>Hb(after)</td>
<td>11.38g/dl</td>
<td>0.08</td>
<td>11.42g/dl</td>
<td>0.09</td>
</tr>
<tr>
<td>Hct (before)</td>
<td>32.42</td>
<td></td>
<td>33.53</td>
<td></td>
</tr>
<tr>
<td>Hct (after)</td>
<td>33.980</td>
<td></td>
<td>34.89</td>
<td></td>
</tr>
</tbody>
</table>

Haematocrit and Haemoglobin were not significantly changed in both groups.

DISCUSSION

Effective medical treatment can improve the excessive menstrual blood loss and may be an alternative to surgery. It is very much important to address the menstrual problems in females to improve their health and quality of life as Lamia Yousaf discussed in her study. A variety of medicines including prostaglandin synthetase inhibitors, antifibrinolytic agents, prostaglandin E1 analogues, herbal and hormonal preparations are proposed for menorrhagia. In this regard, misoprostol (PGE1 analogue)
is assumed to improve the menstrual blood loss by having a potent stimulatory effect on myometrium. Mefenamic acid, a prostaglandin synthetase inhibitor, reduces menstrual blood flow by having an effect on endometrial prostaglandin synthesis. Efikhar et al. proved in his study that misoprostol and mefenamic acid are equally effective in decreasing menorrhagia. Results are consistent with our study. Ibrahim et al. in his study about effect of oral and rectal misoprostol on menorrhagia suggested that both oral and rectal misoprostol were found to be safe and effective in reducing bleeding. Our study showed that misoprostol and mefenamic acid both decreased menstrual bleeding but mefenamic acid significantly reduced severity of dysmenorrhea as compared to misoprostol. A study conducted by Sahil Kumar et al. on women with excessive menstrual blood loss who were treated with mefenamic acid, showed reduction in dysmenorrhea, headache, vomiting and number of pads used and a significant increase in serum ferritin level. The results are consistent with our study but according to our results the frequency of vomiting is more in mefenamic acid group. Kinitis et al. conducted a study on patients with severe dysmenorrhea who were treated with mefenamic acid. After three cycles, 88.6% were pain free and 13% reported mild to moderate pain reduction in placebo group. Our study also showed the same results. Pari Rahi et al. study results are consistent with ours regarding improvement of dysmenorrhea with mefenamic acid. There is no significant change in Hb and Hct in misoprostol and mefenamic acid group, while there seems to be a significant improvement in blood loss. It seems that for significant and detectable changes in these two indices, a large sample size for study and a long duration of follow up is needed.

**CONCLUSION**

Misoprostol and mefenamic acid effectively reduced menstrual blood loss, Menstrual discomfort and lower abdominal pain is more relieved by mefenamic acid.

**Acknowledgment**

The authors deeply acknowledge the support of Gynae department especially Professor Dr. Asma Gul for her kind cooperation and guidance.

**Conflict of Interest**

Authors have no area of conflict.

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Diabetes mellitus (DM) is one of the communal emerging diseases in all over the world. DM associated global mortality was 2.9 million in 2000. According to an estimate globally almost 366 million peoples effected by the year of 2030. In Pakistan, It is estimated that 6.3 million persons have an age adjusted 7.9% prevalence of persons with diabetes among adults, 20 years or older. In Pakistan, in 2030 will have an estimated 11.4 million persons with diabetes and prevalence of 8.9% in the absence of major medications.

Despite extensive data suggesting large benefits with preventive and treatment strategies, and despite increasing media attention, there has been little improvement in diabetes management in the US. The estimated prevalence of diabetes among adults in the United States ranges from 4.4 to 17.9 percent (median 8.2 percent). However, because of the associated micro vascular and macrovascular disease, diabetes accounts for almost 14 percent of US health care expenditures, at least one-half of which are related to complications such as myocardial infarction, stroke, end-stage renal
disease, retinopathy, and foot ulcers. 

Numerous factors, in addition to directly related medical complications, contribute to the impact of diabetes on quality of life and economics. Diabetes is associated with a high prevalence of affective illness and adversely impacts employment, absenteeism, and work productivity.

Almost all obesity in children is strongly influenced by environmental factors, caused by either a sedentary lifestyle or a caloric intake that is greater than needs. The contributions of specific environmental influences are the subject of considerable discussion and research. Environmental factors explain only part of obesity risk, but are important targets for treatment because they are potentially modifiable.

Increasing trends in glycemic index of foods, sugar-containing beverages, portion sizes for prepared foods, fast food service, diminishing family presence at meals, decreasing structured physical activity, increasing use of computer-oriented play activity, and elements of the built environment (e.g., availability of sidewalks and playgrounds) have all been considered as causal influences on the rise in obesity.

Currently, almost one third of children and adolescents in the United States are either overweight or obese.

Childhood obesity is more common among American Indian, non-Hispanic blacks, and Mexican Americans than in non-Hispanic whites. Having an obese parent increases the risk of obesity by two- to threefold. Obesity is also more prevalent among low-income populations. As an example, 14.9 percent of low-income preschool-aged children were obese in 2010, as compared with 12.1 percent in this age group in the general population. Among the low-income children, 2.1 percent had extreme obesity (BMI ≥120 percent of the 95th percentile).

Obesity has become one of the most important public health problems in the United. As the prevalence of obesity increased, so did the prevalence of the comorbidities associated with obesity. For this reason it is imperative that health care providers identify overweight and obese children so that counseling and treatment can be provided.

"Overweight" technically refers to an excess of body weight, whereas "obesity" refers to an excess of fat. However, the methods used to directly measure body fat are not available in daily practice. For this reason, obesity is often assessed by means of indirect estimates of body fat (i.e., anthropometrics).

The body mass index (BMI) is the accepted standard measure of overweight and obesity for children two years of age and older. BMI provides a guideline for weight in relation to height and is equal to the body weight (in kilograms) divided by the height (in meters) squared. Other measures of childhood obesity, including weight-for-height (which is particularly useful for the child younger than two years), measures of regional fat distribution (e.g., waist circumference and waist-to-hip ratio), and the growth standards developed by the World Health Organization (WHO).

Adults with a BMI between 25 and 30 are considered overweight; those with a BMI ≥30 are considered to be obese. Unlike adults, children grow in height as well as weight. Thus, the norms for BMI in children vary with age and sex. In 2000, the National Center for Health Care Statistics and the Centers for Disease Control (CDC) published BMI reference standards for children between the ages of 2 and 20 years. BMI percentiles also can be determined using a calculator for boys and for girls. As children approach adulthood, the 85th and 95th percentile BMI for age and sex are approximately 25 and 30, the thresholds for overweight and obesity in adults, respectively. Present study was planned to determine the correlation between waist hip ratio with duration of diabetes mellitus among diabetic patients presenting to a tertiary care hospital.

**METHODOLOGY**

This cross-sectional study was conducted in medical unit I, Jinnah hospital Lahore during the
period of 1\textsuperscript{st} Jan 2017 to 25\textsuperscript{th} December 2017. Sample size of 110 cases is calculated with 95% confidence level, 5% type I error, 10% type II error and taking value of correlation coefficient as 0.741 between waist hip ratio and duration of diabetes. Non probability consecutive sampling technique was used and 110 cases were enrolled.

Inclusion criteria: (i) Age 20-60 years (ii) Both sexes (iii) Diabetic patients (as per operational definition) for at least 6 months.

Exclusion criteria: (i) Patients not willing to participate in the study (ii) Patients with coronary artery disease determined on history and medical record (iii) Hypertensive patients with BP > 140/90 mm of Hg or taking antihypertensive determined on history and medical record. (iv) Pregnant females (v) Patients with ascites due to any cause determined by presence of fluid in abdominal cavity on ultrasonography.

Diabetes Mellitus: Fasting blood sugar level > 126 mg/dl or HbA1C > 6 mmol or taking antidiabetic treatment for at least 6 months was taken as diabetes mellitus.\textsuperscript{17}

Duration of diabetes mellitus: It was determined by the patient on history and medical record and was noted in the form of months since the diagnosis of diabetes mellitus.

Waist Hip Ratio: Waist circumference was measured at the midpoint between the inferior costal margin and upper iliac crest with the subject standing at the end of expiration in centimeter. Hip circumference was obtained at the level of femoral trochanters with both legs closed with an inelastic measuring tape with a precision of 1 millimeter. Two readings were obtained for each measurement and mean of two readings was taken as final reading. Waist-hip ratio was calculated by dividing the final reading of waist circumference in cm by final reading of hip circumference in cm. About 110 diabetic patients presenting to the medical unit I of Jinnah hospital Lahore and fulfilling the selection criteria were approached. An informed consent was taken from them before enrolling in the study. Information regarding their demographic data was obtained and noted in the proforma. Waist-hip ratio was calculated by dividing the final reading of waist circumference in cm by final reading of hip circumference in cm as per operational definition while duration of diabetes was noted in months in the proforma as well. Confidentiality of the data was ensured. Data was entered and analyzed using SPSS version 17.0. Numerical variables i.e. age, waist hip ratio and duration of diabetes were summarized as mean and standard deviation. Qualitative variables like sex were presented in the form of frequency and percentages. Pearson correlation coefficient was calculated to measure the correlation between waist hip ratio and duration of diabetes.

RESULTS

From 110 patients, it was observed that the minimum age was found 20 years and maximum age was 60 years with mean and standard deviation of the age was 38.07 ± 12.45 years. The minimum duration of diabetes was 6 months and maximum duration was 60 months with mean and standard 38.34 ± 15.54 months. While minimum waist hip ratio was 0.83cm and maximum was 1.01cm with mean and standard deviation of ratio was 0.94 ± 0.03cm. There were 61 (55.5%) male patients while female patients were 49 (44.5%). There was significant correlation found between waist hip ratio and duration of diabetes having Pearson correlation coefficient as -0.282 with p-value = 0.003.

DISCUSSION

A meta-analysis of 35 cross sectional and 17 prospective studies was published in European journal of clinical nutrition. BMI, waist circumference, waist-to-hip ratio was calculated and their association with the increase in the incidence of type II diabetes was assessed. A significant association was
concluded, irrespective of the contentious outcomes on which of these obesity indicators is better. Only two studies of this meta-analysis were in the support of waist circumference among Mexicans African Americans, respectively, one study was in the support of BMI in Pima Indians. Maximum number of studies were exploring greater odds ratio or a little larger area under the ROC curve for waist circumference than for BMI.  

Likewise a meta-analysis consist of 18-74 years study participants was done. There were only four prospective studies resting all were cross sectional studies. it was detected that Tongans had the greatest waist circumference 103 cm. All the races of USA and Uk showed higher values paralleled with their counterparts in their original countries. The ideal waist circumference (WHR) cutoff values were 85 cm (0.83–0.85) and 97–99 cm (0.95) for White women and men respectively, living outside to the USA and UK , for Asian men it was 85 cm (0.90) and for women 75–80 cm (0.79–0.85). For further cultural groups the values were among the range of as for White and Asians. Men had greater values than women in White, Indians Chinese, Japanese, and Bangladeshis, but not in Tunisians, Thai, Iranians, Mexicans, Iraqi, Africans and Tongans. Sensitivity was higher or equal to specificity at these optimal cutoff points 60–70%. There is no standard cutoff value that can be useful around the globe. Therefore a country-specific value should be considered taking into account the purposes and resources.  

Snijder et al reported that logistic regression analyses showed a 1-SD larger hip circumference gave an odds ratio (OR) for developing diabetes of 0.55 (95% CI: 0.36, 0.85) in men and 0.63 (0.42, 0.94) in women, after adjustment for age, BMI, and waist circumference. The adjusted ORs for a 1-SD larger thigh circumference were 0.79 (0.53, 1.19) in men and 0.64 (0.46, 0.93) in women. In contrast with hip and thigh circumferences, waist circumference was positively associated with the incidence of type 2 diabetes in these models (ORs ranging from 1.60 to 2.66). Large hip and thigh circumferences are associated with a lower risk of type 2 diabetes, independently of BMI, age, and waist circumference, whereas a larger waist circumference is associated with a higher risk.  

In present research the minimum waist hip ratio was 0.83cm and maximum waist hip ratio was 1.01 cm with mean and standard deviation of ratio was 0.94 ± 0.03cm. There was significant correlation found between waist hip ratio and duration of diabetes having Pearson correlation coefficient as -0.282 with p-value = 0.003. In existing literature there was a positive correlation between the duration of diabetes and the waist hip ratio and a negative correlation between the duration of diabetes and the thigh circumference. As the duration of diabetes mellitus increases, the anthropometric parameters also increase, and so does the incidence of cardiovascular risk, thus signaling suggesting that a check to must be kept on the much easily measurable anthropometric parameters, which could warn about the future risks. As the duration of diabetes mellitus increases, the anthropometric parameters also increase, and so does the incidence of cardiovascular risk. Hence, a check has to be kept on the much easily measurable anthropometric parameters, which could warn about the future risks.  

In another previous study odds ratios for non-insulin-dependent diabetes mellitus, comparing a high waist-hip ratio (greater than or equal to 0.926 for men, greater than or equal to 0.83 for women) to a low waist-hip ratio were 4.72 with a 95% confidence interval of 2.39-9.34, and 2.17 with a 95% confidence interval of 1.03-4.58, for women and men, Table 2: Correlation between Waist Hip Ratio and Duration of Diabetes

<table>
<thead>
<tr>
<th>Variables</th>
<th>Statistics</th>
<th>Waist hip ratio</th>
<th>Duration</th>
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<tr>
<td>Waist hip ratio</td>
<td>Pearson Correlation</td>
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<td>-0.282**</td>
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<tr>
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<td>Sig. (2-tailed)</td>
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<td>.003</td>
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<td>Duration</td>
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<td></td>
<td>N</td>
<td>110</td>
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</tbody>
</table>

**. Correlation is significant at the 0.01 level (2-tailed).
respectively, controlling for age, overall obesity, and a family history of diabetes. Women with high waist-hip ratios in the presence of these risk factors are notably at risk for diabetes. Central obesity, as measured by the waist-hip ratio, is importantly and independently associated with non-insulin-dependent diabetes mellitus.31

CONCLUSION
The negative correlation was observed between waist hip ratio and duration of diabetes mellitus among diabetic patients presenting to a tertiary care hospital having Pearson correlation coefficient as -0.282 with p-value = 0.003.

REFERENCES
ROLE OF TOCILIZUMAB IN TREATING IMPENDING CYTOKINE STORM IN CRITICALLY ILL COVID-19 PATIENTS

Asif Islam, Zainab Younus, Mujtaba Hasan Siddiqui, Khawar Abbas Chaudhry, Atiq Ahmad, Rizwan Elahi


Abstract

Background: Pakistan is a country of lower economic status which was badly affected in the first wave of COVID-19. The second wave of COVID-19 is at hand which may increase the mortality of these patients. It is hard to control the disease without an available vaccine but some medications have been tried to control the mortality and morbidity. This was a single center study conducted in March 2020 to check the efficacy of tocilizumab among critically ill patients and establish the results that may be helpful to treat these patients in the second wave of Covid-19.

Methodology: For this study, we used 400mg of tocilizumab which was reconstituted with 100 ml sodium chloride solution. The drug was given after 60 minutes for 23 days. We observed the efficacy of the drug by measuring C-reactive Protein (CRP), d-dimer, and serum ferritin levels twice during the study.

Results: Our study did not demonstrate any significant decrease in the mortality rate with tocilizumab. During the study period, only three patients survived, two of them fully recovered and discharged and 1 was discharged with a tracheostomy. Remaining 12 patients died within 7-23 days of follow-up. The survival rate of our study was only 20%.

Conclusion: In our study, we did not find any positive effect of tocilizumab on the mortality of Covid-19 patients. Although it helped to reduce the CRP level, D-dimer level and to some extent reduced the serum ferritin level among the critically ill patients, but it failed to reduce the mortality.

Keywords: Cytokine storm, Covid-19, CRP, Ferritin, D-dimer

At the end of 2019, an outbreak of the coronavirus emerged out from the city of Wuhan, China. In February 2020, the World Health Organization (WHO) declared this disease as pandemic and named it as severe acute respiratory syndrome coronavirus 2” (SARS-CoV-2). In March 2020 this disease spread out to 212 countries and affected more than 5 million people worldwide. In the first 6 months, 347,192 deaths were reported due to Covid-19. This high frequency of deaths was suspected due to “cytokine storm syndrome” (CSS). Recently another study of Cron and Behrens brought attention to the association of CSS with Covid-19. They defined "cytokine storm" as activation of rapid cytokines production due to the unregulated response of the immune system to infections, malignancy, and rheumatic disorder. Tisoncik described cytokine storm as a systemic inflammatory response that leads to extreme activation of immune cells. A study of Wang and Guan reported a high number of white blood cells and very high levels of procalcitonin and C-reactive protein amongst the Covid-19 patients.
who were admitted to the ICU, and classified them as critical cases of the disease. Many other studies observed a higher concentration of pro-inflammatory cytokines among moderate ill Covid-19 patients. Very high levels of cytokines in Covid-19 patients also point out to a poor prognosis. The autopsy of Covid-19 patients revealed the existence of acute respiratory distress syndrome (ARDS) due to the high cytotoxicity of the CD8+ T cells. SARS Cov-2 activates the innate immune response-triggered inflammation among these patients that leads to the cytokine storm. These cytokines cause the death of epithelial and endothelial cells that leads to the mortality of the patient.

SARS Cov-2 causes an increase in interleukin-6 (IL-6) levels which promotes inflammatory responses. Tocilizumab (TCZ) is a recombinant humanized IL-6 receptor monoclonal antibody which helps to prevent the binding of IL-6 in the human body. Recently, a study by Michot et al observed the efficacy of tocilizumab in a 42 years old man who was affected by Covid-19 suffering from respiratory failure. He observed a massive decline in the CRP level of the patient after 4 days of therapy. His CRP level was decreased from 225 to 33 mg/L after the addition of tocilizumab which eventually helped in his recovery. Many other studies reported efficacy of tocilizumab among the Covid-19 patients along with other comorbidities like myeloma, end-stage renal disease and sickle cell disease etc.

**METHODOLOGY**

This single-center study was conducted in the intensive care unit of the EverCare hospital, Lahore, Pakistan. We selected 15 patients of Covid-19 infection according to the WHO classification in March 2020. At the initial stage of hospital admission due to the symptoms similar to Covid-19, all the patients received hydroxychloroquine and azithromycin. Before the administration of azithromycin, we assessed the patient history of cardiac disorder and evaluate the cardiac conditions to avoid any complications. All the information regarding demographic characteristics, clinical baselines and laboratory data were collected and utilized for our analysis. Patients with a serum ferritin level greater than 400 mcg/ml were considered for the administration of tocilizumab. Only severe cases of Covid-19 were selected which were defined as with SpO₂ ≤ 94% on room air, who required supplemental oxygen and needed spontaneous intervention by non-invasive or invasive mechanical ventilation. The time for administration of tocilizumab was decided by the treating physician but we assured that the administration was conducted before the progression of respiratory failure. For this study, we used 400mg tocilizumab which was reconstituted in 100 ml of sodium chloride solution. The prepared drug was infused after 60 minutes for 23 days. We observed the levels of C-reactive Protein level (CRP), d-dimer and serum ferritin twice in the study.

All the collected information was analyzed through the IBM SPSS version 21.0. Nominal variables were presented in the form of percentage whereas continuous variables were presented in the form of mean and standard deviations. p-value of < 0.05 was considered significant in all the analyses.

The study was conducted with all good clinical practices and followed the ethical principles mentioned in the Declaration of Helsinki. An informed consent was obtained from the patient's family before collecting their information.

**RESULTS**

Serum ferritin levels of the selected 15 critically ill patients admitted to ICU were observed at the time of our study. We also observed the adverse effects of tocilizumab on these patients. In 7 patients, ferritin level increased after the administration of tocilizumab while in the remaining 8, it decreased but failed to maintain within the normal limits. So the ratio of tocilizumab on patients was 2:1. All the results were listed in table 1.

As observed in Covid-19 patients, C-reactive protein (CRP) level is also an important parameter of the severity of infection. The results of our study
showed a significant relationship between CRP level and tocilizumab (p-value : 0.0085). Tocilizumab helped to decrease the amount of CRP among critically ill patients which helped to minimize the mortality. However, the results in one of our patient were not in favor of tocilizumab, in whom CRP level increased many fold after the administration of tocilizumab.

D- dimer levels were also observed before and after the administration of tocilizumab. D-dimer usually helps to determine the susceptibility to develop clots in the circulation in these patients. Our results did not reveal a significant relationship between the d-dimer levels and tocilizumab as shown in the table 3.

**DISCUSSION**

We observed the clinical outcomes of 15 patients who received tocilizumab therapy for severe COVID-19 infection. All the patients were in ICU when received tocilizumab therapy. Unfortunately, our study did not demonstrate any significant relationship between the tocilizumab therapy and mortality rate. During the study period, only three patients survived, two of them fully recovered and discharged and 1 was discharged with tracheostomy. Rest 12 patients died within 7-23 days of follow-up. The survival rate of our study was only 20%. Our result was quite similar to the previous study of Grasselli" in which he observed 16% survival and discharge rate of severe Covid-19 patients from ICU. We observed a great positive effect of tocilizumab on the CRP level of our patients. We observed a rapid decline in oral temperature and CRP after the adminis-

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p value = 0.32581

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p value = 0.0085

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p value= 0.16872
tration of tocilizumab. This decrease in CRP levels was according to the results of the research of Michot,16 Zhang,16 Ferrey,17 and Luo.20 Michot and Zhang. They all observed a significant reduction in the CRP level of Covid patients after the administration of tocilizumab. Serum ferritin levels were found to be increased in about half (7) of our patients after the administration of tocilizumab. These results are similar to another single-center study by Luo et al.20 Luo selected critically ill Covid-19 patients and administered 80 mg to 800 mg of tocilizumab in these patients. In 66% of patients he administered Tocilizumab only once while in the remaining it was given twice daily. He observed that the CRP level decreased in all patients except one. Luo observed an increase in serum level of 80% patients and reported three deaths at the time of his study. Overall Luo’s research was in favor of the use tocilizumab, in contrast to the present study.

Abnormal coagulation estimated by high D-dimer levels has a very strong relationship with the progression of Covid-19 infection.21,22 In our study, we analyzed the association of D-dimer and the effect of tocilizumab in critically ill patients of Covid-19 but could not appreciate any positive results. Similar results were observed by Huang who reported an increased level of D-dimer among the Covid-19 patients admitted to ICU.10

There is no proper recommendation of the dose of tocilizumab yet. However different studies demonstrate the efficacy of different doses of tocilizumab among the Covid-19 patients. Genentech recommends a dose of 8mg/kg.24 However, many other studies reported a beneficial effect of 400 mg to 800 mg of tocilizumab in critically ill patients and 200 mg for non-critical patients. Several doses have been tried to date but the majority of studies recommend a single dose and in case of severe disease, a second dose of tocilizumab can be given after 12 hours.25

CONCLUSION

In the pandemic of COVID-19, tocilizumab is considered to be a blessing for patients. It helps to minimize the mortality ratio of Covid patients. Many studies were conducted in favor of this drug. However, in our study, we did not find any positive effect of tocilizumab on the mortality rate of Covid-19 patients. Although it helped to reduce the levels of CRP, D-dimer and to some extent, the serum ferritin yet it failed to decrease the mortality rate. Only 3 patients survived and were discharge after the administration of tocilizumab. We used a dose of 400 mg which was a comparatively lower dose than the other studies. We suggest that further studies should be conducted to monitor the efficacy of the tocilizumab and also about its dosage on severely ill patients and establish a full protocol for its use in Covid-19 patients.

Acknowledgment

We are grateful to Dr. Rizwan Elahi, Consultant Physician & Nephrologist at Madina Munawara, Saudi Arabia for reviewing and sorting out the literature which helped us in writing this research paper.

Conflict of Interest

There was no conflict of interest during this study.

REFERENCES


Acute coronary syndrome associated with elevated ST-segment (ST) demands emergency treatment for coronary artery disease. Many risk factors have been found to be associated with coronary artery disease, few of these factors are also associated with pre-hospital delay.

Objectives: Aim of present study was to determine the frequency and association of pre-hospital delay factors among ST Segment Elevation myocardial infarction (STEMI) patients attended in tertiary care hospital. This descriptive study was commenced in Department of Medicine, Jinnah Hospital Lahore from August 2017 to April 2018.

Methodology: A total of 200 patients of either gender, aged 50 years and above with pre-hospital delay of $\geq$3 hours after onset of symptoms of myocardial infarction (MI) showing elevated ST-segment on ECG were included in present study. After taking an informed written consent a pre-designed questionnaire was used to collect the information. Data was entered and analyzed in SPSS software.

Results: A total of 200 patients consisting 43 male and 157 females with mean age of 64.97±8.009 and age groups of 50-6- years (29.5%), 61-70 (43.5%) and $\geq$71 as 27%. Denial of symptoms has been shown to be the most predominant (75.5%) pre-hospital delaying factor following age > 60years (70.5%), female gender (53.5%), diabetes mellitus (34.5%) with low socioeconomic status (28.5%) remaining the least.

Conclusion: Denial of symptoms, Diabetes, female sex and elderly age of $>60$ years are strongly associated to pre-hospital delay in case of STEMI in this study with rebuttaion of symptoms as of cardiac being the most common. Smoking, Hypertension are very important entities but showed low level of association as compared to other factors.

Keywords: Pre-hospital Delay, STEMI, Hypertension, Elderly age.
FACTORS AFFECTING PRE-HOSPITAL DELAY IN GETTING TREATMENT IN PATIENTS

Incidence of MI is as high as 600 cases per 100,000 populations in United States and STEMI comprises of around 40% of all cases. Pakistan is one of the low and middle income countries; reportedly around 39% deaths under the age of 70 years are due to coronary heart diseases and further 30% people of Pakistan over the age of 45 years are affected by this disease. Scarcity of data and paucity of reporting about estimates are major hurdles to access the actual burden of disease and implementation of control measures in all over the country.

Coronary blood flow restoration of the affected artery is the major standard of treating STEMI. Prompt access to the reperfusion therapy, either pharmacological or catheterization, basic percutaneous intervention restrict extent of infarct ultimately improves survival. Global registry of acute coronary events (GRACE) reported around 40% STEMI patients could not receive therapeutic reperfusion in time however availability of percutaneous intervention facility at primary level has shown greater effect to fibrinolysis hence improves survival and recurrence of MI.

Diagnosis of MI is based on various biochemical tests including cardiac enzymes, troponin and creatin kinase levels however, ECG is recommended in most recent guidelines. This test confirms in 80% of the diagnosis further it is serially performed to look dynamic changes in ST-segment. Many risk factors have been found to be associated with coronary heart disease few of these include diabetes, chronic renal disease, hypertension, obesity, physical activity and diet low in fruits/vegetables.

Some of these factors are also associated with pre-hospital delay among STEMI patients due to low intensity of symptoms and other reasons. Various studies have been done in the past to show correlation among various factors and the pre-hospital delay in treatment of MI with various outcomes, some showing contextual factors while other being focusing on cognitive and affective factors and all of these studies are done abroad. Presently only scarce work on these factors is available in Pakistan and it is necessary to generate a comprehensive data which may help in not only in future practices but also important to recognize the areas where necessary improvements are desired. Therefore the aim of present study was to determine the frequency and association of pre-hospital delay factors among STEMI patients attended in tertiary care hospital.

METHODOLOGY

This descriptive study was commenced in Department of Medicine, Jinnah Hospital, Lahore from August 2017 to April 2018. A total of 200 patients of either gender, aged 50 years and above with pre-hospital delay of ≥ 3 hours after onset of symptoms of MI showing elevated ST-segment on ECG were included in present study. STEMI was diagnosed on the basis of typical chest pain, ECG changes and Cardiac enzymes. ECG changes were defined as ST elevation of at least 1mm in two contiguous leads or new onset LBBB with typical chest pain. Ethical approval was taken from the ethical board committee of the Jinnah Hospital/Allama Iqbal Medical College Lahore. After taking an informed written consent from patients and their relatives a pre-designed questionnaire was used to collect the information like name, age, gender and demography of patients. Similarly qualitative information about important factors including history of circumstances of symptoms onset, nature of the pain, patients perception about the pain along with the severity of the pain on a scale of 0-10 with 10 representing the severest pain with visual analogue scale, patients socioeconomic status as well as educational level, hypertension, diabetes, smoking and body mass index (BMI) >25 was also noted. The approximate time by the primary physician/referring physician was also noted. Data was entered and analyzed in statistical package for social sciences (SPSS) software. Age was only quantitative variable which was presented in mean ± standard deviation. All other qualitative variables were presented in frequency and percentages.
RESULTS

A total of 200 patients consisting 43 male and 157 females with mean age of 64.97± 8.009 were analyzed in this study. Gender distribution with respect to different age groups of STEMI patients is presented in figure 1. Most of 43.5% patients remained in age group of 61-70 years followed by 29.5% in 50-60 years and lowest of 27% were in age of ≥71.

Figure 1: Age and Gender Distribution of STEMI Patients

Denial of the symptoms that they are due to infarction, either due to muscular one, gastroesophageal related and surprisingly a large number of patients thought of this pain due to generalized weakness and will recover spontaneously and took self medications, came out to be the most important and prevalent (75.5%) factor in seeking delayed hospital treatment following age of patients with predominantly participants >60years (70.5%) in the present study.

Another factor was Diabetes mellitus (34.5%) causing decrease perception of pain with vague and non-specific symptoms leading to delaying in obtaining proper treatment.

In-time referral was also delayed in patients having low socioeconomic status (28.5%) as those having good status present earlier for better care as compared to the ones having poor living status obtaining delayed treatment for MI.

Female gender (53.5%) came out to be a significant variable in the present study with more incidence of delayed treatment in older females as compared to the young ones.

DISCUSSION

MI is one of the leading causes of morbidity and mortality. Incidence of disease is decreasing in developed nations due to implementation of effective health policies and improvements in health systems on the other hand it is surging in developing countries. But still there are various factors which pose a concern in obtaining delayed proper treatment leading to poor prognosis and having worse morbidity and mortality. Present study has shown five factors and their proportions involved in pre-hospital delay including denial of symptoms of ischemia/infarction (75.5%), age of patients >60 years (70.5%), female gender (53.5%) and diabetes mellitus (34.5%) and low socioeconomic status (28%) the least respectively.

Low socioeconomic status as shown by various studies have shown a clear relationship with the pre-hospital delay in achieving treatment. It is seen that the rich people usually show up early in emergency departments as compared to the poor ones being more concerned about the health owing due to the availability of resources to get even costly treatment. This is also true in our society as the health care facilities are not totally free and readily available and up to mark especially in government hospitals. This is also show by our study.

The third common factor found in our study population was female gender being 53.5% of the study cases. Female gender also has been associated to be more pre-hospital delay in case of STEMI in present study as around 79.5% of age ≥ 50 years while 53.5% of age >60 years were get affected presently and in concomitant with (a study done by

Table 1: Frequency of Factors Responsible for Pre-Hospital Delay

<table>
<thead>
<tr>
<th>Factors</th>
<th>N</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>Diabetes Mellitus</td>
<td>69</td>
<td>34.5</td>
</tr>
<tr>
<td>Denial of ischemic symptoms</td>
<td>151</td>
<td>75.5</td>
</tr>
<tr>
<td>Low socioeconomic status</td>
<td>57</td>
<td>28.5</td>
</tr>
<tr>
<td>Age &gt;60 Years</td>
<td>141</td>
<td>70.5</td>
</tr>
<tr>
<td>Females</td>
<td>107</td>
<td>53.5</td>
</tr>
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</table>
Leslie WS) a recent study which concluded that women have double mortality rate due to STEMI as compared to men. Cultural values could be one of the female gender based pre-hospital delay in our society as most of the women are dependent on males further they bear the pain for long time, hence delay at home further the arrangements to reach hospital or acquire emergency services significantly get hindered. The females also usually being shy in telling their illness, responding late to their symptoms, more frequency of atypical symptoms as compared to males and thinking that the heart attack can mainly occur in males lead to delayed appearing in the hospital. Several studies confirm our finding. But at the same time few studies counter this finding which may be due to the cultural, socioeconomic and educational differences of the regions as compared to our area.

Presently 34.5% patients had diabetes in this study which is an important comorbidity among patients of MI and STEMI. A recent long term follow up study of STEMI among diabetes revealed higher rates of mortality among diabetics as compared to non-diabetics with worse clinical outcomes among diabetics as compared to non-diabetics following STEMI largely due to atherosclerosis development. It is also reported that patients with diabetes mellitus are 1.4 times more prone to MI as compared to others furthermore; cardiovascular disorders and STEMI are the commonest cause of mortality among diabetics. Although it is perceived that diabetics do not feel chest pain due to MI but a study revealed neglected perception and showed an insignificant difference of chest pain and no chest pain among diabetics so this might lead to delayed seeking of medical help.

Mean age of study subjects in present study remained to be 64.97±8.009, further 70.5% of the cases had their ages >60 years. Our study showed that age is the most common factor leading to pre-hospital delay in attaining medical help which is consistent with other studies. The elderly people usually suffer from different diseases leading to multiple symptoms including body aches and pains that usually wax and wane misleading the ischemic pain as a part of their general illness.

The old ones also have decrease perception of pain, and they also being due to psychological reasons or so don’t want to disturb the family leading to delay in getting early treatment.

Denial of symptoms that I am not having MI, and how can I have this disease leads to pre-hospital delay in the treatment of MI. They often think that the symptoms are not related to heart, either muscular or gastric denying the actual occurrence of ischemia receiving late treatment with bad cardiovascular outcome as compared to their counterparts who present early seeking early treatment also shown by various studies.

Our study is consistent with a study done by J. Pattenden which showed that it constitutes a major factor in pre-hospital delay and in our society where educational level, self-awareness along with socioeconomic status is very low and self-treatment is very common, it becomes even more prominent.

Conclusively, denial of acceptance of having symptoms of MI, elderly age of >60 years, female gender and low socioeconomic status are strongly associated to pre-hospital delay in case of STEMI in this study.

Limitations of study

This study has been mainly done in an urban area where the resources, medical facilities, education level is different from the rural ones. Secondly this study has mainly taken in account of the out of the hospital factors leading to treatment delay.

Conflict of Interest

All authors declare no conflict of interest.

Funding Source

Also we solemnly declare that no funds, no grants or any sort of financial support was provided by any institution, agency or organization.

Author contributions

Nadeem Yousaf: Concept and paper writing
Mukhtar Ahmad: Data Interpretation
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FACTORS AFFECTING PRE-HOSPITAL DELAY IN GETTING TREATMENT IN PATIENTS

29. L.P. Daisy, W. Philip, S.A. Steptoe Causal beliefs, cardiac denial and pre-hospital delays following the onset of acute coronary syndromes J Behav Med, 31 (2008), pp. 498-505

Confidence comes not from always being right but from not fearing to be wrong.
The deficiency of Vitamin D is said to be a global health issue and more than a billion people throughout the world are deficient or insufficient. The “International Association of Endocrinology” defined Vitamin D Insufficiency when level of vitamin D in blood is 21-29ng/ml and level < 20 ng/ml as Deficiency of Vitamin D in adults. There is increased requirement of vitamin D in pregnancy and prevalence of its deficiency has been reported to be 50% to 63.3% among pregnant women. In pregnancy all women should increase their vitamin D intake ten times than normal in order to have fruitful outcome. The elementary role of vitamin D is to keep blood calcium and phosphate values by boosting their intestinal absorption directly and indirectly. Vitamin D level during pregnancy and lactation is utmost important for the development of fetus and its skeleton. In the last trimester of pregnancy the maternal alteration in metabolism of Vitamin D and calcium let the shift of 250 mg of Calcium every day to fetal skeleton, and for a total of 25-30 grams of calcium. The absorption of calcium becomes double in women during first trimester of pregnancy and continues till delivery. Vitamin D deficiency during pregnancy may susceptible to adverse maternal outcomes e. g Preeclampsia and Gestational Diabetes Mellitus. Vitamin D deficiency during pregnancy and breast feeding is also associated with untoward effects on growing baby e.g. infantile rickets, pathetic fetal growth, large fontanelle and poor neonatal development. Deficiency of Vitamin D may lead to diminution maternal bone density especially in last trimester of preg-

**Abstract**

**Objectives:** To determine the prevalence of Vitamin D deficiency in Postpartum Women and their Neonates.

**Methodology:** This Prospective, Cross-Sectional study was carried out at department of Obstet. and Gynae. Special Unit Services Hospital Lahore, over a period of one year from First January 2015 to 31st December 2015 after approval from Institutional Ethical Committee. One hundred (100) women were enrolled in this study, blood samples of enrolled women after delivery and their neonates were taken, labelled and sent to SIMS (Service Institute of Medical Sciences) laboratory for Vitamin D estimation levels.

