JAIMC
The Journal of Allama Iqbal Medical College
October - December 2020, Volume 18, Issue 04

Editorial

Original Articles

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JAIMC
The Journal of Allama Iqbal Medical College
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Outstanding Reviewer of Vol.18 Issue 04 (October – December 2020)

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She is working as a demonstrator in Pathology Department, Allama Iqbal Medical College, Lahore since 2019. She completed her M.Phil in Histopathology from Post Graduate Medical Institute Lahore. She has 2 years of working experience in Pathology Department as a senior demonstrator in University of Lahore, Medical and Dental College. She is eager to learn latest skills, networking with new people and gain valuable work experiences in the field of science and research.

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OPEN YOUR EYES BEFORE AIDS CLOSE THEM

How to cite: Imran M. Open your eyes before AIDS close them. JAIMC. 2020; 18(4): iii-v

December 1st is marked as the World AIDS Day. Acquired Immune Deficiency Syndrome (AIDS) was first recognized as new disease in 1981. Caused by two lentiviruses, human immune deficiency virus types 1 and 2 (HIV-1 & HIV-2); it has become one of the most devastating infectious diseases to have emerged in the recent past. Transmitted through percutaneous, perinatal and sexual routes, the pandemic form of HIV-1, also called the main (M) group, has infected millions of people and the developing countries experiencing the highest morbidity and mortality, with the greatest prevalence rates recorded in sub-Saharan Africa. Although antiretroviral therapy has reduced the number of AIDS-related deaths, access to the treatment is not universal, and the prospects of a targeted curative treatment and an effective vaccine are yet uncertain, thus posing a significant public health threat for decades to come.

The local administration in Pakistan became alert by the media reports of increasing HIV cases on 25 April 2019 especially amongst children in Ratodero Taluka, Larkana district, Sindh. From that day till June 2019, a total of 30,192 people have been screened for HIV in the area, of which 876 were positive and 82% of these patients were below the age of 15 years. The process of screening highlighted many risk factors including: unsafe intravenous injections during medical procedures, unhygienic child delivery practices, unsafe practices at the blood banks; poor implementation of infection control programs, and improper collection, storage, segregation and disposal of the hospital and medical waste. This was the fourth reported outbreak of HIV in Larkana district since 2003. The first outbreak in 2003 was among the people who inject drugs (PWID), the second was among 12 pediatric patients in a local pediatric hospital in 2016, and the third, also in the same year, was among 206 patients in a local hospital dialysis ward. The recent event opened the eyes of the concerned authorities to make strategies to identify sources and the chains of transmission of HIV, point out the high-risk areas, and identify the gaps in HIV diagnosis, care and treatment.

HIV epidemic evolves in three phases. First is a low prevalence phase, when prevalence of the disease is less than 5% in any high-risk group of the country. Second phase is a concentrated epidemic when proportion of infected people in any high-risk group rises more than 5% and the last phase is a generalized epidemic when the prevalence of HIV infection rises over 1% among blood donor or pregnant women. Pakistan is one of the Asian countries where new HIV infections are increasing at an alarming level since 1987. The present HIV epidemic in Pakistan is defined as a concentrated epidemic. It is concentrated among the two main population groups driving the epidemic in our country: people who inject drugs, with a national prevalence of 27.2%, followed by transgender sex workers, standing at 5.2%. In Pakistan in the year 2018; 160,000 people were living with HIV, 22,000 people were newly infected with the virus, 6400 people died from an AIDS-related illness. HIV incidence per 1000 uninfected (the number of new HIV infections among the uninfected population over one year) among people of all ages was 0.1. HIV prevalence (the percentage of people living with HIV) among adults (15–49 years) was 0.1%. There has been a 369% rise in the number of AIDS-related deaths since 2010. The number of new HIV infections has also increased from 14,000 to 22,000 in the same period.

In the WHO fast track commitments to end AIDS by 2030, the 90–90–90 targets envisions that, by 2020, 90% of people living with HIV will know their HIV status, 90% of people who know their HIV- positive status will be accessing treatment and 90% of people on treatment will have suppressed viral loads. In terms of all the people living with HIV, reaching the 90–90–90 targets means that 81% of all people living with HIV are on treatment and 73% of all people living with HIV are virally suppressed. In 2018 in Pakistan 14% of people living with HIV knew their status and 10% of people living with HIV were on treatment. Of all adults aged 15 years and over living with HIV, 10% were on treatment, while 11% of children aged 0–14 years living with HIV were on treatment. 10% of pregnant women living with HIV accessed antiretroviral medicine to prevent vertical transmission. Early infant diagnosis (the percentage of HIV-exposed infants tested for HIV before eight weeks of age) was 2% in 2018. Of the 160,000 adults living with HIV in Pakistan, 48 000 (30.71%) were women. New HIV infections among young women aged 15–24 years were less than those among the

young men: 1800 new infections among young women, compared to 2600 among young men. HIV treatment was lower among women than men, with 7% of adult women living with HIV on treatment, compared to 11% of adult men. Only 4.29% of women and men 15–24 year old correctly identified ways of preventing the sexual transmission of HIV. In 2017, the percentage of people living with HIV and tuberculosis who were being treated for both diseases were 1.3%, up from 0.9% in 2015.

HIV is no more a health problem; rather it has become a security issue. Pakistan is a very vulnerable country, with increasing poverty, low levels of literacy, less condom use, lack of awareness among health workers, a huge population of refugees near border areas, internal and external migrants, long-distance truck drivers known to be engage in sexual practices that put them at risk of contacting HIV and other sexually transmitted diseases (STDs); social and economic disadvantages, a booming commercial sex industry, unsafe transfusion of blood products; high prevalence of STDs with, limited awareness and access to good-quality STD care and treatment, limited safety of medical injection usage and health care practices, extensive use and reuse of unsterilized syringes, increased rate of needle-sharing among estimated 60,000 intravenous drug users and a large proportion with lack of knowledge about HIV transmission, prevention and treatment.

This highlights the current importance of using high-impact interventions to reduce vulnerability and prevent viral transmission. It is high time to address the non-availability of sufficient information to determine the complete extent and magnitude of the disease in the country, lack of information regarding all possible sources of exposure, insufficient treatment options, and past history of repeated HIV outbreaks in the country. Prompt epidemiological and statistical investigations will help in determining the magnitude of the cases representing the tip of iceberg of a larger epidemic. The situation must be closely monitored, and the risks factors must be re-assessed according to the results. It is stressed to take into consideration the prevention of transmission through unsafe blood products, sexual transmission in high risk groups, spread through drug injections usage and the vertical transmission from mother-to-child; and the significance of immediately linking all those diagnosed with HIV infection to antiretroviral therapy and vigilant follow-up in regards to disease related morbidity and complications.

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Education, Knowledge and Prevention are the Key, but Stigmatization and Exclusion from Family is what makes People Suffer Most.
Photograph by: ***Ali Rizvi***

COMPARISON OF RANGE OF MOTION IN DIFFERENT JOINTS OF HAND IN PATIENTS WITH METACARPAL FRACTURE AFTER K-WIRE VERSUS MINIPLATE INTERNAL FIXATION

Muhammad Ali,[1] Usman Zafar Dar,[2] Rashid Hussain,[3] Amjad Ali,[4] Muhammad Omer Sabir,[5] Muhammad Ikram Ullah Khan[6]

How to cite : Ali M, Dar UZ, Hussain R, Ali A, Sabir MO, Khan MIU. Comparison of range of motion at different joints of hand in patients with metacarpal fracture after K-wire versus miniplate internal fixation. JAIMC. 2020; 18(4):571-76.

Abstract

Objective: To compare the range of motion at different hand joints in metacarpal fracture patients after K-Wire versus Miniplate Internal Fixation in our patients at department of Orthopaedics, LGH, Lahore.

Methods: This experimental study was accomplished in Orthopedics ward of LGH Hospital, Lahore. Sampling was done via non-probability convenient method, and the sample size was 50 cases, 25 in each group. The patients in group A underwent treatment with Kirshner wire fixation, while patients in group B underwent miniplate internal fixation. The patients in both groups were trailed upto 4 months postoperatively for improvement checking via range of motion (ROM). Range of Motion was measured using goniometer. The treasured data was interpreted in SPSS version 18.00. Age and range of motion were the quantitative variables, while gender was a qualitative variable. Chi-square test was used for testing of the significance of qualitative variables. P-value were considered significant if ≤ 0.05. Repeated measurement ANOVA test was applied to see the difference of both quantitative variables in both groups.

Results: Among total 50 patients with metacarpal fracture, 50% were managed with K-wire fixation while other 50% with Miniplate internal fixation. In patients, treated using K-wires fixation, there was improvement in ROM of metacarpo-phalangeal joint extension from 10.80±1.88o to 42.01±6.13o at 4th post-op month (final visit). The patients treated with miniplate showed betterment in ROM of metacarpo-phalangeal joint extension from 12.79o±2.32o to 44.39±1.656o at 4th post-op month i.e. final visit. There was an insignificant difference in improvement of ROM of MP joint extension between both study groups (p-value = 0.065) on last follow-up. Similarly, there was an insignificant difference between both study groups (p-value = 0.114) in ROM improvement in MP joint flexion on last follow-up. Similar findings were for ROM of PIP joint flexion and ROM of DIP joint flexion.

Conclusion: Range of motion (ROM) is a quantitative measure of the correction of defect created by hand fracture especially metacarpal fractures. In our study, both K-wire and mini-plate internal fixation technique showed comparable and excellent improvement in ROM at metacarpophalangeal, proximal inter-phalangeal as well as distal interphalangeal joints. There was more ROM achieved with miniplate fixation as compared to K-wire, however inferiority of the K-wire could not be documented because the difference was statistically insignificant.

Keywords: Metacarpal fracture, Range of motion, Kirschner (K) wire, Miniplates

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Submission Date: 24-08-2020
1st Revision Date: 12-09-2020
Acceptance Date: 20-09-2020

Metacarpals are the thin, long bones which are situated between the phalanges in the digits and the carpal bones in the wrist.[1] Metacarpal fractures (MF)[2] are the third most common fractures among upper extremities injuries, and accounts for approximately 40% of all hand fractures.[3] Typical age for metacarpal fractures is 10 to 40 years.[4] The incidence of fracture of metacarpal bone increases

from radial to ulnar side.[2] They empirically happen as a result of a direct hit or directly fall onto the hand.[5] They generally occur during athletic activities, frequently in younger persons.[6] Work-related injuries[7] are the usual reason in middle-aged people, while fall in the elderly.[8] Fifth metacarpal fracture is named as boxer's fracture.[9] Majority metacarpal fractures are managed conservatively; however, some require surgical intervention.[10] Surgery can include close reduction followed by Kirschner (K) wire internal fixation[11] or open reduction with miniplate fixation.[12] In some international literatures, both modalities are found equally effective while other studies has proven superiority of one over the other technique.[13,14] Range of motion (ROM)[15] is a vital element of evaluation of hand function. Historically, a metric ruler was used to measure it; however its use was associated with upto 100 of inaccuracy.[16] By 2006, a new goniometer[17] was made, particularly for the proficient measurement of small joints. The local studies on the comparisons of range of motion at various hand joints in metacarpal fracture after k-wire internal fixation versus miniplate fixation in Pakistani population are infrequent. Therefore, the objective of the present study was to compare the range of motion at different hand joints in metacarpal fracture patients after K-Wire versus Miniplate Internal Fixation in our patients at department of Orthopaedics, LGH, Lahore.

METHODOLOGY

This experimental study was accomplished in Orthopedics ward of LGH Hospital, Lahore. Sampling was done via non-probability convenient method, and the sample size was 50 cases. The patients were divided in two groups, 25 each. Two weeks history of metacarpal fracture, age between 6 to 50 years and both genders were the inclusion criteria, while bone loss during fracture, impossible precise reconstruction with steady cortical apposition, osteoporotic disease, and refracture were the exclusion criterias. The patients in group A underwent treatment with Kirshner wire fixation, while patients in group B underwent miniplate internal fixation. Miniplate fixation involved dorsal incision after aseptic measures. Then, periosteum was incised and lifted to disclose the fracture. After reduction of the fracture, plate was implanted, and fracture was fixed. Then, wound was stitched. During K-wire fixation procedure, close reduction of metacarpals was done. Then, k-wire was proceeded from distal to proximal longitudinally. Then, hand was splinted followed by radiologic imaging (x-ray) to confirm the proper reduction. The patients in both groups were trailed upto 4 months postoperatively for improvement checking via range of motion (ROM). Range of Motion was measured using goniometer. It was defined by calculating the degree of movement on different joints separately, at the metacarpophalangeal (MP) joint hyperextension / flexion (0-45H) /90, at the proximal interphalangeal joint extension / flexion (0/100), at the distal interphalangeal joint extension/flexion (0/80). While examining ROM of finger, the wrist is positioned neutral. This results the tendon excursion of the long extensors and flexors of the fingers. Flexion of a finger was estimated by maximally flexing the other three fingers, and extension of one finger was mapped by maximally extending the other three fingers actively. All the statistics was put into a structured performa. The treasured data was interpreted in SPSS version 18.00. Age and range of motion were the quantitative variables, while gender was a qualitative variable. Chi-square test was used for testing of the significance of qualitative variables. P-value were considered significant if ≤ 0.05. Repeated measurement ANOVA test was applied to see the difference of both quantitative variables in both groups.

RESULTS

Among total 50 patients with metacarpal fracture, 50% were managed with K-wire fixation (group A) while other 50% with Miniplate internal fixation (group B).

In patients, treated using K-wires fixation, there was improvement in ROM of metacarpo-phalangeal

joint extension from 10.80±1.88° to 42.01±6.13° at 4th post-op month (final visit). The patients treated with miniplate showed betterment in ROM of metacarpo-phalangeal joint extension from 12.79°± 2.32° to 44.39±1.656° at 4th post-op month i.e. final visit. There was an insignificant difference in improvement of ROM of MP joint extension between both study groups (p-value = 0.065) on last follow-up (Table 1). We plotted a graph. The both groups showed significant improvement in ROM of MP joint extension; however, with miniplate, there was more improvement than K-wires. (Figure 1).

The patients treated with K-wire showed improvement in ROM of MP joint flexion from 20.81°±10.95° to 85.02±12.07° on final visit after 4th post-op month. On the other hand, the patients treated with miniplate showed the improvement in ROM of MP joint flexion from 26.42°±3.38° to 89.05±2.90° on final visit after 4th post-op month. There was an insignificant difference between both study groups (p-value = 0.114) in ROM improvement in MP joint flexion on last follow-up (Table 2). Both groups showed significant improvement in ROM of MP joint flexion. We plotted the graph. The improvement with miniplate was more than the improvement using K-wires (Figure 2). The patients managed with K-wires showed improvement in ROM of PIP joint flexion from 34.01°±2.03° to 97.01±8.65° on final visit after 4th post-op month. The patients treated with miniplate showed improvement in ROM of PIP joint flexion from 44.02°±6.93° to 99.21±2.76° on final visit after 4th post-op month. There was an insignificant difference between both study groups (p-value = 0.232) for ROM improvement of PIP joint on last follow-up (Table 3). The figure 3 indicates that both groups showed significant improvement in ROM of PIP joint flexion. The difference between both groups was also significant (p-value = 0.000) and with miniplate, there is more improvement than K-wires. The patients treated with K-wires exhibited improvement in ROM of DIP joint flexion from 31.41°±2.28° to 78.41±4.52° on final visit after 4th post-op month. The patients treated with miniplate exhibited improvement in ROM of DIP joint flexion from 44.82°±7.83° to 80.61±4.17° on final visit after 4th post-op month. There was an insignificant for ROM of DIP joint Flexion between both study groups (p-value = 0.079) on last follow-up (Table 4). The figure 4 indicates that both groups showed significant improvement in ROM of DIP joint flexion. The difference between both groups was also significant (p-value = 0.000) and with miniplate, there is more improvement than K-wires.

Table 1: *Comparison of Range of Motion of Metacarpophalangeal (MP joint) Extension in Both Study Groups (n=50)*

		K-wires	Mini plate	p-value
ROM of MP joint extension	**1st post-op day**	10.80°±1.88°	12.79°±2.32°	0.010
	After 2 weeks	24.20°±6.56°	34.00°±6.12°	0.000
	After 4 weeks	24.20°±6.56°	34.00°±6.12°	0.000
	After 6 weeks	30.20°±8.23°	40.20°±7.29°	0.000
	After 8 weeks	36.60°±8.63°	43.80°±4.15°	0.000
	After 10 weeks	40.60°±6.51°	44.20°±2.36°	0.012
	After 3 months	41.80°±6.27°	44.40°±1.66°	0.051
	After 4 months	42.01°±6.13°	44.39°±1.66°	0.065

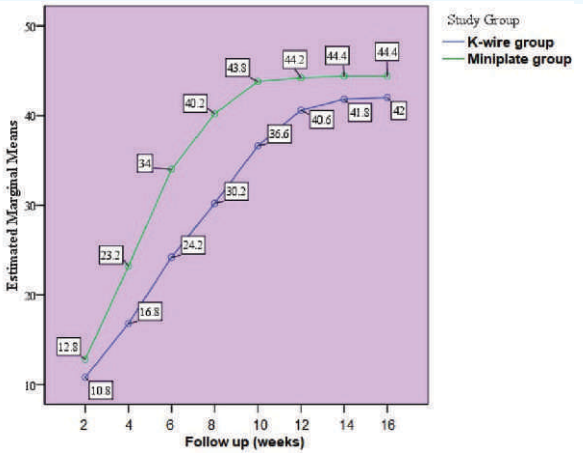

Fig. 1: *Comparison of mean ROM of MP Joint Extension at different Follow-ups (n = 50)*

Table 2: *Comparison of Range of Motion of Metacarpophalangeal (MP joint) Flexion in both Study Groups (n=50)*

		K-wires	Mini plate	p-value
ROM of MP joint Flexion	**1st post-op day**	20.81°±10.95°	26.42°±3.38°	0.018
	After 2 weeks	30.20°±6.69°	46.40°±6.38°	0.000
	After 4 weeks	46.60°±11.70°	69.40°±11.21°	0.000
	After 6 weeks	59.00°±14.72°	79.60°±12.66°	0.000
	After 8 weeks	74.00°±17.08°	88.20°±6.27°	0.000
	After 10 weeks	82.80°±12.59°	88.60°±4.45°	0.035
	After 3 months	84.80°±12.20°	89.00°±2.89°	0.101
	After 4 months	85.02°±12.07°	89.05°±2.90°	0.114

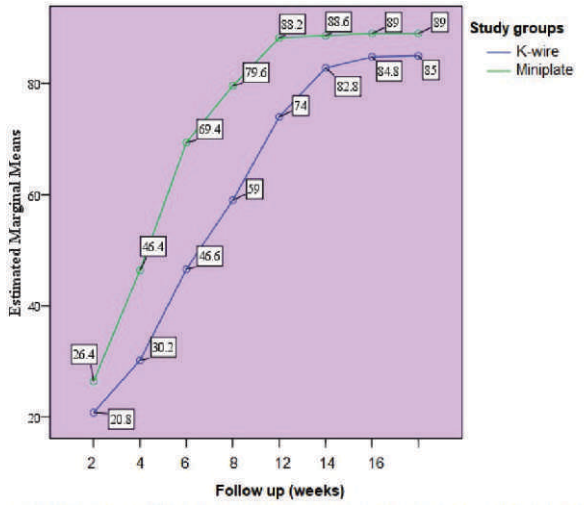

Fig. 2: *Comparison of mean ROM of MP Joint Flexion at different Follow-ups (n = 50)*

Table 3: *Comparison of Range of Motion of Proximal Interphalangeal (PIP joint) Flexion in both Study Groups (n=11)*

		K-wires	Mini plate	p-value
ROM of PIP joint Flexion	1st post-op day	34.01°±2.03°	44.00°±6.92°	0.000
	After 2 weeks	49.80°±9.52°	62.80°±6.78°	0.000
	After 4 weeks	62.20°±10.81°	77.00°±6.77°	0.000
	After 6 weeks	76.20°±16.85°	90.80°±10.28°	0.001
	After 8 weeks	92.00°±16.07°	98.40°±6.25°	0.070
	After 10 weeks	95.60°±11.58°	98.60°±5.31°	0.245
	After 3 months	96.60°±9.21°	99.20°±2.77°	0.183
	After 4 months	97.01°±8.66°	99.20°±2.77°	0.232

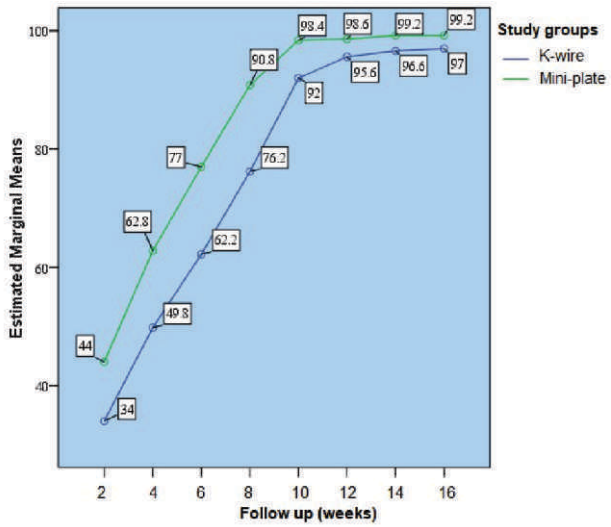

Fig. 3: *Comparison of Mean ROM of PIP Joint Flexion at Different Follow-ups (n = 50)*

Table 4: *Comparison of Range of Motion of Distal Interphalangeal (DIP joint) Flexion in both Study Groups (n=50)*

		K-wires	Mini plate	p-value
ROM of DIP joint Flexion	1st post-op day	31.41°±2.28°	44.82°±7.83°	0.000
	After 2 weeks	47.20°±7.65°	60.40°±7.06°	0.000
	After 4 weeks	58.20°±11.45°	68.40°±6.25°	0.000
	After 6 weeks	66.80°±13.68°	75.00°±7.50°	0.012
	After 8 weeks	76.80°±7.89°	80.20°±5.09°	0.077
	After 10 weeks	77.80°±5.79°	80.40°±4.55°	0.084
	After 3 months	78.40°±4.50°	80.60°±4.16°	0.079
	After 4 months	78.41°±4.52°	80.61°±4.17°	0.079

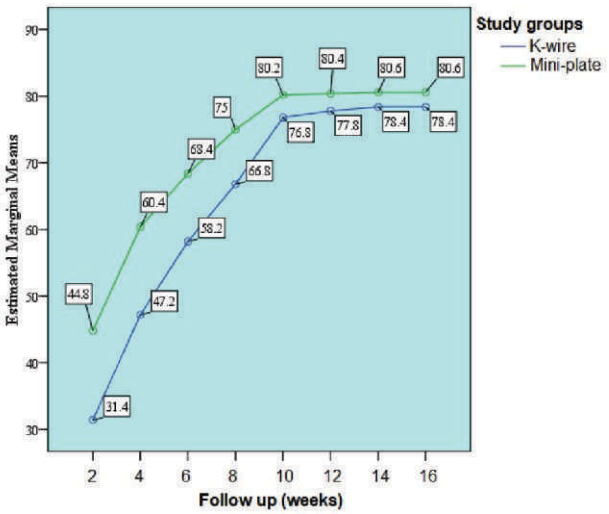

Fig. 4: *Comparison of Mean ROM of DIP Joint Flexion at different Follow-ups (n = 50)*

DISCUSSION

Metacarpal fracture are a common hand injury, which involves a break in one of the five metacarpal bones of either hand.[18] They commonly occur during athletic activities, particularly in contact sport. They are also prevalent among factory workers. The right hand is dominantly involved. Metacarpal fractures are managed efficiently both by conservative approach as well as by surgical intervention. Correction of joints defect is assessed by range of motion (ROM). If there is a difference between joint active and passive ROM, this is called active-passive mismatch, which may be caused by a tendon adhesion. Khalid M. Hassan et al[19] from Egypt compared fixation of metacarpal fractures by titanium metal

plates (group A) with biodegradable plates (group B). In group A, total range of motion was 234±15.05 degrees while in group B, it was 133±17.02 degrees as measured by goniometer. There was insignificant difference in improvement in ROM by two techniques.[19] In a study of 112 patients, Somboon Wutphiriya-angkul[20] found that k-wire internal fixation had comparable improvement in range of motion (ROM) to miniplate technique (p=0.65). On the other hand, Zulfiqar Ahmed and colleagues compared both surgical modalities in metacarpal fracture patients. They observed that total active ROM was greater in miniplate fixation patients compared with K-wire treated patients, and this difference was statistically significant.[21] In our study excellent improvement in ROM was noted with both surgical modalities, however inferiority of single one technique could not be documented; Both were comparably effective. Khan et al[22] did a comprehensive angle elaboration on MFs and described that the head/shaft angle of the fifth metacarpal was 60.60±9.39° preoperatively. However, It was 14.20±7.32° on zero day postoperatively, and 15.60±6.95° on weeks 12 postoperatively. The dissimilarity between postoperative and preoperative angles was extremely significant. The range of motion of the metacarpal joint was uninjured side which was 90.93± 3.18°. It was 86.73±6.13° postoperatively, so both were comparable. The ROM of the metacarpal joint was not remarkably different as compared to uninjured side. The mean union time was 5.46 ± 1.22 weeks. He deduced that this mode under consideration does not disrupt the fracture site itself, the Kirschner wire being inserted in retrograde approach makes it easier to accurately place the wire, which provides courteously stable fixation, gives outstanding results in a high percentage of sorted cases. Huffaker et al,[23] deliberated the factors affecting final ROM in 150 cases. This precise article reported acceptable results of 67% apart from the strategy of treatment. 20% patients had decreased ROM in normal fingers in the same hand. The median TAM was 220° without joint involvement and 174° with joint involvement. Crush injuries involving the flexor and/or extensor tendons or skin significantly affected the final result. Fyfe & Mason, and Massengill et al[24,25] in their studies concluded that Kirschner wire fixation provided weaker fixation than miniplate fixation. Firm stabilization of the Miniplate permitted early ROM. We know that K-wire methodology is the best convenient for a transverse fracture,[26] so further studies with larger sample size are required to validate our findings as well as to compare applicability of two surgical modalities in our population.

CONCLUSION

Range of motion (ROM) is a quantitative measure of the correction of defect created by hand fracture especially metacarpal fractures. In our study, both K-wire and mini-plate internal fixation technique showed comparable and excellent improvement in ROM at metacarpophalangeal, proximal inter-phalangeal as well as distal inter-phalangeal joints. There was more ROM achieved with miniplate fixation as compared to K-wire, however inferiority of the K-wire could not be documented because the difference was statistically insignificant.

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IN HOSPITAL MORTALITY AND ITS PREDICTORS AMONG THE PATIENTS OF LIVER CIRRHOSIS

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How to cite: Akhtar H, Iqbal MA, Riaz A, Idress RH, Janjua AA, Raza MH. In hospital mortality and its predictors among the patients of liver cirrhosis. JAIMC. 2020; 18(4):577-81.

Abstract

Objectives: To determine the frequency of in-hospital mortality and its predictors amongst the patients suffering liver cirrhosis admitted at DHQ teaching hospital, Gujranwala, Pakistan.

Methods: This was a cross-sectional study carried out in Medicine Department of Gujranwala Medical College from Jan 2017 to Dec 2019. All the hospitalized patients having complications of liver cirrhosis with age 12 years or more were enrolled. The principle variable was mortality, where one group was made who died during hospitalization, while second group included the patients whose sequel was recovery at the end of hospitalization. Statistical analysis was executed utilizing the SPSS 25. Bivariate analysis and binary logistic regression were completed to establish the effect of numerous variables like age, gender, weight, diabetes history, hypertension history, viral etiology of cirrhosis, and presentation with hepatic encephalopathy on the probability that death would be the consequence in liver cirrhosis patients. All p-values was considered significant if < 0.05.

Results: Out of the total of 400 hospitalized patients, 16.5% (n=66) died. The mean age of the death group was 54.08 + 14.28 years while the mean weight was 66.09+12.34kilograms. Bivariate analysis suggested that mortality was remarkably more significant in set of patients who had previous history of hospitalization ($p<0.01$), and viral etiology of liver disease ($p<0.01$), and who presented with hepatic encephalopathy ($p<0.01$). Mortality was not significantly associated with male/female gender ($p=0.893$), presence of diabetes mellitus ($p=0.369$), and presence of hypertension ($p=0.622$). Logistic regression disclosed that hepatic encephalopathy patients had 39 times more risk of death than patients without hepatic encephalopathy. Similarly, cirrhotic patients with viral etiology of liver disease were likely to die during hospitalization ($p<0.01$).

Conclusion: The mortality rate was high amongst the studied hospitalized patients suffering liver cirrhosis. The mortality was significantly inflated in group of patients with hepatic encephalopathy and viral etiology for cirrhosis. However, it was not associated with age, weight, gender, presence of diabetes and hypertension. History of previous hospitalization was found significant contributor for mortality in bivariate study; however, association was proved insignificant during logistic regression analysis. Prevention from hepatotropic viruses and marvelous management steps of hepatic encephalopathy can effectively turn down the mortality rate amongst cirrhotic patients in our population.

Keywords: Liver cirrhosis,complications, in-patient mortality, hepatic encephalopathy, cross-sectional study, SPSS

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Submission Date: 20-08-2020
1st Revision Date: 29-08-2020
Acceptance Date: 13-09-2020

Pakistan is now a cirrhotic state where disease burden is very high throughout the country.[1] Hepatitis C is the commonest etiologic factor progressively leading to liver cirrhosis in our people.[2] In the world, liver cirrhosis spans between 4.5 % to 9.5%.[3,4] The patients affected with liver cirrhosis require repeated hospitalization due to its various complications like hepatic coma,[5] spontaneous bacterial peritonitis,[6] and upper gastrointestinal (UGI) bleeding[7]

etc. Themortality rate in hospitalized liver cirrhosis patients is displeasingly high. Its global prevalence ranges from 13.5% to 35%.[8,9]

Formerly, numerous prognostic models10like MELD score and CTP score had been composed for terminal liver disease. However, until now, hospital and person-related aspects responsible for death in hospitalized cirrhotic patients are poorly established. If few hefty etiological factors are recognised in our systems, then precautionary strategies would decrease the mortality rates among admitted cirrhotics and thus hospitalization yield could be revamped. This will, in turn, help to design and reconstruct policies based on the realities and thus prop up the health sector. Therefore, the desire and focus of the present study was to determine the frequency of in-hospital mortality and its predictors amongst the patients suffering liver cirrhosis admitted at DHQ teaching hospital, Gujranwala, Pakistan.

METHODOLOGY

This was a cross-sectional study[11] carried out in Medicine Department of Gujranwala Medical College from Jan 2017 to Dec 2019. After ethical review committee approval, written informed consent was taken from patients. The data was composed by purposive sampling utilizing a definite proforma. All the hospitalized patients having complications of liver cirrhosis with age 12 years or more were enrolled. The principle variable was mortality, where one group was made who died during hospitalization, while second group included the patients whose sequel was recovery at the end of hospitalization.

Statistical analysis was executed utilizing the SPSS 25. Age and the weight of the patients were continuous variable, while gender, diabetes history, hypertension history, viral /non-viral etiology of cirrhosis, previous history of hospitalization, and hepatic encephalopathy at the presentation were the categorical variables. During descriptive interpretation of data, quantitative variables were expressed as mean and standard deviation. Frequencies and percentages were worked out for qualitative variables. The mean age and weight of the patients was compared with the outcome (death/ no death) utilizing Independent sample T test. The chi-square test was used for the bivariate analysis of the categorial predictors of mortality. The p-values was significant if < 0.05.The binary logistic regression[12] was also completed to establish the effect of numerous variables on the probability that dying would be the consequence in cirrhotic patients.

RESULTS

Out of the total of 400 hospitalized patients affected with liver cirrhosis, 16.5% (n=66) died and 83.5% (n=334) recovered (Picture 1).The mean age of the death group was 54.08 + 14.28 years while the mean age of the patients who recovered / discharged from hospital was 53.43+ 14.55 years. The mean age of the death-group patients wasjust 0.65 years higher than that of recovered-group patients, and the difference was statistically insignificant (p=0.743). Similarly, the mean weight of the patients who died during hospitalization was 66.09+12.34 kilograms while the mean weight of the patients who recovered / discharged from hospital was 65.22+ 11.53 years. The mean weight of the death-group patients was just 0.87 years higher than that of recovered-group patients, and the difference was statistically insignificant (p=0.58). (Table 1).

Bivariate analysis propounded that mortality was remarkably more significant in set of patients who had previous history of hospitalization (p<0.01), and viral etiology of liver disease (p<0.01), and who presented with hepatic encephalopathy (p<0.01). Mortality was not significantly associated with male/ female gender (p=0.893), presence of hypertension (p=0.622), and diabetes mellitus (p=0.369)(Table 2).

Binary logistic regression was executed to establish the effect of age, gender, weight, hypertension, diabetes, previous hospitalization, etiology of cirrhosis and hepatic encephalopathy on the likelihood that dying would be the sequel/ consequence of the disease during recent hospitalization. The logistic regression model was noteworthy, p<0.05. The model accurately classified 87% of cases and

described 45.18% (Nagelkerke R2) of the variance in subset of the patients who died. Logistic regression disclosed that hepatic encephalopathy patients had 39 times more risk of death than patients without hepatic encephalopathy. Similarly, cirrhotic patients with viral etiology of liver disease were likely to die during hospitalization (p<0.01)(Table 3).

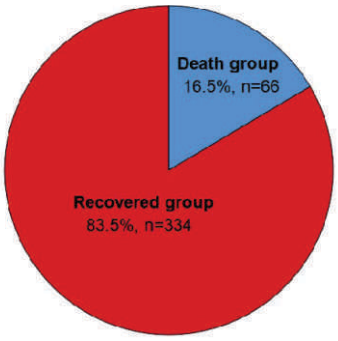

Fig.1: *In-Hospital Mortality Rate Amongst Patients Suffering Liver Cirrhosis (n=400)*

Table 1: *Associations of Mortality with Various Quantitative Variables amongst Liver Cirrhosis Patients (n = 400) **

Quantitative variables	ST elevation settled >50% at 1st post-admission day		Mean difference	p-value
	Yes (mean+SD)	No (mean+SD)		
1. Age (years)	54.08±14.28	53.43±14.55	0.65	0.743
2. Weight (Kilogram)	66.09±12.34	65.22±11.53	0.87	0.580

*Independent sample T-test was utilized

DISCUSSION

High inpatient mortality is a challenging truth in our patients suffering liver cirrhosis. The disease is prevalent world-wide with exorbitant death rates. A study was conducted in North Carolina in 2016 in which in-hospital mortality was 13.5% amongst the patients who presented with the complications of the liver cirrhosis.[8] Similarly, from Colombia, R Zubieta-Rodríguez and his team members[13] noted 23.5% while Alsultan et al[9] from Riyadh, Saudi Arabia acclaimed 35% mortality rates among hospitalized cirrhotic

Table 2: *Factors Affecting the In-Hospital Mortality Among Patients Suffering Liver Cirrhosis (n = 400)**

Factors	Hospitalization end-result		Total	p-value
	Death	No death		
Gender:				
Female	34 (51.5%)	168 (50.3%)	202 (50.5%)	0.893
Male	32 (48.5%)	166 (49.7%)	198 (49.5%)	
Diabetes Mellitus:				
Yes	14 (%)	54 (%)	68 (%)	0.369
No	52 (%)	280 (%)	332 (%)	
Hypertension:				
Yes	12 (18.2%)	73 (21.9%)	85 (21.3%)	0.622
No	54 (81.8%)	261 (78.1%)	315 (78.7%)	
Etiology of cirrhosis:	47 (71.2%)	304 (91%)	351 (87.8%)	<0.01
Viral	19 (28.8%)	30 (9%)	49 (12.2%)	
No-viral				
Previous history of hospitalization:				
Yes	56 (84.8%)	197 (59%)	253 (63.2%)	<0.01
No	10 (15.2%)	137 (41%)	147 (36.8%)	
Hepatic encephalopathy at presentation:				
Yes	51 (77.3%)	47 (14.1%)	98 (24.5%)	<0.01
No	15 (22.7%)	287 (85.9%)	302 (75.5%)	

*Chi-square test was utilized

Table 3: *Binary Logistic Regression of the Predictors of In-Patient Mortality in Cirrhotic Patients (n=400)*

Risk Factors	B	S.E.	Wald-Statistic	p-value	Odds Ratio	95% C.I. for EXP(B)	
						Lower	Upper
Gender (Male/Female)	.130	.352	.137	.712	1.139	.571	2.272
Age (Years)	.012	.011	1.129	.288	1.012	.990	1.034
Weight (Kilogram)	-.011	.014	.592	.442	.989	.963	1.017
Diabetes mellitus (Yes/No)	.456	.584	.611	.434	1.578	.503	4.958
Hypertension (Yes/No)	.834	.580	2.069	.150	2.302	.739	7.168
Etiology of cirrhosis (Viral/non-viral)	-1.748	.459	14.509	.000	.174	.071	.428
History of repeat hospitalization (Yes/No)	.888	.576	2.373	.123	2.431	.785	7.523
Hepatic encephalopathy at presentation (Yes/No)	3.664	.526	48.602	.000	39.007	13.925	109.263
Constant	-1.259	1.382	.830	.362	.284		

Nagelkerke R Square = 45.1% Cox & Snell R Square = 26.7%

patients. This inpatient mortality was 16.5% in our studied cirrhotic patients. Numerous factors influence the sequel of hospitalization in victims suffering complications of liver cirrhosis. Muhammad A Alsultan et al detected poorend results of hospitalization in the liver cirrhosis patients who had advanced age, high MELD score and elevated CTP score.[7] They also concluded that elderly age was amaverick risk indicator for the mortality amongst liver cirrhosis patients (p=0.004). Similarly, Cheng-Yi Chen and team members[14] detected that age more than 75 years was notably associated with in-patient mortality. In our analysis, the death group of the patients has a little higher mean age as compared to recovered patient's group; however, the correlation was insignificant (p=0.743).When we put in the logistic regression, only two factors (viral etiology for cirrhosis and hepatic encephalopathy) were principally predictive of death in cirrhotic patients. In 2017, Jasmohan S. Bajaj et al[15] found the hepatic coma as prime contributor to mortality among liver cirrhosis patients.

In our regression statistics of 8 prognosticator, the highest odds ratio was 39 times higher mortality rate for the hepatic encephalopathy patients. In our societies, patients in hepatic encephalopathy present to medical floors late.[16] The recovery from hepatic encephalopathy is inversely proportional to the length of the period passed after onset of the encephalopathy.[17] So, proper education of the liver cirrhosis patients regarding early hospitalization when encephalopathy starts should be done during their routine follow up visits in out-patient departments (OPD). Secondly, during hospitalization proper steps of the management including adequate purgation where large volume rectal lactulose enemas should be considered. Large volume rectal lactulose enema1[18,19,20] requires rectal tube placement. Such steps are usually missing in our patients now a days. After recovery from hepatic encephalopathy, proper education of these patients must include to inform them to avoid sleeping pills[21] and over-diuresis[22] for cosmetic reason. Most of our cirrhotic patients are fan of undue mobilizing of their mild ascites and ankle edema for cosmetic reason only inspite of the facts that they are facing hepatic encephalopathy repeatedly. General practitioners and quacks help them to take diuretics himself/herself without prescribing by a specialist consultant. Our data proposed that viral etiology for cirrhosis and hepatic encephalopathy at the presentation in hospital are distinct predictors of mortality among admitted cirrhotic patients where viral etiology for liver disease is a preventable and hepatic encephalopathy is manageable condition. So, effective measures can help to reduce the mortality in admitted cirrhotic patients.

CONCLUSION

The mortality rate was high amongst the studied hospitalized patients suffering liver cirrhosis. The mortality was significantly inflated in group of patients with hepatic encephalopathy and viral etiology for cirrhosis. However, it was not associated with age, weight, gender, presence of diabetes and hypertension. History of previous hospitalization was found significant contributor for mortality in bivariate study; however, association was proved insignificant during logistic regression analysis. Prevention from hepatotropic viruses and marvelous management steps of hepatic encephalopathy can effectively turn down the mortality rate amongst cirrhotic patients in our population.

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DEMOGRAPHIC FEATURES AND FREQUENCY OF RISK FACTORS AMONG THE PATIENTS SUFFERING FROM ACUTE ST ELEVATION MYOCARDIAL INFARCTION

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How to cite: Raza MH, Rafiq Q, Riaz A, Akhtar H, Janjua AA, Bilal M. Demographic features and frequency of risk factors among the patients suffering from acute ST elevation myocardial infarction. JAIMC. 2020; 18(4): 582-86.

Abstract

Objectives: To determine the demographic features and frequency of different risk factors of acute ST elevation myocardial infarction (STEMI) among patients admitted at tertiary care hospital, Gujranwala, Pakistan.

Methods: This cross-sectional analysis was carried out in the Department of Cardiology/ Medicine, GMC Teaching hospital, Gujranwala from June 2017 to May 2018. After informed consent, data of acute STEMI patients was collected by purposive sampling. Statistical analysis was executed by SPSS version 25.Age, weight, height and the BMI of the patients were the quantitative variables, while history of (H/O) smoking, hypertension, diabetes mellitus, personal history of ischemic heart disease, obesity, history of ischemic heart disease in male family member of age less than 55, and history of ischemic heart disease in female family member of age less than 45 were the qualitative variables. During descriptive interpretation of the data, quantitative variables were stated as mean and standard deviation. Frequencies and percentages were computed for different qualitative variables.

Results: Out of the total of 430 patients, 78.4% (n-337) were male while 21.6% (n=93) were female. The mean age of the patients was 53.59 + 12.51 years, the mean weight was 74.77 + 11.84 kilogram, the mean height was 65.49 + 2.24 inches, while the mean BMI was 27.03 + 4.19 Kg/m2. 54.7% (235 out of 430 patients) had history of smoking, 54.2% (233 out of 430 patients) were hypertensive, 28.4% (122 out of 430 patients) were diabetics, 22.3% (n=96) were obese, 27.7% (n=119) had personal history of ischemic heart disease, 10.2% (n=44) had history of ischemic heart disease in male family member of age less than 55, and 9.8% (n=42) had history of ischemic heart disease in female family member of age less than 45.

Conclusion: Male gender was mainly affected by acute STEMI in our studied population. The smoking was the most prevalent risk factor for myocardial infarction, followed by hypertension, diabetes, personal history of ischemic heart disease, obesity, history of ischemic heart disease in male family member of age less than 55, and history of ischemic heart disease in female family member of age less than 45. Adequate reduction in the reversible risk factors can minimize the cases of myocardial infarction in our society.

Keywords: Demographic features, risk factors, STEMI, Age, cross-sectional study, SPSS

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Acute ST-elevation myocardial infarction (STEMI) is a lethal disease which is one of the leading causes of death throughout the world.[1] Its happening is related to abrupt occlusion of the blood flow to cardiac tissue from one or more of the heart arteries.[2] As a consequence, myocardial necrosis starts generally in the endocardium and extends towards the epicardium.[3] The most efficacious management for the acute STEMI is the prompt

reinstating the patency of the occluded artery either by PCI or fibrinolysis.[4] The American guidelines about heart diseases propose primary percutaneous coronary intervention (PCI) as the favored treatment stragedity for STEMI patients,[5] however in our environments fibrinolysis is used widely due less availability of PCI. In USA, the incidence of first heart attack is approximately stable during last 10 years, that is 1.7% and 1.1% per year in women and men, respectively.[6] The people of our subcontinent are more prone to myocardial infarction, where annual incidenc is approx 6.44%.[7] The major known risk factors of MI include smoking, diabetes mellitus, hypertension, and dyslipidemia.[8] The recent studies have also linked these risk factors with premature coronary artery disease.[9] The known risk factors of first acute myocardial infarction among youngs diverge from that of eldely,[10] where dyslipidemidemia, smoking, family history of myocardial infarction, and male gender are known common factors among youngs, while diabetes and systolic hypertension are common factors among elderly people.[11] The literature focusing such amplifications from Pakistan is lacking. Therefore, the author is desirous to determine the demographic features and frequency of different risk factors of acute ST elevation myocardial infarction (STEMI) among patients admitted at tertiary care hospital, Gujranwala, Pakistan.

METHODOLOGY

This was a cross-sectional analysis which was carried out in the Department of Cardiology/ Medicine, GMC Teaching hospital, Gujranwala from June 2017 to May 2018. Keeping the confidence interval of 95% and 50% distribution of the response, the calculated sample size was 377 for a total population size of 20000. After written informed consent from all the patients, the data was gathered by purposive sampling using a structured proforma. All the patients diagnosed with ST segment elevation myocardial infarction (STEMI) who were hospitalized were included in this study. The diagnosis of STEMI was made by ST segment elevation and raised cardiac enzymes in a patient with acute chest pain. Left bundle branch block or left ventricular hypertrophy cause secondary ST-T changes. Here cardiac troponins were especially used to help diagnosis. The statistical analysis was executed using the Statistical Package for Social Science (SPSS), version 25. Age, weight, height and the BMI of the patients were the quantitative variables, while history of (H/O) smoking, hypertension, diabetes mellitus, personal history of ischemic heart disease, obesity, history of ischemic heart disease in male family member of age less than 55, and history of ischemic heart disease in female family member of age less than 45 were the qualitative variables. During descriptive interpretation of the data, quantitative variables were stated as mean and standard deviation. Frequencies and percentages were computed for different qualitative variables.

RESULTS

Out of the total of 430patients who presented with acute STEMI, 78.4% (n-337) were male while 21.6% (n=93) were female (Picture 1).The mean age of the patients was 53.59 + 12.51 years with a range from minimum 24 to maximum 90 years. The minimum weight of the patients was 40 kilograms and maximum was 130 kilograms, and the mean value was 74.77 + 11.84 kilogram. The mean height of the patients suffering acute STEMI was 65.49 + 2.24 inches with a range of 57-70 inches. The mean BMI was 27.03 + 4.19 Kg/m^2 with a minimum value of 15.6 Kg/m^2 and maximum limit of 41.1 Kg/m^2 (Table 1). The percentage/ frequency distribution of the risk factors among our studied patients suffering acute STEMI was as follow: 54.7% (235 out of 430 patients) had history of smoking, 54.2% (233 out of 430 patients) were hypertensive, 28.4% (122 out of 430 patients) were suffering diabetes mellitus as well, 22.3% (n=96) patients were obese, 27.7% (n=119) had personal history of ischemic heart disease, 10.2% (n=44) had history of ischemic heart disease in male family member of age less than 55, and 9.8% (n=42) had history of ischemic heart disease in female family member of age less than 45

(Table 2).

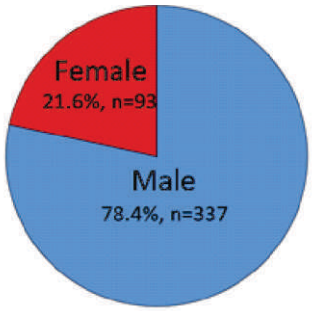

Fig.1: *Gender of the Patients Suffering Acute STEMI (n = 430)*

Table 1: *Descriptive Statistics of Different Quantitative Variables of Patients Suffering Acute STEMI (n=430)*

Quantitative variables	Mini.	Max.	Mean	Standard deviation
1. Age (years)	24	90	53.59	12.510
2. Weight (Kilogram)	40	130	74.77	11.843
3. Height (inches)	57	70	65.49	2.242
4. BMI (Kg/m^2)	15.6	41.1	27.032	4.1850

Table 2: *Frequency distribution of different risk factors among patients suffering acute STEMI (n=430)*

Risk factors of MI	Percentage (Number of cases)
1. H/O Smoking	54.7% (235)
2. H/O Hypertension	54.2 (233)
3. H/O Diabetes mellitus	28.4 (122)
4. H/O Obesity	22.3 (96)
5. Personal H/O IHD	27.7 (119)
6. H/O of IHD in male family member <55years	10.2 (44)
7. H/O of IHD in female family member <45years:	9.8 (42)

DISCUSSION

There are miscellaneous changeable and non-changeable risk factors related with myocardial infarction. The addition of a risk factor results acute myocardial injury at younger age is a known fact,[12] hence changable factors must be inscribed to circumvent the earlier disease. Fifth decade was the mean age of the patients affected by acute STEMI in the majority studies. F kiani et al studied 213 patients suffering acute myocardial infarction, where the mean age of the patients was 58.3 + 12.6 years.[13] In a similar study from Pakistan by Muhammad Ajmal Mlaik and his colleagues, the mean age of acute STEMI patients was 54.99±11.25 years.[14] Similary, in our study, the mean age of the patients was in the same decade i.e. it was 53.59+ 12.51 years. Arsalan Majeed Adam et al from Karachi found dyslipidaemia (91.2%) as the most prevalent risk factor, followed by hypertension, diabetes mellitus, parental history of disease, where smoking (29.2%) was the least prevalent one factor.[15] In our studied population, smoking (54.7%) was the most prevalent risk factor of acute myocardial infarction. Another mith that obesity is found at peak in Gujranwala's people, may not be realistic fact. In our data from this city, prevalence of Obesity (22.3%) among STEMI suffering patients comes at 4th number, after smoking, hypertension and diabetes. Similarly, Abdul Ghaffar Memon studied risk factors of acute Stemi at Hyderabad, Pakistan. His findings were in concordrant to our data. He noted that smoking (65.9%) was the most frequent risk factor followed by hypertension (42.0%) and diabetes mellitus (34.1%).16In Sudan, it was found that Smokers have 3.71 times higher risk of myocardial infarction than non-smokers.[17] According to Emily M. Bucholz, compared to non-smokers, ongoing smokers affected by acute myocardial infarction were younger (mean age 77.20 + 7.40 vs 72.41 + 5.82 years).[18] Diabetes mellitus is an entrenched risk factor that rises the risk of coronary heart disease by two to four times.[19] This is because diabetes smoothens the development of atherosclerotic plaque and rises the rate of atherscleroticprogression.[20] In our study, diabetics were 28.4% among patients suffering acute myocardial infarction which is a big proportion in comparison to prevalence of the diabetes itself among our populations. In old age, hypertension is even deadful for heart and blameworthy for approximately 70% of the cardiac diseases.21In our study, hypertension was seen in more than half of the patients (54.2%). Obese patients suffer coronary artery disease at an

earlier age.[22] In a similar data from North Punjab, Pakistan, Riffat Iqbal et al found that patients with a positive family history of heart disease acomplished myocardial event at an ealier/ immature age (P = 0.0001).[23] A lot number of the risk factors present in our patients suggest that addressing these preventable evils, we may escape the lethal consequences of this acute myocardial event in our people. The preventable risk factors like smoking is prevailing in our people, so hope for the betterment exist for our patients. If awareness programmes address the issue, it will results a decremental response in the myocardial infarction cases.

CONCLUSION

Male gender was mainly affected by acute STEMI in our studied population. The smoking was the most prevalent risk factor for myocardial infarction, followed by hypertension, diabetes, personal history of ischemic heart disease, obesity, history of ischemic heart disease in male family member of age less than 55, and history of ischemic heart disease in female family member of age less than 45. Adequate reduction in the reversible risk factors can minimize the cases of myocardial infarction in our society.

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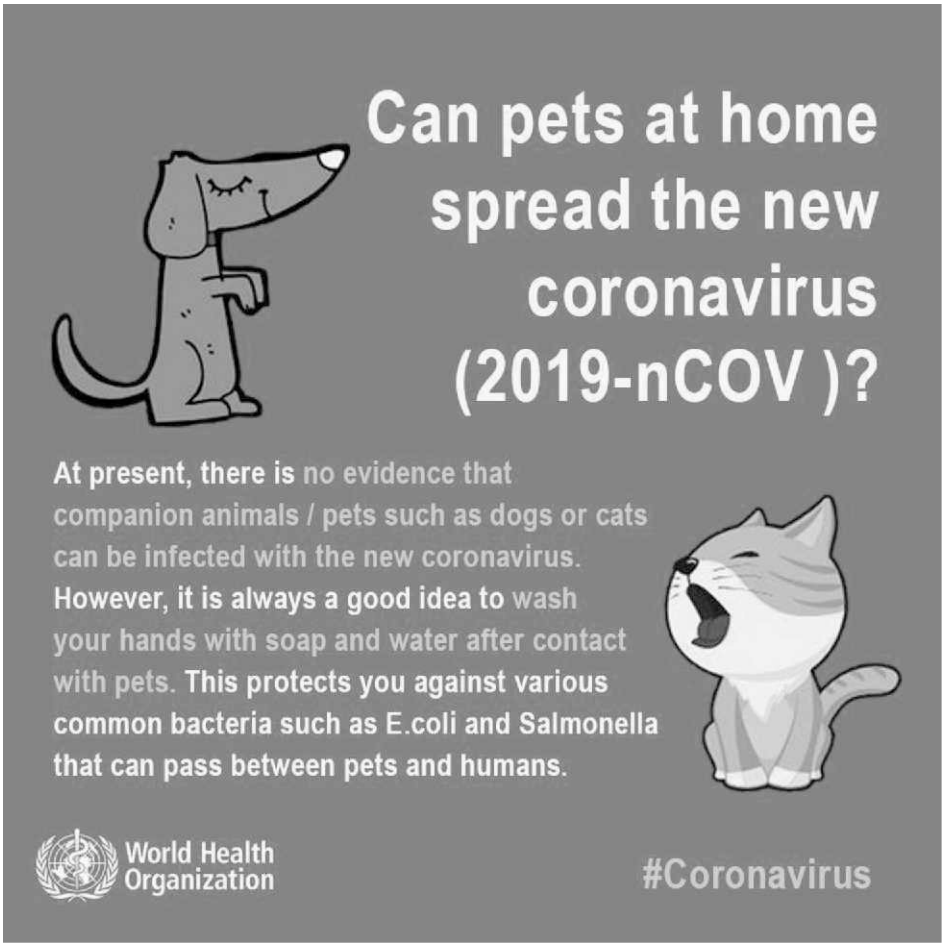

PEDIATRIC AND NEONATAL SEPSIS: BACTERIOLOGICAL PROFILE AND ANTIBIOTIC SUSCEPTIBILITY PATTERN IN A TERTIARY CARE HOSPITAL OF LAHORE

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How to cite: Mubeen A, Jabeen K, Rasheed F, Rashid F, Husnain S, Ahmad I, et al. Pediatric and neonatal sepsis: bacteriological profile and antibiotic susceptibility pattern in a tertiary care hospital of Lahore. JAIMC. 2020; 18(4): 587-90.

Abstract

Background: Septicemia in neonates refers to generalized bacterial infection documented by positive blood culture in the first four weeks of life and is one of the four leading causes of neonatal mortality and morbidity. Blood culture is the gold standard for the diagnosis. Emergence of multidrug resistant bacterial strains is a major problem in the management of sepsis. Present study was undertaken to identify the common bacterial pathogens associated with pediatric sepsis and to determine their antibiotic susceptibility pattern.

Methodology: This cross-sectional study was designed to isolate and identify the bacterial etiologic agents responsible for neonatal sepsis and to determine the susceptibility pattern of isolates in a tertiary care hospital in Lahore Pakistan from 1st august 2019 to 30 January 2020.1545 clinical specimens obtained from both indoor and outdoor patients, were cultured using standard microbiological techniques and antimicrobial susceptibility pattern was evaluated using modified Kirby Bauer disc diffusion method following the CLSI guidelines 2019.

Results: Out of 1545 samples 296 were culture positive. Gram negative organisms were predominant than gram positive. Most common pathogen was E. coli (21%) followed by Klebsiella pneumoniae (18%), Staphylococcus species (16%), Acinetobacter buminai (14%), Salmonella typhi (11%), Pseudomonas aeruginosa (7%), Burkhulderia cepacian (6%), Stenotrophomonas species (2%), Enterobacter (1%), and Proteus mirablis (1%).

Conclusion: Majority of the gram-negative isolates were sensitive to polymyxin and imipenem while gram positive was sensitive to vancomycin, teicoplanin and linezolid.

Key words: Neonatal sepsis, Pediatric, Polymyxin

Blood stream infections (BSIs) are an important cause of referrals, admissions, morbidity and mortality among newborns and infants. Timely diagnosis and treatment of bacteremia is essential.[1]

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Submission Date: 12-06-2020
1st Revision Date: 15-07-2020
2nd Revision Date: 19-08-2020
Acceptance Date: 02-09-2020

World Health Organization has estimated that 1.6 million deaths occur globally every year due to neonatal infections and 40% of all neonatal deaths occur in developing countries.[2]

Several risk factors have been identified in the neonates and children, which make them susceptible to infections. The risk factors for neonatal septicemia include premature rupture of membrane, prolonged rupture, prematurity, Urinary Tract Infection, poor maternal nutrition, low birth weight, birth asphyxia and congenital anomalies.[3] The children at risk of septicemia include infants, children with serious injury and children on chronic antibacterial therapy, malnourished children, children with chronic medical problems, and children with immunosuppressants.

Polymicrobial sepsis occurs in high risk patients and is associated with catheters, gastrointestinal diseases, neutropenia and malignancy.[4]

Knowledge of pathogens causing infections in young infants is essential for designing community-based management strategies[5]. The spectrum of organisms causing neonatal sepsis changes overtime and varies from region to region and hospital to hospital even in the same city/country.[6] Bacteria commonly isolated in the samples included Klebsiella pneumoniae, Escherichia coli, Enterobacter species, Pseudomonas aeruginosa and Staphylococcus aureus.[7]

In developing countries, the rate of detection of bacterial pathogen is generally low due to poor laboratory techniques and lack of technical expertise. In spite of recent advancement in diagnostic molecular techniques for microbiological diagnosis of sepsis, conventional blood culture is still the gold standard. However, it has some limitations, i.e. prolonged time of reporting and high rate of contamination. Overdiagnosis of pathogens leads to administration of unnecessary antimicrobial agent. It will result in high cost and toxicity and diverts the attention of the clinician from treating the actual causative agent.[8,9]

The present study was undertaken to study the bacteriological profile and the antimicrobial sensitivity pattern of septicemia in neonates and infants.

METHODOLOGY

This cross-sectional study was conducted at the of Jinnah Hospital pediatric ward and Pathology Department of the Allama Iqbal Medical College, Lahore, Pakistan, from august 2019 to January 2020.

Blood samples of 1545 individuals were obtained aseptically from peripheral veins with the help of butterfly needles.

One milliliter (neonates) and 5 ml (children) blood was collected and inoculated into 10 and 50 ml, respectively, of brain heart infusion broth (1:10 dilution). The culture bottles were incubated at 37°C aerobically and periodic subcultures were done onto MacConkey's agar and blood agar after overnight incubation on day 3, day 4 and finally on day 7. The growth obtained was identified by conventional biochemical tests.

Analytical profile index (API) was put up for gram-negative pathogen, if necessary. Quality control (QC) was done at the start of the study and after 50 tests. The standard disk diffusion test for susceptibility to routine antibiotics was done by modified Kirby-Bauer method. Zone sizes were measured and interpreted according to CLSI guidelines.

Table 1: *Antibiotic Profiles of Organisms (Percentage Resistant)*

Antibiotics	Acinetobacter spp. N=42	E. coli N=63	Klebsiella spp. N=54	Pseudomonas aeruginosa N=21	Salmonella spp. N=35
Aug (Augmentin)	–	60%	54%	–	–
Amp (Ampicillin)	–	90%	100%	–	79%
TZP(Tazobactam/piperacillin)	30%	30%	60%	100%	60%
CAZ(Ceftazidime)	NA	NA	62%	62%	–
CTR(Ceftriaxone)	65%	50%	62%	–	60%
Amk (Amikacin)	70%	70%	62%	80%	–
Gen (Gentamicin)	73%	80%	65%	64%	–
CPR(Ciprofloxacin)	77%	80%	39%	67%	85%
Imi (Imipenem)	48%	40%	52%	47%	0%
Mero (Meropenem)	63%	30%	42%	70%	0%
Cot(co-trimoxazole)	65%	60%	62%	–	80%
Poly (Polymyxin B)	0%	0%	0%	0%	–
Azt (Azithromycin)	–	–	–	–	0%
CHL(Chloramphenicol)	–	–	–	–	90%

RESULTS

During the 6-month study period, 1545 blood cultures were analyzed. Among them, 107 were from neonates. 296 samples showed growth and all infections were due to a single organism. Gram negative organisms were predominant than gram positive. Most common pathogen was E. coli (21%) followed by Klebsiella pneumoniae (18%), Staphylococcus species (16%), Acinetobacter buminai (14%), Salmonella typhi (11%), Pseudomonas aeruginosa (7%), Burkhulderia cepacian (6%), Stenotrophomonas species (2%), Enterobacter (1%), and Proteus mirablis (1%).

Table 2: *Antibiotic Profiles of Organisms (Percentage Resistant)*

Antibiotics	Burkhulderia N=18	Stenotrophomonas N=7	Staphylococcus spp. N=48
COT(Co-trimoxazole)	25%	0%	-
CPR(Ciprofloxacin)	88%	100%	77%
Mero (Meropenem)	63%	-	-
CPZ(Cefoperazone)	100%	100%	-
Poly (Polymyxin B)	-	0%	-
Aug (Augmentin)	-	-	72%
Amp (Ampicillin)	-	-	81%
CXT(Cefoxitin)	-	-	77%
Pen (Penicillin)	-	-	81%
Amk (Amikacin)	-	-	72%
Gen (Gentamycin)	-	-	72%
Doxy (Doxycycline)	-	-	81%
Ery (Erythromycin)	-	-	77%
CLN(Clindamycin)	-	-	77%
Van (Vancomycin)	-	-	0%
TCP(Teicoplanin)	-	-	0%
LNZ(Linezolid)	-	-	0%
Fus (Fusidic acid)	-	-	43%

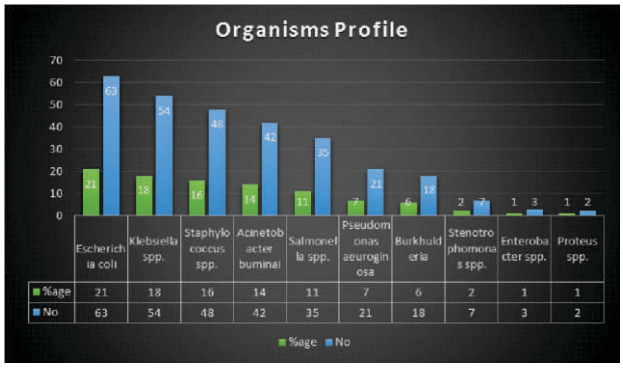

Figure No.1

DISCUSSION

Neonatal Septicemia (NS) has been documented as a leading cause of mortality and morbidity all over the world[10]. World Health Organization (WHO) reported over 4 million neonatal deaths occur each year globally; 3 million of these deaths occur in early neonatal period. Mortality rate of NS has been more prevalent in developing countries which account 98% of deaths in neonates.[11] UNICEF (2009) reported that more than 500 neonates die daily in Pakistan and mortality rate is 54/1000 live births (LBs). About 40% of these deaths are due to infections and asphyxia. Amongst Asian countries, Pakistan has the eighth highest rate of newborns deaths.[12]

In our study 1545 peeds and neonatal blood samples were observed from which 296 samples were culture positive. A similar study was done in Peshawar in which 2,685 blood samples were analyzed. From them 1,534 were found culture positive for bacterial growth. E. coli was the predominant organism in their study followed by other gram negative and positive organisms that was also similar to our study.[13]

A low blood culture isolation rate could be due to administration of antibiotic before blood collection from the primary centers or the possibility of infection with anaerobes. A negative blood culture does not exclude sepsis and about 26% of all neonatal sepsis could be due to anaerobes.[14]

Antibiotic susceptibility pattern was studied for all isolates causing neonatal sepsis. The analysis of drug resistance pattern showed that, among Gram-negative isolates, maximum numbers (97%) were resistant to ampicillin and zero resistance to Polymyxin/ Colistin except intrinsically resistant organisms. Resistance was observed to be against commonly used antibiotics such as ampicillin, co-amoxiclav, and co-trimoxazole. Among Gram-positive isolates, high resistance was seen to penicillin (89%), and co-amoxiclav (72%). Zero resistance was seen to Vancomycin, Teicoplanin and linezolid. Similar results were found in another study that was carried out in India. Gram-negative isolates, maximum numbers

(97%) were resistant to ampicillin and lowest to imipenem (7%). Resistance was observed to be against commonly used antibiotics such as ampicillin, amoxiclav, cephalexin, and co-trimoxazole. Among Gram-positive isolates, high resistance was seen to penicillin (90%), cloxacillin (84%), and amoxiclav (76%). Least resistance was seen to linezolid (9%), followed by tetracycline (32%), and piperacillin/tazobactam (36%).[15]

In this study, maximum sensitivity was observed in Polymyxin, vancomycin, teicoplanin and linezolid. Sensitivity of these drugs was much higher than that to other antibiotics, but these drugs should not be used indiscriminately and be kept as a reserve drugs, otherwise resistance to these drugs may develop, thereby threatening the treatment.

CONCLUSION

Conventional blood cultures are an important aide in sepsis management. Most microorganisms in our study were susceptible to the empirical antibiotics used. Aseptic practices in handling patients helps limiting infection by Staphylococci and MRSA. Large scale studies will further improve our observations.

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EFFICACY OF 1% ACETIC ACID IN SUPERFICIAL SKIN AND SOFT TISSUE WOUNDS INFECTED WITH PSEUDOMONAS AEUREGINOSA

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How to cite: Munir F, Aqeel CM, Ilyas R, Mehmood K, Arshad A, Naveed M. Efficacy of 1% acetic acid in superficial skin and soft tissue wounds infected with Pseudomonas aeureginosa. JAIMC. 2020; 18(4): 591-96.

Abstract

Objective: To study the efficacy of 1% acetic acid in superficial skin & soft tissue wounds infected with pseudomonas aeureginosa.

Methods: All registered patients through Sugical unit II of Gulab Devi hospital OPD were recruited. After taking informed consent, irrigation of wounds and 1% acetic acid soaked gauze dressing for 24 hours were done for 6 days. Culture was sent on 6th day to see results. Efficacy end point was reached by negative culture report of pseudomonas aeureginosa on 6th day by two swabs taken from wound to minimize the error of contamination and outcome was recorded accordingly. The data was entered and analyzed in SPSS version 20.0 computer program. Quantitative variables such as age and BMI were presented as mean and standard deviation. Qualitative variables such as gender, wound category, diabetes mellitus, anemia, smoking (>5pack year), wound site and efficacy were presented as frequency and percentage. Data was stratified for age, gender, BMI, diabetes mellitus, anemia, smoking and wound site to control effect modifiers. Post stratification chi square test was applied taking p-value < 0.05 as significant.

Results: Culture of Pseudomonas aeureginosa on 6th day were negative in 87.69% patients whereas 12.30% patients still had Pseudomnas in their wounds.

Conclusion: The efficacy of 1% acetic acid in the treatment of skin and superficial soft tissues wounds infected with Pseudomonas aeureginosa was 87.69%.

Key words: Pseudomonas aeureginosa, acetic acid, infection

Injury to skin due to various etiology compromises the physical barrier against invading microorganisms and suppresses host immune system that facilitates colonization of pathogens and infection in wounds.[1] Pseudomonas infections are caused by a free-living opportunistic gram negative bacterium, Pseudomonas Aeureginosa. They favor moist areas and are widely found in soil and water. The bacteria can be spread in hospitals via the hands of healthcare workers, or by hospital equipment that is not properly cleaned.[2] Biofilms are bacterial communities residing within a polysaccharide matrix that are associated with persistence and antibiotic resistance in chronic infections. Pseudomonas aeureginosa develops biofilm a special consortium of bacteria which is composed of polysaccharides, protein and DNA. This biofilm is responsible of prolongation of infection by developing resistance against host defense and antibiotics.[3] Due to its resistance Pseudomonas aeureginosa is leading cause of hospital acquired microbial infection with significant mortality.[4] Pseudomonas aeureginosa and staphylococ-cus both are the most common organism in acute and chronic wound infections. Their prevalence in infections as well as trauma and burn is increasing. Poly-

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Submission Date: 06-08-2020
1st Revision Date: 11-09-2020
Acceptance Date: 19-09-2020

microbial burden delays wound healing and also enhances antimicrobial drug resistance by developing biofilm. Pseudomonal infections (eg, bacteremic pneumonia, sepsis, burn wound infections, meningitis) are associated with an extremely high mortality rate. Combination therapy with antipseudomonal antibiotics is used to ensure treatment of resistant strains and to prevent selection of resistant mutants. Carbapenems (eg, imipenem, meropenem) and the monobactam the monobactam antibiotic aztreonam are generally reserved for serious infections caused by organisms resistant to other beta-lactam antibiotics or in those with renal disease who are at risk for aminoglycoside-related nephrotoxicity.[5,6]

Healing is affected by pH of wound environment. Studies show acidic environment increases antimicrobial activity, alters protease activity and promotes angiogenesis and re-epithelization.

Wound toilet has pivotal role in wound management. Irrigation with normal saline and antiseptic has important role in reducing pathogens load of wound. It is observed that irrigation with antiseptic may be toxic to tissue and delays healing. Washing wound with normal saline and natural organic acids for example citric acid, boric acid, acetic acid, ascorbic acid and algenic acid have also role in controlling Pseudomonal wound infection.[7]

Acetic acid eliminated Pseudomonas aeureginosa in 87.5% i.e 14 out of 16 patients. Al-Bran and Khan in 2010 studied effect of 1% acetic acid in burns wounds against Pseudomonas aeureginosa and found it effective in 90% cases.[8] Excellent bactericidal effect of acetic acid against Pseudomonal infection is seen in experimental trial in burn units[9]. Normal saline and topical 1% acetic acid irrigation of wounds eliminated Pseudomonas aeureginosa in 11 and 4.5 days respectively with P-value was < 0.001.[10]

Effect of acetic acid against mature biofilm of Pseudomonas aeureginosa and Staphylococcus aureus is studied which shows 0.5% to 1% acetic acid completely eradicated biofilm.[11,12] Twenty nine different isolates of common wound infecting pathogens were tested against 0.16% to 0.31% of acetic acid and it is found effective antimicrobial and destroy mature biofilm in 23 isolates (79.3%).[13]

No specific local literature in last five years regarding efficacy of 1% acetic acid in Pakistan is available. There is one study efficacy of 1% acetic acid in control of Pseudomonas wound infection control carried in and paper presented in 13th annual symposium of Jinnah Postgraduate Medical center, Karachi, 8-13 December,1976.[14]

Our objective was to see efficacy of 1% acetic acid as it is a cheap, safe and easily available for Pseudomonas aeureginosa control which is common burden of prolong hospital stay of patients on surgical floor. This study will provide a reference point for acetic acid role against Pseudomonas aeureginosa for clinical practice.

METHODOLOGY

This was a Descriptive case study conducted in Surgical unit II, Gulab Devi Hospital, Lahore. Estimation of sample size was 130 and Margin of error was 7%. The Confidence level was 95% in this study. The Sampling technique used was non-probability consecutive sampling. The duration of Study was Six months from feb 2019 to july 2019.

The study was conducted in all adult population of both male and female between 18 years to 70 years of age with pseudomonas infected wounds on culture.

Malignancy, signs of systemic sepsis e.g fever >101oF that needed antibiotic treatment, 3rd and 4th degree burn, mucocutaneous ulcer for example mouth angle, nose and near eyes as acetic acid may cause allergic irritation of mucous membranes are exclusion crieteria in this study.

All registered patients through OPD were recruited and after taking informed consent, their wounds were irrigated with 1% acetic acid. Irrigation of wounds and 1% acetic acid soaked guaze dressing were done for 24 hours for 6 days. Culture was sent on 6th day to see results. Efficacy end point

was reached by negative culture report of pseudomonas aeureginosa on 6th day by two swabs taken from wound to minimize the error of contamination and outcome was recorded accordingly.

The data was entered and analyzed in SPSS version 20.0 computer program. Quantitative variables such as age and BMI were presented as mean and standard deviation. Qualitative variables such as gender, wound category, diabetes mellitus, anemia, smoking (>5pack year), wound site and efficacy were presented as frequency and percen-tage. Data was stratified for age, gender, BMI, diabetes mellitus, anemia, smoking and wound site to control effect modifiers. Post stratification chi square test was applied taking p-value < 0.05 as significant.

RESULTS

One hundred and thirty patients with superficial skin and soft tissue wounds infected with pseudomonas aeureginosa were included in the study.

The BMI was less than 18.5 kg/m^2 (underweight) in 9 (6.92%) patients, between 18.5-25 kg/m^2 (normal) in 30 (23.07%) patients, between 25-30 kg/m^2 (over weight) in 73 (56.15%) patients and more than 30 kg/m2 (obese) in 18 (13.84%) patients.

The surgical site infection of wounds were seen in 54 (41.53%) patients, burns in 47 (36.15%) and post traumatic wounds were seen in 29 (22.30%) patients. (Table 1)

Diabetes mellitus was present among 59(45.38 %) patients while it was not present among 71 (54.61%) patients. Anemia (Hb level <7mg/dl) was observed in 11 (8.46%) patients while it was not observed in 119 (91.5%) patients. Smoking (>5pack year) was present in 38 (29.23%) patients while 92 (70.76%) patients were non-smoker. Out of 130 superficial skin and soft tissue wounds, 5(3.84%) wounds were present on head and neck region, 14(10.76%) wounds on upper limbs, 59 (45.38%) wounds on thorax and abdomen area and 33 (25.38%) wounds were present on lower limbs .

Culture of pseudomonas aeureginosa on 6th day was positive in 16 (12.30%) patients and the cultures of wounds for pseudomonas aeureginosa of 114 (87.69%) patients were found negative on 6th day (Table 2).

Efficacy of 1% acetic acid in the treatment of skin and superficial soft tissues infected with pseudomonas aeureginosa was present among 114 (87.69%) patients while it was not present among 16 (12.30%) patients .

Out of 9 patients whose BMI was less than 18.5 kg/m^2, efficacy of 1% acetic acid in the treatment of skin and superficial soft tissues infected with pseudomonas aeureginosa was seen in 8 (88.89%) patients. Out of 30 patients whose BMI was between 18.5 -25kg/m^2, efficacy of 1% acetic acid was seen in 29 (96.67%) patients. Out of 73 patients whose BMI was between 25-30 kg/m2, efficacy of 1% acetic acid was seen in 64 (87.67%) patients. Out of 18 patients whose BMI was more than 30kg/m^2, efficacy of 1% acetic acid was seen in 13 (72.23%) patients. The p-value was 0.003.

Out of 59 diabetic patients, efficacy of 1% acetic acid in the treatment of skin and superficial soft tissues infected with pseudomonas aeureginosa was seen in 50 (84.74%) patients. Out of 71 non diabetic patients, efficacy of 1% acetic acid was seen in 64 (90.14%) patients. The p-value was 0.001 (Table 3).

Out of 11 patients, whose Hb level was below 7mg/dl, efficacy of 1% acetic acid in the treatment of skin and superficial soft tissues infected with pseudomonas aeureginosa was seen in 9 (81.81%) patients. Out of 119 patients, whose Hb level was above 7mg/dl, efficacy of 1% acetic acid was seen in 105 (88.23%) patients. The p-value was 0.002. (Table 4)

Out of 38 smoker patients, efficacy of 1% acetic acid in the treatment of skin and superficial soft tissues infected with pseudomonas aeureginosa was seen in 33 (86.84%) patients. Out of 92 nonsmoker patients, efficacy of 1% acetic acid was seen in 81 (88.04%) patients. The p-value was 0.001 (Table 5).

Out of 5 patients, whose wounds were present in head and neck region, efficacy of 1% acetic acid in the treatment of skin and superficial soft tissues infected with pseudomonas aeureginosa was seen in 4 (80%) patients. Out of 14 patients, whose wounds were present on upper limbs, efficacy of 1% acetic acid was seen in 11 (78.57%) patients. Out of 59 patients, whose wounds were present on thorax and abdomen area, efficacy of 1% acetic acid was seen in 51 (86.44%) patients. Out of 33 patients, whose wounds were present on lower limbs, efficacy of 1% acetic acid was seen in 29 (87.87%) patients. The p-value was 0.917 (Table 6).

DISCUSSION

In this prospective clinical study of 130 patients, we assessed the efficacy of 1% acetic acid in the treatment of skin and superficial soft tissues infected with Pseudomonas aeureginosa. So far this is the largest clinical trial conducted in Pakistan.

The efficacy of 1% acetic acid in the treatment of skin and superficial soft tissues infected with pseudomonas aeureginosa in our study was 87.69%. The observation was almost similar to the results obtained by Basvaraj S et al. They showed efficacy of acetic acid in the wounds infected with pseudomonas aeureginosa was 87.5%.[7] However, Al-Bran and Khan et al showed efficacy of 1% acetic acid in the treatment of burn wounds infected with pseudomonas aeureginosa was 90%.[8] In a study by Augustine H et al, efficacy of acetic acid in the wounds infected with pseudomonas aeureginosa was 84.8%.[11] A study by Halested FD et al showed 79.3% efficacy of 0.16% to 0.31% acetic acid in the treatment pseudomonas aeureginosa infection.[13] In a study by Fearn J et al, 1% acetic acid was found to be effective against pseudomonas in vitro in 88 per cent of cases.[14] In a study by Sloss JM et al, efficacy of

Table 1: *Distribution of Patients by Wound Category (n=130)*

Wound category	No. of patients	Percentage (%)
SSI	54	41.53
Burn	47	36.15
Post traumatic	29	22.30
Others	0	0

Table 2: *Distribution of Patients by Culture of Pseudomonas Aeureginosa on 6th Day (n=130)*

Culture of pseudomonas aeureginosa on 6th day	No. of patients	Percentage (%)
Positive	16	12.30
Negative	114	87.69

Table 3: *Stratification of Data (Efficacy) with Effect Modifier (Diabetes Mellitus)*

Diabetes mellitus	Efficacy	
	Yes	No
	No.(%)	No.(%)
Present (n=59)	50 (84.74)	9 (15.25)
Not present (n=71)	64 (90.14)	7 (9.85)
P Value*	0.001**	

*Chi Square test **Significant

Table 4: *Stratification of Data (Efficacy) with Effect Modifier (Anemia)*

Anemia (Hb <7mg/dl)	Efficacy	
	Yes	No
	No.(%)	No.(%)
Present (n=11)	9 (81.81)	2 (18.18)
Not present (n=119)	105 (88.23)	14 (11.76)
P Value*	0.002**	

*Chi Square test ** Significant

Table 5: *Stratification of Data (Efficacy) with Effect Modifier (Smoking)*

Smoking	Efficacy	
	Yes	No
	No.(%)	No.(%)
Yes (n=38)	33 (86.84)	5 (13.15)
No (n=92)	81 (88.04)	11 (11.95)
P Value*	0.001**	

*Chi Square test ** Significant

Table 6: *Stratification of Data (Efficacy) with Effect Modifier (Wound Site)*

Wound site	Efficacy	
	Yes	No
	No.(%)	No.(%)
Head & neck (n=5)	4(80)	1(20)
Upper limb (n=14)	11(78.57)	3(21.42)
Thorax & abdomen (n=59)	51(86.44)	8(13.55)
Lower limb (n=33)	29(87.87)	4(12.12)
P Value*	0.917**	

*Chi Square test ** Not significant

0.5-5% Acetic acid in burn and ulcer was 87.5%.[15] In another study by Phillips I et al, efficacy of 5% Acetic acid on wounds was 70.0%.[16]

We also cross tabulated the efficacy of 1% acetic acid in the treatment of skin and superficial soft tissues infected with pseudomonas aeureginosa with effect modifier i.e age which showed significantly higher efficacy in age group 41-50 years i.e 93.1092.30% as compared to other age groups i.e 75% in age group of 18 – 20 years, 91.67% in age group of 21-30 years, 82.92% in age group of 31-40 years, 92.30% in age group of 51-60 years and 71.42% in age group of 61-70 years (P value < 0.05). We found the highest efficacy rate among middle age patient group.

The mean age of the patients in our study was 37.89 ± 9.83 years with an age range of (18 – 70 years). There was a female dominancy in our study (32% were male and 68.48% were female). We did not found any difference in efficacy among male and female population i.e 87.64% and 87.80% respectively (P value > 0.05).

We also cross tabulated the efficacy of 1% acetic acid in the treatment of skin and superficial soft tissues infected with pseudomonas aeureginosa with effect modifier i.e BMI which showed significantly higher efficacy in patients whose BMI is within 18.5-25 kg/m^2 i.e 96.67% as compared to other BMI groups i.e efficacy of 1% acetic acid was 88.89% in patients with BMI less than 18.5 kg/m^2, 87.67% in patients with BMI 25-30 kg/m^2, 72.23% in patients with BMI more than 30 kg/m^2 (P value < 0.05). We found the highest efficacy rate among normal BMI patient group.

We cross tabulated the efficacy of 1% acetic acid in the treatment of skin and superficial soft tissues infected with pseudomonas aeureginosa with effect modifier i.e diabetes mellitus which showed significantly lower efficacy in patients with diabetes mellitus i.e 84.74% while in patients who are non diabetics, the efficacy rate was significantly higher i.e 90.14% (P value < 0.05).

We cross tabulated the efficacy of 1% acetic acid in the treatment of skin and superficial soft tissues infected with pseudomonas aeureginosa with effect modifier i.e anemia which showed significantly lower efficacy in patients whose Hb level was less than 7mg/dl i.e 81.81% while in non anemic patients the efficacy was significantly higher i.e 88.23% (P value < 0.05).

We also cross tabulated the efficacy of 1% acetic acid in the treatment of skin and superficial soft tissues infected with pseudomonas aeureginosa with effect modifier i.e smoking which showed lower efficacy in smoker patients i.e 86.84% while in non smoker patients, the efficacy to 1% acetic acid was higher i.e 88.04% (P value < 0.05).

We also cross tabulated the efficacy of 1% acetic acid in the treatment of skin and superficial soft tissues infected with pseudomonas aeureginosa with effect modifier i.e wound site which showed higher efficacy in wounds over lower limb i.e 87.87 % as compared to the wounds over other regions i.e 80% in head and neck area wounds, 78.57% efficacy in wounds over upper limb and 86.44% efficacy in wounds over thorax and abdomen (P value > 0.05). We found the lowest efficacy rate among wounds over lower limbs.

The study has certain limitations. It was not a double blind study and carried in single centre on limited population size.

CONCLUSION

From the results of present study, it is concluded that 1% acetic acid is nontoxic, inexpensive and efficient topical agent for effective elimination of pseudomonas aeureginosa from superficial skin and soft tissue wounds. It is the best alternative when infection is caused by multiple antibiotic resistant strains and where there is shortage of therapeutic options.

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OBJECTIVE STRUCTURED CLINICAL EXAMINATION AS AN EXAMINATION TOOL-PERCEPTION OF UNDERGRADUATE STUDENTS

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How to cite: Mukhtar S, Azhar T, Nasreen M. Objective structured clinical examination as an examination tool – perception of undergraduate students. JAIMC. 2020; 18(4): 597-99.

Abstract

Background: OSCE –Objective structured clinical examination has been designed to assess students' clinical competence. The OSCE content and scoring procedures are standardized. Each examination station is designed to focus on an area of clinical competence. During OSCE every student experiences the same problem and is asked to perform the same task within the same timeframe.

Methodology: This study was conducted to explore perceptions of students regarding OSCE at the University College of Medicine & Dentistry. A validated questionnaire developed by Russell et al was distributed among the students after completion of their OSCE. The questions asked were related to the exam orientation, content of the exam, incorporation of knowledge, skills and attitude in the exam and comparison of various assessment tools.

Result: In this study 55% of the students considered exam as fair and 66% of the students rated the exam as very stressful. 50% of the students rated that they were fully aware of the nature of the exam, 52%of the students said that the tasks reflected those taught while 36%of the students said that they were satisfied with the duration of each station. Moreover, 54% of the students expressed that OSCE provided a true measure of skills. 60% of the students rated OSCE system to be one of the fairest methods.

Conclusion: Students' were of a viewpoint that OSCE was one of the fairest and standardized assessment tools being used. They perceived OSCE as a valid and reliable tool for assessment.

Key words: OSCE; perception: clinical assessment

In order to assess the clinical competence among the medical students Harden developed OSCE tool in 1975. In order to assess students' clinical competence various tools are being used in examination.[1,2]

The Objective Structured Clinical Examination is a method that involves assessment of various aspects of clinical components in a structured format.[3] An OSCE is structured and time bound, it includes multiple stations in which students perform various tasks which include history taking, performing a clinical method or counseling a patient. The learner at every station is assessed against a standard checklist.[4]

The OSCE was developed to improve the effectiveness of the assessment process at 'the shows how' level of Miller's Pyramid.[5]

This study was conducted at The University College of Medicine & Dentistry. At University College of Medicine and Dentistry we have implemented integrated curriculum. The goal of curriculum renewal was to ensure that the new curriculum was in line with recent educational approaches based on research. The curriculum comprises of both vertical and horizontal integration. The students are

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Submission Date: 07-08-2020
1st Revision Date: 16-08-2020
Acceptance Date: 29-08-2020

exposed to clinical training right form the day one. And their clinical component is assessed by both MCQs and OSCE.

The current study was designed to obtain students perception regarding OSCE as an evaluation tool that would help in further improvement.

METHODOLOGY

The current study was used to obtain the students perception regarding OSCE. Only those students who consented to participate were included. A pre-validated questionnaire developed by Russell et al was used. Permission to use the questionnaire was obtained through email. The questions in the questionnaire were on the domains of exam orientation, exam content, attitude and comparison of different assessment tools that are being used.

There were 20 OSCE stations and each station was of 4 minutes duration. In addition to this there was a rest station as well. The stations assessed students' knowledge, skills and attitude. It included standardized patients as well, all students were marked against a standard check list. The questionnaire was distributed among the students after they've completed their OSCE examination. Students were asked to compasre different assessment methods and assess the content and structure of the OSCE. They were also asked to comment on the usefulness of the OSCE as an examining tool.

RESULT

Half of the class reported that the exam was well structured, covered wide area of knowledge and practical component (54.5%). 60% of the students reported that they need more time for OSCE stations which is probably the reason that the exam was stressful (65%).

Half of the class reported that the exam was fair (55%). Thirty nine percent students reported that they were aware of the information that was required from them and 45% suggested that the exam minimized their chance of failing.

Students reported that they were not fully aware regarding the orientation of the exam. Half of the students reported that the OSCE was a useful experience. Half of the students were not sure whether their scores were an actual representation of their clinical skills or not.

Students rated OSCE as the most difficult tool of assessment. According to them the easiest tool of assessment is MCQs. Moreover, they reported that the most fairest assessment tool is MCQs followed by OSCE, according to them essay questions are the least fair form of the tool. The results showed that OSCE helps the students to learn the most and they learn least from viva and essay questions.

Most of the students reported that OSCE should be used more for their clinical assessment.

DISCUSSION

Half of the study population reported that the exam was fair and well structured which is consistent with the results of the study conducted in University of West Indies and New Castle medical Schools. The 68% students in these studies reported that the exam was fair and 82% reported that it was well structured.

Majority of the students reported that the exam was stressful which is consistent with the various studies that have been conducted previously.[6] Similarly, another study was conducted which showed increased anxiety levels.[7] Another study was conducted in Peshawar which reported that the fear of failing in exams results in increased anxiety levels among the students.[8]

Students in this study stated that OSCE provided them with learning opportunities, they reported that OSCE stimulates learning among them. A similar results in literature suggests that OSCE motivates the learners thus improving their performance.[9]

The last segment of the questionnaire compared different assessment methods. Students suggested that the OSCE was second fairest tool after MCQs they ranked SEQs as the least fairest tool which is consistent with the study conducted in Newcastle Medical School.[10]

In the end students reported that OSCE should be used more to asses their clinical skils. Literature also suggests that OSCE and OSPE are used to assess clinical competence in a structured and comprehensive manner.[11,12]

CONCLUSION

OSCE is an assessment of clinical competence that assesses the knowledge, skills and attitude in a planned and structured manner. In order to ensure the effectiveness of this tool it is essential that the exam is properly planned and executed.

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FREQUENCY AND ANTIMICROBIAL SUSCEPTIBILITY PATTERN OF GROUP B STREPTOCOCCUS IN PREGNANT WOMEN

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How to cite: Hameed F, Mirza IA, Faheem Q, Khurshid U, Danish M, Khalid A. Frequency and antimicrobial susceptibility pattern of group B Streptococcus in pregnant women. JAIMC. 2020; 18(4): 600-4.

Abstract

Objective: To determine the frequency and antimicrobial susceptibility pattern of Group B Streptococcus (GBS) in pregnant women.

Methodology: A cross sectional prospective study was conducted in the department of microbiology Combined Military Hospital Lahore. Consented participants' information was collected using structured questionnaire. A total of 275 recto-vaginal swabs were collected by non probability convenience sampling technique and inoculated on 5% blood agar for isolation of GBS. Antimicrobial susceptibility testing was performed according to the criteria of the clinical and laboratory standard institute (CLSI) guidelines 2015 by disk diffusion method. Data was entered and analyzed using SPSS version 20.0 software. Chi-square test was applied. A P-value of < 0.05 was considered statistically significant.

Result: The prevalence of GBS colonization among pregnant women was 6.5% (18/275). GBS colonization had no association with age or gravidity of the pregnant women ($P>0.05$). All GBS isolated were susceptible to penicillin, vancomycin, linezolid, ceftriaxone. Sensitivity of clindamycin, erythromycin, and doxycycline was 55.6%, 44.4% and 61.1% respectively.

Conclusion: Colonization of GBS in pregnant women and its transmission to the neonates is present in our population. This infection might be a silent clinical problem and therefore, requires awareness and effort for preventive measures. Resistance to the commonly used antibiotics suggests the importance of the screening of GBS colonization in pregnant women at 35-37 weeks of gestation and testing their antimicrobial susceptibilities in order to provide antibiotic prophylaxis.

Key words: Group B Streptococci, prevalence, antimicrobial susceptibility testing.

Group B Streptococcus (GBS) also known as Streptococcus agalactiae belongs to Lancefield group B. It is an established cause of maternal and neonatal morbidity and mortality as shown in many studies.[1] GBS are Gram positive, facultatively anaero-bic, beta-hemolytic diplococci. These are catalase negative. Colonies at 48hrs are 3-4mm in diameter, grayish white surrounded by a narrow zone of beta-haemolysis.[2]

GBS colonizes genital or lower gastrointestinal tract of 10-40% pregnant women.[1] Gastro-intestinal tract serves as the primary reservoir for GBS and is the likely source of vaginal colonization. Vaginal GBS colonization is asymptomatic and varies with the geographical location.[3,4] Vertical transmissions occurs after the onset of labor or rupture of fetal membrane. The rate of vertical transmission at the time of delivery is about 50%. The carriage rate in

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Submission Date: 19-08-2020
1st Revision Date: 27-08-2020
2nd Revision Date: 21-09-2020
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neonates born to GBS colonized mothers is 40-70% and 1-3% of the neonates colonized with GBS develop early onset Group B Streptococcal disease (EOGBSD). The most important risk factor for EOGBSD is maternal GBS colonization at the time of delivery.[5,6] Group B streptococci cause early onset (within 7 days) and late onset (7-89days) neonatal disease. Early onset group B streptococcal disease (EOGBSD) presents as meningitis, neonatal sepsis or pneumonia which are associated with high morbidity and mortality. In pregnant women it causes urinary tract infection, endometritis, chorioamnionitis, pneumonia and puerperal sepsis.[7]

The use of intrapartum prophylactic antibiotics has led to a decrease in rate of neonatal GBS disease.[8]

It is recommended by Centers for Disease Control and Prevention (CDC) that all pregnant women at 35–37 weeks should have prenatal screening of the vagina and rectum for GBS colonization. During labor GBS colonized women are given I/V Penicillin-G for intrapartum prophylaxis. The recommended dose is 5 million units of penicillin initially and then 2.5 million units every 4 hours until delivery. For use in women allergic to penicillin and at low risk for anaphylaxis cefazolin (2g initially, then 1g every 8 hours) is recommended. Those at high risk for anaphylaxis may receive clindamycin. In United States prevalence of resistance for clindamycin is 13-20% and erythromycin 25-32%.[5]

This study was conducted to find out the frequency and antimicrobial susceptibility of GBS in pregnant woman in both vagina and rectum and with the aim to provide this updated information to the physicians and gynecologists to develop local guidelines for the management of pregnant females and to reduce morbidity and mortality in neonates and women.

METHODOLOGY

This cross-sectional study was conducted in Gynecology and obstetrics department CMH Lahore, and lab work was carried out in Microbiology department CMH Lahore from January 2019 to June 2019. Sample size of 275 cases was calculated with 95% confidence interval, taking expected proportion of GBS colonization to be 4.5% in antenatal population and 2.5% margin of error. Pregnant women between 20-35 years at 35-37 weeks of gestation, with no history of recent intake of antibiotics, ruptured membrane, vaginal bleeding, or obstetrical problems were included in the study after taking verbal informed consent. All the data was recorded in predesigned proforma. Approval from Ethical committee was taken.

The specimens for culture from the lower vagina (vaginal introitus) and rectum (through the anal sphincter) were collected using sterilized disposable cotton swabs.

The swabs were transported to the microbiology laboratory within 2 hours and inoculated on 5% sheep blood agar and MacConkey's agar. Plates were then incubated at 37ºC in 5% CO_2 or ambient air for 24-48 hrs. GBS was identified using colonial morphology (presence of β-hemolytic colonies on Blood agar). B-hemolytic colonies morphologically resembling GBS were subjected to Gram stain, catalase test, CAMP test and latex agglutination tests.

Antibiogram was performed by Modified Kirby-Bauer disk diffusion method on MHA with 5% sheep blood agar according to Clinical and Laboratory Standards Institute (CLSI) guidelines 2015. The antimicrobials tested were penicillin (10units), clindamycin (2ug), erythromycin (15ug), Vancomycin(30ug), doxycycline(30ug), ceftriaxone(30ug), linezolid(30ug). Clindamycin and erythromycin disks were placed 20 mm from each other in order to detect inducible resistance to clindamycin (D-zone test).[10]

Data was entered and analyzed in SPSS 20.0 version. Frequencies and percentages for variables like presence of Group B Streptococcus were determined. Quantitative data like gestational age was presented by mean and standard deviation. Data was stratified for age and number of pregnancy to deal with effect modifiers. Gestational age was not

stratified as only those women at 35- 37 weeks of gestation were screened. Post stratification chi-square test was applied. P-value < 0.05 was considered significant.

RESULTS

A total of 275 (non-duplicate) antenatal cases were screened during 35-37 weeks of gestation for GBS colonization with the above mentioned methods. A total of 18 cases were found to harbor Group B Streptococcus. Out of which 4 vaginal samples, 8 rectal samples and 6 rectovaginal samples were positive for GBS (table 1). The frequency of GBS was found to be 6.5 % in women during 35-37 weeks of gestation.

Out of 18 positive cases, 8 females belonged to age group 20-25 years, 3 females in age group 25-30 and 7 females in age group 30-35 years. Chi-square value was 4.127 with P-value 0.127 which showed no association between age and presence of GBS.

Females with GBS colonization were divided into 3 groups according to the number of pregnancies. A total of 9 females were in group 1 (with 1-2 pregnancies), 5 females in group 2 (with 3-4 pregnancies), and 4 females in group 3 (with > 4 pregnancies). Chi-square value was 0.167 and P-value was 0.920, which showed no association between number of pregnancies and presence of GBS.

Mean gestational age of the females was 36 weeks.

Sensitivity pattern revealed susceptibility of Penicillin to be 100%, Clindamycin 55.6%, erythromycin 44.4%, Vancomycin 100%, linezolid 100%, ceftriaxone 100%, and doxycycline 61.1%. Inducible resistance to clindamycin was seen in only 5.6% of isolates (table 2).

DISCUSSION

In this study rectal and lower vaginal specimens of pregnant females at 35-37 weeks of gestation were collected. The GBS colonization rate was 6.5%. A total of 18 cases were found to harbor Group B Streptococcus. Out of which 4 vaginal samples, 8 rectal samples and 6 combined recto-vaginal samples were positive for GBS, with no association between GBS colonization and age or parity. These rates of GBS would have been missed if only vaginal swabs were obtained, suggesting the importance of obtaining combined vaginal and rectal swabs. This is consistent with the findings of other investigators who recommend combined vaginal and rectal swabs to increase culture yield and detection rates.[11,12]

Table 1: *Isolation Sites and Number of GBS Carriers (n = 18)*

Isolation site	Number/n
Only vagina	4
Only rectum	8
Both vagina and rectum	**6**
Total	**18**

Table 2: *Antimicrobial Susceptibility Pattern of GBS (n = 18) Isolated from Pregnant Women*

Antibiotic	Sensitive (%)	Resistant (%)
Penicillin	100	-
Erythromycin	44.5	55.5
Clindamycin	55.6	44.4
Ceftriaxone	100	-
Doxycycline	61.1	38.89
Vancomycin	100	-
Linezolid	100	-

No isolate was resistant to penicillin, vancomycin, ceftriaxone and linezolid. Of the isolates examined 55.5%, 44.4%, 38.89% were resistant to erythromycin, clindamycin and doxycycline respectively. Inducible resistance to clindamycin was only 5.6%. A relatively high level of resistance in this study might be attributed to the wide and non-judicious use of antimicrobials.

A study conducted in 2011 in the Maternity Unit and the microbiology laboratory of the University Hospitals of Geneva, Switzerland showed prevalence rate of 16.3%. Penicillin remained efficacious in all cases, as well as vancomycin. The resistance rate was 28% for clindamycin and 30% to erythromycin.[13] As compared to this study, the

resistance rate to clindamycin and erythromycin in our study is higher, which indicates that antimicrobial susceptibility testing (AST) is crucial for appropriate antibiotic prophylaxis since the resistance to erythromycin and clindamycin is increasing among GBS isolates.

A study carried out in Argentina in 2008 reported 7.6% carriage rate of GBS in pregnant women. No isolate was resistant to penicillin or ampicillin. Of the isolates examined 98.3%, 96.8%, 46.8% and 29.0% were susceptible to nitrofurantoin, rifampicin, trimethoprim-sulphamethoxazole and tetracycline respectively. Susceptibility of quinolones varied, with gatifloxacin being the most sensitive (98.4%) followed by levofloxacin (93.5%) and then ciprofloxacin (64.5%). [9]

In a meta-analysis done in Iran, comprising of 25 studies showed the meta-analyses showed that the prevalence of GBS colonization among Iranian pregnant women was 9.8%.[14]

A study conducted in 2014 in Lahore showed a vaginal carriage rate of 14%, and significant association of GBS colonization with previous history of miscarriage and vaginal discharge.[15]

In a similar study conducted in Saudi Arabia GBS colonization rate among term pregnant women was found to be 27.6% with neonates at greater risk of developing early-onset invasive disease.[16] The carriage rate is quite high as compared to this study attributed to the geographical difference of the area.

It is estimated by the CDC that 300 million dollars are spent in a year to treat almost 7,500 cases of EOGBSD.[2] Attention should be focused on prevention of GBS infection in neonates which is only possible by proper identification and treatment of colonized mothers, so that potential lethal consequences can be prevented.[22,23]

The prevention of GBS transmission from mother to infant is the key to decrease neonatal infections by this etiology.[17,18] Multi-centre studies need to be carried out on GBS colonization in pregnant women in different parts of our country and in case of significant results guidelines should be formulated to prevent the transmission of GBS from the mothers to their neonates. Nationwide epidemiological data on neonatal GBS disease should also be collected. Data suggests that treating GBS infected neonates is more expensive than preventing the infection and proper implementation of guidelines can significantly decrease morbidity and mortality resulting from GBS disease.[19,20,and21]

CONCLUSION

The frequency of GBS among pregnant women in this study suggests that a culture based screening approach for all pregnant women should be done at 35–37 week's gestation to provide antibiotic prophylaxis to GBS carriers. GBS colonization in pregnant women and its transmission to the neonates is present in our population. GBS infection might be a silent clinical problem and therefore, requires need for awareness and concerted effort for preventive measures.

More specific national epidemiological data on the incidence, morbidity, and mortality of neonatal EOGBS infection are required.

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COMPARISON BETWEEN LASER ENDOPYELOTOMY AND OPEN PYELOPLASTY IN THE MANAGEMENT OF SECONDARY PELVIURETERIC JUNCTION OBSTRUCTION

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How to cite: Rehman RA, Durrani AS, Hussain SA, Adnan M, Seerwan M, Rahman F. Comparison between laser endopyelotomy and open pyeloplasty in the management of secondary pelviureteric junction obstruction. JAIMC. 2020; 18(4): 605-8.

Abstract

Background: Open pyeloplasty has been the gold standard for surgical treatment of ureteropelvic junction (UPJ) obstruction, enjoying a long-term success rate exceeding 90%. Still there is need to develop less invasive procedure. Hence this study is planned

Objective: To compare the frequency success of laser endopyelotomy and open pyeloplasty in management of secondary pelviureteric junction obstruction.

Methodology: About 300 patients fulfilling the inclusion criteria from Department of Urology, SZH, Lahore were included in the study after permission from ethical committee and research department. Patients are randomized into two groups. In group A patients were placed in the lithotomy position under general or epidural anaesthesia. All patients underwent a renal scan at 3 months and success rate was assessed.

Results: It was observed that mean age was 28.56 ± 7.09 years. The minimum duration of complain was 2 months and maximum duration of complain was 12 months with mean was 7.05 ± 2.86 months. The male to female ratio was 1:1Success was observed in the open pyeloplasty group in 137(91%) cases and 110(72%) in laser endopyelotomy group with a significant difference (p-value<0.05).

Conclusion: Success rate was significantly higher in open pyeloplasty group as compared to laser endopyelotomy group.

Key words: Secondary Pelviureteric Junction Obstruction, Laser Endopyelotomy, Open Pyeloplasty.

Open pyeloplasty has been the gold standard for surgical treatment of ureteropelvic junction (UPJ) obstruction, enjoying a long-term success rate exceeding 90%.[1] This procedure requires a muscle incision that entails some degree of morbidity. Ureteropelvic junction obstruction causes hydronephrosis and progressive renal impairment may ensue if left uncorrected. The optimum surgical correction of Uretero-pelvic junction obstruction has been a urological challenge for over a century. Open pyeloplasty originally described by Andersen and Hynes remains the gold standard against which new technique must be compared.[2] The morbidity associated with flank incision, however, has led to development of minimally invasive approaches to Uretero-pelvic junction obstruction repair. Over the last two decades the treatment approach to Uretero-pelvic junction obstruction has evolved from open pyeloplasty to various minimally invasive procedures like endopyelotomy, acucise catheter incision, balloon dilatation and laparoscopic pyeloplasty.[3] Rapid development of minimally invasive ap - proaches has enabled minimized trauma, swift convalescence and more exquisite surgical manipulations

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Submission Date: 12-08-2020
1st Revision Date: 22-08-2020
2nd Revision Date: 12-09-2020
Acceptance Date: 14-09-2020

with outcomes equivalent to open procedures.

Endoscopic management of Uretero-pelvic junction obstruction has been reported in a number of centres with either an antegrade (percutaneous) or a retrograde approach.[4] The latter appears more appealing since it brings even less invasiveness by using a natural human orifice. Amid all the modalities a ureteroscope equipped with a Holmium: Yttrium- Aluminium-Garnet (Ho:YAG) laser is widely applied due to its precision and minimal thermal spread in tissue cutting.[5] However, most present reports on Ho: YA G endopyelotomy consist of small series of patients with limited aetiologies.[6] More accumulated data andtechnical tips should be gathered before establishing an instructive guideline for the procedure.

In a study by Fahad AH, showed the success rate of open pyeloplasty was higher in management of secondary pelviureteric junction obstruction.[(7)] while another study reported contrary to the findings by Fahad AH.[8] No such study has been done before in our local population. Moreover no randomized controlled trial have been found in international literature comparing these two approaches. Therefore I have planned to compare the success rate of laser endopyelotomy and open pyeloplasty in management of secondary pelviureteric junction obstruction in our local population.

METHODOLOGY

A randomized controlled trial study was conducted in department of urology, SZH, Lahore. The study was conducted form 26.05.2018 to 25.05.2020. A sample size of 300 (150 in each group) and there was non-probability consecutive sampling method for sampling was used. Inclusion criteria was: i) age 15-40 years, ii) Both Gender and secondary pelviureteric junction obstruction. All the cases were excluded who have obstructions longer than 2 cm by intravenous urography/pyelography (IVU/P), Ipsilateral upper urinary calculi on ultrasound, crossing vasculature at the posterior or lateral wall(s) of the obstruction identified by CT Angiography, pregnancy on ultrasound/medical record.

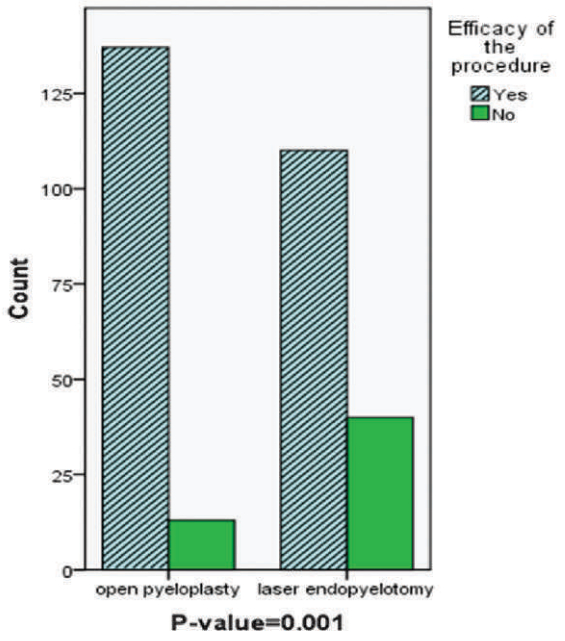
A computer generated randomization list was generated to produce two parallel groups (1:1 ratio) of patients, 150 in each group. Each patient was assigned a number at enrolment which defined a study procedure assignment. 150 sample size for laser endopyelotomy Group or Group A while 150 sample size for open pyeloplasty group or Group B.

In group A patients were placed in the lithotomy position under general or epidural anaesthesia. A 0.035 inch guidewire was introduced for passage of the62ureteroscope through the ureteral orifice. No balloon dilation was used and fluoroscopic monitoring was maintained throughout the procedure. The Wolf 8/9.8F semi-rigid ureteroscope was initially applied with caution for sharp distortions and transmitted pulsations at the UPJ. Significant kinking required a second wire to diminish the torsion. Nonetheless, intraoperative change of a Storz flexible ureteroscope was immediately exerted if the double railed guidance was still insufficient without forced or duplicate attempts with the semi-rigid device. Delivery of the holmium laser (Versa Pulse Select) was conducted through a 200-µm fibre at the initial energy of 1- 1.5 J and pulse rate of 10- 15 Hz. A retrograde cutting pattern was achieved by slowly advancing the ureteroscope into the renal pelvis. The incision was commenced at approximately 0.5 cm below the obstruction and was performed over the obstruction with another 0.5 cm distance. Completely under direct visual monitoring, the obstruction was incised lamina by lamina. The ureteroscope was used to assist the procedure by gentle passage into the pelvis and mild lateral parting of the cut edges. Haemorrhage encountered was cauterized by the defocused laser beam and the incision was deepened until the peripelvic and periureteral fat was perceived. The procedure was completed with passage of the ureteroscope through the incised part into the pelvis for dilation. A 6 F endopyelotomy stent was implanted in the ureter and was left indwelling for 4 to 8 weeks with urethral catheterization of 1 to 2 days.63In group B, the tech-

nique was performed by dissecting the part of the ureter and renal pelvis with the obstruction, then spatulating the ureter, and making ananastomosis to the renal pelvis. All patients underwent a renal scan at 3 months and success rate was assessed asper operational definition in both group and noted by researcher himself.

RESULTS

It was observed that the minimum age was 15 years and maximum age was 40 years with mean and standard deviation of the age was28.56 ± 7.09 years. The minimum duration of complain was 2 months and maximum duration of complain was 12 months with mean and standard deviation was 7.05 ± 2.86 months. The minimum BMI was 20 m^2/kg and maximum weight was 30 m^2/kg with mean and standard deviation was 25.16 ± 2.96 m^2/kg. There were 54 (54%) male patients and 46 (46%) were female patients. Success was observed in the open pyeloplasty group in137(91%) cases and110(72%) in laser endopyelotomy group with a significant difference (p-value<0.05, Graph#1).



Graph 1: *Comparison of the Success Rate in the both Operative Group*

It was observed that there was significant difference for the age, gender, duration of complaint and body mass index for the success of the operative procedure. (Table#1)

Table 1: *Impact of the Demographical Variables on the Success Rate in the both Procedural Groups*

Group of age		Efficacy of the procedure		P-value
		Yes	No	
<30 year	open pyeloplasty	69(90.8%)	7(9.2%)	0.001*
	laser endopyelotomy	53(67.9%)	25(32.1%)	
>30 year	open pyeloplasty	68(91.9%)	6(8.1%)	0.024*
	laser endopyelotomy	57(79.2%)	15(20.8%)	
Male	open pyeloplasty	76(90.5%)	8(9.5%)	0.007*
	laser endopyelotomy	59(74.7%)	20(25.3%)	
Female	open pyeloplasty	61(92.4%)	5(7.6%)	0.002*
	laser endopyelotomy	51(71.8%)	20(28.2%)	
8 months	open pyeloplasty	89(91.8%)	8(8.2%)	0.004*
	laser endopyelotomy	74(77.1%)	22(22.9%)	
>8 months	open pyeloplasty	48(90.6%)	5(9.4%)	0.002*
	laser endopyelotomy	36(66.7%)	18(33.3%)	
<25	open pyeloplasty	54(93.1%)	4(6.9%)	0.001*
	laser endopyelotomy	50(71.4%)	20(28.6%)	
>25	open pyeloplasty	83(90.2%)	9(9.8%)	0.007*
	laser endopyelotomy	60(75%)	20(25%)	

DISCUSSION

Existing literature showed that the mean operative time was 2 hours and 3 hours in open& laparoscopic pyeloplasty groups, respectively. Mean hospital stay was shorter (24 hours) in the laparoscopic group and (48 hours) in open group. Mean-follow-up period was 9 months. Postoperative complication rates were 45% and 55% in laparoscopic & open pyeloplasty groups, respectively. Success rates were95% and 90 % for open and laparoscopic pyeloplasty groups, respectively. Redo 76 surgery was needed in 2 patients of laparoscopy and 1 of open surgery |groups due to recurrence of stricture.[9]

In present study, there were 54% male patients and 46% were female patients. Overall success rate was 85% while in open pyeloplasty group success rate was 94% and success rate was 76% in laser endopyelotomy group. It was found that success rate was significantly higher in open pyeloplasty group

as compared to laser endopyelotomy group having p-value = 0.012. In a previous study it was described that the evidence available has significant limitations in terms of the heterogeneous study design and the definitions of outcomes. The average overall success rate of the pooled data was 75% with a mean follow-up of 29 months. Complications were predominately minor with an average rate of 12.5%. [10]

After stratification and by using chi-square test it was found that success rate was significantly associated with study group having p-value = 0.048 in males but not significantly associated in females with p-value = 0.127. In age group of < 30years the success rate was not significantly associated with study group having pvalue= 0.383 but significantly associated in in age group of > 30 years with pvalue= 0.010. In duration of complain of < 8 months the success rate was not significantly associated with study group having p-value = 0.131 but significantly associated in duration of complain of > 8 months with p-value = 0.035. In BMI <7725 m^2/ kg the success rate was not significantly associated with study group having p-value = 0.121 but significantly associated in weight of > 25 m^2/ kg with p-value = 0.042.