**Results:** In postpartum women Vitamin D deficiency prevalence was 67% and in their neonates 58%. There was a statistically significant correlation among delivered women and their neonates regarding Vitamin D deficiency P-value was <0.004. There is also statistically significant correlation between parda/veil observer and non parda P value<0.002.

**Conclusion:** The majority of Pakistani women and their neonates are Vitamin D deficient, a serious issue. There is an urgent need to make strategies and its implementation to prevent deficiency of Vitamin D both in the mothers and their neonates.

**Key Words:** Vitamin D levels, Postpartum Women, Neonates

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<table>
<thead>
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<td>2nd Revision Date:</td>
<td>24-03-2021</td>
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<tr>
<td>Acceptance Date:</td>
<td>29-03-2021</td>
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2. Iqra Ahmad  
3. Iqbal Ahmad Azhar  
4. Nuzhat Gull  
5. Nabila Abdullah  
6. Masooda Shafi  

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nancy and may lead to backache, and severe cramps in legs. It has been observed that adequate amount of Vitamin D in early life may reduce the different health problem risks later on in life e. g Asthma, various respiratory, cardiovascular, autoimmune and psychiatric disorders in neonates. According to NICE guidelines it is mandatory to give 10 microgram of Vitamin D in pregnancy and breast feeding period to all pregnant women. The objectives of this study was to ascertain the prevalence of deficiency of Vitamin D in Postpartum Women and their Neonates so that strategies and its implementation could be streamlined to deal this issue.

METHODOLOGY

A Prospective, Cross-Sectional study was carried out at Obstet and Gynae. Special unit Services Hospital Lahore, a tertiary care teaching hospital, over a period of one year from First January 2015 to 31st December 2015 after the Institutional Ethical Committee approval. Sample size was calculated by using “WHO sample size determination software with 95% confidence interval”. Non probability purposive sampling technique was used, a total of 100 pregnant women at term fulfilling the inclusion criteria were enrolled in the study. Inclusion criteria include all healthy at term pregnant women and their newborns. Pregnant women having chronic illnesses like Hypertension, Diabetes Mellitus, cardiac, renal, respiratory, psychiatric illness and carcinoma were excluded from the study. After taking informed consent blood samples were drawn from mother immediately after delivery and cord blood of newborn was collected labelled properly and then sent to SIMS (Service Institute of Medical Sciences) laboratory for estimation of vitamin D levels. Data was collected by filling specially designed proforma, demographic information like age, parity, address, parda/veil, Gestational age, socioeconomic and educational status and birth weights of newborns were filled in Performa. All the data was entered, rechecked and then analyzed with the help of SPSS software version 19.

RESULTS

A total of 100 maternal blood and cord blood samples were collected, properly labelled and sent to SIMS laboratory for estimation of vitamin D levels. Table 1 highlight the demographic features of the participants. Major chunk of the women (65%) were between 21-30 years of age mean age was 25.48±2.6 years. Majority of women (58%) were having 2-4 kids. The 74% of the women having BMI < 25 mg/m², the deficiency of Vitamin D was found in 67% (67) women, and the mean vitamin D level in women was 27.31 ng/ml. Out of 100 women 38% were wearing parda / veil and 62% were not. It had been observed that deficiency of Vitamin D was frequent and severe in women with parda and in their neonates, All women (100%) with parda were Vitamin D deficient in this study, there is a statistically important correlation between parda/veil observer and non parda P value<0.002.

Table II illustrate the maternal and neonatal Vitamin D levels in blood, there is statistically signi-
significant relationship in between mother and in her neonatal blood regarding Vitamin D deficiency, P value <0.004. Vitamin D deficiency prevalence in neonates was 58%, the 62.68% in women with Vitamin D deficiency and 48.48% in women without Vitamin D deficiency. There was a statistically significant correlation within maternal and neonatal blood Vitamin D deficiency levels, P-Value<0.002 was observed. The birth weight of all newborn babies ranges between 2.5 kg to 3.5 kg.

Table 2: Maternal & Neonatal Blood Levels of Vitamin D (n=100)

<table>
<thead>
<tr>
<th>Maternal Levels</th>
<th>Neonatal blood</th>
<th>Levels</th>
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<tbody>
<tr>
<td>ng / ml</td>
<td>&lt; 30 ng / ml</td>
<td>≥ 30 ng / ml</td>
</tr>
<tr>
<td>&lt; 30 (n=67) (67%)</td>
<td>42 (62.68%)</td>
<td>25 (37.31%)</td>
</tr>
<tr>
<td>&gt;30 (n=33) (33%)</td>
<td>16 (48.48%)</td>
<td>17 (51.51%)</td>
</tr>
</tbody>
</table>

DISCUSSION

Deficiency of Vitamin D leads to significant health issues, not in mothers only but in their neonates too, as Vitamin D store of the pregnant women is the leading root of Vitamin D for the growing fetus. According to WHO recommendation a pregnant women should take Vitamin D 200 IU/day throughout pregnancy, but recent studies reported that every pregnant women should take more than 1000 IU/day to attain satisfactory levels. Vitamin D deficiency prevalence found in the study in women was 67% that is quite high and consistent with other national and international studies. The consequence of this deficiency could affect the mother’s health, and may also affect the development of growing neonates because most of the women breast fed their newborns 1-2 years in our setup. The developing fetus is totally depend on the mother for Vitamin D supply. In our study population the Vitamin D levels were deficient and not matching with IOM Committee. In our study 38% of the women were wearing veil/ parda, it has also been observed that 35 women (92.10%) were Vitamin D deficient that is quite high and similar with other studies. Parda/ Veil wearing women, Congested residential areas where sunlight is hardly seen, more deficiency could be explained because of lack of exposure to sunlight, different studies also support this finding that women living in indoors only are more deficient with Vitamin D. But a study conducted in Tehran reported that there is no dispute in Vitamin D deficiency within two groups with parda/veil or without. Low BMI is a contributory factor in deficiency of Vitamin D, and in our study 74% of the women had BMI < 25 mg/m², and this finding is tallying with other studies. Socio-economic status is a big denominator in Vitamin D deficiency because it is observed that low and middle class women are highly affected reason being poor dietary intake. In our study 58% of the neonates were Vitamin D deficient, there is no discrimination between two genders. There is no statistically difference in birth weight and head circumference of Vitamin D deficient and non-deficient women, these findings were consistent with other studies.

Limitations of Study

As this study was conducted in only one institute so its results could not be generalized more longitudinal studies are mandatory to see the long term effects of Vitamin D deficiency on development of growing kids.

CONCLUSIONS

The deficiency of Vitamin D is a rampant in our society and significant contributor to the disease burden. The majority of Pakistani women and their neonates are Vitamin D deficient, a serious issue. There is an urgent need to make strategies and its implementation to prevent deficiency of Vitamin D both in mothers and in their neonates.

REFERENCES


COVID-19 PNEUMONIA: PATTERN OF FINDINGS IN HIGH RESOLUTION CT-SCAN OF CHEST

Madeha Hussain,1 Nazish Hameed,2 Najaf Abbas,3 Sadia Khanum,4 Aftab Ahmad,5 Saba Maqsood6

Abstract

Background: Novel Corona virus also known as SARS COV-2 (Severe acute respiratory syndrome corona virus 2), which causes a disease known as Covid-19, is an extremely contagious virus. Real time polymerase chain reaction is being taken as a standard diagnostic test to label covid-19. Recent studies have shown numerous CT scan features in patients with Covid-19 therefore it has an important role not only in assisting in diagnosis but also for the monitoring of disease. Hence, it is necessary for the Radiologists to be well familiar with these findings and their pattern.

Objective: This study has been carried out to determine the HRCT chest scan findings and their pattern of prevalence in our patients with Covid-19 pneumonia.

Methodology: This is a retrospective study of fifty patients with Covid-19. Only the patients who were diagnosed with PCR were included in this study. HRCT chest scans of all patients were done and evaluated for different pulmonary findings and their pattern.

Results: All of the fifty patients had shown findings on their respective HRCT scans. Out of 50 patients 29 (58%) were male whereas 21(42%) were female. The mean age was 50 years (22 to 80 years) with standard deviation of ± 17.46. GGO (Ground glass opacities) was the most commonly present pattern that was found in 49 out of 50 patients (98%) either alone or in addition to other features. Reticular pattern was the second most commonly seen pattern and it was present in 26 out of 50 patients (52%). In 46 out of 50 patients (92%) bilateral involvement was noted. In 96% (48/50) patients lower lobes were involved while upper lobe involvement was seen in 70% (35/50) of the patients. In 90% (45/50) of the patients the lesions were peripheral.

Conclusion: GGOs (Ground glass opacities) are the most common HRCT scan features in patients with Covid-19. Bilateral chest involvement was also more prevalent as compared with unilateral. The involvement of lower lobes was more common than the upper ones.

Key Words: HRCT-Scan chest, Ground glass opacities, Covid-19 Pneumonia.
chest HRCT scan (Computerized tomography) has a very important role not only in assisting in diagnosis but also for the monitoring of disease. Unfortunately, PCR has got a high false negative ratio for novel corona virus and this fact has further increased the importance of CT scan in helping the diagnosis as its sensitivity is 98%. Recent studies have shown numerous CT scan features in patients with Covid-19. Due to important role of CT-scan in these patients, it becomes extremely necessary for the Radiologists across the globe to be well familiar with these findings and their pattern.

This study has been carried out to determine the HRCT chest scan findings and their pattern of prevalence in our patients with Covid-19 pneumonia.

**METHODOLOGY**

This study was conducted in Radiology department of Islam central hospital, Sialkot. It is a retrospective analysis of 50 patients of Covid-19. Approval for the study was taken from hospital ethical committee. Informed consent was waived by the ethical committee because; being retrospective analysis, there was no harm to patients. Moreover, the identity of patients was also been kept confidential in this study.

We analyzed the data of 50 patients of Covid-19 who underwent chest CT scan at the Radiology department of Islam central hospital. We only included those patients who were diagnosed to have developed Covid-19 and proven by a positive PCR for Corona virus. The nasopharyngeal sampling of the admitted patients was done in coordination with ENT and pathology department and PCR was done by Shokat khanum laboratories. The patients with suspicion of disease but negative PCR were NOT included in our study.

CT scans were performed in supine position and during inspiration. Multiple thin slice sections were obtained using 16-CT Emotion (Siemens Healthcare). Following is the protocol used for performing CT scans of chest: (Siemens Healthcare) 130 kV, 30–150 mAs, 8-mm slice thickness. All of the CT scans were done by using the same machine.

The CT scans of the patients were reviewed retrospectively. These images were assessed for pulmonary parenchymal pathologies. The abnormalities were assessed using following four parameters:

Firstly, location of abnormality (which lobe/lobes were involved?). Secondly, the distribution of abnormalities (e.g. sub-pleural, peribronchovascular or random). Thirdly, the morphology (patchy, irregular, lobar, nodular or segmental). Finally, the density of abnormalities which was categorized broadly into Ground glass opacities (GGO), others or mixed pattern. The images were also assessed for extra-pulmonary involvements like pleural thickness, pleural effusion or lymphadenopathy (mediastinal). For statistical analysis of our data we used SPSS software (Version 21).

**RESULTS**

A total of 50 patients were included in this study. Out of them 29 (58%) were male whereas 21(42%) were female. In this study the age of our patients was from 22 to 80 years. The mean age was 50 years with standard deviation of ± 17.46.

In our patients subpeural GGO (Ground glass opacities) was the most commonly found pattern. Ground glass opacities were found in 49 out of 50 patients (98%) either alone or mixed with other features. Reticular pattern was the second most commonly seen pattern and it was present in 26 out of 50 patients (52%). The CT scans of 9 patients (18%) shown consolidation. Pleural effusion and bronchiectasis were also seen in 2(4%) and 1(2%) patients respectively. No CT scan was found to be absolutely normal.

Another important finding, that we observed, was bilateral involvement by disease in most of the patients. In 46 out of 50 patients (92%) bilateral

<table>
<thead>
<tr>
<th>Table 1: Frequency Distribution of Patients Gender</th>
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<tbody>
<tr>
<td>Gender</td>
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<tr>
<td>----------</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
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</table>
involvement was noted. The CT scans of only 4 (8%) patients demonstrated unilateral findings. Similarly, another notable finding was the predominant involvement of lower lobes. In 96% (48/50) patients lower lobes were involved while upper lobe involvement was seen in 70% (35/50) of the patients. As far as the distribution is concerned, the lesions were usually peripheral. In 90% (45/50) of the patients the lesions were peripheral, while in 10% (5/50) they were central.

DISCUSSION

The purpose of this study was to find out the pattern of CT scan findings in our patients with Covid-19. This study was carried out on 50 patients. GGOs (Ground glass opacities) were the most common feature noted in these patents and they were present in 98% of our patients. This finding is consistent with the study of Zhan et el, where 65.4% patients were having GGOs in their CT scans. Another important thing, that we noticed, was that most of our patients shown bilateral lung involvement (92%). Literature review suggests that previous researches have also reported more bilateral involvement as compared to unilateral, but their percentage is less than ours, For instance Bergheim et el found bilateral lung involvement in 73% of their patients. According to Ding et el initial CT scans (within first four days of developing symptoms) showed bilateral disease involvement only in 42.3% of their patients which increased to 95.6% in subsequent CT scans after eighteen days of developing the symptoms of Covid-19. This is an important finding which suggests that as the disease progresses it involves both lungs. The results of Zhan et el have also shown a similar pattern where bilateral lung involvement increased from 71% (averaged fourth day, after the development of symptoms) to 93.5% (Follow up scan that was done at a mean interval of 5.3 days) thus further supporting this hypothesis. Probably the reason why bilateral involvement is much higher in our study is the late presentation of patients in our part of the world. Therefore, their disease is mostly at an advance stage before they get it evaluated by costly investigations like CT scan.

In spite of all these limitations, we believe that this study is a contributory effort towards developing the radiological diagnostic criteria and knowing the pattern of CT scan findings in patients of Covid-19. The future studies need to include more clinical data so that we can correlate it with the pattern of CT scan findings.

CONCLUSION

Our study concludes that GGOs (Ground glass opacities) are the most common HRCT scan feature in patients with Covid-19. Similarly bilateral chest involvement was also more prevalent as compared with unilateral. The involvement of lower lobes was more common than the upper ones. We also suggest further studies with large sample size to validate these findings.

Limitations of the study
As we have already described that it is retrospective study, hence, there are certain limitations of our study. First of all, we don’t have complete clinical data of patients especially the clinical severity of their illness, blood oxygen saturation, oxygen requirement and their relation with CT scan findings. Secondly, majority of the patients were referred patients who were referred just for CT scan and then they went back to their primary treating physician so we don’t have access to follow them up.

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Conflict of Interest

It is hereby declared that authors have no conflict of interest.

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Contributions of Authors

Conceptualization: Madeha Hussain, Nazish Hameed, Saba Maqsood
Data collection: Madeha Hussain, Nazish Hameed, Saba Maqsood
Formal analysis: Najaf Abbas, Aftab Ahmad, Sadia Khanum, Madeha Hussain
Sampling for PCR: Najaf Abbas
Patient Referral for CT-Scan: Najaf Abbas, Aftab Ahmad, Sadia Khanum
Methodology: Madeha Hussain, Nazish Hameed, Saba Maqsood
Project administration: Madeha Hussain
Supervision: Madeha Hussain, Najaf Abbas
Writing – Madeha Hussain, Najaf Abbas
Writing – review & editing: Nazish Hameed, Saba Maqsood, Aftab Ahmad, Sadia Khanum

REFERENCES

Lower back provides support to the upper body weight and plays a role in the mobility and stability of different parts of body. The lower back paraspinal muscles help in movement of hips when walking in addition to providing stability to the spine.

Two important muscles of lower back are erector spinae and multifidus. Erector spinae consists of three muscles out of which longissimus and iliocostalis play a role in lower back stability. Longissimus occupies the central position of erector spinae. The origin of its fibers is from the accessory process as well as the medial half of the posterior surface of the transverse process of each of the five lumbar vertebrae. The lateral most component of erectorspine is iliocostalis.

The origin of its lumbar fibers is from the tips of the first four lumbar transverse processes and the posterior surface of the middle layer of thoracolumbar fascia lateral to these tips. These fibers insert into the medial end of the iliac crest and the dorsal segment of the iliac crest along with the fascicle. The function of thoracic and lumbar components of erector spinae is the extension of the vertebral column and when acting unilaterally they can laterally flex

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**Abstract**

**Objective:** To determine the association of lumbar paraspinal muscle atrophy with lumbar disc herniation and spinal stenosis.

**Methodology:** Prospective study of 160 consecutive patients was done who presented with lower back pain and had disc herniation on MRI lumbar spine. Disc herniation with its pattern and spinal stenosis with its grade were analyzed. Paraspinal muscle atrophy of Multifidus, Longissimus and Iliocostalis was noted at each level of disc herniation and spinal stenosis and their correlation with muscle atrophy grade and laterality was studied.

**Results:** 79% patients with disc herniation showed Multifidus muscle atrophy however no significant association was seen between paraspinal muscle atrophy and disc herniation (P = .15). Significant correlation was seen between muscle atrophy laterality and disc herniation pattern (P < .001). 90% patients with spinal stenosis showed paraspinal muscle atrophy. Significant association was also seen between paraspinal muscle atrophy and spinal stenosis of any grade (P < .001).

**Conclusion:** There is correlation between paraspinal muscle atrophy and spinal stenosis. Pattern of disc herniation and symmetry of paraspinal muscle atrophy also has significant correlation but more studies need to be done with large sample size.

**Key Words:** Paraspinal muscle atrophy, Spinal stenosis, Disc herniation pattern, MRI

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the trunk\(^2\). The multifidus muscle is the back muscle which is medial most in location. It is also the largest muscle spanning the lumbosacral junction. Its function is to maintain the erect posture of the trunk and also abduction and rotation of the trunk.\(^2\) The origin of Multifidus is in the form of fascicles arising from the lower edge of the lateral surface of the spinous process and from the lower end of its tip. These fibers course caudally to their insertion into the transverse elements of vertebrae which are two, three, four and five levels below. Fascicles that extend beyond the fifth lumbar vertebra insert into the dorsal surface of the sacrum. The longest fascicles from the first and second lumbar vertebrae insert into the dorsal segment of the iliac crest.\(^2\)

Lower back pain is becoming more prevalent day by day and according to an estimate it affects 65-85% of the general population at some point throughout their lifetime.\(^4\) Low back pain causes a lot of disability hampering day to day activities. It is prevalent in people belonging to all cultures and interferes with overall quality of life also affecting performance at work. It is also one of the most frequent causes for medical consultations. The low back pain is an issue faced by many people on daily basis. It commonly occurs among the masses yet poses serious questions for the physicians. It is a cause for social as well as economical problems.

One of the most common causes of lower back pain in adult population is herniation of lumbar disc. It is also a frequent cause of sciatic pain in adults. The protruded disc causes compression on the dorsal and/ or the ventral nerve roots leading to low back pain and other symptoms such as sciatica, muscular spasm, and restricted trunk movements.\(^5\) Likewise lumbar spinal stenosis is another important cause of backache and becomes more common with increasing age and seen frequently in elderly people. Spinal stenosis patient can present with neurologic deficit pain or disability.\(^5\)

Young to middle aged population is affected by lower back pain secondary to degenerative disc disease. Its peak incidence occurs at approximately 40 years of age. If radiologic evidence of lumbar disc degenerative disease is considered, disc degeneration becomes more prevalent with age. When disc degenerative disease was studied as a cause of back pain it was found to affect men more than women. Patients having lumbar disc degenerative disease can present with symptoms of sensory disturbances in legs, claudication and pain relief upon bending forwards.\(^6\)

Magnetic resonance imaging (MRI) is increasingly applied in finding out the underlying cause for back pain. It plays a role as a diagnostic tool in patients with lower back pain for evaluation of underlying anatomical pathology. It can also provide valuable information about muscle quality, atrophy or other contributing factors including herniated disc, spinal stenosis or compression of the nerve roots. In recent studies the importance of fatty infiltration of lumbar paraspinal muscles and their size (cross sectional area or volume) has been highlighted as a tool in helping to predict the disability related to lower back pain, chances of recurrence of symptoms and whether the symptoms would improve with exercise or not. Magnetic Resonance Imaging (MRI) is frequently used in the assessment of the lumbar spine and related structures such as paraspinal muscles and ligaments. Studies have been conducted that have suggested the role of fatty infiltration of the lumbar paraspinal muscles in predicting patient response to treatment for lower back pain.\(^4\)

There are many factors which make MRI the ideal and standard modality for the detection of disc related pathology including its lack of ionizing radiation and ability for multiplanar imaging. It also provides excellent spinal soft-tissue contrast and can precisely localize the pathological changes in intervertebral discs.\(^6\)

Although lower back pain is highly prevalent, many questions remain unanswered with respect to its pathophysiology. More work needs to be done to establish definite association between the imaging findings and patient’s symptoms. Previously only
limited information was available regarding the role of the paraspinal muscles in causing lower back pain. Recently increasing number of studies have been conducted attempting to highlight the possible association between the paraspinal muscle atrophy, lower back pain and spinal disc disease. However no conclusive evidence is available in this respect till date and more work needs to be done to establish convincing relationship between paraspinal muscle atrophy and lumbar disc herniation. Our study aims to focus on the assessment of paraspinal muscles atrophy and possible relationship with lumbar disc herniation and spinal stenosis.

**METHODOLOGY**

We studied total 160 patients ranging in age between 21 to 65 years old from both genders between August 2019 and January 2020. Those were included who presented with history of lower back pain with or without associated symptoms of numbness and stiffness. Patients were referred from outpatient clinic by physician after clinical exam was done. Symptoms were noted and family history of spine disease was also interrogated. Systemic disease was also excluded on history and type and location of symptoms were recorded. Those patients were excluded who had incomplete MRI done due to some reason and those who had surgeries of spine. Patients with backache and having no disc herniation on MRI were also not included in study. Patients with congenital or development disease of musculoskeletal system and those with diagnosed spondylitis or spondylodiscitis and neoplasm either primary or secondary of the spine were also excluded.

The participants were subdivided on the basis of:

1- Education level
   a- Low level below high school b- Regular level until high school c- High level college or university
2- Lifestyle a- Passive b- Regular
c- Active for example sportive.

Two ethnic groups were noted among the patients and they belonged to either Punjabi or Pathan.

We collected and analyzed the data on IBM SPSS version 23 and applied Chi square test to determine the significance of P value. Different variables were assessed for their frequency and their associations were determined. P value <0.05 was taken as statistically significant.

We studied MRI of total 160 patients according to the selection criteria described above. All patients were imaged on Toshiba 1.5 Tesla MRI in Radiology department of Sir Ganga Ram Hospital, Lahore. Same sequences of images were acquired in all patients including T1 weighted, T2 weighted and STIR images in sagittal plane with T1 weighted and T2 weighted images in axial planes at all lumbar levels. Paraspinal muscle atrophy was assessed by two radiologists in consensus to decrease the controversies in the study. Atrophy of paraspinal muscles including multifidus, longissimus and ileocostalis were assessed on T1 weighted as well as on T2 weighted axial images and correlation with disc herniation was noted. Muscle atrophy was graded with semi-quantitative method as per the criteria,

Grade 0: Normal (normal size, homogeneous signals without fatty infiltration)
Grade I: Size reduction (less than 50 % with fatty infiltration)
Grade II: Size reduction (over 50% with fatty infiltration)
Grade III: Complete fatty infiltration (complete absence of muscle fibers)

Disc herniation was taken as 2 mm beyond the vertebral margin. Patients with complex pattern of disc herniation showing more than one pattern were also not included to make the study and results more specific. Spinal stenosis was graded as mild, moderate and severe subjectively and some effacement of thecal sac was taken as mild, near total effacement of CSF in thecal sac was taken as moderate and total effacement was taken as severe.

**RESULTS**

Prospectively we studied MRI of 160 consecutive patients who had disc herniation on MRI,
ranging in age between 21 to 65. Out of them 107 were males and 53 were females. We noticed that most common pattern of disc herniation was circumferential and was seen in 127 patients followed by central disc protrusion and then by paracentral herniation. Most common level of disc herniation was L4-L5 followed by L5-S1 and then L3-L4.

A- Association between disc herniation and paraspinal muscles atrophy:

Out of total 160 patients with disc herniation of any pattern 127 (79%) patients showed multifidus muscle atrophy. Majority of these patients had grade I and bilaterally symmetrical atrophy. 56% patients showed grade I and 32 % showed grade II and p value was insignificant (P = .15). Table 1 Likewise in case of longissimus coli muscle atrophy was seen in 109 (68%) patients (P= .588) and in ileocostalis was seen in 83 (52%) patients (P= .127) and most common pattern was grade I.

Table 1: Type of disc herniation and multifidus muscle atrophy cross tabulation

<table>
<thead>
<tr>
<th>Type of disc herniation</th>
<th>Multifidus muscle atrophy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grade 0</td>
</tr>
<tr>
<td>Circumferential</td>
<td>23</td>
</tr>
<tr>
<td>Right</td>
<td>3</td>
</tr>
<tr>
<td>Left</td>
<td>0</td>
</tr>
<tr>
<td>Central</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
</tr>
</tbody>
</table>

Paraspinal muscle atrophy is bilaterally symmetrical.

Figure 1: T2W axial image at L3-4 level showing diffuse disc bulge (thick arrow) with multifidus atrophy (thin arrow), longissimus atrophy (arrow head) and ileocostalis atrophy (open arrow).

Figure 2: T2W axial image at L4-5 level showing central disc herniation (thick arrow) with bilateral symmetrical multifidus atrophy (arrow heads) and mild atrophy of longissimus and ileocostalis muscles.

Figure 3: T2W axial image at L4-5 level showing moderate spinal canal stenosis with multifidus atrophy (thin arrow), longissimus atrophy (arrow head) and ileocostalis atrophy (open arrow). Paraspinal muscle atrophy is bilaterally symmetrical.

Figure 4: T2W axial image at L4-5 level showing diffuse disc bulge with asymmetrical multifidus atrophy more on right side (arrow head). There was right paracentral disc herniation at one level above but atrophy on right side was more prominent at this
Multifidus muscle atrophy was seen bilaterally symmetrical in majority of patients (table 2) who showed circumferential disc herniation while unilateral/predominant atrophy was observed in only 10 patients and all of them showed paracentral disc herniation either right or left (P < .001).

Longissimus atrophy was also bilateral in patients with circumferential disc herniation and only 5 patients had unilateral/dominant atrophy with paracentral disc herniation pattern (P < .001). Same pattern was observed in ileocostalis atrophy but with less number of patients and P value was significant too (P<.001).

Among three paraspinal muscles examined multifidus was affected most frequently followed by longissimus and then ileocostalis. The level of muscle atrophy correlated with the level of disc herniation on all three muscles and also inferiorly in many cases.

**B- Association between spinal stenosis and paraspinal muscle atrophy:**

We noticed that out of total patients, 141 patients showed some degree of spinal stenosis. Out of 141 patients 127 (90%) patients had multifidus muscle atrophy. In patients with mild stenosis atrophy was seen in 66 patients (74%) and with moderate spinal stenosis in 93% and with severe stenosis 88% cases (P<.001) p value was significant. We noticed that atrophy was seen in association with all grades of spinal stenosis including mild, moderate and severe. Majority of cases showed grade I muscle atrophy followed by grade II and then grade III (Table 3). In case of longissimus same kind of trend was observed and muscle atrophy was seen in 77% of patients with spinal stenosis (P < .001). In case of ileocostalis 65% of cases showed atrophy (P < .001). We saw muscle atrophy more in ethnic group of punjabi than pathan and p value was not significant (P=.165).

It was observed that of all patients with disc herniation the majority of them had high school education level and p value was insignificant (P=.910).

Most of the patients with regular life style showed muscle atrophy. In patients with passive life style 93 % showed atrophy and with active life style 81 % and with regular life style 76% showed muscle atrophy (P=.008).

We also noticed that grade I and II muscle atrophy was more common in male patients however cases with grade III atrophy were mostly females. In multifidus muscle atrophy out of 15 patients with grade III atrophy 11 were females (P=.006) and same was true with longissimus.

**DISCUSSION**

In adults chronic lower back pain is reported as high as 20.3 percent and increases with life starting from the age of 30 years onwards. Decreased physical activity and sedentary lifestyle has been established as contributor to development of lower back pain and they inturn are related to weakness and atrophy of paraspinal muscles. Nerve root compression and disc herniation have effect on innervation of paraspinal muscles resulting in atrophy. 

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**Table 2: Type of Disc Herniation and Multifidus Muscle Atrophy Laterality/Symmetry Cross Tabulation**

<table>
<thead>
<tr>
<th>Type of disc herniation</th>
<th>Multifidus atrophy laterality</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Unilateral/Dominant</td>
</tr>
<tr>
<td>Circumferential Right</td>
<td>0</td>
</tr>
<tr>
<td>Right</td>
<td>5</td>
</tr>
<tr>
<td>Left</td>
<td>5</td>
</tr>
<tr>
<td>Central</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
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</tbody>
</table>

**Table 3: Spinal Stenosis Type and Multifidus Muscle Atrophy Cross Tabulation**

<table>
<thead>
<tr>
<th>Spinal stenosis type</th>
<th>Multifidus muscle atrophy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grade 0</td>
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<tr>
<td>Mild</td>
<td>23</td>
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<tr>
<td>Moderate</td>
<td>3</td>
</tr>
<tr>
<td>Severe</td>
<td>1</td>
</tr>
<tr>
<td>Absent</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
</tr>
</tbody>
</table>

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Sadaf Batool Faisal
Several studies have assessed atrophy of paraspinal muscles in patients with low back pain in correlation with pain. Multifidus atrophy and fatty infiltration has been shown in unilateral lower back pain on the same side. They found correlation between the side of lower back pain and ipsilateral atrophy of paraspinal muscles in patients with either acute or chronic back pain. Association has also been seen between backache and decreased CSA and fatty infiltration of paraspinal muscles and also between disc herniation, radiculopathy with paraspinal muscle atrophy. Review studies have noticed lack of adoption of uniform methods for paraspinal muscles evaluation in several studies which highlights the need for more studies to understand cause and effect relationship between changes in paraspinal muscles and spinal degenerative changes. They concluded that multifidus muscle atrophy has role in cause of disc herniation / degeneration specially at L3- L4 level in one study. Muscle atrophy should be considered in treatment of lumbar disc herniation and lumber extension muscles strengthening program could be helpful in preventing muscle atrophy and spinal degeneration.

In other studies they noticed that paraspinal muscle atrophy was seen in patients not having lower back pain but due to aging however when they compared with patient having neuromuscular diseases then they found atrophic changes were more severe and there was total fat replacement. This shows that problems affecting the innervation of muscles can aggravate the atrophy in addition to other factors, which can even occur as age related phenomenon. Less improvement was seen in patients with more severe muscle atrophy or fatty infiltration after corrective surgery in one study.

But none of the above mentioned studies analyzed disc herniation pattern in correlation with laterality/ dominance of paraspinal muscle atrophy. In our study we compared type of disc herniation with muscle atrophy grade and noticed that paraspinal muscle atrophy was quite frequent in patients with disc herniation independent of pattern. In our sample the majority of patients had circumferential disc herniation pattern but the atrophy was also noted in some patients with paracentral and central disc herniation and no specific pattern was responsible for atrophy. We could not find significant association between disc herniation pattern and muscle atrophy grade however we concluded that in majority of patients with degenerative disc herniation it has effect on paraspinal muscle volume which can alter the biomechanics of spine.

It was noticed in our study that majority of the patient had bilaterally symmetrical muscle atrophy at the level of disc herniation or inferior mostly with circumferential disc herniation pattern but unilateral/ dominant atrophy was observed also in patients with paracentral disc herniation on the same side. We found significant relationship between side of disc herniation and side of muscle atrophy however limitation was limited number of patients with paracentral disc pattern because we included only consecutive patients with any type of disc disease. More studies need to be done to see the significance of side of disc herniation and muscle atrophy with greater sample.

Multifidus muscle was most commonly affected in atrophy followed by longissimus and then iliocostalis indicating that multifidus muscle is the most important muscle in the back giving strength and stability to the spine. No isolated atrophy of the erector spinae muscle was seen without multifidus atrophy.

Lumbar spinal stenosis is among the spectrum of degenerative spine changes and is common in older individuals. It has been proven in studies that paraspinal muscle denervation occurs in patients with spinal stenosis and posterior passing ramus is the main cause for this denervation rather than nerve root compression. In one prospective study they assessed correlation between paraspinal muscle atrophy and spinal stenosis. They compared asymptomatic subjects and subjects with mechanical low back pain with symptomatic spinal stenosis and they found that paraspinal muscle atrophy was more significantly in spinal stenosis group than low back
pain than asymptomatic group. In this study the limitation was smaller sample size. In one study they found poor correlation between degree of spinal stenosis and symptoms and functional impairment of the spine. They saw association between functional performance of patient with lumbar spinal stenosis and cross sectional area of multifidus and psoas major. In this study more decreased cross sectional area of muscles was seen in females than males and in our study we also noticed that severe atrophy patients were more females.

Significant association was seen in our study between muscle atrophy and spinal stenosis suggesting that spinal stenosis is a contributing factor in muscle atrophy resulting from compression on the nerve roots. In patients with severe stenosis almost all of them showed atrophy of muscles. Muscle atrophy was seen in all grades of spinal stenosis however more prevalence was seen in patients with having severe spinal stenosis. We also noticed that even patient not having spinal stenosis also showed muscle atrophy suggesting that there are also other multiple causes contributing to paraspinal muscle atrophy. We did not correlate the duration of symptoms with muscle atrophy and this was the limitation.

In conclusion paraspinal muscle atrophy has significant prevalence in patients with degenerative disc herniation of any pattern and has significant association with spinal stenosis. More studies need to be done to determine the significance of correlation between side of disc herniation and unilateral or dominant atrophy of paraspinal muscle on same side so that therapeutic management can be directed towards specific exercises for unilateral muscle strengthening for these cases.

REFERENCES
Allergic rhinitis (AR), often misconstrued as a trivial issue amongst the myriad of chronic diseases, is in actuality a ‘chronic’ nuisance for many sufferers. Although not immediately life threatening, the profound impact of this disease on quality of life cannot be understated. AR is highly prevalent with

Abstract

Background: Allergic rhinitis(AR) is a highly prevalent disease that has a profound effect on the functionality of the sufferer and can severely affect quality of life. It has far reaching consequences on health resources and the economy in general. Effective management is key to lessening the toll of the disease on the individual and the economy in general. In this article we look into adherence to the management protocol in young, educated individuals in Lahore and reasons for nonadherence.

Objective: To find out the perceived adherence to treatment of AR of the young educated population of Lahore and identify the reasons for nonadherence.

Methodology: A cross sectional study was conducted in Lahore, Punjab, Pakistan from December 2020 to January 2021. Questionnaires of the research topic were provided to individuals that met the inclusion criteria. The questionnaires were distributed both online and manually, with the majority of responses coming from individuals receiving the questionnaire online. Efforts were made to clarify what allergic rhinitis was to the possible respondents. One hundred and one questionnaires were filled and 15 were disregarded as they did not meet the inclusion criteria or were improperly filled. Data from 96 questionnaires was compiled, statistical data tabulated and finalized. Common trends and patterns were found and written.

Results: Only 23(24.0%) individuals reported to always take the appropriate dose of their AR medication at the right time. The major reasons for not adhering to appropriate doses at the right time included 58(60.4%) individuals stating that ‘they tend to forget’ to take their medication and 21(21.9%) individuals cited side effects of the medication as a reason for not adhering to their regimen. The majority of patients, 44(45.8%), reported to only taking medications when having symptoms and stopping when symptoms cease. 29(30.2%) individuals stated that they always use preventative measures. On asking the reasons for non-adherence (if present) to these preventative measures/ lifestyle changes advised, 23(24.0%) individuals identified job constraints as the reason for non-adherence whereas 24(25.0%) stated non availability of alternative means of transportation as the reason for non-adherence.

Conclusions: Adherence to medications and preventative measures in AR in young educated individuals of Lahore is generally low. Forgetfulness and side effects were the major reasons for non-adherence to medication. The main reasons for non-adherence to preventative measures were that job constraints and non-availability of alternative means of transportation made it difficult to avoid potential allergens.

Key words: allergy, allergic rhinitis, Lahore, adherence, non-adherence

Allergic rhinitis (AR), often misconstrued as a trivial issue amongst the myriad of chronic diseases, is in actuality a ‘chronic’ nuisance for many sufferers. Although not immediately life threatening, the profound impact of this disease on quality of life cannot be understated. AR is highly prevalent with
ADHERENCE TO MANAGEMENT OF ALLERGIC RHINITIS AND REASONS FOR NON ADHERENCE

more 500 million affected globally and is the most common chronic disease in children. Even though many individuals do not seek medical advice for AR it accounted for 15.2 million visits to healthcare providers in 2003 in the US. With advancements in medication protocols and better understanding of AR, management strategies have been refined such that they allow sufferers to lead relatively normal lives.

Allergic rhinitis, as the name implies has an allergic etiology. AR is an inflammatory disease of the upper airways related to an history of family atopy and is usually manifested in childhood or adolescence. AR is mediated by an Ig E related mechanism. AR is a chronic allergic disease and in this way is similar to asthma. Indeed, a significant number of sufferers of AR suffer from asthma. Note, AR is as debilitating as severe asthma.

AR can affect an individual throughout the year or be seasonal, the many symptoms of AR include sneezing, rhinorrhea, post nasal drip, irritation in the nose, blocked nose etc.

There are various modalities for treating AR which include pharmacotherapy, immunotherapy and preventative measures. Recommendations support continuous rather than on demand treatment. Quality of life can be greatly impacted by allergic rhinitis. The symptoms (frequent sneezing, rhinorrhea, blocked nose etc.) can interfere with social interactions, work and adversely affect sleep. Not only does it affect the individual but it poses a great burden on resources in the form of direct economic cost, loss of man hours and poor work performance.

A key component in the effectiveness of any treatment protocol is how strictly the sufferers adhere to it. This is especially necessary in chronic diseases such as AR where the prolonged clinic course can be vexing and the monotonous application of medications can in itself be grievance and something that requires immense amounts of discipline. Indeed, even the most state of art treatments will fail if proper instructions regarding timing, administration and dosing are not followed. By questioning sufferers of AR about the various factors that lead to their noncompliance, health professional will be able to more aptly gauge which areas need to be addressed in more detail during consultation and channel their efforts in a more focused manner to tackle these concerns in efforts to allay any possible fear or apprehensions that the patient may have and in turn possibly improve compliance to treatment. We therefore took keen interest in attaining further insight into how the compliance was amongst young educated individuals of Lahore and what the reasons were for non-compliance amongst this demographic. We focused on this demographic specifically as we came across no study focusing primarily on this cohort and present our findings in this article.

METHODOLOGY

It was a cross sectional study conducted in Lahore, Punjab, Pakistan from December 2020 to January 2021. Individuals with AR that were between the ages of 18 and 35 years of age and had completed their matriculation/equivalent or higher. Exclusion criteria included non consenting individuals, individuals below 18 years of age and above 35 years of age and individuals that haven’t completed their matriculation/equivalent.

Questionnaires of the research topic were provided to individuals that met the inclusion criteria. The questionnaires were distributed both online and manually, with the majority of responses coming from individuals receiving the questionnaire online. Efforts were made to clarify what allergic rhinitis was to the possible respondents. 111 questionnaires were filled and 15 were disregarded as they did not meet the inclusion criteria or were improperly filled. Data from 96 questionnaires was compiled, statistical data tabulated and finalized. Common trends and patterns were found and written.

RESULTS

Of the initial 111 responses, 15 were disregarded due to the individuals not falling into the inclusion criteria or improper filling of the questionnaire.
As such, the sample population comprised 96 individuals with ages ranging from 19 years to 32 years with the majority (89-92.7%) falling in the 21 years to 28 years age range. 24(25.0%) individuals were suffering from other concomitant diseases, most of which were chronic in nature. Asthma was the most common concomitant disease and 10(10.4%) individuals suffered from diseases (specifically asthma, eczema and allergic conjunctivitis) that have allergic etiologies.

When inquired whether they experienced perennial or seasonal symptoms, 58(60.4%) answered that they experienced seasonal symptoms and 36(37.5%) answered that they experienced perennial symptoms with 2(2.1%) individuals failing to answer.

When given a list of possible symptoms to choose from 14(14.6%) individuals identified as having 1 of the symptoms, 12(12.5%) individuals had 2 symptoms, 24(25%) individuals had 3 symptoms, 29(30.2%) individuals had 4 symptoms, 8(8.3%) individuals had 5 symptoms and 9(9.4%) individuals had all 6 of the listed symptoms. 28(29.2%) individuals described their symptoms as mild. i.e. few symptoms that occur occasionally, 49(51.0%) individuals described their symptoms as moderate. i.e. few symptoms which are frequent or persistent and 19(19.8%) individuals described their symptoms as severe. i.e. multiple symptoms which are frequent or persistent.

On questioning the respondents on how the symptoms effected the quality of their life 39(40.6%) individuals stated that it adversely effects their work, 49(51.0%) individuals identified their symptoms as a reason for disturbed sleep, 35(36.5%) individuals stated that their symptoms interfere with social interactions. 17(17.8%) respondents felt that their symptoms did not affect their quality of life in the above-mentioned ways with 1(1.0%) respondent failing to answer.

Oral antiallergics were by far the most used medications with 70(72.9%) individuals stating that they used them, followed by nasal decongestants used by 38(39.6%) individuals. Nasal steroids were used by 29(30.2%) individuals, Oral decongestants were used by 17(17.8%) individuals, 3(3.1%) individuals used oral steroid pills whilst 15(15.6%) individuals stated that they did not take any of the medications mentioned.

The majority of individuals had been prescribed their medications for more than 1 year with 39(40.6%) individuals falling in this category. At the other end of the spectrum 34(35.4%) individuals had been prescribed their medications for less than one month. 8(8.3%) Individuals had been prescribed their medications between 1 to 6 months prior and 6(6.3%) individuals had been prescribed their medications between 6 months and a year prior. 9(9.4%) individuals failed to respond. 19(19.8%) individuals believed that their medications confereed great benefit in relieving their symptoms, double this number 38(39.6%) of individuals stated that they did benefit from their medications whilst 34(35.4%) individuals stated that they somewhat benefit from their medications. Only 2(2.1%) individuals felt that they did not benefit from taking their medications. 3(3.1%) individuals failed to give a response. 42(43.8%) individuals reported to not have received any guidance for the application of nasal sprays and 52 (54.2%) stated that they did so. 2(2.1%) individuals failed to give a response.

When inquired on how often they experienced the taste of the nasal spray in their mouth on applying nasal sprays, few 15(15.6%) reported never experiencing the taste, with 34(35.4%) occasionally experiencing the taste and 40(41.7%) often experiencing the taste. 7 (7.3%) individuals failed to give an answer.

On asking how strictly they adhere to the timing and number of doses of the medication 23(24.0%) reported to always take the appropriate dose at the right time, 50(52.1%) stated that they occasionally forget to take a dose or occasionally take the dose at the wrong time whereas 18(18.8%) individuals reported that they often forget to take medications or often take doses at the wrong time. 5(5.2%) parti-
pants did not answer the question.

The respondents were asked about reasons for not adhering to medications appropriately. 5(5.2%) individuals cited cost as a reason, similarly 5(5.2%) individuals found the dosing protocols hard to follow. 58(60.4%) individuals stated that ‘they tend to forget’, 21(21.9%) individuals cited side effects of the medication as a reason for not adhering to their regimen. 11(11.5%) individuals found the drugs to be ineffective/ not curative, 4(4.2%) individuals stated that they were not able to understand the prescribing physician’s instructions adequately.

On questioning how strictly did they adhere to the duration of the doses (‘number of days you should take the medication for’) of the prescribed medications, the majority 44(45.8%) reported to only taking medications when having symptoms and stopping when symptoms cease. 29 (30.2%) reported that they always took medications for the prescribed duration with 19(19.8%) individuals only taking medications when symptoms become severe. 27 (28.1%) individuals reported that they avoid exhaust fumes by decreasing travel by rickshaw or motor bike, when inquired on what lifestyle changes/preventative measures they followed. 29(30.2%) individuals reported that they limited outdoor activity during pollen season, 18(18.8%) individuals reported on using nasal douching, 48(50.0%) individuals reported that they used a facemask, 6(6.3%) individuals reported that they had stopped smoking whilst 18(18.8%) individuals stated that they did not use any of the mentioned preventative measures/lifestyle changes.

The majority of individuals had been advised preventative measures/lifestyle changes more than 1 year with ago 38(39.6%) individuals falling in this category. At the other end of the spectrum 11(11.5%) individuals had been advised preventative measures/lifestyle changes between 6 months and one year ago. 15(15.6%) Individuals had been advised preventative measures/lifestyle changes 1 to 6 months prior and 17(17.7%) individuals had been advised preventative measures/lifestyle changes less than a month prior. 15(15.6%) individuals failed to respond.

When participates were asked to what extent do you feel using lifestyle changes/preventative measures helps with your allergic rhinitis 46(47.9%) individuals stated that they benefited from their lifestyle modification whilst 32(33.3%) individuals stated that they somewhat benefit. Only 6(6.3%) individuals felt that they did not benefit. While 4(4.2%) individuals stated that they greatly benefited from lifestyle change. 2(2.1%) individuals failed to give a response.

When participates were asked how is your adherence to the lifestyle changes/preventative measures advised? 29(30.2%) individuals stated that they always use preventative measures whilst 48(50.0%) individuals stated that they only use preventative measures when having symptoms, and stop when symptoms cease benefit. Only 12(12.5%) individuals only use preventative measures when symptoms become severe. 7(7.3%) individuals failed to give a response.

On asking what are the reasons for non-adherence (if present) to these preventative measures/lifestyle changes advised? 23(24.0%) individuals identified Job constraints as the reason for non-adherence whereas 24(25.0%) stated non availability of alternative means of transportation as the reason for non-adherence. 13(13.5%) individuals were not able to understand the prescribing physician’s instructions adequately 10(10.4%) individuals stated that the cost (of masks/nasal douches) was the cause of non-adherence while 8(8.3%) individuals stated that they find it difficult to stop

Table 1: Reason for Non Adherence to Timing and Number of Doses of the Medication

<table>
<thead>
<tr>
<th>Reason</th>
<th>Frequency</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of medication</td>
<td>5</td>
<td>5.2</td>
</tr>
<tr>
<td>Found dosing protocol hard to follow</td>
<td>5</td>
<td>5.2</td>
</tr>
<tr>
<td>Forgetfulness</td>
<td>58</td>
<td>60.4</td>
</tr>
<tr>
<td>Side effects of medications</td>
<td>21</td>
<td>21.9</td>
</tr>
<tr>
<td>Drugs are ineffective/not curative</td>
<td>11</td>
<td>11.5</td>
</tr>
<tr>
<td>Did not understand the prescriber’s</td>
<td>4</td>
<td>4.2</td>
</tr>
<tr>
<td>instructions adequately</td>
<td></td>
<td></td>
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</tbody>
</table>

adherence whereas 24(25.0%) stated non availability of alternative means of transportation as the reason for non-adherence. 13(13.5%) individuals were not able to understand the prescribing physician’s instructions adequately 10(10.4%) individuals stated that the cost (of masks/nasal douches) was the cause of non-adherence while 8(8.3%) individuals stated that they find it difficult to stop

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smoking. 35(36.5%) individuals failed to respond.

**DISCUSSION**

Compliance/adherence\(^{10,19}\) is a term that encompasses a compendium of factors\(^{20,21}\), each contributing to a varying degree depending on the individual case. It is this case-to-case variability combined with the generally broad management protocol which includes not only medications but also lifestyle changes compounded with the chronic nature of allergic rhinitis that makes describing compliance with allergic rhinitis treatment and pinpointing reasons for noncompliance a particularly arduous task. Our article excludes any mention of immunotherapy despite it being a major and effective means of managing allergic rhinitis.\(^{22,23,24,25,26,27}\) This exclusion stems from the fact that Pakistan, as a whole, has very few facilities providing the treatment and it thus is not a norm to include it as part of a typical management protocol.

In our study we found that 22(22.9%) individuals were suffering from other concomitant diseases, most of which were chronic in nature of which asthma was the most common. Indeed the majority of allergic rhinitis patients suffer from respiratory problems.\(^{28}\) Another study found that individuals with rhinitis were at a significant risk of asthma with a adjusted odd ratio of 3.2.\(^{29}\) These findings are similar to our findings.

58(60.4%) answered that they experienced seasonal symptoms and 36(37.5%) answered that they experienced perennial symptoms of allergic rhinitis in our survey. Meltzer et al\(^{30}\) found that 20% of adults and 21% children experienced allergic rhinitis symptoms throughout the year, whilst 95% experienced symptoms in spring, 63% in summer and 74% experienced symptoms in fall. This study was conducted amongst US patients. We believe the dusty environment and poor air quality leads to a larger number of people experiencing perennial symptoms in Lahore.

Mild symptoms were experienced by 28(29.2%) individuals, 49(51.0%) individuals described their symptoms as moderate and 19(19.8%) individuals described their symptoms as severe. In another study\(^{31}\) it was found that 59% sufferers felt that their symptoms were moderately severe or severe. These findings further highlight the need to pay utmost attention in dealing with this issue. In a study conducted by Marple et al\(^{32}\) where 1 in 5 individuals felt that their symptoms weren’t taken seriously enough.

The overwhelming majority of individuals in our study felt that allergic rhinitis affected their quality of life in one way or the other with only 17.8% stating that their quality of life wasn’t affected. The literature is replete with studies emphasizing the effects of allergic rhinitis on quality of life. With effects documented on cognitive impairment, learning, decision making, psychosocial wellbeing, self-attractiveness and quality of life in general.\(^{33,34,35,36}\) Bollinger et al\(^{37}\) found that 39.1% were taking monotherapy whilst 11.0% were taking concurrent AR therapy. Of those taking monotherapy the most commonly prescribed were cough/cold medications (28.3%), intranasal corticosteroids (26.7%) and antihistamines (25.9%). Surprisingly 13.6% adults took oral steroids as monotherapy to treat their symptoms. Only 3(3.1%) individuals used oral steroid pills in our study and antihistamines were used by more than 70% individuals (note: this figure is the total value of individuals who use antihistamines as one of the medications in their protocol).

In our study, 77.1% of individuals complained of experiencing the taste of nasal sprays in their mouth with most stating that they often experienced the taste of sprays. One third of patients found the dripping of medication to be bothersome in another
ADHERENCE TO MANAGEMENT OF ALLERGIC RHINITIS AND REASONS FOR NON ADHERENCE

study. This is a highly concerning pattern as it implies that the patients were either not given adequate guidelines regarding nasal spray application or despite being given appropriate instructions were not following them properly.

Only 2 individuals in our study felt that their medication protocol conferred no benefit. The remaining felt that they experienced at least some benefit from using medications. In contrast a UK study found 54% of individuals felt that their symptoms were poorly controlled with a combined protocol of an intranasal corticosteroids and an antihistamine. Another study found that only 3% felt that their intranasal corticosteroid conferred no benefit at all.

Non adherence to medical treatment is high in chronic conditions 30-60% and can be as high as 80% for preventative measures. Sanchez et al also found adherence to pharmacotherapy was very low in AR.

35% individuals in another study indicated that they were non adherent for at least some time during the treatment, 38% stated that they discontinued treatment once they felt better the MASK Study also found that adherence to treatment in AR was low. 41% adults and 26% children reported taking medications year round in a study conducted by Meltzer, this study also found that two thirds of individuals took their medication exactly as advised with a further 20% stating that they only took medications on the appearance of symptoms.

Our study found that only 23(24.0%) individuals reported to always take the appropriate dose at the right time and only 29(30.2%) %) reported that they always took medications for the prescribed duration which is in line with the findings of low adherence in other publications.

Numerous studies identify cost, forgetfulness, lack of efficacy and side effects and lack of efficacy as major reasons for non-adherence. In our study forgetfulness and side effects were identified as the most prevalent factors contributing to non-adherence. Complex treatment regimens and inadequate communication are also cited as factors for poor compliance.

The authors despite thorough review of available literature found very few articles talking about the reasons for non-adherence to preventative measures despite these guidelines being commonly advised. Allergen avoidance is the main basis of the preventative measures advised to manage allergic rhinitis. We were able to find one study that looked into pets as source of allergens and feasibility of implementing avoidance measures, this study found that only 4% of individuals followed medical recommendations regarding allergen avoidance with regards to pets.

CONCLUSION

Adherence to medications and preventative measures in AR in young educated individuals of Lahore is generally low. Guidance regarding proper use of medications is inadequate. Forgetfulness and side effects were the major reason for non-adherence to medication. The main reasons for non-adherence to preventative measures are that job constraints and non-availability of alternative means of transportation make it difficult to avoid potential allergens.

Limitations of the Study

As we used convenience sampling to select the population group, this may slightly distort the results. Furthermore, as online questionnaires were a method employed by the authors it is possible that some of the questions weren’t fully understood by the cohort despite efforts to ensure that the questionnaire was as easy to understand as possible. Since the authors did not have physical access to a large number of participants, it was not possible to confirm whether or not the individuals met the criteria to be considered sufferers of AR. As a result, some participants may consider themselves to have AR due to misdiagnosis by their physician, management by quacks etc. even though in reality they may not. One major limitation is that we did not use quantitative methods to quantify adherence and the responses were all subjective.
Recommendations

Studies focused on the adherence to different preventative measures should be performed as the region is vastly undiscovered. Strides should be taken to ensure that patients are given adequate instruction regarding proper administration technique; which will presumably lead to increased effectiveness of therapy. The importance of following medical instructions and risk factors vs benefits of all treatment modalities employed by health professionals should be properly conveyed to the patient thereby empowering patients to make an informed decision about the management of their disease.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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The authors did not receive any funding for this project.

Contributions of the Authors

- Conception or design of the work- Dr Syed Ahmed Shahzaeem Hussain
- Data collection- Dr Syed Ahmed Shahzain Hussain
- Data analysis and interpretation - Dr Syed Muzahir Hussian
- Drafting the article- Dr Syed Muzahir Hussian
- Critical revision of the article- Dr Muhammad Hasnain Haider
- Final approval of the version to be published - Dr Anas Zahid

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43. Bender BG. Motivating patient adherence to allergic
EFFECT OF INTRA OPERATIVE GLOVE CHANGING DURING ELECTIVE CESAREAN SECTION ON POST OPERATIVE WOUND COMPLICATIONS

Afroze Ashraf,1 Rehana Ayub,2 Nasreen Akhtar,3 Sadaf Zahra Syed4

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Abstract
Background: The single most important factor associated with post-partum infection is caesarean section and has a 5-20 fold increase risk of infection. The glove which is contaminated when reintroduced into the abdominal cavity and the operative field that otherwise would be sterile, causes wound complications.

Objective: To compare outcome of changing gloves by entire surgical team vs no glove change by surgical team intra-operatively before abdominal closure on post-operative infectious morbidity and wound complications during elective caesarean.

Methodology: After approval from ethical committee and informed consent, 60 females fulfilling selection criteria were enrolled in study. Subjects were randomly divided into two groups by using lottery method. In group A, outer pair of sterile gloves were changed by entire surgical team including surgeon, assistant and scrub nurse before abdominal closure during caesarean section, while group B, gloves were not changed during the procedure. All patients were given prophylactic pre-operative antibiotics. Patients were followed up in post-operative ward for signs and symptoms of fever, endometritis, cellulitis, wound seroma or the wound dehiscence daily till second post-operative day, patients were discharged if there is no post-operative complication and finally were observed at the day of stitches removal. Data was entered and analyzed statistically by using SPSS version 26. Quantitative variables like patient age, gestational age at delivery, estimated blood loss, pre & post-operative Hb etc were presented in the form of mean + S.D. Qualitative variables like parity, wound complications etc were presented in the form of frequency and percentage. Comparison of two groups, Group A and Group B was done by applying Chi-Square with p-value ≤ 0.05 as significant.

Results: 60 patients were included in the study and mean age was 26.17 + 5.7 years. Mean gestational age was 36.7 + 5.6 weeks. 96.7% were more than 30 years. 100.0% were from urban area. 61.7 % were illiterate, 33.3% had primary education. Outcome among groups were compared, In group A (with gloves) fever and purulent discharge from site were present in 3.3% of subjects as compared to Group B in 26.7%. (p< .05). 13.3% in Group B developed endometritis. (p < .05) and 6.7% developed wound dehiscence. (p > .05). (Table no: 2)

Conclusion: Use of intraoperative glove changing during cesarean section significantly reduced postoperative wound infection and complications.

Key Words: Caesarean section, morbidity, infection, wound infection,

The single most important factor associated with post-partum infection is caesarean section. It carries a 5-20 fold increase risk of infection when compared with vaginal delivery. After Caesarean delivery, infectious morbidity and material mortality may result from a number of post-partum infections. These include endometritis, urinary tract infection and surgical site infection. These lead to an increase in hospital stay and expense. Inspite of modern standards of pre-operative techniques and prophylactic antibiotics, post-operative wound infection still remains a
serious issue of any surgery. The use of prophylactic antibiotics has become a standard practice in many centres, but its indiscriminate use has led to the evolution of many multi resistant organisms.4

Many investigators are attempting to identify the factors that may predispose the patients undergoing Caesarean Section to post-operative infection. A consistent agreement in defining these factors has not been decided upon. Endogenous micro flora of the lower genital tract is frequently a cause of the development of post-operative infections after obstetric surgery. These bacteria gain entrance to the upper genital tract and pelvic cavity during labour or Caesarean Section. A large number of aerobic and anaerobic gram negative and gram positive bacteria including staphylococci; streptococci, members of enterobacteria, bacteroids and other aerobes colonize the lower genital tract.4 A few workers documented about the frequent surgical glove contamination during extraction of fetal head. The dorsal aspect of surgeons gloves are frequently contaminated after extraction of fetus; non staphylococcal bacteria are significantly present.4 They suggested that bacteria are inoculated directly into surgeons hand because during the process of extraction, the dorsal aspect of the surgeons hand usually comes in contact with either the vaginal wall or the endocervical canal, and thus gets contaminated. The contaminated glove is again reintroduced into the abdominal cavity and the operative field that otherwise would be sterile, which causes wound complications.4 Hence, the intra-operative glove changing technique has been studied here.

A review of literature showed that only 2 studies, 1st small study of 92 patients was published in 2004 in journal of Reproductive Medicine,4 2nd study was conducted in Karantaka, India in 2014 including 150 patients in study.7 Both of these studies concluded that obstetricians may decrease the number of post-operative cesarean infections by having the entire team change surgical gloves after delivery of placenta,6,7 but both of these studies lacked power and timing of change of gloves. Changing gloves after the delivery of placenta was not very practical during course of surgery. Recent study performed in 2018 by Buvana,9 Jonathan Scrafford published in ACOG concluded that changing gloves before abdominal closure brings down the rate of wound infection by almost 50% in cesarean section.8 But further research is needed to aid in findings of Buvana9 and Scrafford,12 which is the rationale of conducting this study. The objective of the study was to compare the efficacy of changing gloves by entire surgical team vs no glove change by surgical team intra-operatively before abdominal closure on post-operative infectious morbidity and wound complications during elective cesarean.

METHODOLOGY

A Randomized Controlled Trial was done at Department of Obstetrics and Gynaecology, Lady Willingdon Hospital, Lahore, from June – December 2020. Sample size of 60 patients, 30 patients in each group is estimated by using 95% confidence level, 10% absolute precision with expected %age glove changing group as 6.4% and control group as 13.6%4 were after approval from ethical committee and informed consent. Subjects of age 20-40 years, at gestational age >37 weeks undergoing elective LSCS having Hb>10g/dL with intact membranes prior to surgery and less than 3 vaginal examinations prior to surgery were selected through non probability consecutive sampling. Previous history of gape wound, morbid obesity (BMI>30), rupture of membranes >4 hours prior to surgery and uncontrolled GDM or Chronic Diabetes and subjects with placenta Previa/ accrete were excluded from study.

Random selection of subjects was into two groups by using lottery method. In group A, outer pair of sterile gloves will be changed by entire surgical team including surgeon, assistant and scrub nurse before abdominal closure during cesarean section, while group B, will be the controlled group in which gloved will not be changed during the procedure. All patients were given prophylactic pre-
operative antibiotics. Patients will be followed up in post-operative ward for signs and symptoms of fever, endometritis, cellulitis, wound seroma or the wound dehiscence daily till second post-operative day, patients will be discharged if there is no post-operative complication and finally will be observed at the day of stitches removal. Outcome was infectious morbidity in terms of Febrile morbidity: Defined as 2ºC temperature elevations ≥38ºC was observed 24 hours after surgery on 2 occasions 6 hours apart, wound infection defined as a presence of cellulitis (Hyperemia, Induration, and wound dehiscence (separation of at least 1 cm). We hypothesized that glove changing technique before abdominal closure by surgical team during elective cesarean section may decrease the post-operative infectious morbidity and wound complications. Data was entered and analyzed statistically by using SPSS version 26. Quantitative variables like patient age, gestational age at delivery, estimated blood loss, pre & post-operative Hb etc were presented in the form of mean ± S.D. Qualitative variables like parity, wound complications etc were presented in the form of frequency and percentage. Comparison of two groups, Group A and Group B was done by applying Chi-Square with p-value ≤0.05 as significant.

RESULTS

60 patients were included in the study and mean age was 26.17 ± 5.7 years. Minimum age was 16 years and maximum was 41 years. 76.7% were less than 30 years. Mean parity was 3.2±3.0 years. 46.7% were with parity between 2 to 5. Mean gestational age was 36.7 ± 5.6 weeks. 96.7% were more than 30 years. 100.0% were from urban area. 61.7 % were illiterate, 33.3% had primary education. (Table no: 1). Outcome among groups were compared, In group A (with gloves) fever and purulent discharge from site were present in 3.3% of subjects as compared to Group B in 26.7%. (p< .05). 13.3% in Group B developed endometritis. (p<.05) and 6.7% developed wound dehiscence. (p> .05). (Table no: 2)

DISCUSSION

An increasing body of literature suggests that during cesarean section infectious morbidity increases when vaginal floral bacteria are introduced in to

Table 1: Demographic and Obstetrics Profile of Subjects

<table>
<thead>
<tr>
<th>Variables</th>
<th>n=  60</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Mean=26.17</td>
<td>41</td>
<td>66.7</td>
<td></td>
</tr>
<tr>
<td>SD=5.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min=16 Max=41</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 30 years</td>
<td>46</td>
<td>76.7</td>
<td></td>
</tr>
<tr>
<td>&gt; 30 years</td>
<td>14</td>
<td>23.3</td>
<td></td>
</tr>
<tr>
<td>Parity Mean=3.2</td>
<td>5</td>
<td>25.0</td>
<td></td>
</tr>
<tr>
<td>SD=3.0 Min0=Max=5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P/G</td>
<td>15</td>
<td>25.0</td>
<td></td>
</tr>
<tr>
<td>&lt; 2</td>
<td>17</td>
<td>28.3</td>
<td></td>
</tr>
<tr>
<td>2 – 5</td>
<td>28</td>
<td>46.7</td>
<td></td>
</tr>
<tr>
<td>Gestational age</td>
<td>42</td>
<td>66.7</td>
<td></td>
</tr>
<tr>
<td>Mean=36.7 SD=5.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min4=Max=42</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 30 weeks</td>
<td>2</td>
<td>3.3</td>
<td></td>
</tr>
<tr>
<td>&gt; 30 weeks</td>
<td>58</td>
<td>96.7</td>
<td></td>
</tr>
<tr>
<td>Residential status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>60</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Illiterate</td>
<td>37</td>
<td>61.7</td>
<td></td>
</tr>
<tr>
<td>Elementary</td>
<td>20</td>
<td>33.3</td>
<td></td>
</tr>
<tr>
<td>Matric – FA</td>
<td>3</td>
<td>5.0</td>
<td></td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Housewife</td>
<td>60</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Outcome among groups

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Group</th>
<th>Group A (n=30) (With Glove change)</th>
<th>Group B (n=30) (Without Glove change)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Fever</td>
<td>Freq.</td>
<td>%</td>
<td>Freq.</td>
<td>%</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>3.3%</td>
<td>29</td>
<td>96.7%</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>0</td>
<td>0.0%</td>
<td>30</td>
<td>100.0%</td>
</tr>
<tr>
<td>Purulent Discharge from the incision site</td>
<td>0</td>
<td>0.0%</td>
<td>30</td>
<td>100.0%</td>
</tr>
<tr>
<td>Endometritis</td>
<td>0</td>
<td>0.0%</td>
<td>30</td>
<td>100.0%</td>
</tr>
<tr>
<td>Wound Seroma</td>
<td>0</td>
<td>0.0%</td>
<td>30</td>
<td>100.0%</td>
</tr>
<tr>
<td>Wound Dehiscence</td>
<td>0</td>
<td>0.0%</td>
<td>30</td>
<td>100.0%</td>
</tr>
</tbody>
</table>
normally sterile environment. An important vehicle of bacteria to the abdominal wall are Surgeon’s gloves, exposed to the lower genitourinary tract during delivery of an infant. The incidence of wound complications following cesarean section can be drastically reduced by changing gloves during cesarean prior to abdominal wall closure.

A previous small randomized controlled trial in which women were assigned to either usual care or glove changing after delivery of the placenta, the results are consistent with our study. In this study, glove changing showed a significant reduction in wound infections (25% to 5.5).

No benefit of intra-operative glove changing was seen in second randomized study of 228 women undergoing cesarean delivery in which the primary outcome was rate of endometritis (17.7% vs 15.7%). This difference is likely due to the extremely low rates of endometritis and inadequate power in this relatively small study.

There have been several studies evaluating the use of a surgical bundle conducting among women undergoing cesarean sections, however none of these included glove changing, in order to reduce the rates of surgical site infection (SSI). A meta-analysis showed these bundles when implemented can lead to decreased SSI. Several studies have looked at the role of introduction of a SSI reduction bundle to reduce surgical site infections in other specialties. In all of these studies, glove changing has been included as part of the bundle and all have shown an improvement in the rates of SSI with the introduction of the bundle. Interestingly, it was not shown to improve SSI when glove changing was studied in urological, gynecologic oncology and colorectal procedures as a single intervention, outside of the bundle in a randomized trial. The difference in results between this study and ours may be because cesarean sections and these surgical procedures are different procedures.

In study by Buvana et al showed that in the first 409 patients analyzed, a significant decrease in ‘composite wound complications’ is seen in the glove-changing group (11/185, 5.9%) as compared to the control group (29/224, 12.9%), with p-value 0.018.

Strengths of this study are that there is a large sample size, randomized design, and broad inclusion criteria which makes the results potentially applicable to most clinical practice cesarean sections. In a study by Scrafford et al which was on the effect of intra-operative glove-changing during cesarean section on post-operative complications, Intra-operative glove changing did cause a significant reduction in composite wound complications from 13.6% in the control group to 6.4% in the intervention group (p=0.008). This concluded that prior to abdominal closure during cesarean section, intra-operative glove changing significantly reduced the incidence of post-operative wound complications.

Several found that there is a significant reduction in rates composite wound infection if the surgical team practiced this protocol of changing their gloves prior to closure of the abdomen during a cesarean section. Based on these results, it is recommend that this intervention should be included as a routine part of an obstetrician’s surgical practice, and encourage its adoption into surgical bundles for the population. In this study there are a few limitations. First, was the lack of blinding of the surgeons, some of whom were responsible for the choice of vaginal preparation and also performing post-operative examinations on these patients. Second, there was no control and record of whether the surgeons and other staff completed the glove change in the medical record, though the final analysis of the was conducted using intention to practice methods as opposed to routine methods. Finally, this study is limited by its single institution design and might not be applicable to other types of hospital settings or patient populations.

CONCLUSION

Use of intraoperative glove changing during cesarean section significantly reduced postoperative wound infection and complications.
Acknowledgments

We are grateful for department of Gynaecology and Obstetrics Unit of Lady Willington Hospital for processing samples collected by the researchers. We would like to appreciate hospital ethical review board of above mentioned hospitals for providing us opportunity for data collection and sampling.

Limitations of the study

There are a few limitations or constraints in our research. The data was obtained from single operation theatre of gynae-cology and obstetrics units of a tertiary care hospital, so results cannot be generalized to population. Another drawback of this study was small sample size and confounding factors like immune status of subjects cannot be controlled especially during pregnancy.

Conflicts of interests

None

Funding sources

None

Authors contributions

Following participants contributed in research

1. Dr. Afroze Ashraf – Assistant Professor – King Edward Medical University Lahore/Lady Willington Hospital Lahore-Unit 1: Principal investigator, data collection and discussion writing

2. Dr. Rehana Ayub – Associate Professor – Gynae Obstetrics – Fatima Jinnah Medical University Co-investigator, data collection and discussion writing

3. Dr. Nasreen Akhtar – Associate Professor Department of Forensic Medicine and Toxicology: Data analysis and report writing

REFERENCES


In January 2020, World Health Organization announced eruption of a current communicable Coronavirus disease named (COVID-19), and it has globally spread rapidly causing infectious pneumonia. In March 2020, according to WHO assessment COVID-19 would be a pandemic problem in future. China is the First country who reported COVID-19 patient and according to China’s National Health Commission report 49824 COVID-19 patients are confirmed. The Government of China, Health care provider team and Public are facing great pressure

Abstract

Objectives: To ascertain the prevalence of stress and anxiety disorders among Medical Students, Pregnant Women and Health Care Providers during Pandemic of COVID-19 and to do Comparison which group is affected more amongst three so strategies could be streamlined to cope.

Methodology: Using 7-items (GAD-7) instrument we conducted three cross-sectional studies “Psychological Impact of COVID-19 Pandemic on Medical Students (1), on Pregnant Women (2) and on health care providers (3), (Junior-doctors, Nurses, and Paramedical-staff) of Gulab Devi Educational Complex attached with Al- Aleem medical college over a period of two months from November 2020 to December 2020 after approval from Institutional Review Board. Non probability convenience sampling technique was used, a total of 350 willing participants were recruited in this study, 150 medical students 50 from each 1st, 2nd, 3rd year, 100 pregnant women and 100 Health Care Providers. The data was collected by handing over “The 7-item Generalized Anxiety Disorder Scale (GAD-7)” Performa. Data was entered, analyzed and compare by SPSS version 23.

Results: The total prevalence in medical students, pregnant women and HCP was 81%, 97% and 86% respectively. The most affected group was of pregnant women. Mild degree of anxiety was present in all groups almost equally, moderate degree was maximally (59%) found in pregnant women. Severe degree (21%) of anxiety was observed in Medical students. Kruskal-Wallis Test was applied to get P-Value it was 0.041, said to be statistically significant.

Conclusions: Significantly high level of stress and anxiety disorders (97%) was found in pregnant women during pandemic of COVID-19, Medical students and Health Care Providers are also affected. This is an alarming issue and need of the hour to deal both at community and government levels, in order to keep psychological wellbeing.