It was described in the previous study that the "safety and efficacy" of"laparoscopic pyeloplasty" is comparable to that of open pyeloplasty, with better cosmetic results and shorter hospital stay, therefore laparoscopic pyeloplasty can replace open surgery and may be considered the gold standard technique form an aging of "ureteropelvic junction obstruction" in expert hands.[9]

CONCLUSION

Overall success rate was 85% while in open pyeloplasty group success rate was 94% and success rate was 76% in laser endopyelotomy group. It was found that success rate was significantly higher in open pyeloplasty group as compared to laser endopyelotomy group having p-value = 0.012.

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BURDEN OF GYNECOLOGICAL MALIGNANCIES IN PUBLIC SECTOR HOSPITAL

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How to cite: Amjad Z, Rehman H, Ajmal O, Bano B, Abid C, Amjad M, et al. Burden of gynecological malignancies in public sector hospital. JAIMC. 2020; 18(4): 609-14.

Abstract

Background: Burden of malignancy is rising alarmingly worldwide. Gynecological malignancies are causing morbidity and mortality across the globe. Developing countries facing grave situations to cope with malignancy .Pakistan having only five Public cancer hospitals .Gynecology departments in Public hospitals receive a lot of malignancy burden .Moreover most of them are not even well equipped and personnel not trained in gynecological oncology. We need to know our statistics of gynecological malignancy to devise a strategy to deal with it.

Method: A Prospective study carried out in Jinnah Hospital Lahore Gynecology Department (three units) from June 2013 to July 2018.Women presenting with gynecological malignancy were enrolled in study after informed consent and identity kept anonymous.

Results: About 375 patients admitted with gynecological malignancies. Cancers were least common below age 20 years (3%) and 49% in age group above 50 years. Ovarian cancer was most common (52%), second commonest uterine cancers (20%), third common cervical cancer (17%), GTN (4.8%), vulvar cancer 3.2% and vaginal cancer 1.8%. Ovarian cancers presented at late stage about 63% at stage III, 50% cervical cancers presented at stage II and 30% presented at stage III. Uterine cancers were mostly presenting at early stages .About 53% uterine cancers presented at stage I and 47% at stage II. Epithelial ovarian cancer was the most common histopathological diagnosis (50%) among ovarian cancers. Endometrial carcinoma 32% and 90% of cervical cancers were squamous cell carcinoma.

Conclusion: Gynecological malignancy is the most common cause of death among non-communicable diseases. Awareness and provision of screening modality is required to cope with the problem.

Key words: Gynaecological, Malignancy, public sector hospital

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Submission Date: 29-07-2020
1st Revision Date: 12-09-2020
2nd Revision Date: 20-09-2020
Acceptance Date: 26-09-2020

Global data suggests that global cancer burden has risen to 18.1 million cases and 6 million cancer deaths. International agencies for research on Gynecological cancers constitute an important burden of disease around the world. Estimates from GLOBOCAN 2018 reveal approximately 1,247,300 incident cases and 596,000 related deaths of cancers of cervix, uterus and annually around the world. According to the American Cancer Society, there were an estimated 110,070 new cases diagnosed and approximately 32,120 deaths from gynecological cancers in 2018.[1] Gynecological cancers include cancers of ovary, uterus, cervix, vagina and vulva. These cancers constitute 1:4 of cancers among women. 25% 0f gynecological cancers occur in low

resource countries contrary to 16% in developed countries. Advancement in industrialization, sedentary lifestyle, lack of awareness and lack of provision of screening programs for genital tract cancers are contributory factors to the rise in malignancies in underprivileged countries.[2]

Cervical cancer is fourth most common occurring cancer in women and top most among gynecological cancers with an estimated 570,000 new cases in 2018 representing 6.6% of all female cancers. Approximately 90% of deaths from cervical cancer occurred in low and middle income countries. Pakistan is among top 10 countries where cervical cancer prevalence is on rise. It is estimated that twenty patients contract cervical cancer each day.[1;3]

Endometrial cancer is sixth most commonly occurring cancer in women and 15th most commonly occurring cancer overall and third common among genital tract malignancies. There were over 380,000 new cases in 2018. Sixty percent cases occurred in developed countries but as a result of increased prevalence of obesity endometrial cancer is on rise in low income countries like Pakistan.[4]

Ovarian cancer is the second most common among gynecological cancers, eighth most commonly occurring cancer in women and the 18th most commonly occurring cancer overall. There were nearly 300,000 new cases in year 2018. Most of ovarian malignancies present in late stage and five year survival rate is less than 30%.[1,5]

Cancers for vulva, vagina, placenta and ill-defined sites together constituted 74900 cases. Vulva and vaginal malignancies are uncommon in Pakistan and globally as well. Due to the increase in the life span of women, it is now on the rise. Mostly women in underdeveloped countries present at advanced stage and are reluctant to seek advice at early stage due to social taboos.[1,6]

The Punjab Cancer Registry was set up in February 2005 to determine the population level cancer statistics in the region. Initially, attempts were made to collect information from cancer patients in the region of Punjab. Effective July 1, 2008, the Registry started collecting data on cancers diagnosed and treated among the residents of Lahore district. In 2014, the Registry expanded to four other districts of Punjab including Faisalabad, Sheikhupura, Kasur, and Nankana Sahib. In 2016, the Registry included Sialkot and Narowal districts. In 2018, the Registry included Okara, Gujrat, Jhelum, Rawalpindi/Islamabad districts. At present, the Registry has around 47 members in over 24 participating institutions. The Central Office of the Registry is located within the Shaukat Khanum Memorial Cancer Hospital & Research Center (SKMCH& RC), Lahore, Pakistan. The running of the Registry is also sponsored by SKMCH & RC. The Punjab Cancer Registry is registered under the Societies Act of Pakistan, 1860, and its registration is renewed every year. The Registry is also a member of the International Association of Cancer Registries, Lyon, France.[7,8]

METHODOLOGY

This study was carried out at Jinnah Hospital Lahore from January 2013 to December 2018. Jinnah Hospital Lahore is a 1500 bedded hospital. It has three gynae units with almost 200 patients received in the outpatient department daily. Approximately 75-80 patients admitted and treated with gynecological malignancies annually. Total 375 Women presenting with gynecological malignancies enrolled in study after taking their informed consent. Information regarding age, Tumor site, stage of tumor, histopathology and treatment taken.

RESULTS

Total 375 patients admitted with diagnosis of gynecological malignancies. Regarding age of presentation 3%(11) women aged less than 20 years, 20%(76) were between 20-40 years, 28%(105)

Table 1:

Age in years	N=375	%
<20	11	3%
20-40	76	20%
40-50	105	28%
>50	183	49%

women were in age ranging from 40-50 years, and almost half of women were more than 50 years old. i.e., 49%(183) . Most common malignancy seen was ovarian cancer contributing to 52 % (197) of malignancies in our study. Second common was uterine cancer 20% (76), cervical cancer 17.6 %(66), GTN were 4.8% (18), while least common were vulvar and vaginal cancers contributing to 3.2%[12] and 1.6%[6] respectively. Table 3 shows the stage of malignancies at presentation. Ovarian cancer was found to be present at a late stage. 63% ovarian cancer presented at stage 3. Only 10% cases presen-ted at stage I. 50% of cervical cancer presented at stage II and 30 % cases presented at stage III. 53% uterine cancer presented at stage I, 46% presented at stage II. Almost all vulval and vaginal cancers presented at stage II. Regarding age of presentation of different gynecological malignancies it was seen that incidence of these malignancies was very low below 20 years of age. Ovarian cancer was seen in 7.6%,[15] uterine cancer 2.6%[2] and cervical cancer in 1.5% cases under 20 years. Most common cancer seen between 20-40 years was gestational tropho-blastic neoplasia 94.4%[(17)], second commonest in this age group was cervical cancer 39.3%,[26] while ovarian and uterine malignancies were 15%[30] and 10%[8] respectively among this age group. Uterine cancer was most common 34%[26] up to age 50 years .Ovarian cancer was seen in 27%,[54] vulval /vaginal cancer in 22%[4] and cervical cancer in 16.6%[11] women in this age . Approximately 50% (98) cases of ovarian malignancy, 52 %[40] cases of uterine malignancies and 77%[14] cases of vulval vaginal malignancies seen in age above 50 years. Table 5 showed histopathological diagnosis of ovarian malignancies. Most common was papillary serous diagnosed in up to 50 %[99] and serous cyst adenocar-cinoma in 15 %[30] cases. Brenner and yolk sac tumors were 3% each. Regarding histopathology of uterine malignancies adenocarcinoma was the most common diagnosis 32.8%,[25] GTN and endometrioid were 23.8%[18] each, Sarcoma 7.8%[6] and papillary serous 3.9%.[3] Approximately 90% of cervical cancer turned out to

Table 2:

Malignancy	N=375	%
Ovarian	197	52.5
Uterine	94	25.06
Cervix	66	17.6
Vulva	12	3.2
Vagina	6	1.6

Table 3: *Stage of Malignancy at Presentation*

Malignancy	Stage of malignancy %			
	I	II	III	IV
Ovarian	10	17.5	63.7	8.7
Uterine(excluding GTN)	53	46	1	-
Cervical	7	50	31	12
Vulva	-	100	-	-
GTN		100		

Table 4: *Age at Presentation of different Malignancies*

Age	Ovarian n=197	Uterine N=76 (excluding GTN)	Cervical N=66	Vulva/ Vagina N=18	GTN N=18
< 20	15 (7.6%)	2 (2.6%)	1 (1.5%)	-	-
20-40	30 (15.2%)	8 (10.5%)	26 (39.3%)	-	17 (94.4%)
40-50	54 (27.4%)	26 (34.2%)	11 (16.6%)	4 (22.2%)	1 (5.5%)
50-70	98 (50%)	40 (52.6%)	28 (42.4%)	14 (77.7%)	-

Table 5: *Histopathological Diagnosis of Ovarian Cancer*

Histopathology	Number (n=197)	%
Epithelial ovarian cancer Serous	(n=157)	(79.5)
cystadenocarcinoma	30	15.2
Mucinous cystadenocarcinoma	18	9.1
Papillary serous	99	50.2
Endometrioid	10	5
Brenner	5	2.5
Germ cell		
Yolk sac	6	3
Dysgerminoma	3	1.5
Struma ovarii	2	1
Granulosa cell	9	4.5
Krukenberg	6	3
Struma ovarii	2	1

Table 6: *Histopathological Diagnosis of Uterine Malignancy*

Histopathology	Number (n= 76)	%
Endometrial	(n=46)	(60.3)
• Adenocarcinoma	25	32.8
• Papillary serous	3	3.9
• Endometrioid	18	23.6
Sarcoma	6	7.8
Mixed mullerian tumors	6	7.8
GTN	18	23.6

Table 7: Histopathological Diagnosis of Cervical Cancer

Histopathology	Number (n=66)	%
Squamous cell carcinoma	59	89
Clear cell	7	11

be squamous cell carcinoma on histopathology.

DISCUSSION

According to WHO classification Pakistan falls in the low to middle income group. Total population of Pakistan is 207 million approximately according to the demographic health survey 2018. Prevalence of malignancies is 310132, new cases are 173937 and death occurring due to malignancy is 118442. Gynecological malignancies are increasing worldwide particularly in developing countries. According to GLOBBOCAN 2018 incidence of gynecological malignancies is 7.8% (cervical cancer 3.25%, ovarian 2.6%, uterine 1.7%, vulva and vagina cancer 0.17%&0.13% respectively).[9]

Age of presentation of all cancers was in the range of 40-50 years and more than 50 years. Most of the cases in our study were found in the age group 50 years or above. Ovarian cancer was seen in only 7% of patients under age twenty. Uterine and cervical cancers were seen in 2.6% and 1.5% cases respectively, while no GTN vulvar and vaginal cancers were seen in this age group. More than 50% of ovarian and uterine malignancies seen in 5th and 6th decade of life. Research carried out by Briggs[10] showed 72% of ovarian and uterine malignancies in this age group. Bimodal pattern of cervical cancer seen in our study. About 42% of cases presented in the age group 50-70 years while 39% of cases were seen in the younger age group about 20-40 years. It is contrary to other studies carried out which showed a mean age of 51- 53 years for cervical cancer. Regarding vulvar and vaginal cancers 77% presented in the 5th to 7th decade of life and 22% cases of vulval &vaginal cancers seen below 50 years of age which is comparable to other studies. Gestational trophoblastic neoplasia seen in reproductive age group i.e. 20-40 years in about 95% of cases while only 5% cases seen in age above 40 years. A study conducted by Javaid N showed that GTN was second commonest malignancy and seen in peak fertility age groups.[11]

Incidence of ovarian cancer in Pakistan is increasing at an alarming rate as around 13.6 percent of women have been suffering from this cancer and, of them, over 70 percent are diagnosed at later stages only, making it highly difficult for the healthcare providers to treat the deadly disease. Our study showed that ovarian cancer was most common malignancy. Almost half of women presenting with malignancy were having ovarian cancer n=197 (52.5%). A study conducted by H. Manzoor at CENAR Quetta (center of nuclear medicine and radiotherapy showed similar results where ovarian cancer was most prevalent. Analysis done at other hospitals in Pakistan also showed the same results. While cervical cancer was found to be most prevalent worldwide and studies conducted in Africa and India.[12,13] Also a research carried out at Liaquat University Jamshoro showed cervical cancer was most common at about 41%.[14] Uterine malignancy was second commonest in our study. About 25% of cases seen, it is contrary to other local and international studies. Some studies showed that ovarian cancer was commonest of gynecological malignancies while most of the studies carried out in India, Africa and even in Pakistan showed that cervical cancer was commonest .In our study cervical cancer was 3rd most common cancer about 17% of cases. It may be due to reason that being a Muslim country sexual practices are not but there is trend towards increase in cervical cancer as no screening program is available. Uterine cancer presented with vaginal bleeding in form of irregular, heavy or postmenopausal bleeding which forced patients to seek medical care. Vulval and vaginal cancers were least common making up to 3.2 and 1.6% respectively. Primary vaginal cancer is very rare and usually present as a result of extension of cervical cancer. (Zang et al).[15]

About 63% ovarian cancer presented at FIGO stage 3 and 17% presented at FIGO stage 2 .Research carried out at India by Maheshwari et al showed that about 60 % of ovarian cancers presented at FIGO stage III and 20% cases presented at stage II which closely resemble to our study. Delayed presentation was due to vague symptoms of ovarian malignancy, lack of awareness and hesitance to consult a doctor if symptoms develop. Most of patients presented at an advanced stage when ascites and abdominal mass was evident clinically .More than 50% of uterine malignancies presented at FIGO stage 1. As already mentioned vaginal bleeding was cause for early presentation. 50% of cervical cancer presented at stage II and 30% at stage III. It was comparable to the study carried out by Ghanna. Rest of gynecological malignancies presented at stage 2. Delayed presentation of cervical cancer was lack of cervical screening program and taboos associated with cervical

cancer in our country.[16,17]

Regarding histopathological diagnosis epithelial ovarian cancers were most common about 79.5% of all ovarian cancers. Among epithelial cancers papillary serous variety was most frequent contributing 67% of epithelial variety. Similar results were shown by a study conducted by Ahmad et al. Next common was germ cell tumors accounting for 5.5% of cases. Yolk sac tumor was more prevalent among germ cell tumors and 2 cases of struma ovarii which is a very rare variety of immature teratoma also found. Patients presented with features of hyperthyroidism. Most of the available studies had not mentioned this type of ovarian malignancy. Among uterine cancers endometrial carcinoma was most prevalent making 60% of all uterine cancers .Second common uterine cancer was GTN (23%) of uterine malignancies. It was comparable to study carried out at Peshawar. Uterine sarcomas and mixed mullerian tumors were 7.8% each. Most studies National and international have not described mixed mullerian tumors. Regarding cervical cancer 89% had squamous cell carcinomas and 11% had clear cell carcinoma. It was comparable to study carried out by Baummann et al. A research conducted in Nepal by Pardhan M showed that squamous cell carcinoma was the commonest histological type in cervical, vaginal and vulvar cancers whereas serous adenocarcinoma and endometrial adenocarcinoma were commonest histological types in the ovary and endometrium respectively.[18,19,20]

In 90% of patients with ovarian cancers debulking surgery was done. About 95% endometrial and uterine cancers total abdominal hysterectomy with bilateral salpingo oophorectomy done. In patients presenting with cervical cancers only 7% had surgical treatment (Wertheim OR Total hysterectomy) and 93% referred for chemo radiation. In vulval/ vaginal tumors few had local excision and rest sent for radiotherapy.

CONCLUSION

Ovarian cancer was commonest malignancy contrary to cervical cancer worldwide. Lack of infrastructure for the health system and improper use of resources are hurdles dealing with cancer patients. Most of the health budget is used on communicable diseases treatment where prevention plays a key role. A lot of input and motivation is required at political, government and public level to overcome malignancy burden.

RECOMMENDATIONS

- Establish cervical screening programs.
- Awareness among the general population regarding signs and symptoms of malignancies.
- Lifestyle and dietary modification as obesity is a major risk factor for endometrial cancer.
- Establishment of cancers hospitals and provision of training in gynecological malignancy and screening modalities at public hospitals.

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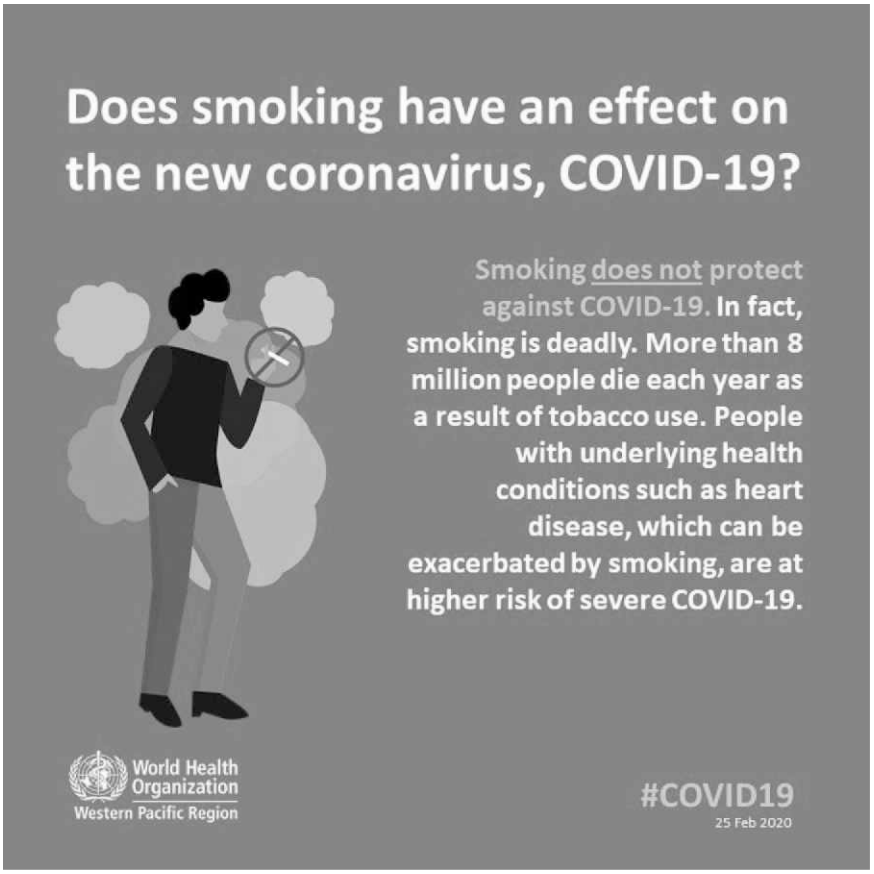

DIAGNOSTIC ACCURACY OF BRONCHIAL WASHINGS FOR AFB IN SMEAR NEGATIVE PULMONARY TUBERCULOSIS

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How to cite: Musharaf MS, Javed A, Usman U, Riaz S. The diagnostic accuracy of bronchial washing for AFB in smear negative pulmonary tuberculosis. JAIMC.2020; 18(4): 615-20.

Abstract

Background: Diagnostic modalities for sputum smear negative pulmonary tuberculosis are multiple with different accuracies. Bronchial washing may help reduce the non-indicated use of anti-tuberculosis treatment.

Objective: To determine the diagnostic accuracy of bronchial washing for AFB in smear negative pulmonary tuberculosis (PTB) taking sputum culture as gold standard. It was prospective, cross-sectional, comparative study conducted at Pulmonology unit of Al-Aleem Medical College Lahore, conducted from July 2019 to March 2020.

Methodology: 180 patients with suspected smear negative pulmonary tuberculosis were enrolled in the study. After taking informed consent, all patients underwent bronchoscopy procedure according to standard protocol and their bronchial washings were sent for smear examination immediately. Results of both post bronchoscopy sputum culture and bronchial washings were recorded. Diagnostic accuracy of bronchial washing was calculated.

Results: The mean age in our study was 35.34 ± 9.144 years (23 to 56 years).105 patients (58.3%) were male and 75 patients (41.7%) were female. The sensitivity of bronchial washing came was 62%, specificity 31%, positive predictive value 72%, negative predictive value 23%, taking culture as gold standard in patients with tuberculous. There was no effect of gender and age on diagnostic accuracy.

Conclusion: It is concluded that bronchial washing can be used as a proxy indicator of tuberculosis in patients with sputum smear negative pulmonary tuberculosis till we may wait for results of culture as it has shown high sensitivity.

Keywords: Sputum smear negative pulmonary tuberculosis, bronchoscopy, AFB culture.

Tuberculosis (TB), an infection caused by mycobacterium tuberculosis, has been known to mankind since prerecorded history. With advent of highly effective anti-tuberculous therapy, the incidence of TB has decreased after 1960s but there is again a rise since 1980's due to emergence of mono and poly resistance tuberculosis. Now it is considered as reemerging infection.

World health organization declared it a global health emergency in 1991.Tuberculosis is prevalent in Pakistan and it ranks at 5th amongst the countries with highest burden of disease in the world. Pakistan contributes about 44% of the disease burden in EMRO region. According to WHO, Pakistan has incidence of 80/100000 smear positive cases per year and 177/100000 for all types of cases.[2]

Major diagnostic procedures employed for diagnosing pulmonary tuberculosis are chest radio-

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Submission Date: 18-08-2020
1st Revision Date: 12-09-2020
Acceptance Date: 19-09-2020

graphy and sputum culture and smear for detection of Acid- Fast bacilli (AFB).[1] In those who have strong clinical and radiological suspicion of tuberculosis it is pertinent to demonstrate presence of AFB either through sputum smear or culture to avoid unnecessary empiric therapy.

Diagnosis of sputum/smear-negative pulmonary tuberculosis patients can be challenging and time consuming and many patients may receive empirical anti-tubercular treatment unnecessarily. Fiberoptic bronchoscopy may assist early diagnosis in such patients, as sometimes patient is unable to produce the sputum.

Altaf et al demonstrated that smear of bronchial washing was able to detect in 48% of the sputum smear negative cases.[3] Ganguli KC et al demonstrated that the sensitivity of AFB-smears in samples from post bronchoscopy sputum and bronchial washings were 74% and 58% respectively, with specificity being 70%.[4]

Gold standard criterion for starting anti tuberculosis treatment is sputum culture for AFB. Different techniques have been applied to increase the yield of sputum microscopy. There is no local study available showing the diagnostic accuracy of bronchial washing. Present study will evaluate the diagnostic accuracy of bronchial washing smear for diagnosis of pulmonary tuberculosis.

Results of this study will help the physician make a definite diagnosis of pulmonary tuberculosis and help the patient to refrain from undue anti tuberculosis treatment.

METHODOLOGY

The objective of the study to determine the diagnostic accuracy of bronchial washing for AFB in smear negative pulmonary tuberculosis (PTB) taking sputum culture as gold standard. The study was conducted in Pulmonology department Al-Aleem Medical College/ Gulab Devi Hospital Lahore. It was conducted from July 2019 to March 2020. It was prospective, cross-sectional, analytical study. The sample was collected through Non-probability consecutive sampling.

Inclusion Criteria

1. Both male and female.
2. Age from 18 to 60 years.
3. Patients who are suspected of smear negative pulmonary tuberculosis with sputum smear and chest x ray done in last six months.

Exclusion Criteria

1. Patients who have used empirical therapy for tuberculosis for more than 2 weeks determined by history and clinical record.
2. Patients who are unwilling to undergo bronchoscopy.
3. Patients who do not give consent for the study.

One hundred and eighty patients with suspected smear negative pulmonary tuberculosis were enrolled in the study. After taking informed consent demographic profile (name, age, sex) was recorded and data was collec-ted through structured questionnaire.

Patients underwent bronchoscopy procedure according to standard protocol. Their bronchial washings and post bronchoscopy sputum was sent for smear examination immediately to local pathological laboratory. Results of both post bronchoscopy sputum culture and bronchial washings were recorded.

Outcome variables were detection of AFB positivityin sputum smear negative PTB by bronchial washings smear and post bronchoscopy sputum AFB culture.

Data was entered and analyzed in SPSS 21 version. Data was analyzed for description i.e. for continuous variable like age Mean+S.D., and for categorical variable like proportion of patients detected positive by bronchial washings or post sputum bronchoscopy or combined, frequencies and percentages were calculated. Data was stratified for age and gender. Post stratification chi square test was applied to determine the significant difference, a p value ≤0.05 was considered significant. A 2×2 table was made to find sensitivity, specificity, positive

predictive value and negative predictive value, and diagnostic accuracy of bronchial washings for AFB taking sputum culture as gold standard.

RESULTS

180 patients were included with mean age of 35.34 ± 9.144 ranged from 23 to 56 years. 60 patients (33.3%) were below 30 years of age and remaining 120 patients (66.7%) were either 30 years of age or above. (Figure 1). 105 patients (58.3%) were male and 75 patients (41.7%) were female. (Figure 2)

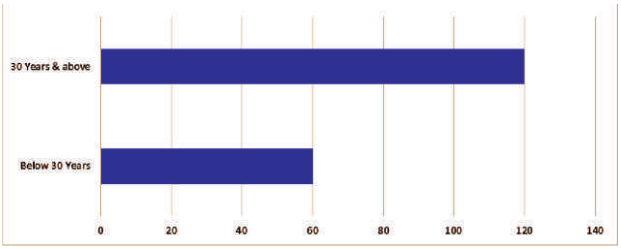

Fig. 1: *Frequency Distribution of Sampled Population by Age Groups*

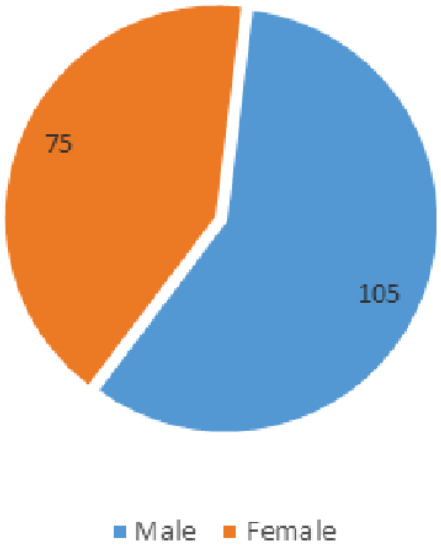

Fig. 2: *Frequency Distribution of Sampled Population by Gender*

115 patients (63.9%) showed positive results for AFB on bronchial washing in our study sample (n=180) whereas remaining 65 patients (36.1%) showed negative results(Figure 3). In 133 patients (73.9%), post bronchoscopy sputum (PBS) culture was positive and in 47 patients (26.1%) had negative sputum culture(Figure 4).

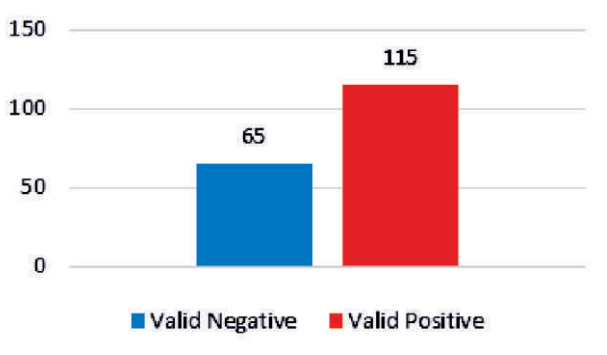

Fig. 3: *Frequency Distribution of Sampled Population by Bronchial Washing*

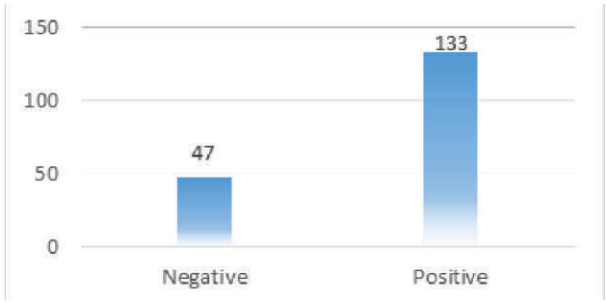

Fig. 4: *Frequency Distribution of Sampled Population by Results of PBS Culture*

When we cross tabulated bronchial washing with sputum culture, out of 115 with Bronchial Washing, 85 showed positive results for sputum culture remaining 32 were negative (Table 1).

Among 115 patients with bronchial washing,

Table 1: *Cross Tabulation between Results by Bronchial Washing &PBS Culture*

		Sputum Culture		Total
		Positive	Negative	
Bronchial Washing	Positive	83	32	115
	Negative	50	15	65
Total		133	47	180

Table 2: *Sensitivity Specificityof Bronchial Washing with AFB Culture*

Outcome	Sensitivity (%)
Sensitivity	62.4
Specificity	31.9
Positive predictive value	72.1
Negative predictive value	23.07
Diagnostic accuracy	54.4

51 male patients showed positive results for the culture and 32 female patients showed positive results for PBS culture.

For male patients, sensitivity of bronchial washing came out 62%, specificity 41%, positive predictive value 78%, negative predictive value 25%, taking culture as gold standard in patients with tuberculous.For female population, sensitivity of bronchial washing came out 61.5%, specificity 41%, positive predictive value 78%, negative predictive value 25%, taking culture as gold standard in patients with tuberculous (Table 3).

Among 115 patients of bronchial washing, 31 patients out of 39 showed positive results for culture who had age below 30 years meanwhile in 76 patients with bronchial washing, 52 showed positive results for culture for those who had age either 30 years or above. For younger patients, sensitivity of bronchial washing came out 63%, specificity 27%, positive predictive value 98%, negative predictive value 14.2%, taking culture as gold standard in patients with tuberculous. For patients above 30 years of age, sensitivity of bronchial washing came out 62%, specificity 33%, positive predictive value 68%, negative predictive value 27%, taking culture as gold standard in patients with tuberculous (Table 4).

Table 3: *Crosstab Bronchial Washing & Culture for Gender*

Gender			Culture		Total
			Positive	Negative	
Male	Bronchial Washing	Positive	51	14	65
		Negative	30	10	40
	Total		81	24	105
Female	Bronchial Washing	Positive	32	18	50
		Negative	20	5	25
	Total		52	23	75

Table 4: *Age Stratification for Diagnostic Accuracy*

Age groups			Culture		Total
			Positive	Negative	
Below 30 Years	Bronchial Washing	Positive	31	8	39
		Negative	18	3	21
	Total		49	11	60
30 Years & above	Bronchial Washing	Positive	52	24	76
		Negative	32	12	44
	Total		84	36	120

DISCUSSION

More than 2 billion peoples (about one-third of the world population) are estimated to be infected with Mycobacterium tuberculosis the causative agent of Tuberculosis. The global incidence of tuberculosis (TB) peaked around 2003 and appears to be declining slowly. According to the World Health Organization (WHO), in 2019, 8 million individuals became ill with TB and 1.4 million died.[2] Twenty-2 high-burdencountries account for about 80% of the total TB disease burden worldwide. Although sub-Saharan Africa has the highest incidence rate, Bangladesh, China, India, Indonesia, and Pakistan together account for half of the global TB burden[2]. But situationin Pakistanis improving as appreciated by WHO EMRO region report "Pakistan National Tuberculosis Program (NTP) has achieved a remarkable and steady improvement in numbers of TB cases detected, from 11 050 in 2000 to 248 115 in 2008, and treatment success rates reached 91% in 2007".[2]

Major diagnostic procedures employed for diagnosing pulmonary tuberculosis are chest radiography and sputum culture and smear for detection of Acid- Fast bacilli (AFB).[1] In those who have strong clinical and radiological suspicion of tuberculosis it is pertinent to demonstrate presence of AFB either through sputum smear or culture to avoid unnecessary empiric therapy.

In our study, sensitivity of bronchial washing came out 62%, specificity 31%, positive predictive value 72%, negative predictive value 23%, taking culture as gold standard in patients with tuberculous. Altaf et al demonstrated that smear of bronchial washing was able to detect in 48% of the sputum smear negative cases.[3] Nikbakhsh Net al demonstrated that the sensitivity of AFB-smears in samples from post bronchoscopy sputum and bronchial washings were 74% and 58% respectively, with

specificity being 70%.[4]

Among 115 patients with bronchial washing, 51 male patients showed positive results for the culture and 32 female patients showed positive results for PBS sputum culture. For male patients, sensitivity of bronchial washing came out 62%, specificity 41%, positive predictive value 78%, negative predictive value 25%, taking PBS culture as gold standard in patients with tuberculous. For female population, sensitivity of bronchial washing came out 61.5%, specificity 41%, positive predictive value 78%, negative predictive value 25%, taking PBS culture as gold standard in patients with tuberculous.

Among 115 patients of bronchial Washing, 31 patients out of 39 showed positive results for culture who had age below 30 years meanwhile in 76 patients with bronchial washing, 52 showed positive results for culture for those who had age either 30 years or above. For younger patients, sensitivity of bronchial washing came out 63%, specificity 27%, positive predictive value 98%, negative predictive value 14.2%, taking PBS culture as gold standard in patients with tuberculous. For patients above 30 years of age, sensitivity of bronchial washing came out 62%, specificity 33%, positive predictive value 68%, negative predictive value 27%, taking culture as gold standard in patients with tuberculous. It implies that there is no effect of age of patient on diagnostic accuracy of bronchial washing.

Altefet al. did study on 75 sputum smear-negative suspected patients for PTB and revealed that the yield of FOB was 83.33%. This yield is slightly higher than with our study5. In another study conducted on sputum smear-negative patients, Yuksekol et al. demonstrated that BAL smears and culture for M. tuberculosiswere positive in 13(23%) and 28(50%) patients, respectively on 56 patients. They thus concluded that FOB was useful and mandatory tool in the selected patients to avoid unnecessary treatment.[6] Similarly, previous studies have reported that FOB and BAL play significant roles in diagnosis of PTB with a sensitivity of 80-93% and a specificity of 70-95%.[7-9] Jacomelli et al. reported 60% sensitivity and 100% specificity of BAL. Although the sensitivity is in line without result, they obtained higher specificity and showed that bronchoscopy was a essential technique in ruling out of tuberculosis.[10]

Limitation of current study is its small sample size and population selection from a tertiary care hospital which is not representative of our total population.

CONCLUSION

It is concluded that bronchial washing can be used as a proxy indicator of tuberculosis in patients with sputum smear negative pulmonary tuberculosis till we may wait for results of culture as it has shown high sensitivity. BAL is safe and effective method with good sensitivity, specificity, positive and negative predicted value for diagnosis of PTB in sputum smear-negative patients, further studies for cost-effectiveness of this procedure are required for recommendation in resource-limited countries.

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COMPARISON OF DEXMEDETOMIDINE AND BUPRENORPHINE AS AN ADJUVANT TO BUPIVACAINE DURING SPINAL ANAESTHESIA

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How to cite: Farooq U, Butt MM, Shahid A, Aslam MU, Aslam M. Comparison of dexmedetomidine and buprenorphine as an adjuvant to bupivacaine during spinal anesthesia. JAIMC. 2020; 18(4): 621-26.

Abstract

Objective: To compare the mean duration of analgesia between buprenorphine and dexmedetomidine as an adjuvant to intrathecal bupivacaine in patients undergoing elective surgical procedures.

Methodology: 60 patients, aged 12-70 years, ASA I and II, undergoing elective surgical procedures under spinal anesthesia were randomly allocated either in Group B or D. During spinal anesthesia with 2 ml (15 mg) 0.75 % hyperbaric bupivacaine, Group B was given 60 µg buprenorphine and Group D was given 5 µg dexmedetomidine as an additive. Patients were observed for next 24 hours. The duration between spinal anesthesia and first dose of analgesia was recorded in minutes as duration of analgesia. The whole information was collected using specially designed Performa.

Result: Mean duration of analgesia was 234.2 ± 25.3 minutes with buprenorphine and 297.8 ± 26.7 minutes with dexmedetomidine ($p<0.0001$).

Conclusion: Both Buprenorphine and Dexmedetomidine can be successfully used in spinal anesthesia, to prolong the analgesia in all age groups and genders. Dexmedetomidine provides longer analgesia duration as compared to Buprenorphine and results are statistically significant ($p<0.0001$).

Keywords: Buprenorphine; Dexmedetomidine; Bupivacaine; Spinal Anaesthesia; Analgesia.

Spinal anesthesia is the favorite technique of most of the anesthesiologist worldwide. It is has been used over decades for surgery of lower half of body.[1] Recently a few upper thoracic surgeries have also been done under spinal anesthesia.[2,3,4] With a dense motor, sensory, and autonomic blockade, spinal anesthesia provides excellent surgical conditions in most of cases. It may provide post operative analgesia depending upon duration of surgery and type of drug used.

Bupivacaine is the most common drug used for the spinal anesthesia. 0.5 or 0.75% hyperbaric solutions are commonly available spinal preparations. This addition of dextrose increases the specific gravity of the drug and changes its anesthetic profile.[5,6] Multiple drugs among opioids like morphine, sufentanyl, fentanyl, tramadol, buprenorphine; α-2 agonists like clonidine and dexmedetomidine; and vasopressors like epinephrine; steroids like dexamethasone; NSAIDs like parecoxib and lornoxicam; induction agents like midazolam and ketamine; neostigmine and magnesium sulfate can be added with bupivacaine to prolong the post operative analgesia with varying degree of effects and complication.[7,8,9,10]

Buprenorphine is thebaine analogue and a weak agonist at µ-opioid receptor. It provides supraspinal and spinal analgesia. It has been used for long to prolong the spinal analgesia. It dissociates slowly

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Submission Date: 28-08-2020
1st Revision Date: 22-09-2020
Acceptance Date: 30-09-2020

from μ receptor, resulting in long duration of action and less addiction potential. Like other opioids, it may cause pruritis, drowsiness, nausea and vomiting.[10,11]

Dexmedetomidine is a recently introduced α-2 agonist, claimed to be best friend of anesthesiologist. It has been used intrevenous, intrathecal, epidural and in peripheral nerve blocks to prolong the anesthetic effects and to provide sedation and analgesia. Dosage of 5 to 10 μg have been used in spinal anesthesia to prolong the effects. It may cause bradycardia and hypotension if given in high dose and rapid infusions.[10,11,12]

Dexmedetomidine is being compared to old drugs in order to understand its safety profile. Multiple trials have been completed and some are still under process.[10,11,12] This randomised control trial was designed with an objective to compare the mean duration of analgesia between buprenorphine and dexmedetomidine as an adjuvant to intrathecal bupivacaine in patients undergoing elective surgical procedures. We hypothesized that there is a difference in mean duration of analgesia with intrathecal bupivacaine with additives buprenorphine and dexmedetomidine.

METHODOLOGY

The randomized control trial was conducted in Department of Anaesthesiology, DHQ teaching Hospital, Gujranwala medical college, Gujranwala from January to June 2019. The sample size of 60 cases (30 in each group) was calculated with 80% power of test, 5% level of significance and taking magnitude of mean duration of analgesia i.e. 289.66 ± 64.94 minutes with buprenorphine and 493.56 ± 38.95 minutes with dexmedetomidine in patients undergoing elective surgical procedures. Non probability consecutive sampling method was used for the selection of sample. Patients aged 12-70 years, of both genders, ASA I and II, undergoing elective surgical procedures under spinal anesthesia were included in this study. Patients with known allergy to study drugs were excluded from this study.

After ethical approval by local research and ethic committee, 60 patients fulfilling the criteria were enrolled in this study from inpatient department. After an informed consent, Patients were allocated randomly using random number table to one of the two groups comprising 30 patient each. (Group B: Buprenorphine and Group D: Dexmedetomidine). All patients did fasting for at least 6 hours before anaesthesia. All patients were monitored with ECG, heart rate, NIBP and SpO_2 in operating room. After intravenous access, all patients were given Ringer Lactate infusion at 10 ml / Kg and then spinal anesthesia was given as per standard protocol. During spinal anesthesia with 2 ml (15 mg) 0.75 % hyperbaric bupivacaine, Group B was given 60 μg buprenorphine and Group D was given 5 μg dexmedetomidine as an additive. The time of spinal anesthesia was recorded and considered zero point for the study parameter. After assessing the effect and level of spinal anesthesia, surgery was started. When surgery was completed, patients were shifted to post operative wards where they were observed for next 24 hours for pain evaluation. Whenever pain score > 4 on VAS, intravenous analgesia was given for pain control. The duration between spinal anesthesia and first dose of analgesia was recorded in minutes as duration of analgesia. The whole information was collected using specially designed Performa. All the collected information was entered and analyzed using IBM SPSS version 23.0. Quantita-tive data like age and duration of analgesia was presented as mean and SD. Qualitative data like gender and ASA status was presented as frequency and percentage. Both groups were compared for mean duration of analgesia by using independent sample t-test. p-value < 0.05 was considered as significant. Data was stratified for age, gender, and ASA status. Post-stratification, independent sample t-test was applied to check the effect of effect modifiers and p-value ≤ 0.05 was considered as significant.

RESULTS

In this study 60 patients were enrolled and

randomly divided into 2 groups each group having 30 patients each. 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

Spinal anesthesia provides immediate and dense motor blockade as compared to Epidural anesthesia. Slow onset of epidural makes it a less favorable choice when time factor is important.

Table 1: *Descriptive Statistics for Age According to Treatment Groups*

	Group-B	Group-D	Total
N	**30**	**30**	**60**
Mean	39.73	40.70	40.22
SD	13.87	10.78	12.32
Minimum	17	23	17
Maximum	66	63	66

Group-B = Buprenorphine
Group-D = Dexmedetomidine

Table 2: *Gender Distribution of Patients in Treatment Groups*

Gender	Group-B	Group-D	Total
Male	17(56.7%)	14(46.7%)	31(51.7%)
Female	13(43.3%)	16(53.3%)	29(48.3%)
Total	30	30	60

Group-B = Buprenorphine
Group-D = Dexmedetomidine

Table 3: *ASA Distribution Among Groups*

ASA	Group B	Group D	Total
I	15	12	27
II	15	18	33
Total	30	30	60

Group-B = Buprenorphine
Group-D = Dexmedetomidine

Table 4: *Analgesia Duration (in Minutes) in Treatment Groups*

Group	N	Mean	Standard Deviation	Minimum	Maximum
Group B	30	234.23	25.276	190	300
Group D	30	297.77	26.723	210	340
Total	60	266.00	41.125	190	340

Group-B = Buprenorphine
Group-D = Dexmedetomidine
Independent t = -9.461
p-value= 0.000

Epidural catheter, on the other hand, provide excellent post operative pain control and is indicated in multimodal analgesia and chronic pain. Techniques like continuous spinal anesthesia using an intrathecal catheter; and combined spinal epidural (CSE) have been employed to get most out of neuraxial blockade. These techniques provided excellent operative condition and post operative control, but are not cost effective and require technical training and supervision. Spinal anesthesia is a relatively simple technique and cost effective as well. It would have been ideal if we could prolong the analgesic effect of single dose spinal. Multiple drugs have been studied so far. The list includes Opioids like morphine, sufentanyl, fentanyl, tramadol, buprenorphine; α-2 agonists like clonidine and dexmedetomidine; vasopressors like epinephrine; steroids like dexamethasone; NSAIDs like ketorolac, parecoxib and lornoxicam; induction agents like midazolam and ketamine; neostigmine and magnesium sulfate. Most of them prolonged analgesia with varying duration and complication.[7,8,9,10]

Most common complication of opioids were respiratory depression, itching/ pruritis, nausea/ vomiting, constipation, and addiction potential. Buprinorphine is a highly lipid soluble thebaine analogue that provides rapid onset and long

duration. Its weak agonism at μ opioid receptors causes less respiratory depression and addiction as compared to strong agonist. Bupinorphine has been widely compared to other opioids like fentanyl, morphine and tramadol. It has been found significantly superior in prolonging duration of analgesia.[13,14,15,16] Its a partial opioid receptor agonist but provided prolonged pain relief due to its local anesthetic properties. However it may increase the risk of post operative nausea/vomiting. [17,18]

Dexmedetomidine is an α-2 agonist which is getting popularity in all fields of anesthesia. Its induces sedation and analgesia by decreasing activity of nor-adrenergic neurons in the locus ceruleus of brainstem, thereby increasing the activity of inhibitory GABA neuron in the ventrolateral pre optic nucleus. It has been used in pre anesthetic sedation; as an induction agent; in maintenance of anesthesia; as a part of TIVA; for conscious sedation and sedation in ICU. When used in regional anesthesia it tends to prolong the effect of local anesthetics.[17,18]

In this study, the duration of analgesia between buprenorphine (60 μg) and dexmedetomidine (5 μg) was compared in intrathecal hyperbaric bupivacaine (0.75%). These dosages of test drugs has been proven safe in multiple studies.[8,9,19,20,21] We found in our study that both drugs prolonged the duration of analgesia. Dexmedetomidine with 297.8 ± 26.7 minutes was significantly better than buprinorphine with 234.2 ± 25.3 minutes ($p<0.0001$). These results are comparable to other studies. Gupta et al found in their study that dexmedetomidine with 493.56 ± 385.95 minutes is significanly better than buprinorphine with 289.66 ± 64.94 ($p=0.015$). [11]

Amitha S and Pradeep R in a randomized control trial compared dexmedetomidine 5 μg with buprenorphine 30μg. They concluded that dexmedetomidine is significantly better as the time for first analgesic requirement was 240 ± 30.2 minutes with dexmedetomidine as compared to 210±22.4 minutes with buprinorphine ($p=0.0001$). [22]

Kaur N et al in their study concluded that both buprenorphine and dexmdetomidine prolong the time for first analgesic but they could not find any statistically significant difference in both groups.[23] In comparison to this our study proved that dexmedetomidine is significantly better than buprinorphine.

Very few studies are available on this subject, as mentioned above, there are still many trials ongoing. Buprinorphine has also been compared to clonidine, another α-2 agonist, and found significantly better in prolonging the time for first analgesic.[24] Interestingly dexmedetomidine has also been compared to clonidine and is found equally effective 25 or significantly better 26 in some studies.

Our study has certain limitations. We have studied a single outcome variable i.e, time for first analgesic requirement. The duration between spinal anesthesia and time for first analgesic requirement was labeled as duration of analgesia. We could not study the onset of blockade; the extent of sensory and motor blockade; the time for regression of sensory and motor blockade; and adverse effects, if any, of the test drugs. Further clinical trials are needed in this aspect to assess all these parameters.

CONCLUSION

Both Buprenorphine and Dexmedetomidine can be successfully used in spinal anesthesia, to prolong the analgesia in all age groups and genders. Dexmedetomidine provides longer analgesia duration as compared to Buprenorphine and results are statistically significant ($p<0.0001$).

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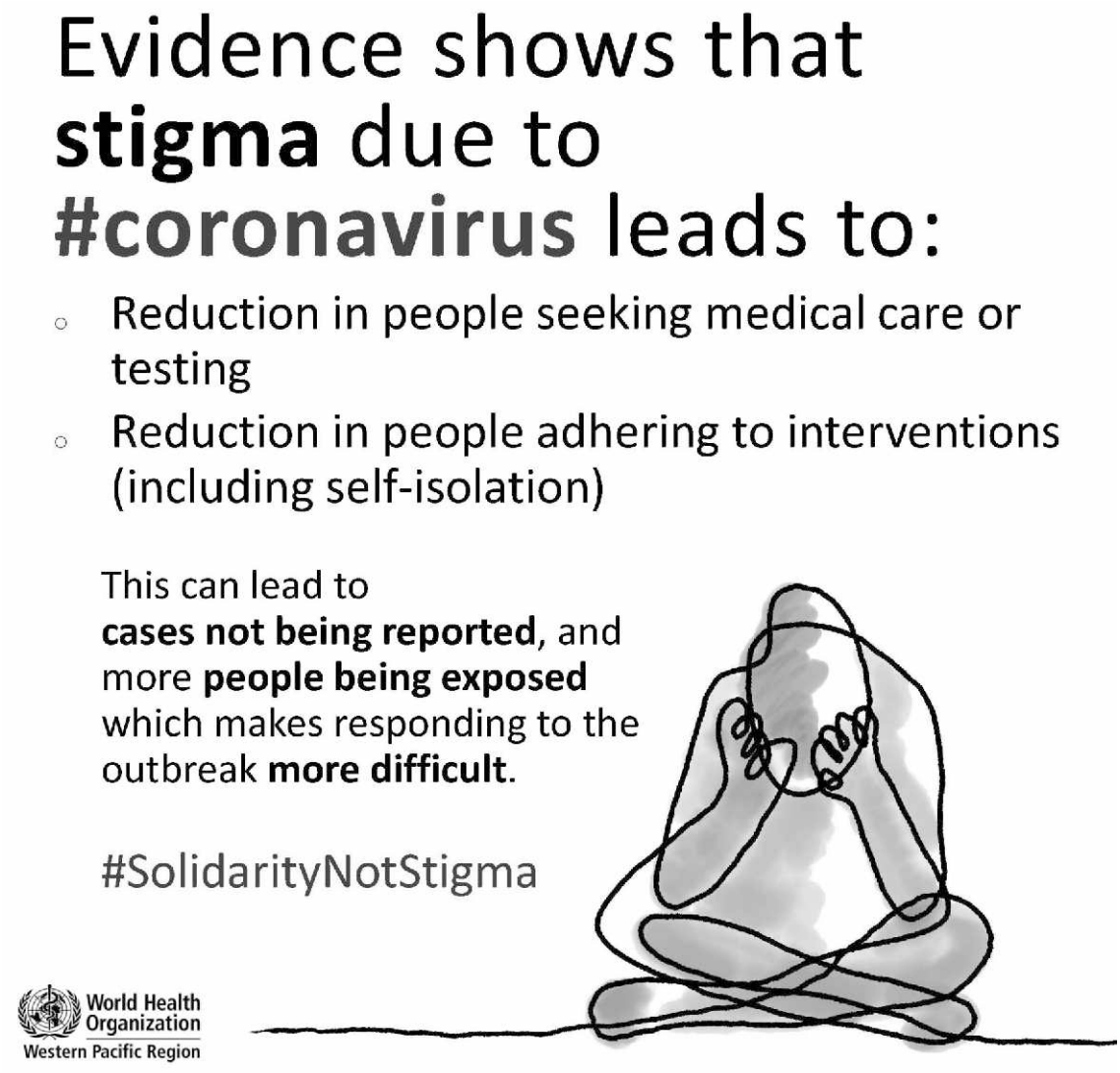

BURNOUT AND ITS INTER-SPECIALTY VARIATION IN DOCTORS OF JINNAH HOSPITAL LAHORE

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How to cite: Tufail H, Hanif H, Tariq H, Ahmad F, Haseeb M. Burnout and its inter-speciality variation in doctors of Jinnah Hospital Lahore. JAIMC. 2020; 18(4): 627-32.

Abstract

Background: Burnout is a "triad" of emotional exhaustion, depersonalization and reduced personal accomplishment. Taking in account the heavy emotional requirements of the work environment, doctors are vulnerable to burnout above and beyond the usual workplace stress.

Objective: To determine the prevalence of burnout in postgraduate doctors according to their specialty, in Jinnah Hospital, Lahore.

Methodology: It was a cross sectional study conducted at Allama Iqbal Medical College / Jinnah Hospital, Lahore from May, 2019 – June, 2019. A sample size of 200 was taken and non-probability purposive technique was used and burnout was assessed using MBI (Maslach burnout inventory). The data was then analyzed by using SPSS version 21.0.

Results: The burnout according to the specialty in pathology, gynecology, surgery, medicine and others were following: 17.5%, 30.0%, 55.0%, 90.0% and 42.5%

Conclusion: Burnout of varying degrees is present in all the specialties, with highest levels being observed in medicine and surgery while lowest was seen in pathology. Gender, age , time served as post graduate and number of working hours per day also appeared to influence the prevalence of burnout. The high incidence of burnout demonstrates the need of appropriate strategies to prevent adverse effects on doctors' quality of life and on the quality of care patients receive.

Keywords: burnout syndrome, MBI, Maslach burnout inventory, postgraduates, doctors,

In 1970s, the American psychologist Herbert Freudenberger presented the term "burnout" as a state of chronic stress leading to physical and emotional exhaustion (i.e. cynicism, detachment, feelings of inadequacy) and lack of accomplishment.[1] In short, burnout is a "triad" of emotional exhaustion, depersonalization and reduced personal accomplishment.[2]

Another interesting fact to ponder upon is that although, no specific diagnosis of burnout is mentioned in the Diagnostic and Statistical Manual of Mental Disorders, even then burnout is categorized as a clear syndrome with noticeable outcomes which indeed is a recurrent reason for medical excuses from work, and thus the impact on health-related economics is observed significantly.[3]

Taking in account the heavy emotional requirements of the work environment, doctors are vulnerable to burnout above and beyond the usual workplace stress. Hence, burnout is linked with a various kinds of undesirable pessimistic effects on patient's wellbeing.[2]

Burnout is a potential harbor for psychosocial adversities affecting not only the subjects but also the organizations which hire them. It can target physical and/or mental health, leading to psychopathological (e.g. anxiety, obsession-compulsion, interpersonal sensitivity, depression, hostility, para-

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Submission Date: 07-08-2020
1st Revision Date: 21-08-2020
Acceptance Date: 13-09-2020

noid ideation, alcoholism and addictions) and/or psychosomatic disorders (e.g. Cardiorespiratory alterations, severe headaches, gastritis, ulcers, insomnia, dizziness etc.).While on the other hand, organization suffers quantitative as well as qualitative loss of its output.[4]

The latest researches emphasize greatly on the disappointing observation i.e. "The rate of burnout among doctors is gradually increasing worldwide".

Burnout specialists at the AMA and Mayo clinic carried out a survey of 6880 doctors, with the objective of assessing and comparing burnout rates of 2011 with 2014. The results (given below) favored the stated observation completely.[5] Family medicine (51.3% in 2011 versus 63% in 2014), General surgery (42.4% versus 52.7%), Pathology (37.6 versus 52.5%) and General pediatrics (35.3% versus 46.3%).