Keywords: Medical Students, pregnant women, Health Care Providers (Junior Doctors, Nurses, Paramedical Staff), Stress, Anxiety, Depression.
COMPARISON OF PSYCHOLOGICAL IMPACT OF COVID-19 PANDEMIC AMONG MEDICAL STUDENTS

because of huge scale infectious disease. In Pakistan COVID-19 virus was reported first time on 26 February 2020, when report of the student confirmed positive of COVID-19 in Karachi when he came back from Iran. From 18 March 2020 onward COVID-19 positive patients had been registered in all provinces including Islamabad. COVID-19 a new disease has affected the attitude and behaviors of the general population, students, health care providers and pregnant women throughout the world and is responsible for different types of anxiety disorders. Quarantine, lockdown, fear of getting COVID-19 infection and death has been responsible for psychological disturbances in general population, students, pregnant women and in health care providers. In the well-developed countries different preventive measures like use of mask, social distancing, quarantines, curfew and lockdown were taken for public safety, similar measures were also taken by our government. The objectives of this study was to ascertain the prevalence of stress and anxiety disorders among Medical Students, Pregnant Women and Health Care Providers during Pandemic of COVID-19 and to do Comparison which group is affected more amongst three, so that strategies could be streamlined to cope and reduce it.

METHODOLOGY

Using 7-items (GAD-7) instrument we conducted three cross-sectional studies “Psychological Impact of COVID-19 Pandemic on Medical Students (1), on Pregnant Women (2) and on health care providers (3), (Junior-doctors, Nurses, and Paramedical-staff) of Gulab Devi Educational Complex attached with Al- Aleem medical college over a period of three months from November 2020 to December 2020 after approval from Institutional Review Board. Non probability convenience sampling technique was used, a total of 350 willing participants were recruited in this study, 150 medical students 50 from each 1st, 2nd, 3rd year, 100 pregnant women and 100 paramedics. The Data was collected by handing over “The 7- item Generalized Anxiety Disorder Scale (GAD-7)” Performa to all participants after informed consent including demographics. The purpose of study, importance of anxiety disorders and how to fill the Performa was explained in first 5 minutes. The filled Performa’s were then collected after 4-5 minutes. Generalized Anxiety Disordered Scale (GAD-7) is most popular instrument for detection and screening of Anxiety Disorders, now a days it is used for screening, diagnosis, and the assessment of anxiety disorders, social phobias, post traumatic and post pandemic disorders. “The 7-item Generalized Anxiety Disorder (GAD-7; range 0-21)” was utilized to appraise the severe-ness of symptoms of anxiety. The score (0-4) was considered as normal, (5-9) showed mild anxiety, (10-14) moderate anxiety, and (15-21) severe anxiety/depression. The data was entered, rechecked by an expert one for confirmation of correct entry and then analyzed using SPSS version 23. Descriptive Statistics was used to check the prevalence and percentage of all quantitative variables, the response rate was 100 percent.

RESULTS

Table-I highlight the prevalence of stress and anxiety disorders, in medical students it was 81%, in pregnant women 97% and in HCPs 86%. The most affected group was of pregnant women. Table-Ill depict the degree of anxiety disorders among three groups. Mild degree of anxiety was present in all groups almost equally, moderate degree was maximally (59%) found in pregnant women. Severe degree (21%) of anxiety was observed in Medical students. Kruskal-Wallis Test was used to get P-Value it was 0.041 said to be statistically significant.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Numbers</th>
<th>Prevalence</th>
<th>Mean Rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Students</td>
<td>150</td>
<td>81%</td>
<td>168.60</td>
</tr>
<tr>
<td>Pregnant Women</td>
<td>100</td>
<td>97%</td>
<td>187.38</td>
</tr>
<tr>
<td>Health Care Prov.</td>
<td>100</td>
<td>86%</td>
<td>172.18</td>
</tr>
<tr>
<td>Total</td>
<td>350</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
DISCUSSIONS

World Health Organization “define Health as a state of Physical, Mental, and social wellbeing and not merely the absence of disease or infirmity”. Stress and anxiety disorders including depression are considered to be a normal emotional response to any pandemic condition. Medical Students of any Institution are the future consultants, their health both physical, mental and grooming is utmost important to become a seven star doctors. Health Care Providers (Junior doctors, Nurses, Paramedics) are the assets of any hospital, also called First line defenders, their health both physical and mental is significantly important for proper carrying of patients. Pregnant Females belongs to special class, during pregnancy proper carrying in respect of food and health play an important role at the time of delivery and in puerperium. According to Literature review any sort of outbreak or pandemic situation would cause psychological problems e.g. anxiety, fear, depression, lack of sleep or concentration to people from all walks of life. The prevalence of stress and anxiety disorders in our study among three group was highest in Pregnant Women 97%. The reason could be because of lack of awareness among health care providers along with improper infrastructure for delivery and neonatal care in COVID-19 positive patients in Pandemic situation this finding is consistent with other studies. Development of stress and anxiety disorders during outbreak mainly depend upon the mental health, duration of pregnancy and living conditions of the women. Moderate degree of anxiety was maximally found in pregnant women amongst three groups. The Second group that was affected in this study was Health Care Providers, Prevalence was 86% that is significantly high. It could be increasing work load, limited preventive resources, sleep deprivation, lack of knowledge and skills to handle the COVID-19 positive cases and this high prevalence in Pakistan is tallying with others studies. The Third group in our study that affected during COVID-19 Pandemic was of Medical Students, the prevalence of stress and anxiety disorders was 81% that is an alarmingly high suggesting emergency measures should be taken to reduce it in order to produce good quality doctors, these findings was quite high from other studies. It was found in the study that that severe degree of anxiety was found in medical students 21%, that is significantly high and is responsible for affecting the cognitive and psychomotor skills. Medical students are next generation of doctors, their mental and physical health is vitally important to make them fruitful doctors both for Local and National level. Kruskal - Wallis test was applied to get the P-Value among three groups and it was 0.041, showing significant result of the study, any P-Value < 0.05 is considered as statistically significant. The results of our study are alarmingly high, so immediate preventive strategies and their implementation are the need of the hour in order to reduce the psychological impact of COVID-19 at Community and Government levels. Our government is focusing on personal protective equipment’s, quarantine, social distancing, facial masks and social activities for the safety of public, but Focused Policy is urgently required to address physical, mental, psychological and social morbidities and mortalities linked with COVID-19 emergencies.

Limitation of the Study: As the study is conducted only in one teaching hospital so results of this study could not be generalized but this data would act as a platform for generation of new data’s for future researches.
CONCLUSIONS

This study highlight the high level of stress and anxiety disorders among three groups during COVID-19 Pandemic in Pakistan. Significantly high levels (97%) in pregnant women, (86%) in Health Care Providers and (81%) in Medical Students was found in the study. This is an alarming issue and need of the hour to deal both at community and government levels in order to keep psychological well-being. To reduce the stress and anxiety special preventive strategies and its implementation are urgently required. Effective Leadership, Training and Coaching Classes and provisions of Personal Protective Equipment’s at community level are top priorities of the society and local government.

Acknowledgments

I am really thankful to my team especially Dr. Faiza Nisar and Dr. Amna Rafique at Gulab Devi Educational Complex Lahore for their sincere practical help in this study.

Conflicts of Interest

I don’t have any conflicts of interest regarding the study.

Funding Sources

No external funding is used.

Author’s Contributions

NI and IAA conceptualized the idea and made research proposal, FN collected the data, KM, NN, helped in entering data and made tables, AR helped in analyzing data and Editing. MZUM, NK, NA supervised the study.

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Management of Hypoxia Using High-Flow Nasal Cannula Versus Non-Invasive Ventilation in Hypoxemic Patients Undergoing Flexible Bronchoscopy

Muhammad Saqib Musharaf, Umar Usman, Mehr Muhammad Imran, Asad Javaid, Faisal Hassan Zahid Chaudhry, Syed Arif Saeed Zaman

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Abstract

Background: Bronchoscopy enables to analyse and visualize the trachea-bronchial passage by placing an optical instrument inside the airways. Non-invasive ventilation (NIV) is a well-known procedure, is about the supply of ventilatory assistance by using the individual's upper airway through a mask or identical device. Hi-Flow Nasal Cannula (HFNC) refers to a device that delivers oxygen at a high flow rate. It provides 0.21 – 1.00% FiO2 with flow rates. The present study wants to evaluate the application of NIV vs HFNC in patient undergoing flexible bronchoscopy so to combat the hypoxia which often occurs during bronchoscopy.

Methodology: Objective: To compare the effect of relieving hypoxia undergoing flexible bronchoscopy by applying NIV versus HFNC in hypoxic patients. It was randomized, cross sectional study performed at District Head Quarter Faisalabad, from July 2019 to September 2020. According prior research the lowest SpO2 had been 95%±5% [14]. To detect a three percent variation in the lowest SpO2 during the FB course along with a power of eighty percent as well as a degree of significance of five percent, 45 patients were calculated to be enrolled in each group.

Result: The mean age in our study was 46.5±12.2 years, with male predominance 71% (n=31). The mean oxygen saturation was 88.3±6.7% on room in NIV group and 91.3±5.6% in HFNC group on room air pre-bronchoscopic. The mean oxygen saturation was 94.3±4.3% in after application of NIV and 90.3±7.6% in HFNC group with bronchoscopic. Three patients from NIV group vs one patient required ETI. No significant cardiac arrythmias, haemoptysis or pneumothorax demonstrated in both groups.

Conclusion: NIV and HFNC are effective means of oxygenation during FB procedure. In hypoxemic patients, NIV provided more suitability and feasibility of oxygenation and cardiopulmonary specification than HFNC.

Key Word: Bronchoscopy, Non-invasive ventilation, High flow nasal flow cannula, Oxygen saturation.
invasive. Application of NIV thus avoid the need of intubation and at the same time support the respiratory system to help in breathing.\textsuperscript{2}

Hi-Flow Nasal Cannula (HFNC) refers to a device that delivers oxygen at a high flow rate. It provides $0.21 - 1.00\% \text{FiO}_2$ with flow rates as high as sixty litres/min. Both $\text{FiO}_2$ and the flow rate are often separately titrated determined the patient’s flow as well as the requirements of $\text{FiO}_2$.\textsuperscript{1}

The present study wants to evaluate the application of NIV vs HFNC in patient undergoing flexible bronchoscopy so to combat the hypoxia which often occurs during bronchoscopy. To our knowledge there is no comparison study conducted in our country so far. So, the date will enhance our knowledge of understanding.

**METHODOLOGY**

The objective of the study was to compare the effect of relieving hypoxia undergoing flexible bronchoscopy by applying NIV versus HFNC in hypoxic patients. It was randomized, cross sectional study performed at District Head Quarter Faisalabad, from July 2019 to September 2020. According prior research the lowest $\text{SpO}_2$ had been $95\% \pm 5\%$.\textsuperscript{14} To detect a three percent variation in the lowest $\text{SpO}_2$ during the FB course along with a power of eighty percent as well as a degree of significance of five percent, 45 patients were calculated to be enrolled in each group.

**Inclusion Criteria**

1. Adult patients age more than 18 years
2. Both genders
3. Flexible bronchoscopy advised by consultant pulmonologist.
4. Patient requiring diagnostic or therapeutic bronchoscopy.
5. Patients who have hypoxemia pre-procedure i.e., $\text{SpO}_2 < 94\%$ despite supplemental oxygen.

Following the registration, individuals have been randomized in the 1:1 ratio to receive either HFNC or NIV to correct hypoxemia during bronchoscopic procedure with target $\text{SpO}_2 \geq 94\%$.

With the dedicated machine of NIV (By Philips Respironics), individuals in the group of NIV were ventilated. Along with elastic banding, the full-face mask adjunct was utilized whilst the interface. The (T-adapter) swivel connector had been placed within the face mask and ventilator tubing allowing the bronchoscope insertion. Bi-range positive airway pressure mode has been set as ventilator parameters, along with 6 cm H$_2$O (EPAP) expiratory positive airway pressure as well as IPAP (inspiratory positive airway pressure) with the range which reached 8 mL/kg of tidal volume or a minimum of 10cm H$_2$O.

HFNC had been provided constantly by using the nasal cannula. The rate of inspiratory flow had been 40 L/min, as well as the $\text{FiO}_2$ had been maintained at 0.6 all through and 30 minutes just after the process.

Bronchoscopic procedure was performed six to eight hours of pre-procedure fasting was done. No premedication with sedation was done. Before procedure oxygen saturation, heart activity and blood pressure were examined, and monitored continuously throughout the procedure. A physical exam was performed, and an informed consent was obtained from the patient after explaining the risks, (pneumothorax, life threatening bleeding, infection, and adverse effects due to medications) benefits and alternatives to the procedure which the patient appeared to understand and so stated. The patient was connected to the monitoring devices. IV was saved. Lidocaine 4%, 2%, viscous lidocaine, were used for local anaesthesia. The bronchoscope was inserted through mouth in case of HFNC and through special port made in full face mask. No sedation was given during procedure to avoid the effect of CNS suppression as a contributory factor to worsening hypoxemia. BF-P180, flexible bronchoscope (made by Olympus, Japan; as external diameter, 4.9 mm; channel diameter, 2.0 mm) was used in procedure in both groups.

Patient oxygen saturation was monitored and recorded on Performa by a third person at two
minutes interval during procedure and 15 minutes after procedure.

Patient’s vitals (pulse, blood pressure, respiratory rate) and oxygen saturation was analysed just before application of NIV or HFNC (labelled as T0), soon after application of HFNC or NIV (T1), then monitored and recorded at two minutes interval (T2), and fifty minutes soon after FB (T3), before switching to nasal oxygen therapy. This is shown in figure 1.

![Figure 1: Assessment of Various Parameters](image)

The visual analogue scale of dyspnoea had been also assessed upon T0, T1, T2, and T3 by using a 10-cm long horizontal line with anchor statements on the left (no dyspnoea) and on the right (extreme dyspnoea). It had been advised the patient to mark the point on the line that best corresponds to their symptom severity.

Complications like haemoptysis, cardiac arrhythmias, cardiac arrest, over sedation, lowest \( \text{SpO}_2 \) (defined as sustained fall in oxygen saturation for upon least thirty seconds during FB), pneumothorax, need for (ETI) endotracheal intubation soon after FB, have been documented.

**RESULTS**

The lowest \( \text{SpO}_2 \) during the FB course had been the major outcome. Secondary outcomes were variations within hemodynamic parameters, dyspnoea scale, oxygen saturation, were recorded.

All values have been indicated as mean ± standard deviation (SD) for constant variables as well as percentages for specific variables. Between the comparisons of groups about constant variables have been practiced with Student’s two-tailed t-test or nonparametric Mann-Whitney U-test in the case of a normal distribution. In the case of low expected frequencies, the Chi-square test or Fisher’s exact test was applied for comparisons of specific variables. ETI at 7 days and mortality at twenty-eight days as soon as FB had been evaluated through the Kaplan-Meier technique, as well as variations between the HFNC and NIV had been evaluated through the log-rank test. Each statistical test had been two-sided, and \( P<0.05 \) was regarded as statistically significant. Each data had been examined by using the SPSS statistical software package, version 20.0 for Windows (SPSS, Chicago, IL).

**DISCUSSION**

The mean age in our study was 46.5±12.2 years, with male predominance 71% (n=31). The mean oxygen saturation was 88.3±6.7% on room in NIV group and 91.3±5.6% in HFNC group on room air pre-bronchoscopic. The mean oxygen saturation was 94.3±4.3% in after application of NIV and 90.3±7.6% in HFNC group with bronchoscopic. Three patients from NIV group vs one patient required ETI. No significant cardiac arrhythmias, haemoptysis or pneumothorax demonstrated in both groups.

In our study, we compared HFNC with NIV in hypoxemic patients undergoing flexible bronchoscopy to correct their hypoxemia. These sorts of studies have been conducted in past with comparison of HFNC to NIV in different clinical situations such as acute hypoxemic respiratory failure and preoxygenation prior to intubation, post-operative cardiothoracic surgery, COPD. In hypoxic patients both these methods, i.e., NIV and HFNC were able to improve oxygenation.

NIV has some pros over HFNC. HFNC is not effective to improve EPAP. But its flow can generate positive airway pressure in the upper airway to
alveoli. It can also increase expiratory pressure breathing with a closed mouth. The flow rate of HFNC is also very much improved at fixed FiO₂. NIV provides EPAP which is helpful in the prevention of rising of mean airway pressure, alveolar collapse and decrease of breathing. IPAP is also helpful in tidal volume at low efforts. NIV provides high inspiratory flow at constant FiO₂.

Our research demonstrates that NIV is more effective than HFNC. The reason for this during flexible bronchoscopy at first EPAP decreases when the mouth is opened, as closed mouth is often required for proper delivery of air to lungs. On contrary, EPAP is maintained with NIV facemask even with the open mouth of patients. It is because of the closed loop of the NIV facemask. Moreover, HFNC ensures a constant flow lower inspired FiO₂ results as inspiratory efforts and expiratory efforts increase during the procedure and flow may not be enough. In comparison, in NIV the flow can be sufficient to attain the target inspiratory pressure. In conclusion, NIV and HFNC are well tolerated and effective for oxygen supplementation during the FB procedure in patients with hypoxemia. NIV provided more adequacy and stability of oxygenation and cardiopulmonary parameters.

The need for endotracheal intubation (ETI) was mostly required in the NIV group. In previous studies, if ETRI was performed ETI within 8 hours after the FB procedure, it was considered as a procedure related to ETI. In our study, the reason for increase ETI in NIV vs HFNC although statistical not significant, baseline SpO₂ was lower in the NIV group, reflecting in more severe pulmonary diseases in this group.

**CONCLUSION**

To sum up, NIV and HFNC are effective means of oxygenation during FB procedure. In hypoxemic patients, NIV provided more suitability and feasibility of oxygenation and cardiopulmonary specification than HFNC.

**Limitations of the study**

Limitations of this studies are that ABGs were not used instead on SpO₂ we relied. Sample size is small, larger sample with diverse population will clarify the ambiguity between which modality is preferred i.e., HFNC versus NIV for management of hypoxia.

**Conflicts of interest**

None

**Funding sources**

None

**REFERENCES**


FREQUENCY OF DEPRESSION IN INFERTILE WOMEN

Abdul Haleem, 1 Nabeel Ibad, 2 Junaid Rasool, 3 Rabia Asghar, 4 
Muhammad Imran Sharif, 5 Manzoor Ali 6


Abstract

Background: The desire of many young women to become parents may be influenced by the premium placed on children by society. Children are highly valued for social, cultural and economic reasons. Infertile and childless women in South Asia are therefore confronted with a series of societal discrimination and stigmatization which may lead to psychological disorders such as anxiety and depression. Even though some research has been done on the prevalence of infertility in worldwide, very little is known about the psychological impact of childlessness among infertile women. The present study aimed to examine prevalence and severity of depression in relation to age, type of infertility and duration of infertility in Local infertile women. The objective of the study was to determine the prevalence of depression among infertile women.

Methodology: Data of 220 infertile women patients, visiting Infertility centre, Jinnah Hospital, were collected, after filling proforma and informed consent forms. Socio-demographic information including age, duration of infertility, educational level were obtained from the respondents. The occupation, monthly income and whether the subjects presenting with primary or secondary infertility were also obtained. Data relating to psychiatry impact of infertility were obtained using the Hamilton Depression Rating Scale (HDRS).

Results: The prevalence of depression among the women was 64.1% with the level of depression showing a significant positive correlation with age of the women and the duration of infertility. The level of depression was significantly higher among subjects with low or no formal education and among the unemployed. Women with primary infertility also presented with high depression scores as measured by HDRS.

Conclusion: In conclusion, the prevalence of depression among the infertile women is high, especially among infertile women age 26 and above, those who are less educated, those with primary infertility, as well as those who have been diagnosed as infertile for more than 3 years. Interventions to decrease and prevent the development of severe depression among these patients should be considered.

Key Words: Fertility, Infertility, Anxiety, Depression.

Infertility as defined by WHO and others is the inability of a sexually active non-contraceptive using, non-lactating woman to have a live birth after 12 or more months of regular sexual intercourse. The type and prevalence of infertility varies widely from one country to the other. In Sub-Saharan Africa, secondary infertility is the most prevalent type of infertility.

Secondary infertility is defined as the inability of a sexually active non-contraceptive using woman who has previously had a live birth to have a child.
FREQUENCY OF DEPRESSION IN INFERTILE WOMEN

Despite cohabitation and the wish to become pregnant for at least 12 months. The inability to have children is undeniably a very distressing experience in women which can lead to major psychological disorders such as depression.

Depression is said to be a major problem associated with infertility especially in Africa where children are highly valued for socio-cultural and economic reasons. Childlessness often creates enormous problems for women, who are generally blamed for the infertility status of women. Studies from communities in Nigeria showed that infertile women are often excluded from social events and ceremonies or may even be despised and perceived as inauspicious.

Prevalence of infertility is highest in South/Central Asia, Sub-Saharan Africa, North Africa/Middle East, and Central/Eastern Europe. Prevalence of infertility among young women was estimated 10% in the United State, 11.5% to 15.7% in Canada, 12.6% in India, 1.72% in China.

Depression is a common mental disorder affecting about 121 million people worldwide. This psychiatric disorder is usually diagnosed by a number of signs and symptoms like depressed mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy, and poor concentration.

Depression contributes to the global burden of diseases and is estimated to become the second leading cause of disability by the year 2020. Infertility has a tremendous psychiatry impact on infertile women like anxiety and depression. This disorder may increase the duration of infertility. It is estimated that about 40% of infertile women experience anxiety and 86% experience depression.

Several studies have been conducted in Iran in order to investigate prevalence of depression among infertile women. The prevalence of depression in infertile women is reported from a minimum of <5% to a maximum of >50%.

In a study, the prevalence of depression among the infertile women was 62% with the level of depression showing a significant positive correlation with age of the women and the duration of infertility. The level of depression was significantly higher among subjects with low or no formal education and among the unemployed. Women with primary infertility also presented with high depression scores.

In a Pakistani study (2014), of the 120 subjects, the two groups had 60 (50%) each. The mean age of fertile women was 27.48±160.75 and that in the infertile group was 27.36±160.75. Depression among fertile women was 21.85±10.98 compared to 32.01±12.49 among the infertile women. Corresponding values for anxiety was 24.45±9.63 and 36.20±12.51. The difference was significant.

The study was to determine the prevalence of depression among infertile women.

Infertility: The inability of a sexual active non-contraceptive using woman to have a live birth after 12 or more months of regular sexual intercourse without a male factor.

Primary Infertility: A woman is unable to ever bear a child, either due to the inability to become pregnant or the inability to carry a pregnancy to a live birth will be classified as having primary infertility.

Secondary Infertility: A woman is unable to bear a child, either due to the inability to become pregnant or the inability to carry a pregnancy to a live birth following either a previous pregnancy or a previous ability to carry a pregnancy to a live birth will be classified as having secondary infertility.

Depression: For measuring the severity of depression, Hamilton Depression Rating Scale (HDRS) scale was used. Scale (0-7) as no depression and above 7 was considered as depression.

METHODOLOGY

The study was conducted in Infertility centre, Jinnah Hospital, Lahore from 30/06/16 to 30/12/16. Non-probability consecutive sampling was done. It was a cross sectional study. The sample size of 220 was estimated by using 95% confidence level and 6.5% margin of error with expected percentage of depre-
Depression among infertile women i.e. 62%. Inclusion Criteria
Infertile women (as per operational definition) Ages between 20-50 years
Exclusion Criteria
History of in-vitro fertilization
History of male factor infertility
Pregnant women
Data of 220 infertile women patients, visiting Infertility centre, Jinnah Hospital, was collected, after filling proforma and informed consent forms. Socio-demographic information including age, duration of infertility, educational level, number of previous children were obtained from the respondents. The occupation, monthly income, whether the subjects were presenting with primary or secondary infertility were also obtained. Data relating to psychiatry impact of infertility were obtained using the Hamilton Depression Rating Scale (HDRS). The test was used is a modified and validated Urdu version.

Data were entered and analyzed by using Statistical Packages for Social Sciences (SPSS) v22.0. Frequencies and percentages were used for qualitative data like Occupation, Education, Conception, Type of infertility, Duration of infertility and depression. Quantitative data like Age were presented by using Mean±S.D. For comparisons, chi-square was used. Data were stratified for Age, Duration of infertility, education and conception to address the effect modifiers. In all statistical tests, a value of P < 0.05 was considered significant.

RESULTS
The mean age of the subjects was 34.58±9.03. Majority of the subjects 37.7% (83/220) were within 20-30 years age group followed by those in the 31-40 year group (33.6%). About 5.9% of the women were self-employed engaging in petty trading and dress making with only 9.1% of them being employed as civil servants in the formal sector.

A significant number of them (85.0%) were unemployed. In all 56.4% of the study subjects had not attained any form of formal education with only 23.2% attaining at least basic formal education.

Majority of the women presented with secondary infertility (61.8%) with 38.2% presenting with primary infertility. The results of the HDRS showed that 64.1% of the subjects had some form of depression with only 35.9% of them showing no symptoms of depression.

The type of infertility presented by the women and previous conception both had significant effect on the level of depression, with women presenting with both primary and secondary infertility (0.412) and those who had never conceived (0.007) tending to be more depressed.

Depression was more common in women age 26 years and above and highly significant in those women age 35 years and above (P < 0.001). Stratified by duration of infertility 66%, 22% and 12% of the women had been suffering from infertility ranging from 1-5 years, 6-10 years, and >10 years respectively. Duration of infertility showed a significant position correlation with HDRS score (r = 0.4736, P = 0.001).

DISCUSSION
The aim of this study was to assess depression among women with infertility. The findings of this study revealed that the level of depression increases with age which is not an unexpected result, because
it is logical that when a woman gets older she might be anxious since she knows there is an age limit to fertility. This could even be more dissatisfying in an African country like Nigeria, where emphasis on fertility of a woman determines social identity as well as acceptance into the family. The fact that most of the respondents had a minimum of secondary education, points to the fact that the group were moderately educated. It is therefore not surprising that this could have contributed to the persistent worry associated with the group as they might have sourced for educational materials to improve their knowledge on infertility. Studies have shown that the more educated an individual is, the more knowledgeable they are about their condition.

It is an uncommon finding that duration of infertility did not have any effect on depression. This disagrees with previous studies, who reported that depression increases with duration of infertility and there was a trend of increasing psychological stress with lengthening of infertility time.

However, it could be that the pressure mounted on couples from onset after marriage could have reached the peak at an early stage and early years of marriage making them to develop resistant and therefore, are not moved by the duration of infertility because they have been stressed to their limit.

Such insinuation at an early stage could have affected their psychological and emotional reaction and might have led to early depression. Therefore, it is not surprising that depression peaked between the 1-5 years of infertility and decreased at about more than 10 years in the study. The predominance of secondary infertility in this study (74.7%) agrees with other studies in our country.

Similarly, findings from a New York study that women who have previous miscarriage are at risk for depression and anxiety symptoms in subsequent years is in line with it.

This contrast the situation in other developed world where depression is higher among women with primary infertility. Near half of the respondents had mild depression, while approximately 30% of the respondents had moderate depression and severe depression was above 20%. This agrees with previous studies. The variation could be explained by the fact that fertility is one of the main and most important reason for marriage in this culture.

Equally important to this, is the issue of being a mother; nursing their children and having satisfying relationship. For instance, studies of post mastectomy clients in Nigeria assure that while their counterpart in United States are concern with the cosmetic effect of the surgery, the Nigerian women were mainly disturbed by their inability to breastfeed and concern about their husband's reaction.

It is therefore necessary that nurses should be equipped with many culturally adapted answers that could offer comfort to women with infertility. That exclusion of women with infertility from friends and families' children's parties was significant, confirms studies in Nigeria and Malawi that women were more likely to suffer the social and psychological consequences of infertility such as physical and mental abuse, neglect, abandonment, economic deprivation, social ostracism and marital breakdowns.17

Table 1: Comparison between Infertility and Depression

<table>
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<th>Depression</th>
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<th>P-value</th>
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</thead>
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</tr>
<tr>
<td>Primary</td>
<td>51</td>
<td>33</td>
<td>84</td>
</tr>
<tr>
<td>Secondary</td>
<td>90</td>
<td>46</td>
<td>136</td>
</tr>
<tr>
<td>Total</td>
<td>141</td>
<td>79</td>
<td>220</td>
</tr>
</tbody>
</table>

Table 2: Age groups wise stratification for Depression.

<table>
<thead>
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<th>Depression</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>20-30</td>
<td>48</td>
<td>35</td>
<td>83</td>
</tr>
<tr>
<td></td>
<td>57.8%</td>
<td>42.2%</td>
<td></td>
</tr>
<tr>
<td>31-40</td>
<td>56</td>
<td>18</td>
<td>74</td>
</tr>
<tr>
<td></td>
<td>75.7%</td>
<td>24.3%</td>
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<td>41-50</td>
<td>37</td>
<td>26</td>
<td>63</td>
</tr>
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<td></td>
<td>58.7%</td>
<td>41.3%</td>
<td></td>
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<tr>
<td>Total</td>
<td>141</td>
<td>79</td>
<td>220</td>
</tr>
<tr>
<td></td>
<td>64.1%</td>
<td>35.9%</td>
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</table>
The Yoruba infertile women experience social exclusion as they are often accused of being a witch and of having devoured their own children. Their exclusion is a usual finding but invitation cards can be sent. The women may have decided not to attend because it is children's party.

More than half (54.4%) of the women were coping effectively but depression was high among respondents who used positive reappraisal, planned problem solving and escape avoidance coping strategies. Positive reappraisal and planned problem solving may be because these strategies were associated with a lot of expectations that would change their conditions.

Escape avoidance coping strategies occur as a result of disappointment and lack of emotional support in all efforts to change the situation. This disagrees with previous studies. However there may be need to replicate the study using a larger sample and a prospective approach to fully appreciate the effect of these strategies.

CONCLUSION

In conclusion, the prevalence of depression among the infertile women is high, especially among infertile women age 31 and above, those who are less educated, those with secondary infertility, as well as those who have been diagnosed as infertile for more than 3 years. Interventions to decrease and prevent the development of severe depression among these patients should be considered.

Limitations of study

Our study being a cross sectional study has a limited value regarding evidence based medicine. We would also like to replicate the study in other cities to see if there are any differences in prevalence rates or associated factors of depression.

Acknowledgments

We would like to thank house officers of gynaecology department, Jinnah hospital Lahore for their help in collecting the data.

Conflicts of interest

None

Funding sources

None

Authors contributions

All six authors have contributed equally in conceptualization and detailed work of our project.

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FREQUENCY OF DEPRESSION IN INFERTILE WOMEN


Retinopathy of prematurity (ROP) is abnormal blood vessel development in the retina of the eye. It occurs in infants that are born too early (premature). Surviving children born very preterm (VPT: \( \leq 32 \)wks) or with very low birth weight (VLBW: \( \leq 1250 \)g) are at high risk of long-term developmental problems. Furthermore, many infants having VLBW and VLBW suffer from morbidities during their hospitalization, such as respiratory distress syndrome (RDS), patent ductus arteriosus (PDA), sepsis, necrotizing enterocolitis (NEC), intraventricular hemorrhage (IVH), retinopathy of prematurity (ROP), and chronic lung disease (CLD). These conditions not only expose the premature infants to a higher risk of mortality and lengthen their hospitalization period but also cause great psychological burden to their families and higher social costs.

Normal retinal vascularization in humans occurs predominantly in the second and third trimester in utero and reaches maturity at 36–40 weeks’ gestation through vasculogenesis and angiogenesis. Physiologic hypoxia in the fetus stimulates angiogenesis through the production of vascular endothelial growth factor (VEGF). Both oxygen-dependent and oxygen-independent factors play a role in the genesis of ROP. Nonoxygen-related growth factors such as insulin-like growth factor-1

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**Abstract**

**Background:** Retinopathy of prematurity (ROP) is a potentially blinding disease of the retina. It is still a major cause of blindness in children in the developing and developed world despite current screening and treatment guidelines.

**Objective:** To identify the frequency of retinopathy of prematurity in low birth weight and very preterm neonates in a tertiary care hospital of Lahore, Pakistan.

**Methodology:** It was a Cross sectional study conducted at, NICU of Ittefaq Hospital, department of Pediatrics, Lahore over a duration of 6 months i.e. September 2017 to February 2018. A total of 145 low birth weight and very low birth weight meeting sample selection criteria were included. Indirect ophthalmoscopy done by an experienced ophthalmologist at 2nd to 3rd weeks of life by 28 diopter lens and ROP was noted. All collected data was entered and analyzed using SPSS version 23.

**Results:** The mean age of cases was 14.13 ± 2.83 days with minimum and maximum age as 8 and 20 days. The mean gestational age was 29.84 ± 1.51 weeks with minimum and maximum gestational age as 28 and 32 weeks. The mean birth weight was 1295.20 ± 120.52 g with minimum and maximum 1103.00 and 1494.00 g. A total of 18(12.41%) of cases had ROP.

**Conclusion:** The frequency of retinopathy of prematurity in low birth weight was considerably higher.

**Key Words:** Retinopathy of Prematurity, Preterm, Very-Low-Birth-Weight

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FREQUENCY OF RETINOPATHY OF PREMATURITY (ROP) IN LOW BIRTH WEIGHT AND VERY PRETERM NEONATES

(IGF-1) also interact with VEGF in the pathogenesis of ROP. Preterm infants are susceptible to the development of ROP because of incomplete neurovascular development of the retina at birth.

Timely screening of premature infants at risk of developing ROP is important in ROP management as early treatment can result in improved visual outcome. The current screening guideline of ROP in the United States calls for dilated fundus examination by indirect ophthalmoscopy for all premature infants below 30 week gestational age or less than 1500g birth weight with the first examination performed by 31 week postmenstrual age or by 4 weeks chronologic age, with additional examinations performed repeatedly thereafter to detect late stage ROP requiring treatment.

Management includes screening with a dilated fundus examination, treatment of acute severe ROP with ablation of the peripheral a vascular retina, surgery for tractional retinal detachment resulting from progressive stage 4 or stage 5 ROP and visual rehabilitation.

The potential visual and developmental impact of ROP requires lifelong follow-up of affected patients. Although the complications are more prevalent in infants with severe stages of ROP that required treatment, continued follow-ups are also recommended for children with mild or moderate disease that regresses spontaneously. Myopia, for example, is more prevalent in premature infants, affecting approximately 70% of infants, with ROP, during the first year after birth. Similarly, the incidence of strabismus is significantly increased in ROP infants affecting up to 20%, of patients. Finally, astigmatic refractive errors are increased in ROP patients affecting up to 40% of eyes with a history of ROP.

A study was done recently and found frequency of ROP as 32.4% in in VPTB and VLBW infants admitted to NICU. One local research reported frequency of ROP was 10.5% in such infants. In a prospective study from Sweden in infants with a gestational age of less than 28 weeks at birth, retinopathy of prematurity (at any stage) was reported in 73% (368/506) and severe retinopathy of prematurity was reported in 35% (176/506). In a study in Norway of infants with a gestational age of less than 28 weeks at birth, retinopathy of prematurity (at any stage) was reported in 33% (95/290). Investigators of a study in Belgium in which infants with a gestational age of less than 27 weeks at birth were included reported severe retinopathy of prematurity in 26% (45/175). A study from Australia and New Zealand of infants with a gestational age of less than 29 weeks at birth reported severe retinopathy of prematurity in 10% (203/2105). In a study in Austria, severe disease was reported in 16% (50/316) of babies with a gestational age of less than 27 weeks at birth. In a Finnish study in infants with birth weight s of less than 1000 g, severe retinopathy of prematurity was seen in only 5–10% (no numbers reported). Thus, prevalence estimates from population-based studies vary even among countries with similar neonatal intensive care facilities. This variation might be partly accounted for by differences in the proportions of infants at high risk of retinopathy of prematurity who survive when born at an early gestational age—in Sweden 11.5% of survivors were born in weeks 22–23, compared with 0–6% in the other studies. An alternative to non-uniform and intermittent data collections in many countries or regions would be occasional snapshots of the burden of severe disease in one geographical area with uniform care. There is huge disparity between the frequency of ROP in these infants with range of 10.5%-15-32.4%. The local study reported lower frequency that should be ruled out again to as with early detection of ROP we can reduce the related complications that include severe nearsightedness and blindness. If we find high frequency then through collaboration of ophthalmologists and early detection higher risk for developing other eye problems in later life, such as retinal detachment, myopia (near-sightedness), strabismus (crossed eyes), visual field defects, amblyopia (lazy eye), colored vision perception and glaucoma can be
decreased. The objective of this study was to find the frequency of retinopathy of prematurity in low birth weight and very preterm neonates.

**METHODOLOGY**

This was a descriptive cross-sectional study conducted over a period of six months from August 2017 till Feb 2018 at NICU Ittifaq Hospital Lahore. 145 infants admitted to NICU due to VLBW and VPTB. The sample size is estimated using expected frequency of ROP as 10.5%. We used 95% confidence level and 5% margin of error, 10.5%. Non-probability consecutive sampling was used. All very preterm (baby born before 32 weeks of gestation by history confirmed on dating scan) having very low birth weight (baby born with weight of <1500 grams assessed on history/medical record) admitted to the NICU of either gender within 2nd to 3rd weeks of life. All cases with congenital cataracts or syndrome assessed on slit lamp at time of admission and cases with major congenital malformations that was assessed through available medical record were excluded.

After taking informed consent from parents or attendants a total of 145 neonates meeting sample selection criteria was taken from NICU Ittifaq Hospital Lahore. Their demographic (age and gender) birth history (gestational age and birth weight) was taken. A single senior ophthalmologist did all examinations at 2nd to 3rd weeks of life. Indirect ophthalmoscopy was performed by 28 diopter lens. Mydriatic eye drop was instilled 30 minutes before examination. We labeled ROP as defined in operational definition. All data was recorded by researcher herself on prescribed proforma.

All collected data was entered and analyzed using SPSS version 23. Frequency and percentage was used for qualitative variables like sex and ROP. Mean ± S.D was applied for quantitative data like age in hours, birth weight and gestational age. Data was stratified for gender, birth weight (> 1200, ≤ 1200g) and gestational age (<30 weeks, 30-32 weeks) to address effect modifiers. Post stratification Chi-square test was used taking p-value ≤0.05 as significant.

**RESULTS**

There were 77(53.10%) male and 68(46.90%) female cases with higher male to female ratio. Fig-1

There were 94(64.83%) cases who borne <30 weeks and 51(35.17%) cases born during 30-32 weeks. Fig-2

Among 18 cases who had ROP they all were born before 30 weeks of gestation while none of them had gestational age >30 weeks, the frequency of ROP was statistically higher in cases who born <30 weeks of gestation, p-value < 0.05. Table-1

Among those 18 cases who had ROP, there were 10(55.6%) with birth weight ≤ 1200 g and 8(44.4%) cases had birth weight 1220-1499g, the frequency of ROP was statistically higher in cases who had birth weight ≤ 1200 g, p-value < 0.05. Table-2
DISCUSSION

Retinopathy of Prematurity (ROP) or retrolental fibroplasia is a potentially serious condition and common cause of blindness of preterm newborns. Timely and correct identification of individuals at risk of developing a serious form of ROP is therefore of paramount importance. ROP or vascular abnormality of retina in premature infants is a common cause of blindness and accounts for up to 10% of childhood blindness in developed countries. Also before surfactant became available in the NICU, an incidence of 11% to 60% was reported in the VLBW population.17 Epidemiological studies have shown falling mortality rates among ELBW infants in developing countries but unfortunately neonatal morbidities. The incidence of ROP and the need for laser treatment for this condition were increased. In some studies 66 percent of infants weighing less than 1250 grams and 82 percent of infants less than 1000 grams had ROPs.18 In a study conducted in Mashhad (Saedii et al) in 2008, the frequency of ROP was less than that of developed countries.19

In Brazil the incidence of severe visual impairment or blindness due to ROP is estimated to be around 500–1500 cases/year.20 The most important risk factors for ROP are the degree of prematurity and low birth weight (BW), but there are other risk factors associated with infant postnatal morbidity such as days of ventilation, sepsis, hyperglycemia, blood transfusions, and bronchopulmonary dysplasia.21 In recent years, studies have consistently identified poor postnatal weight gain as a strong predictor of ROP.22 Study findings have, however, been contradictory as to whether or not prenatal growth restriction is a risk factor for ROP. Prenatal growth restriction can be defined as the infant's deficit from normal birth weight standard deviation score (BWSDS). The term small for gestational age (SGA), defined as BW per GA below a certain percentile or confidence interval based on growth charts, is also frequently used to describe infants' prenatal growth restriction. SGA was found to be a risk factor for ROP in some studies.23 However, in other studies no significant differences were found between infants born SGA and those with a BW appropriate for their gestational age and the risk of developing ROP. A possible explanation for these inconsistent results may be differences in the characteristics of the study populations and study designs. The definition of SGA has varied in previous studies where it has been defined as a BW ranging from below the 3rd (approximately corresponding to 2 SD below the gestational-age related mean) to below the 10th percentile. Furthermore, the definition of normal BW in relation to GA varies according to different growth charts. Growth charts used throughout the world vary in design; some are based on longitudinal fetal ultrasound weight estimations and thereby aim to reflect undisturbed intrauterine growth, some are based on live births, and others on live as well as still births.

We found that a total of 18(12.41%) of cases had ROP while other 127(87.59%) cases had not ROP. A study was done recently and found frequency of ROP as 32.4% in in VPTB and VLBW infants admitted to NICU.7 The frequency of ROP in current study as less than this study while the ROP was

| Table 1: Comparison of ROP with Respect to Gestational Age (Weeks) |
|-------------------------|-------------------|-----------------|
|                        | ROP               | No              | Total           |
| Gestational age (weeks) |                   |                 |                 |
| <30 weeks              | 18(100.0%)        | 76(59.8%)       | 94(64.8%)       |
| 30-32 weeks            | 0(0.0%)           | 51(40.2%)       | 51(35.2%)       |
| Total                  | 18(100.0%)        | 127(100.0%)     | 145(100.0%)     |
| Chi-square = 11.150    | P-value = 0.001   |

| Table 2: Comparison of ROP with Respect to Birth Weight (g) |
|-------------------------|-------------------|-----------------|
|                        | ROP               | No              | Total           |
| Birth weight (g)        |                   |                 |                 |
| ≤ 1200                 | 10(55.6%)         | 38(29.9%)       | 48(33.1%)       |
| 1200-1499              | 8(44.4%)          | 89(70.1%)       | 97(66.9%)       |
| Total                  | 18(100.0%)        | 127(100.0%)     | 145(100.0%)     |
| Chi-square = 4.678     | P-value = 0.031   |
higher than a study on local population i.e. ROP was found in 10.5% infants.46 Recently, a cross-sectional study was performed to determine the incidence of ROP in LBW infants. In this study 152 LBW infants were screened admitted at Imam Reza Hospital, Mashhad, Iran, between October 2013 and October 2015. The patients were examined by neonatologist and ophthalmologist. The result has showed that 152 LBW infants, including 79 males and 73 females, were evaluated. The mean gestational age was 30.32 ± 2.84 (26-37). In this study author identified 31 patients (20.39%) with ROP.19 patients with 26 to 29 weeks gestational age and 9 patients between 30 to 33 weeks and just 3 patients between 33 to 37 weeks of gestational age. However, there were no meaningful relationship was found with gender. (P=0.395) Hence it can be concluded that ROP is rising in Iran and low birth weight is an important risk factor for ROP and screening program is very important in this group of newborns.

Similarly, another study is conducted to evaluate the incidence and risk factors of ROP in preterm babies at neonatal intensive care units, Mansoura city. The study included 402 preterm infants admitted to neonatal intensive care units in Mansoura city in the period from March 2013 to March 2015. The study result has showed that out of the 402 screened preterm babies, 237 (59%) cases had ROP, among whom 101 (42.6%) had stage 1, 114(48.1%) had stage 2, 12(5.1%) had stage 3, 10(4.2%) had aggressive posterior retinopathy, and 24 (10.1%) presented with plus disease.26

In 2015, Hwang et al. conducted a study to describe the incidence, risk factors, and current treatment status of retinopathy of prematurity (ROP) in very-low-birth-weight (VLBW) infants registered in the Korean Neonatal Network database. The total incidence of ROP was 34.1%. Of the patients, 11.6% showed ROP stage ≥3 and 11.5% received treatment of VLBW. In conclusion, the high incidence of ROP is associated with low GA and BW, and attempt to reduce the aforementioned risk factors could reduce the incidence of ROP stage ≥3 in VLBW infants.27

CONCLUSION
We concluded that the frequency of retinopathy of prematurity in low birth weight and very preterm neonates was considerably higher. So, low birth weight very preterm neonates should be assessed for ROP and preventive and therapeutic strategies must be adopted to minimize the risk because timely screening of premature infants at risk of developing ROP is important in ROP management as early treatment can result in improved visual outcome.

Limitations of Study
Categorization of sample on the basis of inhaled oxygen(FIO2)was not done in the study

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Conflicts of Interest None
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Reviewers: Prof. Dr. Saima Batool and Dr. Muhammad Naveed

REFERENCES
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DETECTION OF MYOCARDIAL ISCHEMIA WITH DOBUTAMINE STRESS ECHOCARDIOGRAPHY

Muhammad Ijaz Bhatti, Saira Azeem, Maria Sadiq, Nasir Iqbal, Hassan Abbas Abdullah, Rajia Liaqat

Abstract

Objective: The objective of this study is to assess clinical utility of dobutamine stress test to detect myocardial ischemia in patients who are being evaluated for suspected ischemic heart disease.

Methodology: The descriptive cross sectional study design was conducted in Cardiology department of Gulab Devi teaching hospital for 6 months from August 2017 to January 2018. Total 144 patients were enrolled by estimating inclusion and exclusion criteria. Data was analyzed by SPSS version 21. Pearson Chi square test for independence was used to assess the association of dobutamine stress test on echocardiography with chest pain and wall motion abnormalities.

Results: Out of total 144 patients, Dobutamine stress Echocardiography (DSE) was positive in 73 patients and negative in 71 patients. The positivity of (DSE) was based upon the presence of new wall motion abnormalities with and without ECG changes and chest pain. At rest WMAs were present in 16 (11.11%) patients while no WMA was noted in 128 (88.88%) patients. At peak new WMAs were present in 73 (50.69%) patients while no new WMA was present in 71 (49.30%) patients. Sixty (42.36%) patients noticed chest pain during dobutamine infusion and 83 (57.63%) had no chest pain. At Peak 55 (38.19%) patients had no ECG changes while ST/T wave changes were observed in 89 (61.80%) patients.

Conclusion: This study shows that dobutamine stress test is safe, well tolerated, low cost and clinical useful modality for those patients who have chest pain and needs stress testing for further evaluation for myocardial ischemia.

Key Words: Myocardial ischemia, Dobutamine Stress echocardiography, Chest pain, Wall Motion abnormalities.

Stress echocardiography permit dynamic estimation of cardiac performance during physical exertion or the pharmacologic simulation by increasing heart rate and myocardial oxygen demand.

S

Stress echocardiographic imaging techniques is additionally accustomed to assess myocardial ischemia, viability and valvular dysfunction. Dobutamine stress echocardiography (DSE) is oftenly used for detection of myocardial ischemia. It is a sort of echocardiography in which dobutamine is infused intravenously to increase heart rate and myocardial oxygen demand patient.

Dobutamine is a synthetic catecholamine with predominant beta-stimulation. Its half-life is approximately 2 minutes. DSE is done by achieving an adequate stress level by increasing heart rate to at least 80% of target heart rate. Failure to achieve required heart rate results in inconclusive tests.

The utilization of Dobutamine stress echocardiography for the assessment of myocardial ische-
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Myocardial ischemia (MI) is rapidly expanding. Safety of Dobutamine stress echocardiography has been sufficiently documented with few rare complications like myocardial infarction or hypotension. In general a variety of traditional risk factors (hypertension, diabetes, smoking, and known history of myocardial ischemia) predict positive test result.

Previous studies have shown a large range positivity of stress induced ischemia in patients referred for evaluation for chest pain or dyspnea from 19% to 42% by stress echocardiography. Patients with dyspnea referred for stress testing had high mortality, although it's not clear whether this can be due to high rates of ischemia.

As compared with traditional radionuclide imaging, pharmacologic stress echocardiography has the benefit of not requiring specialized radionuclide imaging equipment. In contrast with radionuclide imaging, echocardiographic images can be obtained anywhere along the continuum from rest to peak physiologic stress. Dobutamine stress echocardiography (DSE) avoids radiation and has relatively high sensitivity and specificity for varied forms of cardiovascular pathophysiology. For these reasons, its utility and applicability are increasing in clinical practice. Stress echocardiography is today the foremost cost-effective possible imaging option for diagnosis of stress induced myocardial ischemia.

The rationale of this study is to detect myocardial ischemia with dobutamine stress echocardiography in patients who are referred to a tertiary care center for evaluation of suspected ischemic heart disease.

Myocardial ischemia: It is a condition in which inadequate blood supply to heart muscles is clinically manifested either by chest pain or ST/T changes on ECG.

Dobutamine stress test: It is a type of echocardiography in which dobutamine is infused intravenously to increase heart rate of the patient.

a) Positive Dobutamine stress test: Dobutamine stress test is declared positive when new wall motion abnormalities (WMAs) appear during stress phase, with and without ECG changes and chest pain.

b) Negative Dobutamine stress test: Dobutamine stress test is declared negative when no new wall motion abnormalities (WMAs) appear, with and without ECG changes and chest pain.

METHODOLOGY

This cross-sectional study was conducted in the Cardiology department of Gulab Devi Chest Hospital Lahore. Using non-probability purposive sampling 114 subjects (irrespective of gender and age) having history of chest pain who were advised stress testing for further evaluation were enrolled. Patients who were already diagnosed with ischemic heart disease and those with severe uncontrolled hypertension were excluded from the study. Informed consent was taken from all patients. The clinical data including history, risk factor, echocardiographic changes, dobutamine infusion rate, hemodynamic effect and wall motion abnormalities (at rest and peak) were recorded on a structured Performa. Later on a master data sheet was developed and all the information was entered on SPSS. Version 21.0 by using original data of the clinical trials. Level of significance was set at $p \leq 0.05$

RESULTS

One hundred and forty four consecutive patients were enrolled into the study. In this study 46 (31.94%) patients were male, and 98 (68.06%) patients were female. Minimum and maximum age of patients was 24 and 82 years respectively. Mean age of total sample population (144 patients) was 52 years. Dobutamine stress echocardiography (DSE) was positive in 73 patients and negative in 71 patients. The positivity of (DSE) was based upon the presence of a new regional left ventricular wall motion abnormality (WMA) with and without ECG changes and chest pain and vice versa for negative dobutamine stress test. Resting WMAs was noted in 16 (11.11%) patients and 128 (88.88%) patients had no WMA at rest before start of stress phase. At peak
new regional WMAs were present in all 73 (50.69%) patients with positive DSE, while 71 (49.30%) patients having negative test did not develop any new wall motion abnormality.

Sixty one patients experienced chest pain in which 60 patients had chest pain with positive dobutamine stress test and 1 patient had chest pain with negative dobutamine stress test. Out of 83 patients 13 patients had no chest pain but their dobutamine stress test was positive and 70 patients had neither chest pain nor positive dobutamine stress test.

At rest 71 patients had minor ECG changes (ST/T wave changes) and 73 patients had no ECG changes (ST/T wave changes). At peak ECG changes (ST/T wave changes) were observed in 89 patients in which 9 patients had T-wave inversion, 55 patients had ST depression, 8 patients had T-wave inversion and ST depression, 13 patients had T-wave depression and elevation, 4 patients had T-wave inversion and ST depression and elevation and 55 patients had no ECG changes (ST/T wave changes).

### Table 1: DSE Findings on Echocardiography

<table>
<thead>
<tr>
<th>Chest Pain during DSE</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>60</td>
<td>1</td>
<td>61</td>
</tr>
<tr>
<td>No</td>
<td>13</td>
<td>70</td>
<td>83</td>
</tr>
<tr>
<td>Total</td>
<td>73</td>
<td>71</td>
<td>144</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Wall Motion Abnormalities</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>73</td>
<td>0</td>
<td>73</td>
</tr>
<tr>
<td>No</td>
<td>0</td>
<td>71</td>
<td>71</td>
</tr>
<tr>
<td>TOTAL</td>
<td>73</td>
<td>71</td>
<td>144</td>
</tr>
</tbody>
</table>

p-value < 0.05

### Table 2: Frequency of Echocardiographic Changes at Peak

<table>
<thead>
<tr>
<th>Changes</th>
<th>Total</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-wave inversion</td>
<td>09</td>
<td>6.25%</td>
</tr>
<tr>
<td>ST-depression</td>
<td>55</td>
<td>38.19%</td>
</tr>
<tr>
<td>T-wave inversion &amp; ST-depression</td>
<td>12</td>
<td>8.34%</td>
</tr>
<tr>
<td>ST depression &amp; elevation</td>
<td>13</td>
<td>9.03%</td>
</tr>
<tr>
<td>No Changes</td>
<td>55</td>
<td>38.19%</td>
</tr>
</tbody>
</table>

DISCUSSION

Dobutamine stress echocardiography has several benefits over currently used non-invasive stress testing techniques. It is cost effective as compared with competing technologies and provides an alternative modality for patients who cannot do leg or arm exercise. The equipment required is highly portable, and thus, studies can be performed within the intensive and coronary care units.

High-quality images from Dobutamine stress echocardiography may be obtained more easily than those from exercise stress echocardiography because of the absence of patient motion and limited respiratory interference. The extent of stress achieved can be controlled and potentially, the suppression of heart rate by b-blockers may be overcome.

A previous study evaluated role of dobutamine stress echocardiography to detect myocardial ischemia in patients presented with dyspnea. The mean age of patients was 58.9 years and range of age was 28 to 85 years. Out of 103 patients 39 were female and 64 were male. DSE was positive for ischemia in 19% of patients with dyspnea.

In our study out of 144 patients, minimum age of patients was 24 years, maximum age was 82, and mean of age was 52.63. Risk factors assessment showed 73.61% hypertensive patients, 34.3% diabetic, 29.17% had positive family history, 13.89% were smoker and 32.64% patients were obese. Dobutamine stress Echocardiography (DSE) was positive in 73 (50.69%) patients and negative in 71 (49.30%) patients. The positivity of (DSE) was based upon the presence of a new wall motion abnormality with and without ECG changes and chest pain. At rest WMAs were present in 16(11.11%) patients while no resting WMA was present in 128 (88.88%) patients. At peak of test new segmental WMAs were present in all 73 (50.69%) patients who had positive DSE while no new WMA was noted in 71 (49.30%) patients.

Dobutamine stress echocardiography (DSE) is an exercise independent non-invasive stress test and is especially useful for those patients who are unable
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to perform exercise due to poor functional capacity or joint disorders. The sensitivity and specificity of DSE for detection of coronary artery disease is 80% and 84% respectively.10 A study revealed that dobutamine stress echocardiography is superior to exercise stress testing for detection of myocardial ischemia and significant coronary artery disease in patients referred for evaluation of chest pain.11 Addition of DSE to resting ECG and echocardiography helps to detect patients who may be at elevated risk of developing adverse cardiac events during non cardiac surgery, further highlighting its significance in everyday clinical practice.12

CONCLUSION

Dobutamine stress echocardiography is a quite useful non invasive imaging modality which can be carried out at almost every cardiac department of a tertiary care hospital. It is safe and well tolerated test to detect stress induced myocardial ischemia in patients who are referred for evaluation of chest pain.

Limitations of Study

Main limitation of this study is that this is a single center study. Large scale study with more than one centers are required before a firm final conclusion is achieved.

Conflict of Interest

No conflict of interest shown by any author.

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REFERENCES


HOW TO DRESS FOR WORK: THE PREFERENCE OF PATIENTS FOR THEIR PHYSICIAN'S ATTIRE AND ITS EFFECT ON THEIR CONFIDENCE

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Abstract

Objective: To identify the perceptions of patients from different gender and background about how physician's attire affect their preference and confidence

Methods: This quantitative descriptive study was carried out between December'19-March'20 on patients coming to the outpatients department at public and private hospitals of Lahore. Patients aged between 14-80 years were surveyed. The questionnaire was adopted from a study done by Christopher M. Petrilli.

Results: 387 surveys were returned. 27% of the participants had done their bachelor’s, 25% were masters and 22% were matric in their qualification. 52.7% of the participants were males whereas 47.0% were females. All the participants preferred white coats with scrubs for males. For the females the preferred choice of attire by primary, intermediate, matric and bachelor participants was white coat followed by abaya (cloak), however for the participants who had done masters they preferred white coats with scrubs.

Conclusion: It was seen that there was a significant difference between opinions of patients between genders and from different educational backgrounds about how they wanted their doctor to be dressed.

Key Words: Attire, Professional, Preferences, Patients, Physician, Hospital, Survey, Quantitative

Patient satisfaction is the main aim of the health care department. A better understanding of the patient doctor relationship results in better organization of healthcare and better training of doctors. 1

We reflect ourselves even before verbal communication, the way we walk, our facial expressions especially smile and the way we dress, all these define the individuality and the uniqueness of a person. This is also called the Halo Effect, in which people associate positive attributes with the overall outlook of the person. 2 In the patient doctor relationship, the style of the physicians dressing, has a paramount important role to play in the doctor patient relationship. 3 According to Petrilli et al, patients had a certain preference for their physicians attire when they had their first encounters at the hospitals. 4 In a study by Gherardi et al, they also stated that the first thing that a patient sees in their doctor is their attire which helps build a good doctor-patient relationship. 5 This was also stated by Rehman et al that doctor’s attire is an important component of the first impression on the patient, which then helps build a level of trust and confidence. 6

With the absence of a strict dress code policy, doctors wear anything from shorts, tees, sneakers to shalwar kameez (traditional attire) to suits. The white coat is also becoming unpopular among the new
graduates mainly due to the risk of spreading infections and the high temperatures in summer. Few senior physicians from the UK when inquired about wearing white coat said that they did not wear so that they could be distinguished from their junior colleagues. Previous studies revealed that patients prefer white coats since it helps them in easy identification of the doctors and it makes the doctor look more professional. A properly dressed physician gives an image that patient contact is important and they should be well prepared for it. Studies also suggested that patients felt that doctor’s attire had nothing to do with their professionalism and that it did not matter how a doctor dressed. In Pakistan, there is no well-defined documented formal dress code for the doctors.

**METHODOLOGY**

The survey was conducted at two hospitals in Lahore (Fatima Memorial Hospital and Sheikh Zayed hospital) between February to March 2020. Informed consent was taken before handing over the questionnaire.

Sample was collected using the non-probability convenience sampling technique. 450 questionnaires were distributed among the participants and 387 were returned. Six questionnaires were discarded due to incomplete information. Patients below 14 years of age and hospital employees were also excluded from the study. The study took seven months to complete following the approval of the abstract.

A questionnaire comprising of three (A, B, C) parts and sixteen questions was administered to the participants. The instrument had previously been developed and used in 2018 by Christopher M Petrelli in his study. Permission to use the instrument was taken from the author through e-mail. Part A of the questionnaire had questions about the demographics of the patients which included the age, gender, marital city, city/background, visits to the hospital and the educational background. Part B had 4 general questions that investigated the importance of doctor’s attire, patient’s confidence, and the importance of a white coat. The patients were required to answer these questions on a five point Likert scale 1(Strongly Disagree) to 5(Strongly Agree). The part C had 6 questions to be answered in response to a picture of a doctor dressed in different attires (Fig 1). The background, light, and facial expressions all stayed constant for all the pictures with the doctor’s attire as the only variable. The questionnaire was first translated into the native language that is Urdu by an Urdu expert and then piloted before use for the actual research process.

**Figure 1: Photographs of Male and Female Physician Models in Different Attires**

The data from the questionnaires were imported into IBM SPSS Statistics Version 26. Responses from the survey were compared against the demographic group (Educational background and gender). The data was found to be non-normally distributed (p<0.05)
**RESULTS**

The response rate came out as 86%. There was almost equal participation by both genders with males (52.5%) being slightly greater in number than females (47%). Majority of the patients fell in the 30 years (7%) age group with a mean score of 34 years for males and 32 years for females. Majority of the patients were from Lahore (79.1%). 27.1% had done their BA, M.A (25.1%) followed by matric (22.2%). Three hundred and sixty seven (94.6%) of the patients said that they had visited the hospital before for other purposes whereas 20 (5.2%) said that this was their first visit to a hospital. The number of patients surveyed in each demographic category is given in Table 1.

For section B there were a total of four questions with a 5 point Likert scale, with a minimum score allotted to strongly disagree\(^1\) and strongly agree.\(^2\) The maximum number of participants from both genders opted for either strongly agree or agree options for all the four questions. For the first question that inquired the patients how much the doctor’s attire was important to them there was a significant difference between the answers of participants from different educational backgrounds to question number 1 ($H_{(2)} = 11.13$, $p= 0.025$). The null hypothesis was rejected. Mann Whitney U test gave a significance value of 0.010 ($p<0.05$) when primary and masters were compared to each other, $p=0.010$ when matric and masters were compared and hence showing that there was a significant different in the responses of the two groups. 52.9% males and 47.3% females agreed to the statement. For the third question which inquired if the patients feel it is okay for a doctor to dress casually on duty the results showed no significance between participants from different educational backgrounds ($H_{(2)}= 3.81$, $p=0.43$). Null hypothesis was retained. 53.9% males and 51.6% females agreed to the statement that it did not bother them if their doctors dressed casually while on duty. For the last question in this section which asked the patient’s opinion about white coat gave a significant difference between the answers of participants from different educational backgrounds ($H_{(2)}=11.35$, $p=0.023$).The null hypothesis for this question was rejected. Mann Whitney U test gave a significance value of 0.020 ($p<0.05$) when primary and masters level of education was compared, $p =0.031$ when matric and primary were compared, $p=0.022$ when Matric and Intermediate were compared, $p=0.010$ when intermediate and masters were compared hence showing that there was a significant difference in the answers of participants from these groups. 61.8% males and 63.7% females agreed with the statement.

<table>
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<th>Age 16-20</th>
<th>21-30</th>
<th>31-40</th>
<th>41-50</th>
<th>51-60</th>
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<tbody>
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<td></td>
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<td>Female</td>
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<td>1</td>
<td>1</td>
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<td>0</td>
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<td>0</td>
</tr>
<tr>
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<td>0</td>
<td>14</td>
<td>11</td>
<td>17</td>
<td>15</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
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<td>5</td>
<td>6</td>
<td>7</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Bachelors</td>
<td>5</td>
<td>5</td>
<td>26</td>
<td>22</td>
<td>19</td>
<td>9</td>
<td>3</td>
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<td>22</td>
<td>27</td>
<td>15</td>
<td>9</td>
<td>9</td>
<td>2</td>
</tr>
</tbody>
</table>

\(^1\)strongly disagree
\(^2\)strongly agree
For the third section of the questionnaire which had pictorial questions frequencies were calculated for each question and Chi-Square was performed.

Chi square for all the questions gave a significance value of 0.00 hence the null hypothesis was rejected and it was inferred that there was a significant difference between the responses of male and female participants as well as participants from different educational backgrounds. For the first question which inquired which doctor the patients would prefer for their treatment based on the pictures provided to them. The majority selected white coat for males (64.3%), 18.1% selected scrubs. 62.3% selected white coat for females followed by scrubs (14.2%) and Abaya (cloak) 13.7%. The second question required the patients to pick the doctor which they thought would be more knowledgeable based on their appearance. For the male physicians 58.9% participants selected doctors wearing white coat followed by, 19.9% selecting males in the scrub.

<table>
<thead>
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<th>Table 2: Strengths and Limitations of the Study</th>
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<tbody>
<tr>
<td><strong>Strengths</strong></td>
</tr>
<tr>
<td>The study sample is large hence a large number</td>
</tr>
<tr>
<td>of perceptions is gathered</td>
</tr>
<tr>
<td>Theoretical framework and hypothesis was well</td>
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<tr>
<td>structured</td>
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<tr>
<td>The questionnaire was translated into the native</td>
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<td>language so that it could be easy for the</td>
</tr>
<tr>
<td>participants to understand</td>
</tr>
<tr>
<td>It was a validated survey</td>
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<tr>
<td></td>
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<tr>
<td>It was conducted in two different clinical</td>
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<tr>
<td>settings, therefore, encompassing a widespread</td>
</tr>
<tr>
<td>population</td>
</tr>
<tr>
<td>The study was not biased against the age, facial</td>
</tr>
<tr>
<td>expressions of the doctor, or the background.</td>
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</table>

59.2% preferred females in white coat followed by 15.5% who preferred Abaya. The third question stated which doctors the patient would prefer when in the hospital based on how they dressed. 63% of the respondents selected males in white coat and 16.3% selected males in scrubs. 63.8% selected females in the white coat as their preference when coming to the hospital followed by 13.7% selecting a female abaya. The fourth question inquired patients who do they think would be able to provide better care to them based on how they dressed. 64.6% of the participant’s selected male white coat and 15.5% preferred male scrubs. 62.3% participants selected white coat for females followed by abaya 13.2%. The fifth question inquired what kind of doctor the patients felt comfortable talking to. The majority selected males with white coats (62%) and males with scrubs (14.7%). For the females majority selected white coats (57.6%) followed by abaya (13.2%). The final question inquired the patients about which doctor they found more approachable and easy to talk to base on their attire. White coat for males (64.1%) followed by scrubs (14.5%) was the most common answer. For the females white coat (60.2%) followed by abaya (14.2%) was preferred for females.

A difference of opinion was observed between the choices of male and female participants when it came to the second choice of attire for female physicians. It was observed that majority males preferred female physicians to wear an abaya (cloak) underneath the white coat whereas female participants preferred them to wear scrubs underneath the white coats.

Figure 2: Gender Wise Preferences for Female Physicians
DISCUSSION

A similar study was conducted about doctor’s attributes in Peshawar in 2019 which slightly touched how doctors dress when seeing their patients. In this study it was observed that male and female doctors dressed in white coats were preferred by patients from both the hospitals. This could be due to the general perception among patients where they associate white coat to professionalism and competence hence they tend to be more confident in such doctors. My study is similar to other studies done in the past except that this kind of a study has not been done in a country with a literacy rate as low as Pakistan. The current study found out the perceptions of patients about their doctor’s attire in a country where literacy rates are much lower than that of the west.

Participants who had primary level of education showed a stronger preference for the physician’s attire with a mean rank of (231.6, 211.2, 202.9, 229.6) for questions 1 to 4 respectively. The second question inquired about the influence of a physician’s attire on their satisfaction or the confidence they felt in their treating doctor after receiving care. This was an important question in judging whether a doctor’s attire affected patient confidence or not. Majority participants from all the five educational backgrounds agreed with the statement hence revealing that attire plays a pivotal role in making a first impression and thus encouraging the patient to have confidence and inclination towards a well-dressed doctor when they first encounter them in the OPD. However participants who had done their masters had a lower mean rank score (166.36) when compared to those who had only done primary level education ( mean rank= 211.20). Here it can be seen that as patients became more educated they were less bothered by the attire of their physician. Majority of the participants felt that the white coat was an essential part of a doctor’s attire and strongly felt that it should be worn when seeing patients. This was supported by a study done by Dunn et al which proved that more than 50% of the participants were in favor of their attending physician to be wearing a white coat and majority also believed that a formal dress should be dawned underneath it. In the third section which had 10 pictures of doctors in different attires both males and females against a set of questions that required the participants to select an appropriate picture when asked about the knowledge, trust, approachability, and competency of a doctor based on how they dressed. Again the most common answer was male and female in a white coat as compared to all other options. These results were consistent with a previous study done in 2018. The difference between the opinion of male and female participants over the female physicians attire need to be further researched upon as to why such a difference exists. The patients gave a number of reasons for choosing the white coat for doctors over other options the most common of which was it made them easily recognizable and it made them look professional, which concept is supported by studies.

However, some patients were also of the opinion that the white coat was confusing for them since everyone in the hospital from the pharmacist to the technicians and nurses wear them and that they should not be allowed to do so. Male scrubs and female cloak or abaya was the second most common answer. It can be seen that the results of the first four education levels that are primary/middle, matric, intermediate and bachelors are consistent with each other for both male and female doctors however there is a difference in the responses of those who had master level of education. The difference of opinion can also be seen among the different genders. Thus it can be deduced from the above results that education and gender has a role to play in different opinions or preferences of patients for their physicians’ attire. Patients from both genders with a higher level of education had a different opinion from those who were bachelors or below.

CONCLUSION

The following table describes the strengths and limitations of the study.
Acknowledgment

We are thankful to all the participants and head of institutes where the study was conducted.

Conflict of interest

None

Financial disclosure

None

REFERENCES


BE STRONGER THAN YOUR EXCUSES
Mental health is one of God’s greatest gifts to mankind. Conversely mental illness has debilitating effects not only on one’s life but affects others in the environment as well. This becomes all the more detrimental to society at large if it assumes the form of a negative and hostile reaction towards the world. Neurological disorder affecting one’s state of thoughts, emotions and daily routine activities, depression affects an estimate 121 million people globally according to the World Health Organization. Life events, medical treatment like beta blockers, neurological and physiological disorders are among the numerous causes of depression among the general population.

Major depressive disorder (MDD) is a common psychiatric illness with high levels of morbidity and mortality. It is estimated that 10% to 15% of the general population will experience clinical depression during their lifetime, and 5% of men and 9% of women will experience a depressive disorder in a given year, according to the World Health Organization. Genetic factors play important roles in the development of MDD, as indicated by family. It suggests a heritability of 40% to 50%, and family studies indicate a twofold to threefold increase in lifetime risk of developing MDD among first-degree relatives.
relatives. This degree of familial aggregation, coupled with the high heritability from twin studies, generated optimism that molecular genetic techniques would reveal genes of substantial influence on MDD risk. The high prevalence of psychiatric disorders among prisoners compared to the general population has long been recognized. Around half of the prisoners worldwide are in the United States, Russia and China, with the United States having the highest incarceration rate in the world. Human Rights Commission of Pakistan reported that by the end of 2012 there were 75,444 detainees in Pakistan’s prisons in total, against a total authorized capacity of 44,5786.

The rationale of the study is that the previous data is significantly variant regarding the frequency of depression in prisoners, the reason behind this difference may be racial and geographical, however, this study will be helpful to estimate this morbidity in prisoners of Lahore in absence of any recorded magnitude. If a high frequency is recorded then psychiatric care may be provided to prisoners and measures to should be taken to screen depression.

METHODOLOGY
The objective of the study was to determine the frequency of depression in prisoners at Central and Kotlakhpat Jail Lahore

Prisoners: In our study all subjects who were arrested and held in prisons of Jails at Lahore District for at least 6 months
Depression: DSM-IV criteria were used to assess the depression (Annexure-B).
Study Design: Descriptive Cross Sectional Survey
Place of Study: Central Jail and Kotlakhpat Jail Lahore
Sample Technique: Non probability Consecutive sampling.
Inclusion Criteria: Age between 18 to 70 years.
Both male and female gender. Prisoners at Central Jail and Kotlakhpat Jail(as per operational definition)
Exclusion Criteria: Already diagnosed cases of depression before prisontment (on history and medical record)
• Patients with history of substance abuse, e.g. cocaine, alcohol, cannabis etc. (based on history)
• Comorbid psychiatric illness, like anxiety disorders and schizophrenia etc (on the basis of history and mental state examination).
• Patients with history of neurological disorder. e.g. epilepsy, migraine etc (excluded on basis of history and examination)
• Already on treatment of depression or psychiatric illness (on history and medical record).

Any other chronic morbidity i.e., Hepatitis B & C, Diabetes Mellitus, Any type of malignancy and Coronary Artery Disease (on history and medical record). The calculated sample size is 175 with 7% margin of error, 95% confidence level taking expected percentage of depression among prisoners i.e. 24.3%.

Descriptive Cross-Sectional Survey of prisoner at Central Jail and Kotlakhpat Jail Lahore. A total of 175 prisoners fulfilling the inclusion/exclusion criteria and under prisonment at Central and Kotlakhpat Jail, Lahore was enrolled in the study. The permission from hospital ethical committee and Jail Superintendent was obtained to examine the prisoners. Informed consent of the prisoners was taken to include their data in the study. The prisoners were evaluated for depression according to DSM-IV criteria (attached as Annexure-B). Frequency of depression in prisoners was recorded on a pre-designed proforma (Annexure-A) by the researcher himself.