Pakistan, being a developing country not only lacks scientific basis (including relevant researches) for this entity but also the standards for its diagnosis, classification and treatment are not well established.[3]

This research was aimed to study the rate of burnout among the post graduate doctors in Jinnah Hospital Lahore. The goal of this review is to provide medical educators and leaders with an overview of the existing factors that contribute to burnout, its inter-specialty variation, and suggestions for interventions to decrease burnout. Objective was to find out prevalence of burnout syndrome and its inter-specialty variation in postgraduates physicians of Jinnah Hospital Lahore.

METHODOLOGY

A Cross sectional study from May – August 2019 at Allama Iqbal Medical College/Jinnah hospital Lahore. 200 post graduates doctors who have been working for more than 6 months were selected through a non probability purposive technique. After an informed consent each doctor was given maslach burnout inventory, it is 3 sections based self-assessment instrument intended to evaluate degree of burnout syndrome according to inter-specialty variation. All information will be entered in a structured questio-nnaire (attached).

The data was entered and analyzed in SPSS version 17 or 21. Mean and Standard deviation will be calculated for variables e.g. number of working hours of post graduate doctors. Frequency and percentages were calculated for qualitative variables. Mean and SD was calculated for quantitative variables.

RESULTS

A total of 200 postgraduates participated in the survey. Out of these, 103 (51.5%) were female and 97 (48.5%) were male doctors. MBI research was carried out in five specialties. 40 post-graduates (20%) were taken from each of the five fields; Pathology, surgery, gynecology, medicine and others. 153 (76.5%) were of the age group 23-29 and 47 (23.5%) doctors fell in the age group of 30-36 years. Out of 200, 145 (72.5%) doctors served time for about 6 months–3 years while rest of them, 55 (27.5%) served for about 4-6 years. 173 (86.5%) doctors had 6-12 working hours and 27 (13.5%) doctors had 13-19 working hours. The means (M) for

Table 1:

Variables n=200	Frequency	Percent
Age		
23-29	153	76.5
30-36	47	23.5
Gender		
Male	97	49.5
Female	103	51.5
Emotional Exhaustion		
Low	73	36.5
Moderate	104	52.0
High	23	11.5
Depersonalization		
Low	14	7.0
Moderate	54	27.0
High	132	66.0
Personal Achievement		
Low level burnout (Score > 40)	85	42.5
Moderate burnout (Score 34 - 39)	42	21.0
High Level burnout (Score < 33)	73	36.5

Table 2:

		Burnout Grade			Total
		Low Burnout 1-3	moderate burnout = 4-6	high burnout 7-9	
gender of postgraduates	Male	5 5.2%	30 30.9%	62 63.9%	97 100.0%
	Female	0 0.0%	71 68.9%	32 31.1%	103 100.0%
age of postgraduates	23-29	2 1.3%	73 47.7%	78 51.0%	153 100.0%
	30-36	3 6.4%	28 59.6%	16 34.0%	47 100.0%
Total		5 2.5%	101 50.5%	94 47.0%	200 100.0%

Emotional exhaustion, De-personalization and Personal Achievement are 20.48, 16.09 and 36.01 and standard deviations (SD) of 8.17, 7.38 and 8.14 have been calculated respectively . Three aspects of MBI Inventory were explored. Out of 200 people the ratio of emotional exhaustion from low to medium to high was 73: 104: 23 and in percentage 36.5: 52.0: 11.5. The assessment of de-personalization showed the following results, 14: 54: 132 burnout in percentage 7.0: 27.0: 66.0.

The evaluation of personal achievement showed the following results 85: 42: 73 burnouts and in percentage 42.5: 21.0: 36.5.

The percentages of high burnout with respect to emotional exhaustion, depersonalization and personal accomplishment in pathology, surgery, medicine gynecology and others were: (00.0%, 22.5%, 5.0%, 7.5%, 22.5%), (35.0%, 55.0%, 100%, 70.0%,70.0%) & (22.5%, 45.0%, 67.5%, 25.0%, 22.5%).Conclusively, the total high burnout grade in pathology, surgery, medicine gynecology and others were: 17.5%, 55.0%, 90.0%, 30.0%& 42.5%. Other contributory factors to the prevalence of burnout causing high burnout rate were: gender(more in male with 63.9 % high burnout as compared to 31.1 % in females), age of post graduates (more in 23-29 with 51.0 % high burnout as compared to 34.0 % in 30-36 years old postgraduates), time served by postgraduates (more in doctors who served for 6 months -3 years with 53.8 % high burnout as compared to 29.1 % in postgraduates who served for 4-6 years) & number of working hours per day (more in physicians who work for 13-19 hours per day with 70.4 % high burnout as compared to 43.4 % in postgraduates working for 6-12 hours per day).

DISCUSSION

The study investigated burnout in post graduate doctors using MBI in five different specialties Pathology, Surgery, Gynecology, Medicine and Others (Dermatology, Cardiology, Eye and ENT) in Jinnah Hospital Lahore. The means for emotional exhaustion, depersonalization and personal achievement were calculated as 20.48, 16.09, 36.01 respectively and were found to be similar to those among physicians in Saxony Germany1, which were, 21.3, 9.9, 36.3 respectively.

As far as degree of burnout was concerned , emotional exhaustion from low to medium to high was 73:104:23 among the 200 postgraduates of JHL when compared to those in Germany 42:28:30, the results for depersonalization were 14:54:132 when compared with those in Germany 25:27:48. Likewise the results for personal achievement were, 85:42:73, which were similar to that of the physicians in Saxony Germany, 36:33:31. Even though the results were almost similar in the two researches, however, in Jinnah Hospital degree of burnout was much more severe in comparison with the physicians of Saxony, Germany.

The research conducted in Jinnah Hospital Lahore's post graduate trainees revealed that the highest degree of burnout was found to be associated with post graduates belonging to specialty of Medicine where 36 out of 40 (90%) trainees showed high degree burnout. Second highest burnout rate was found in post graduate trainees of Surgery where 22 out of 40 (55%) candidates had high burnout, third highest burnout i.e. 17 out of 40 (42.5%) was found in the specialty categorized as Others having Dermatology ,Eye, ENT and Cardiology included in it, followed by Gynecology department's post graduate trainees having fourth highest burnout i.e. 12

out of 40 (30%) and the specialty having least burnout rate turned out to be Pathology where only 7 out of 40 candidates revealed high degree burnout. The research conducted by Mayo Clinic of US in 2014 revealed that the highest degree of burnout was associated with the post graduate trainees of Medicine, followed by Surgery and least with Pathology. This finding is consistent with the results of our research which was conducted in Jinnah Hospital, Lahore. 28 out of 40 post graduate trainees of the Gynecology department of JHL revealed moderate degree of burnout, whereas the post graduates trainees of Gynecology department of Mayo Clinic US revealed low degree of burnout and high level of satisfaction with work-life balance. Hence the burnout in post graduate trainees of JHL is very high as compared to the candidates of research in Mayo Clinic at Gynecology department, the possible reasons for this difference being the lengthier working hours per day, poor working conditions in JHL and the female gynecologists finding it hard to manage their job along with their household chores.

Our research included 200 post graduate doctors. Out of these 103 were females and 97 male. One worth noting aspect was that males were more prone to depersonalization (tendency to opt for cynicism) than females. This finding was consistent with the research in Saxony, Germany. Emotional exhaustion was also found to be more prevalent among men with 15.5 % with high emotional exhaustion values compared to 7.8% of females. These tendencies reflected that the burnout was generally found to be higher among males than females in general. The plausible reason appearing to be more stress on men being the dependant part of our population.

With regard to age, burnout in almost all its forms affected more doctors who fell in the 23-29 age group and who were in their early specialization years. These findings were also consistent with the results of research among the medical residents of United States of America with the prevalence rate ranging from 27 to 75 %.[2] However with respect to emotional exhaustion in the post graduates in Jinnah hospital, Lahore, the 30 onward age group was found out to be more prone with 19.1 % as compared to 9.2 % of those below 30. In general a greater burnout among the young post graduates can be attributed to the lack of coping skills with the relatively novel workload and due to the absence of career counseling. Dissatisfaction with the monthly income is also a major contributory factor for high burnout among the younger age group in Jinnah Hospital, Lahore.

The next facet that our research comprised of included different specializations and their relative burnout degrees. In Medicine with the exception of emotional exhaustion which was 5%, they reported to have the greatest burnout with regard to personal achievement and depersonalization of 67.5 % and 100 % respectively. This was due to the greater number of cases reported to the medicine department and the consequent burnout. On the other hand the lowest degree of burnout was seen in Pathology department. Emotional exhaustion was 00.0%, depersonalization 35.0% and personal achievement was 22.5% .This being due to stress-free environment, less number of working hours per day and systematic management of the work place with lower work load.

It should be acknowledged that factors measured in the context of this study can also be the reasons for increased job turnover and wishes to leave the country to avail better opportunities abroad. Men were found to be more prone to these tendencies whereas women due to early marriage and having children were comparatively less aspiring. Such results were consistent with the French and German physicians.

CONCLUSION

Young postgraduates experience high levels of professional burnout due to intense and stressful working conditions this explains the reason behind high burnout in medicine and surgery and low burnout in pathology. Young male doctors due to long working hours and the pressure of supporting their families are more to developing high degree of

burnout.

Immediate attention needs to be payed to the above mentioned contributory factors in order to improve the mental, physical and emotional status of the doctors so that they can provide their patients with better care without compromising their health and quality of life.

RECOMMENDATIONS

- In order to reduce the development of burnout the working conditions in the hospital setting should be improved.
- The number of working hours per day must not be more than 10 and if the duty hours are more, then there must be sufficient breaks in between.

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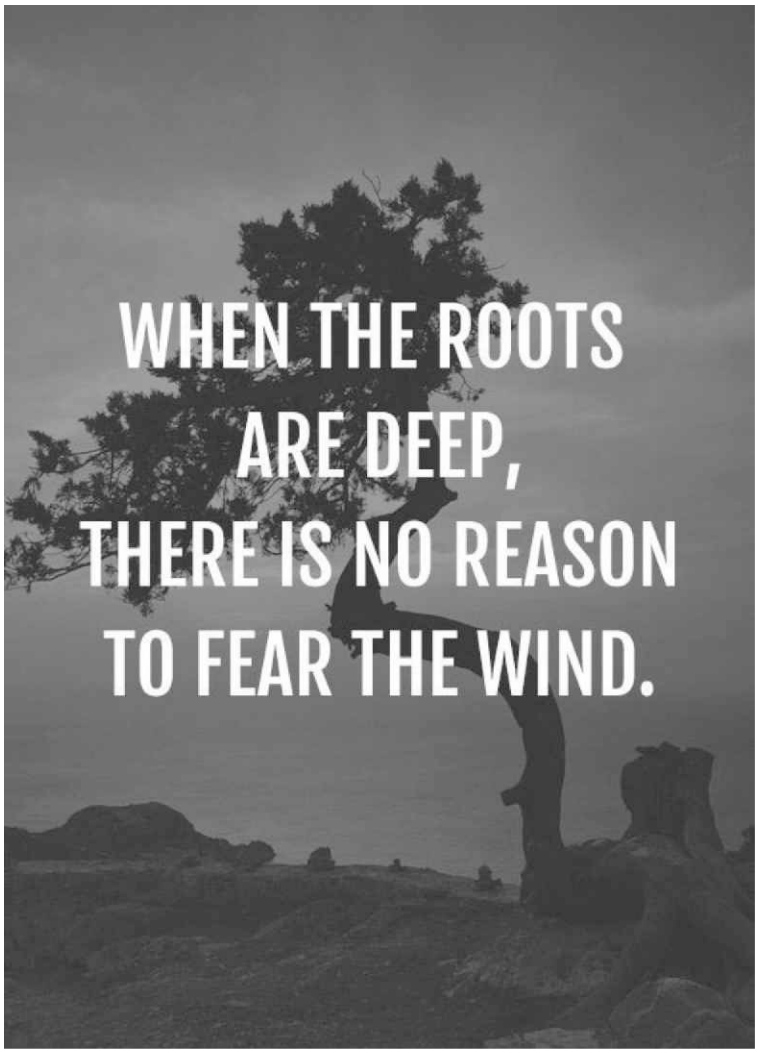

PERIPARTUM CARDIOMYOPATHY - STILL A DILEMMA

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How to cite: Iqbal N, Latif L, Salman N, Nisar M. Peripartum cardiomyopathy – still a dilemma. JAIMC. 2020; 18(4): 633-36.

Abstract

Objectives: To determine the risk factors and fetomaternal outcomes in women with PPCM. It was an observational prospective Cohort, conducted in Obstetric and Gyne Department of Al-Aleem Medical College, Gulab Devi Educational Complex, from 1st April 2019 to 31st March 2020.

Methodology: All women admitted or referred with PPCM were enrolled in this study after informed consent. Data regarding age, parity, booked/unbooked, socio economic status, and fetomaternal were recorded and analyzed.

Results: During this period there were 900 deliveries and 20 women were having PPCM giving an incidence of 2.2%. Majority of the women 65% were between 31-40 years and 65% were multipara. Maternal mortality was 5% and neonatal was 6.67%. The booked women were 95%.

Conclusion: The PPCM is an obstetric catastrophe associated with high maternal and perinatal morbidity and mortality in developing countries. The study showed multiple risk factors are associated with it, the most important being advance age, multiparty, obesity and hypertension.

Key Words: Pregnant women, Peripartum Cardiomyopathy.

Peripartum cardiomyopathy (PPCM) is said to be a myocardial lesion linked up with pregnancy associated with failure of heart because of pronounced systolic dysfunction of the left ventricle, resulting significant maternal morbidity and mortality.[1] Globally its incidence varies, uncommon as 1 per 2500 to 4000 live births in United States, Canada, Europe; and common as 1 in 1000 live births in South Africa and up to 1 in 300 live births in Haiti,[2,3,4] In Pakistan it is 1 in 837 deliveries in one study[5] and 1 in 960 in another study6. The Risk factors related with PPCMP are age of mother 25 years or more, African race, para 4 or more, twins/triplets, marked anemia, pregnancy-induced hypertension, elevated liver enzymes, and low platelet count (HELLP Syndrome).[4,7] The underlying cause of PPCMP is still in a grey zone. This could be because of previous viral illness or atypical immune response, though definite evidence is still lacking, that antiviral or immunosuppressant therapy are fruitful.[3] Many studies were supporting that genetic mutations play an important role to this disease.[8] Some studies were focusing on the hormonal cause that is raised prolactin levels in Peripartum and post-partum period resulting abnormal immune response and leading to disease.[9] Because there is fundamental overlapping of symptoms which are pregnancy related, especially at the end or immediate after delivery, and heart failure, this is the reason that diagnosis could be delayed[2]. Patients with Peripartum cardiomyopathy may present with fatigue, dyspnea, orthopnea, cough, ankle edema, chest pain and more weight gain in third trimester of pregnancy. For diagnosis ECG and Echocardiography are important tools, Echocardiographic findings show an ejection fraction (EF) <45 % and fractional reduction <30% along with left ventricular end diastolic measure 4.8 cm/m^2 of body surface area.[10] The Maternal Mortality in in United States has been notified 25%-50% with Peripartum

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Submission Date: 02-08-2020
1st Revision Date: 21-09-2020
Acceptance Date: 30-09-2020

Cardiomyopathy.[11,12] Counseling of the patients is utmost important in the subsequent in order to reduce the risks of maternal morbidity and mortality.[13] In Pakistan data regarding this disease is significantly low. There are only three studies quoting a small number of patients.[5,6,14] The purpose of this study was to find out the risk factors and fetomaternal outcome in PPCMP, presenting at AL-Aleem Medical College affiliated with Gulab Devi Educational Complex.

METHODOLOGY

This Observational Prospective Cohort was carried out at department of Obstetric and Gyne in AL-Aleem Medical College affiliated with Gulab Devi Educational Complex after approval from the Ethical Review Board. The period of study was one year from 1st April 2019 to 31st March 2020. All patients admitted and referred to the institute with PPCMP were included in the study after formal informed consent. The patients were evaluated by a joint team of a Cardiologist and a Gynecologist. Clinical evaluation includes a detailed history, physical examination, determination of functional capacity, and assessment on the basis of New York Heart Association functional class. Patients' previous records were checked for any known cardiac disease and associated conditions. Patients' height and weight, blood pressure, pulse and electrocardiography were done. Baseline investigations including blood complete examination, renal function tests, liver function tests, serum electrolytes, and blood sugar levels were carried out. Echocardiography was done to evaluate the LV systolic function and to rule out any other cardiac pathology leading to heart failure. All the data were entered, rechecked and then analyzed using SPSS version 12. Descriptive statistics was used to check the frequency and percentage of all quantitative variables.

RESULTS

A total of twenty pregnant women with cardiomyopathy were recruited in the study. The mean age of the woman was 29.2±2.4 years. Majority 65% were between 31-40 years of age as shown in Table l. The 95% women were booked.

Presentation of women with Peripartum cardiomyopathy varies according to New York Heart Association classification. Major chunk of the women 85% presented with class ll and lll as shown in Table ll.

Table I: *Demographic Data of Woman (n=20)*

Variables	No. of Women	Percent
Age Years		
20 – 30	6	30
31 – 40	13	65
>- 40	1	5
Parity		
Gravida 2	7	35
Gravida 3	11	55
Gravida 4 & more	2	10

Risk factors observed in our study were highlighted in Table lll.

Maternal outcomes was shown in Table lV. All the women were saved except one (5%), That woman was 35 years para 4 delivered at home 2 days back, unbooked, presented with severe shortness of breath and cardiac failure, admitted in ICU, her ejection fraction was 26% expired after 3 days.

Table II: *Distribution as per NYHA Classification (n=20)*

Class	No. of Women	Percentage
Class I	1	5
Class II	10	50
Class III	7	35
Class IV	2	10

Table III: *Risk Factors (n=20)*

Variables	No of Women	Percentage
Maternal Age > 30	14	70
Parity > 4	2	10
Hypertension	4	20
Pregnancy Induced H.T	6	30
HELLP	3	15
Hypothyroidism	2	10

Neonatal outcome was shown in Table V. Only

one baby expired that was preterm with low birth weight.

DISCUSSION

Table IV: Maternal Outcome (n=20)

Cardiac Outcome	No. of Women	Percentage
Dyspnea	14	70
Palpitation	7	35
Pulmonary edema	8	40
Thromboembolism	1	5
Chest Pain	1	5
Mortality	1	5
Obstetrical Outcome		
First Trimester loss	3	15
Second Trimester loss	2	10
Preterm Labour	3	15
Preterm delivery	2	10
Mode of Delivery (n=15)		
LSCS	7	46.67
Vaginal delivery	8	53.33

Peripartum cardiomyopathy is rare but potentially harmful to maternal health, responsible up to 9%-11% of maternal death.[15] The incidence in our study was 2.2% and this is supported by other studies.[5,6,14] The common risk factors associated with PPCM are increased maternal age, multiparty, black race, hypertension, hypothyroidism, low social class, anemia, Obesity, use of alcohol, tobacco and oncolytic agents.[16] In our study important risk factors found were advance maternal age 70%, multiparty 65%, poor social class 75%, Obesity 65% anemia 60% hypertension 35% and hypothyroid 10%, this is similar with other studies[5,6,14] but the study conducted in India showed no traditional risk factors.[17] Majority of our patients 85% presented in class II (50%) and III (35%) according NYHA classification this is mimic with other studies.[5,6,18,19] Echocardiography was used as gold standard test to diagnose and manage PPCM in the study, this is supported by other studies.[5,10] The Successful managing the Peripartum cardiomyopathy women is still a great challenge to the obstetric team because of increased risks in such patients. Pregnancy induced hyper dynamic circulatory alterations are responsible for up rise in left atrial pressure, that leads to increased risk of left ventricular failure accompanying pulmonary edema.[20] In our study 53.33 percent had vaginal delivery and 46.67 percent required caesarean section because of obstetric reasons, this is tallying with other studies.[5,6,17] A multidisciplinary approach was used consisting of an experienced Obstetrician, Cardiologist, Anesthesiologist, Perinatologist and Staff nurse. Following delivery 50% of women required ICU care under supervision of cardiologist and anesthesiologist. Maternal cardiac outcomes observed in our study were dyspnea 70%, pulmonary edema 40%, palpitation 35%, thromboembolism 5% and chest pain 5% such complications were also observed in other studies.[5,6] Obstetrical outcomes in our study were first trimester pregnancy loss 15%, second trimester pregnancy loss 10%, preterm labour 15% and preterm delivery 10%. Maternal mortality in our study was 5%, this is mimic with other studies,[5,6] that woman was 35 years para 4 delivered at home 2 days back, unbooked, presented with severe shortness of breath and cardiac failure, admitted in ICU, her ejection fraction was 26% expired after 3 days in spite of close vigilant monitoring. Regarding neonatal outcome in our study 20% babies were preterm, low birth weight was found in 33.33% neonates, 40% babies required nursery admission, only neonatal mortality was 6.6% it was preterm and low birth weight, this is supported by other studies.[5,6,21] The prognosis of women with PPCM mainly depends on both normalization of function and size of left ventricle,[22] it took almost 5-6 months. Counseling regarding contraception is utmost important to prevent maternal morbidity.

Table V: Neonatal outcome (n=15)

Outcome	No. of neonates	Percentage
Preterm Births	3	20
Low Birth Weight	5	33.33
Nursery Admission	6	40
Neonatal mortality	1	6.67

CONCLUSION

The prognosis mainly depend upon advanced multidisciplinary approach.

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COMPARISON OF ANTIEMETIC EFFECTS OF DEXAMETHASONE AND ONDANSETRON IN LAPROSCOPIC CHOLECYSTECTOMY

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How to cite: Khan MA, Aslam M, Ajmal MO, Dodhy AA, Butt MM. Comparison of antiemetic effects of dexamethasone and ondansetron in laproscopic cholecystectomy. JAIMC. 2020; 18(4): 637-42.

Abstract

Background: Although there is rapid growth in the field of modern anaesthesia, the incidence of postoperative nausea and vomiting still remains high. Dexamethasone has been used as an antiemetic in patients undergoing laparoscopic cholecystectomy with limited side effects. Ondansetron a 5- HT3 receptor antagonist has provided effective antiemesis in surgical patients undergoing laparoscopic cholecystectomy.

Objective: To compare the effects of dexamethasone and ondansetron as an antiemetic in laparoscopic cholecystectomy.

Methodology: This randomized controlled trial was done at Department of anaesthesia and ICU, Lahore General Hospital Lahore for one year. Sixty patients were included in the study through convenient, non-probability sampling. In-group D, patients who were given dexamethasone for laparoscopic cholecystectomy and in group O, patients were given ondansetron for the same procedure. Both groups were given the drugs intravenously after induction of general anaesthesia with endotracheal tube. The effects of both drugs were assessed.

Results: In group D, 18.3% of patients had complaints of nausea, and 26.7% had complaints of vomiting. While in-group O, 18.3% of patients complained of nausea, and 16.7% had complaints of vomiting. The difference was statistically insignificant, but on seeing the data it can be derived that there were more complaints of vomiting in dexamethasone group while no difference in complaints of nausea in both the groups.

Conclusion: It was concluded that there is no significant difference in the efficacy of both the drugs. These drugs have markedly reduced the incidence of nausea and vomiting in patients undergoing for laparoscopic cholecystectomy.

Key Words: Postoperative nausea and vomiting, dexamethasone, ondansetron, laparoscopic cholecystectomy

Although there is rapid development in the field of modern anaesthesia, the incidence of postoperative nausea and vomiting (PONV) still remains high. Independent of a patient's baseline risk of postoperative nausea and vomiting, ondansetron and dexamethasone can reduce PONV.[1] In patients undergoing laparoscopic cholecystectomy, high incidences of PONV have been reported (50-70%).[2]

Dexamethasone has been used as an antiemetic for more than 20 years in patients undergoing chemotherapy, with limited side effects. Dexamethasone or methylprednisolone is more effective or better tolerated (or both) than the phenothiazines or benzamides.[3] Antagonists to 5-HT3 receptors are also effective antiemetic agents when used with such chemotherapeutic regimens. Ondansetron a 5- HT_3 receptor antagonist has provided effective antiemesis in surgical patients.

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Submission Date: 23-07-2020
1st Revision Date: 20-08-2020
Acceptance Date: 11-09-2020

Recently dexamethasone has been reported to be effective in reducing the incidence of postoperative nausea and vomiting in paediatric patients undergoing tonsillectomy, adenoidectomy and strabismus repair,[4] women undergoing gynaecological surgery[5] and in patients undergoing laparoscopic cholecystectomy.[6] Combination of antiemetic drugs could be an effective method to control severe postoperative nausea and vomiting.[7]

The aim of this study was to determine the efficacy of ondansetron and dexamethasone for the prevention of PONV in laparoscopic cholecystectomy. Objective of the study was to compare the effects of dexamethasone and ondansetron as an antiemetic in laparoscopic chole-cystectomy.

METHODOLOGY

Study Design: Randomized controlled trial

Setting: Department of anaesthesia and ICU, Lahore General Hospital Lahore

Duration of study: One year i.e. 01/01/2019 to 31/12/2019

Sampling: Convenient, non-probability sampling

After approval from hospital ethical committee and informed written consent, all patients were premedicated with midazolam 2 mg intravenously thirty minutes before surgery in the preoperative room. By using random number table, the patient was allocated to one of the two groups before induction; Group D, those who were given intravenous dexamethasone 8mg and group O, those who were given intravenous ondansetron 4mg. Patients in both of these groups received general anaesthesia with endotracheal tube and were induced with Propofol 2mg/kg intravenously and atracurium 0.6mg/kg intravenously, maintained with isoflurane in 40% oxygen and 60% nitrous oxide. After induction, one of the two study drugs was given to the patient. Injection ketoralac 30mg and injection nalbuphine 6mg intravenously were given intra operatively. Intermittent doses of atracurium was given during anaesthesia to maintain adequate muscle relaxation throughout the procedure. Reversal of neuromuscular blockade was achieved with neostigmine 2.5 mg and atropine 1 mg intravenously. Post-operative analgesia with injection nalbuphine 4mg intravenously 4 hourly and injection ketoralac 30mg intravenously 8 hourly and on demand given. Following variables were evaluated: mild nausea, moderate nausea, severe nausea and number of vomitings per hour, rescue antiemetic and complete response. Vomiting was taken in numbers per hour. Rescue antiemetics, metoclopramide 10mg intravenously were given when vomiting occurred. The complete response was defined as no nausea, no vomiting and no antiemetic medication during 24 hours postoperative period.

Mild nausea defined as slight sensation associated with awareness of urge to vomit, moderate nausea (more intense sensation associated with awareness of urge to vomit), and severe nausea (intense sensation associated with urge to vomit). Vomiting was defined as forceful expulsion of gastric contents from mouth.

Data was analyzed by using SPSS version 21. The outcome variables were mild nausea, moderate nausea, severe nausea and number of vomiting per hour, rescue antiemetic and complete response and the two groups were compared by using chi-Square test. $P \leq 0.05$ was taken as significant.

RESULTS

The mean age of patients was 41.20± 12.15 years. There were 54 (90%) females while 6 (10%) were males. The mean duration of surgery was 68.75±16min. Table 1

Overall view of nausea given for both the groups. In dexamethasone group, 3(5%) patients complained mild nausea, 5(8.3%) had moderate nausea while severe nausea was present in 3(5%) patients. On the other hand in ondansetron group 4(6.7%) patients complained mild nausea, 2(3.3%) patients complained moderate nausea while 5(8.3%) patients had severe nausea. The difference was insignificant ($p>0.05$).

In 8 (26.7%) patients in dexamethasone group

and 5 (16.7%) patients in ondansetron group had vomiting. In 8 (26.7%) patients in dexamethasone group and 5 (16.7%) patients in ondansetron group required rescue medication. In dexamethasone group 19(63.3%) patients had complete response while 19(63.3%) patients in ondansetron group also had complete response. The difference was insignificant (p>0.050). Table 2

DISCUSSION

Laparoscopic cholecystectomy for the treatment of cholelithiasis is popular amongst surgeons as well as patients due to its associated advantages, which includes a short hospital stay. The latter advantage has been negated by PONV, which is turning out to be the leading cause of unexpected readmission after day surgery. The incidence of PONV has been reported to be as high as 53–72%. After laparoscopic cholecystectomy up to 70% patients have PONV if they are not on any antiemetic prophylaxis. The etiology of PONV after laparoscopic cholecystectomy is not wholly understood. Risk factors such as a prolonged CO_2 insufflation, gall bladder surgery, intraoperative use of isoflurane, fentanyl and glycopyrrolate, female sex and postoperative use of patient controlled analgesia with opioids may contribute to these episodes. CO_2 insufflation significantly increases peritoneal pressure, reduces intestinal blood flow and leads to intestinal ischemia and release of emetogenic substances. Also, the emetic center is stimulated by the afferents from the gastro-intestinal tract manipulated during surgery. Intraoperative hypotension may cause brainstem hypoxia and thus trigger the vomiting center to induce emesis. Further, the intestinal tissue is active metabolically and has a poor tolerance for even brief periods of hypoxia or ischemia.

Table 1:

N	60
Age	41.20±12.15
Female	54 (90%)
Male	6 (10%)
Time duration for surgery	68.75±16

Table 2:

		Group		p-value
		Dexamethasone	**Ondansetron**	
Severity of nausea during surgery	No Nausea	19 (31.7%)	19 (31.7%)	0.587
	Mild	3 (5.0%)	4 (6.7%)	
	Moderate	5 (8.3%)	2 (3.3%)	
	Severe	3 (5.0%)	5 (8.3%)	
Vomiting		8 (26.7%)	5 (16.7%)	0.347
Rescue Medication		8 (26.7%)	5 (16.7%)	0.347
Complete Response		19 (63.3%)	19 (63.3%)	>0.999

An important intestinal response to ischemia is the release of serotonin, a highly emetogenic substance. There are various drug therapies for the prevention of PONV. Droperidol is an effective antiemetic, but is associated with side effects such as agitation, sedation, extra-pyramidal reactions and delayed awakening with large doses. Smaller doses of (0.625 mg) of droperidol are as effective as larger doses (1.25 mg) and 4 mg IV ondansetron. Lower doses of droperidol may also be associated with restlessness. Transdermal scopolamine decreases PONV after laparoscopic surgeries, but 91% of patients experience side effects. Phenothiazines and antihistamines can produce sedation and lethargy. Metoclopramide is also an effective antiemetic but not without side effects including dystonic reactions, restlessness and tachycardia. Symptoms resembling parkinsonism have also been reported in children. Antagonists at the NK1 receptor represent a new class of antiemetics, which is still under investigation. Ondansetron, a 5-hydroxy tryptamine subtype 3 (5HT3) receptor antagonist, is an effective antiemetic for the prevention and treatment of PONV. It has been extremely useful in reducing PONV in patients undergoing laparoscopic cholecystectomy. Despite its advantages, including minimal side effects, it is expensive compared with other antiemetics.

5-hydroxytryptamine 3 (5-HT3) receptor antagonists were earlier shown to prevent effectively chemotherapy-induced nausea and vomiting. During the past few decades, 5-HT3 receptor antagonists have been investigated extensively in the

prevention of PONV.[8] Dexamethasone, which similarly was first used to prevent chemotherapy-induced emesis, has been lately investigated for the prophylaxis of PONV. The effective dose of dexamethasone is 8–10 mg in adults and 1–1.5 mg/kg in children.[9]

Dexamethasone reduces the incidence of nausea and vomiting after major gynecologic surgery[10] (i.e., hysterectomy), laparoscopic cholecystectomy, thyroidectomy, or pediatric tonsillectomy[11,12]. The exact mechanism of dexamethasone for the prevention of postoperative nausea and vomiting is not known, but there have been some suggestions, such as central or peripheral inhibition of the production or secretion of serotonin, central inhibition of the synthesis of prostaglandins, and changes in the permeability of the blood-brain barrier to serum proteins.[13]

Multiple interventions, including prophylaxis using two or more antiemetic drugs, were recommended for patients at high risk of PONV.[14] Dexamethasone with ondansetron is an attractive combination, because ondansetron is most effective against early vomiting. The optimum prophylactic dose of ondansetron alone appears to be 4–8 mg[8], whereas dexamethasone is effective against both early and late (2–24 h) nausea and vomiting, its late efficacy being pronounced.[15] Dexamethasone 8–10mg is widely used but smaller doses are effective for ambulatory laparoscopic surgery.[16]

In our study it can be seen that 5 patients complained of vomiting in ondansetron group which was 16.7% of the patients of that group. In dexamethasone group, 8 patients had complaints of vomiting which was 26.7% of that group.

Kashmiri ZU et al. used dexamethasone 8 mg for PONV prophylaxis in laparoscopic cholecystectomy patients, observed a significant reduction in PONV. In a study comparing dexamethasone at the same doses, a 5 mg dose appeared to be optimal for preventing PONV in patients undergoing thyroidectomy.[17] Henzi et al in a review have seen that a single prophylactic dose of dexamethasone, compared with placebo appeared to be an antiemetic displaying a more apparent late efficacy. The antiemetic effect of dexamethasone seems to start after 2 hours after its administration, thus the role of dexamethasone in the treatment of PONV is limited to the most intractable symptom not responding to any other antiemetic agent. Easy availability, being economical and absence of significant side effects are the features that suggest more frequent use of dexamethasone in these patients.

In our study, the complaint of nausea was 18.3% in each group, which is 36.6% of total patients in the study. 11 patients in dexamethasone group had complaints of nausea and the same number of patients had similar complaints in ondansetron group. Ondansetron is most effective against early vomiting. The optimum prophylactic dose of ondansetron alone appears to be 4–8 mg, whereas dexamethasone is effective against both early and late (2–24 h) nausea and vomiting, its late efficacy being pronounced. Similar efficacy of dexamethasone 8 mg was observed when used as prophylaxis for reducing PONV in different laparoscopic cholecystectomy. The antiemetic efficacy of ondansetron has been proven to be superior to placebo and metoclopramide and equal to that of droperidol and dexamethasone.[18] In one of the systematic reviews, the anti-vomiting effect of ondansetron was more pronounced than its anti-nausea effect. Ondansetron appears to be more effective in controlling postoperative vomiting than nausea. The effect of 5-HT3 receptor antagonists on the treatment of vomiting is confirmed, but the anti-nausea effect is not so clear. Dexamethasone 8mg was used for PONV prophylaxis in laparoscopic cholecystectomy patients and observed a significant reduction in PONV.[19] Laiq N et al. comparison of dexamethasone prophylaxis with saline placebo in gynecological laparoscopic surgical patients was done and observed a significant reduction in the incidence of PONV. Dexamethasone 8 mg prophylaxis was used for reducing PONV in a different laparoscopic cholecystectomy patient population. No problems with wound healing, or

disturbances of glucose metabolism have been reported after a single prophylactic dose.

In our study complete response, which was no nausea, no vomiting, no rescue medication, was in 19 patients in each group who underwent laparoscopic cholecystectomy. This was 63% in our study.

Biswas BN et al compared ondansetron 4mg, dexamethasone 8mg, and ondansetron plus dexamethasone vs. placebo in their laparoscopic tubal ligation patients. They found a complete response of 60% and 63% respectively in ondansetron and dexamethasone groups, they found no significant difference. The incidence of PONV in the ondansetron plus dexamethasone group when compared with ondansetron or dexamethasone alone was also statistically insignificant. Yuksek MS et al. while comparing ondansetron 4mg with dexamethasone 8mg in gynaecological laparoscopic surgeries found ondansetron to be better than dexamethasone, incidence of PONV 35% vs. 55% respectively, with significant difference only in the first 3 hours postoperatively when used for PONV prophylaxis at induction.

Finally It was concluded from this study that incidence of nausea is equal in both the groups but incidence of vomiting was less in ondansetron group. Our study did not show a statistically significant difference between the dexamethasone and ondansetron groups in controlling nausea and vomiting in laparoscopic cholecystectomy.

CONCLUSION

On the basis of this study, it can be concluded that:

1. Use of dexamethasone and ondansetron as an antiemetic in laparoscopic cholecystectomy reduced the incidence of nausea and vomiting.
2. Although the results are statistically insignificant but on seeing the data it can be confidently concluded from this study that ondansetron reduces vomiting better than dexamethasone and there is no difference between ondansetron and dexamethasone to control nausea.

RECOMMENDATIONS

The sample size (n=60) in our study was too small to validate the results within the groups for comparison with other studies. It is therefore suggested that bigger sample size should be chosen for evaluation of both drugs as an antiemetic in laparoscopic cholecystectomy. Dexamethasone is cheaper than ondansetron, and side effects with single dose are not frequent so it should be used more frequently. As we used only one drug in our patients for each group, it is suggested that combination of drugs can be used to get better results to control nausea and vomiting in laparoscopic cholecystectomy.

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COMPARISON OF MIRABEGRON AND TAMSULOSIN FOR THE TREATMENT OF URETERAL STENT RELATED SYMPTOMS

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How to cite: Durrani AS, Saifullah M, Javed MS, Rehman A, Yousaf MH, Rahman F. Comparison of mirabegron anf tamsulosin for the treatment of ureteral stent related symptoms. JAIMC. 2020; 18(4): 643-49.

Abstract

Background: Double J stents is an important auxiliary being used in urological surgeries. DJ stents are safe, still may be associated with lower urinary tract symptoms (LUTS) secondary to smooth muscle spasm, vesicoureteric irritation, back reflux of urine and urinary bladder mucosal irritation. This LUTS can be treated with different pharmacological agents including tamsulosin and mirabegron.

Objective: To compare the efficacy of Mirabegron and Tamsulosin for the treatment of ureteral stent related symptoms.

Methodology: This randomized controlled trial was carried out at Sheikh Zayed Hospital, Lahore during January 2019 to December 2019. We enrolled 194 patients (97 in each group) using non-probability consecutive sampling technique. Patients were randomized into group A and B. Group A received 0.4 mg Tamsulosin once daily at bedtime whereas group B received 50mg Mirabegron once daily. The medication was started on the 1st post-operative day and was continued until stent removal. IPSS questionnaire was used to assess LUTSs on 1st day after removal of Foley catheter. After 4 weeks, IPSS was re-assessed just before removal of DJ stent. All the data was analyzed using SPSS version 23.

Results: Mean age was calculated as 39.96+5.04 years in Group A and 41.24+4.09 years in Group B. Gender distribution revealed 68.81 % (n=64) in Group A and 64.21% (n=61) in Group B were male while 31.19% (n=29) in Group A and 35.78% (n=34) in Group B were females. Mean IPSS on 1st day after removal of catheter was 10.23+2.01 in Group A and 10.89+1.67 in Group B ($p = 0.0152$). IPSS after 4 weeks was 6.02+1.12 in Group A and 4.54+0.89 in Group B ($p < 0.0001$) while the change in IPSS was calculated as 4.21+0.89 in Group A and 6.35+0.78 in Group B ($p < 0.0001$) showing a significant difference between the two groups.

Conclusion: Mirabegron single therapy showed good results as compared to Tamsulosin in treating LUTS caused by DJ stents.

Key word: Mirabegron, Tamsulosin, DJ stent, Stent related symptoms.

Upper tract endourological procedures are usually supplemented by temporary urinary drainage using ureteric stents (US).[1] These stents are soft plastic tubes which are designed in such a way that urine flows through or around them. They are usually called double-J (DJ) stents or pig-tailed catheters because of soft coils at both the ends. This helps in prevention of stent migration.[2] There are certain qualities which should be present in stents. Ideally ureteric stent should be cheap, radio-opaque, chemically stable and show good flow characterstics. Furthermore, it should allow easy insertion, internal placement and prevent migration as well as encrustations.[3] Usual indications of DJ stenting include ureteric obstruction, infected hydronephro-

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Submission Date: 03-08-2020
1st Revision Date: 12-08-2020
2nd Revision Date: 28-09-2020
Acceptance Date: 30-09-2020

sis and prevention of iatrogenic ureteric injuries.[4,5] Moreover, it is used for ureteric splintage after different endourological, laparoscopic and open procedures.[6] Not only these stents help in securing renal function but also helps in treatment of pain caused by obstructive uropathy. Ureteric stents expedites healing of mucosal trauma, transit of broken stones and prevents ureteric stricture formation.[7,8] Although ureteric stents have their benefits but 19-80% of patients experience their side effects which significantly deteriorates the quality of life (QoL). 9-11 These are collectively known as the so-called "stent syndrome".[9] These side effects include frequency, sexual dysfunction, reduced work capacity, urgency, dysuria, flank pain, incomplete emptying, suprapubic pain, hematuria and reduced QoL.[4,12] Different questionnaires have been used to quantify these symptoms like international prostate symptom score (IPSS), overactive bladder questionnaire (OAB-q) and QoL questionnaire.[11] As far as medical management for control of these symptoms is concerned, different drugs have been proposed and studied including analgesics, muscarinic receptor blockers, alpha receptor antagonists, phosphodiestrase-5 (PDE5) inhibitors and combination therapy.[12] Tamsulosin is a well studied selective α-1a receptor blocker which reduces smooth muscle contraction of bladder neck and trigone[6,13] It is hypothesized that relaxation of these smooth muscles will reduce voiding pressure and in turn provide benefit in patients with stent related symptoms.[14] On the other hand, smooth muscle of the bladder and ureter also contains β_3 adrenoreceptors.[15] Mirabegron is well known β_3 agonist which has proven efficacy in treatment of irritative lower urinary tract symptoms (LUTSs) due to overactive bladder (OAB).[16,17] As ureteric stent causes irritative or storage LUTSs like OAB syndrome, therefore a theoretical advantage exists that Mirabegron can benefit patients with LUTSs due to ureteric stent.[18]

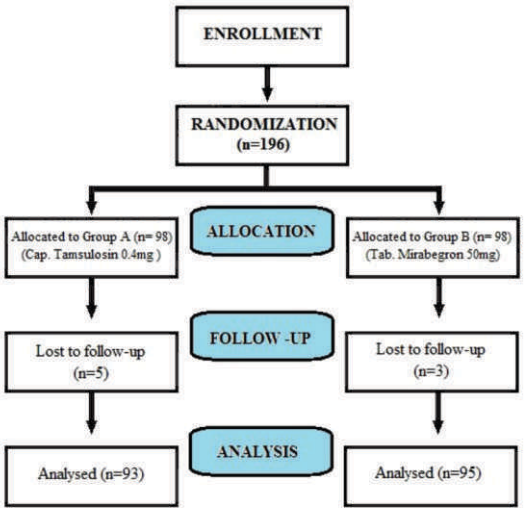
The rationale of our study was to aim at the medical management of stent related symptoms by comparing β_3 agonists with α-1a blockers. This would help in better tolerability of DJ stents and thus improve quality of life.

The objective of the study was to compare the efficacy of Mirabegron and Tamsulosin for the treatment of ureteral stent related symptoms.

METHODOLOGY

This single blind randomized controlled study was carried out at Sheikh Zayed Hospital, Lahore during March 2019 to May 2020. After taking approval from ethical review committee, informed consent was obtained from all the patients. Patients aged 18 years or more who underwent semi-rigid ureteroscopy for ureteric stones followed by DJ stenting were included in the study. However, patients with active urinary infection, pre-existing overactive bladder syndrome and benign prostatic enlargement were excluded from the study. Moreover, the patients who encountered ureteric injury during ureteroscopy were also excluded from the study. Under spinal anesthesia, ureteroscopy and intra-corporeal lithotripsy was performed with a semi-rigid ureteroscope and pneumatic lithoclasts. After stone retrieval, the 4.8 Fr polyurethane DJ stent (Boston) was placed in situ. Digital x-ray KUB was used to confirm the stent position before discharge. We enrolled 194 patients (97 in each group) using non-probability consecutive sampling technique. Patients were randomized into two groups i.e., A and B using computer generated random number table. Group A received Tamsulosin (0.4 mg) once daily at bedtime whereas group B received Mirabegron (50 mg) once daily. The medication was started on the 1st post-operative day and was continued until stent removal. Diclofenac sodium 50 mg was given to all patients for pain relief. IPSS questionnaire was used to assess LUTSs on 1st day after removal of Foley catheter. After 4 weeks, IPSS was re-assessed just before removal of DJ stent. All the data was analyzed using SPSS version 23. The quantitative variables like age, IPSS score on 1st day after removal of catheter, IPSS score after 4 weeks of procedure and mean change in IPSS

were presented as mean and standard deviation. The qualitative variable like gender was presented as frequency and percentage. Independent sample t-test was used to compare the change in IPSS scores. Independent sample t-test was applied. P-value < 0.05 was taken as significant.



FLOW DIAGRAM (CONSORT)

RESULTS

Mean age was calculated as 39.96+5.04 years in Group A and 41.24+4.09 years in Group B. Amongst these 39.78% (n=37) patients in group A and 35.79% (n=34) in group B were aged 18-35 years, whereas 60.22% (n=56) in group A and 64.21% (n=61) in group B were aged between 36 and 50 years. (Figure # 1) Gender distribution revealed 68.81 % (n=64) in Group A and 64.21% (n=61) in Group B were male while 31.19% (n=29) in Group A and 35.78% (n=34) in Group B were females. (Figure. 2)

Figure # 1: Age distribution

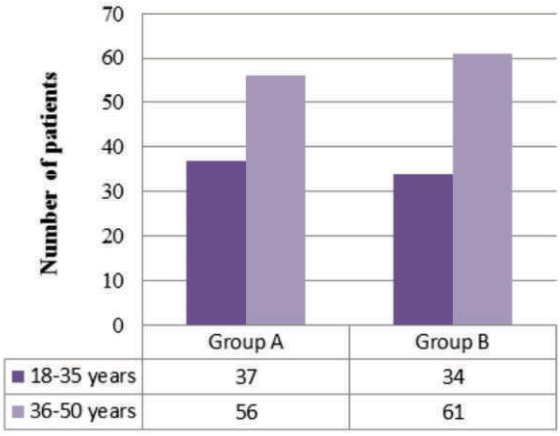
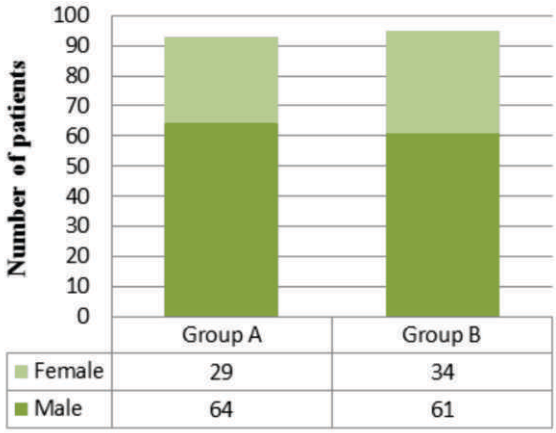


Figure # 2: Gender distribution



Mean IPSS on 1st day after removal of catheter was 10.23+2.01 in Group A and 10.89+1.67 in Group B (p = 0.0152). IPSS after 4 weeks was 6.02+1.12 in Group A and 4.54+0.89 in Group B (p < 0.0001) while the change in IPSS was calculated as 4.21+0.89 in Group A and 6.35+0.78 in Group B (p < 0.0001) showing a significant difference between the two groups. (Table 1) The mean change in IPSS was stratified for age and gender to control the effect modifiers in Table 4 & 5 respectively.

Table 1: *Mean IPSS in both groups (n=188)*

IPSS	Group A (n=93)		Group B (n=95)		P-value
	Mean	S.D	Mean	S.D	
On 1st day after removal of catheter	10.23	2.01	10.89	1.67	P=0.0152
After 4 weeks of treatment	6.02	1.12	4.54	0.89	P<0.0001
Change in IPSS	4.21	0.89	6.35	0.78	P<0.0001

Table 2: *Stratification of Mean Change in IPSS According to Age (n=188)*

Mean change in IPSS	Group A (n=93)		Group B (n=95)		P-value
	Mean	S.D	Mean	S.D	
18-35 years	5.12	1.01	7.04	0.85	P < 0.0001
36-50 years	2.83	0.71	5.11	0.65	P < 0.0001
Total	4.21	0.89	6.35	0.78	P < 0.0001

Table 3: Stratification of Mean Change in IPSS According to Gender (n=188)

Mean change in IPSS	Group A (n=93)		Group B (n=95)		P-value
	Mean	S.D	Mean	S.D	
Males	4.78	0.95	5.89	0.62	P < 0.0001
Females	3.95	0.86	6.61	0.86	P < 0.0001
Total	4.21	0.89	6.35	0.78	P < 0.0001

DISCUSSION

DJ stent is widely used in urological practice and has become an integral part of urological surgeries, being important in post-operative circumstances after renal and ureteric stone injuries, renal and ureteric reconstructive surgeries and repair surgeries. Where DJ stent is making post-operative recovery easy and eventless, also has been found associated with certain complications like lower urinary tract symptoms, overactive bladder, encrustation, biofilm formation and infection[19]. Among these, lower urinary tract symptoms have been a rule and is present in almost all patients, These lower urinary tract symptoms is mainly due to irritation caused by indwelling vesical end of DJ stent causing irritation to vesicoureteric junction, trigone and bladder neck while other causes are smooth muscle spasm and bladder mucosal irritation[20]. LUTSs is the most bothersome post-operative complication in immediate circumstances, increasing patient distress and causing bothersome[21] impact on quality of life[22]. It was first described in 1967 by Zimskind et al. USs are not complication free.[23] These problems can vary from commonly experienced stent symptoms to serious issues like forgotten stent. Symptoms which are commonly encountered by patients include sensation of incomplete evacuation (76%), frequent urination (60%) and urgency (57-60%). Apart from these, painful micturition, hematuria, lumbar pain and suprapubic discomfort is experienced by 19-40% patients. This reduces quality of life in nearly 80% patients.[4,24] Transmission of high pressure to the renal pelvis during voiding and distal ureteric / bladder spasm caused by irritation of US are blamed to be the cause of these symptoms.[25] Debate has been found among clinicians about appropriate treatment for lower urinary tract symptoms, still it's a matter of controversy and no established treatment modality is still known. Among treatment modalities to be used, medical management is the most commonly treatment method and among medical management most commonly prescribed medication consists of use of alpha blockers; mainly tamsulosin.

Alpha blockers have been used for the treatment of stent related symptoms worldwide.[26,27] Tamsulosin is uroselective alpha antagonist, causing antagonist response to alpha receptors present in trigone and bladder neck area, causing dynamic response towards lower urinary tract symptoms. Previously conducted studies have found that tamsulosin has been unable to treat lower urinary tract symptoms secondary to indwelling catheter effectively[28,29] and different other pharmacological agents and combinations have been tried in past but no conclusive evidence can be obtained from previous studies[30,31]. So in search of another medication which has potential response for treatment of LUTS, mirabegron have been used by clinicians. Mirabegron, a β_3 agonist, causes agonist activity towards the beta receptors present in bladder, and show promising response for treatment of LUTS secondary to indwelling double J stents. Bladder as well as ureteric smooth muscles harbour β_3 receptors which help in relaxation.[32] β_3-adrenergic receptor agonist which is used for treatment of overactive bladder symptoms include Mirabegron.[33]

It is reported in one study that spasms of smooth muscles of ureter can be relaxed using β_3-adrenergic agonists.[32] Furthermore, β_3–agonists also relax smooth muscles of the bladder which leads to decreased bladder pressure. This in turn prevents vesicoureteric reflux which helps in decreasing pressure inside the renal pelvis and ureter.[34] Comparative studies comparing tamsulosin and mirabegron with each other and with placebo have been done. Yavuz A et al compared Tamsulosin and Mirabegron with placebo. He quoted that urinary symptoms score was lower in Tamsulosin group than it was in

the control group (22.1 vs 27.8). He recommended that Mirabegron can only be used for pain relief and it has no effect on ureteral stent related symptoms.[15] Otsuki H et al concluded that Mirabegron alleviated urinary symptoms due to the patients' ureteral stents. According to his study mean IPSS score significantly improved from 16.2 to 14.3 by using Mirabegron.[35] Sahin A et al studied that Mirabegron single therapy showed good results in treating LUTS and better results in treating OAB symptom related with DJ stents than other therapies. He noted that Postoperative IPSS in Mirabegron group was 13.65 ± 4.97 which was lower than Solifenacin/ Tamsulosin group (15.6 ± 4.37) and hydration group (21.78 ± 2.54).[36] In another study, comparison of Mirabegron vs placebo revealed that USSQ urinary symptom scores were insignificantly lower in Mirabegron group (33.19 vs. 24.38). It was further recommended that 50 mg Mirabegron once daily can be used to treat discomfort and irritative symptoms caused by indwelling ureteral stents.[37] Chandna A et al conducted a randomized control trial and compared Mirabegron with Solifinacin and Tamsulosin. He concluded that Mirabegron has comparable benefit in alleviating stent related symptoms and may be use as an alternative to Tamsulosin or Solifenacin.[38] A basic comparative study has been lacking in our part of world which can compare the two concerned drugs and find out drug of choice for treatment of LUTS secondary to indwelling double J study. So, this study was initiated with the aim to find appropriate drug for patients suffering bothersome LUTS secondary to indwelling double J stent. Our studies showed that mean IPSS on 1st day after removal of catheter was 10.23+2.01 in Group A and 10.89+1.67 in Group B ($p = 0.0152$). IPSS after 4 weeks was 6.02+1.12 in Group A and 4.54+0.89 in Group B ($p < 0.0001$) while the change in IPSS was calculated as 4.21+0.89 in Group A and 6.35+0.78 in Group B ($p < 0.0001$) showing a significant difference between the two groups, concluding that mirabegron has shown good results for treatment of LUTS secondary to indwelling DJ stent as compared to tamsulosin.

CONCLUSION

Based upon our study we concluded that mirabegron single therapy showed good results as compared to tamsulosin in treating LUTS caused by DJ stents.

Conflict of interest

The author has no conflict of interest.

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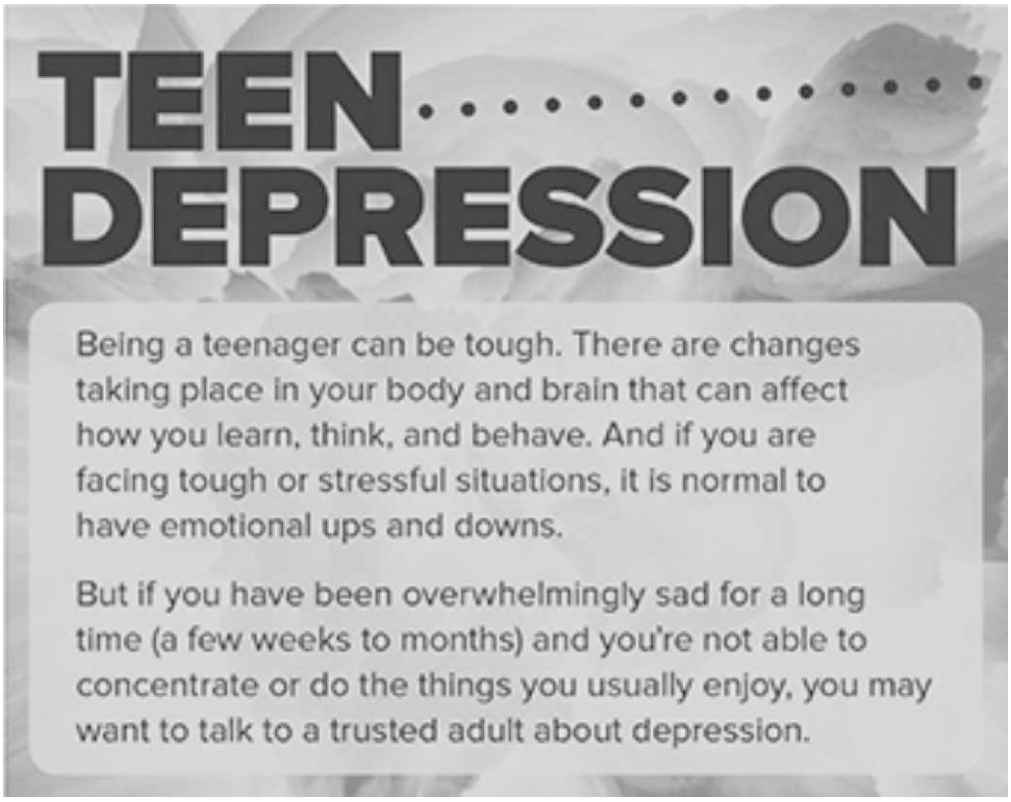

COMPARISON OF CYTOCHEMISTRY WITH FLOWCYTOMETRY IN DIAGNOSIS OF ACUTE LEUKEMIA

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How to cite: Arshad H, Haider S, Khan SH. Comparison of cytochemistry with flowcytometry in diagnosis of acute leukemia. JAIMC. 2020; 18(4): 650-53.

Abstract

Objectives: To compare the efficacy of cytochemical stain (Sudan Black B) with Flowcytometry for the diagnosis of acute leukemia. This cross sectional comparative study was conducted in the Pathology Department of Allama Iqbal Medical College, Lahore from September 2019 to February,2020.

Methodology: 60 patients of either sex, aged 5 - 65 years, with provisional diagnosis of acute leukemia were selected by non probability purposive sampling. 2-3 cc of venous sample was collected from them. A complete blood count and a peripheral smear was made. Another slide of the same sample was stained with Sudan black B. Leukemia cell analysis was performed by standard immunofluorescence methods using monoclonal antibodies. Sensitivity, Specificity, Positive and negative predictive values were calculated to assess the diagnostic accuracy of cytochemistry. Data was stratified for type of leukemia, age and gender for diagnosis by cytochemistry.

Results: out of 60 cases 44 were diagnosed to be acute lymphoid leukemia and12 were labeled as acute myeloid leukemia on the basis of cytochemistry with the special stains, followed and confirmed by flowcytometry. 6 cases were inconclusive on cytochemistry (out of which, 3 were Acute myeloblastic leukemia (AML)M0 ,2 were AML M1 and 1 was diagnosed as Acute lymphobnlastic leukemia (ALL) on flow cytometry. Sensitivity of Cytochemistry turned out to be 75%, Specificity 97.6% and accuracy 90%.

Conclusion: Cytochemistry seems quite promising in early diagnosis of acute leukemia and therefore rendering its timely treatment.

Key words: Acute leukemia, flowcytometry, sudan black B.

Acute leukemia are malignant neoplastic diseases that arise when a hematopoietic stem cell undergoes malignant transformation into a primitive, undifferentiated cell with abnormally prolonged existence. Acute leukemia being a diverse group of malignancies, that differ in clinical, morphologic, immunologic and molecular features and warrant specific therapy.[1] Acute leukemia can be broadly classified into acute lymphoblastic and myeloblastic leukemia. Incidence of leukemia is generally higher in males, with a male to female ratio of 1.4. In 2018, worldwide estimate for acute leukemia were a total of 437.0 thousand new cases and 309.0 thousand cancer deaths.[2] Another study also claims that the incidence of acute leukemia and disease burden is increasing globally.[3] AML accounts for approximately 25% of all leukemias in adults in the Western world, while ALL represents 75% to 80% of acute leukemia among pediatric group, making it the most common form of childhood leukemia;[4] by contrast, ALL represents ~20% of all leukemia amongst adults.[b]

With growing occurrence of acute leukemia, its timely diagnosis at an early stage has become a matter of prime importance. The gold standard for

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Submission Date: 10-08-2020
1st Revision Date: 31-08-2020
Acceptance Date: 14-09-2020

diagnosis of acute leukemia is flow cytometric analysis. This technique is expensive, requires special equipment and is sparsely available in developing countries. Cytochemistry with special stains (Sudan Black B in our study), on the other hand, is easy, affordable and does not require any special equipment yet diagnoses acute leukemia in most cases. Some studies support the fact that through cytchemistry upto 96% of the acute leukemia cases can be diagnosed with no further need of confirmation from flowcytometry.[6]

By proving the value of cytochemistry in resource constrained laboratory set ups, we can provide early and easily available diagnosis for clinicians, suggest an alternate way of acute leukemia diagnosis at a cheaper rate for authorities and guide policy makers to incorporate this cost effective technique in diagnostic laboratories.

METHODOLOGY

This cross sectional comparative study was conducted at Pathology Department of Allama Iqbal Medical College, Lahore from September 2019 to February, 20. About 60 patients of either sex, aged 5 - 65 years, having a provisional diagnosis of acute leukemia were selected by non probability purposive sampling. Hemolyzed Samples and those having blast count < 20 percent and Total leucocyte count < 5×103 / u liter were excluded from the study The study was approved by Ethical Review board Allama Iqbal Medical College. Informed and written consent was taken by all the participants.

All the data was collected in structured questionnaire designed by researchers. Under aseptic measures, 2-3 cc of venous sample was collected from the subjects in EDTA vacutainers. A complete blood count was run using a SYSMELX KX-21 , with a peripheral smear stained by Geimsa. Another slide of the same sample was stained with special stains, namely Sudan black B. Lastly, Leukemia cell analysis was performed by standard immunofluorescence methods using monoclonal antibodies directed against cMPO, CD33, CD64, CD11c, HLA-DR, CD2, CD19, CD5, CD7, CD34, CD 10, CD19, CD 20 , CD79a, CD 14and CD45, KAPPA , LAMBDA, and TdT. Flow cytometric analysis was performed with a four colored BD FACS CALIBUR cytometer. Positivity was taken from the reference quadrant of isotype control along the logarithmic scale either on forward or side scatter. Positivity was expressed as dim, moderate and bright, depending on the expression with reference to control quadrant. It may also be expressed as 1+, 2+ or 3+, on the basis of intensity of expression.

Data was entered and analyzed in IBM SPSS statistics version 24. Cross tabulation was done for diagnosis by flow cytometric immunophenotyping and cytochemistry for accuracy of the technique. Sensitivity, Specificity, Positive predictive values and negative predictive values were calculated to assess the diagnostic accuracy of cytochemistry. Data was stratified for type of leukemia, age and gender for diagnosis by cytochemistry.

RESULTS

We enrolled 80 patients in the study,20 did not fulfill the inclusion criteria and were dropped out. 44 of the 60 cases were diagnosed to be acute lymphoid leukemia and[12] were labeled as acute myeloid leukemia on the basis of cytochemistry with the special stains, followed and confirmed by flowcytometry.[6] cases were inconclusive on cytochemistry (out of which, 3 were Acute myeloblastic leukemia (AML) M0, 2 were AML M1 and 1 was diagnosed as Acute lymphobnlastic leukemia (ALL) on flowcytometry) (Table. 1). Age and gender wise distribution of cases are shown in Table No.2. Results of sudan black B and flow cytometery are given in Table no. 3. Table no.4 shows breakdown of results and comparison of lymphoid and myeloid leukemia in terms of special stain and flowcytometric CD markers.

DISCUSSION

To determine the diagnosis of acute leukemia, flowcytometry has been considered the gold standard, for a long time. Although reliable, it is an expensive technique with limited availability in

Table 1: Case Distribution of AML and ALL

Total cases of acute leukemia	No of ALL cases	No of AML cases	No of aberrant cases
60	42	12	06

Table 2: Age and Gender Wise Distribution of the Study Population

Variables	No. Of Patients
Age groups	
5—15	35
16—25	05
26—35	03
36—45	05
46—55	02
56—65	10
Gender	
Male	49
Female	11

Table 3: Results for Sudan Black B and Flow Cytometry

Acute leukemia on SBB	Positive (Myeloid/ Lymphoid)	Negative (Myeloid/ Lymphoid)	Aberrant	Total
SBB +ve	12 +ve For myeloid markers	12 –ve For lymphoid markers	1 borderline positive for SBB,-ve for FC myeloid CD markers	13
SBB –ve	42 +ve for Lymphoid markers	42 –ve for myeloid markers	5 -ve for SBB,positive for myeloid markers on FCM	47
Total	60			60

Sensitivity of Cytochemistry= true positive/ true positive + false negative =12/12+4 *100= 75%
Specificity of Cytochemistry =true negative/true negative+ false Positive =42/42+1 *100 = 97.6%
Accuracy of Cytochemistry = true positives+ true negatives/ all cases tested = 12+42/60 * 100 = 90%

Table 4: Comparison of Sudan Black B with Flow Cytometery

Type Of Leukemia	Sudan Special Stain	Flowcytometry Cd Markers
Acute lymphoblastic leukemia	Negative	Positive for lymphoid markers*
Acute Myeloid leukemia	Positive	Positive for Myeloid markers**
Aberrant cases***	Negative /Borderline SBB	3 identified as M_0(AML)** 2 as M_1(AML)** 1 as ALL*

*These are the limited panel of CD markers employed for diagnosis of suspected lymphocytic leukemia, in our setting. These include CD45, CD10, CD19, CD34, CD79a, Tdt, HLA-DR.
** These are the limited panel of CD markers employed for diagnosis of suspected myeloid leukemia, in our setting. These include CD10, CD19, CD 45, CD33, CD34, CD79, CD 11c, MPO, HLA-DR.
*** Total of 6 Aberrant cases
In our study, the CD marker positivity in flowcytometry correlated positively with the cases diagnosed on Sudan black B and PAS cytochemistry.

countries like Pakistan. The constraint of resources with the increasing burden of acute leukemia among our population in all age groups warrants adaptation of techniques which are cheap, easier and readily available. Development of strategies and policies in this regard in the light of ongoing research is inevitable and dire need of the time.

Myeloperoxidase, an enzyme which is present in the primary granules of myeloid cells is an unequivocal marker of myeloid lineage. Its importance is being emphasized in mixed phenotypic acute leukemia. SBB was used, which gives comparable information to that of MPO staining.[7] Many studies have compared the efficacy of both the techniques, as both have a huge cost difference. Sudan black B is an easy, cheap and reliable staining technique. It identifies the granular component in myeloid cells by staining them in the cell cytoplasm.

In a study conducted by Akhiwal et al, it was deduced that 96% of the cases could be diagnosed by cytochemistry.[6] Although 4% of the cases were left undiagnosed and sent to higher centers, diagnosing 96% with limited resources without needing tertiary care specialization or major financial burden to the patient says a big yes to cytochemistry. They used multiple stains in cytochemistry, which can increase its sensitivity and should be studies further.

Ahuja et al compared the results of immunohistochemistry, cytochemistry and flowcytometry in acute leukemia.[8] 92 cases were identified as AML and ALL by Cytochemistry whereas 28 cases showed discrepancy. Out of these 28, 22 cases were resolved when immunohistochemistry was added to the diagnostic process. It highlights the importance of another cheap technique i.e. of immunohistochemistry along with cytochemistry can play a vital role

in classifying most of the acute leukemia cases.

Our study concluded that the results of Cytochemistry are comparable with those of flowcytometry. In cases of acute leukemia, early diagnosis is of utmost importance. Barbera J. Bain in her internationally acclaimed textbook of Hematology encourages the Hematologists in limited resource countries to diagnose acute myeloid leukemia M1—M5 and ALL L1 with the help of morphology and Cytochemistry, taking further support from immunohistochemistry as a 3rd step, if and when required.[9] This helps save resources, provides timely diagnosis and ensures early and proper treatment of the patients with leukemia. Rest of the cases like M0, M5, M6 and few phenotypically mixed / inconclusive on Cytochemistry and immunohistochemistry cases should be referred for flowcytometry.

At primary and secondary health level, Provision of basic techniques like cytochemistry which require minimal expense as well as expertise can help in early diagnosis and prompt treatment of acute leukemia patients. Moreover, referral of only those cases of acute leukemia for final diagnosis with flowcytometry, which can not be diagnosed by cytochemistry alone e.g cases of acute lymphocytic leukemia, will also help in a better budget allocation helping more people in need. Moreover, more studies need to be conducted combining more stains and techniques like immunohistochemistry. This will help achieve the goal of prompt, cheap and reliable diagnosis to the acute leukemia cases. Although, Flowcytometry has indisputable advantages over Cytochemistry when it comes to diagnosing AML M0 and M6. The expense, however, is of concern in resource constrained set ups, in regards to conduction of flowcytometry for all cases of AML. Therefore, limiting its use to the cases which are not clearly diagnosed by Cytochemistry will save a lot of finances, directing the savings to be used in diagnosis and treatment of more people in need.

CONCLUSION

Cytochemistry with a specificity of 90 % and sensitivity of 75%, although an old technique, seems quite promising in early diagnosis of acute leukemia and therefore rendering its timely treatment. More research needs to be carried out with inclusion of other cytochemical stains and may be, addition of other techniques like immunohistochemistry may help in increasing the sensitivity of this technique.

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COVID-19 OUTBREAK: ITS PSYCHOLOGICAL AND BEHAVIORAL EFFECTS IN PAKISTAN

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How to cite: Shahid A, Badar A, Cheema HA, Tayyba A, Ilyas MA, Umer M. Covid-19 outbreak: its psychological and behavioral effects in Pakistan. JAIMC. 2020; 18(4): 654-67.

Abstract

Background: COVID-19 was declared a pandemic in March 2020 by WHO. With the constant rise in the number of cases worldwide and the increasing number of deaths, COVID-19 is a threat to the psychological wellbeing of the people. Data is needed to form evidence-based strategies to cater to the psychological needs of the people

Objectives: This study aims to assess the impact of the pandemic on the mental health of the people and to identify their major concerns regarding the current situations. So that our findings can be used to form future strategies to provide adequate psychological aid to the people of Pakistan.

Methodology: From 10th April to 14th April we conducted an online survey to assess the initial psychological response of people of Pakistan to the pandemic. We used the snowball sampling strategy to collect the data. We collected information on demographic data, major concerns of the people, state of awareness about telemedicine facilities, and psychological responses to the spread of misinformation and practices like panic buying. The psychological well-being of people was assessed using the DASS-21 scale for anxiety, stress and depression.

Results: Out of our 906 respondents, 40% of respondents reported moderate to extremely severe symptoms of depression, 36.2%% of respondents showed symptoms of moderate to extremely severe anxiety, and 19.9%% of respondents were moderate to extremely severely stressed. Women, young adults (age 18-24), people who had a history of contact with a confirmed or suspected case of COVID-19, and people who showed symptoms like cough, fever, and shortness of breath had comparatively higher DASS scores. The spread of misinformation and practices like panic buying also showed to harm the psychological health of people. 47.4% of respondents were unaware of any telemedicine facility. The majority of the respondents identified WhatsApp as the major source of misinformation 71.1% of respondents said that they would want professional advice on how to cope with the stress of the pandemic.

Conclusion: During the initial stages of the pandemic in Pakistan, more than one-third of the respondents reported their psychological effect as moderate to extremely severe. Our findings suggest that women, people with contact history, adults from ages 18 to 24, and people who show symptoms like cough, fever, etc. are high-risk groups. Moreover, the spread of misinformation, and practices like panic buying are associated with poor psychological health. Our findings identify the major concerns of the general population of Pakistan and can be used to formulate future policies.

Keywords: Pandemic, psychological impact, COVID-19, mental health, concerns, anxiety, depression, stress.

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Submission Date: 27-07-2020
1st Revision Date: 12-09-2020
Acceptance Date: 16-09-2020

The coronavirus which causes COVID 19 is a previously unknown virus called the severe acute respiratory syndrome virus-2 (SARS-COV-2). It was first identified in December 2019 when several cases atypical pneumonia appeared in Wuhan, China[1] whose basis was traced to a local fish market in the district.[2] Within weeks of the outbreak, the number of patients started increasing dramatically and spread beyond the borders of China and has now spread to at least 185 countries all around the world. The disease

was declared as a pandemic on 11th March 2020 by the WHO.[3]

The SARS-CoV-2 has a long incubation period of almost 2-14 days, after which it appears as non-specific symptoms of fever, cough, and malaise. The disease might progress especially in the elderly or in people who are immune-compromised, leading to dyspnea and respiratory failure, requiring respiratory support.[4] The infection fatality rate is estimated to be 1.4 percent.[5] The transmission of the coronavirus from human to human is by the inhalation of respiratory droplets or direct contact with the infected individual. It can also be transmitted by coming in contact with surfaces contaminated with the virus.[6] Transmissibility of the virus can be estimated by its RO number which is estimated to be around 2.0-2.5.[7]

In order to control the spread of the virus, the governments all around the world have ordered a lockdown of their respective countries. The quarantine has created an unusual condition worldwide, requiring the people to socially isolate themselves. This has brought the world at a dramatic halt, creating circumstances the people have never faced before. The closure of businesses to contain the virus and quarantining has negatively impacted the economies of the countries, directly affecting the financial situation of the general population.[8,9]

In Pakistan, the first case of COVID-19 was confirmed on 26th February 2020 in the city of Karachi. From there, more cases were reported, who were mostly people arriving in the country after international travel. In early March, the virus started spreading locally causing the cases to pile up. A complete lockdown was declared in most provinces of Pakistan on 24th March 2020 when there were a total of 991 positive cases and 7 deaths.[10]

With the country's 50% of the population living on daily wages and struggling to make the ends meet, it has been very difficult for the people. The massive unemployment and the wave of idleness sweeping across the country might have negative effects on the mental health of the population. The government's unclear policy and confusion have translated into the general population being susceptible to becoming a target of misinformation and rumors, further weakening the response to the deadly pandemic on a national level. This might lead to people falling prey to quacks and using prevention methods that might be harmful in the long-term. The social isolation and the uncertainty about the future to come, along with the crippling economy of the country might have very harsh impacts on the mental health of the people because previous studies have suggested that the general public is likely to experience anxiety, depression and panic attacks when affected with highly contagious diseases.[11,12]

At the time of our survey, there were a total of over 4500 positive cases and 63 deaths in Pakistan. This research is meant to understand the negative impact of the circumstances on the psychology and behavior of the people of Pakistan and to find out ways in which the impacts can be controlled.

METHODOLOGY

We designed a cross-sectional study to assess the immediate psychological and behavioral effects of the COVID-19 outbreak on the public by using an anonymous online questionnaire. We used a snowball sampling approach to recruit the general public living in Pakistan. The online survey was first distributed to university and school students who were then asked to forward it to others.

Due to the lockdown enacted by the Pakistani Government with the aim of preventing face-to-face interaction and promote social distancing, potential respondents were invited to fill in the survey through social media sites mainly (WhatsApp, Facebook, Instagram). They filled out the questionnaires in English through the online survey platform Google Forms. All the respondents provided informed consent before starting the survey. The survey was conducted from 10 to 14 April 2020.

The survey was divided into several parts covering both the effect of COVID-19 outbreak on the behavior and mental health of the public as well as

some of the associated factors:

(1) general demographic information consisting of gender, age and educational status; (2) physical symptoms in the past 14 days including fever, cough, sore throat, runny nose and breathing difficulty; (3) contact history with COVID-19 in the past 14 days comprising of close contact with a confirmed COVID-19 case, and contact with a suspected COVID-19 case or infected material; (4) behavioral and mental health effects of COVID-19 including how the people felt that the outbreak had affected their mental health, their feelings about it, whether they thought the outbreak had negatively affected the mental health of their family or friends or not, whether have they been constantly checking for updates about COVID-19 or not, and whether they or someone in their family had been panic buying or not, and if yes, what was the reason to do so; (5)awareness about telemedicine facilities comprising of whether they would seek professional help as a coping mechanism if given the opportunity or not; (6) coping mechanisms including whether the respondents felt that they were receiving adequate emotional support from their family/friends or not, whether they knew about any telemedicine facility that they could avail or not; (7) Misinformation about COVID-19 outbreak regarding what the people felt was the biggest source of misinformation in their opinion out of forwarded messages on social media sites (e.g. WhatsApp), newspapers, news channels and posts by inauthentic sources on social media, and whether this spread of misinformation was negatively affecting their or their family's mental health; and lastly (8) Concerns about COVID-19 outbreak comprising of asking the respondents: (i)who were they most concerned about out of their family, themselves and their friends; (ii) what were their major concerns regarding COVID-19 outbreak including their academic loss, theirs and their family's health, setback faced by the economy of Pakistan, being isolated and cutoff due to lockdown, financial setback faced by them/their family, and safety and survival of the people of Pakistan; and (iii)how satisfied were they with the measures taken by the government of Pakistan to contain the spread of COVID-19. The mental health status of respondents was measured using the Depression, Anxiety and Stress Scale (DASS-21).[13] DASS-21 is based on a ternary model of psychopathology that consists of a general distress construct with distinct characteristics.[14] The DASS-21 was previously used in research related to the COVID-19 pandemic.[15,16,17]

The collected data was analyzed using SPSS version 26.0 (IBM SPSS Statistics, New York, United States). Descriptive statistics were calculated for all of the variables involved in the study. Percen-tages of response were calculated according to the number of respondents per response with respect to the number of total responses of a question. The scores of DASS-21 scale and subscales were expre-ssed as mean and standard deviation. Linear regre-ssion was used to calculate the univariate associa-tions where appropriate between sociodemographic variables, physical symptoms, contact history variables, behavioral and mental health effects variables, coping mechanisms and awareness about telemedicine facilities variables, concerns about COVID-19 variables, and the scores of DASS-21 subscales. All tests were two-tailed, with a significance level of $p < 0.05$. We also used contingency tables and chi-square tests to analyze the associations between DASS-21 subscales and whether the respondents would seek professional advice as a coping mechanism variable; as well as the associations between DASS-21 subscales and how the COVID-19 outbreak has affected the mental health of the respondents variable. $P < 0.05$ was considered statistically significant.

RESULTS

We received a total of 906 responses in 5 days from 10 April to 14 April. The effect of the COVID-19 outbreak on the mental health of the general population was measured using DASS 21-item scale which revealed a sample mean score of 30.72 (SD=25.72). For the depression subscale, the sample mean score was 11.97 (SD=10.27). 418 (46.1%)

were considered to have a normal score (score 0-9); 125 (13.8%) were considered to be mildly depressed (score:10-13); 194 (21.4%) were considered to be moderately depressed (score:14-20); 81 (8.9%) were considered to be severely depressed (score:21-27); and 88(9.7%) were considered to suffer from extremely severe depression (score: 28-42). For the anxiety subscale, the sample mean score was 8.11 (SD= 8.28). 511 (56.4%) were considered to have a normal score (score: 0-7); 67 (7.4%) were considered to suffer from mild anxiety (score: 8-9); 146 (16.1%) were considered to suffer from moderate anxiety (score: 10-14); 74 (8.2%) were considered to suffer from severe anxiety (score:15-19); and 108 (11.9%) were considered to suffer from extremely severe anxiety (score:20-42). For the stress subscale, the sample mean score was 10.64 (SD=9.59). 648 (71.5%) were considered to have a normal score (score: 0-14); 78 (8.6%) were considered to suffer from mild stress (score:15-18); 87(9.6%) were considered to suffer from moderate stress (score:19-25); 68 (7.5%) were considered to suffer from severe stress (score:26-33); and 25 (2.8%) were considered to suffer from extremely severe stress (score:34-42).

Sociodemographic variables are presented in Table 1. The majority of the respondents were female (51.2%), aged 18 to 24 (77.8%) and well educated (59.2% were doing/had done bachelors). Female gender was significantly associated with higher scores in the DASS depression subscale (B = 1.86, 95% Confidence Interval (95% CI): 0.52 to 3.19), DASS anxiety subscale (B = 1.96 95% CI: 0.89 to

Table 1: *Association between Demographic Variables and Adverse Mental Health Status During the COVID-19 Outbreak (n = 906).*

Variables	N (%)	Depression			Anxiety			Stress		
		R-Squared (R^2)	Adjusted R-Squared (AR^2)	Beta (95% Confidence Interval) B (95% CI)	R-Squared (R^2)	Adjusted R-Squared (AR^2)	Beta (95% Confidence Interval) B (95% CI)	R-Squared (R^2)	Adjusted R-Squared (AR^2)	Beta (95% Confidence Interval) B (95% CI)
Gender										
Female	442(51.2)	0.008	0.007	1.86 ** (0.52 to 3.19)	0.014	0.013	1.96 *** (0.89 to 3.03)	0.014	0.013	2.28 *** (1.03 to 3.52)
Male	442(48.8)			Reference			Reference			Reference
Age (Years)										
18 to 24	705(77.8)			3.54 * (0.61 to 6.47)			1.44 (-0.94 to 3.82)			2.95 (0.20 to 5.70)
24 to 30	109(12.0)			1.19 (-2.23 to 4.61)			1.60 (-1.17 to 4.38)			1.29 (-1.91 to 4.50)
30 to 40	26(2.9)	0.018	0.013	-0.66 (-5.50 to 4.18)	0.004	-0.001	0.97 (-2.96 to 4.90)	0.010	0.004	2.65 (-1.89 to 7.19)
40 to 50	12(1.3)			-1.95 (-8.39 to 4.48)			-0.97 (-6.20 to 4.26)			0.88 (-5.16 to 6.92)
50 to 60	4(0.4)			-2.12 (-12.52 to 8.28)			-3.80 (-12.25 to 4.65)			-3.62 (-13.38 to 6.14)
Below 18	50(5.5)			Reference			Reference			Reference
Education										
Bachelors	536(59.2)			1.51 (-0.21 to 3.24)			1.16 (-0.24 to 2.55)			1.72 (0.11 to 3.33)
Doctorate	45(5.0)			-2.39 (-5.73 to 0.96)			0.20 (-2.50 to 2.91)			-0.45 (-3.58 to 2.68)
Lower Secondary	10(1.1)			0.13 (-6.40 to 6.65)			1.42 (-3.85 to 6.70)			1.04 (-5.06 to 7.14)
Masters	129(14.2)	0.014	0.007	-0.45 (-2.76 to 1.86)	0.007	0.000	1.74 (-0.13 to 3.61)	0.010	0.004	0.72 (-1.44 to 2.88)
None	3(0.3)			-8.61 (-20.30 to 3.08)			-5.84 (-15.30 to 3.62)			-8.89 (-19.83 to 2.04)
Primary School	1(0.1)			4.73 (-15.41 to 24.86)			-1.18 (-17.47 to 15.12)			0.44 (-18.40 to 19.28)
Upper Secondary	182(20.1)			Reference			Reference			Reference

3.03) and DASS stress subscale (B = 2.28 95% CI: 1.03 to 3.52). 18 to 24 age group was signi-ficantly associated with higher scores in the DASS depression subscale (B = 3.54 95% CI: 0.61 to 6.47). Other age groups and educational attainment were not associated with DASS subscale scores.

Physical symptoms are displayed in Table 2. It shows that 5.8% of the sample reported a fever for at least 1 day within the previous two weeks, 20.0% had a cough, 22.2% had a runny nose, 17.2% had a sore throat and 8.3% had encountered breathing difficulty all within the previous two weeks. Overall, 495 respondents reported no symptoms (54.6%) while 411 respondents (45.4%) reported at least one symptom. Linear regression showed that the presence of fever was significantly associated with higher DASS anxiety subscale scores (B = 2.52 95% CI: 4.81 to 0.24) but not associated with the other DASS subscales. Having a cough was only significantly associated with higher DASS stress subscale scores (B = 1.77 95% CI: 3.41 to 0.13). The presence of breathing difficulty was significantly associated with higher DASS depression, anxiety and stress scores. In contrast, the other symptoms were not found to be associated with any of the DASS subscales. Also, the presence of a dyad of symptoms such as fever and cough was not associated with any of the DASS subscale scores.

Table 3 shows the contact history of confirmed and suspected COVID-19 cases. Overall, 1.9% of the people had been in contact with a confirmed COVID-19 case while 4.2% had been in contact with a suspected COVID-19 case or infected material. Contact with a confirmed COVID-19 case was found to be significantly associated with very high DASS anxiety scores indeed (B = 6.60 95% CI:

Table 2: *Association between Physical Symptoms and Adverse Mental Health Status during the COVID-19 outbreak (n = 906).*

Variables	N (%)	Depression			Anxiety			Stress		
		R-Squared (R^2)	Adjusted R-Squared (AR^2)	Beta (95% Confidence Interval) B (95% CI)	R-Squared (R^2)	Adjusted R-Squared (AR^2)	Beta (95% Confidence Interval) B (95% CI)	R-Squared (R^2)	Adjusted R-Squared (AR^2)	Beta (95% Confidence Interval) B (95% CI)
Persistent fever (>100°F for at least 1 day)										
No	853 (94.2)			-0.47 (-3.39 to 2.45)			-2.52 * (-4.81 to -0.24)			-0.26 (-2.96 to 2.45)
Yes	53 (5.8)			Reference			Reference			Reference
Cough										
No	725 (80.0)			-0.86 (-2.63 to 0.91)			-1.13 (-2.52 to 0.26)			-1.77 * (-3.41 to -0.13)
Yes	181 (20.0)			Reference			Reference			Reference
Runny nose										
No	705 (77.8)	0.016	0.010	-0.02 (-1.68 to 1.65)	0.07	0.065	0.06 (-1.25 to 1.36)	0.033	0.028	-0.25 (-1.79 to 1.29)
Yes	201 (22.2)			Reference			Reference			Reference
Sore throat										
No	750 (82.8)			0.63 (-1.26 to 2.53)			-1.11 (-2.60 to 0.37)			-0.29 (-2.04 to 1.46)
Yes	156 (17.2)			Reference			Reference			Reference
Breathing difficulty										
No	831 (91.7)			-4.27 ** (-6.80 to -1.74)			-6.15 *** (-8.13 to -4.16)			-4.96 *** (-7.31 to -2.62)
Yes	75 (8.3)			Reference			Reference			Reference

10.56 to 2.64). Contact with a suspected COVID-19 case or infected material was found to be significantly associated with higher depression (B = 4.05 95% CI: 7.38 to 0.72) and stress scores (B = 4.55 95% CI: 7.66 to 1.44). There were no other significant associations.

12.8% of the people said that they were experiencing symptoms of anxiety while the majority of people (38.2%) said that they only worry when they hear the news (or read online) about further developments. Unsurprisingly, people who said that they were experiencing symptoms of anxiety or those who said that they found themselves worrying about the situation now and then were found to be significantly associated with higher DASS depression, anxiety and stress subscale scores (with those who were experiencing anxiety showing the highest B values). People who reported that they only worried when hearing news about recent developments were not significantly associated with any of the DASS subscale scores.

Majority of the people, when asked about their feelings about the COVID-19 outbreak, said that they had a feeling of uncertainty about the whole issue (35.1%) while the others reported a range of feelings including anxiety (10.3%), fear (9.5%), isolation (20.8%) and being rather calm (15.2%). As expected, people who said that they were rather calm were significantly associated with lower DASS depression, anxiety and stress scores.

72.4% of the respondents reported that they thought that the current situation has negatively affected the mental health of their family or friends. All of these people were also significantly associated with higher DASS depression, anxiety and stress scores.

62.4% of the respondents said that they have found themselves constantly checking for updates or news about COVID-19 within the previous two weeks but this was not found to be significantly associated with any of the DASS subscales.

35.3% of the respondents said that they or someone in their family has been involved in panic buying. This was also significantly associated with higher DASS anxiety scores (B = 1.94 95% CI: 3.07 to 0.82) but not with DASS depression and stress

Table 3: *Association between Contact History and Adverse Mental Health Status during the COVID-19 Outbreak (n = 906).*

Variables	N (%)	Depression			Anxiety			Stress		
		R-Squared (R^2)	Adjusted R-Squared (AR^2)	Beta (95% Confidence Interval) B (95% CI)	R-Squared (R^2)	Adjusted R-Squared (AR^2)	Beta (95% Confidence Interval) B (95% CI)	R-Squared (R^2)	Adjusted R-Squared (AR^2)	Beta (95% Confidence Interval) B (95% CI)
Do you have a history of contact with a CONFIRMED COVID-19 case during the last 14 days?										
No	889 (98.1)	0.000	-0.001	-0.40 (-5.33 to 4.54)	0.012	0.011	-6.60 ** (-10.56 to -2.64)	0.001	-0.001	-1.63 (-6.23 to 2.98)
Yes	17 (1.9)			Reference			Reference			Reference
Do you have a history of contact with a SUSPECTED COVID-19 case or infected material during the last 14 days?										
No	868 (95.8)	0.006	0.005	-4.05 * (-7.38 to -0.72)	0.003	0.002	-2.30 (-4.99 to 0.39)	0.009	0.008	-4.55 ** (-7.66 to -1.44)
Yes	38 (4.2)			Reference			Reference			Reference

scores. Moreover, 61.3% of the people said that they have been indulging in panic buying because of the feeling that there is or will be a shortage of goods, 19.5% said it was because they have been reading about this trend on social media and 19.2% said that it was due to them seeing or hearing people around them buying or storing things. (see Figure 1)

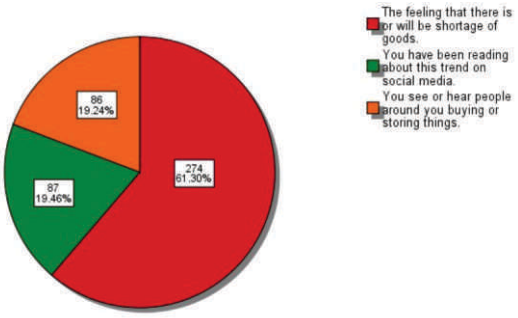

Figure 1 – *Reasons for Panic Buying (n = 906).*

Nearly half of the respondents had no knowledge of any telemedicine facility that they could avail (47.4%) but this was not associated with scores in any of the DASS subscales

81.8% of the respondents said that they are receiving adequate emotional support from their friends or family. The small percentage of people who said that they are not receiving adequate emotional support (18.2%) were significantly associated with higher scores in the DASS depression subscale (B = 5.32 95% CI: (3.62 to 7.02), anxiety subscale (B = 3.94 95% CI: 2.56 to 5.31) and stress subscale (B = 5.69 95% CI: 4.12 to 7.27).

On the other hand, 71.1% of the respondents said that if given an opportunity they would indeed seek professional advice for coping mechanisms in times like this. But a contingency table showed that 3.9% of the respondents were suffering from severe to extremely severe depression yet said that they would not seek professional advice even if given an opportunity. This was a significant association ($X2(1) = 10.9, p < .05$).

Contingency tables also showed that 5.9% of people suffering from moderate to extremely severe depression said that they would rather not characterize themselves as "anxious or stressed"; this was a significant association ($X2(12) = 91.7$, $p < .001$). 4.4% of people suffering from moderate to extremely severe anxiety also said that they would rather not characterize themselves as "anxious or stressed"; this was a significant association ($X2(12) = 124.8$, $p < .001$). And 1.9% of people suffering from moderate to extremely severe stress also said that they would rather not characterize themselves as "anxious or stressed"; this was a significant association ($X2(12) = 106.3, p < .001$).

62.7% of the respondents were of the opinion that forwarded messages on social media (e.g. WhatsApp) were the biggest source of misinformation about COVID-19 while others believed that the biggest source of misinformation was news channels (14.2%) and posts on social media (e.g. Twitter, Facebook, etc.) (22.4%). Only 0.7% of the participants thought that newspapers were the biggest source of misinformation. Moreover, 68.0% of the people also felt that their or their family's mental health was being negatively affected by this spread of misinformation.

Table 7: *Cross Tabulation between DASS Depression Levels and Willingness to Seek Professional Advice for Coping Mechanisms during the COVID-19 Outbreak (n = 906).*

Crosstab*					
			If given an opportunity, would you seek professional advice for coping mechanisms in times likethis?		
			No	Yes	Total
Depression level	Extremely Severe	Count	22	66	88
		% of Total	2.4%	7.3%	9.7%
	Mild	Count	40	85	125
		% of Total	4.4%	9.4%	13.8%
	Moderate	Count	69	125	194
		% of Total	7.6%	13.8%	21.4%
	Normal	Count	117	301	418
		% of Total	12.9%	33.2%	46.1%
	Severe	Count	14	67	81
		% of Total	1.5%	7.4%	8.9%
Total		Count	262	644	906
		% of Total	28.9%	71.1%	100.0%

* $p < 0.05$.

Table 8(A): *Cross Tabulation between DASS Depression Levels and People's Opinion about their Mental Health Status during the COVID-19 Outbreak (n = 906).*

Crosstab***							
			How do you think the recent COVID-19 outbreak has affected your mental health?				
			You are experiencing symptoms of anxiety (loss of sleep, frequent headaches etc).	You find yourself worrying about the situation every now and then.	You worry only when you hear news (or read online) about the recent developments.	You would rather not characterize yourself as "anxious or stressed".	Total
Depression level	Extremely Severe	Count	22	31	25	10	88
		% of Total	2.4%	3.4%	2.8%	1.1%	9.7%
	Mild	Count	15	29	51	30	125
		% of Total	1.7%	3.2%	5.6%	3.3%	13.8%
	Moderate	Count	33	59	74	28	194
		% of Total	3.6%	6.5%	8.2%	3.1%	21.4%
	Normal	Count	23	82	174	139	418
		% of Total	2.5%	9.1%	19.2%	15.3%	46.1%
	Severe	Count	23	21	22	15	81
		% of Total	2.5%	2.3%	2.4%	1.7%	8.9%
Total		Count	116	222	346	222	906
		% of Total	12.8%	24.5%	38.2%	24.5%	100.0%

*** p < 0.001.

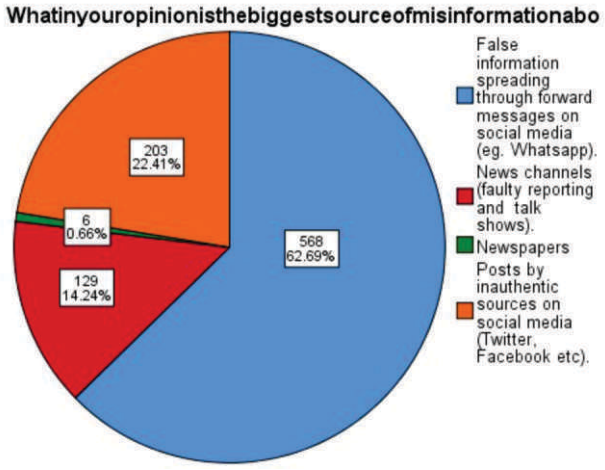

Figure 2: *People's Opinion about the Biggest Source of Misinformation (n = 906).*

Table 11 shows that an overwhelming majority of the respondents (91.4%) said that they were concerned about their family's health and safety the most while only a small number said that they were concerned the most about their friends (2.8%), and their health and safety (5.8%).

When asked about their major concerns regarding the COVID-19 outbreak (Table 12), the majority of the people (75.3%) said that they were concerned about the safety and survival of the people of Pakistan. 60.3% of the respondents were also concerned about their academic loss while 66.1% were concerned about the setback faced by the economy of Pakistan. Only 43.4% of the people were concerned about the financial setback faced by them or their families. Being isolated and cut-off due to lockdown was also a concern of about half of the participants (51.0%).

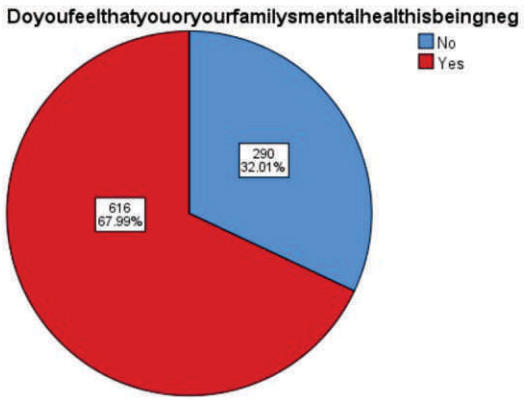

Figure 3: *People's Opinion about Whether their or their Family's Mental Health is being Negatively Affected by the Spread of Misinformation about COVID-19 (n = 906).*

Table 13 shows how satisfied the people are with the steps taken by the government to contain the spread of COVID-19. The majority of the respondents (58.1%) were somewhat satisfied with the government's steps so far while 8.9% of the respondents were highly dissatisfied, 17.3% were some-

what dissatisfied and 15.7% were highly satisfied. However, linear regression showed that there was no significant association between the level of satisfaction and any of the DASS subscale scores.

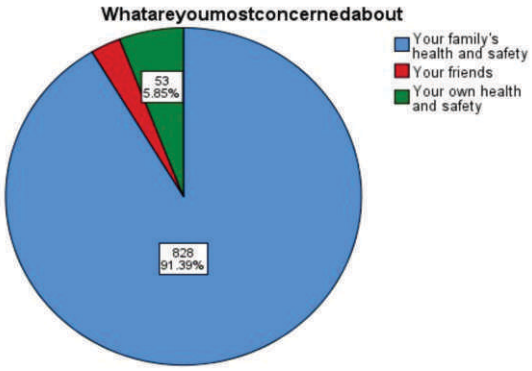

Figure 4: *What People are most Concerned About (n = 906).*

DISCUSSION

Through our survey conducted from 10 April to 14 April, about a month after COVID-19 was declared a pandemic by WHO,[18] the initial psychological response of the general public of Pakistan was assessed. At the time of the survey, there were 4601 recorded cases of COVID-19 in Pakistan with a total of 66 deaths reported across the country.[19] The psychological impact was assessed using DASS-21 scale for anxiety, stress and depression. This scale characterizes symptoms as mild, moderate, severe and extremely severe on individual subscales of anxiety, stress and depression. According to our results, 21.4% of participants were moderately depressed, 8.9% were severely depressed, and 9.7% were extremely severely depressed. For the anxiety subscale, 16.1% were moderately anxious, 7.5% were severely anxious, and 2.8% were extremely severely anxious. Moreover, 9.6% were moderately stressed, 7.5% were severely stressed, and 2.8% were extremely severely stressed.

Table 12: Frequencies of what is the Major Concern of People Regarding the COVID-19 Outbreak (n = 906).

What is your major concern regarding the COVID-19 outbreak?		
Levels	**Counts**	**% of Total**
Your academic loss.	546	60.3%
Your and your family's health.	603	66.6%
Setback faced by the economy of Pakistan.	599	66.1 %
Being isolated and cutoff due to lockdown.	462	51.0 %
Financial setback faced by you/your family.	393	43.4 %
Safety and survival of the people of Pakistan.	682	75.3 %

In our survey, most of the respondents had no symptoms pointing towards COVID-19. Moreover, most of the respondents did not have any contact history with confirmed or suspected cases of COVID -19. However, as expected the contact history with confirmed or suspected cases of COVID-19 was associated with a higher DASS score of anxiety (in case of confirmed COVID-19 case) and a higher level of depression and stress (in case of contact with the suspected case). When asked if they found themselves checking for constant updates on COVID-19, 62.4% of our participants responded with yes. Surprisingly, these respondents, however, did not have significantly high DASS scores. Even though it is suggested by mental health experts to not constantly look for updates and signs of illness[20] for the fear of exacerbating anxiety, our findings suggested otherwise. This proves that an overall better state of awareness and being up to date on the recent advancements regarding COVID-19 can help people cope better rather than triggering anxiety.

When asked to describe their feeling regarding the current situation 20% of respondents said that they felt isolated, 10% said they felt anxious, 9.5% admitted feeling afraid while 15% respondent said that they would characterize themselves as rather calm. The dominant feelings of isolation and fear can be dealt with by creating a sense of community among the people. As most of the people are quarantining and are homebound, the use of social media to create a sense of community can help in dealing with these emotions.[21]

When asked about the need to look for advice on how to cope with the current situation of the pandemic, 71.1% of our respondents said that if given the opportunity they would seek professional advice. This highlights the need for the provision of immediate psychological aid to the people.

When asked about panic buying 35.3% of

people said that they or their family did indulge in it. Unsurprisingly these people had higher scores on the DASS scores of anxiety. 61.3% people said that their reason for panic buying was that they feared that there would be a shortage of goods, 19.5% people said that their panic buying was prompted by reading posts about this practice on social media and 19.2% respondents said that they did it because they saw other people doing it. Panic buying is a psychological response or manifestation of the current situation that might be due to primitive response of the humans for survival, exacerbation of anxiety, fear of losing control over the environment, and social learning. Lack of trust in the government to meet the needs of the people is also one of the core reasons behind the panic buying phenomenon.[22]

As COVID-19 continues to spread our findings will prove to be useful for developing strategies to cater to the psychological needs of the general population of Pakistan. They can prove helpful while forming policies to make the current healthcare scenario of the country better suited to overcome the hurdles in the way of delivery of proper, immediate, and effective psychological first aid. The discussion of the results that we compiled using our survey draws attention to the steps needed to be taken by the healthcare workers as well as the Government officials to ensure the psychological safety of the people. First, the healthcare authorities need to identify the higher risk groups in terms of the psychological consequences of the pandemic. Our findings conclude that women are at a higher risk of developing anxiety, depression and stress. This finding corresponds to previously done epidemiological studies that found that women are generally at higher risk for depression.[23] Moreover, participants between the ages of 18 to 24 have also shown higher levels of anxiety. This suggests that young adults seem to be in a need of proper counseling for coping mechanisms to deal with COVID-19. Our findings also suggest that people who have shown symptoms that point towards a COVID-19 infection are associated with higher DASS scores. Complaints of fever, cough, and shortness of breath have the most effect on the psychological well-being of the people. Fever caused a higher anxiety rate; cough was associated with higher stress while people with a complaint of shortness of breath had higher DASS scores for all three i.e. anxiety, stress and depression. This suggests that adequate information regarding the symptoms, disease pattern of COVID-19, and preventive measures against the infection should be freely available to the general public, so the unnecessary panic can be avoided. People should be well informed of when they need to worry about their symptoms. Also, it needs to be pointed out that mass testing can help with the psychological well-being of the people who show any symptoms in addition to the early diagnosis and isolation of the COVID-19 positive patients. Healthcare officials can play an important role in this regard by providing proper counseling to the patients who visit the hospitals with symptoms of fever, cough, or shortness of breath, as these cases are a high-risk group for the psychological impact of COVID-19.

Second, the government should devise policies to ensure that the most accurate information on COVID-19 reaches the maximum number of people immediately. This can reduce the impact of rumors and misinformation and unnecessary panic among the people can be avoided.[24] Lack of awareness along with the wrong information from inauthentic sources can be a major factor contributing to the psychological distress of people. Our findings show that 67.99% of people suggested that their and their family's mental health is being negatively affected by the spread of misinformation regarding COVID-19. Unsurprisingly, these participants showed higher scores on the DASS scale. When asked about the major sources of misinformation in their opinion 62.7% of people said that forward/chain messages on sites like WhatsApp contribute towards the spread of misinformation the most. While 14.2% of people said it is the posts on social networking sites e.g. Twitter and Facebook. This suggests the need to make policies to have a strict check on the informa-

tion spread via the said sites. In today's time when social media has become the major source of communication and has a wide audience anything that is put on it can have a drastic effect on the state of awareness of the general population. While the chances of spread of misinformation resulting in distress among the public increase, so do the chances of running effective and widely popular awareness campaigns. The government should use these platforms to make sure that the authentic and necessary information reaches the public. Our findings also suggest that print media (e.g. newspaper) remains one of the most trusted sources of information for people. Thus the government should use it for the awareness regarding COVID-19, to make people observe the social distancing measures, and to advertise the telemedicine facilities set up to facilitate people.

Third, in addition to the lack of awareness and the spread of misinformation regarding COVID-19, government officials have a burden to make sure the measures taken in this regard are proving effective or not. Our findings show that despite many telemedicine desks set up by the government, 47.4% of our respondents stated that they did not know of any telemedicine facilities that they can approach in times of need. Thus, in addition to setting up the telemedicine desks, making sure that these facilities are easily accessible and that people are aware of these facilities is important. Effective campaigning can only be done if the major concerns of the public are assessed and are used to get due attention from the people. For example, 91.4% of our respondents said that they worry about their family's physical health more than their own. This fact thus can be used to motivate people to observe social distancing and SOPs. By telling people that their lack of preventive measures can put their families at risk we can motivate them into following guidelines given by WHO to prevent the spread of COVID-19.

Fourth, new policies should be made to provide online psychological support to people. Our results show that the current state of the general public in terms of the psychological impact of COVID-19 is somewhat worrisome. There is a need to immediately provide psychological first aid to the people. Considering the countrywide lockdown that is being observed in Pakistan the electronic media and social media have become an important link in the chain of the flow of information between the healthcare officials and the general public. Thus, healthcare workers should also mold their expertise to better suit the needs of the current situation. Making use of social networking sites to spread awareness, provide medical advice and psychological support to the people is important. However, this is not just limited to making helplines and telemedicine desks. As mental health remains an issue that is not well taken or much discussed in our society, providing psychological aid can become much more intricate. Tackling this issue step by step starting from the grassroot level is the only way to make sure the psychological well-being of the people is well taken care of. Our findings show that 5.9% of people who have symptoms of moderate to severe depression when asked to comment about their mental health said that they would rather not characterize themselves as anxious or depressed. This suggests that people might be in a state of denial about their psychological distress; this denial may sprout from the lack of proper awareness or understanding of mental health issues. This might also be due to the social stigma that is associated with mental health problems in our society. Lack of awareness and acceptance about mental health issues have always been a problem in our society but now, due to the COVID-19 pandemic, their effect has been magnified several-fold and it is contributing to the worsening state of the psychological health of people. It is important now, more than ever, to take appropriate steps to eradicate this problem before it leaves long term effects on the psychological health of the people. Our findings also suggested that 3.9% of the severely depressed people said that they won't look for help or advice for coping mechanisms from a professional. This might be due to the social stigma associated with 'seeking

help', which further points to the importance of proper education and awareness given to the people on the issue of mental health. Thus the successful delivery of psychological aid to people has to start from spreading awareness among the people, of how the pandemic can affect their mental health and why it is normal and important to look for help or advice from a professional. This would bring us to the last step in delivering successful psychological aid which is the modification of the contents of the current psychological interventions (e.g. CBT) to better suit the needs of the people during the country-wide lockdown situation. CBT should be provided through online networking and telephone.[25] Telemedicine facilities that are already working should be modified to create a separate desk for psychological aid or new facilities should be set up. For people with no access to the internet, helplines should be made and professionals should be recruited to ensure the delivery of proper psychological care to the people.

Fifth, in order to cater to the needs of the people, the government needs to identify major concerns of the people of Pakistan. Through our survey we asked people about their major concerns about the current situation, majority of the people said that they were concerned about the safety and survival of the people of Pakistan; 60.3% of people were also concerned about their academic loss due to the lockdown. This suggests that, during the pandemic, educational authorities need to establish online portals to meet the educational needs of the students.[26] Moreover, more than half of the people were also worried about the setback faced by the economy of Pakistan, and being isolated.

When asked about their opinion on the performance of the government regarding COVID-19 majority of the respondents appeared to be satisfied. The major suggestions people gave to improve the current situation in the country were to impose a strict lockdown, making sure people stay indoors, and setting up better quarantine centers to isolate infected and suspected cases. People also suggested that, in their opinion, mass testing can improve the current healthcare scenario. Mass testing is the ideal response of the healthcare officials to the COVID-19 outbreak; this can lead to early isolation and treatment of the infected patients, thus, improving the health condition drastically.[27]

This study has several limitations. First, the results might vary with time i.e. at an early or later stage of the pandemic. As the study was conducted via the internet and the confidentiality and privacy of the participants had to be maintained, a follow-up study cannot be conducted. The mental health evaluation done in this study is self-reported and the results may vary greatly if the assessment is conducted by a professional. Moreover, there is an over-sampling of some groups of people (age group 18-24) leading to sample bias, thus the results may not be generalized. This was because we used the snowball sampling strategy which was necessary because the psychological effect on the public had to be evaluated in a timely manner. Another limitation is that due to the cross-sectional nature of the study, it cannot reflect trends of psychological changes of people in Pakistan.

CONCLUSION

During the initial stages of the pandemic in Pakistan, more than one-third of the respondents reported their psychological effect as moderate to extremely severe. Our findings suggest that women, people with contact history, adults from ages 18 to 24, and people who show symptoms like cough, fever, and shortness of breath are high-risk groups. Moreover, the spread of misinformation, and practices like panic buying are associated with poor psychological health. Setbacks faced by the economy of Pakistan, the well-being of the people of Pakistan, the academic loss of the students, and the health of their families are among the major concerns of the population. Nearly half of our respondents were unaware of any telemedicine facility and more than three fourth would want professional advice to cope with the stress of the

current situation. Three fourth of our respondents showed satisfaction towards the steps taken by the government to face the pandemic. Our findings also identify the major concerns of the general population of Pakistan and can be used to formulate future policies for psychological interventions to improve the mental health of the Pakistani population.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgements

We wish to thank all participants for putting their time into giving us sincere answers.

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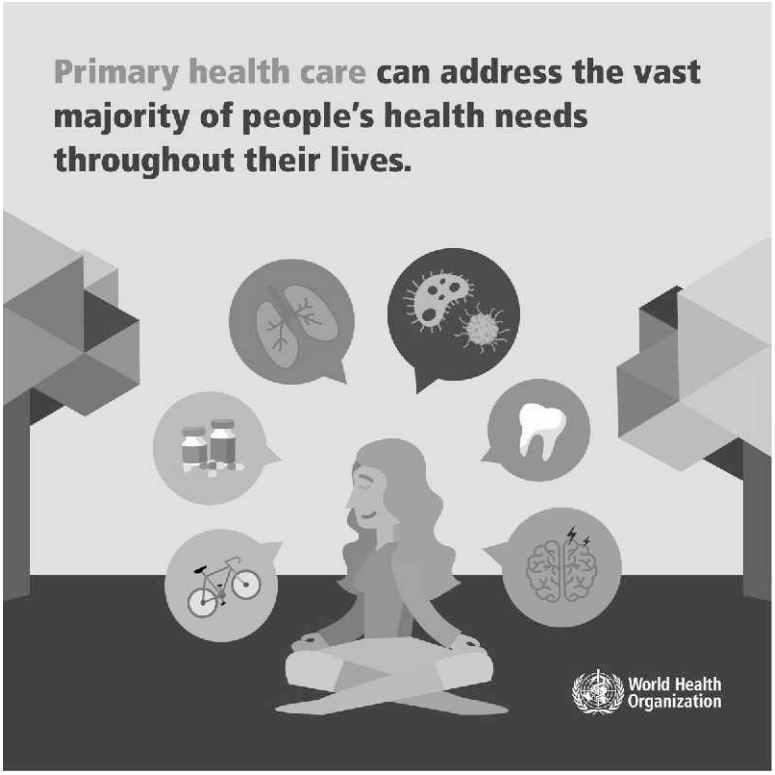

ACCURACY OF DIAGNOSTIC LAPAROSCOPY AS A PRIMARY INVESTIGATIVE TOOL IN THE DIAGNOSIS OF ABDOMINAL TUBERCULOSIS WITH HISTOPATHOLOGY AS GOLD STANDARD

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How to cite: Nasim A, Malik S, Jabbar N. Accuracy of diagnostic laparoscopy as a primary investigative tool in the diagnosis of abdominal tuberculosis with histopathology as gold standard. JAIMC. 2020; 18(4): 668-72.