All the collected data was entered and computed by using Statistical Package for Social studies (SPSS version 16). The qualitative data like gender and depression (Yes or No) was presented as frequency distribution and percentages. Quantitative data in the study like age (in years) was presented as means and ± standard deviations. The data was stratified for age, gender, duration of prisonment, socio-economic status (low, middle, high) Central/
kotlakhpat Jail to address the effect modifiers. Post stratification chi square test was applied to check the significant effect modifier with p value <0.05 as significant.

RESULTS

A total of 175 cases fulfilling the inclusion/exclusion criteria were enrolled to determine the frequency of depression in prisoners at Central and Kotlakhpat jail Lahore.

Age distribution of the patients was done, it shows that 54.86%(n=96) were between 18-50 years of age and 45.14%(n=79) were between 51-70 years of age, mean+sd was calculated as 48.10±10.98 years. Table No.1

Gender distribution shows that 89.71%(n=157) were male and 10.29%(n=18) were females, Table 2

Frequency of depression in prisoners at Central and Kotlakhpat jail Lahore was recorded as 57.71%(n=101). Table 3

We compared our results with previous local study reveals 42.4% of the prisoners had depression. Another study conducted in Egypt recorded these findings in 82.5% of the prisoners while a European study recorded these findings in 24.3% (10.2% in male prisoners and 14.1% in female) prisoners. The findings of our study are in agreement with the local study with slightly higher difference, while Egyptian and European studies are not in agreement with our findings.

Sergio Baxter Andreoli and others determined the prevalence of psychiatric disorders in the prison population in the State of São Paulo, Brazil, they recorded that lifetime and 12-month prevalence rates differed between genders. Lifetime and 12-month prevalence of any mental disorder was, respectively, 68.9% and 39.2% among women, and 56.1% and 22.1% among men. Lifetime and 12-month prevalence of anxious-phobic disorders was, respectively, 50% and 27.7% among women and 35.3% and 13.6% among men, of affective disorders was 40% and 21% among women and 20.8% and 9.9% among men, and of drug-related disorders was 25.2% and 1.6% among women and 26.5% and 1.3% among men. For severe mental disorders (psychotic, bipolar disorders, and severe depression), the lifetime and 12-month prevalence rates were, respectively, 25.8% and 14.7% among women, and 12.3% and 6.3% among men. Some prevalence studies of personality disorders in prisoners are problematic for similar reasons. Large high quality studies using clinically based diagnoses have reported prevalence of 7–10% compared with 65% found in reviews of studies that have used diagnostic instruments. The discrepancy could be partly explained by the inclusion of antisocial personality disorder, the most common personality disorder in prisoners, for which diagnostic criteria overlap with the

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<tr>
<th>Age(in years)</th>
<th>No. of patients</th>
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<tbody>
<tr>
<td>18-50</td>
<td>96</td>
<td>54.86</td>
</tr>
<tr>
<td>51-70</td>
<td>79</td>
<td>45.14</td>
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<tr>
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<th>No. of patients</th>
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<tr>
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<td>Female</td>
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DISCUSSION

In our study, out of 175 cases, 54.86%(n=96) were between 18-50 years of age while 45.14%(n=79) were between 51-70 years of age, mean age was calculated as 48.10±10.98 years, 89.71%(n=157) were male and 10.29%(n=18) were females, frequency of depression in prisoners at Central and Kotlakhpat jail Lahore was recorded as 57.71%(n=101).
reasons for entering prison. Three of these criteria (disregard of norms and rules, low threshold for aggression or violence, and inability to profit from experience) are together highly correlated with criminogenic factors.

However, our study is helpful to estimate this morbidity in prisoners of Lahore in absence of any recorded magnitude and considering the high frequency we are of the view that psychiatric management may be provided to the prisoners and measures should be taken to screen depression.

CONCLUSION

We concluded that the frequency of depression is higher among prisoners at Central and Kotlakhpat Jail Lahore.

Limitations of Study

Our study being a cross sectional study has a limited value in 2 jails of big city. We would also like to replicate the study in other cities to see if there are any differences in prevalence

Funding sources

None

Self, no external funding

Authors contributions

All six authors have contributed equally in conceptualization and detailed work of our project.

Acknowledgments

We would like to thankful our Jail Superintendent of Central and Kotlakhpat Jail Lahore for facilitating this research.

REFERENCES

Infertility is defined as inability of couple to conceive after one year of unprotected intercourse. The prevalence of infertility in Pakistan is 21.9%. The most common cause of medically treatable infertility is polycystic ovarian syndrome (PCO). In PCO, increased ovarian androgen production leads to premature adrenarche, menstrual irregularity, acne, hirsutism, and infertility by means of elevated luteinizing hormone to follicle stimulating hormone production and hyperinsulinemia. Rotterdam criteria is used to diagnose polycystic ovarian syndrome. Revised diagnostic criteria have been proposed based upon a 2003 consensus meeting held in Rotterdam (European Society of Human Reproduction and Embryology/ American Society of Reproductive Medicine consensus workshop group). These criteria encompass a broader spectrum of phenotypes considered to represent PCOS. In the revised criteria, two out of three of the following are required to make the diagnosis: Oligo- and/or anovulation, Clinical and/or biochemical signs of hyperandrogenism and Polycystic ovaries (by ultrasound). In an Indian study, the frequency of PCOs

**Abstract**

**Background:** Ultrasound can be used as diagnostic modality for polycystic ovarian syndrome (PCOS) among infertile women. There is scarce data available regarding use of ovarian volume > 8ml as cut off for diagnosis. So current study was undertaken.

**Methodology:** This cross sectional study was conducted in Radiology Department of Military Hospital, Lahore during February 2018—March 2019, to determine the diagnostic accuracy of ovarian volume > 8ml on transvaginal sonography in diagnosing polycystic ovarian syndrome among 150 infertile women taking Rotterdam criterion as gold standard.

**Results:** 150 patients were included in our study population with mean age of 32.93 ± 2.942 years. 116 patients (77.3%) had polycystic ovarian disease according to Rotterdam criterion. 137 patients (91.3%) were having ovarian volume above 8ml. When we took Rotterdam criterion as gold standard, for ovarian volume >8ml, sensitivity was 88.80% and positive predictive value was 75.18% while specificity and negative predictive value was zero. We stratified diagnostic yield for age and BMI > 30 . Sensitivity came out higher for older and obese patients.

**Conclusion:** It is concluded that ovarian volume > 8ml can be used as a proxy indicator of polycystic ovarian syndrome as it has shown high sensitivity but low specificity.

**Key Words:** Polycystic ovarian syndrome, Rotterdam criterion, Diagnostic accuracy Transvaginal sonography, Infertile women
in female related infertility was 38.5%. All women presenting with complaints of menstrual disturbances, male pattern hair growth or infertility were included. Sensitivity of 79.49% and specificity of 90.67% was achieved. In another study, an ovarian volume of 10 ml had an 81% sensitivity and 84% specificity. Differentiation between treatable and non-modifiable factors is needed to treat infertility. Polycystic ovarian syndrome falls in treatable conditions list. It needs a cascade of high tech test. Rationale of current study is that there is no local study available regarding the diagnostic accuracy of ovarian volume >8ml in diagnosing polycystic ovarian syndrome among infertile Pakistani women. A simple modality like transvaginal sonography may reduce the cost of diagnosis of PCO among infertile women.

Objective of this study was to determine the diagnostic accuracy of ovarian volume > 8ml on transvaginal sonography in diagnosing polycystic ovarian syndrome among infertile women taking Rotterdam criterion as gold standard. Infertile women was defined as a married woman with no conception after one year of unprotected sexual activity.

The volume of the ovary was calculated with the formula of ellipse: \(\frac{1}{2} (A \times B \times C)\), where A is the longitudinal diameter, B is the anteroposterior diameter; and C is the transverse diameter of the ovary on transvaginal sonography. Ovary volume > 8ml was taken as cutoff value for diagnosis of PCO.

Rotterdam criterion: Two out of three of the following are required to make the diagnosis:

- Oligo- and/or anovulation (defined as the absence of menstruation for \(\geq 35\) days or <8 cycles/year and amenorrhea as no menstruation for >6 months
- Clinical signs of hyperandrogenism (modified Ferriman-Gallwey (FG) score \(\geq 8\))
- Polycystic ovaries (presence of 12 or more follicles in each ovary measuring 2 to 9 mm in diameter and/ or increased ovarian volume >10 mL on ultrasound.

True Positive: Case having ovary volume > 8ml as well as positive for PCOS on Rotterdam criterion.
True Negative: Case having ovary volume < 8ml as well as negative for PCOS on Rotterdam criterion.
False Positive: Case having ovary volume > 8ml but negative for PCOS on Rotterdam criterion.
False Negative: Case having ovary volume < 8ml but positive for PCOS on Rotterdam criterion.

**METHODOLOGY**

This cross sectional study was conducted in Radiology Department of Military Hospital, Lahore during February 2018—March 2019, to determine the diagnostic accuracy of ovarian volume > 8ml on transvaginal sonography in diagnosing polycystic ovarian syndrome among 150 infertile women taking Rotterdam criterion as gold standard. At 95% level of significance estimated sample size is 150 with 5% of margin of error, 79.49% sensitivity, 90.67% specificity and 38.5% prevalence of polycystic ovarian syndrome among infertile patients. The sampling technique was non-probability consecutive sampling. Females with history of hypothyroidism, autoimmune disease, uncontrolled diabetes and chronic steroid use were excluded. After informed consent, 150 infertile women aged 18-40 yrs presenting to department of radiology were included in study. Included patient had transvaginal sonography on 5th to 7th day of menstrual cycle. The volume of the ovary was calculated. A single consultant radiologist reported the ovarian volume on transvaginal sonography without prior knowledge of diagnosis of polycystic ovarian syndrome by Rotterdam criterion. Data was collected on structured proforma containing background information i.e. age and body mass index. Researcher herself recorded data according to operational definitions. PCOS was diagnosed according to Rotterdam criterion. Ultrasound system SonoAce R5 with transvaginal probe model EVN4-9 was used in every patient. Data collected was entered and analyzed in the SPSS version 17. Mean with standard deviation was calculated for quantitative variables like age, BMI and frequency and percen-
tage was calculated in case of categorical variables like ovarian volume > 8ml on transvaginal sonography and on Rotterdam criterion. Data was stratified for age and BMI. Post stratification sensitivity, specificity was measured.

RESULTS

150 patients were included in our study population with mean age of 32.93 ± 2.942 years ranged from 27 to 38 years. (Table I) Among study population (n=150), 137 patients (91.3%) were having ovarian volume above 8ml. (Table II) 116 patients (77.3%) had polycystic ovarian disease according to Rotterdam criterion. (Table II) 135 patients (90%) had duration of symptoms for disease above 5 years. (Table II) 125 patients (83.3%) had body mass index above 30kg/m2 whereas rest of 25 patients (16.7%) had below 30kg/m2. (Table II) In our study population, 122 patients (81.3%) were either 30 year or above and remaining 28 patients (18.7%) were below 30 years. (Table II) When we cross tabulated ovarian volume above 8ml with polycystic ovarian disease, among 116 patients 103 patients had polycystic ovarian disease with ovarian volume above 8ml. (Table III) When we took Rotterdam criterion as gold standard, for ovarian volume >8ml, sensitivity was 88.80% and positive predictive value was 75.18% while specificity and negative predictive value was zero. (Table III) We stratified diagnostic yield for age and BMI > 30 Kg/m2. Sensitivity came out higher for older and obese patients. (Table IV)

DISCUSSION

Polycystic ovarian syndrome falls in treatable conditions list. It needs a cascade of high tech test. Rationale of current study is that there is no local study available regarding the diagnostic accuracy of ovarian volume > 8ml in diagnosing polycystic ovarian syndrome among infertile Pakistani women. A simple modality like transvaginal sonography may reduce the cost of diagnosis of PCO among infertile women. In our study, when we took Rotterdam criterion as gold standard, for ovarian volume >8ml, sensitivity was

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</tr>
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<td>No</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Table 3: Validity of Ovarian Volume Against Rotterdam Criteria (Gold Standard) for Polycystic Ovarian Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovarian Volume &gt; 8 ml</td>
</tr>
<tr>
<td>Polycystic Ovarian disease</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 4: Stratification Analysis of Diagnostic Yield of Ovarian Volume &gt;8ml with Polycystic Ovarian Disease for Age and BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Groups</td>
</tr>
<tr>
<td>-----------------------------------</td>
</tr>
<tr>
<td>Age 30 yrs &amp; above</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Below 30 yrs</td>
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<tr>
<td></td>
</tr>
<tr>
<td>BMI</td>
</tr>
<tr>
<td>BMI &gt; 30 Kg/m2</td>
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<tr>
<td></td>
</tr>
<tr>
<td>BMI &lt; 30 Kg/m2</td>
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<tr>
<td></td>
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</tbody>
</table>
88.80% and positive predictive value was 75.18% while specificity and negative predictive value was zero. It implies that in infertile population (as in our case) transvaginal ultrasonography can be used to diagnose polycystic ovarian syndrome without additional cost. But zero specificity make it unreliable for excluding the cases. Our results match with previous studies up to some extent. In an Indian study, the frequency of PCOs in female related infertility was 38.5%. All women presenting with complaints of menstrual disturbances, male pattern hair growth or infertility were included. Sensitivity of 79.49% and specificity of 90.67% was achieved with a cutoff of 8 mL as ovarian volume. These differences can be attributed to study population characteristics. Our sampling technique was non probability consecutive sampling, so usually in our sampled age group infertile women appear. In another study, an ovarian volume of 10 ml had an 81% sensitivity and 84% specificity.\(^\text{11}\) We can attribute the minor difference in sensitivity to the population included. Mean age in our study population was 32.93 ± 2.9 years showing a delayed age marriage trend. 116 patients (77.3%) had polycystic ovarian disease according to Rotterdam criterion. Out of 116 patients, 103 patients were correctly diagnosed. Another study has emphasized to determine Ovarian volume in both ovaries for diagnosis of PCOs, the approach used in our study.\(^\text{12}\) We stratified diagnostic yield for age, BMI > 30 and duration of symptom. Sensitivity came out higher for older and obese patients.

Limitation of current study is its small sample size and population selection from a single tertiary care hospital which is not representative of our total population. In future studies controls should be included so as to comment on Specificity.

CONCLUSION

It is concluded that diagnostic accuracy of ovarian volume > 8ml by transvaginal ultrasonography is acceptable for diagnosis of polycystic ovarian syndrome among infertile women. It can be used as a proxy indicator of polycystic ovarian syndrome as it has shown high sensitivity but low specificity. Obese patients and those in higher age group can benefit more with this screening test.

Limitations of the Study

This study has recruited all the infertile females reporting to radiology department. If this study had included more subjects and some fertile females as well, it could have yielded more valid results.

Acknowledgments

We acknowledge the support and guidance provided Brig Imran Masoud Qasmi.

Conflicts of interest

No conflict of interest

Funding Sources

None

Contributions of the Authors

Dr. Yusrah Liaqat: Conception of idea, Data Collection, Literature review.

Dr. Jawairiah Liaqat: Literature Review, Write up of article.

Dr. Sana Iftikhar: Data entry, statistical Analysis, Referencing

REFERENCES


Diabetic nephropathy (DN) is one of the long-term complications of diabetes that affects small blood vessels. It is a major factor of causing end stage renal disease (ESRD) and pragmatically manifests as albumin concentration in urine, ranging from microalbuminuria to macroalbuminuria and ultimately leading to ESRD. Major and potentially modifiable risk factors for diabetic nephropathy in at risk individuals, are persistent hyperglycemia and uncontrolled blood pressure. Other putative hazardous factors are glomerular hyperfiltration due to other causes that are smoking, dyslipidemia, severity of proteinuria and nutritional factors such as the quantity and origin of fat and protein in the diet. Once the diagnosis of micro-or macroalbuminuria is established, patients should withstand complete assessment including a work-up for other causes of albuminuria, an evaluation of renal function and the
CORRELATION BETWEEN DIABETIC NEPHROPATHY AND MEAN NEUTROPHIL TO LYMPHOCYTE RATIO

existence of other associated comorbidities. There is a necessity to establish early onscreen diagnostic marker of DN which can modify the disease progression. Asians are more widely affected with DN in contrast to Caucasians. Association between diabetic nephropathy, inflammation, and coronary artery disease has been defined.

Many inflammation related makers are linked to DN like cytokines, TNF-α, transforming growth factor beta 1 and IL1, IL6, IL8. However, their estimation is not used rigorously and cost burden on economics. In this respect, neutrophil to lymphocyte ratio has appeared as an innovative marker. An index, i.e. the neutrophil/lymphocyte ratio has lately been created to consider both high level of neutrophils, which reflects the critical condition of inflammation, and lymphopenia, which depicts physiological stress. The NLR has proved as an approving index of the inflammatory status. Purpose of the study was to find the frequency of DN in type II Diabetes Mellitus (DM) patients and comparison of NLR among patients with or without diabetic nephropathy. The results would add local data and we would be able to recommend the timely screening of patients for NLR and if found deranged, they would be managed earlier to halt progression of diabetic nephropathy.

METHODOLOGY

The research was conducted at the department of Medicine, Jinnah Hospital Lahore. Duration of this was study was six months. The study was endorsed by the Research Evaluation Unit of College of Physicians and Surgeons Pakistan. Inclusion criteria set for this study includes enrollment of patients of age 50 to 80 years, belonging to either gender, with type II diabetes (as per operational definition) and diagnosed at least 1 year ago. Diseases that can affect urinary albumin excretion, cardiac disease, blood diseases that can affect neutrophils and lymphocytes and TLC < 4.0 × 10^9/L or > 11.0 × 10^9/L were excluded for this study. 130 patients fulfilling selection criteria were enrolled from Outdoor patient of Department of Medicine, Jinnah Hospital, Lahore. Informed consent and demographic details (name, gender, age, BMI) were obtained. Urine sample was obtained from each patient and was stored in separate container. All samples were sent to the hospital laboratory for microalbuminuria (30 – 300mg/d). If microalbuminuria was present then patient was labeled having diabetic nephropathy. Venous blood samples of these patients were also obtained and sent to the hospital laboratory for assessment of NLR. Reports were assessed and NLR calculated (as per operational definition). All data analysis was performed in SPSS version 20.0. All measureable variables i.e. age, NLR, BMI and diabetes duration were presented as mean standard deviation. The qualitative variable i.e., gender and diabetic nephropathy was obtained as frequency and percentage. Independent sample T–test was used to compare neutrophil to lymphocyte ratio. P-value smaller than or equal to 0.05 was considered significant. Data was stratified for gender, age, BMI and type II diabetes duration. Chi-square test for diabetic nephropathy and independent sample T–test for NLR were applied with p-value smaller than 0.05 taken as statistically significant.

RESULTS

Mean age ± S.D. of the subjects was 59.4 ± 12.4 years (range: 50 – 78 years). Highest number of subjects (44.6%) was from the age group 50 – 60 years. There were 68 (52.3%) males and 62 (47.7%) females in the study with female to male ratio being 1:1.1 (Table 1)

<table>
<thead>
<tr>
<th>Age Groups (Years)</th>
<th>Number of Subjects (N=130)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-60</td>
<td>58</td>
<td>44.6</td>
</tr>
<tr>
<td>61-70</td>
<td>52</td>
<td>40</td>
</tr>
<tr>
<td>71-80</td>
<td>20</td>
<td>15.4</td>
</tr>
<tr>
<td>Total</td>
<td>130</td>
<td>100</td>
</tr>
</tbody>
</table>

(Mean Age:59.4±12.4 years) (Range: 50-78years)

female subjects in the study with female to male ratio being 1:1.1 (Table 1)

The mean age of the males and females were 62.3±13.4 and 58.69 ±14.8 years respectively. The difference between the mean age of the male and
female population was statistically significant with p-value = 0.037.

The mean duration of diabetes in the study population was 8.9 ± 3.6 years with 8.4 ± 3.5 years and 9.1 ± 3.7 years in the male and female population respectively. The mean BMI of the patients was 26.2 ± 4.2 Kg/m² and the difference between the male and female population was statistically not significant with p-value: 0.762. Similarly, the serum albumin level was 4.1 ± 0.6 g/dL in the study population and it does not differ significantly between the male and the female patients. The frequency of diabetic nephropathy, as calculated by presence of microalbuminuria, was found to be 43.1%. Female population had higher prevalence of microalbuminuria (45.2%) than male population (41.2%) but the difference was statistically not significant with p-value > 0.05 (Table 2).

Table 2: Difference in the Age of the Male and Female Patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Categories</th>
<th>N</th>
<th>Mean± SD</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Male</td>
<td>68</td>
<td>62.3±13.4</td>
<td>0.037</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>62</td>
<td>58.69±14.8</td>
<td></td>
</tr>
</tbody>
</table>

Post-stratification, chi-square test for diabetic nephropathy and independent sample T–test for NLR were applied. This difference in the age of the patients with and without diabetic nephropathy was statistically significant (p-value: 0.012). The differences in the gender distribution study participants was not statistically significant (p value: 0.952)

The patients with diabetic nephropathy had significantly higher mean duration of diabetes than without diabetic nephropathy (10.2 ± 45 versus 8.1 ± 3.8 years; p-value: 0.001). However, the differences in the BMI and serum albumin of the patients with and without diabetic nephropathy were not statistically significant i.e. p>0.05.

The mean neutrophil count was 4.8 ± 1.8 and 4.4 ±1.6×10⁹/L in the cases with and without diabetic nephropathy (p-value: 0.024). Similarly, the mean lymphocyte count was 1.9 ± 0.7 and 2.6 ± 0.8 x 10⁹/L in the patients with and without diabetic nephropathy (p-value <0.001) respectively. The mean value of NLR in the cases with diabetic nephropathy came out to be 2.7 ± 1.0 as opposed to 1.9 ± 0.8 in the patients without diabetic nephropathy. The difference in the NLR between the two study subgroups was statistically significant with p-value <0.001.

DISCUSSION

Diabetes mellitus (DM) type 2 may have hazardous socioeconomic consequences because of microvascular (diabetic neuropathy, retinopathy and nephropathy) and macrovascular complications. Diabetic Nephropathy leads to noteworthy difficulties in 25–40% of diabetic patients and is the utmost cause of end case renal failure. The urine microalbumin excretion rate (UMAER) can be considered for detection and surveillance of DN progression. Glomerular damage is considered as an early sign of DN and it can be detected by presence of microalbuminuria, while worsening proteinuria is a strong indicator of progression DN. Increase in proteinuria due to DN is a part of the inevitable chain of clinical incidences involving high blood pressure and ongoing fall in Glomerular filtration rate. Clinical and experimental studies have showed the notable role of inflammatory markers like adhesion molecules, chemokines, adipokines and cytokines) and endothelial dysfunction in the background of DN. In addition to that, it has also been reported that renal inflammation has a pivotal place in progression and advancement of DN. WBC count and its subtypes, depicts the equilibrium between lymphocytes and neutrophils in the body and can be predictors of systemic inflammation. Neutrophil to lymphocyte ratio can easily be premeditated by taking peripheral blood. Several Investigators determined a remark-
able association between White blood cell count and the DN prevalence.

Okyay et al. reported that Neutrophil to lymphocyte ratio had a direct association with IL-6 and was sensitive to C-reactive protein as well. These results showed that NLR assessment may be used as an assay marker of systemic inflammation in Chronic kidney disease. In another study, Huang et al found notable difference between the diabetic patient group and controls regarding NLR. In our study, we found that neutrophil and lymphocyte counts were dissimilar among the groups, which is in agreement with the previous studies.

The main results of this study was that NLR levels were found to be remarkably related with patients who have an early-stage DN in contrast to those without DN. This study was first in Pakistan to evaluate the correlation in between NLR and DN. The exact pathological process of DN is unidentified. However, pathological cascade of incidents (with glomerular damage being an initial indicator, which gives rise to proteinuria, followed by advancement of renal damage, fibrosis, inflammation, and finally depletion of functional nephrons) is known to play an pivotal role in the development and advancement of DN. Inflammation in kidneys in the background of DN is thought to have a crucial role. WBC count and its subtypes are amid the promptly available and cost effective inflammatory markers.

NLR is a innovative indicator of chronic inflammation that depicts an equilibrium of two dependent components of the immune system; neutrophils that are the active indifferent inflammatory mediator forms main line of defense whereas lymphocytes regulates inflammation. Interestingly, NLR was found to have a positive relation not only with the existence but also with the austerity of metabolic syndrome. Initially, Neutrophil to Lymphocyte ratio was identified as a prognostic marker in numerous types of cancer that may helps in patient stratification and individual risk assessment. Recently, numerous studies have recommended that NLR might be a prognostic marker for vascular diseases also. In this study, the average NLR value among diabetic patients with albuminuria (2.7 ± 1.0) was considerably high than patients without albuminuria (1.9 ± 0.8). In concordance with our results, Huang et al. have also reported that NLR values were remarkably high in diabetic patients with indication of nephropathy (2.48 ± 0.59) than in diabetic patients with absence of nephropathy (2.20 ± 0.62) and healthy controls (1.80 ± 0.64) (9).

**Limitation of Study**

Limitations of this study includes the conduction of a cross sectional analysis and small sample size. Since this study is not a prospective controlled study, any decisive contributory associations between NLR and DN could not be inspected.

**CONCLUSION**

The results of this study showed a notable association between NLR and DN, suggesting that endothelial dysfunction and inflammation might be a fundamental part of DN. NLR was independently and significantly high in patients affected with type 2 DM and increased albuminuria. Therefore, NLR may be appraised as a future diagnostic and prognostic risk marker of DN. NLR can be calculated easily by detecting the differential leukocyte value. The test is easy, rapid and cost effective and can be done on daily basis. With limited laboratory facilities, NLR is a manageable check marker which can be a substitute for other high priced inflammation related markers like TNF, cytokines, ILs and C-reactive protein. Much research with a futuristic design and many NLR measurements will open light on the function of NLR as an inflammatory marker and a likely risk factor for DN.

**Acknowledgment**

Dr. Muhammad Masood, Ex Head Medical Unit 4, JHL

**Conflict of Interest**

None

**Funding Statement**

None

**Contributions of Authors**

Rabia Arshad: Manuscript writing, data collection and supervised research

Faiza Muzahir: Design of research work and review manuscript

Navaira Arshad: Perform statistical analysis and data analysis.
Sana Zafar: perform statistical analysis and data analysis
Sundus Mariyum Haroon: Data collection and data record
Sabeen Aftab: manuscript writing, data record
Prof Muhammad Masood: critical data analysis and supervised research

REFERENCES
Anxiety is a natural reaction arising in response to entering a different environment, such as an operating theatre. The role of sedation is important in such scenarios as the pregnant woman’s anxiety and preoperative stress are intense. While sedation has a wide sphere of use in today’s regional anaesthesia procedures, its probable depressant effect on the newborn in Caesarean section operation explains its rare or non-existent employment.

Midazolam is the benzodiazepine most commonly used for sedation, since it produces a faster onset, more complete amnesia, less pain on injection, and improved awakening when compared with diazepam. Midazolam possesses a relatively high volume of distribution (Vd) compared with other benzodiazepines because of its lipophilicity. The Vd is greatly amplified in obese patients, resulting in an increased half-life from 2.7 hours to 8.4 hours. Midazolam is cleared by hepatic hydroxylation to 1-hydroxymidazolam (elicits about 10% of the pharmacologic activity as parent compound). In comparison, diazepam has an extremely long half-life (0.8-2.25 d) that

Abstract

Objective: To compare mean anxiety scores in obstetric patients undergoing caesarean section, which are pre-medicated with midazolam versus normal saline (as placebo). A randomized controlled trial was conducted at the Department of Anesthesiology, Shalamar Hospital, Lahore from 15th September, 2017 to 14th March, 2018.

Methodology: A total of 100 patients of ages between 18 and 40 years indicated for caesarean section were included. Patients with hypertension, antepartum haemorrhage and congenital malformations and contraindicated for regional anaesthesia were excluded. The patients were randomized to receive either intravenous premedication with 0.025 mg/kg midazolam (group M, n = 50) or an equal quantity of Normal Saline (group S, n = 50). The Amsterdam Preoperative Anxiety and Information Scale (APAIS) was used for the objective analysis of anxiety in all patients.

Results: The mean age of patients in group M was 28.38 ± 6.50 years and in group B was 27.84 ± 5.83 years. The mean weight of patients in group M was 63.44 ± 9.18 kg and in group S was 62.90 ± 9.16 kg. In this study, mean anxiety score was 8.92 ± 2.62 for midazolam group as compared to 17.38 ± 3.28 of saline group with a p value of 0.0001.

Conclusion: This study concluded that mean anxiety scores is less in obstetric patients, scheduled for elective caesarean section under regional anaesthesia technique, who were administered sedation using midazolam as compared to those receiving normal saline.

Key Words: caesarean section, midazolam, anxiety score.
COMPARISON OF PREMEDICATION WITH MIDAZOLAM VERSUS NORMAL SALINE

is markedly increased in obese or elderly patients (3.9 d and 3.29 d, respectively). Additionally, its active metabolites have long half-lives (i.e. N-desmethyldiazepam[1.6-4.2 d]; nordiazepam [about 8 d]).

While there are several studies concerning the use of midazolam in regional anaesthesia, the number of studies regarding its use in Caesarean section is limited. Although it crosses the placental barrier, in small doses, it does not cause any adverse effects in the neonate. The preoperative stress response leads to vasoconstriction in the uterine arteries and may cause fetal distress. Many researchers have reported that increased preoperative anxiety means the use of more peri-operative as well as postoperative analgesia and longer hospitalization.

In a study by Senel AC et al, patients undergoing caesarean section under regional anaesthesia, who received midazolam 0.025 mg/kg as premedication had significantly low anxiety scores (p=0.0001) and the new born Apgar scores were not reported to differ between the group administered the midazolam and the control group (p>0.05). The baseline anxiety scores in both groups were comparable i.e. 18.24 ± 4.23 and 17.84 ± 3.77 with a p value of 0.725. However, anxiety scores were lower in the group after premedication with midazolam i.e. 10.84 ± 3.51 as compared to 15.00 ± 3.29 in the control group with a significant p value of 0.0001. Also the APGAR score at 5th minute after birth was 9.12 ± 0.58 and 9.16 ± 0.73 in both groups with a p value of 0.83.

In another prospective randomized controlled trial, mothers pre-medicated with low doses of midazolam showed a lower level of preoperative anxiety and a higher degree of postoperative satisfaction than the control group. The preoperative anxiety scores of two groups before any premedication were 17.10±3.19 and 16.81±2.60 with a p value of 0.618. After premedication, anxiety score was 11.98±1.99 for midazolam group as compared to 14.15±2.11 of control group with a p value of 0. The APGAR scores 5 minutes after birth were 9 in both groups. No significant differences were found between the two groups regarding the Apgar scores of the new born and the pH, PaCO2, PaO2, and base deficit in the umbilical arterial samples (p>0.05).

This study was intended to compare anxiety scores in obstetric patients scheduled for elective Caesarean section under regional anaesthesia technique, in groups administered sedation using midazolam or without sedation. This will help us to improve our practice and will update local guidelines as well.

METHODOLOGY

After approval of hospital ethics committee, 100 patients were included in the study through operational theatre of obstetrics and gynaecology at Shalamar hospital, Lahore. After taking informed written consent from the participant cases, demographics were noted (name, age, weight). Patients of ages between 18 and 40 years scheduled for Caesarean section with ASA physical status I & II were included in the study. Patients with Systemic problems e.g. hypertension (BP > 140/90mm hg), Diabetes mellitus (BSR>186mg/dL), obstetric complications such as antepartum haemorrhage and cases contraindicated for regional anesthesia or refusing a regional anaesthetic technique were excluded from the study. The patients were randomized to receive either intravenous premedication with 0.025 mg/kg midazolam (group M, n = 50) or an equal quantity of Normal Saline (group S, n = 50) in the operating room before surgery by coin tossing method. All patients were booked on a morning list, instructed for the same preoperative fasting protocol and were educated as to how to complete the questionnaires required for the study. On arrival of the patients to the operation theatre, routine monitoring (electrocardiography, pulse oximetery, and a non-invasive blood pressure cuff) were applied, and venous access established for the infusion of lactated Ringer's solution.

After the institution of spinal anaesthesia, group (M) was given intravenous premedication with midazolam (0.025 mg/kg) in 2 mL solution, whereas group (S) was given an equal quantity of normal saline. Same anaesthesia personnel administered the medication to either group. The Amsterdam Preope-
Perioperative Anxiety and Information Scale (APAIS) was used for the objective analysis of anxiety in all patients. It consisted of six questions receiving a score between one (none) and five (most), with a total score of 30, investigating patient’s concerns and anxiety. It is short, reliable, and easy to administer. APAIS was applied twice by the same anaesthesia assistant to all patients in the operating theatre before and after the completion of surgery. All spinal blocks were performed by the researcher himself. For spinal anaesthesia, 12 mg of intrathecal hyperbaric bupivacaine (0.75%) was injected using a 25-gauge spinal needle with patients in the sitting position at the L 3/4 interspace, under strict aseptic precautions. Parturient were then immediately placed in the tilted supine position. The level of sensory block was determined with cold and pinprick tests. Oxygen by nasal cannula (2 L/min) was applied to all patients. Urinary catheterization was performed, and surgery was started when a sufficient level of sensory block (T4) is achieved. Following spinal anaesthesia, systolic arterial blood pressure was maintained above 90 mmHg. Cases falling below this level were given 10-50 ug intravenous boluses of phenylephrine. Anxiety scores was recorded just before and after the surgery (as per operational definition). After completion of surgery, patients were kept in the recovery room for 1 hour and then shifted to the ward when they fulfil criteria.

Data were entered and analysed into SPSS version 21. Quantitative variables such as age and weight were presented as mean and standard deviation. Both groups were compared for anxiety score by applying independent t test with p value ≤0.05 as significant. Data were stratified for age, weight to address effect modifiers. Post-stratification independent sample ‘t’ test was applied with p-value ≤0.05 as significant.

**RESULTS**

Age range in this study was from 18 to 40 years with mean age of 28.13 ± 6.12 years. The mean age of patients in group M was 28.38 ± 6.50 years and in group B was 27.84 ± 5.83 years. Majority of the patients 60 (60.0%) were between 18 to 20 years of age.

<table>
<thead>
<tr>
<th>Table 1: Age Distribution for Both Groups (n=100)</th>
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<tbody>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>-------------</td>
</tr>
<tr>
<td>18-30</td>
</tr>
<tr>
<td>31-40</td>
</tr>
<tr>
<td>Mean ± SD</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2: Weight for Both Groups (n=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
</tr>
<tr>
<td>&lt;=60</td>
</tr>
<tr>
<td>&gt;60</td>
</tr>
<tr>
<td>Mean ± SD</td>
</tr>
</tbody>
</table>

- P-value = 0.0001 which is statistically significant
COMPARISON OF PREMEDICATION WITH MIDAZOLAM VERSUS NORMAL SALINE

age as shown in Table I.

The mean weight of patients in group M was 63.44 ± 9.18 kg and in group S was 62.90 ± 9.16 kg (Table II).

The mean anxiety score was 8.92 ± 2.62 for midazolam group as compared to 17.38 ± 3.28 of saline group with a p value of 0.0001 as shown in Figure I.