Abstract

Background: Abdominal tuberculosis is seen in 20% of cases of extra peritoneal TB (Tuberculosis).Its diagnosis can be confirmed by histopathology of the involved viscera. In most surgical centers patients with abdominal tuberculosis have to undergo open surgical procedures for diagnosis and treatment. Now a days diagnostic laparoscopy is gaining popularity.

Objective: To determine the diagnostic accuracy of laparoscopy in abdominal tuberculosis taking histopathology as gold standard.

Methodology: A total of 210 patients were admitted through outpatient department. Surgeries were performed by consultant surgeons, having years of experience in the procedures, to avoid bias. Diagnostic laparoscopy was done by inserting three ports. Lymph nodes and peritoneal biopsy were taken and sent for histopathology. All patients were managed according to standard departmental protocols.

Results: Male patients were 139 (66.2%) and 71 (33.8%) were female. Mean age was 29.9±8.6 years In the comparison of laparoscopic findings vs histopathological findings in detection of abdominal tuberculosis,130 (61.9%) patients were true positive, 11 (5.2%) patients false positive, 19(9.0%) patients false negative and 50 (23.8%) patients were true negative. The sensitivity of laparoscopic was 87%, specificity 82%, diagnostic accuracy 86%, positive predictive value 92%, and negative predictive value was 72%.

Conclusion: It was concluded that diagnostic accuracy of laparoscopy is high i.e. 86% in diagnosing abdominal tuberculosis taking histopathology as gold standard. In abdominal tuberculosis early laparoscopy is secure and helpful in confirmation of diagnosis.

Keywords: Abdominal tuberculosis, laparoscopy, histopathology, diagnostic accuracy, sensitivity, specificity.

Tuberculosis is a disease that affects almost 33% of the world's residents.[1] It is very common in developing countries including the South Asian countries like India and Pakistan.[2] Pakistan ranks sixth among the twenty two high disease burden countries. It has 44% of the case load of Eastern Mediterranean Region. Out of this, 25% of total disease burden is borne by Punjab alone. Worldwide, the incidence of new cases of tuberculosis has male to female ratio of 2:1 respectively. It is a bacterial infection caused by Mycobacterium tuberculosis.[1,3] It affects almost all the organ systems of human body including lungs brain, gastrointestinal tract, bones and urinary tract. Its constitutional symptoms are anorexia, weight loss and low grade fever and specific symptoms depend on the type of the viscera involved. Abdominal tuberculosis is seen in 20% of cases of extra peritoneal TB (Tuberculosis).[4] It can involve the ileocecal region and the mesenteric lymph nodes. Tuberculous peritonitis is commonly divided into four type's i.e. ascitic, encysted, fibrous

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Submission Date: 03-08-2020
1st Revision Date: 12-09-2020
Acceptance Date: 18-09-2020

and purulent. Each has different signs and prognosis.[3] Tuberculosis of small bowel is either of hyperplasic, sclerotic or ulcerative type depending on the source of infection, virulence of bacteria and immune status of the patient.[5] In Pakistan there is no central database for registration of patients suffering from Tuberculosis so it's hard to estimate its incidence and prevalence. Local studies from all over the country showed that it's common in Pakistani population .[4,5,6,7]

The diagnosis of abdominal tuberculosis can be extremely difficult at times because of its non-specific symptoms and limited methods of diagnosis.[6] Its diagnosis can be confirmed by histopathology of the involved viscera. In most of the surgical centers patients with abdominal tuberculosis have to undergo open surgical procedures to get their pathology diagnosed and treated. Now a day's laparoscopic surgery in the diagnosis of abdominal tuberculosis is gaining popularity.

Laparoscopic surgical techniques have the advantage of being less invasive and require less cutting. That's why such techniques are associated with less post operative pain, decreased hospital stay and less time off work.

With recent advances the open surgical procedures are widely being replaced by minimal access techniques. Although it needs sophisticated facilities and expertise but has proven to be beneficial in terms as mentioned above.[8]

In an international study patients recorded as positive for abdominal tuberculosis by using laparoscopic surgery had a sensitivity of 58%.[8] A local study highlighted that abdominal tuberculosis can be detected early by laparoscopy and recorded 82% patient's positive for abdominal tuberculosis.[2] The only international study to publish the sensitivity and specificity of diagnostic laparoscopy was an Indian one in which sensitivity was 92% and specificity 76%. The total number of cases being 92.[9]

The rationale of the study is to determine how sensitive and specific is diagnostic laparoscopy in diagnosing abdominal tuberculosis as compared to the gold standard. The studies mentioned above are very much varied in their results (58% in one and 92% in the other as mentioned above). None of the studies conducted locally have calculated the diagnostic accuracy of laparoscopy in abdominal tuberculosis. Also the local studies have obscure results i.e. no data on specificity and have failed to set local guidelines based on available evidence from scientific research, local circumstances and cultural issues for the prompt diagnosis of abdominal tuberculosis.

The purpose of this study was to conduct research on a large sample size so that the evaluation of laparoscopic surgical procedures as diagnostic tool in patients of abdominal tuberculosis may be recorded. The outcome of this study would be a guideline and documented local reference for the surgeons who are working in the field.

METHODOLOGY

This cross sectional study was conducted in Department of Surgery, Jinnah Hospital, Lahore for two year from June 2017 to June 2019.

Total 210 cases were included using non-probability purposive sampling technique. All the adult male and female patients (more than 15 years old and less than 50) of suspected abdominal tuberculosis undergoing laparoscopy admitted through outpatient department and diagnosed clinically, the symptoms of abdominal tuberculosis being taken into consideration i.e. relative constipation (passing flatus but not faeces), weight loss (>10 percent of their weight in the last 3 months), altered bowel habits were included in the study. All unwilling patients, patients less than 15 years or more than 50 years of age, ASA III, IV and V patients, patients having malignancies, patients having diabetes mellitus, patients having chronic liver disease and immunocompromised patients & patients undergoing recurrent surgery were excluded.

After the approval of synopsis the study was submitted to the Institutional Research Ethical

Committee of Jinnah Hospital Lahore for ethical approval. All the patients were admitted through outpatient department. The purpose of this study and all the possible outcomes were explained to the patients fulfilling the inclusion criteria. All patients incorporated in the study were informed and permission was taken. Information was obtained from patients at the time of admission. All diagnostic laparoscopies were performed under general anesthesia.

Surgeries were performed by consultant surgeons, well experienced in the procedures, to avoid bias. Laparoscopic surgery was done by inserting three ports. Lymph nodes and peritoneal biopsy were taken and sent for histopathology. All patients were managed according to standard departmental protocols. All observations were documented.

Statistical package for social sciences version 13 (SPSS 13, Chicago, and II, USA) was used. Categorical variable i.e. positive and negative cases of abdominal tuberculosis and gender were expressed as frequencies and percentages. Continuous variable like age was expressed as mean and standard deviation. For estimation of the positive predictive value, negative predictive value, the sensitivity and specificity and accuracy of diagnostic laparoscopy as a definitive diagnostic tool in abdominal tuberculosis by taking histopathology as gold standard, a 2×2 contingency table was made.

Table 1: *Distribution of Patients by Age (n=210)*

Age (Years)	No. of patients	Percentage
15-20	36	17.1
21-30	70	33.3
31-40	79	37.6
41-50	25	12.0
Mean±SD	29.9±8.6	

RESULTS

29.9±8.6 years was the mean age. Age distribution is shown in table 1.

Table 2: *Distribution of Patients by Sex (n=210)*

Sex	No. of patients	Percentage
Male	139	66.2
Female	71	33.8
Total	210	100

There were 139 (66.2%) male and 71 (33.8%) female patients (Table 2).

Table 3: *Distribution of Patients by Laparoscopic Finding (n=210)*

Laparoscopic Finding	No. of patients	Percentage
Positive	141	67.1
Negative	69	32.9
Total	210	100

141 (67.1%) patients had positive laparoscopic findings and 69 (32.9%) patients had negative (Table 3).

Table 4: *Distribution of Patients by Histopathological Finding (n=210)*

Histopathological Finding	No. of patients	Percentage
Positive	149	71.0
Negative	61	29.0
Total	210	100

In the distribution of patients by histopathological findings, there were 149 (71%) patients had positive and 61 (29%) patients had positive (Table 4).

In the comparison of laparoscopic findings vs histopathological findings in detection of abdominal tuberculosis, there were 130 (61.9%) patients were true positive, 11 (5.2%) patients were false positive,

Table 5: *Comparison of Laparoscopic vs. Histopathological Findings in Diagnosing Abdominal Tuberculosis(n=160)*

Laparoscopic	Histopathological		Total
	Positive	Negative	
Positive	130 (TP)	11 (FP)	141
Negative	19 (FN)	50 (TN)	69
Total	149	61	**210**

Key: TP = True positive FP = False positive
FN = False negative TN = True negative

Table 6: *Sensitivity, Specificity and Accuracy of Diagnostic Laparoscopic*

Sensitivity	87%
Specificity	82%
Accuracy	86%

Table 7: *Positive Predictive and Negative Predictive Value of Laparoscopic findings*

$$\text{Predictive value of Positive test} = \frac{\text{True Positive}}{\text{True Positive} + \text{False Positive}} \times 100$$

$$= \frac{130}{130 + 11} \times 100 = 92\ \%$$

$$\text{Predictive value of Negative test} = \frac{\text{True Negative}}{\text{True Negative} + \text{False Negative}} \times 100$$

$$= \frac{50}{50 + 19} \times 100 = 72\ \%$$

19 (9.0%) patients were false negative and 50 (23.8%) patients were true negative (Table 5).

The sensitivity, specificity, and diagnostic accuracy of laparoscopic is as follow Table 6).

DISCUSSION

Abdominal tuberculosis should be considered in differential diagnosis of patients having vague abdominal symptoms, history of weight loss or coming from areas where tuberculosis is common.[10] Non-specific presenting features, false-negative ultrasound & CT scans, unhelpful laboratory tests and negative results with tuberculin skin tests & Ziehl–Neelsen staining are the common diagnostic problem which clinicians often face.[10,11]

Many of the times computerized tomography of the abdomen, used commonly after ultrasound, is marginally more specific for abdominal TB.[12,13] Diagnostic laparoscopy is the most specific test for abdominal TB with its advantage of histological confirmation.[14,15,16] Our experience is also the same in this regard. Till now laparoscopy is not very commonly used to establish the diagnosis of abdominal TB at early stage and widely underutilized.[17,18] In the past laparotomy was being used for this,[19,20] and there was usually hesitancy to intervene .The morbidity of laparoscopy is not an issue now as the surgeons are much experienced and trained in laparoscopy. Our findings are in line with the evidence[21] that patients having background and history of Tuberculosis, laparoscopy is the investigation of choice.

It's difficult to access intraperitoneal pathology noninvasively so diagnosis of abdominal TB and its histopathological confirmation is not easy. Sensitivity and specificity of imaging and culture of ascitic fluid in clinically suspected cases is not very high. Laparoscopy provides an opportunity and insight of abdomen to get tissue for biopsy resulting in histopathological diagnosis of abdominal TB. So it should be early in management plan of suspicious cases.[21]

In different studies, laparoscopy was found helpful in the diagnosis up to 87%-92% abdominal tuberculosis.[22]

Mohamed et al[23] depicted the mean age of the patients with abdominal tuberculosis is 29 years which is comparable with our study i.e. 29.9±8.6 years.

According to our data there were 66.2% male patients and 33.8% female which is comparable with the study of Rai et al[24] that showed 66.7% male and 33.3% female patients.

Krisnan P concluded that in patients suspected to have abdominal tuberculosis without evidence of extraabdominal disease, early laparoscopy is 80% sensitive in establishing diagnosis histologicaly.[25] An other study showed that Laparoscopy was safe and helped in the diagnosis of peritoneal as well as intestinal tuberculosis in 87% of patients.[26]

In our study the sensitivity and specificity of laparoscopic findings was 87%, and 82%. As compared with the study of Mir et all, the sensitivity and specificity of laparoscopic findings was 92% and 76%, which is like our experience.

In our research the diagnostic accuracy of laparoscopic findings was 86%. As compared with the study of Mohamed et al[22] the diagnostic precision of laparoscopic findings was 95%, which is in accordance with our study.

Positive predictive value of laparoscopic was 92%, and negative predictive value was 72%. On the above discussion it is concluded that diagnostic accuracy of laparoscopy is high in diagnosing abdominal tuberculosis taking histopathology as gold standard. Timely Laparoscopy is harmless and valu-

able in the confirmation of abdominal TB.

CONCLUSION

It is concluded from this study that diagnostic accuracy of laparoscopy is high i.e. 86% in diagnosing abdominal tuberculosis taking histopathology as gold standard. Timely Laparoscopy is harmless and valuable in the confirmation of abdominal TB.

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DIAGNOSTIC ACCURACY OF MAGNETIC RESONANCE IMAGING IN THE DETECTION OF PITUITARY TUMOURS TAKING HISTOPATHOLOGY AS GOLD STANDARD

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How to cite: Rashid F, Jabeen K, Ali F, Amin A. Diagnostic accuracy of magnetic resonance imaging in the detection of pituitary tumors taking histopathology as gold standard. JAIMC. 2020; 18(4): 673-77.

Abstract

Objectives: To determine the diagnostic accuracy of Magnetic Resonance Imaging in the detection of pituitary adenoma taking histopathological confirmation of pituitary tumour as gold standard. Simple descriptive/observational study. All MRIs were conducted at Department of Diagnostic Radiology, Lahore General Hospital, Lahore whereas Histopathology studies were performed by various public & private sector facilities.

Methodology: A total of 150 patients strongly suspected to be having pituitary adenoma on clinical or laboratory basis referred for MRI over a period of 6 months (March to Sept, 2016) were included in the study after taking their informed consent. Every patient's demographic data was documented i.e. age, gender and address. After ruling out all possible contraindications for MRI studies; Axial, Coronal and Sagittal images of brain in T1W, T1W with contrast and T2W sequences were obtained using a 1.5 Tesla MRI PHILIPS SCANNER having standard imaging coil. The results of Magnetic Resonance Imaging and Histopathology were compared taking histopathological diagnosis as gold standard.

Results: In this study the mean age of all patients was 35.66 ± 10.07 years with 85(56.7%) being Males and 65(43.3%) being Females cases. The sensitivity, specificity, PPV and NPV of MRI was 85.11%, 96.12%, 90.91% and 93.4% respectively. The overall diagnostic accuracy of MRI was 92.67% taking histopathological confirmation of pituitary tumour as gold standard.

Conclusion: Through the findings of this study we found MRI to have a very high diagnostic accuracy. Therefore, despite the limited number of cases it can be safely recommended as the non-invasive test of choice regarding diagnosis of pituitary tumours in clinically suspected cases provided there are no contraindications to MRI studies. It can also help in establishing accurate tumour location & extent to help neurosurgeons planning the surgical approach accordingly.

Keywords: Pituitary adenoma, diagnostic, radiology, MRI, histopathology.

Pituitary adenomas are quite common among CNS neoplasias[1]; comprising 10 to 25% of all intracranial neoplasm[2] with its reported incidence of 10%[3] and prevalence as high as 20%[1]. Commonly categorized as microadenomas (<10mm) or macroadenomas (>10mm) depending on size; nonfunctional (non-hormone secreting) or functional (hormone secreting);[2] or based on cell type, including lactotrophs, gonadotrophs, somatotrophs, corticotrophs, and thyrotrophs).[1] Prolactinomas are the most common (~40%) followed by non-functioning adenomas (28% to 37%).[1] Microadenomas are more common in women, whereas macroadenomas are more frequent in men.[4]

Clinical presentations are diverse & at times vague; making diagnosis difficult.[1] Both plain skull radiographs as well as CT scan are not a sensitive indicator of pituitary tumours and carry radiation

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Submission Date: 16-08-2020
1st Revision Date: 10-09-2020
Acceptance Date: 19-09-2020

risk.[5]

Magnetic Resonance (MR) imaging is an excellent diagnostic method in the investigation of pituitary adenomas due to its superior soft tissue contrast, multiplanar capability and lack of ionizing radiation.[5,6] Although intravenous gadolinium-based contrast material (IV-GBCM) provide higher detection rates of adenomas; T2-weighted coronal images may be important for the detection of the pituitary adenomas without administration of IV-GBCM.[6]

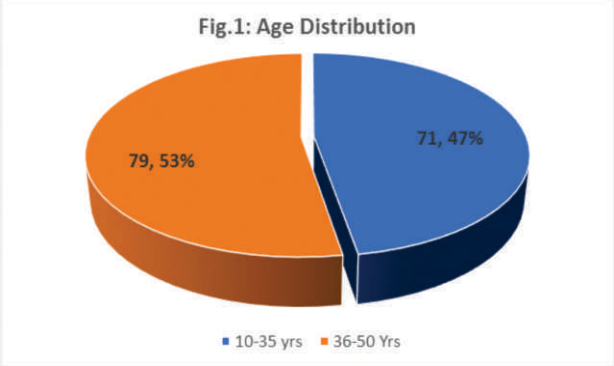
Reported sensitivities of MRI in the detection of adenomas vary widely, but are about 85-90% for contrast-enhanced studies[7] with a specificity of 88% to 90%.[1] The purpose of current study is to assess the usefulness of MR imaging in our settings as a diagnostic tool for pituitary tumours. Internationally MR imaging is emerging to the modality of choice for pituitary lesions.[8]

METHODOLOGY

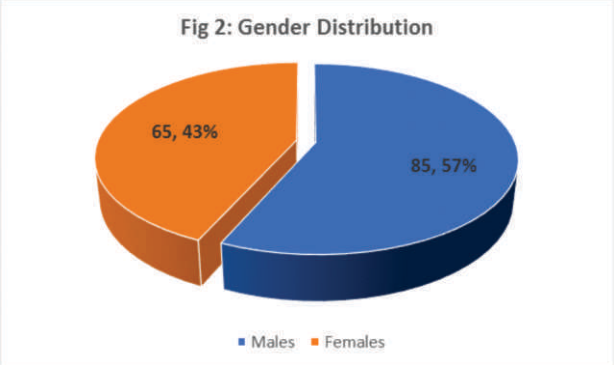
A total of 150 patients strongly suspected to be having pituitary adenoma on clinical or laboratory basis referred for MRI over a period of 6 months (March to Sept, 2016) were included in the study after taking their informed consent; excluding inoperable cases as well those where MRI was contraindicated. Every patient's demographic data was documented i.e. age, gender and address. Axial, Coronal and Sagittal images of brain in T1W, T1W with contrast and T2W sequences were obtained using a 1.5 Tesla MRI PHILIPS SCANNER having standard imaging coil. All patients were initially imaged without gadolinium (T1-SE) proceeded by gadolinium diethylenetriaminepentaacetic acid (DTPA), given intravenously for contrast imaging. Dynamic study was also performed. Magnetic Resonance diagnosis i.e. presence or absence of micro or macro adenoma was made. All the operable cases then were operated and histopathological findings was recorded. The results of Magnetic Resonance Imaging and histopathology were compared taking histopathological confirmation of pituitary tumour as gold standard. Data was compiled and analyzed utilizing the SPSS Statistical Package.

RESULTS

In this study the mean age of all patients was 35.66 ± 10.07 years with minimum and maximum ages being 10 and 50 years respectively. A total of 71 (47.33%) cases were 10-35 years of age and 79 (52.67%) were 36-50 years old (Figure 1).



There were 85 (56.7%) male and 65 (43.3%) female cases in this study (Figure 2).



According to size of tumour 16 (10.7%) patients had Microadenoma (< 10mm) and 134 (89.3%) cases had Macroadenoma (≥10mm).

Table 1: Frequency distribution according to the size of the tumours

		Frequency	Percent
Size (mm)	<10	16	10.7
	⩾10	134	89.3
	Total	150	100.0

According MRI findings pituitary adenoma was diagnosed in 44 (29.3%) and on histopathology it was diagnosed in 47 (31.3%) of the cases (Table-2,3).

Table 2: Frequency Distribution of MRI Findings

		Frequency	Percent
MRI findings	Positive	44	29.3
	Negative	106	70.7
	Total	150	100.0

Table 3: Frequency Distribution of Histopathology Findings

		Frequency	Percent
Histopathology findings	Positive	47	31.3
	Negative	103	68.7
	Total	150	100.0

There were 40 cases that were diagnosed positive on both MRI and Histopathology and 103 cases were negative on both MRI and Histopathology. There were 4 false positive and 7 were false negative. The sensitivity, specificity, PPV and NPV of MRI was 85.11%, 96.12%, 90.91% and 93.4% respectively. The overall diagnostic accuracy of MRI was 92.67% taking histopathological confirmation of pituitary tumour as gold standard (Table 4).

Table 4: Comparison of MRI and Histopathology Findings

		Histopathology findings		Total
		Positive	Negative	
MRI findings	Positive	40	4	44
	Negative	7	99	106
Total		47	103	150

Sensitivity	85.11%
Specificity	96.12%
Positive Predictive Value	90.91%
Negative Predictive Value	93.40%
Diagnostic Accuracy	92.67%

When data was stratified for age, gender and size of tumour we found sensitivity, specify, PPV, NPV and diagnostic accuracy > 80% for each strata other than for patients whose tumour size was < 10 mm (Table-5,6,7).

DISCUSSION

Pituitary adenomas are quite common among CNS neoplasias;[1] comprising 10 to 25% of all intracranial neoplasm[2] with its reported incidence of

Table 5: Comparison of MRI and Histopathology Findings - Stratified for Age (Years)

Age (years)			Histopathology findings		Total
			Positive	Negative	
10-35 Years	MRI findings	Positive	24	2	26
		Negative	6	39	45
36-50 Years	MRI findings	Positive	16	2	18
		Negative	1	60	61

	Age groups(years)	
	10-35	36-50
Sensitivity	80%	94.12%
Specificity	95.12%	96.77%
Positive Predictive Value	92.31%	88.89%
Negative Predictive Value	86.67%	98.36%
Diagnostic Accuracy	88.73%	96.2%

Table 6: Comparison of MRI and Histopathology Findings when Stratified for Gender

Gender			Histopathology findings		Total
			Positive	Negative	
Male	MRI findings	Positive	23	1	24
		Negative	4	57	61
Female	MRI findings	Positive	17	3	20
		Negative	3	42	45

	Gender	
	Male	Female
Sensitivity	85.19%	85%
Specificity	98.28%	93.33%
Positive Predictive Value	95.83%	85%
Negative Predictive Value	93.44%	93.33%
Diagnostic Accuracy	94.12%	90.77%

Table 7: Comparison of MRI and Histopathology Findings when Stratified for Size of Tumour

Size			Histopathology findings		Total
			Positive	Negative	
<10 mm	MRI findings	Positive	6	0	6
		Negative	4	6	10
⩾ 10 mm	MRI findings	Positive	34	4	38
		Negative	3	93	96

	Size (mm)	
	<10 mm	⩾10 mm
Sensitivity	60%	91.89%
Specificity	100%	95.88%
Positive Predictive Value	100%	89.47%
Negative Predictive Value	60%	96.88%
Diagnostic Accuracy	75%	94.78%

10%[3] and prevalence as high as 20%.[1] Pituitary adenomas are the most common type of pituitary disorders.[9]

Clinical presentations are diverse & at times vague; making diagnosis difficult[1]. Both plain skull radiographs as well as CT scan are not a sensitive indicator of pituitary tumours and carry radiation risk.[5]

Magnetic Resonance (MR) imaging is an excellent diagnostic method in the investigation of pituitary adenomas due to its superior soft tissue contrast, multiplanar capability and lack of ionizing radiation[5,6]. Although intravenous gadolinium-based contrast material (IV-GBCM) provide higher detection rates of adenomas; T2-weighted coronal images may be important for the detection of the pituitary adenomas without administration of IV-GBCM.[6]

Magnetic resonance imaging (MRI) is now used routinely in the investigation of the pituitary gland, and is accepted as the most sensitive imaging method for the diagnosis of pituitary microadenomas.[10] Gupta R et al., concluded that contrast-enhanced MRI is the preferred modality for the detection of ACTH-secreting adenomas, which are difficult to visualize on CT scans due to their small size.[11]

Reported sensitivities of MRI in the detection of microadenomas vary widely, but are about 85-90% for contrast-enhanced studies[12]. Yuksekkaya R et al., reported that positive predictive value, negative predictive value, sensitivity, specificity, and diagnostic accuracy rates of T2-weighted coronal images on the detection of the presence of lesions were 100%, 17.4%, 68.7%, 100%, and 87.4%, respectively.[13]

In this study the mean age of all patients was 35.66 ± 10.07 years with 85(56.7%) being Males and 65(43.3%) being Females cases. The sensitivity, specificity, PPV and NPV of MRI was 85.11%, 96.12%, 90.91% and 93.4% respectively. The overall diagnostic accuracy of MRI was 92.67% taking histopathological confirmation of pituitary tumour as gold standard. Our findings are consistent with the fore mentioned studies with an even higher diagnostic accuracy.

Tabarin A. et al., and Peck WW et al., however reported a relatively lower accuracy and specificity than our findings but these studies are almost two decades old and significant advanced in MR technology has occurred since; hence the slightly different findings.[14,15] Newer studies however report a much higher sensitivity and diagnostic accuracy of MRI in the detection of adenomas, being 85-90% for contrast-enhanced studies[7] and specificity of 88% to 90% respectively.[1]

CONCLUSION

Through the findings of this study we found MRI to have a very high diagnostic accuracy. Therefore, despite the limited number of cases it can be safely recommended as the non-invasive test of choice regarding diagnosis of pituitary tumours in clinically suspected cases provided there are no contraindications to MRI studies. It can also help in establishing accurate tumour location & extent to help neurosurgeons planning the surgical approach accordingly.

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FREQUENCY OF HEMATOLOGICAL MANIFESTATIONS IN NEONATAL JAUNDICE

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How to cite: Arshad S, Farhan S, Khanum A, Kashif A, Hareem S, Aslam N. Frequency of hematological manifestations in neonatal jaundice. JAIMC. 2020; 18(4): 678-81.

Abstract

Background: Neonatal Jaundice defined as a total serum bilirubin level above 5 mg per dl (86 µ mole per L) is the most common problem and a life threatening condition faced by neonates in the first week of life; 60% in full-term infants and 80% in preterm infants. Jaundice may not be a major cause of mortality in this age group but a significant burden of untreated severe neonatal jaundice causes potential neurological abnormalities, in developing countries such as ours. This study was conducted to determine the frequency of various changes in hematological parameters and ABO incompatibility in patients with neonatal jaundice.

Methodology: A cross sectional study was done. Study was conducted in Department of Haematology and transfusion medicine, The Children's Hospital and Institute of Child Health, Lahore for a period of six months (2017 -2018). All data was analysed by SPSS version 20. Mean & SD were calculated for quantitative variables Frequency and percentage were calculated for qualitative variables.

Results: This study included 140 jaundiced neonate of which 108 (77.1%) neonates were males and 32(22.9%) were females. The mean age of neonates was 3.10+ 1.78 days.70% babies were preterm and 30% babies were full term. Hematological manifestations showed that 107(76.4%) were anemic, 79 (56.4%) neonates showed leukocytosis and reticulocytosis. 78(55.7%) neonates showed ABO incompatibility as a cause of jaundice.

Conclusion: Hyperbilirubinemia is a very severe condition in newborns. Therefore an overview of the changes in hematological parameters during the course of disease can help the clinicians to diagnose and treat the disease timely and properly. Parents should screen their ABO blood groups as well as Rh factor before marriage.

Keywords: Neonatal Jaundice (NNJ), Hyperbilirubinemia, ABO incompatibility, Hematological manifestations

Neonatal Jaundice defined as a total serum bilirubin level above 5 mg per dl (86 µ mole per L) is the most common problem and a life threatening condition[1] faced by neonates in the first week of life; in 60% of full-term infants and 80% of preterm infants.[2] About 65% of healthy newborns develop hyperbilirubinemia in the first week of life. Severe hyperbilirubinemia defined as total serum bilirubin >95th percentile occurs in 8% to 9% of neonates during the first week; approximately in 4% after 72 hours of life. Breast feeding is one of the important causes of hyperbilirubinemia.[3] Yellowish discoloration of skin and mucous membranes after 14 days in term neonates, and 21 days in preterm neonates are considered for prolonged jaundice.[4]

Neonatal jaundice is a very common syndrome provoking neonatologists world over as well as in Pakistan but there are no reliable data to exactly estimate the load of this condition in our country and

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Submission Date: 09-08-2020
1st Revision Date: 11-09-2020
Acceptance Date: 21-09-2020

is 25% of newborn admission and readmission to hospitals in Pakistan.[5] A study conducted about exchange transfusion of hyperbilirubinemia in Nepal showed out of 481 cases of hyperbilirubinemia 6% required exchange transfusion. 13.8% had ABO incompatibility and 44.8% were with exaggerated physiological jaundice.[6] A study conducted in Asia showed ABO incompatibility and G6PD deficiency as the leading causes of neonatal jaundice with frequencies 18% and 12% respectively.[7] but higher than 4.2% was observed in a case-control study in Taiwan.[8] Important hematological manifestations associated with this condition are anemia, leukocytosis and increase in reticulocyte count. Certain screening tests such as hemoglobin levels, reticulocyte count, leukocyte count, and blood grouping might advance the diagnosis. Various studies have been conducted to demonstrate various parameters of hematological profile and show how they influence the different etiologies of neonatal jaundice.[9] Anemia is one of the common problems in neonates and its evaluation should be performed in a step-wise process including manual review of the peripheral blood smear by the hematologist.[10] Reticulocyte count more than 4% on the third day of life is called reticulocytosis in neonates and should be done for any baby with jaundice requiring phototherapy and is advisable to screen all the jaundiced babies with reticulocytosis and negative coomb's test; for irregular antibodies to detect rare variants in blood group.[11]

Present study determined the frequency of various hematological manifestations and ABO incompatibility in patients with neonatal jaundice.

METHODOLOGY

A cross sectional survey with 140 sample size calculated by using WHO sample size calculator and taking anticipated population of neonatal jaundice with ABO incompatibility as 22.5%, confidence interval 95%, and margin of error 7%. The study was conducted in Department of Haematology and Transfusion, The Children's Hospital and The Institute of Child Health, Lahore. The inclusion criteria were that patients diagnosed with neonatal jaundice on operational definition defined above and age of one week. The exclusion criteria were that infants who are the product of mothers with history of hepatitis B and C confirmed on screening and presenting with any congenital anomaly. Samples collected in EDTA vial were run on Sysmax KX 21 for CBC, reticulocyte count. 1 ml samples collected in 5 ml syringe were run for blood grouping. Investigations included CBC showing Hb (haemoglobin) and TLC(total leucocyte count), reticulocyte count done by stain –Brilliant cresyl blue and blood group of mother and baby using known antisera with tube method. Anaemia, leucocytosis, reticulocytosis and ABO incompatibility were outcome variables. All data was entered and analysed by SPSS version 20. Mean and standard deviation were calculated for quantitative variables like age, serum bilirubin and CBC findings. Frequency and percentage were calculated for qualitative variables like gender, blood group of mother and baby and ABO incompatibility and haematological manifestation. Data was stratified for age, gender and term /preterm, birth weight to deal into the effect modifiers. Post stratification chi square test applied by taking P value < 0.05 as significant.

RESULTS

This study included 140 jaundiced neonates of which 108 (77.1%) neonates were males and 32(22.9 %) were females. The mean age of neonates were 3.10+1.78 days. 32(22.9%) fell in age group less than 2 days, 91(65%) in age group between 2 to 5 days and 17(12.1%) in group aged > 5days. Mean and standard deviation of Hemoglobin, TLC and Bilirubin was 9.57+2.043, 8.12 + 4.60 and 7.83 + 1.73. 70% babies were preterm and 30% babies were full term. Hematological manifestations showed that 107(76.4%) were anemic of which 59(75.6%) had ABO incompatibility. 79 (56.4%) neonates showed leukocytosis and reticulocytosis of which 32(41%) were ABO incompatible with raised TLC and

Table 1:

Mean ± Standard Deviation			
Age	**Bilirubin**	**HB**	**TLC**
3.10± 1.78	7.83± 1.73	9.57± 2.04	8.12± 4.60

Table 2:

		ABO incompatibility		
		Yes	**No**	**P value**
Anemia	**Yes**	59(75.6%)	48(77.4%)	
	No	19(24.4%)	14(22.6%)	0.805
Leukocytosis	**Yes**	32(41%)	47(75.8%)	
	No	46(59%)	15(24.2%)	0.000
Reticulocytosis	**Yes**	63(80.8%)	16(25.8%)	
	No	15(19.2%)	46(74.2%)	0.004

Table 3:

Gender	**Male**	**Female**
	108(77.1%)	32(22.9%)
Age Groups	Less than 2 days	32(22.9%)
	2 to 5 days	91(65%)
	More than 5 days	17(12.1%)
ABO incompatibility	Yes	78(55.7%)
	No	82(44.29%)

63(80.8%) showed ABO incompatibility with increase in reticulocyte count. Of total 78(55.7%) neonates showed ABO incompatibility. 48(34.3%) data showed positive coombs test and 92(66.7%) had negative coombs test.

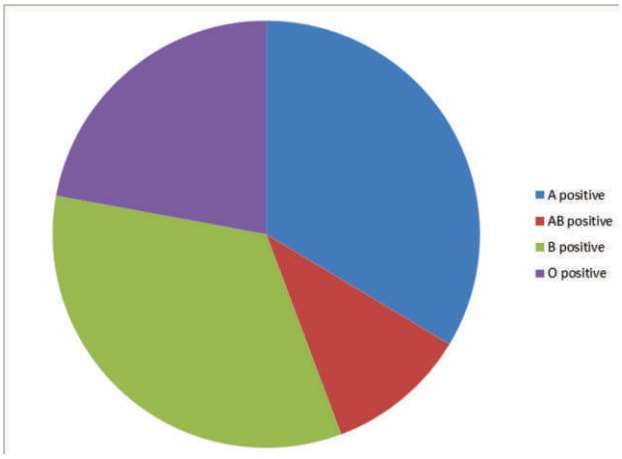

Figure. 1 *Frequencies of Baby Blood Groups*

DISCUSSION

A significant trouble of untreated severe neonatal jaundice in developing countries is leading to the potential neurological abnormalities and guidelines are needed for screening and appropriate management of neonatal jaundice in this aspect.[12] Newborns with jaundice are a vulnerable population of 4 million infants born yearly in US and over 3.5 million infants are born at 35 or more weeks of gestation. All healthy infants have some degree of hyperbilirubinemia and over 60% develop jaundice during their first week of life and is associated with a variety of physiologic and pathologic conditions. In a study, factors associated with severe neonatal jaundice in babies requiring exchange blood transfusion (EBT) included low birth weight, ABO incompatibility (30.0%), glucose-6-phosphate dehydrogenase deficiency (34.4%) and septicemia (26.1%). 27 neonates developed features of kernicterus; 26 before admission while 1 during admission; all except one were delivered outside the hospital. 11.3% cases were result of ABO incompatibility as compared to our study where 55.7% cases were ABO incompatible.[13] Similarly another study showed ABO incompatibility in 22.5% followed by Rh incompatibility in 12.4% of patients with neonatal jaundice.[14] Lower hemoglobin concentration was seen in ABO incompatibility, septicemia, Rh incompatibility and neonatal jaundice due to prematurity. While our study results also showed lower hemoglobin concentration with ABO incompatibility as compared to those new borns having normal hemoglobin level had no ABO incompatibility[15]. In litereature , most of the significant factors associated are like home delivery, sepsis, ABO diseases as compared to our study there is a significant relationship between ABO incompatibility with anemia, Leukocytosis and Reticulocytosis. 76.4% respondents of ABO incompatibility have anemia while 23.6% have no anemic. It also shows that those 75.6% respondents have ABO incompatibility and anemia as compare to 24.4% have no anemic. 41% respondents of ABO incompatibility have Leukocytosis while 59 % have no leukocytosis. It also shows that those respondents did not have ABO incompatibility but 75.8% have leukocytosis as

compare to 24.2 % have no leukocytosis. Most of the hospital could not perform a Coombs test until day 4 or 5 in neonates. False-negative tests were likely to occur, and it is possible that we underestimated the true incidence of ABO hemolytic disease in the out born neonates. It is difficult to make a firm diagnosis of ABO hemolytic disease unless a Coombs'-positive neonate has a rapidly rising bilirubin level in the first few days after birth. The presence of jaundice on day 4 or 5 in a breast-fed, Coombs'-positive, ABO-incompatible neonate, however, does not mean that we can conclude that the jaundice is due to ABO incompatibility In our study coombs test done on neonates to check the positivity of the test, 34.3% showed positive combs test and 65.7% showed negative test.

CONCLUSION

Hyperbilirubinemia is more severe in newborns. Therefore preventive measures should be accepted by both parents, and clinicians to diagnose and treat the disease properly. Basic investigations like CBC and reticulocyte count can indicate the severity of condition. Management and community health organizations should assemble seminars, workshops and trainings for mothers regarding neonatal jaundice. Partners should screen their ABO blood groups as well as Rh factor before marriage. Consanguineous marriages should be avoided.

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EFFECT OF GENERAL ANAESTHESIA VERSUS SPINAL ANAESTHESIA ON APGAR SCORE IN ELECTIVE CAESAREAN SECTION

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How to cite: Mumtaz H, Aslam M, Rukh S, Haider AS, Saqib M, Butt MM. Effect of general anesthesia versus spinal anesthesia on apgar score in elective caesarean section. JAIMC. 2020; 18(4): 682-85.

Abstract

Introduction: The outcome of anaesthesia either spinal or general depends upon the condition of the mother and more importantly effects on newborn. APGAR score is the best parameter to assess the immediate condition of the baby after cesarean section under spinal and general anesthesia.

Objective: The objective of this study was to compare the frequency of Apgar score ≥7 in babies delivered by elective cesarean section after general vs. spinal anaesthesia.

Methodology: It was a randomized controlled trial, done in Department of Anaesthesiology, Lahore General Hospital Lahore, affiliated with College of Physicians and Surgeons Pakistan. Using non probability purposive sampling 106 cases were enrolled in this study. Patients were divided into two groups, General anaesthesia + ETT was given in Group-A and in Group-B, patients were spinal anaesthesia.

Results: In this study the mean age of all subjects was 25.94 ± 4.197 with minimum age 20 years and maximum age 38 years. In GA group mean age was 26.68 ± 4.28 years and in Spinal group the mean age was 25.21 ± 4.02 years. In GA group APGAR ≤7 was seen in 15(28.3%) and in Spinal group APGAR score ≤7 was seen in 19(35.8%). APGAR >7 in GA and Spinal group was seen in 38(71.7%) and 34(62.2%) of the patients respectively. APGAR score >7 was statistically same in both study groups, p-value = 0.405.

Conclusion: According to our results we conclude that there is no significant difference between the effects of general and spinal anaesthesia on Apgar score (> 7) among neonates at 5 minutes interval after birth.

Keywords: Caesarean section, neonatal complications, apgar score general anaesthesia, spinal anaesthesia

Caesarean section is the most commonly performed operation in females. The operation has become very safe over the years, it is still associated with greater maternal mortality and morbidity.[1] The risk of maternal death with caesarean section is four times that associated with all types of vaginal birth, which is 1 per 10,000 births.[1] It is known that there is a greater risk of neonatal respiratory distress with caesarean section than vaginal delivery, regardless of gestational age.[1] This has been described as mild and transient, however, and caesarean section is usually considered safe for the fetus.[2]

Caesarean section can be performed under general or regional anaesthesia like spinal or epidural technique.[3] The anaesthetic techniques and agents chosen should provide good anaesthesia and analgesia with minimal effects on feto-maternal well being.[4]

In developed countries, the proportion of caesarean births is 21.1%[5] and regional anaesthesia is being preferred as the anaesthetic technique of

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Submission Date: 07-08-2020
1st Revision Date: 29-08-2020
Acceptance Date: 13-09-2020

choice due to its safety even in emergency situations.[6] In parts of United Kingdom, use of regional anaesthesia has reached nearly 95%.[6,7] In Turkey, only 44.5% of patients were submitted to regional anaesthesia[8] compared to 80% in the USA.[9]

International obstetric guidelines recommend spinal over general anaesthesia for most caesarean sections.[10,11] The drugs required for general anaesthesia are multiple, most of the drugs affect the baby in two ways: by direct effect from placental drug transfer and by indirect effect resulting from maternal physiological and biochemical changes, which appear to be much more important. They may produce systemic effects in the baby like low Apgar score and sedation.[12-14]

A local study reported an Apgar score ≥ 7 in spinal anesthesia was 60(75%) and in General Anesthesia group 74 (92.5%) at 05 minutes in neonates with significant p =0.028. Moreover they observed Apgar score at 05 min was 9.89 ± 0.32 in Spinal and 9.34 ± 1.07 in general anesthesia with significant p-value ≤0.001.[3] Another local study reported an APGAR score ≥ 7 at 5 minute in General and Spinal anesthesia was seen in 29(96.66%) and 30 (100%) respectively, so they concluded there was no significant difference between the effects of general anaesthesia and spinal anaesthesia on Apgar score of neonates at 5 minutes interval after birth, born after full term elective cesarean section, p-value >0.05.[15] According to the above statistics the APGAR score ≥ 7 at 5 minutes is controversial in local studies (one study reported significant, p-value ≤ 0.0013 and other reported insignificant value p-value >0.05),[15] hence rationale of this study to compare the Apgar score of baby delivered after general and spinal anaesthesia. We use spinal anesthesia quite commonly without any statistics, so after this study we will use spinal or general anesthesia for better outcome on Agar score on new born baby.

METHODOLOGY

It was a randomized controlled trial, done in Department of Anaesthesiology, Lahore General Hospital Lahore, affiliated with College of Physicians and Surgeons Pakistan. Using non probability purposive sampling 106 cases were enrolled in this study. Patients were divided randomly using random number table into two groups, General anaesthesia + ETT was given in Group-A and in Group-B, patients were spinal anaesthesia. Apgar score at 1 minute and then at 5 minutes after the delivery was calculated. Data was collected on predesigned proforma and was analyzed using SPSS version 20. Quantitative variables like age, Apgar score was presented in the form of mean and S.D. Qualitative variable like Apgar score ≥ 7 was presented in the form of frequency and percentages and was compared between both groups. Chi-square test was used to compare the Apgar score ≥7 in both groups. P-value ≤0.05 was considered as significant.

RESULTS

In this study the mean age of all subjects was 25.94 ± 4.197 with minimum age 20 years and maximum age 38 years (Table-1).

In GA group mean age was 26.68 ± 4.28 years and in Spinal group the mean age was 25.21 ± 4.02 years (Table-2).

Overall (n=106) the mean APGAR score was 7.28 ± 0.98 with minimum and maximum APGAR score 5 and 9 respectively (Table-3).

The mean APGAR score in GA group was 7.7 ± 0.93 and in Spinal group mean APGAR was 7.26 ± 1.04 (Table-4).

In GA group APGAR ≤7 was seen in 15(28.3%) and in Spinal group APGAR score ≤ 7 was seen in 19(35.8%). APGAR > 7 in GA and Spinal group was seen in 38(71.7%) and 34(62.2%) of the patients respectively. APGAR score > 7 was statistically same in both study groups, p-value=0.405 (Table-5).

Table 1: Descriptive Statistics of Age (Years)

	Age
Mean	25.94
Std. Deviation	4.197
Minimum	20.00
Maximum	38.00

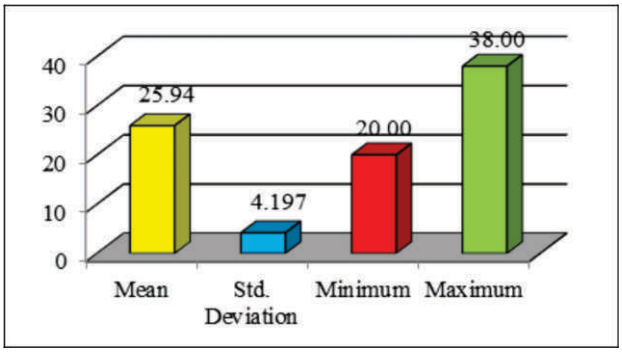

Figure-1: *Descriptive Statistics of Age (Years)*

Table 2: *Comparison of Age (Years) in both Study Groups*

	Study Group	
	GA Group	Spinal Group
Number of patients	53	53
Mean	26.68	25.21
Std. Deviation	4.28	4.02
Std. Error Mean	0.58	0.55

Table 3: *Descriptive Statistics of Five Minutes Apgar Score*

	Five Minutes
Mean	7.28
Std. Deviation	0.98
Minimum	5.00
Maximum	9.00

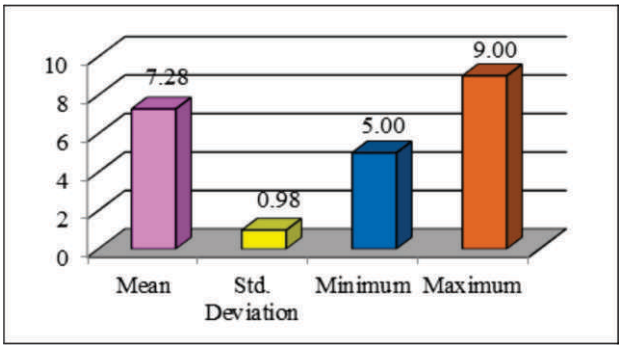

Figure-2: *Descriptive statistics of five minutes apgar score*

Table 4: *Comparison of 5 Minutes Apgar Score in both Study Groups*

	Study Group	
	GA Group	Spinal Group
Number of patients	53	53
Mean	7.30	7.26
Std. Deviation	0.93	1.04
Std. Error Mean	0.128	0.14

Table 5: *Comparison of 5 minutes Apgar Score (≤7 or >7) in Both Study Groups*

		Study Group		Total
		GA Group	Spinal Group	
Apgar Score	≤7	15 28.3%	19 35.8%	34 32.1%
	>7	38 71.7%	34 64.2%	72 67.9%
Total		53 100.0%	53 100.0%	106 100.0%

DISCUSSION

In present study we found that in GA group APGAR ≤ 7 was seen in 15(28.3%) and in Spinal group APGAR score ≤ 7 was seen in 19(35.8%). APGAR >7 in GA and Spinal group was seen in 38(71.7%) and 34(62.2%) of the patients respectively. APGAR score >7 was statistically same in both study groups, p-value = 0.405. So the results of this study are similar to those above cited literature who are in favor of both but it is comparable to the study who reported significant results regarding significant lower Apgar score in general anesthesia. A study reported no difference in Apgar scores between the groups while others reported lower Apgar scores and worse outcomes with the use of general anesthesia.[16]

One more study an Apgar score >7 was observed at 01 and 05 minutes in 78(97.5%) and 80 (100%) neonates respectively in group A while it was 60(75%) and 74 (92.5%) in group B neonates. Apgar score >7 was observed in significantly more neonates in group A as compare to group B (p = 0.028). Average Apgar score at 01 and 05 minutes was also significantly higher in group A than group B; 8.04±0.82 vs 7.10±0.92 (p=0.0001) and 9.89± 0.32 vs 9.34±1.07 respectively (p=0.0001). Umbilical artery blood pH>7.2 was observed significantly high in group A93.8% as compared to group B 83.8% (p=0.045). Also average pH was significantly high in group A than group B e.g. 7.38±0.15 vs 7.21±0.16 (p=0.017).[3]

According to Yegin A, in contrast to regional anesthesia, general anesthesia offers a very rapid and

reliable onset, control over the airway and ventilation and potentially less hypotension. The major adverse fetal effect of regional anesthesia and its sympathetic blockade is utero-placental hypo-perfusion which leads to an acute fall in intervillous blood flow with the potential for fetal academia.[17]

In views of Zahir J, spinal anaesthesia is relatively easy to perform, gives excellent anaesthesia with a low potential of toxicity. It is preferred as it allows mother to be awake and interact immediately after the birth of baby. Compared to general anesthesia it offers less maternal morbidity, ability to use few drugs, comparable less blood loss and provision of excellent pain control.[6]

Internationally, obstetric anaesthesia guidelines recommend spinal and epidural over general anaesthesia (GA) for most caesarean sections (Css). The primary reason for recommending regional blocks is the risk of failed endotracheal intubation and aspiration of gastric contents in pregnant women who undergo GA.[18] While there is evidence that GA is associated with an increased need for neonatal resuscitation, evidence about specific delivery indications and about neonatal outcomes subsequent to resuscitation is limited.[18]

CONCLUSION

According to our results we conclude that there is no significant difference between the effects of general and spinal anaesthesia on Apgar score (> 7) among neonates at 5 minutes interval after birth. Any of the anesthesias can be used for c/section but relatively spinal anesthesia is an easy procedure to perform and allows mother to be awake and interact immediately after the birth of baby.

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KNOWLEDGE OF EPISTAXIS - DOCTOR'S PERSPECTIVE

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How to cite: Hussain SAS, Hussain SAS, Hussain SM. Knowledge of epistaxis – doctors' perspective. JAIMC. 2020; 18 (4): 686-91.

Abstract

Background: Epistaxis is a common problem that the vast majority of doctors have encountered throughout their professional careers. As an important cause of hospital visits, knowledge of the condition is necessary and steps to deal with this issue should be ingrained within a doctor's mind for appropriate management steps in a timely and orderly manner.

Objective: To assess the knowledge of young doctors regarding etiology and management of epistaxis and determine whether it meets the thresholds of adequacy

Methodology: A structured questionnaire assessing knowledge about epistaxis was provided to the doctors that met the inclusion criteria. The questionnaires were distributed mostly online and some were handed out to on duty doctors. The data from 108doctors was compiled, statistical data tabulated and finalized. All the data collected was entered in SPSS ver: 17. The qualitative variables were presented as frequency and percentage and the quantitative variables were presented as mean and standard deviation. Cross tabulation was done for knowledge and independent variables for statistical significance ap value of <or=0.05 was taken as statistically significant.

Results: The study showed that of 108 doctors of various hospitals in Pakistan vast majority of respondents had an adequate knowledge of causation of epistaxis (80.6%), however, many less respondents had adequate knowledge pertaining to management of epistaxis (49.1%). Amongst the respondents, whom had adequate knowledge of both causation and management of epistaxis (42.6%), there was considerable overlap amongst those who had adequate knowledge of management and those who had adequate knowledge of both management and causation, implying the majority of people who knew how to manage epistaxis

Conclusion: Most doctors have adequate knowledge regarding epistaxis. Many more doctors have adequate knowledge of causation of epistaxis as compared to management.

Key words: Epistaxis, young doctors, causation, management

Epistaxis or a nose bleed, as known by the lay man, is a menacing problem. It isextremely prevalent, affecting the majority of the population at one time or the other during their lifetime, having an estimated lifetime prevalence of 60% in the United States,[1] of which 6% will receive medical attention.[2] Its bimodal distribution seems to affect those factions of the population (those below 10 and those above 50)[3,4] in which management is particularly arduous. Com-pounding this problem, some researchers suggest that management of the common problem is poorly taught.[5,6]

Epistaxis is a problem that most physicians will inevitably encounter, whether it be the primary problem or secondary to other disease processes.[7] There is a myriad of situations in which epistaxis can present from a minor nose bleed in an ENT OPD to massive epistaxis in a patient presenting to the surgical emergency department and can be due to variety

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Submission Date: 10-08-2020
1st Revision Date: 12-09-2020
Acceptance Date: 15-09-2020

of different causes.[8,9] It is absolutely essential that all doctors regardless of the field that they belong to have adequate knowledge of epistaxis so that they may promptly and appropriately manage the problem such as to alleviate the anxiety that goes hand in hand with epistaxis. Loaec et al. reported frequent epistaxis to be associated with a decrease in QOL index[10] epistaxis was also associated with higher stress scores.[11]

Not only are doctors the primary care takers of such patients but ultimately, they should be their teachers. A study conducted in Tabuk city[12] showed that there were no significant correlations between educational level and knowledge of cause and how to deal with epistaxis, meaning every individual regardless of education may benefit from the teaching of management of epistaxis. It is incumbent that doctors provide apt and necessary information to their patient regarding this common problem. However, this is not possible if the doctor has inadequate knowledge of epistaxis. They should be their primary educators regarding matters pertaining to health. However, there is a wide disconnect between doctors and patients in this regard.[13] Most epistaxis stems as an outpatient problem, as such it is vital that first aid measures are known by the general population to decrease morbidity and mortality associated with this common problem and allay the misery of the patient by saving them considerable time and effort of repeated hospital visits. Indeed, first aid measures reduce morbidity and mortality in patients[14] particularly in those with continuous bleeding.[15]

As such we think it necessary to gauge the knowledge of doctors regarding epistaxis and as such we have put together this article addressing the situation particularly focusing on young doctors that do not hold a post graduate degree as this group constitutes the major chunk of the work force and often have the very initial contact with patients. The objective of the study was to assess the knowledge of young doctors regarding etiology and management of epistaxis and determine whether it meets the thresholds of adequacy.

METHODOLOGY

A Cross Sectional study was conducted at Allama Iqbal Medical College from April – June 2020. 108 young doctors of either gender, working for any duration in a clinical capacity in a tertiary care hospital public or private, in Lahore, Pakistan. The doctor must be consenting and carry MBBS degree or equivalent. Dentists, physiotherapists and doctors with post graduate degrees were excluded. A structured questionnaire assessing knowledge about epistaxis was provided to the doctors that met the inclusion criteria. The questionnaires were distributed mostly online and some were handed out to on duty doctors. The data from 108 doctors was compiled, statistical data tabulated and finalized. All the data collected was entered in SPSS ver: 17. The qualitative variables were presented as frequency and percentage and the quantitative variables were presented as mean and standard deviation. Cross tabulation was done for knowledge and independent variables for statistical significance ap value of <or = 0.05 was taken as statistically significant.

RESULTS

Although knowledge of epistaxis in general (e.g most common site of epistaxis) and knowledge regarding causes of epistaxis is very useful to any clinician or surgeon, knowledge of management of epistaxis is extremely necessary.

As such, our questionnaire focused mainly on the management of epistaxis however a handful of questions were also dedicated solely for the causation and general knowledge of epistaxis. Of the total questions: 3 related to causation of epistaxis from which a cumulative score was derived, the cumulative score looked into whether each individual had knowledge of the cause of epistaxis with any individual getting 2 out of 3 questions correct deemed to have adequate knowledge. However, if the question regarding risk factors of epistaxis was correct, the individual was deemed to have adequate

knowledge (even if the individual only managed to answer this particular question out of the 3 correctly). This was because it was felt unanimously by the authors that this question held enough weightage to deem the individual who answered this question to have adequate knowledge.

Whoever met the mentioned criteria was given a cumulative score of knowledge of cause>/ 50 (adequate). 12 questions of the questionnaire were focused on the management of epistaxis and a cumulative score of knowledge of management of epistaxis was given. An individual who correctly answered 6 or more of these questions was given a cumulative score of knowledge of management >/ 50 (adequate).

The study was conducted on a sample of 108 doctors of various hospitals in Pakistan out of which 65 (60.2%) were male and 43(39.8%) were female. The year of graduation of the correspondents fell in the range 2012 to 2019. of the 108 correspondents 52 (48.1%) were employed in medicine or its allied fields 40 (37.0%) employed in surgery or its allied fields& 16(14.8%) were general physicians. Only 26 (24%) had any work experience & out of these 13(12.0%) had 3 months (duration of HJ rotation) 13 (12%) had >/ 1 year experience working in ENT. 11(10.2%) respondents were currently working in a rural area and 93 (86.1%) were currently working in urban area. Also 2 (1.9%) were working in both.

There were 3 questions pertaining to the causes of epistaxis. 62(57.4%) were able to correctly identify the essential points in the history taking, the majority of respondents were able to correctly identify the most common cause of epistaxis with only 13(12.0%) incorrect responses and 47(43.5%) knew the % prevalence of epistaxis.