DISCUSSION

Patients scheduled for surgery experience varying levels of anxiety, due to different factors like, cultural diversity, type of surgery, previous anaesthesia experience, and preoperative information.69 Previous studies have reported anxiety of being awake during surgery as one of the most common reasons for choosing general anaesthesia (GA),10,11 but whether higher level of preoperative anxiety influences patient's decision to refuse regional anaesthesia (RA) needs to be determined. Literature has reported a higher level of preoperative anxiety in obstetric patients compared to general surgical population.12,13 Caesarean section (CS) is one of the most common surgical procedures performed on obstetric patients, and regional anaesthesia is the preferred technique of anaesthesia in terms of risk and benefits for both mother and fetus. In modern obstetric anaesthesia practice, percentage use of regional anaesthesia for Caesarean section has become a marker of quality.14 Like all surgical patients, obstetric patients also feel operative stress and anxiety. This can be prevented by giving patients detailed information about their operation and with preoperative pharmacological medications. Because of depressive effects of sedatives on new born, pharmacological medications are omitted, especially in obstetric patients. The literature contains few studies concerning preoperative midazolam use in caesarean section patients.15

I have conducted this study to compare mean anxiety scores in obstetric patients undergoing caesarean section, which were pre-medicated with midazolam versus normal saline (as placebo). Age range in this study was from 18 to 40 years with mean age of 28.13 ± 6.12 years. The mean age of patients in group M was 28.38 ± 6.50 years and in group B was 27.84 ± 5.83 years. Majority of the patients 60 (60.0%) were between 18 to 20 years of age. In this study, mean anxiety score was 8.92 ± 2.62 for midazolam group as compared to 17.38 ± 3.28 of saline group with a p value of 0.0001. In a study by Senel AC et al, patients undergoing caesarean section under regional anaesthesia, who received midazolam 0.025 mg/kg as premedication had significantly low anxiety scores (p=0.0001) and the new born Apgar scores were not reported to differ between the group administered the midazolam and the control group (p>0.05). The baseline anxiety scores in both groups were comparable i.e. 18.24 ± 4.23 and 17.84 ± 3.77 with a p value of 0.725. However, anxiety scores were lower in the group after premedication with midazolam i.e. 10.84 ± 3.51 as compared to 15.00 ± 3.29 in the control group with a significant p value of 0.0001.6

Premedication to facilitate neuraxial blockade remains the rare exception in pregnant patients, based on concerns about potential untoward effects of fetal drug exposure. In fact, in the 1960’s several case reports described decreased motor tone in infants born to mothers who had been treated with diazepam during their pregnancy.129 Another reason for the relative infrequent use of benzodiazepines during pregnancy is probably related to their putative association with facial malformations in animals when given during the teratogenic period of pregnancy, although, in a recent review, the alleged association of benzodiazepine use during pregnancy with facial malformations has been completely dismissed.16,17 Therefore, women in some cases may endure a great deal of anxiety and discomfort when undergoing placement of a spinal or epidural block for Caesarean delivery.

In another prospective randomized controlled trial, mothers pre-medicated with low doses of midazolam showed a lower level of preoperative anxiety and a higher degree of postoperative satisfaction than the control group. The preoperative anxiety scores of two groups before any premedication were
17.10±3.19 and 16.81±2.60 with a p value of 0.618. After premedication, anxiety score was 11.98±1.99 for midazolam group as compared to 14.15±2.11 of control group with a p value of 0.

Sun GC et al., studied the effects of two different doses of midazolam premedication on age and gender. In this study the dosage of intravenous midazolam chosen were 0.02 and 0.06 mg/kg midazolam. They concluded that midazolam is effective for producing sedation and anxiolytic effect at a dose of 0.02 mg/kg, with minimal effects on cardio-respiratory system and oxygen saturation to patients. In a placebo controlled trial comparing the effects of 0.025 mg/kg midazolam with saline in patients undergoing caesarean section, it was found that anxiety scores were lower in mothers receiving intravenous midazolam. These findings were similar to our findings where midazolam premedication considerably reduced the anxiety scores.

CONCLUSION

We concluded that mean anxiety score is less in obstetric patients, scheduled for elective caesarean section under regional anesthesia technique, who are administered sedation using midazolam as compared to those receiving normal saline. So, we recommend that premedication with midazolam in patients undergoing caesarean section should be used routinely in our general practice for preventing anxiety.

Ethical Approval

Ethical approval was obtained from the Hospital Review Committee.

Patients’ Consent

Informed consent was signed by every patient before enrolment in the study.

Conflict of Interest

Authors declared no conflict of interest.

Authors’ Contribution

Muhammad Imran Aslam: Conceived idea, study designed, Data Collection.
Itrat Kazmi: Study designed, Data Collection, literature review, Manuscript writing
Aamir Bashir: Data collection, literature review, Manuscript writing
Aamir Waseem: Data Analysis, Manuscript writing, Proof reading

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19. Ahmet C, Fatih M. Premedication with midazolam prior to caesarean section has no neonatal adverse effects. 2014;64:16-21.
Fracture of femoral shaft is the most common orthopedic injury after those of the radius, ulna and tibial shaft fractures. Common mechanisms of injury are child abuse, road traffic accidents, fall from height, fall of heavy object on the affected limb and the pathological fractures.

Although various methods of treatment of the fracture of femur in children are in current practice. The choice of a specific method is generally based upon the fracture pattern, age of the child, weight of the child, experience of the surgeon and the presence of associated injuries. Age is one of the most important factor. Our treatment modalities change according to the age. Fracture of the femoral shaft affect social and economic status of a country.

Angular deformity, leg-length discrepancy,
Comparision of clinical outcome of immediate versus delayed spica casting

Rotational deformity, and nonunion are commonly reported complications following pediatric femoral shaft fracture. Other complications include muscle weakness, neurovascular injury, re-fracture, compartment syndrome, infection, and knee subluxation (with skeletal traction). Orthopedic surgeons remain divided about the optimal method of treatment for children's femoral fractures. The choice of treatment may be influenced by the age of the child, the level and pattern of the fracture and to a great extent, by regional, institutional or surgeons' preferences. Mechanism of injury and associated injuries are also considered. The psychological and economical outcome are being considered more frequently regarding the mode of treatment. A systematic review of the literature provides little evidence to support one method of treatment over another.

Non-operative treatment is still the treatment of choice for closed fractures of the femoral shaft in children. So standard for the management of most femoral fractures in children has always been conservative i.e a period of traction to maintain the reduction until early stabilization by fracture callus, followed by hip spica until fracture union. Children between 2-10 years of age can be treated either with balanced traction for 2-3 weeks followed by hip spica cast for another 4 weeks or by early reduction under anesthesia and a hip spica cast from the outset.

Young children have traditionally been treated conservatively with good results. The great problems encountered by the family caring for a child in spica cast were transportation, cast intolerance by the child and keeping the child clean. The primary problem with immediate spica casting are shortening and angulation of the fractures in high energy patients. Enthusiasm for treatment that decreases hospital stay has led to the use of external fixator & flexible intramedullary nails in children 6 years of age through adolescense. Given the excellent fracture healing potential in children, it is believed that skin traction followed by spica casting achieves favourable outcomes and should not be excluded as a viable treatment option in older children. An international study has reported that the limb length discrepancy was in 22% of patients managed with traction & casting, hence in 78% there was no leg length discrepancy. In another international study 207 patients were treated by this method, no significant residual angular deformities were seen in any of children.

I reported a randomized clinical trial to compare mean days in bone union in immediate versus delayed spica casting in uncomplicated fracture shaft of femur in children.

**Methodology**

152 patients with unilateral close mid diaphyseal femur fracture presenting in the emergency and outdoor departments of Nishtar Hospital Multan, Pakistan. Patients between 6 months to 6 years of age both male and female were enrolled in the study. Patients with open fractures, bilateral fractures and associated injuries were excluded from study. Approval was taken from ethical committee of the hospital. Patients were divided into two groups.

Group A consisting of 76 patients were treated by initial skin traction and then delayed Spica casting.

Group B consisting of 76 patients were treated by immediate Spica Casting. The Spica cast was applied by consultant orthopedic surgeon who has five year experience of application of Spica casting.

Patients were sedated or general anesthesia was given under proper protocol and supervision. The Spica cast was applied keeping the hip and knee in 90 degree flexion (sitting spica technique) with foot in neutral position. Supporting rods were used to connect the fracture leg with normal one for stability in slight abduction. Patient was observed for 24 hours for any neurovascular compromise and then discharged. The same technique was used for group B patients. Patients were followed up after every 2 weeks and X-Rays were repeated up to (90 days), number of days for bone reunion were noted by observing all the four cortices in anteroposterior (Ap) and lateral Views.
and movements at fracture site were noted clinically.

All the data was entered on SPSS for windows version 10. Frequency and percentage were calculated for gender. Independent t. test was applied to compare the union in days taken for bone union in both groups. A p-value ≤ 0.05 will be considered statistically significant. Stratification was done especially for age and sex and type of fracture and to see the effect of these on outcome variables. Post stratification Chi-square test was applied.

RESULTS

152 cases of femoral shaft fracture in children of either sex aged between 6 months to 6 years of age were treated in the study having 76 patients in each group.

Results were evaluated according to number of days in union by radiography.

Patients in group A who underwent delay spica casting showed delayed bone healing and took more days for bone reunion (83.81 ± 0.3124) as compared to group B who underwent early spica casting (64.13 ± 0.09806)

Graph-1 Outcome (Number of days of bone reunion) of immediate versus delayed spica cast in paediatric femur shaft fractures.

Majority of the children (50.7%) were between 4–6 years, while rest 41.4% children were between 1-3 years and 7.9% were between 6 months-1 year as shown in graph no. 2.

There were 97(63.8%) male and 55(36.2%) female cases. Male to female ratio being 1.8:1.

Results were evaluated according to type of fracture, the number of children having transverse fracture were 44(28%), children with short oblique fracture were 73(48%) which is the most common type of fracture seen in children, children having long oblique fracture were 31(20.4%), children with spiral fracture were 4(4.2%).

Results were evaluated according to weight of children and number of days taken in bone union, children having weight 5-10 kg were 12(7.9%), children with weight 10-15 kg were 26(17.1%), children weighing 15-20 kg were 81(53.3%), children weighing 20-25 kg were 33 (21.7%). Patients between 5-10 kg treated with early and delayed spica cast were 8 versus 4 respectively. Regarding children falling between 10-15 kg, 6 were treated with early spica as compared to 20 patients treated with delayed spica. Regarding majority of children between 15-20 kg, 43 were treated with early spica and 38 were treated with delayed spica. Among children between 20-25 kg, 19 were treated with early spica cast as compared to 14 who were treated with delayed spica cast.

Results were evaluated according to number of days in union (by radiography). Union was achieved in 63 days in 30 children (19.7%), 64 days in 28 children (18.4%) and 65 days in 18 children (11.8%) after removal of early spica. After removal of delayed spica, union was achieved in 83 days in 14 cases (9.2%), 84 days in 31 children (20.4%) and 85 days in 31 children (20.4%) as shown in table no 1. The mean number of days in bone union after early and delay spica group were 63.84 days and 84.22 days respectively as shown in Graph no. 3.

<table>
<thead>
<tr>
<th>Table 1:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bone Union in Days</strong></td>
</tr>
<tr>
<td><strong>63 Days</strong></td>
</tr>
<tr>
<td>6-12 months</td>
</tr>
<tr>
<td>1-3 years</td>
</tr>
<tr>
<td>3-6 years</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>
DISCUSSION

Paediatric femoral fractures are common and expensive. Numerous options are available for treatment. Non operative treatment options include pavlick harness, skin or skeletal traction and spica casting. While operative treatment options include closed reduction and external fixation, open reduction and internal plate fixation, closed reduction and minimally invasive plate osteosynthesis (MIPO), closed reduction and intramedullary nailing with either flexible or rigid nails.

Conventional treatment of femoral shaft fractures in children is by traction followed by a hip spica. Early closed reduction and hip spica casting has gained popularity as an effective treatment modality.

Present study dealt with immediate spica cast and delayed hip spica cast application as a definitive treatment option for the fracture of femur shaft. Regarding demographic data, in present study mean age of the children with early spica was 41.26 months and mean age of children with delayed spica was 38.18, with a male to female ratio of 1.8:1.

In our study the outcome after removal of spica cast and after final assessment revealed that the average number of days in bone union after immediate spica cast were 63.8 and the average number of days in bone union after delayed spica cast were 84.22. our study showed that early spica casting has better outcome in terms of bone healing and time taking for bone to heal. It was concluded in our study that patients treated with early spica casting has lesser length discrepancy, less joint stiffness, less deformity and lesser period of immobilization.

In a recent Pakistani study, Siddiqui et al compared the results of skin traction followed by spica cast versus early spica cast in femoral shaft fractures of children. The results of their treatment were satisfactory in 95% and unsatisfactory in 5% cases.

They found satisfactory results in children treated with early spica cast and good results in children treated with skin traction followed by spica cast and there were fewer complications in this group. However, they concluded that the latter method was better because of lesser length discrepancy, less deformity, less joint stiffness, lesser period of immobilization in spica cast, and fewer complications like ulceration, pressure sores and loss of reduction.

CONCLUSION

Skin traction and spica cast immobilization is simple, effective and definitive method of treatment for most femoral shaft fractures in children. There are fewer complications with this mode of treatment with no risks of surgical intervention. Although the period of immobilization is less with early spica cast as compared to patients managed with delayed spica cast. Early spica casting is a better approach in treating femoral shaft fracture in children as it reduces complication and hospital stay, lessening the patient burden in a tertiary care hospital.

Limitations of Study Limitation of the study is that we did not include above 5 years age.
Acknowledgements I would like to express a deep and sincere gratitude to Prof. Dr. Sajjad Hussain Goraya Head of Orthopaedics unit 2, Jinnah Hospital, Lahore who gave me opportunity to do research and providing invaluable guidance through this research.

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Research design and planning by: Dr. Aamir Shabab, Dr. Muhammad Imran
Reviewers: Prof. Dr. Sajjad Goraya, Dr. Waqar Ahmad Siddiqi and Dr. Muhammad Imran

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22. Dirk Leu, MD1; M. Catherine Sargent, MD1; Michael C. Ain, MD1; Arabella I. Leet, MD2; John E. Tis, MD1; Paul D. Sponseller, MD1 Spica Casting for Pediatric Femoral Fractures: A Prospective, Randomized Controlled Study of Single-Leg Versus Double-Leg Spica Casts. J Bone Joint Surg Am, 2012 Jul 18; 94(14):1259-1264. doi: 10.2106/ JBJS. K. 00966
I
schemic heart disease is one the most common type of acquired heart diseases occurring due to plaque build-up along the arterial wall resulting in its narrowing and impaired blood flow to heart tissue. Heart disease has become one of the leading causes of death and disability worldwide and is considered to be a burden on the society’s health-care system. Its incidence is estimated to rise continuously during the next few decades. It has also been estimated that the number of people affected throughout the world is expected to double by 2025 and to triple by 2050¹ (Sasayama, 2008). The disease alone is responsible for a death rate of 16.7 million annually in both developing and developed countries.² (Jafar et al., 2005).

Atherosclerosis is an immune-inflammatory disease of arteries that causes their walls to become thickened. It is by far the most common cause of underlying ischemic heart disease. The arterial wall thickens due to accumulation of leukocytes and

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proliferation of smooth muscles in intima that leads to formation of a plaque. The haemostatic function of blood platelets has long been recognized that results in attachment of platelets to areas of endothelial injury. The process of atherosclerosis is thought to result from the interaction of platelets and endothelial cells at atherosclerotic-susceptible sites.³ (Kaplan et al., 2011).

Platelets are known to participate in all stages of haemostasis in vivo. This haemostatic plug is formed by the interaction of platelets with sub endothelial matrix proteins including VWF, collagen, fibronectin and laminin. The immobilized VWF on sub endothelial matrix provides binding sites for the attachment of platelets via their GPIbα receptors. This interaction is however unstable and requires firm binding which is mediated by platelets and other matrix molecules.³ (Kaplan et al., 2011).

Light transmission aggregometry is known as the historical Gold standard platelet function test in which platelet-platelet aggregation is stimulated by addition of various agonists in platelet rich plasma⁴ (Gurbel et al., 2007). LTA is also the most commonly used test to measure the efficacy of antiplatelet drugs such as clopidogrel and aspirin⁵ (Michelson, 2004). Apart from the advantages LTA offers, it also has certain disadvantages like requirement of large sample size, time consuming, technically challenging and expensive. Clopidogrel resistance measured by LTA is defined as the change in baseline platelet aggregation to post-treatment aggregation in response to 5 and 20 µmol/L ADP⁶ (Lev et al., 2006). Impedance aggregometry is also based on the same principle as LTA, the only difference being the use of whole blood instead of platelet rich plasma.

Measurement of ADP induced receptor expression is done by flow cytometry with the help of monoclonal antibodies. Receptor activity assessed by VASP phosphorylation with monoclonal antibodies also assessed by flow-cytometry, has also been used for detection of clopidogrel response.⁷ (Barragan et al., 2003).

In a study carried out in 2002 the effect of a loading clopidogrel dose of 600 mg followed by 75 mg daily in patients with stable angina pectoris was studied and a significant variation in clopidogrel induced platelet inhibition was observed⁸ (Jaremő et al., 2002). A year later Gurbel et al.⁴ assessed the variation in clopidogrel efficacy by platelet aggregation studies where clopidogrel resistance was defined as less than 10 % with 5 µmol ADP as the agonist in comparison with the baseline aggregation.

Further work was done on the subject in later years. The frequency of clopidogrel non-responsive individuals among 105 patients with coronary artery disease was assessed in 2003. Patients received loading dose of 600 mg clopidogrel followed by maintenance dose of 75 mg/day. Clopidogrel resistance was estimated by aggregation studies using 5 and 20 µmol ADP as the agonist. It was observed that with 5 µmol 5% and with 20 µmol 10% individuals were found to be clopidogrel resistant. On further follow-up it was found that clopidogrel resistance was associated with stent thrombosis and hence had clinical relevance⁹ (Muller et al., 2003).

The work of Serebruany et al was also consistent with Jaremo and Gurbel showing that patients taking clopidogrel were divided mainly into two groups; responders and non-responders. His work ascertained that further trials were required to demonstrate the clinical implication of non-responsiveness.

The frequency of stent thrombosis in CAD patients is 1-3% despite treatment (Tollesson et al., 2003). It is therefore essential to establish the relationship between clopidogrel resistance and adverse clinical outcomes.¹⁰

In a prospective study Matetzky et al studied the effect of clopidogrel resistance on the clinical course of the disease. The study showed significant results with 40% patients having lowest platelet inhibition suffering from adverse clinical outcomes.¹¹ In a retrospective analysis of 1684 stented patients it was found that 16 patients who had stent thrombosis were found to have high platelet activity despite treatment compared to 30 normal controls⁷ (Barragan et al., 2003).
The objective of study was

- To find out the frequency of clopidogrel resistance among ischemic heart disease patients.
- To determine the relationship of comorbidities and concomitant drug usage on clopidogrel response.

**METHODOLOGY**

Study design: A cross-sectional study was conducted at Department(s) of Hematology and Biochemistry.

Duration of study: This study was conducted during a time period of 6 months from September 2014 to March 2015.

Sample collection: After approval from ethical committee subjects those fulfilling the inclusion criteria of diagnosed patients of IHD who are more than 21 year of age, taking clopidogrel 75mg for more than 07 days were recruited from Punjab Institute of Cardiology, Lahore using simple random sampling technique during the time period of September, 2014 to September, 2015. A sample size of 220 was calculated keeping the confidence level equal to 95% and the margin of error equal to 6% with anticipated proportion of 29%. Patients having history of bleeding disorders or on unfractionated or low molecular weight heparin therapy 24 hours or taking drugs like ketoconazole, rifampicin and erythromycin were excluded from the study.

Hemoglobin and hematocrit: Five ml of blood was obtained from each patient using aseptic technique. It was divided into two vacutainers. Two ml of blood was transferred to sodium citrate vacutainer for platelet aggregation studies. Three ml was transferred to EDTA vacutainer for measurement of Hemoglobin and Hematocrit. Haemoglobin (Hb) level was determined by using automated Complete Blood Count (CBC) analyzer Sysmex XT-1800i. Any patient with Hb <8 g/dl and >18 g/dl was excluded. Haematocrit (Hct.) was measured by using automated CBC an analyzer. A value of 40-52% for males and 36-48% for females was kept for all patients. Sample was excluded if Hct was not in normal range. Platelet count was also measured by using automated CBC analyzer. Samples having platelet count less than 150 and more than 450 × 10^9/L were excluded.

Platelet aggregation studies: The Innovance® PFA-200 system was used for the detection of inhibition of aggregation in patients undergoing clopidogrel therapy. The results of INNOVANCE® PFA P2Y were reported by the PFA Systems as Closure Time (CT) in seconds (s). INNOVANCE® PFA P2Y closure times more than 106 seconds were considered normal and were classified as responders while those with less than 106 seconds were viewed as non-responders or resistant.

**RESULTS**

The study comprised of 237 diagnosed patients of ischemic heart disease who were taking clopidogrel for more than one week. 51.5% had ischemic heart disease without PCI (percutaneous coronary intervention) or CABG (coronary artery bypass graft). 36.2% had IHD with angioplasty and 12.2% were treated with CABG. 77.6% were male and 22.4% were females. Mean age of the patients was 55.4 ± 9.6 years with a mean duration of illness of 27.2 ± 17.6 months. BMI of ischemic heart disease patients was just above normal with a mean value of 25.2 ± 3.9 kg/m². 29.1% of the patients were smokers.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Total no. of patients (N=237)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>55.4 ± 9.6</td>
</tr>
<tr>
<td>Gender M/F</td>
<td>184/53</td>
</tr>
<tr>
<td>Duration of illness (months)</td>
<td>27.2 ± 17.6</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.2 ± 3.9</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>29.1%</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>34.2%</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>59.1%</td>
</tr>
<tr>
<td>Dyslipidemia (%)</td>
<td>45.6%</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>14.1 ± 1.6</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>41.3 ± 4.3</td>
</tr>
<tr>
<td>Platelet count (x10^9/µl)</td>
<td>302.5 ± 68.5</td>
</tr>
<tr>
<td>Clopidogrel non-responders</td>
<td>14.3%</td>
</tr>
</tbody>
</table>

BMI=Body mass index, M=Male, F=Female
The body-mass index is the weight in kilograms divided by the square of the height in meters.
and the percentage of diabetics, hypertensive and dyslipidemia patients was 34.2%, 54.1% and 45.6% respectively. Patient’s mean hemoglobin (14.1 ± 1.6), hematocrit (41.3 ± 4.3) and platelet count (302.5 ± 68.5) were all in normal range as shown in Table 1.

Aggregation studies were done on INNOVANCE® PFA-200 system on the same day, within 5 hours of sample collection. Patients with Closure Time (CT) less than 106 sec were put in the category of clopidogrel resistant, and those with Closure time (CT) equal to or above 106 sec were classified as clopidogrel responders. A total of 240 patient's samples were run on PFA-200 system, however 3 patients gave invalid aggregation results so they were excluded. According to the PFA-200 results a total of 34 (14.3%) patients were found to be non-responders, whereas 203 (85.7%) were labeled as responders (figure 1).

It was observed that out of the 34 non-responders 20 were male and 14 were females. The gender wise distribution of clopidogrel resistance showed that 20 (10.9%) out of a total of 184 males and 14 (26.5%) out of a total of 53 females were clopidogrel non-responsive. This finding was highly significant with a p value of 0.004. The comparison of clopidogrel responsive and non-responsive groups with smoking and diabetes came out to be statistically significant. It was found that a higher no. of smokers (92.7%) were clopidogrel responsive as compared to non-smokers (82.7%). A higher percentage of diabetics (22.2%) and hypertensives (16.4%) were clopidogrel non-responsive as compared to non-diabetics (10.2%) and non-hypertensives (11.3%). However the correlation of clopidogrel response with hypertension was not statistically significant as shown.

No significant association of clopidogrel response was observed with aspirin (0mg, 75mg, 150mg, and 300mg) dosage. The correlation of Statin dosage with clopidogrel response did not show an increase in resistance with increasing doses of statins. A higher percentage of non-responders (29%) were present in the group who were not taking statins as compared to group who were taking 10mg (5.08%), 20mg (14.6%) and 40mg (25%) statins. These findings were significant with a p value of <0.05. A higher percentage of non-responders (19.5%) and (25%) were found in the group of patients who were taking Ca channel blockers and proton pump inhibitors respectively as compared to non-responders who were not taking those drugs. However, these finding were not statistically significant (p >0.05).

In case of beta blockers a significantly higher number i.e. 20 (58.8%) out of 34 non-responders were found in the group of patients who were taking the drug.

**DISCUSSION**

Clopidogrel has become a mainstay of treatment by preventing platelet aggregation and activation in patients with ischemic heart disease. Current data shows that some patients do not achieve optimum
The percentage of non-responsive patients varies from 5-44% in various studies as shown in Table 4.1. The present study demonstrated that 14.3% ischemic heart disease patients were clopidogrel resistant. Our findings were closest to Rizvi et al. (2013) (17%) who adopted Cone and Plate(let)® analyzer for measuring clopidogrel resistance. The approximation in results could be explained by the fact that similar

**Table 2:** Correlation of Clopidogrel Response with Patient's Risk factors and Drugs

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Total (n=203)</th>
<th>Clopidogrel responders (n=179)</th>
<th>Clopidogrel non-responders (n=24)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male 184</td>
<td>164 (89.1%)</td>
<td>20 (10.9%)</td>
<td>0.004</td>
</tr>
<tr>
<td></td>
<td>Female 53</td>
<td>39 (73.5%)</td>
<td>14 (26.4%)</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>Yes 69</td>
<td>64 (92.7%)</td>
<td>5 (7.9%)</td>
<td>0.046</td>
</tr>
<tr>
<td></td>
<td>No 168</td>
<td>139 (82.7%)</td>
<td>29 (17.2%)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>Yes 81</td>
<td>63 (77.7%)</td>
<td>18 (22.2%)</td>
<td>0.013</td>
</tr>
<tr>
<td></td>
<td>No 156</td>
<td>140 (89.7%)</td>
<td>16 (10.2%)</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>Yes 140</td>
<td>117 (83.5%)</td>
<td>23 (16.4%)</td>
<td>0.272</td>
</tr>
<tr>
<td></td>
<td>No 97</td>
<td>86 (88.6%)</td>
<td>11 (11.3%)</td>
<td></td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>Yes 108</td>
<td>92 (85.1%)</td>
<td>16 (14.8%)</td>
<td>0.851</td>
</tr>
<tr>
<td></td>
<td>No 129</td>
<td>111 (86%)</td>
<td>18 (13.9%)</td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>0mg 30</td>
<td>23 (76.6%)</td>
<td>7 (23.3%)</td>
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</tr>
<tr>
<td></td>
<td>75mg 62</td>
<td>55 (88.7%)</td>
<td>7 (11.2%)</td>
<td></td>
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<tr>
<td></td>
<td>150mg 143</td>
<td>124 (86.7%)</td>
<td>19 (13.2%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>300mg 2</td>
<td>1 (50%)</td>
<td>1 (50%)</td>
<td></td>
</tr>
<tr>
<td>Statins</td>
<td>0mg 31</td>
<td>22 (70.9%)</td>
<td>9 (29%)</td>
<td>0.019</td>
</tr>
<tr>
<td></td>
<td>10mg 59</td>
<td>56 (94.9%)</td>
<td>3 (5.08%)</td>
<td></td>
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<td></td>
<td>20mg 143</td>
<td>122 (85.3%)</td>
<td>21 (14.6%)</td>
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</tr>
<tr>
<td></td>
<td>40mg 4</td>
<td>3 (75%)</td>
<td>1 (25%)</td>
<td></td>
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<tr>
<td>Ca channel blocker</td>
<td>Yes 46</td>
<td>37 (80.4%)</td>
<td>9 (19.5%)</td>
<td>0.261</td>
</tr>
<tr>
<td></td>
<td>No 191</td>
<td>166 (86.9%)</td>
<td>25 (13%)</td>
<td></td>
</tr>
<tr>
<td>Beta Blocker</td>
<td>Yes 180</td>
<td>160 (88.8%)</td>
<td>20 (11.1%)</td>
<td>0.012</td>
</tr>
<tr>
<td></td>
<td>No 57</td>
<td>43 (75.4%)</td>
<td>14 (24.5%)</td>
<td></td>
</tr>
<tr>
<td>Proton pump inhibitor</td>
<td>Yes 20</td>
<td>15 (75%)</td>
<td>5 (25%)</td>
<td>0.155</td>
</tr>
<tr>
<td></td>
<td>No 217</td>
<td>188 (86.6%)</td>
<td>29 (13.3%)</td>
<td></td>
</tr>
</tbody>
</table>

antiplatelet effect with conventional doses of clopidogrel (Nguyen et al. 2005). The variation in clopidogrel response among IHD patients is multifactorial. Among the more common ones are factors such as non-compliance, drug interactions or genetic defects. For assessment of patients that are poor responders to the pharmacological effect of clopidogrel Platelet Function Analyzer-200 was utilized in our study. Several other analyzers are also available for clinical use. However, it should be noted that the sensitivity of different laboratory tests used to identify patients that may have reduced antiplatelet effect achieved by clopidogrel differs according to the test employed. A brief review of some analyzers along with their principle and the incidence of resistance are given in Table 3.

The percentage of non-responsive patients varies
CLOPIDOGREL RESISTANCE IN ISCHEMIC HEART DISEASE PATIENTS

response is that estrogen in women may elevate plasma levels of fibrinogen, protein S, and plasminogen activator inhibitor (Berger et al. 2009). Our results indicate significant but inverse relation with smoking i.e. smokers had a lower percentage of non-responders (p<0.05). These results are in accordance with previous studies that suggest greater inhibition of platelet aggregation by clopidogrel in subjects who smoke ≥ 10 cigarettes/day. Similar observations have been made in another study which, shows that cigarette smoking positively modifies clopidogrel response in STEMI patients (Jeong et al., 2010). These results can be explained on the basis of the background knowledge that cigarette smoking induces CYP1A2, which converts clopidogrel into its active metabolite (Desai et al., 2009).

In the current study a higher percentage (22.2%) of diabetic patients were found to have poor clopidogrel response. This finding was in agreement with prior studies which show that type-2 diabetes mellitus promotes thrombosis and leads to clopidogrel resistance. It has been observed that platelet function profiles in Type 2 diabetic had a higher number of non-responders as compared to controls (Angiolillo et al., 2005). Type 2 diabetes (T2D) is associated with several defects in haemostasis that predispose to thrombosis. Moreover, reduction in antiplatelet response to clopidogrel has been related to Type 2 diabetes (Samoš et al., 2016).

Although the relation of clopidogrel response with hypertension came out to be statistically insignificant, however; it shows that a higher percentage of hypertensives are resistant. Our findings are also in concordance with those of Akturk et al.

The effect of concomitant drug usage was also observed in this study. Statins are the most commonly prescribed anti-hyperlipidemic drugs for management of ischemic heart disease. CYP3A4 is involved in the metabolism of both Clopidogrel and Atorvastatin and simultaneous use of these drugs leads to reduction in antiplatelet effects of clopidogrel (Lau et al., 2003). The results in this research however did not show effect of statin intake on clopidogrel responsiveness. A higher percentage of non-responders were found amongst the individuals who were not taking statins than those who were on 10-40mg atorvastatin individually. Our findings are supported by other researchers (Saw et al., 2003) and (Mukherjee et al., 2005). However, in a larger long-term follow-up study no adverse effect on clinical outcome was observed with coadministration of clopidogrel and statins, despite metabolism of drugs with of CYP3A4 enzyme (Saw et al, 2007).

Calcium channel blockers (CCB) and Proton pump inhibitors (PPI) are two important and commonly prescribed classes of drugs for treatment of ischemic heart disease. Although our results show a higher percentage of non-responders among patients who were taking clopidogrel with CCB and PPI; however, no significant association of CCB and PPI with clopidogrel resistance was found (p value 0.261). This could be due to the limited number of patients who were on PPI (n=46) and CCB (n=20).

Beta blockers are also prescribed to Ischemic heart disease patients. The results of this study showed that a significantly higher percentage of non-responders were present among patients who were on beta blockers. However, based on the previous knowledge which suggests that platelets possess beta adrenergic receptors, which if blocked by beta blockers lead to reduced platelet aggregation causing increased responsiveness (Bonten et al., 2014). Our results however are in concordance with Knight et. al. who studied the effect of three major classes of antiangiinal drugs namely nitrates, Ca antagonists and beta blockers on platelet function and found that of the three; beta blockers enhanced aggregation.

CONCLUSION

The results of this study show that among 237 ischemic heart disease patients, 34 patients (14.3%) were non-responders to clopidogrel. We concluded that resistance clopidogrel therapy is seen in significant number of patients and female patients are at high risk of developing the resistance to clopidogrel therapy. These patients can be identified by perform-
ming platelet aggregation studies. Furthermore the effect of smoking on clopidogrel response was favorable and it revealed that a higher percentage of smokers were clopidogrel responsive. Statins intake in our study did not affect clopidogrel response. However, clopidogrel response was adversely affected by beta blocker use i.e. a higher percentage of non-responders were present among ischemic heart disease patients who were on beta blockers.

**Limitations of the study** Sample size was a limitation in the study due to limited financial resources.

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**Conflicts of interest** There was no conflict of interests in this study.

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**Contributions of the authors** Nabila Akram performed the research work. Nabila Akram did the statistical analysis. Nabila Akram wrote the paper.

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CLOPIDOGREL RESISTANCE IN ISCHEMIC HEART DISEASE PATIENTS


One of the growing, major public health issues is chronic kidney disease. In a small number of patients, impairment in functions of kidneys occur rapidly and few patients reach the end stage renal disease. It is of prime significance in terms of predicting the long-term prognosis of such patients. Some of the factors that can predict it are arterial hypertension, proteinuria and functions of kidneys at baseline. Interstitial fibrosis also helps in provision of valuable data that can predict prognosis of disease.

Doppler ultrasonography (US) yields a prime and useful data regarding the morphological features of the kidneys and its vasculature. The pattern of intra-parenchymal flow in the renal arteries is affected by factors, that are present both structurally and functionally, and the flow wave that is formed by the vascular resistance and its compliance. Because of this, pathologies like interstitial fibrosis strongly
CUT-OFF PARAMETERS OF RENAL DOPPLER ULTRASONOGRAPHY TO DETERMINE END STAGE RENAL DISEASE

Effects the indices that are obtained from examination done with the help of Doppler. Studies conducted recently revealed that doppler parameters (specifically the resistive index) and damage to the tubulointerstitial area as well as to the vasculature are closely related to each other. In current study, parameters of arterial flow, both intrarenally and extrarenally, were evaluated by Doppler in patients who had renal disease at an advanced stage and further determined the relation of renal disease stage and parameters of Doppler.

METHODOLOGY

After taking approval from the Ethical Committee of Avicenna Medical College, Lahore, this prospective study was conducted from January 2017 to July 2020. Written informed consents were taken from all the patients prior to study. A total of 50 patients, of both genders, were enrolled in the study. The criteria of inclusion was patients with renal disease at an advanced stage who had proteins in the urine and high creatinine levels in the serum persistently. Proteinuria was defined as levels of proteins in the urine of >0.3gm/gm creatinine, whereas, raised serum creatinine level was labeled if it was >1.08 mg/dl in males and >0.84 mg/dl in females. The patients that were excluded from the study were individuals with renal artery stenosis, acute renal failure and hepatorenal syndrome.

According to the glomerular filtration rates (GFR), patients were divided into 5 stages. The categories were: Stage 1, 2, 3, 4 and 5 with GFR> 90, 61 – 89, 31 - 60, 16 - 30 and <15 ml/min/1.73m² respectively. GFR calculation was done according to the Modification of Diet in Renal Disease (MDRD) formula.

Evaluation of all participants was done by B-Mode and Doppler US in the lateral decubitus position, which was followed by a period of 6 hours of fasting. Single, experienced radiologist performed the US and Doppler US examinations by using a 3.5 MHz abdominal convex transducer of a Mindray DC-7 machine. Firstly, the kidneys were evaluated morphologically. Longest axes was measured along with measurement the mean thickness of parenchyma of kidneys bilaterally and findings were noted down. Assessment was made of increased echogenicity of parenchyma of kidneys and were classified as grade 1 (light), 2 (moderate) and 3 (advanced) in a sequential order.

Samples of doppler flow was gathered from the segments of the main renal arteries of both sides, at the proximal or median end, utilizing the angle of Doppler of 30˚ - 60˚. From the renal arteries, measurements were made of Maximum systolic (RA PSV) and end-diastolic (RA EDV) flow velocities. RA PSV-RA EDV/RA PSV formula was used to assess the value of resistivity index (RI) from the renal arteries. RA PSV-RA EDV/Mean Renal Arterial Flow Velocity formula was used to determine the pulsatility index (PI) from the renal arteries. At least twice all measurements were carried out and mean of these measurements was taken as the final value. Similar procedure was carried out to make measurements at interlobular arteries that were located at the top, middle and bottom portions of the kidneys. The mean values were taken again as final values. The control group consisted of 15 patients which were of same age and with normal levels of creatinine in the serum and no proteinuria. From renal arteries of both sides, the values of PI were obtained and were added to record their sum. Similarly, values of PI obtained from the interlobular arteries of both sides were added up too and sum was calculated. This was followed by comparison of these sums with those who were healthy (control).

For analyzing data, comparison of two groups i.e. the patient (Group A) and the control group (Group B) was done using T-test, whereas, for evaluating the results that were gathered from different stages of renal disease, the Variance Analysis (ANOVA) test was used. A p-value of ≤0.05 was considered as statistically significant. Receiver Operating Characteristics (ROC) curve analysis method was used to assess the cut off value of the RI and PI values.

RESULTS

A total of 50 patients (Group A) fulfilling the criteria of inclusion were included in the study. The control (Group B) comprised of 15 healthy individuals. With respect to gender, there were 29 (58%) males and 23 (42%) females in group A, whereas in group B, males were 8 (53%) and females were 7 (47%) in total. The difference in the
frequency of gender between the two groups was not significant statistically. Participants’ mean age (in years) in the study vs control group was 60.7± 11.2 and 53.5± 13.7 respectively and this difference was of no significance statistically. Doppler measurements were not assessed in 5 individuals on one side due to the presence of gaseous artefacts and difficulty in holding breath by the patient. Bilaterally the measurements could not be assessed in one patient.

**Figure 1:** Doppler Sonograms and Spectral Waveforms of A 56-year-old Woman with Chronic Kidney Disease Show Elevated Ri and Pi Values.

In the patient vs healthy group, the mean RI from the right main renal artery (RMA) was 0.71 ± 0.06 vs 0.63 ± 0.03 respectively, whereas, the mean PI was 1.45 ± 0.35 and 1.04 ± 0.23 respectively. The mean RI from the left main renal artery (LMA) in the study vs control group was 0.72 ± 0.076 and 0.64 ± 0.04 respectively and mean PI values were 1.62 ± 0.43 and 0.98 ± 0.13, respectively.

Differences found between the value of RI and PI were significant statistically as recorded in the main renal arteries (MRA) of both sides. The mean RI in the interlobular arteries (ILA) in the study vs control group was 0.69± 0.075, vs 0.63± 0.035 respectively and the mean PI recorded was 1.27 ± 0.32 vs 1.01 ± 0.15 respectively. The difference in the RI values recorded from the ILA in both groups was not significant statistically, whereas, difference was found to be of significance statistically in terms of mean values of PI values between the two groups. In study vs control group, mean RI values gathered from the left ILA were 0.68 ± 0.05 vs 0.63 ± 0.02 respectively and the PI values were found as 1.27 ± 0.24 and 1.05 ± 0.11, respectively. Difference in these values between two groups was significant statistically.

In the study vs control group, the mean diameter along the long axis of the right kidney in was 94.8 ± 15.8 mm vs 108.4 ± 10.6 mm respectively and the mean thickness of the parenchyma for the same kidney was measured as 10.02 ± 2.64 mm and 13.4 ± 1.37 mm respectively. In comparison, the mean diameter along the long axis of the left kidney in the study vs control group was 97.83 ± 14.2 mm and 111.5 ± 8.08 and the mean thickness of parenchyma of left kidney was found to be 11.3 ± 3.02 mm vs 12.61 ± 17.76 mm respectively. The difference was significant statistically in terms of mean kidneys' dimensions. The difference was significant statistically between two groups in terms of thickness of parenchyma of right kidney but it was no significant with regards to left kidney.

**Figure 2:** Doppler Sonograms and Spectral Waveforms of a 69-year-old Man with Chronic Kidney Disease. Intrarenal Artery Shows Elevated Ri And Pi Values.

Additionally, an important finding was that in terms of stages of renal disease, there was difference between the two groups in all parameters that were studied and this difference was found to be significant statistically. The results obtained by summing up all the PI values that were taken from renal arteries or interlobar arteries of both sides between the two groups were compared too. The resultant PI values was labeled after adding up all the PI values together from the main renal arteries and was similarly done for interlobular arteries of both sides too. The value of resultant PI was compared with the control group findings and a cut-off value of 2.15 was obtained, which had 90.2% and 86.7% sensitivity and specificity respectively.
DISCUSSION
A factor that is of risk for renal disease at an advanced stage and cardiovascular diseases is chronic renal disease. Establishing diagnosed earlier and provision of prompt medical management is necessary for preventing these diseases. Evaluation of renal functions is of prime importance and it can help in predicting outcomes over long term. Generally, interstitial fibrosis and capillaries as well as tubular loss occurs due to renal disease that is progressive and decline of GFR and it is closely associated with functions of kidneys and prognosis over long term. Previous studies have reported a relationship between RI and conditions that occur pathologically such as glomerulosclerosis and tubulointerstitial as well as vascular damage. Numerous studies have investigated relation between parameters on doppler of kidneys and conditions such as functions of kidneys and histological damage. Izumi et al. reported that by means of the renal resistivity index, differential diagnosis can be made of acute tubular necrosis and prerenal azotemia. At the end of a study, Sugiura and Wada reported that by determining the atrophic index and RI, evaluation of injury to the interstitium can be done. Hanamura et al. revealed that for establishing diagnosis of chronic tubulointerstitial nephritis, the RI value can play an important part.

In the current study as well, differences were present between the two groups with chronic renal disease of stage II-IV, in terms of values of RI which were determined from the MRA and ILA and the difference was significant statistically. Despite that the differences were statistically significant in terms of values of PI that were measured from the intrarenal arteries of both groups, there was no statistically significant differences in values of PI that were gathered from the MRA.

These results denote the value and significance of the RI value that can be used as an indicator of tubulointerstitial damage in patients with CRD in whom the GFR is reduced. In current study, RI values in various stages of renal disease was studied and comparison was made, which was not similar to the other studies previously conducted. As a result of current study, it was revealed that RI values were increased linearly in patients who had advanced renal pathology. These results have indicated clearly the significance of evaluating renal parameters on doppler as well as RI values in individuals who have chronic renal disease that is proven both on clinical basis and histopathological evaluation, in determining the stage of disease and its prognosis. An individual's height and weight effects the dimensions of kidneys and thickness of renal parenchyma. On the other hand, dimensions of kidneys are increased in certain diseases such as glomerulonephritis that is rapidly progressive and amyloid nephropathy. For establishing diagnosis of chronic kidney disease and its follow up, parameters such as dimensions of kidneys and thickness of parenchyma do not seem to be of practical importance. In our study as well, differences were found between the control and patients' groups that were significant statistically and also in terms of dimensions of kidneys and thicknesses of parenchyma related to the stage of kidney pathology, but emphasis should be laid still on the fact that these parameters are not helpful in determining CRD and its stage.

Comparative evaluation of Renal parameters on doppler and stages of parenchymal disease of kidneys were done in this study. However, staging on evaluation done histopathologically could not be done that affects the doppler parameters directly because of the invasive nature of biopsy and procedural cost. This was the limiting factor of the current study.

CONCLUSION
In patients with renal parenchymal disease at an advanced stage, use of doppler ultrasound must be carried out routinely. The values of RI obtained from the MRA and ILA were related to each other and the relation was significant statistically and with an increase in the stage of disease, the relation became strong. The values of RI and PI obtained from these arteries if show an increment must raise the suspicion of advanced renal disease and interstitial fibrosis. differentiation of groups with and without damage to parenchyma of kidneys can be done by making comparison of the total mean values of PI that is gathered from MRA and ILA of both sides. This differentiation can be performed over a cut-off
value of 2.15, with a sensitivity and specificity of 90.2% and 86.7% respectively.

Conflicts of Interest
None

Funding Sources
None

REFERENCES


Elbow joint comprised of complicated anatomy, providing a mechanical connection between hand and wrist on one side and shoulder on the other contributing to significant function. Nearly 7% of the adults accounted for elbow fractures with the prevalence of distal humerus fracture accounted for 30%. Occurrence of distal humerus fractures showed bimodal distribution in relation to age, with pattern of high energy among adults and teenagers, and osteoporosis with less energy blow in the elderly.

For most of the displaced fractures, open reduction with internal fixation is most appropriate method with aim to restore the fractured segment anatomically providing appropriate stability and is reported to have better functional results. Surgical management of these fractures is preferable due to complex anatomy and moreover, braces or casts alone failed to restrict segment and provide unsatisfactory stability. However, post-operative casts requires longer period of immobility and rest which eventually lead to contractures and stiffness around the elbow region further limiting the activity.
EFFECTS OF SUPERVISED VERSUS HOME-BASED REHABILITATION ON FUNCTIONAL OUTCOME

However, most of daily activities required 30 to 130 degrees of elbow flexion and almost 100 degrees of rotation with both supination and pronation contribute equally. Shoulder abduction compensates for any loss of pronation, but no secondary mechanism exists for compensation of any supination loss.

The focus for early postoperative motion in stable fixation is aimed at good restoration of joint anatomy in relation to movements, strength and joint play. But this is difficult to achieve which can lead to complications and unsatisfactory results among 15% of individuals. So, the present study focused on the functional outcomes after the plate fixation of distal humerus fractures, aiming at early mobilization, adhesions prevention and joint play restoration and contrast the supervised post-operative rehabilitation regimen with the home-based exercise program in the form of visually assisted exercises diagrams to evaluate and distinguish satisfactory results and movement dysfunctions.

METHODOLOGY

This study recruited 60 participants who sustain distal humerus fractures and were operated surgically at Department of Orthopedics, Sahiwal Medical College, Pakistan between 2017 and 2020. Any patient who sustained isolated, closed, or open, displaced intra-condylar or intra-articular fracture of distal humerus was included in the study. Patients with involvement of proximal radius or ulna, skeletally immature, an ipsilateral or contralateral upper-extremity injury and preexisting musculoskeletal condition were excluded.

Patient were classified according to American Orthopedics (AO) classification into C1, C2 and C3. All the patients were operated using medial or lateral plating with appropriate surgical approach with regards to segment involved and feasibility of anatomical reconstruction like olecranon osteotomy for intra-articular fracture.

All the patients were monitored for signs of infection and appropriate care was initiated with antibiotics and NSAIDs. After the careful examination and X-ray, cast was removed partially at 2nd week and patient was allowed to do guided activities. Range of motion (ROM) exercises of hand and shoulder was started earlier at 1st day post-operatively.

An external assistant randomly allocated the patients to either the home-based rehabilitation or supervised rehabilitation group using a computer-generated random sequence (randomized.com). Patients were divided into two groups:

After the partial removal of cast at post-operative 2nd week, patient was taught about self-mobilization of elbow using any belt, self-distraction technique with cotton roll while monitoring the pain, diagrams of exercises showing active and passive movements and gentle stretching with protocols of duration, intensity, and frequency.

The treatment group received gentle elbow mobilization and distraction, active and passive ROM and stretching.

Elbow distraction: Patient was comfortable in lying supine. The Clinician apply a traction belt around the proximal part of forearm with elbow flexed to 90 degrees. With the scooping of both hands of clinician along with grasping of belt, a gentle traction was applied and sustained for 20 seconds. Shoulders of clinicians are used to provide stability to distal forearm.

Elbow Mobilization with Movement: With the patient lying supine on couch, a mobilization belt was placed around the proximal part of forearm and surrounded the pelvis of clinician at the same level. One hand of therapist stabilizes the distal part of humerus while the other provide stability to distal forearm. A gliding force was applied in lateral direction and patient was instructed to actively flex and extend his/her elbows.

A blind assessor assessed the patient at baseline usually after the removal of cast at 2nd week post-operatively to check stability and take baseline measurements, at 10th week post-operative after regular exercises and physiotherapy, and at 6 months post-operatively. Signed informed consent was taken and protocol of the study was approved form
Ethical Review Committee of Sahiwal Medical College & Allied Hospital, Sahiwal.

Visual analogue scale (VAS) was used to quantify pain subjectively. Mayo Elbow performance scale (MEPS), The Disabilities of Shoulder Arm and Hand (DASH) quantify the functional outcomes. Gonio-metry examined the ROM of elbow flexion and elbow extension.

The data was analyzed using SPSS v 27. The normality of the data was assessed using Shapiro-Wilks test of normality and uniformity, based on which parametric or non-parametric test were applied to determine across the group difference in two groups. Independent sample T test was applied to determine any significant difference across the two groups. A difference with p value less than 0.05 was considered as significant.

### Table 1: Demographics and Patients Related Outcomes

<table>
<thead>
<tr>
<th>Variables</th>
<th>Supervised Rehabilitation</th>
<th>Home Based Rehabilitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Age (Years)</td>
<td>34 (SD 8)</td>
<td>38 (SD 8)</td>
</tr>
<tr>
<td>Gender</td>
<td>Male 22, Female 8</td>
<td>Male 21, Female 9</td>
</tr>
<tr>
<td>AO Fracture Type</td>
<td>C1 9, C2 16, C3 5</td>
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<tr>
<td>Side of Injury</td>
<td>Right 19, Left 11</td>
<td></td>
</tr>
<tr>
<td>Average Bone Healing Time (weeks)</td>
<td>9.66 (SD 1.37)</td>
<td>10.1 (SD 1.65)</td>
</tr>
<tr>
<td>Complications</td>
<td>Wound 1, Mal or Non-Union 1</td>
<td></td>
</tr>
</tbody>
</table>

**RESULTS**

The total 60 patient, 30 in each group who sustained the distal humerus fractures were included in the study with the average of 36 (SD 8, Range 55-20) years of age and majority were males (72%). Patients were classified according to American Orthopedic (AO) classification system into C1 (n=9), C2 (n=16), and C3 (n=5), and the average healing time after surgery evaluated by radiographs and clinical assessment were about 9-12 weeks. There were only three exceptions about healing with two patients had wound complication and one patient had recurrent trauma causing implant failure which needed revision surgery (Table 1).

**Figure 2: Consort Diagram**

Patients who were included in the supervised rehabilitation groups showed overall greater MEPS score, with 27 patients scored as excellent and 3 cases were catagorized as good, with no fair or poor reporting. In the home based rehabilitation group, participants showed comparitively less improvement with only 10 patients with the excellent score (figure 3).

The MEPS score was measured to classify the elbow function. An independent sample T-test was
conducted to compare the average MEPS among both groups. There was significant difference in MEPS at 6th month follow up for supervised rehabilitation (M=96.50, SD= 4.93) and home-based rehabilitation (M=83.33, SD= 10.23) with p value of 0.00 (two-tailed). Significant difference between two groups also observed after 8 weeks of rehabilitation (post-operative 10th week) with p = 0.00. However, patient in home-based rehabilitation obtained an excellent/ good MEPS among 66% of the cases although this is less than the supervised rehabilitation group. Similar results were obtained in DASH score and elbow arc of motion as the independent sample t-test showed significant difference among both groups. Mean difference of DASH= 15.78 at 10th week, DASH=13.60, p=0.00, elbow arc of motion (difference in elbow flexion and extension) was 17.23 at 10th week, 15.43 at 6 months, p= 0.00 was calculated (Table 2).

**DISCUSSION**

This study compared the functional outcome of surgically operated distal humerus fractures in contrast with home-based exercise program done by patient after specified instructions provided in the leaflet, and supervised rehabilitation provided by the physiotherapist. Exercise program was equally designed for both groups in term of technique, intensity, frequency, and type of exercises. After analyzing 60 cases of distal humerus fractures, supervised rehabilitation would confer superior functional outcomes in contrast with home-based rehabilitation. However, both groups showed significant improvement in terms of functional outcomes with an excellent/good MEPS in majority of cases.

**Figure 3: Comparison of MEPS Among both Groups**

The study appends four different variables in terms of functional outcomes in both post-operative groups with the fracture of distal humerus. In recent

| Table 2: Functional Related Outcomes and their Significance |
|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
|                            | Supervised Rehabilitation   | Home-Based Rehabilitation   | Mean Difference             | 95% CI                      | P               |
| **VAS**                    |                            |                             |                             |                             |                 |
| Baseline                   | 5.80 ± 2.73                | 6.20 ± 2.99                 | -0.4                        | -1.88, 1.08                 | 0.13            |
| At 10th week               | 1.33 ± 2.05                | 3.20 ± 2.26                 | -1.86                       | -3.11, -0.62                | 0.04            |
| At 6 Months                | 0.66 ± 0.36                | 0.66 ± 0.36                 | 0                          | 1.88, 0.18                  | 1               |
| **Total MEPS**             |                            |                             |                             |                             |                 |
| Baseline                   | 40.46 ± 11.49              | 38.00 ± 13.49               | 2.46                        | -4.01, 8.94                 | 0.44            |
| At 10th week               | 87.50 ± 6.79               | 68.01 ± 17.25               | 19.50                       | 12.64, 26.35                | 0.00            |
| At 6th Month               | 96.50 ± 4.93               | 83.33 ± 10.23               | 12.16                       | 9.07, 17.25                 | 0.00            |
| **DASH Score**             |                            |                             |                             |                             |                 |
| Baseline                   | 90.26 ± 2.78               | 91.16 ± 2.32                | -0.9                        | -2.22, 0.42                 | 0.18            |
| At 10th week               | 28.56 ± 3.71               | 44.34 ± 8.00                | -15.78                      | -19.03, -12.53              | 0.00            |
| At 6th Month               | 17.65 ± 2.41               | 31.25 ± 7.05                | -16.80                      | -16.36, -10.83              | 0.00            |
| **Elbow Arc of Motion**    |                            |                             |                             |                             |                 |
| (flexion-extension)        |                            |                             |                             |                             |                 |
| Baseline                   | 10.01 ± 3.05               | 11.33 ± 3.55                | -1.33                       | -3.04, 0.37                 | 0.12            |
| At 10th week               | 124.36 ± 7.34              | 107.46 ± 10.70              | 17.23                       | 2.36, 12.47                 | 0.00            |
| At 6th Month               | 127.46 ± 6.04              | 112.03 ± 10.72              | 15.43                       | 10.93, 19.93                | 0.00            |

Test of normality was confirmed and parametric test (independent sample t-test) was applied to check the difference between two groups. P value less than 0.05 considered to give statistically significant results.

MEPS: Mayo Elbow Performance Score
DASH: The Disabilities of the Arm, Shoulder and Hand (DASH) Score
CI: Confidence Interval
P: Independent sample t-test (2-tailed significance value)
study, average MEPS was reported 96.50 (SD=4.93) in supervised rehabilitation group in contrast with 83.33 (SD 10.23). There was significant result in MEPS (p=0.00, CI, 95%) among both groups and this is because the supervised rehabilitation more efficiently breaks the adhesion, maintained joint play, and restrict the joint stiffness. However, patient with home-based program also provide satisfactory results and supported by the research. Vivek Trikha et al, studied the functional outcome of extra-articular distal humerus fracture and concluded that 34 patients (94.44%) had complete union within 3 months. Average MEPS was 90.8 + 9.9 with average follow up of 1 year without proper physiotherapy. So, our study not only decreases the average follow up period, but also reported increase MEPS score.

In our study, mean DASH score was comparatively more in both treatment as well as control group in comparison with previous studies. It was 17.65 (SD=5.4) in the supervised rehabilitation group and 31.25 (SD=7.05) in home-based group. Kanthan Theivendran et al, studied the functional outcome after internal fixation using precontoured anatomic plates. The mean DASH score was 46.1, grip strength was 56% of the uninjured side, and the mean MEPS score was 72.3 with average 24 months follow up. Available studies on recovery after fracture of the elbow joint focus on the cause and treatment of stiffness of the joint but the recovery of the range of motion of the elbow joint after a simple elbow fracture has not yet included in the literature. Our study shows similar results on VAS among both groups using postoperative rehabilitation regimen. In term of elbow arc of motion, supervised rehabilitation group was reported 127.46 (SD= 8.9) while 112.03 (SD=9.3) was in home-based group. Our study also focused on early mobilization after 2 weeks post-operatively which resulted in no implant failure or non-union reported.

In spite of leaving search terms broad and employing two highly utilized databases, the possibility of missing studies on distal humerus fractures still existed. On the other hand, weak obedience with follow-up and physical therapy appointments was fairly common, leading possibly to the limitation of motion range. The reasons for insufficient enforcement include other medical problems and overall health issues, lack of transportation access as well as physical therapy procedure difficulties.

Overall, our study supports no more variability in the findings obtained from the patients who undergone treatment and the others who did not in some variables. While treatment sessions are only better in improving the range of motion and functionality of the patients.

**CONCLUSION**

Supervised and home-based exercises were equally effective in reducing pain, disability and improving elbow function after plate fixation of distal humerus fracture. Supervised exercise was better in reducing disability and improving elbow function clinically as compared to home-based rehabilitation. The variability found in the reported outcome measures apparently makes it a problem for the orthopedic surgeons to decide about which current treatment modalities would be better for acute distal humerus fractures but in our study, there are no more complications for the surgeons to decide either the treatment modalities would be better or the home plan while keeping the ROM and functionality in mind which is a major point to be clear about in different major treatment centers. The results obtained in our ROM are consonant with those of other studies on the healing of distal humeral fractures.

**REFERENCES**


Urinary tract infections (UTIs) are one of the most common infections among hospital acquired infections as well as community acquired infections. Evolving Antibacterial resistance among Gram positive as well as Gram negative bacteria is lead to search for options to deal with these bugs. The objective of this study was to assess the activity of Fosfomycin against clinical isolates from patients presenting to a tertiary care hospital, Lahore.

Methodology: Urine specimens were cultured on CLED agar according to WHO protocol. A total of 124 isolates including Gram negative bacilli and Gram positive cocci were included in this study. Patients from out door as well as indoor were included in this study. Antibacterial susceptibility testing was performed by using standard modified Kirby Bauer disc diffusion method, following guideline of CLSI 2014. Fosfomycin 200-μg disc was used and zone diameter ≥16 mm was considered as susceptible.

Results: Out of 81 isolates of Escherichia coli 81%(66) were susceptible to Fosfomycin, out of 15 isolates of Enterococcus faecalis 80% (12) were susceptible to Fosfomycin, one isolate of Enterococcus faecium was susceptible (100%) to Fosfomycin, out of 13 isolates of Klebsiella pneumoniae 54% (7) were susceptible to Fosfomycin and one isolate of Klebsiella oxytoca was susceptible (100%) to Fosfomycin, out of 7 isolates of Staphylococcus saprophyticus 57% (4) were susceptible to Fosfomycin, 4 isolates of Citrobacter freundii were susceptible (100%) to Fosfomycin and one isolate of Citrobacter braaki and Enterobacter cloacae each were susceptible(100%) to Fosfomycin. Out of total 124 isolates 78% (97) were susceptible to Fosfomycin.

Conclusion: Fosfomycin is very good option for urinary tract infections. It has many advantages over other drugs like single dose therapy is required for uncomplicated UTI. Resistance to Fosfomycin is very low. It is active against both Gram positives as well as Gram Negative organisms. It do not posseses cross resistance with Beta lactam drugs. As our study shows it is active against even highly resistant isolates. It was also active against ESBL producing fours isolate of Escherichia coli and one isolate of Klebsiella pneumoniae.

Key Words: Fosfomycin, Urinary Tract infections (UTI), Escherichia coli, Klebsiella pneumoniae
venous form. It is a broad spectrum antimicrobial agent with activity against various gram-positive as well as gram-negative bacteria which includes staphylococci, enterococci, E. coli and other gram-negative bacteria. It is a bactericidal antibiotic which interferes with cell wall synthesis by inhibiting phosphoenol pyruvate transferase which is the first enzyme involved in the peptidoglycan synthesis. There is no cross resistance of this antibiotic with others and it can be administered safely in combination with many other antibiotics.

Fosfomycin has very good oral absorption with a bio-availability of 40% and majority of the drug is excreted unchanged in urine with very high concentration levels achieved in urine after a single oral dose.

Renal elimination of Fosfomycin is of 95% and no tubular secretion occurs. It has a relatively long elimination half-life, which varies between 4 and 8 hours. Urine levels remain high for prolonged period which makes it a suitable drug for the treatment of UTI. Besides urine.

E. coli is the most common organism causing the UTIs. With the inappropriate and inadvertent use of higher antibiotics, antimicrobial resistance emergence among these bacterial isolates has lead to difficulty in treating these infections. As the antibiotic pipeline is getting empty with only few alternatives available for treating these resistant infections, old antibiotics like fosfomycin, nitrofurantoin, colistin have gained importance recently again. In the present study we have evaluated the antibacterial activity of fosfomycin against isolates causing UTIs.

**METHODOLOGY**

This cross sectional study was conducted at pathology department, Allama Iqbal Medical College, Lahore, from January 2018 to October 2018. Midstream Urine specimens collected from different wards like surgical wards, medical wards, ICU, gynaecology ward, urology ward and also from outpatient department (OPD) were included in this study. Specimens from the both the genders were included in this study. Repeat specimens during same episode of illness, specimens having mixed growth, specimens from urine collection bag and Folley’s catheter tips were excluded from the study. All urine specimens were cultured on Cysteine Lactose Electrolyte Deficient (CLED) agar according to WHO protocol.

A total of 124 isolates including Gram negative bacilli and Gram positive cocci were included in this study. Gram negative rods which are intrinsically resistant to fosfomycin like Acinetobacter baumannii were excluded from this study. Bacterial isolates were identified on the basis of colonial morphology, Gram staining, Catalase test, coagulase test, Oxidase test, and biochemical profile using API 20 E and API 20NE. Antimicrobial susceptibility testing was performed by using standard modified Kirby bauer disc diffusion method. Zone sizes were interpreted following CLSI 2014 guideline. Fosfomycin 200-μg disc was used and zone diameter ≥ 16 mm was considered susceptible.

**RESULTS**

A total of 124 isolates were included in this study during study duration. 101 isolates were Gram negative rods and 23 were Gram positive cocci. Out of 81 isolates of Escherichia coli 81%(66) were susceptible to Fosfomycin, out of 15 isolates of Enterococcus faecalis 80% were susceptible to Fosfomycin, one isolate of Enterococcus faecium was susceptible (100%) to Fosfomycin, out of 13 isolates of Klebsiella pneumoniae 54% were susceptible to Fosfomycin and one isolate of Klebsiella oxytoca was susceptible (100%) to Fosfomycin, out of 7 isolates of Staphylococcus saprophyticus 57% were susceptible to Fosfomycin, 4 isolates of Citrobacter freundii were susceptible (100%) to Fosfomycin and one isolate of Citrobacter braaki and Enterobacter cloacae each were susceptible(100%) to Fosfomycin. Out of total 101 Gram negative rods 79% (80) were susceptible to fosfomycin. Out of 23 Gram positive cocci 74% were susceptible to fosfomycin. Out of total 124 isolates 78% (97) were susceptible to Fosfomycin. Out of 81 isolates of
Escherichia coli, four were extended spectrum beta lactamase (ESBL) producer, all of them were susceptible to fosfomycin. Out of 13 isolates of Klebsiella pneumoniae, only one was ESBL producer and it was susceptible to fosfomycin. So 5 ESBL producing gram negative rods were 100%(5) susceptible to fosfomycin.

**DISCUSSION**

Fosfomycin is very good option for urinary tract infections. It has many advantages over other drugs like single dose therapy is required for uncomplicated UTI. Resistance to Fosfomycin is very low. It is active against both Gram positives as well as Gram Negative organisms. It do not posseses cross resistance with Beta lactam drugs. It is active against even multidrug resistant (MDR) isolates. It was active against ESBL producing fours isolate of Escherichia coli and one isolate of Klebsiella pneumoniae.

In our study, out of total 124 isolates 78% (97) were susceptible to Fosfomycin. Out of total 101 Gram negative rods 79% (80) were susceptible to fosfomycin. Out of total 23 Gram positive cocci 74%(17) were susceptible to fosfomycin.

So many studies have been conducted on fosfomycin against organism causing urinary tract infections. Neuner et al conducted a study on fosfomycin against MDR urinary isolates in 2012. Fosfomycin was susceptible to 86% of urinary isolates. These isolates included both Gram positives as well as Gram negatives like Enterococcus species, Pseudomonas aeruginosa, Escherichia coli, Klebsiella species. Most of the isolates were MDR including 13 carbapenem-resistant Klebsiella pneumoniae, 8 Pseudomonas aeruginosa, and 7 vancomycin-resistant Enterococcus faecium (VRE) isolates, 7 extended-spectrum beta-lactamase (ESBL) producers. Like our study most of the isolates (86%) were susceptible to fosfomycin.

Maraki et al conducted a study from Greece in 2009. A total 578 urinary isolates were included in this study. Both Gram positives as well as gram negatives were included in this study. Over all more than 89% of theses isolates were susceptible to fosfomycin. These results are even better than our study results. In this study fosfomycin was susceptible to most of the MDR isolates including Vancomycin resistant Enterococci (VRE), Methicillin resistant Staphylococcus aureus (MRSA), ESBL producing Gram negative rods.

Matthews et al conducted a study in 2016. Among all urinary isolates tested during study duration, fosfomycin resistance was documented in 1 % of E. coli vs. 19 % of Klebsiella spp. They only tested Gram negative rods. Even these results are better than our study results in terms of resistance of fosfomycin.
Noor et al conducted a similar study on urinary isolates in 2004 from Karachi, Pakistan. In this study 94% isolates were susceptible to fosfomycin. This study included only 56 Gram negative rods, most of them were MDR. In comparison our study included both Gram positive as well as Gram negative isolates and sample size of our study is more than double of this study.

Wali et al conducted a study from Rawalpindi, Pakistan, in 2016. This study included 200 Gram negative urinary isolates. Out of which 97 were MDR and 103 were non MDR. Fosfomycin susceptibility was better among MDR urinary isolates. 98% of MDR isolates were susceptible to fosfomycin as compared to non MDR isolates. Fosfomycin susceptibility in this study is much better than our study especially against MDR isolates.

Khan et al conducted a study on ESBL producing Gram negative rods causing urinary tract infections from Rawalpindi Pakistan in 2014. A total of 381 isolates were included in this study. Results were comparable with our results, as 84% of these ESBL producing isolates were susceptible to fosfomycin. In our study, all isolates were not ESBL producer but those who were ESBL producer were 100% susceptible to fosfomycin as compared to over 78% susceptibility of fosfomycin.

CONCLUSION

Fosfomycin is a very good option for uncomplicated urinary tract infections against both gram positive and gram negative bacteria. It is easy to administer as single oral dose. It is more active against MDR isolates and ESBL producers. So it is proved to be better option in an era of high antibiotic resistance where we are left with limited choices.

REFERENCES

A UNIQUE PRESENTATION OF SYNOVIAL OSTEOCHONDROMATOSIS IN WRIST JOINT

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Abstract

Synovial osteochondromatosis is a rare self-limiting disease of benign etiology. It results in the formation of hyaline cartilage nodules in the subsynovial tissue of a joint, tendon sheath and bursa with varying degrees of mineralization. It is mostly a monoarticular disease but sometimes it has a polyarticular presentation. Knee joint is the most typical intraarticular presentation site but sometimes it arises at an extraarticular site where it is most seen in wrist joint along the tenosynovium and bursae. Computed Tomography (CT) is the optimal imaging modality for diagnosis. Here I present a rare case of both intra and extra articular presentation of synovial osteochondromatosis in an adult male along the wrist joint taking peroperative findings as the gold standard.

Key Words: Synovial osteochondromatosis, intraarticular, extraarticular, tenosynovium and bursal variety.

An old patient (age: 75 years) came for 3D CT wrist joint with complaint of swelling of left hand and no prior history of trauma. His case details are as follows:

Case Description

The 75 year old male presented to radiology department for 3D CT examination of his left wrist joint. He had a history of pain and swelling of left hand and forearm for the last one year. The pain was radiating to the whole arm. Movements of wrist joint were restricted, however, shoulder joint showed normal mobility. He was non-diabetic and non-hypertensive. His hemoglobin was 12.5 g/dl with normal LFT’s. His RFT’s were deranged with serum creatinine level of 1.55 g/dl restricting the contrast study. No other joint deformity or abnormality was reported. His X-ray was performed as a part of general routine. It showed multiple calcified and non-calcified soft tissue deposits in both intra and extra-articular compartments as well as in thenar and hypothenar compartments. His CT was performed and was reconstructed in coronal, sagittal and 3D planes. Contrast could not be given due to deranged RFT’s. The CT showed variable sized predominantly calcified foreign bodies around the wrist joint. Multiple large soft tissue deposits with calcifications in the ring and arc configuration were identified along the bursae and course of tendons. Both the flexor and extensor compartments showed edematous tendons with fluid tracking within the retinaculum. No definite collection was seen. Metacarpals, phalanges and large bones showed pressure erosions with relatively preserved bone density. No overhanging bony lips were noted. No alignment deformity was noticed. The case was diagnosed as synovial osteochondromatosis of tenosynovial and bursal variety. The patient was referred to orthopedic department. His surgery was planned after acquiring surgical fitness. His per-operative findings confirmed the above findings. Multiple calcified and partly calcified soft tissue deposits were scraped from the tendons. No malignant change was observed. The patient was referred for rehabilitation to recover from any movement disability.
DISCUSSION

Synovial osteochondromatosis was described in detail by Jaffe in 1985. It is a benign self limiting disease with rare potential. It has high incidence of local recurrence. It exists in both primary and secondary forms. Primary synovial chondromatosis is the metaplastic conversion of the chondroid matrix in the synovium with the formation of multiple intraarticular loose bodies. Secondary synovial chondromatosis is associated primarily with abnormalities of joints as trauma, arthritic disabilities or deformities. However, in some rare cases as it has been presented in this article, this formation of chondroid loose bodies can spread along the synovium involving the tendons and bursae where it is referred to as tenosynovial or bursal chondromatosis.

This rare extra-articular presentation of the synovial chondromatosis mostly occurs in adults over 20 years of age with mean age of 50 years. Men are generally more affected, however, for extraarticular disease when diagnosed in older patients, there is a female preponderance (2:1 ratio). Clinically, it presents as mild tenderness or pain over swelling. Extraarticular presentation rarely presents with limitation of joint movement. Duration of symptoms is frequently long i.e. upto 2 years. Most common sites involved inextra-articular presentation are commonly hands (57%), feet (22 %), wrists (11%) and ankles (5%). Although knee joint is the most common presentation for intraarticular presentation, it is a rare presentation site for extraarticular presentation.

Pathologically, it is the hyperplastic synovium that results in the formation of numerous chondroidnodules of variable size. The extraarticular presentation involves the subsynovium of tendons and bursae. These nodules may detach and reside within joint cavity or in the parenchyma of tendons and bursae. Since these loose bodies absorb their nutrition from the synovial fluid, they continue to grow in size and may reach several cm. They may exhibit different levels of peripheral or central dystrophic calcification in ring and arc configuration. In a long standing disease, they may progress to enchondral ossification or target appearance showing a central punctate focus and single peripheral rim of calcification. Extrinsic erosion of the bone is identified on both sides of bone, however, juxtaarticular osteopenia is not a typical feature of the disease. Adjacent joints also appear normal. Surgical resection is the mainstay of the disease. In a study by Maurice et.al. and Roulot and Le Viet, there was no recurrence following local resection. However, in a large study of Fetschet.al. recurrence rate of 88% was observed. Arthroscopy can prove further helpful in the
management of the disease. There is 5% prevalence of malignant transformation to chondrosarcoma in cases of primary osteochondromatosis with extensive soft tissue component. This requires amputation as treatment strategy. Metastasis to lung are common, 56 % of follow up of patients showed metastasis in a study conducted by Bertoniet.al. Death rate was 44% and 67% in studies by Bertoniet. al. and Davis et.al. respectively.  

REFERENCES