As a whole 80.6% had a cumulative score of knowledge of cause>/ 50 % and had knowledge regarding causation of epistaxis that met the threshold of adequacy, however, many less respondents had adequate knowledge pertaining to management of epistaxis (49.1%). Amongst the respondents, 42.6% had adequate knowledge of both causation and management of epistaxis.

12 questions pertained to the management of epistaxis. Of the 108 respondents, 9 (8.3%) knew when an emergency referral to ENT was to be done and 14 (13.8) knew when an immediate emergency transfer was to be done. The majority of correspondents were aware of the correct site of nose pinching with 73(67.6) able to identify the correct option, only a few correspondents did not know the 1st step to control anterior epistaxis with 99(91.7%) answering the question correctly.

On the question regarding what the position of the patient should be during epistaxis 67(59.3%) were correct. When inquired on whether the blood from the nose should be spat out, collected or ingested, 86(79.6%) were able to answer appropriately. During the course of the research it was encouraging to find that the majority of individuals were able to correctly identify the 1st line antibiotics given to patients with epistaxis with 89(82.4%) answering correctly.

In contrast, few knew when prophylactic antibiotics should be used for epistaxis with only 14(12.9%) answering with the correct response. Similarly, only 49(45.4%) knew not to discharge a patient home after doing nasal packing. Of the test subjects, most did not know how long nasal packing should be kept in the nose for, as is reflected by the fact that 44(40.7%) were able to answer correctly.

We attempted to gauge their knowledge about cauterization of bleeding points in the nose and when it is indicated and when it is contraindicated. We found 9(8.3%) knew when cautery should be done whilst 10 (9.3%) knew when it is contraindicated. In total, 42.6% of the researched population had adequate knowledge of epistaxis. Only those who had adequate knowledge of both causation and management were considered to have adequate knowledge of epistaxis as a whole.

'Knowledge' of a subject is difficult to define and it is even harder to delineate the knowledge of a subject as either inadequate or adequate. Generally,

we found the results to show that the vast majority of respondents had an adequate knowledge of causation of epistaxis (80.6%), however, many less respondents had adequate knowledge pertaining to management of epistaxis (49.1%). Amongst the respondents, whom had adequate knowledge of both causation and management of epistaxis (42.6%), there was considerable overlap amongst those who had adequate knowledge of management and those whom had adequate knowledge of both management and causation, implying the majority of people who knew how to manage epistaxis were also aware of causation which is encouraging. In a similar study in Aseer,[16] Saudia Arabia, it was found that amongst residents 23% had good knowledge about epistaxis. Slightly below half of respondents in our research (42.6%) were deemed to have adequate knowledge. However, their criteria to classify an individual as having 'good' knowledge was more restrictive as at least 60% of the total questions had to be answered correctly.

Although not directly linked to our research, it is fascinating to see how the different levels of medical education respond to the same question and it allows to gauge how medical knowledge matures. Therefore, we have included researches not only targeting doctors/medical personnel but also medical students and the general population.

The same study conducted in Aseer[16] showed that only 56.4 % where able to identify the most common cause of epistaxis, whereas in our research 88% were able to identify the most common cause as trauma correctly. In a research conducted amongst medical students in Saudia Arabia[17] only 40% were able to identify the most common cause of epistaxis. Albouq et al[18] reported 87.1% incorrectly identified the most common cause of epistaxis as bleeding disorder, showing the disparity of knowledge even in the same country amongst medical students. A study[19] conducted amongst the general population saw that 71.2% knew that nasal manipulation was a risk factor, in the same study 77.9% knew that environmental factors contributed to epistaxis. These results are in contrast to findings in a study[20] of 600 respondents from amongst the general population, the large majority of whom did not know that medication or chronic disease were risk factors (74% and 82% respectively).

Alhejaily et al[12] conducted a study amongst the general population which showed that 34.8% knew that chronic disease causes epistaxis. 42.2% and 68.9% were aware of the fact that certain drugs and excessive nasal manipulation can cause epistaxis respectively.

Doctors in Aseer,[16] outperformed doctors in our research when asked about relevant points in history taking, 66.3% of the doctors in Aseer were able to correctly recall relevant points to be asked in history compared to 57.4 % of doctors in our research.

When inquired about the position in which a patient of epistaxis should be managed in, 59.3% of respondents in our research were correct, much fewer than the 88.5% of patients in Aseer[16] who were able to correctly identify the position. Our result was similar to that of Mugwe et al[21] in which 60 % of the individuals identified the correct position.

When studying the knowledge of correct position in medical students we saw a significant number knew the correct position at 80.6%. Moving on to the general population, 45.2% knew the correct position to stop epistaxis in a study conducted in Tabuk[(12)]. Another study carried out amongst the general population[22] showed that 56.9% of respondents knew the right position which was higher than the numbers reported by Strachan D and England J[23] at 36%. It was good to see 73(67.6%) of the respondents of our research were able to identify the correct site of nose pinching, at the other end of the spectrum only 38.1% of the respondents were able to correctly identify this point in a survey amongst clinical staff employed in Accident and Emergency in Kenya.[21] Only 41.3% of medical students[17] were aware of this site. One study[13] found 15% of the general population knew the lower part of the nose should be pinched. Many studies showed that the general population knew that nasal compression was

beneficial in stopping bleeding with 55.6%,[12] 77.7%[20] of the respondents in different studies aware of this point.

An outstanding 91.7% of doctors in our research knew the correct initial step of controlling epistaxis, much greater than the 60.6% of the residents in Aseer.[16]

There were some limitations to our study. We had a relatively small sample size. Also, we did not include post graduates in our research. Some questions carry more value than others in that they must be known by all physicians and therefore they should have carried a higher mark in our scoring system.

CONCLUSION

Most doctors have adequate knowledge regarding epistaxis. Many more doctors have adequate knowledge of causation of epistaxis as compared to management.

RECOMMENDATIONS

- Specialized workshops should be carried out to teach the management of epistaxis.
- Regular screening tests should be taken to assess doctor's knowledge regarding epistaxis in order to gauge the effectiveness of such workshops and open-ended feedback should be encouraged to improve productivity and efficacy of such workshops.

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Variables n=108	Frequency		Percentage %	
	Correct	Incorrect	Correct	Incorrect
When should emergency referral to ENT be done?	9	99	8.3	91.7
Whenshould an immediate emergency transfer to ENT be done?	14	94	13.8	86.2
What is the correct site of nose pinching?	73	35	67.6	32.4
What is the 1st step to control anterior epistaxis?	99	9	91.7	8.3
What is the correct position of the patient during epistaxis?	67	41	59.3	40.7
Should blood be spat out, collected or ingested?	86	22	79.6	20.4
What are the 1st line antibiotics given to patients with epistaxis?	89	19	82.4	17.6
When should prophylactic antibiotics be used for epistaxis?	14	94	12.9	87.1
Should a patient be discharged home after doing nasal packing?	49	59	45.4	54.6
How longshould nasal packing be kept in the nose?	44	64	40.7	59.3
When should nasal cautery be done?	9	99	8.3	91.7
When should nasal cautery not be done?	10	98	9.3	90.7
Adequate knowledge pertaining to management of epistaxis (cumulative score of knowledge of management>/ 50 %)= 49.1%				

Variables	Frequency		Percentage%	
	Correct	Incorrect	Correct	Incorrect
What are the essential points in the history ofpatient who presents with epistaxis?	62	46	57.4	42.6
What is the most common cause of epistaxis?	95	13	88	12
What is the % prevalence of epistaxis?	47	53	43.5	56.5
Adequate knowledge regarding causation of epistaxis (cumulative score of knowledge of cause>/ 50%) = 80.6%				

Adequate knowledge pertaining to management of epistaxis (cumulative score of knowledge of management>/ 50 %)	49.1%
Adequate knowledge regarding causation of epistaxis (cumulative score of knowledge of cause>/ 50%)	80.6%
Whom had adequate knowledge of both causation and management of epistaxis	42.6%

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TRENDS OF LIPID ABNORMALITIES IN MIDDLE-AGED ADULTS RESIDING IN HARBANSPURA & TULSPURA REGIONS OF DISTRICT LAHORE-PAKISTAN

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How to cite: Saeed U, Saeed S, Malik AI. Trends of lipid abnormalities in middle-aged adults residing in Harbanspura & Tulspura regions of district Lahore, Pakistan. JAIMC. 2020; 18(4): 692-96.

Abstract

Objectives: This research aimed to measure the plasma triglycerides and cholesterol levels in both adult males and females, regarding lipid abnormalities in the given population of Harbanspura and Tulspura regions in district Lahore, Pakistan.

Methodology: Three hundred middle aged individuals were included in the study.Blood samples were analysed for levels of triglycerides and cholestrol after taking informed consent.

Results: The results showed an overall prevalence of hyper-triglyceridemia (24.3%), while mixed hyperlipidemia was 2nd most common lipid abnormality, and was observed in 21.3% individuals. In contrast, hypercholesterolemia was detected in 11.7% individuals in the same population.

Conclusion: Hypertriglyceridemia was more prevalent in females (14.3%) compared with males (10%), while hypercholesterolemia was observed to be more common in males (7.6%) compared with females (4.1%). Mixed hyperlipidemia, however, showed a near equal trend in both males and females (11% and 10.3% respectively)

Key Words: Plasma triglyceride, cholesterol, middle-aged adults

Harbanspura and Tulspura are densely populated semi-urban regions located in the south of cosmopolitan Lahore. People residing in these regions are considered less aware of dietary planning and life-style modifications to control obesity, diabetes, hypertension and cardiovascular mortalities.

Dietary triglycerides (TAGs) are carried from the small intestines in the form of chylomicrons, whereas, endogenous TAGs are transported from the liver via very-low-density lipoprotein (VLDL) molecules. After meals, more than 90% of the circulating TAGs are derived from dietary lipids from small intestines and transported via chylomicrons, while in fasting conditions, endogenous triglycerides packaged by the liver as VLDL particles dominate in the blood circulation. This increase in plasma levels of TAG rich lipoproteins is primarily derived from the small intestines and liver.

The normal reference range of plasma triglyceride (TAG) is considered as 150 mg/dl (JAMA. 2001). Primary hypertriglyceridemia is caused by genetic defects in endogenous TAG synthesis, while secondary hypertriglyceridemia is caused by various clinical conditions such as obesity, hypothyroidism, diabetes mellitus, chronic kidney disease and some medications. It has been demonstrated that hypertriglyceridemia is the predominant cause of acute pancreatitis in approximately 1% to 4% of patients (Kota S et al. 2012). Hypertriglyceridemia charac-

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Submission Date: 10-08-2020
1st Revision Date: 19-08-2020
2nd Revision Date: 22-09-2020
Acceptance Date: 30-09-2020

teristically does not occur independently, but is commonly associated with other lipid disorders, and all these eventually lead to coronary artery disease (Ford ES et al; 2002). Prevalence of hypertriglyceridemia varies in different sections of populations, and this was demonstrated by a National Health Survey conducted in Saudi Arabia in 2018, which highlighted the occurrence of coronary artery disease risk in 43% cases of hypertriglyceridemia. In South Asia, the burden of ischemic heart diseases is considered to be caused primarily by dyslipidemias, such as hypertriglyceridemia and hypercholesterolemia (Enas et al; 2007). A study conducted on urban & rural Pakistani population, estimated serum lipids fractions and concluded that 63% of the population included in the study demonstrated impairment of any one major lipid fraction in their serums (Zaid M. 2018). High plasma cholesterol levels are associated with a substantial risk of cardiovascular diseases (CVD) and its increasing global prevalence is posing a grave threat to our lives (Hassankhani H et al; 2012).

Cholesterol is vital for neuronal physiology in adults and also important during developmental stages of life. Cholesterol maintains the fluidity of all the biological membranes, and determines the biochemical and physical properties of cellular proteins. Clinical data and epidemiological studies have observed both elevated plasma levels of low-density lipoprotein (LDL) cholesterol, and decreased high-density lipoprotein (HDL) cholesterol, linked with the development of CVD. Association of hypercholesterolemia with cardiovascular disease (CVD) has been well established, worldwide (Ramos et al; 2012). This increased risk of CVD was significantly observed among patients having high plasma lipid levels, while in patients with controlled hypercholesterolemia, the risk of CVD was statistically non-significant (Huerta et al;2010). Presence of coronary artery disease in close relatives of patients with hypercholesterolemia is observed to be very low and estimated to be approximately 3% in a separate research study (Alonso et al; 2014).

Mixed hyperlipidemia, also known as combined dyslipidemia, is characterized by elevated plasma levels of cholesterol (LDL-cholesterol) and triglycerides, often accompanied by reduced plasma levels of HDL (high density lipoprotein). It is already known that mixed hyperlipidemia significantly contributes to the risk of development of cardiovascular diseases (CVD) worldwide (Reaven et al; 1993). Although the etiology of combined hyperlipidemia is unclear, but it is known this condition is expressed resulting due to interaction of genetic, metabolic and a variety of environmental factors including dietary habits of individuals (Carmena et al; 1999). Mixed hyperlipidemia is frequently associated with insulin resistance and elevated risk of cardiovascular diseases (CVD). This common occurrence of combined hyperlipidemia, insulin resistance and CVD was observed in a study conducted by Sergio et al who worked on 20 individuals suffering from combined hpyerlipidemia (Sergio et al; 2006).

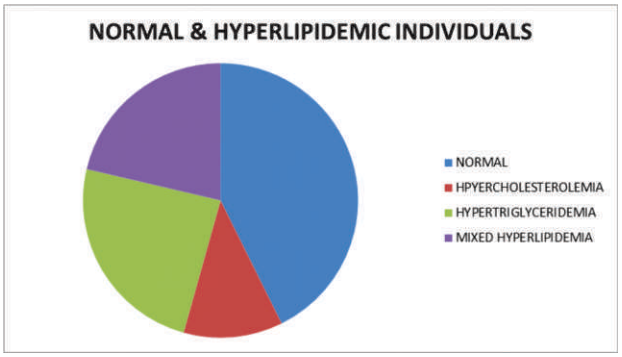
METHODOLOGY

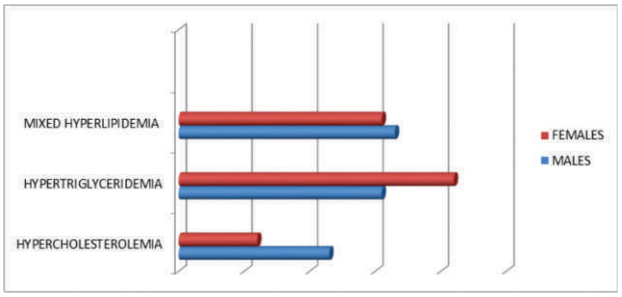
Three hundred middle-aged individuals, both males and females, ranging between 25 and 70 years of age are randomly selected in this study. After taking consent from each subject, approximately 5 ml venous blood is drawn, preferably from the median cubital vein of left forearm. The collected blood is then immedia-tely transferred into yellow-capped 'gel vacutainers' for proper storage and subsequent sample handling. Each vacutainer is carefully labeled. All blood samples are immediately centrifuged, and serum triglycerides and cholesterol levels are determined by using the standard protocols and employing spectrophotometric analysis of each sample.

RESULTS

Out of 300 individuals, 128 had normal plasma triglycerides and cholesterol levels (42.6%), hypertriglyceridemia was detected in 73 individuals (24.3%), hypercholesterolemia in 35 individuals

(11.6%), and mixed hyperlipidemia in 64 individuals (21.3%). Mean age of normal individuals including both males and females was 37.5 years, while individuals with hypercholesterolemia was 56 years; mean age of individuals with hypertriglyceridemia was 47 years, and mean age with mixed hyperlipidemia was 59 years. In normal individuals (n=128), 53 were males (17.6%), while 75 were females (25%), among the individuals with hypercholesterolemia (n= 35), 23 were males (7.6 %), 12 were females (4.1%), in the individuals with hypertriglyceridemia (n=73), 31 were males (10.3 %), while 42 were females (14%), in individuals with mixed hyperlipidemia (n=64), 33 were males (115) while 31 were females (12.3%). (TABLE-4)





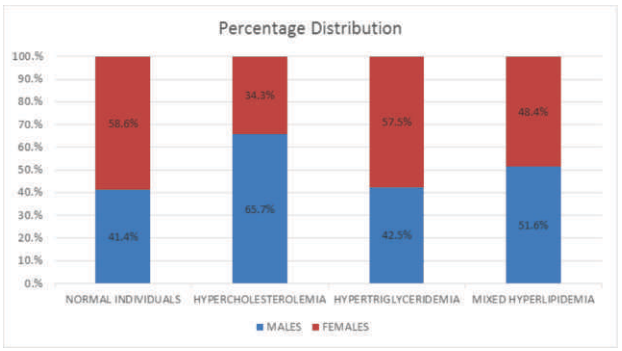


Table 1: *Serum Cholesterol and Triglyceride Levels in Female Population*

Parameters	Units	Mean ± SD	p- value
Age	Years	36.8±2.10	0.00
Serum cholesterol Levels	mg/dl	236.30±12.10	0.00
Serum Triglyceride levels	mg/dl	228.40±22.12	0.00

<0.005

Table 2: *Serum Cholesterol and Triglyceride Levels in Male Population*

Parameters	Units	Mean ± SD	p- value
Age	Years	35.5±2.10	0.00
Serum cholesterol Levels	mg/dl	245.30±22.05	0.00
Serum Triglyceride levels	mg/dl	239.20±12.10	0.00

<0.005

Table 3: *Mean Age of Normal Individuals and Hyperlipidemic Patients in Males and Females*

NORMAL INDIVIDUALS/PATIENTS n = 300	MEAN AGE (years)
Normal	37
Hypercholesterolemia	56
Hypertriglyceridemia	47
Mixed hyperlipidemia	59

Table 4: *Mean Age of Normal Individuals and Hyperlipidemic Patients in Males and Females*

Normal Individuals (n=128) Patients (n=172)	% Age n=300	Males	Females
Normal Individuals n = 128	128 (42.6%)	53 (17.6%)	75 (25%)
Hypercholesterolemia n = 35	35 (11.7%)	23 (7.6%)	12 (4.1%)
Hypertriglyceridemia n = 73	73 (24.3%)	31 (10.3%)	42 (14%)
Mixed Hyperlipidemia n = 64	64 (21.3%)	33 (11%)	31 (10.3%)

The results showed overall prevalence of hypertriglyceridemia (24.3%), out of which 10.3% were males and 14% were females; indicating that females have high incidence of hypertriglyceridemia, compared with males (228.40±22.12 mg/dl). In contrast, hypercholesterolemia was detected in (11.7%) individuals, out of which 7.6% were males, while only 4.1% were females; showing high incidence of hypercholesterolemia in adult males, compared with females (245.30±22.05 mg/dl). Mixed hyperlipidemia was observed in 21.3%

individuals; among them 11% were males and 10.3% were females, indicating that mixed hyperlipidemia is the 2nd most common lipid disorder in the given population, involving both males and females almost equally in this study.

DISCUSSION

Dyslipidemias are considered as potential risk factors for coronary heart diseases, hypertension and insulin resistance. World Health Organization (WHO) has previously reported that lipid disorders are significantly related to the occurrence of ischemic heart diseases worldwide. The current study aims at detecting dyslipidemias in local adult population in both males and females. Prevalence of lipid disorders and its association with coronary artery diseases has been documented in several studies in the past. Despite the evaluation of dyslipidemias in selected populations in different countries, definite statistics on the prevention of incidence and progression of these disorders are scarcely available (Franco et al; 2005). Hamid Najafipour in 2016 demonstrated high prevalence of diagnosed cases of dyslipidemia in a local population, simultaneously highlighted the influence of obesity, strong family history and advancing age on the occurrence of these dyslipidemias (Hamid et al; 2016). A study conducted in Iran documented hypercholesterolemia in 35.4% individuals (Sharifi et al; 2008). In the same lines, another study conducted in Jordan reported hypercholesterolemia in 48.8% of population and hypertriglyceridemia in 43.6% individuals included in the study (Khader; 2010). Recently a gender based plasma lipid analysis in Pakistani population documented a high incidence of hypertriglyceridemia in males than in females, and observed that 63% of the population included in the study had dyslipidemia characterized by abnormal plasma lipid levels of at least one major lipid-fraction (M. Zaid; 2018). In the current study high prevalence of dyslipidemia was observed (52.7%), while 42.6% individuals had normal plasma cholesterol and triglyceride levels. Females have an overall high incidence of hypertriglyceridemia (14%) while hypercholesterolemia was more frequently observed in males (7.6%), mixed hyperlipidemia was almost equally distributed in both males and females (115 and 10.3 & respectively). The findings suggest the need for improved health education, effective region-based screening and strict dietary management of lipid disorders in Pakistani population.

CONCLUSION

It is, therefore, concluded that hypertriglyceridemia (24.3%) is far more common in the given population, compared with hypercholesterolemia (11.7%), while mixed hyperlipidemia (21.3%) is second most common lipid abnormality observed in the same population. Regarding the overall incidence of dyslipidemia, 57.3% individuals were affected, while 42.6% individuals had normal plasma cholesterol and triglyceride levels in the same population.

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MEAN DECREASE IN SERUM FERRITIN LEVELS WITH DEFERASIROX MONOTHERAPY VERSUS DEFERASIROX-DESFERRIOXAMINE COMBINATION THERAPY IN PATIENTS OF BETA THALASSEMIA WITH IRON OVERLOAD

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Abstract

Objective: This study is aimed at comparing the mean decrease in serum Ferritin with DFX monotherapy versus DFX-DFO combination therapy in paediatric patients with iron overload suffering from Beta Thalassemia Major bearing the hypothesis that there is a difference in mean decrease in serum Ferritin with DFX monotherapy vs DFX-DFO combination therapy in patients of Beta Thalassemia Major.

Methodology: One hundred and twenty peadiatric patients of Beta Thalassemia Major with iron overload having serum Ferritin > 1000ng/ml, ages between 2 and 15 years of age of either gender were selected from The Heamatology Department of The Children's Hospital and ICH, Lahore . They were divided in two groups randomly. Group A underwent DFX monotherapy while group B patients underwent DFX-DFO combination therapy to reduce iron overload. Serum Ferritin levels were performed with a serum sample run on Siemens Immunulite 2000, Statistical analysis was done using SPSS version 19.

Results: The mean age of the patients who underwent this trial was 7±3 SD. 58(48.3 %)of the patients were male while 62(51.7%)were female. The mean of the initial serum Ferritin levels was 2071±491 SD. The mean serum Ferritin after three months was 1817±491 SD. The overall mean decrease in serum Ferritin was 254±96 SD with the mean decrease in serum Ferritin with DFX monotherapy being 158±5 SD while the mean decrease in serum Ferritin with DFX-DFO combination being 349±3 SD. The p value came out to be <0.001 which is statistically significant.

Conclusion: From these results it was concluded that DFX-DFO combination therapy is more effective at reducing serum Ferritin level than DFX monotherapy because of a greater mean decrease in serum Ferritin after three months. This is in accordance with other international studies published.

Key words: Beta Thalassemia Major, Serum Ferritin, Deferasirox(DFX), Desferrioaxamine(DFO) , DFX-DFO combination therapy, Iron overload.

Thalassemia, an inherited genetic anemia. renders patients dependent on regular blood transfu-sions because of ineffective hemoglobin synthesis. However frequent blood transfusions and chronic hemolytic anemia can result in excessive iron over-load with subsequent organ damage and death.[1]

After 10 to 20 repeated blood transfusions, the serum Ferritin level is expected to exceed 1000 pg/L. This level is a signal for iron chelation therapy to be initiated.

There are 3 iron chelators marketed for clinical

use; Desferrioaxamine (DFO), which is administrated parenterally, and another two, Deferiprone (DFP) and Deferasirox (DFX), which are given orally. Important points for ideal iron chelation therapy include: slow rate of metabolism, able to penetrate tissues and cells, nontoxic, affordable, no redistribution of iron, oral availability, and high chelating efficiency.[2]

Desferrioxamine (DFO) or Deferiprone (DFP) or Deferasirox (DFX) monotherapy and DFO and DFP combination therapy (DFO+DFP) were four commonly implemented chelation regimens for the iron overloaded of β-thalassemia major.[3]

Background Patients with severe iron overload may require a more rapid and efficient therapy for reduction in iron burden than what can be provided with chelation monotherapy. [4]

Deferasirox is an oral iron chelator which is rapidly absorbed after administration and has a bioavailability of about 70%.The elimination half-life of 8 to 16 hours allows a once daily administration after the tablets have been added to water or juice. Excretion is mainly through the faeces[5] Side effects include renal dysfunction with elevations in serum creatinine, skin rash, gastrointestinal disturbances and serious ocular side effects including decreased vision, lens opacities and retinopathy[6].

DFO acts by binding free iron in the bloodstream with a 1:1 ratio and enhances its elimination mostly in the urine and to a lesser extent in the feces. It is administered by slow subcutaneous infusion at the usual dosage of 40–60mg/kg 5–7 days per week.[7]

Its adverse effects include local reactions that are managed by local anesthetics or topical steroids, growth delay, and bony abnormalities due to epiphyseal dysgenesis, impaired hearing and visual disturbances, and sepsis, such as Yersinia enterocolitis and Klebsiella infections, Ophthalmologic and audiologic toxicities are more likely to occur when the DFO dose is high relative to the iron burden.[8]

This study is aimed at comparing the mean decrease in serum Ferritin with DFX monotherapy versus DFX-DFO combination therapy in paediatric patients with iron overload suffering from Beta Thalassemia Major bearing the hypothesis that there is a difference in mean decrease in serum Ferritin with DFX monotherapy vs. DFX-DFO combination therapy in patients of Beta Thalassemia Major.

METHODOLOGY

This was a randomized control trial carried out in the hospital from February to August 2016. Institutional Ethical Review board approved the study.120 patients were randomly divided into two groups by the lottery method. The sample size of 60 in each group was calculated with 95% confidence level and 80% power of test .Patients with Beta Thalassemia Major between 2 years to 15 years of age and of both genders were included in the study. All the patients included had Serum Ferritin levels greater than 1000ng/ml with CRP levels in the normal range (≤6mg/L) since serum Ferritin is an acute phase reactant.Exclusion criteria were: Children with Beta Thalassemia Major associated with other co morbidities such as Hepatitis C, Ascorbic acid deficiency(clinically determined by connective tissue defects and gum bleeding with levels < 0.2mg/dl, pre-existing cardiac (on echocardiography), hepatic (deranged LFT'S) or renal disease (deranged RFT'S), Children with raised CRP (>6mg/L) levels or fever (>100°F) during serum ferritin measurement, Children with deranged LFT's and RFT's (deranged from the normal. Normal LFT'S : AST 10-40 U/L and ALT 7-56 U/L and normal RFT'S : S/Creatinine 0.7-1.3mg/dl and BUN 6-20mg/dl.

Group A patients underwent DFX monotherapy. Deferasirox was given as an oral iron chelator , daily with a starting dose of 25mg/kg/day and taken up to 40mg/kg/day. Administered half an hour before breakfast dissolved in a glass of water. It is available in preparations of 100mg and 400mg. A standard preparation was used for all patients. Group B patients underwent DFX-DFO combination therapy to reduce iron overload. Deferasirox was given daily

as an oral iron chelator with a starting dose of 25mg/kg/day and taken up to 40mg/kg/day. Desferrioxamine was given along with daily Deferasirox. Desferrioxamine was given 40mg/kg/day subcutaneously over eight hours at night via an infusion pump five days a week with a gap of two days on which only oral Deferasirox was given. In younger children, Desferrioxamine was given at a dose of 20mg/kg to minimize adverse effects. It is available in a preparation of 500mg. A standard preparation was used for all patients.

All data was collected using a proforma. Informed consent was taken from the patients before data collection. Serum Ferritin levels were perfor-med with a serum sample run on Siemens Immu-nulite 2000.

RESULTS

The mean age of patients who underwent iron chelation therapy was 7±3 S.D as shown in Table 158(48.3%) of the patients were male while 62 (51.7%) were female as shown in Table 5. The mean initial serum Ferritin levels taken were 2071± 491 S.D as shown in Table 2.The mean serum Ferritin after three months was 1817±491 S.D as shown in Table 3.The mean decrease in Serum Ferritin was 254± 96.S.D as shown in Table 4.75(62.5%) of the patients were in the age group of 2-8 yrs while 45(37.5%) were in the age group of 9-15 yrs as shown in table 6.94(78.33%) of the patients had initial serum ferritin in the range of 1000-2500 while 26(21.66%) had initial serum ferritin in the range 2501-3500 as shown in table 7.The mean decrease in serum ferritin has been stratified with three effect modifiers: with gender in Table 8, with age in groups in table 9 and ranges of initial serum ferritin in table 10.The mean decrease in serum Ferritin with DFX monotherapy was 158±5 S.D. while it was 349±3 in combination therapy as shown in table 11. The p value came out to be <0.001 as shown in table 11 which is highly significant.

DISCUSSION

Tahir and colleagues assessed the utility of

Table 1: *Quantitative Variables Presented By Calculating Mean And Standard Deviation*

N	120
Minimum	2.00
Maximum	15.00
Mean	7.7333
Standard Deviation	3.51643

Table 2: *Initial Serum Ferritin Levels*

N	120
Minimum	1200.0
Maximum	3126.00
Mean	2071.4667
Standard Deviation	491.46563

Table 3: *Serum Ferritin Levels After Three Months*

N	120
Minimum	990.0
Maximum	2845.00
Mean	1817.3750
Standard Deviation	491.53478

Table 4: *Decrease In Serum Ferritin*

N	120
Minimum	148.00
Maximum	355.00
Mean	254.0917
Standard Deviation	96.07980

Table 5: *Distribution Of Gender*

GENDER	GROUP A		GROUP B		TOTAL	
	N	%	N	%	N	%
MALE	28	46.66	30	50	58	48.3
FEMALE	32	53.34	30	50	62	51.7
TOTAL	**60**	**100%**	**60**	**100%**	**120**	**100%**

Table 6: *Distribution Of Age*

AGE IN GROUP	GROUP A		GROUP B		TOTAL	
	N	%	N	%	N	%
2-8	39	65	36	60	75	62.5
9-15	21	35	24	40	45	37.5
TOTAL	**60**	**100**	**60**	**100**	**120**	**100**

Table 7: *Distribution Of Initial Serm Ferritin*

Ranges of Initial Serum Ferritin	Group A		Group B		Total	
	N	%	N	%	N	%
1000-2500	48	80	46	76.66	94	78.33
2501-3500	12	20	14	23.33	26	21.66
Total	**60**	**100%**	**60**	**100%**	**120**	**100%**

Table 8: *Stratification For Mean Decrease In Ferritin With Respect To Gender*

GENDER	GROUPS	MEAN DECREASE IN FERRITIN		P - VALUE
		N	MEAN±SD	
MALE	A	28	160.6 ± 4.03	0.001
	B	30	349.47 ± 3.46	
FEMALE	A	32	156.66 ± 5.80	0.001
	B	30	349.87 ± 3.28	

Table 9: *Stratification For Mean Decrease In Ferritin With Respect To Age In Groups*

AGE IN GROUPS	AGE IN GROUPS	MEAN DECREASE IN FERRITIN		P - VALUE
		N	MEAN±SD	
2-8	2-8	39	159.26 ± 5.08	0.001
		36	349.89 ± 3.38	
9-15	9-15	21	157.14 ± 5.81	0.001
		24	349.33 ± 3.38	

Table 10: *Stratification For Mean Decrease In Ferritin With Respect To Ranges Of Initial Serum Ferritin*

Ranges Of Initial Serum Ferritin	Regimen Groups	Mean Decrease In Ferritin		P - Value
		N	MEAN±SD	
1000-2500	A	48	158.15 ± 4.92	0.001
	B	46	349.83 ± 3.46	
2501-3500	A	12	160.00 ± 7.06	0.001
	B	14	349.14 ± 3.01	

Table 11: *Comparison Of Mean Decrease In Serum Ferritin Between Both Groups*

Decrease In Serum Ferritin	Regimen Group	Mean Decrease In Serum Ferritin		p value
		N	MEAN± S.D	
	Monotherapy	60	158.52 ± 5.39	0.001
	Combination therapy	60	349.67 ± 3.35	

Deferasirox in heavily iron-overloaded Thalassemia patients. This was a prospective trial that followed 237 patients (162 were between 2 and 16 years of age) for 1 year. A majority of patients completed the trial on 30 mg/kg/day. Deferasirox was effective and resulted in statistically significant decreases in liver iron concentrations and serum Ferritin levels.[9]

Another study on DFX monotherapy is included in the review. The aim of this study was to evaluate the long-term efficacy and tolerability of Deferasirox in Taiwanese patients with transfusion-dependent β-thalassemia who have been treated with Deferasirox for 7 years. Taiwanese patients aged ≥2 years with transfusion-dependent β-thalassemia whose serum Ferritin levels were ≥1000 ng/mL and had started Deferasirox treatment since December 2005 at the National Taiwan University Hospital were enrolled. Sixty patients were recruited for analysis, and 11(18.3 %) patients discontinued Deferasirox during the study. In the 42 patients included in the efficacy analysis, the mean serum Ferritin levels decreased significantly by 2566 ng/mL after 7 years of treatment ($P < 0.001$)[10]

Case reports and series on DFX-DFO combination have shown that this combination is safe and effective. In the clinical realm, in 2011, Voskaridou et al reported the first case of a patient with TDT successfully and safely treated with a combination of DFX and DFO. A 40-year-old male with β-TM, who had been regularly transfused from the age of 2, had been administered in the past iron chelation with DFO, DFP, and DFX monotherapy, without major improvement on his iron overload status. Liver and cardiac magnetic resonance imaging (MRI) revealed severe iron overload, while serum Ferritin was persistently greater than 2500 μg/L. After the patient gave informed consent, he was administered combination therapy of DFX at 30 mg/kg/day for 7 days per week and DFO at 2500 mg/day for 4 days every week and routinely followed up for compliance. Eighteen months later, serum Ferritin was reduced to 680 μg/L, while both liver and cardiac MRI T2* values improved, reflecting lower iron overload. The combination regimen was well tolerated and no adverse events were documented11 Similarly, Lal et al ran a pilot clinical trial to evaluate the safety and efficacy of combined therapy with DFX (20–30 mg/kg/day) and DFO (35–50 mg/kg on 3–7 days/week) in 22 patients with persistent iron overload or organ damage. In the 18 patients who completed the study, SF, LIC, and cardiac iron load significantly decreased proving that simultaneous administration of DFO and DFX rapidly reduced systemic and myo-

cardial iron without increase in toxicity. This study demonstrated a significant improvement in systemic (as measured by LIC) and myocardial iron, also reducing the toxic labile plasma iron species.[12] Grady et al used 34-day metabolic iron balance studies in six patients to evaluate monotherapy with DFX (30 mg/kg/day) versus monotherapy with DFO (40 mg/kg/day) versus combination therapy with DFX (30 mg/kg/day) and DFO (40 mg/kg/day).They determined that supplementing the daily use of DFX with 2–3 days of DFO therapy would place all patients into net negative iron balance.[13]

In this quasi-experimental study, serum Ferritin levels were evaluated in 32 β-thalassemia major patients with severe iron overload before and after receiving combined Deferasirox (30-40 mg/kg/ day) and Desferrioxamine (40-50 mg/kg/day) 2 days a week. The mean of serum Ferritin levels significantly reduced from 4031 ± 1955 to 2416 ± 1653 ng/mL after 12 months of therapy ($P < 0.001$).

No drug toxicity was observed by monitoring serum creatinine, liver enzymes and blood urea nitrogen (BUN) during the study period. This study suggests that combination chelating therapy with Deferasirox and Desferrioxamine can effectively reduce iron burden in β-thalassemia major patients with heavy iron overload without any significant complications.[14]

In 256 consecutive TDT patients, BMD was measured by dual-energy X-ray absorptiometry in lumbar spine and femoral neck regions. Treatment outcome of five iron chelation regimens including Desferrioxamine (DFO), Deferiprone (DFP), Deferasirox (DFX), and combination therapy was evaluated to compare the mean differences of serum Ferritin and BMD indices pre- and post-treatment during 12-months follow-up period. Combination therapy with DFX and DFO had the highest impact on reducing serum Ferritin. [15]

To date, no data are available regarding the effects of once-daily DFX administration on the reversal of heart damage and improvement of survival. Level C Evidence was observed for the effects of twice-daily administration of DFX on SF.[16]

In a study of 20 TM patients who were treated for 1year with DFO (32±4mg/kg/day, 3–4days/ week) plus DFX (20±2mg/kg/day), Cassinerio et al, observed a marked reduction in LIC (6.54 vs. 11.44mg/g dw at baseline) and in the median SF (1346 vs. 2254µg/l at baseline). Moreover, an improvement in cardiac T2* values (26.34±15.85 vs. 19.85±12.06 at baseline) was reported.17There is a need for better chelators while search for optimum chelation regimen combining different chelators continues. [18]

Similarly in our study the mean decrease in serum Ferritin with DFX monotherapy is 158±5 SD while the mean decrease in serum Ferritin with DFX-DFO combination being 349±3 SD. The p value came out to be <0.001 which is highly significant. Our study strongly suggests that simultaneous use of DFO and DFX has the potential to offer higher potency. Combination therapy could be considered as an option for patients who require a swift and predictable reduction in iron overload, or are unable to maintain negative iron balance with a single chelator due to toxicity or high iron-loading rate.

CONCLUSION

From these results it was concluded that DFX-DFO combination therapy is more effective at reducing serum ferritin level than DFX monotherapy because of a greater mean decrease in serum ferritin after three months. This is in accordance with other international studies published.

Ethical Approval: The institutional review board approved the research.

Patients' Consent: Informed consent was taken from every patient's parents

Conflict of Interest: Authors declare no conflict of interest in this study.

Authors' Contribution:

SR: Corresponding author, Research planning, data acquisition and analysis, literature research, manuscript writing and final review.

SY: Literature research, manuscript writing and final

review.
JF: Literature research, manuscript writing and final review.
SG: Drafting of work, data acquisition and statistical analysis
SH: Drafting of work, data acquisition and statistical analysis
SF: Manuscript writing and final review.
NA: Literature research and final review

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COMPARISON OF LIGNOCAINE AND KETAMINE FOR PREVENTION OF PROPOFOL-INDUCED INJECTION PAIN

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How to cite: Shahid A, Butt MM, Taqi M, Farooq U, Khan MA. Comparison of lignocaine and ketamine for prevention of propofol-induced injection pain. JAIMC. 2020; 18(4): 703-9

Abstract

Background: Propofol is very popular anesthetic agent frequently used for intravenous induction in short procedures, day care and ambulatory surgery and for sedation in critical care. Due to its high lipid content causing pain or discomfort on injection remains its greatest disadvantage.

Objective: To compare the lignocaine and ketamine for prevention of propofol induced injection pain in healthy adults undergoing elective surgical procedures under general anaesthesia.

Methodology: This Randomized controlled trial was conducted in Department of Anesthesiology, SIMS/Services Hospital, Lahore from August, 2015 to February, 2016. 300 patients were allocated randomly to one of the two groups (Group L: Propofol-Lignocaine and Group K: Propofol-Ketamine). Group L was given 2 mL 2% lignocaine before propofol and Group K was given 100 µg/kg of ketamine before propofol. Propofol was administered by an anesthesiologist blinded to the Group who immediately asked the patient to rate any sensation of pain during the propofol injection, using a 0–3 scale (verbal rating scale [VRS]) as per operational definition. The highest pain score was recorded. Whole information was recorded using a proforma (attached). Pain prevention was labeled as per operational definition.

Results: The mean age of patients was 40.16±7.76 years 184(61.33%) male and 116(38.76%) female cases. Pain prevention was achieved in 73(48.7%) patients of ketamine group and in 120(80%) patients of Lignocaine group. The frequency of pain prevention was significantly higher in Lignocaine group as compared to Ketamine, p-value < 0.001. When data was stratified for age groups, gender, ASA and Obesity, Pain prevention was significantly high in lignocaine group in case of gender and ASA groups p-value < 0.05. When Verbal rating scale was compared to gender ,VRS 1 and 3 were more in males (84% and 95.4% respectively) and VRS 2 and 4 were more in female (75.6% and 73.8% respectively) p-value < 0.001.

Conclusion: Lignocaine is better than ketamine for prevention of propofol induced injection pain.

Keywords: Injection Pain, propofol, lignocaine, ketamine, prevention

Propofol provides rapid onset, rapid recovery, and a short duration. These properties make it the most popular induction and sedation agent specially for day care and ICU. Adverse effects include pain on injection, involuntary movements, Apnea, Hypotension, and Infection due to egg-phosphatide content.[1-3] Pain on injection remains the most common clinical problem during induction of anesthesia with propofol.[4] Incidence of pain varies between 28% - 90% in adults and 28% - 85% in children.[5] Several methods which has been used to reduce or avoid this pain include dilution of drug, injection through large veins, reducing the speed of injection, warming or cooling the solution and prior or concomitant injection of another drug. Drugs used for this purpose are lignocaine, metoclopramide, thiopental, benzodiazepines, tramadol and other opioids, flurbiprofen, ondansetrone, ephedrine, and

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Submission Date: 10-08-2020
1st Revision Date: 12-09-2020
Acceptance Date: 16-09-2020

ketamine.[6-8] Among these drugs, Lignocaine is most commonly purposed but its failure rate is between 13% - 32%.[8] Ketamine (a phencyclidine derivative) has potent analgesic effects and local anesthetic properties. It is likely that the reduction in propofol injection pain is the result of a peripheral action which attenuated the afferent pain pathways.[8] Ketamine has been used in various studies to reduce the propofol injection pain, either pretreatment or as propofol admixture.[8-10] Results of previous studies done to compare these two drugs are contradictory. Polat et al found in their research that Pretreatment with 2% lidocaine 40 mg, and ketamine 100 µg/kg prevents propofol induced pain 76%, and 58% respectively.[11] Seung-Woo Koo et al found the number of patients perceiving any pain or discomfort and the intensity of pain were less in ketamine Group than in lignocaine Group with a median pain score 0 and 1 respectively.[12] The rationale of this study was to solve this contradiction in literature and to use the outcome of this study in future patients. The objective of the study was to compare the lignocaine and ketamine in terms of prevention of propofol induced injection pain in healthy adults undergoing elective surgical procedures under general anaesthesia.

METHODOLOGY

This Randomized controlled study was conducted in Department of Anesthesiology, SIMS / Services Hospital Lahore, from August 11, 2015 to February 10, 2016. The calculated sample size was of 300 cases (150 in each group) by taking expected percentage of prevention of propofol induced injection pain in both group with 5% level of significance and 80% power of test i.e. 76%[11] in Lignocaine group versus 58%[11] in Ketamine group in healthy adults undergoing elective surgical procedure under GA. Non-probability consecutive sampling technique was used. ASA (American Society of Anesthesiologists) physical status I & II patients of both genders, age between 12-50 years undergoing elective surgical procedures were included in the study. Patients with diagnosed Diabetes mellitus (BSF>126 mg/dl), Ischemic heart disease, Acute confusional state and/or dementia were excluded from the study. After approval by local research and ethical committee and informed written consent, 300 patients fulfilling the criteria were enrolled in this study from in-patient department. Patients were allocated randomly using random number table to one of the two groups comprising 150 patients each. (Group L: Propofol + Lignocaine and Group K: Propofol + Ketamine). All patients were kept fasting for at least 6 hours before induction of anesthesia. A 20-gauge intravenous cannula was inserted into a vein of the dorsum or wrist of the left hand, approximately 120 min before the induction of anesthesia and slow infusion of Ringer's lactate solution was commenced. All patients were monitored with ECG, Heart rate, Noninvasive blood pressure and Oxygen saturation (SpO_2) in operating room. Group L was given 2 mL 2% lignocaine as a test solution before propofol and Group K was given 100 µg/kg of ketamine as a test solution before propofol. The drugs were kept and prepared at room temperature and used within 10 min of preparation. The syringes of test solution were prepared by a doctor not involved in induction of anesthesia. Induction was done by a doctor blinded to the nature of the solution. Immediately after the administration of the test solution, 1% solution of propofol 2.5 mg/kg was injected slowly over 30 seconds through a three-way tap directly connected to the IV catheter, with the IV infusion line closed, after which crystalloid was administered at maximal gravity flow. Before the administration of propofol, each patient was asked by an anesthesiologist, blinded to the type of test solution; to immediately rate any sensation of pain during the propofol injection, using a 0–3 scale (verbal rating scale [VRS]) where 0 is No pain: No response to questioning about pain, 1 is Mild pain: Pain reported only in response to questioning without any behavioral signs, 2 is Moderate pain: Pain reported in response to questioning and accompanied by a behavioral sign or pain reported sponta-

neously without questioning and 3 is Severe pain: Strong vocal response or response accompanied by facial grimacing, arm withdrawal or tears. The highest pain score was recorded. VRS score ≤ 1 was labeled as pain prevention. Whole information was recorded using a proforma. Anesthesia was continued after induction as per procedure requirements. All the collected information was entered and analyzed using SPSS version 23.0. The age of the patients was presented by calculating mean and standard deviation. Gender and pain prevention was presented by calculating frequency and percentage and was compared using chi square test. Data was stratified for age, gender, ASA status and BMI to deal with effect modifiers. Post stratification Chi-square test was applied. P ≤ 0.05 was considered as significant.

RESULTS

Mean age of patients was 40.16±7.76 years with age range of 36 years (minimum 14 maximum 50). 82(27.3%) Patients were aged between 12-35 years and 218(72.7%) were > 35 years old. 184(61.3 %) were male and 116(38.7%) were female. 143 (47.7%) were ASA-I and 157(52.3%) were ASA-II classification. 45(15%) were obese and 225(85%) were non-obese. Pain prevention was achieved in 193(64.3%) and not achieved in 107(35.7%). Pain prevention was achieved in 73(48.7%) patients of ketamine group and in 120(80%) patients of Lignocaine group. The frequency of pain prevention was significantly higher in Lignocaine group as compared to Ketamine, p-value =0.00 (Pearson Chi-square = 32.09). Table-1

When data was stratified for age groups, gender, ASA and Obesity, Pain prevention was significantly high in lignocaine group in case of gender (p-value = 0.002) and ASA groups (p-value = 0.009) Table-2

When Verbal rating scale was compared to gender, VRS 1 and 3 were more in males (84% and 95.4% respectively) and VRS 2 and 4 were more in female (75.6% and 73.8% respectively) p-value = 0.00. Figure-1

Table 1: *Comparison of Pain Prevention in Both Study Groups*

		Study groups		Total
		Ketamine	Lignocaine	
Pain prevention	Yes	73 48.7%	120 80.0%	193 64.3%
	No	77 51.3%	30 20.0%	107 35.7%
Total		150 100.0%	150 100.0%	300 100.0%
Chi-square = 32.09			p-value = 0.00	

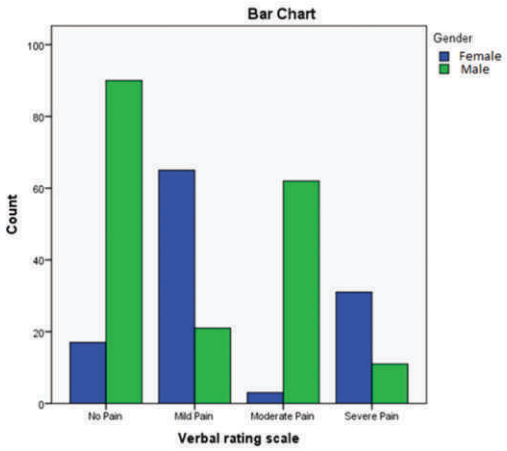

Figure-1: *Comparison of Verbal rating scale and Gender*

Table 2: *Comparison of Pain Prevention in Both Study Groups with Respect to Age Groups, Gender, ASA and Obesity.*

Pain Prevention		Age groups (years) n & %		Gender n & %		ASA n & %		Obesity n & %	
		12-35	> 35	Male	Female	ASA I	ASA II	Yes	No
Ketamine	Yes	23 31.5%	50 68.5%	48 65.8%	25 34.2%	35 47.9%	38 52.1%	9 72.9%	64 27.1%
	No	15 19.5%	62 80.5%	48 62.3%	29 37.7%	41 53.2%	36 46.8%	12 77.6%	65 22.4%
	p-value	0.091		0.663		0.516		0.566	
Lignocaine	Yes	38 42.2%	82 57.8%	63 52.5%	57 47.5%	60 50%	60 50%	19 73.3%	101 26.7%
	No	6 29.7%	24 70.3%	25 83.3%	05 16.7%	7 23.3%	23 76.7%	5 75.9%	25 24.1%
	p-value	0.209		**0.002**		**0.009**		0.911	

DISCUSSION

Propofol is very popular intravenous induction agent, especially for brief procedures, day care surgery or when using a laryngeal mask airway. It is also used for sedation in critical care and maintenance of anesthesia. It has been found to be very helpful in preventing PONV and for treating pruritis. Its frequently used for tracheal intubation without neuromuscular blocking drugs especially in pediatric population.[13] Among its very few and manageable adverse effects pain on injection remains the most common problem. Often injection pain just before going blank remains the only painful memory of patient. Incidence of pain varies from 28% to 90% in adults and it may be severe in intensity.[14,15] Pain on propofol injection (POPI) has been reported in a survey, to be the seventh most important problem in current anesthesia practice.[16] Multiple studies have been published for multiple drugs for POPI also including two systematic reviews in 2000 and 2011. A quantitative systematic review in 2000 concluded that "IV lignocaine (0.5 mg/kg) should be given with a rubber tourniquet on the forearm, 30–120 s before the injection of propofol to prevent pain in approximately 60% of the patients".[17] In young patients, incidence of pain varies from 28% to 85%.[18,19] The younger the patient, the higher is the incidence and severity of pain.[20] This may be attributed to the smaller veins in children. Gender association for this pain has not been reported in previous literature. When compared to other intravenous anaesthetic agents Propofol has highest incidence of pain on injection. The incidence of pain on induction with thiopentone is about 7%,[15] whereas with methohexitone it varies between 12% and 64%.[21,22]

While the systematic review in 2011 recommends two efficacious interventions to reduce POPI, namely, injection in the antecubital vein or pretreatment with lignocaine in conjunction with venous occlusion when hand veins are used.[23] A third practical intervention suggested in this review was pretreatment with either lignocaine or ketamine and use of medium chain triglyceride /long chain triglyceride MCT/LCT propofol. The authors also suggest the use of a small dose of opioids to halve the risk of POPI. However, none of the reviews indicated elimination of POPI in 100% of patients using only one intervention.[23] Use of lignocaine with propofol is almost a norm since many years and hence perhaps maximum numbers of clinical trials were with lignocaine either alone or in combination with other drugs. The most effective dose for lignocaine with venous occlusion was 60 mg in one study, whereas 40 mg is the most commonly used dose when premixed with 200 mg of propofol.[24] Venous occlusion with lignocaine is an effective method in relieving propofol-induced pain, Massad et al. recommend 60 s occlusion time in their report while another study did not find difference when the duration of venous occlusion was 15, 30, or 60 s.[25,26] Pretreatment with lignocaine for propofol infusion did not show any benefit in pediatric group of patients in one study.[27] Bano et al believed that using a rubber tourniquet and pretreating with ketamine 0.5 mg/kg 1 minute before lipid emulsion propofol administration reduced pain on injection without causing hemodynamic changes.[28] Fujii and Nakayama found that the pretreatment of a mixture of Lignocaine and ketamine significantly reduced pain on injection from lipid emulsion propofol more than pretreating with Lignocaine alone.[29] Most studies used ketamine as pretreatment while some other mixed it with propofol or applied venous occlusion after pretreatment or used it in conjunction with lignocaine. The reported effective dose varied from 0.1 mg/kg to 1 mg/kg. In two studies a small dose 0.1 mg/kg was very effective while two other studies quoted a higher dose of 0.3mg/kg to be effective.[8,30-32]

Currently, a study is done to compare the efficacy of ketamine or lidocaine on relieving the pain during the injection of a new formulation of propofol containing a mixture of medium-chain triglyceride/ long-chain triglyceride (MCT/LCT). This study including patients, ASA I and II, was conducted as double-blinded and placebo controlled randomized trial on 75 subjects aged 18-65 years scheduled for

elective surgical operation under general anesthesia. Propofol MCT/LCT 1% (2.5 mg/kg) plus 40 mg lidocaine, 10 mg ketamine, and normal saline were administered in groups I, II, and III, respectively. Scores of pain intensity and arm withdrawal were assessed during the propofol injection. The study result showed that there was no significant difference among the study groups with regard to the ratios of no and mild pain ($p>0.05$); however, the ratios of moderate pain of the lidocaine and ketamine groups were significantly lower than that of the normal saline group (2% vs. 28%; $p<0.05$). Hence, Propofol MCT/LCT as the new formation of propofol generally cause less pain during injection and for reducing its pain, ketamine 10 mg has similar effects with lidocaine 40 mg.[33] In current study the primary outcome of prevention of pain, so we found that in group-K prevention of pain was achieved in 73(48.7%) cases while in group-L 120(80%) did not have prevention of pain. The frequency of pain prevention was significantly higher in group-L when compared to group-K, p-value < 0.001. Polat et al performed a randomized, double-blind, prospective trial to compare various drugs with saline, lidocaine and together at the same time. In this study a total of 250 patients (ASA I-II) undergoing elective surgery with general anesthesia were randomly allocated into five groups. The study result showed that pretreatment with % 2 lidocaine 40 mg and ketamine 100 microg/kg yields propofol induced pain 76% and 58% respectively. Pretreatment with lidocaine significantly reduced the incidence and severity of propofol induced pain. They concluded that lidocaine were most effective treatments in attenuating pain during intravenous injection of propofol compared to pretreatment with ketamine.[34] These findings confirmed the findings of our study. Similarly one more study reported that pretreatment using lidocaine (lignocaine) in conjunction with venous occlusion was similarly effective (0.29, 0.22 to 0.38). Other effective interventions were a lidocaine-propofol admixture (0.40, 0.33 to 0.48); pretreatment with lidocaine (0.47, 0.40 to 0.56), opioids (0.49, 0.41 to 0.59), ketamine (0.52, 0.46 to 0.57), or non-steroidal anti-inflammatory drugs (0.67, 0.49 to 0.91); and propofol emulsions containing medium and long chain triglycerides (0.75, 0.67 to 0.84).[23] Another study was done on 130 patients who were undergoing elective surgery under general anesthesia were enrolled. The patients received IV lidocaine 40 mg plus ketamine 25 mg (Group LK, n = 43), lidocaine 40 mg (Group L, n = 42), or ketamine 25 mg (Group K, n = 45). The pain score was assessed by a 4-point verbal rating scale (VRS) at 10 seconds after injection of micro emulsion propofol 30 mg and during the injection of the remaining total dose. The study result explored that the incidence and severity of pain was significantly lower in Group LK than Group L or Group K at 10 seconds after the injection of micro emulsion propofol 30 mg ($P < 0.05$). And the incidence and severity of pain was significantly lower in Group LK and Group K than Group L during the injection of the remaining total dose ($P < 0.05$). So, this study concluded that pretreatment with IV lidocaine 40 mg plus ketamine 25 mg with a rubber tourniquet on the forearm 1 min before the injection of micro emulsion propofol is more effective than lidocaine 40 mg or ketamine 25 mg alone in preventing pain from the injection of micro emulsion propofol.[35] So, Lignocaine can prevent pain on propofol injection. Lignocaine is not only effective as a local anesthetic effects on the vein but also as a stabilizer for the kinin cascade.[36] King et al mixed 5, 10, and 20 mg of Lignocaine with lipid emulsion propofol and found that a greater dose reduces pain on injection.[37] Jonson et al stated that Lignocaine 40 mg is more effective than 20 mg in reducing pain on injection from lipid emulsion propofol.[38]

CONCLUSION

Lignocaine is superior to ketamine for prevention of propofol induced injection pain, when used as pretreatment.

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FREQUENCY OF POSTPARTUM DEPRESSION AMONG OBESE WOMEN

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How to cite: Malik KK, Rasheed M, Kanwal S, Sohail R. Frequency of postpartum depression among obese women. JAIMC. 2020; 18(4): 710-14.

Abstract

Background: Obesity is on rise in Pakistan especially in women. It predisposes women to a lot of health risks with or without pregnancy. Pregnancy is already a state which puts women's health to a lot of challenges in all trimesters and post natal period. Obesity adds another challenge in this stressful condition. Mental health problems are researched less than physical complications associated with obesity in literature; this study aims to estimate frequency of postpartum depression in obese mothers.

Objectives: The objective of this study was to determine the frequency of postpartum depression among obese mothers presenting in a tertiary care hospital.

Methodology: The descriptive observational study was carried out at Services Hospital Lahore, Department of Obstetrics & gynaecology Unit 1 from November 2018 to November 2019. Total 184 women fulfilling inclusion criteria were enrolled with their consent, and post partum depression was assessed by Edinburgh postnatal scale, at six and twelve weeks postpartum.

Results: 24% mothers in the obese postpartum group were diagnosed to be suffering from postnatal depression, which is a significantly higher frequency as compared to background risk in the literature. **Conclusion:** Obstetrician must be vigilant in case of obese mothers not only for physical complications but mental health problems also especially in the postpartum period.

Key words: Obesity. Postpartum depression, Body Mass Index (BMI)

Obesity is an alarming problem in most of the parts of the world and estimated to be around 30%. Initially it was considered the health problem of the developed world but now it is realized world-wide that unhealthy weight gain is a global issue. In 2013, a study estimated that 20% of women are obese in USA when they get pregnant.[1] According to data, obesity is on rise and 27% and 41% women in the reproductive age are overweight or obese in 2015 and 2016 respectively in USA. At conception, 21 percent of women have a BMI of 30kg/m^2 or more and 9 percent have a BMI of 35 kg/m^2 or more.[2]

There is a rise in risk of complications which can be attributed to obesity and over weight in pregnancy as pre- eclampsia, gestational diabetes, postpartum hemorrhage, spontaneous and medically indicated preterm birth, risk of congenital fetal malformation, increased rate of induction, elective cesarean section, cesarean delivery, shoulder dystocia, pelvic infection, wound infection or complication, large for gestational age fetus and fetal macrosomia, stillbirth and deep venous thrombosis.[3] The effects of excess weight in pregnancy especially the physical effects has been studied extensively especially in the high income countries, but its impact on maternal mental health needs attention. Now Obesity is not only the health issue in high income countries rather it is affecting the low income and middle income countries immensely. A list of the world's "fattest countries" was published on Forbes in 2007 and Pakistan was at number 165 (out of 194

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Submission Date: 16-08-2020
1st Revision Date: 23-09-2020
Acceptance Date: 30-09-2020

countries) with regards to its overweight population, with 22.2% of population over the age of 15 above the threshold of overweight or obesity. In 2016, WHO estimated overweight population in Pakistan to be around 28% with 4.8% obese. Now Pakistan stands as the 9th most obese nation in the globe and excess weight is affecting all age groups, and children and females are affected more as compared to men. It is perceived that the prevalence will become double in future as a result of high carbohydrate intake and less exercise or physical activity along with other environmental factors. In 2013 WHO stated that the rate of excess weight was 28% for men and 38 % for women, which is alarming and depicting more weight problems in women. In urban areas 56% of men and 67% of women are obese which is higher as compared to rural areas. Even in our youth obesity is growing at a fast pace. 2013 statistics reveal that obesity in young individuals was 10%, and it is a huge figure (4).

As obesity is increasing in women and younger age group so it is definitely affecting pregnancy and child birth. Literature shows that obesity and overweight not only affects maternal and neonatal physical but also mental health. In antenatal period anxiety disorders and in postpartum period the incidence of postpartum depression and mood disorders has been linked to unhealthy weight. Postpartum period or peurperium brings a lot of physical and psychological changes in a mother's life and these changes make it a stressful time for the family. Postnatal depression usually presents around six weeks postpartum and even has been reported to exist around even one year postpartum. It is mainly characterized by emotional instability, tearfulness, despondency, loss of appetite, feelings of guilt, suicidal ideas and tendencies, sleep deprivation as well as emotions of low capability and inability to cope with the infant, poor concentration and memory, fatigue, and irritability. Probably body image perception can be linked to it.[5] Hence to assess the burden of the mental disorders in this group this observational study was carried. This study aims to estimate frequency of post partum depression among obese mothers. The objective of this study was to determine the frequncy of postpartum depression among obese mothers presenting in a tertiary care hospital.

Department of Obstetrics and Gynaecology Unit 1 Services Hospital Lahore for a period of one year.

METHODOLOGY

The study was carried out in a tertiary care public sector hospital for one year from November 2018 to November 2019. Sample size was calculated with 95% confidence interval with 5 % margin of error. Total 200 women were included in the study from labour room and postnatal ward. It was an observational, descriptive study and included those women whose Body Mass Index- BMI was more than 30kg/m^2, and gave singleton birth at term. Sampling was by done by non probability purposive sampling. Obesity was defined as class 1with BMI 30-34.9 kg/m^2 , class II 35-39.9, class III > 40 kg/m^2 BMI. The women with history of depression, having all female issues (daughters), multiple gestation and fetal or neonatal death or anomaly were excluded from the study. These women fulfilling inclusion or eligibility criteria were followed at six and twelve weeks postpartum and on their visits they were asked to fill or answer the Edinburgh Postnatal Depression Scale (EPDS). The Edinburgh Postnatal Depression Scale (EPDS), is a ten-item self-report questionnaire, was used to measure the severity of postnatal depression. Each question is scored 0–3 (range 0–30), depending on how the women felt in the past 7 days and answering or completion of the full EPDS takes around 5 minutes. The cut-off score was taken as thirteen and scores on the EPDS at or above 13 were considered as postnatal depression. The EPDS has been shown to have overall reliability (Cronbach's alpha) of 0.79, sensitivity of 86%, and a specificity of 78% at score of 13 taken as cut off. Question ten of the EPDS specifically asked for suicidal ideation. Those who scored 13 or more than 13/30 were labeled suffering from postpartum

depression which was the primary outcome. The patients who suffered in between these visits with mental disorder symptoms and were diagnosed by consultant psychiatrist as suffering from postpartum depression were also considered as cases. Maternal demographic data, medical complications, intrapartum and delivery events (postpartum hemorrhage, prolonged second stage), postpartum wound infection, deep venous thrombosis along with neonatal death or development of any other physical complication in the post natal period were recorded on a Performa. Patients who did not come for follow up were contacted on phone and asked questions. Data was collected and analyzed on SPSS 20 and frequency of postpartum depression was calculated in obese postpartum women as a primary outcome.

RESULTS

Total 184 patients were included in the study who gave consent and fulfilled the inclusion criteria (singleton birth and BMI > 30 kg/m^2). Initially 200 women were included but thirteen were lost to follow up and even could not be contacted on phone and three had neonatal deaths and were excluded from the study. Mean age was 25.6+/- 5.1 year. The range of score on EPDS was maximum 19 and minimum zero. Mean score was 6.38.+/-5.81. Out of 184 mothers -114 women(62%) were in class I, 65 women(35%) were in class II and 5 (3%) were in Class III on the basis of WHO definitions. On the basis of EPDs score 45 patients were labeled as having postpartum depression and this translates into 24% mothers who were obese and developed postnatal depression. Out of these 12% had suicidal tendencies depicted by question no 10 in EPDS but no one had severe suicidal tendency or attempt. Out of 45 women fifteen that is 13% were para one. Moreover, in this group of 45 mothers, 18 women had caesarean delivery which translates into 40% and annual rate of caesarean section rate of the unit is around 38%. 30% of the depressed mothers had education at least till 5th class and 15% more than matric. One woman was a widow and 2 had been divorced. In the table no.1 different characteristics and features, noted during study are given below. Tests of significances/ analytical tests were applied on these characteristics in these groups. Both groups were obese and one group comprises of women who suffered from post natal depression n= 45 and the other group who remained mentally healthy n=139. Analytical tests show that these characteristics though had different frequencies but were not statistically significant.

Table 1: *Characteristics of Mothers with and without Depression*

	Characteristics	Women with score 13 or more on EPDS n=45	Women with score less than 13 on EPDS n=139	P value
1.	Education			
	Less than primary	28.8% (n=13)	32.3%	
	Primary	31% (n=14)	30%	0.06
	Secondary	24.4% (n= 11)	28.5%	
	More than secondary	15.5% (n=7)	19.1%	
2.	Primipara	13.3% (n=6)	16%	0.17
3.	Multi para	86.6% (n=39)	84%	0.09
4.	Vaginal delivery	60% (n=27)	62.4%	0.10
5.	Caesarean delivery	40% (n=18)	37.61%	0.11
6.	Single (divorce/widow)	6.6% (n=3)	5%	0.06
7.	Wound infection	6.6% (n=3)	4.5%	0.05

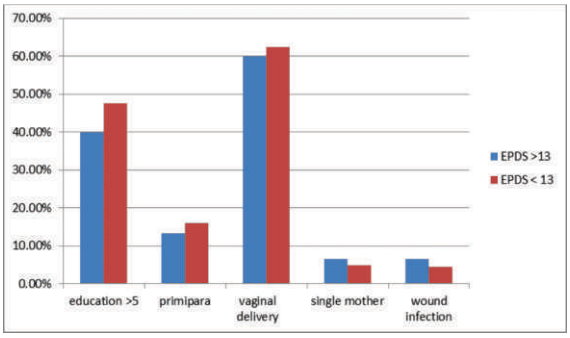

Figure No.1: *Graph Representing Characteristic in two groups of obese mothers with and without depression*

Figure No.2 *Frequency of Postpartum Depression in Obese Mothers: 24%*

DISCUSSION

Women of reproductive age group are being affected worldwide by obesity and there is an increasing trend seen in this already high prevalence. Moreover the women in low as well as in middle income countries are facing a double edge sword of obesity and under nutrition.[6] These nutritional and dietary imbalances put pregnant women with unhealthy weight and their fetuses in a situation where they face a lot of physical and mental issues and complications.

The institute of Medicine (IOM) has published maternal weight gain guidelines based on pre pregnancy BMI. For overweight and obese pregnant women, the IOM recommends a range of total weight gain of 15-25 and 10-20 lb, respectively, and recommendation for rates of weight gain in the second trimester is: 0.6ib/week and in third trimester: around 0.5 lb/week. Weight loss during pregnancy is not recommended.[7,8] In our study the prevalence of postpartum depression is quite high as compared to background risk of postpartum depression in women. This may be explained by negative body image perceived by women due to excessive fat deposition. This negative wave propels them towards depression and decreases their interest in life and neonate.[5] In another study, after applying a cox proportional hazard model to control for maternal age, preterm labor, maternal diabetes, hypertensive disorders of pregnancy, and birthweight as confounding factors even then, maternal obesity was found to be independently associated with long-term neuropsychiatric morbidity of the offspring. Hence it not only affects the mother but the child also.[9] In a recent study done by Adkins LD. and others the results show that pre pregnancy obesity is clearly linked to a rise in postpartum depression though gestational weight gain especially in Class III obese mothers was not associated with depression.[10] In our study as class III obese patients were very few so interpretation of results only in them is not possible, however further studies can be done and mental disorders can be evaluated in all groups separately with adequate sample size. Moreover qualitative studies may give an insight in depth about reasons of differences seen in these groups.[11,12] In a study done in India prevalence of post natal depression was around 39% in women with abnormal waist to hip ratio, so in this study along with other parameters as BMI, anthropometric parameters were also taken in account.[13] The correlation between depression and obesity has been shown to be moving in both directions, and depression can lead to significant weight gain and elevated BMI and vice versa and regression analysis in this study revealed that shows that even postnatal BMI has a role in risk assessment of postnatal depression, as does pre natal height, weight, and total weight gain.[14] Postnatal depression prevalence is not exactly known in Pakistani women but around the world as literature shows it has been around 11% and in countries around us has been reported to be around 10-20%.[15,16] In our study the prevalence is 24%, which is quite high.

Though, study has limitations as there is no control group, lack of consideration to: presence of family support, gender base violence and financial status, even then the prevalence is high as compared to background risk in the literature. Violence was not asked or assessed in data collection as this is a sensitive issue in our society and women do not easily disclose about verbal or physical abuse. This may have led to wrong information and acted to affect data interpretation. This requires more awareness in society and empowerment of women and then we can rely on data collected on gender base violence. As in different studies violence has been implicated as a major factor associated with ante partum and post partum depression so this can be considered limitation of our study.[17]

Moreover in this study overweight women were not included to decrease the bias as pre pregnancy weight is usually not known especially in un booked or delayed booked women and gestational weight gain cannot be quantified and can affect the results. The woman may be not overweight at start of their pregnancy and later on fall in this group while

there is less chance for a woman with normal BMI to be obese at delivery.

Evaluation of these results alarms obstetrician to consider obese women as a more vulnerable group for mental health issues in pregnancy and postpartum period.

CONCLUSION

Important obstetric health problems include Overweight and obesity. Obesity is not only associated with numerous maternal and neonatal physical complications but mental health problems also. The prevalence of postnatal or post partum depression is more in obese population. To prevent adverse maternal and neonatal outcomes management should be done in all stages of the pregnancy, from pre conception time through the antenatal, intra partum and postpartum period. Obstetrician should be more careful in such group of women as unhealthy weight can predispose to mental illness. This will help in early referrals and effective management in these women and hence grave consequences can be minimized.

Conflict of interest: None

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CHANGE IN HEMOGLOBIN CONCENTRATION WITH PREOPERATIVE VERSUS POSTOPERATIVE MISOPROSTOL IN ELECTIVE CESAREAN SECTION

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How to cite: Farrukh R, Kanwal S, Afridi T, Raana G, Naeem R. Change in hemoglobin concentration with preoperative versus postoperative misoprostol in elective cesarean section. JAIMC. 2020; 18(4): 715-20.

Abstract

Objective: The objective of the study was to find change in hemoglobin concentration in primigravida undergoing elective cesarean section with preoperative versus postoperative misoprostol. Upto 1000 ml of blood loss during c section is acceptable. Greaterloss is considered as postpartum hemorrhage. It was a randomized controlled trial. Study was conducted at department of Obstetrics and Gynecology Unit 3, Sir Ganga ram hospital Lahore from 14th May 2018 to 13th November 2018, a period of 6 months.

Methodology: This study included 64 pregnant women between 18-35 years of age, undergoing cesarean section at 38 to 42 weeks of gestation. These patients were randomly distributed into two treatment groups. Women in group A received preoperative misoprostol while those in group B were given postoperative misoprostol. Hemoglobin was estimated before and after 24 hours ofthe surgery and mean changein hemoglobin was measured and studied between the groups. Written informed consent was taken from each patient.

Result: The mean age of women was 28.0+ 5.3 years. Mean duration of gestation was 39.6+ 1.4 weeks while the mean BMI was 26.5+3.6 Kg/m2.Hemoglobin level in postoperative period was significantly lower in both study groups compared to the preoperative hemoglobin level. preoperative misoprostol (10.4 +1.4 vs 11.6+1.3g/dl; p -value<0.001)and postoperative misoprostol(9.9+1.3 vs 11.6+1.4 g/dl; p-value< 0.001). Mean change in hemoglobin was significantly less in patients receiving preoperative misoprostol in comparison to those receiving postoperative misoprostol (1.2+0.4 vs 1.8+0.4 g/dl; p-value <0.001). Same difference in mean change in hemoglobin was observed between the groups across various subgroups based on patients age, gestational age and BMI.

Conclusion: Pre-operative misoprostol resulted in significantly lesser mean change in hemoglobin than post-operative misoprostol in patients undergoing cesarean section .

Key Words: Cesarean Section, Obstetric blood Loss, Pre-operative Misoprostol, Post-operative Misoprostol

History of cesarean section on alive women dates back to 16th and 17th century but it was not supported by higher authorities of that era .with the passage of time nearly in mid-19th century it was considered as a much safer procedure than before mainly due to improved anesthetic techniques as well as improved aseptic measures and technique of surgery leading to reduced maternal mortality.[1]

Crude birth rate of Pakistan was reported as 30/1000 people.[2] The frequency of caesarean section in Pakistan is 31.26% leading toincreased cost of healthcare.[3]

There is a long list of expected morbidities with cesarean section, for example torrential hemorrhage,

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Submission Date: 10-08-2020
1st Revision Date: 15-09-2020
Acceptance Date: 22-09-2020

extension of surgical incision towards broad ligament or cervix, bladder or bowel injury and obstetric hysterectomy.[4-6]

Obstetrical hemorrhage is one of the major causes of severe maternal morbidity and mortality in the low per capita income countries. There are various pharmacologic agents used to prevent it like oxytocin, prostaglandin F2α. But due to their undesirable effects like nausea, vomiting, cardiovascular and respiratory effects, their use is not liked by anesthetist. On the other hand incidence of anemia in pregnant women is very high, 50-80 % in developingand underdeveloped countries[5]5, nutritional deficiency being a leading cause. This predisposes them to increased risk of intra partum and post-partumblood loss. For the last couple of decades misoprostol has gained popularity due to lesser side effects and greater effectiveness for the treatment and prevention of postpartum hemorrhage.

Misoprostol, prostaglandin El analogue is used for multiple pathologies in obstetrics and gynecology like miscarriages, management of prolonged pregnancy, priming of cervix preoperatively and prevention and treatment of excessive bleeding after childbirth. That is why WHO essential medicine list contains this drug.[7] Misoprostol effects myometrium by increasing its sensitivity to prostaglandin which causes uterine muscles to contract tonically thus minimizing blood loss from venous sinuses.[8]

According to one study it was concluded that misoprostol used preoperatively led to reduction of blood loss during surgery and in postoperative period,as there was significantly lower mean change in hemoglobin concentration (10.4±0.67 vs. 10.8± 0.45 g/dl; p<0.001).[9] In another study, there was more difference in preoperative and postoperative hemoglobin when misoprostol was given postoperatively rectally (1.9±0.45 g/dl) as compared to group in which it was given preoperatively(1.2±0.67 g/dl; p=0.032).[10]

Misoprostol is used mostly post-delivery or post C-section to reduce the post-partum blood loss. If given preoperatively, misoprostol leads to increase uterine muscles tone leading to decrease in the amount of blood loss during surgery and in postoperative period. The observed adverse effects of drug are not related to the time of administration of drug. However, the available local research is limited regarding this topic. The aim of the current research is to conduct this trial in local population. If the result of study shows significantly lower mean change in hemoglobin with preoperative misoprostol, it will enable us in better management of future patients and can help in reducing the mean blood loss which can lead to decreased need of blood transfusions intra and postoperatively, leading to fewer incidences of transfusion related complications.

METHODOLOGY

This study was carried out at obstetric and gynae unit 3, Sir Ganga Ram hospital Lahore, atertiary care hospital from May to November 2018, a period of six months. It was arandomized controlled trial in which 64 women scheduled for elective cesarean section were recruited. Written informed consent was taken and study conducted after approval from ethical committee.

64 pregnant women who met eligibility criteria were included in study and they were allocated one of the two groups by non-probabilityconsecutive sampling technique. Group A in which misoprostol was given preoperatively while in group B misoprostol was given postoperatively.

Inclusion Criteria: Term (38 to 42 weeks gestation), primigravida with uncomplicated singleton pregnancy, scheduled for elective cesarean section.

Exclusion Criteria: Patients with diagnosed hypertension, diabetes, multiple pregnancy, placenta previa, abnormal laboratory results and preoperative hemoglobin less than 10 g/dl were excluded from the study.

Mean Change in Haemoglobin Concentration: 5 ml of venous blood was sampled 2 hours before C section and 24 hours after C section and was sent for hemoglobin estimation. It was measured as g per dl and has been presented as change.

Change = Pre-Operative haemoglobin - Post Operative haemoglobin

The postulated hypothesis was "there is a difference in the mean change in haemoglobin concen-tration with preoperative versus post-operative misoprostol in primigravida undergoing elective caesarean section".

After getting approval from ethical review committee of the hospital, 64 women who presented in the outpatient department of, Sir Ganga Ram Hospital, Lahore and who fulfilled the above criteria were counseled and explained the details of the study. After written informed consent, detailed history was taken from each patient. These patients were then randomly allocated into following two groups using lottery method.

- Group A: Misoprostol preoperatively
- Group-B: Misoprostol postoperatively

Hemoglobin concentrations was tested 2 hours before operation and 24 hours after operation. Patients belonging to group A were given misoprostol (400µg) rectally 5 minutes before the skin incision. Patients belonging to group B received misoprostol (400µg) rectally 5 minutes after the skin was closed. All the cesarean sections were carried out under spinal anesthesia and uterus was closed with Vicryl 1 suture ,using continuous non-locking suturing technique in two layers, peritoneum was left un-sutured, rectus sheath was repaired with Vicryl 1 and the skin was approximated by simple interrupted suturing technique with Prolene 2/0. The preoperative and post-operative hemoglobin levels were entered into the attached proforma along with demographic details of the patient. All patients were operated upon by same surgical team. Allth laboratory tests were done at hospital laboratory for standardization. Difference in preoperative and postoperative hemoglobin was calculated.

Whole data was entered and analyzed on spss version 20.

RESULTS

The age of the patients ranged from 18 years to 35 years with a mean of 28.0±5.3 years. Gestational age of the patients ranged from 38 weeks to 42 weeks with a mean of 39.6±1.4 weeks while the BMI ranged from 20.5 Kg/m^2 to 33.0 Kg/m^2 with a mean of 26.5±3.6 Kg/m2 as shown in Table 1.

Both the study groups were comparable in terms of mean age (p-value=1.000), mean gestational age (p-value=0.796), mean BMI (p-value = 0.789) and mean pre-operative hemoglobin. Distribution of various subgroups based on patient's age (p-value=0.616), gestational age (p-value=0.802), BMI (p-value=0.877) and preoperative hemoglobin (p-value 0.9710 are shown in Table 2.

Post-operatively hemoglobin was lower in both the study groups; pre-operative misoprostol (10.4± 1.4 vs. 11.6±1.3 g/dl; p-value<0.001) and post-operative misoprostol (9.9±1.3 vs. 11.6±1.4 g/dl; p-value <0.001) and the difference was statistically significant (paired sample t-test). Although the mean post-operative hemoglobin was higher in the pre-operative misoprostol group as compared to post-operative misoprostol group (10.4±1.4 vs. 9.9±1.3; p-value=0.122) yet the difference was statistically insignificant. However, the mean change in hemoglobin was significantly lower in patients receiving pre-operative misoprostol as compared to those receiving post-operative misoprostol (1.2±0.4 vs. 1.8±0.4 g/dl; p-value<0.001) as shown in Table 3. Similar difference in mean change in hemoglobin was observed between the groups across various subgroups based on patient's age, gestational age and BMI as shown in Table .4.

DISCUSSION

Massive hemorrhage is the nightmare inobstetrics that can happen to any woman at the time of parturition. If it is not managed timely and effectively it can cost the life of the woman).[11] Nearly one fourth of mothers die due to obstetric hemorrhage. It accounts for nearly 50% maternal deaths in developing countries.[11,12] Caesarean section is the most commonly performed operation in obstetrics and associated

with complications and risk of mortality. Blood loss is relatively more during surgery so it is important to reduce the extent of bleeding during and after c section.[13]

Misoprostol is asynthetic analogue of prostaglandin E1 and it is found to be effective for binding to prostanoid receptor in pregnant uterine myometrium(14)[14] so it is used to treat and prevent postpartum hemorrhage. Routes of administration are varied like oral, sublingual, rectal and vaginal.[15] Misoprostolis convenient to use because of its low cost, stability at room temperature and varied routes of administration.

Table 1: *Baseline Characteristics of Study Sample*

Characteristics	Participants n=64
Age (years)	28.0±5.3
• 18-26 years	34 (53.1%)
• 27-35 years	30 (46.9%)
Gestational Age(weeks)	39.6±1.4
• 38-39 weeks	33 (51.6%)
• 40-42 weeks	31 (48.4%)
BMI (Kg/m^2)	26.5±3.6
• 20-25 Kg/m^2	21 (32.8%)
• 25-30 Kg/m^2	32 (50.0%)
• 30-35 Kg/m^2	11 (17.2%)

Table 2: *Baseline Characteristics of Study Groups n=64*

Characteristics	Pre-Operative Misoprostol n=32	Post-Operative Misoprostol n=32	P-value
Age (years)	28.0±5.5	28.0±5.1	1.000
• 18-26 years	16 (50.0%)	18 (56.2%)	0.616
• 27-35 years	16 (50.0%)	14 (43.8%)	
Gestational Age (weeks)	39.6±1.4	39.7±1.5	0.796
• 38-39 weeks	17 (53.1%)	16 (50.0%)	0.802
• 40-42 weeks	15 (46.9%)	16 (50.0%)	
BMI (Kg/m^2)	26.4±3.4	26.6±3.9	0.789
• 20-25 Kg/m^2	10 (31.3%)	11 (34.4%)	
• 25-30 Kg/m^2	17 (53.1%)	15 (46.9%)	0.877
• 30-35 Kg/m^2	5 (15.6%)	6 (18.7%)	
Pre-Operative Hemoglobin (g/dl)	11.6±1.3	11.6±1.4	0.971

Chi-square test and Independent Sample t-Test, observed difference was statistically insignificant

Table 3: *Change in Hemoglobin Level after the Surgery across the Study Groups n=64*

Hemoglobin (g/dl)	Pre-Operative Misoprostol n=32	Post-Operative Misoprostol n=32	P-value~
Pre-Operative	11.6±1.3	11.6±1.4	0.971
Post-Operative	10.4±1.4	9.9±1.3	0.122
Change	1.2±0.4	1.8±0.4	<0.001*
P-value!	<0.001*	<0.001*	

~ Independent Sample t-Test comparing hemoglobin values between the groups
! Paired sample t-test comparing pre-operative and post-operative hemoglobin of same group
*Observed difference was statistically significant

Table 4: *Comparison of Mean Change in Hemoglobin between the Study Groups across Various Subgroups n=64*

Subgroups	n	Mean Change in Hemoglobin (g/dl)		P-value
		Pre-Operative Misoprostol n=32	Post-Operative Misoprostol n=32	
Age				
• 18-26 years	16/18	1.2±0.4	1.8±0.4	<0.001*
• 27-35 years	16/14	1.2±0.4	1.8±0.4	0.001*
Gestational Age				
• 38-39 weeks	17/16	1.2±0.4	1.8±0.4	<0.001*
• 40-42 weeks	15/16	1.2±0.3	1.8±0.5	0.001*
BMI				
• 20-25 Kg/m^2	10/11	1.1±0.3	1.6±0.4	0.004*
• 25-30 Kg/m^2	17/15	1.2±0.4	1.7±0.4	0.001*
• 30-35 Kg/m^2	5/6	1.5±0.4	2.1±0.4	0.038*

Independent Sample t-Test, * observed difference was statistically significant

Though misoprostol is time tested drug for prevention and treatment of postpartum hemorrhage there is limited evidence to support its use as an intraoperative preventive therapy for reducing blood loss. In these trials, misoprostol was given postoperatively[7]. However, according to a recent study it was found that pre-operative misoprostol was more efficacious than conventional practice of post-operative misoprostol evident from lesser mean change in hemoglobin after Cesarean section and recommended it for future practice[10]. However, the available

evidence was limited while there was no such local study available which arose the need for current study.

The objective of this study was to compare mean change in haemoglobin concentration with preoperative versus post-operative misoprostol in primigravida undergoing elective caesarean section.

In the present study, patient's mean age was 28.0±5.3 years. Similar mean age of 28.4±4.7 years among women undergoing C-section at Aga Khan University Hospital, Karachi was reported by Khan et al16. A slightly higher mean age of 30.8+5.1 years has been reported by Raees et al. among pregnant women undergoing elective cesarean section at Lady Reading Hospital Peshawar.[17] While Eusaph et al. reported it to be 31.9±2.3 years at Lady Willington Hospital, Lahore[18]. Akinola et al. reported comparable mean age of 30.4±4.9 years in Nigeria.[19] While Chen et al. reported it to be 31.6±3.0 years in Chinese such women.[20]

In this study it was noted that the mean duration of gestation 39.6±1.4 weeks while the mean BMI was 26.5±3.6 Kg/m^2. Osmundson et al. and Wortman et al. reported similar mean duration of gestation of 39.20±1.80 weeks and 38.07±2.30 weeks respectively among American women undergoing elective C-section.[22,23] While Chen et al. reported similar mean BMI of 26.1±4.0 Kg/m^2 in Chinese such women.[20]

In the present study, the mean change in hemoglobin was significantly lower in patients receiving pre-operative misoprostol as compared to those receiving post-operative misoprostol (1.2±0.4 vs. 1.8±0.4 g/dl; p-value<0.001). Similar difference in mean change in hemoglobin was observed between the groups across various subgroups based on patient's age, gestational age and BMI. Our results were similar to those of Abd-Ellah et al. whose study revealed similar significant difference in the mean change in hemoglobin with pre-operative versus post-operative misoprostol in women undergoing elective cesarean section (1.2±0.67 vs. 1.9±0.45 g/dl; p-value=0.032)10 In another similar study, Ragab et al. also revealed similar results regarding mean change in hemoglobin with pre-operative versus post-operative misoprostol in women undergoing elective cesarean section (10.4±0.67 vs. 10.8± 0.45 g/L; p-value<0.001) 9

This study is first of its kind in local population and adds to the limited available research evidence on the topic. In this study it was observed that pre-operative misoprostol resulted in significantly lesser mean change in hemoglobin than the conventional practice of post-operative misoprostol in patients undergoing cesarean section which suggests optimal control of blood loss during surgery and subsequent decreased need of blood transfusion with associated side effects. This observation with possible implications advocate preferred pre-operative use of misoprostol in women undergoing elective C-section in future practice.

The limitation of the current study was that the spectrum of various fetomaternal side effects between these two regimens was not recorded which could further help in the selection of more appropriate regimen in such women. Further research needs to be carried out on large scale including assessment of fetal risk as well.

CONCLUSION

Pre-operative misoprostol resulted in significantly lesser mean change in hemoglobin than the conventional practice of post-operative misoprostol in patients undergoing cesarean section which suggests optimal control of blood loss during surgery with pre-operative misoprostol and is therefore recommended regimen in future practice.

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SATISFACTION TO ONLINE TEACHING DURING COVID-19 PANDEMIC: RESIDENT'S PERSPECTIVE

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How to cite: Ahsan U, Nasim A, Tabbasum S, Yusuf L. Satisfaction to online teaching during covid-19 pandemic: resident's perspective. JAIMC. 2020; 18(4): 721-26.

Abstract

Objective: To present a brief snapshot of the effect of online courses and explore the residents' satisfaction with their learning experiences and their perceptions on effectiveness and quality in online learning.

Methodology: It was mixed method study. Data was collected through an email survey with 129 postgraduate residents; and focus group discussions were carried out with 8 residents. Data were collected through pre-designed questionnaires comprising of open- and close-ended questions. The data were entered into SPSS version 21 and analyzed.

Results: A total of 129 residents participated. The mean age of residents was 29.8+-1.1. Among these 129 respondents, 85(66%) were males and 44 (34%) were females. In this study, majority of residents responded in agreement to the questions pertaining to the learning environment, technological characteristics and course management. Residents who were satisfied with online teaching programs ranged between 60-90%. All the diverse responses were coded into theme and we identified 4 major themes during data analysis, which were apparently related directly to the questions asked in focus group interview. These were "instructional efficiency", "learner's achievement", limitatios" and "quality indicators".

Conclusion: The present study recommends the use of online learning facilities during COVID-19 Pandemic, for residents at various levels of training in Pakistan.

Keywords: Online teaching, Satisfaction, Residents, Medical Education

Medical education has evolved immensely over past two decades across the globe. With worldwide advancements in information technology and internet services, E-learning platforms have become dominant tools of teachings. Online learning resources are now widely used globally and include the use of variety of modalities. They not only provide opportunities to deliver academic content and learning materials in undergraduate and postgraduate training but provide the advantage of flexibility of scheduling the courses according to the student's own schedules.[1]

The novel corona virus (SARS-CoV-2) pandemic has suspended the academic activities worldwide. This has created a remarkable transformation in the way our residents and fellows are educated.[2] Currently, most of the academic physicians have shifted from traditional to online teaching. This transition has provided a unique opportunity to formulate long-term instructional plans for the residents and maintain continuing medical education (CME) as a specialty.[3]

The introduction to digital teaching and learning is testing not only for the institutions but for the faculty and residents as well. Effective and authentic online teaching, assessment and interactive formative feedback can enhance the learners experience and provide valuable learning. In the crisis driven

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Submission Date: 12-08-2020
1st Revision Date: 17-09-2020
Acceptance Date: 23-09-2020

context, the effectiveness of online teaching programs can be examined by evaluating the resident's satisfaction with such teachings.[4] We therefore decided to assess the students satisfaction towards the online courses conducted during COVID-19 Pandemic. The aim of the study is to present a brief snapshot of the effect of online courses and explore the residents' satisfaction with their learning experiences and their perceptions on effectiveness and quality in online learning environment. We believe that the analysis of resident's satisfaction will draw attention to the areas of improvement in E-learning practices, which in turn could be helpful in achieving the learning objectives. To the best of our knowledge, this was the first study of its kind that will analyze satisfaction to online teaching courses among trainee residents of various specialties in the local context.

METHODOLOGY

This mixed method study was conducted in Sharif Medical and Dental College from April 2020 till June 2020. Quantitative data was collected from a total of 129 residents of various specialties using non-probability consecutive sampling. Students were approached via their email. They were briefed about the objectives of the study. Only those residents who gave consent were sent the questionnaire which was prepared through computer generated software. From the participants, 8 residents were reselected through purposeful qualitative sampling for focus group discussion. Responses were kept anonymous. The participants filled a demographic form with information about gender, age, qualification, years in the course. Items or questions of Residents Satisfaction Survey Questionnaire were developed following the steps of AMEE guideline no 87.[5] A pilot test was conducted for establishing reliability and validity of instruments. Items in quantitative survey were characterized into three main dimensions of learning environment, technological characteristics and course management. The participants rated on a Likert-type scale ranging from one (1=Strongly Disagree to 5=Strongly Agree).

Data analysis was done using SPSS 21.0. Numerical data was presented as mean and standard deviation; and categorical data as frequencies and percentages. Percentages of the respondents in each domain of questionnaire were calculated using Likert scale. 1 & 2 being highly dissatisfied (strongly disagree) and 4&5 were taken as satisfied (Strongly agree) and 3 were considered as uncertain.

Qualitative data was analyzed through thematic analysis. Initial data reduction was followed by data presentation in templates by recognition of themes and trends and calculation of their frequencies. Words comprising of answers to research questions with same conclusions were clustered in one theme with least overlap. Themes and codes (sub-themes) were then reevaluated through member checking among the researcher and were finalized by passing through phases of familiarization with data, generating initial codes, searching for themes among codes, reviewing themes, defining and naming themes, and drawing conclusions using this iterative scheme.

Several measures were taken to ascertain validity. For establishing interpretive validity, we followed a participatory approach with member checking. The participants went through the transcripts to confirm the precision of interviews. The excerpts shown in each of the themes, further confirmed descriptive validity. Conclusions were finally drawn by following a regular iterative process of re-visiting research questions, transcriptions and matrices by a set of researchers (member checking) by putting each other's interpretations to the test of plausibility, sturdiness and conformability.

RESULTS

A total of 129 post-graduate residents participated. The mean age of residents was 29.8±1.1. Among these 129 respondents, 85(66%) were males and 44 (34%) were females. 60 (46.5%) were working in public sector, 53(41%) from private sector, 16(12.4%) from armed forces. Of these 129

respondents, 77(59.6%) residents were from Punjab, 32(24.8%) from Sindh, 13 (10%) from KPK, 1(0.7%) from Baluchistan 6(4.6%) from Federal Capital Islamabad.

Table 1: *Speciality wise Distribution of the Respondents*

Specialty	Number of Respondents(n)	%
Dermatology	45	36%
Pathology	18	14.4%
Nephrology	14	11.2%
Radiology	12	9.6%
Pediatrics	10	8%
Rheumatology	09	7.2%
Surgery	08	6.4%
Internal Medicine	08	6.4%
Endocrinology	04	3.2%
Total	129	100%

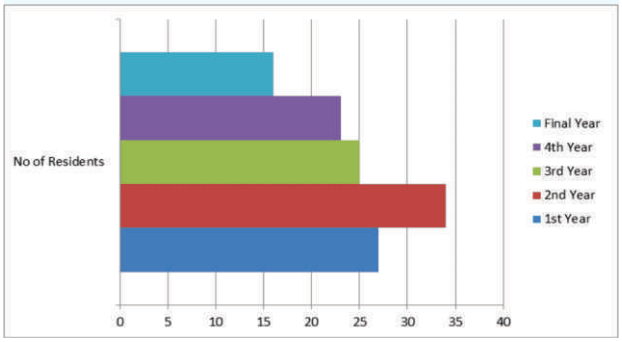

Figure-I: *Distribution of Data as per year of training.*

Participant's responses to items in questionnaire were calculated as frequencies and percentages and presented in Table-II

Focus group discussion was carried out using Zoom video call, with 8 residents. The aim of the focus group interview was to explore the range of ideas and feelings of the residents about online teachings. The interviews were audio recorded and transcribed afterwards. Accuracy was verified by the researcher. For identification of themes and concepts, content analysis was done. This methodology was directed to explore the residents view point of what represents an effective online teaching, what impact an online teaching creates on the learning experience of the students. They were also inquired about the indicators of Quality Assurance (QA) and Quality Improvement (QI) being utilized in their respective courses and finally about the assessment techniques. All the diverse responses were coded into theme and we identified 4 major themes during data analysis, which were apparently related directly to the questions asked in focus group interview. These were "instructional efficiency", "learner's achievement", limitatios" and "quality indicators".

Table 2: *Frequencies of Student's Satisfaction with Online Teaching during COVID19 Pandemic*

Domain	Items	Dissatisfied n (%)	Uncertain n (%)	Satisfied n (%)
Learning Environment	The classroom was distraction free	22 (17%)	39(30.3%)	68(52.7%)
	I was satisfied with the quality of online learning material	6(4.6%)	30(23.2%)	93(72%)
	Instructional techniques (presentations) aided student learning	10 (7.7%)	33(25.6%)	86(66.7%)
	The assignments were clearly communicated	13(10%)	21(16.3%)	95(73.6%)
	The instructor facilitated discussions in course	13(10%)	25(19.4%)	91(70.5%)
	I felt comfortable interacting with other participants	21(16.2%)	42(32.5%)	66(51.1%)
	Computer mediated communication is an excellent medium for distant learning	16(12.4%)	28(21.7%)	85(65.9%)
Technological Characteristics	I was satisfied with the audiovisual quality	25(19.4%)	32(24.8%)	72(55.8%)
	I felt confident that the class will not be cancelled due to technical errors	37(28.7%)	31(24%)	61(47.2%)
	The instructors promptly responds to the queries on tele-response system	21(16.2%)	33(25.5%)	75 (58.1%)
	The picture and sound quality was appropriate on Zoom	15(11.6%)	26(20.2%)	88(68.2%)
Course Management	Online teaching was great learning opportunity	14(10.8%)	20(15.5%)	95(73.6%)
	Online teaching is stimulating	17(13.17%)	29(22.5%)	83(64.3%)
	I look forward to online teaching in future	28(21.7%)	33(25.5%)	68(52.7%)

Theme	Subtheme	Excerpts
Instructional Effectiveness	• Distant learning • Interactive • Stimulating/Challenging • Accessibility • Effective time management	• "I found it useful as it allowed for a distant learning opportunity during this COVID-19 Pandemic" • "I was always encouraged for any questions, and the discussion that was generated afterwards cleared many points" • "When I am asked a question, during these online sessions about something clinically relevant or important, I feel like my mind has been stimulated… it actually is more interesting rather than just a topic discussion" • "These sessions kept us involved with the academics and our clinical courses, we were able to discuss important topics with senior faculty" • " Instead of wasting our time during the rotational duties, such classes allowed us to effectively manage our time and I feel better prepared for my exam"
Learner's Achievement	• Self Directed learning • Motivated • Goal Oriented • Receptive to change	• " We chose to discuss difficult topics and topics of clinical and exam relevance to discuss, instead of wasting our times in general lectures" • " I feel it was a good learning opportunity and helped clearing my difficult concepts" • "I found them useful, as those areas in text were discussed which are normally ignored, but have significance in exams" • "It was a positive activity, utilizing technology which was user friendly and we felt enlightened"
Limitations	• Lack of real time patients • Inability to perform procedural skills • Lack of feedback • Resource limitations	• " Theory parts were discussed and covered properly, but clinical skills could not be practiced and assessed" • "This program did not allow us for learning the procedures, this is the major shortcoming. Our trainings will be ending with major gap and that is quite alarming" • "We were not assessed, so we never knew about our mistakes. Such online programs should have some form of test or assignment at the end, so that we can know our deficiencies" • "Zoom was limited to only 40 minutes session and could share only specific type of presentations, it could have been more useful if other apps are used which allow for real time clinical discussion, or institution buys a package of Zoom with more time and participants"
Quality Assurance	• Incorporation of CBD • Faculty Training • Regular Formative Assessment & Feedback • Orientation on Virtual Patients	• "It would be more useful if we add case discussion to online teachings" • " seniors are not very much familiar with the use of technology, if the supervisors and senior faculty gets trained on the use of new applications, then such programs will be more fruitful" • "We have no idea about are we doing right or wrong? The seniors should give us tasks or assignments and provide us feedback about our performance. This is the only way to learn" • When will this pandemic end; no one knows about it. We are lacking the clinical practice and skills. I think institutions should allocate resources for simulated patients and virtual patients to improve our learning"

DISCUSSION

Online education has changed the teaching and learning pattern globally. It is being practiced for a long time, but its role has been recently highlighted during COVID-19 pandemic in education. In this study, majority of residents responded in agreement to the questions pertaining to the learning environment, technological characteristics and course management. Residents who were satisfied with online teaching programs ranged between 60-90% (Table-II). This is in accordance with Cipriano et al, where all the participants reported to improve their clinical knowledge after the online program. In the current scenario of COVID-19 pandemic, there has been a transition from a clinical to online instruction, opted by various specialties.[6] Several societies have involved the residents in active online learning to maintain continuing medical education (CME). A variety of instructional modalities are being utilized in such programs. We however, couldn't find any study that has assessed the resident satisfaction with these programs in current pandemic. On undergraduate level, currently a few studies have highlighted

the advantages of online teaching programs as being flexible and student centered.[7] This was in accordance with our findings as well. The participants reported it to be an effective instructional strategy.[8] They believed that online teaching was interactive, stimulating and allowed effective time management. Such flexibility in accessing the resource material and in learning has been mentioned in literature as well.

Residents in our study linked the programs with certain achievements as they felt motivated, self directed, goal oriented and receptive to change. All such accomplishments enable the students to develop into a self directed learner; a capability that should ideally be acquired by health professionals to continue their lifelong learning skills.[9]

Our study participants also pointed out the limitations associated with the online teaching programs. They observed the inability to teach clinical skills and lack of patient interaction as the major limitation. Resource and time limitation was also highlighted, as Zoom provided only 40 minutes of teaching, which they believed was a limited time. Residents recommended allocating financial resources for an improved provision e- learning facilities.

For future improvement in standards of online teachings and quality assurance participants suggested having a formative feedback to improve their academic performance. Literature also highlights the importance of mutual feedback to improve self-efficacy and motivation.[10] They also suggested using virtual patients to improve their clinical skills of reasoning and management. This has been highlighted in literature as well. Virtual patients are considered to be valid tools for building up self directed learning skills and support in curricular advancement and delivery in distant areas.[11] Change in the academic content was suggested by incorporation of case based discussions instead of only lectures, so that the sessions can become more interactive and productive. Training and orientation of faculty for using the modern apps and tools for online teaching and assessment was recommended as well, for smooth execution of classes.[12]

Limitations

Result of this study needs to be seen in framework of its limitations. We relied on self-report and study population was only the residents, therefore the findings can be pertinent only in corresponding context. Additionally, number of studies included for comparison was limited. Our results couldn't be compared due to non-availability of particular data during COVID-19 Pandemic. In the local context, no comparison could be done due to same reason. Despite these limitations, study has much strength including an excellent response rate & participation of substantial number of respondents across different levels of training and inclusion of multiple teaching institutions throughout the country leading to better generalizability of results.

CONCLUSION

The present study recommends the use of online learning facilities during COVID-19 Pandemic, for residents at various levels of training in Pakistan. Such courses are not only flexible and interactive but also allow the residents to develop their self directed learning abilities. It started as 'distant learning during Covid crisis", however the limitations can be addressed with additional investment of time and resources. Faculty orientation and training for the use of modern computer software and online teaching applications is required to decrease the cognitive load and enhance the interactiveness.

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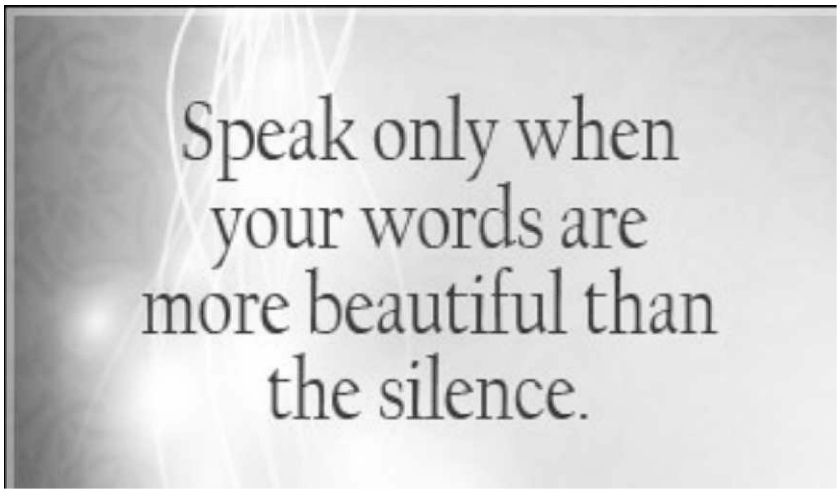

ETIOLOGY AND SURGICAL OUTCOMES OF UROGENITAL FISTULA

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How to cite: Channa AA, Akhtar SMH, Khanum S, Cheema NA, Waqar MS, Shafiq N. Etiology and surgical outcomes of urogenital fistula. JAIMC. 2020; 18(4): 727-31.

Abstract

Background: Urogenital fistula has been recognized as a repetitive maternal sickness in developing countries. Since 1980's, it's been known to cause maternal deaths.

Objective: To find out the etiology and outcomes of surgical repair of urogenital fistula.

Methodology: The descriptive observational study was conducted at Islam Medical College/ Teaching Hospital, Sialkot and all patients with urogenital fistula during May 2015 to May 2018 were included. All 23 women were referred from different clinics and hospitals of our region with varying types of urogenital fistula falling in age range of 20years to 52 years. We clinically examined the number, size, and location of the fistula and reported their pre and post-operative results. SPSS Version-26 was used for data entry and analysis.

Results: Overall, mean age was 35.91±11.05 years. Success was reported in 22(95.6%)i.e. urinary leakage got improved completely in 1 week post operation. Out of the 23 patients, 70% were vesicovaginal fistula, 22% ureterovaginal, 4% uretherovaginal, vesicouterine fistula with 4% and fistulae caused due to hysterectomy and 22% due to obstructed labor.

Conclusion: Hysterectomy and obstructed labor remained the most common cause of urogenital fistula. Surgical treatment to manage urogenital fistula proved effective in our study and it helps in reducing urinary incontinence.

Key Words: Etiology, Urogenital fistula, surgical repair, urine incontinence

Urogenital fistula has been recognized as a repetitive maternal sickness in developing countries.[1] Since 1980's, it's been known to cause maternal deaths. Precisely what amount of people are affected by urogenital fistula is not recorded yet however WHO wrote that above 2 million young women exist all around the world who are unaware and untreated while they also recorded that about 50,000 to 100,000 more women every year are being exposed to it.[2] From Africa, it was reported that around 30,000 to 130,000 new cases of urogenital fistula develop yearly.[3,4] Considering the spread of obstetric fistula, the statistics range from 0.16% to 4.7% in Sub-Sahara Africa while in south Asia, and the number goes down to 0.08 to 2.7% however fistula caused due to pregnancy and labor estimates from 1 to 1200 cases. While gynecologic fistula approximates 1 in 1200 from gynecologic procedures.[5]

An abnormal tract that forms between the urethra, urinary tract, bladder and genital organs is called urogenital fistula .This can develop anywhere

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Submission Date: 11-08-2020
1st Revision Date: 09-09-2020
Acceptance Date: 17-09-2020

in the organs in pelvis.[6] However fistula allows urine to pass and exit through the urogenital tract. Due to the gastrointestinaltract and urinary system being closed, fistula formation is very much probable. Further sub-classifications includes which covered the size of the fistula, extent of scarring, and vaginal length.[7] Simple fistulas are usually small in size (≤ 0.5 cm) and are present as single non-radiated fistulas. Complex fistulas include previously failed fistula repairs or large-sized (≥2.5 cm) fistulas, more often a result of chronic diseases or radiotherapy. Most authors consider intermediate-sized fistulas (between 0.5 and 2.5 cm) as complex ones.[8]

Usually fistula is caused due to injuries, infections, obstructed labor, and delay in childbirth, hysterectomy and radiation therapy. Physicians take the history of patients who usually present with continuous urinary incontinence symptomsor watery discharge along with normal voiding.[9] physically examination of the genitals is important while specifically assessing perineal dermatitis, ulceration, infection and presence of scars or fistula repairs. Assessment of fistulae is done regarding its size and number followed by Dye test which involves filling the bladder and closing urethra passage to note any dye leakages. Hemoglobin is tested for nullifying any other infections.

Genitourinary tract fistulas are among the worst complications of obstetric and gynecologic procedures.[10] Patient are frequently treated with conservative techniques however in order to handle urinary continence, surgery is the best way. Not much local experience is on view regarding etiology and outcomes of urogenital fistula and therefore our objective was to find out the etiology and outcomes of surgical repair of urogenital fistula.

METHODOLOGY

This descriptive observational study was conducted at the Department of Urology, Islam Medical College/Teaching Hospital Sialkot and 23 female patients with urinary leakage during May 2015 to May 2018 were included in our study. Patients with acute inflammation on surgical site, or with other skin issues or those who had co-existing bladder problems were excluded. Approval from Institutional Ethical Committee was acquired and written consent was sought from all study participants.

We performed complete blood count, serum biochemistry, urine analysis and culture, Ultrasonography, cystography (AP, lateral view) and CT IVU was performing before surgery. Three swab test was performed with the help of tablet Phenzopyridine orally and methelene blue intravesical installation.

After induction of anaesthesia, patient was made to lie in a high lithotomy position and the patients is thorough examined under anaesthesia, using cystoscopy to identify fistula and bilateral retrograde catheterization for ureteral potency, and vaginal examination using speculum with 3 swab test for identification of fistula. And making plan for surgery which approach is best for either transvaginal repair in low vv fistula and for high fistula using transabdominal transperitoneal or transvesical approach.

We used Patients profile sheet to examine the age, etiology, duration, size, location and number of fistula. Our team took follow-ups and clinically assessed patients for 30 days and check patterns of urogenital fistula operating modality and recorded the outcomes post-repair.

SPSS Version 26 was used for data entry and analysis. Age (years), height (cm) and BMI (kg/m^2) of patients, fistula size (cm), operation time (minutes) and estimated blood loss (ml) were represented in terms of mean and standard deviation. Etiology and outcomes of urogenital fistula were represented in terms of frequencies and percentages.

RESULTS

Overall, the mean age of patients was 35.91± 11.05 years (ranging from a minimum of 20 years to a maximum of 52 years). Table number 1 shows distribution of types of urogenital fistula with regards to various etiologies found. Vesicovaginal

fistula were the commonest type, found among 16 (69.6%) cases while abdominal hysterectomy was the commonest cause noted among 10 (43.5%).

The vesicovaginal fistula was observed in 70% while 22% ureterovaginal fistulae and 1 patient was vesicouterine fistula and 1 of uretherovaginal fistula i.e. 4% respectively. (Table-2) The mean fistula size was 3.42±0.5 cm and mean operating time was 164 mines and mean estimated blood loss was 62 ml (ranging from 35ml to 70 ml) however the hospitalization was minimum 6 days. (Table No.2) All patients had their catheter removed post-operatively except for the uretherovaginal fistula patient who took 1 month for removal.

Out of the 16 cases of Vesicovaginal Complex fistula, 7 patients were repaired with O Connor technique Trans peritoneal with Omental flap and 3 with transvesical and 6 lesser complex fistulas were treated with Transperitoneal transvesical technique. In 5 cases of ureterovaginal fistula; 1 was treated through end-to end anastomosis and 3 ureteric-reimplantation and 1 using Baaries Flap while DJ Stent was kept in all patients which was removed successfully in all .And a single case of vesicouterine repair by trans abdomen transperitoneal and another single case of uretherovaginal fistula which is repair in lithotomy position in which labial fat flap (martius technique) used and foley's catheter was kept, and 1 month post operation catheter was removed.(Table No.3)

Success was reported in 22 (95.6%)i.e. urinary leakage got improved completely in 1 week post operation. None of the patient developed any bowel related complication and all patients were continent following procedures.

Table 1: *Frequency of Allergies in a Sample of 300 Medical Students in Lahore, Pakistan, in 2014*

Type & Procedure	Complexity		
	High Fistula	Low Fistula	Low Fistula
	Trans-abdominal	Trans-abdominal	Trans-vaginal
Ureterovaginal fistula-n=5	**1**	**4**	
End-to end anastomosis	1		
ureteric re-implantation		3	
Bories Flap		1	
Uretherovaginal fistula n=1			**1**
Vesicouterine fistula n=1		**1**	
Vesicovaginal fistula n=16	**10**	**2**	**4**
Connor Technique transperitoneal transvesical	3		
Connor Technique transabdomin Transperitoneal	7		

Table 1: *Etiology and Types and Urogenital Fistula (n=23)*

Types of Urogenital Fistula	Causes of Urogenital Fistula					P-Value
	Abdominal Hysterectomy	Difficult Vaginal Delivery	Elective Cesarean Section	Forceps Delivery	Prolonged Obstructed Labour	
Ureterovaginal Fistula	5	-	-	-	-	0.114
Uretherovaginal Fistula	-	-	-	1	-	
Vesi couterine Fistula	-	-	-	-	1	
Vesicovaginal Fistula	5	2	3	2	4	

Table 2: *Types of Fistula and Characteristics of Stud Participants*

Types of Fistula	n	Mean Values					
		Age (years)	BMI (kg/m^2)	Fistula Size (cm)	Operation time (min)	Hospitalization (days)	Blood Loss (ml)
UVF	5	48.8	26	3.44	162.60	6.2	40
URVF	1	52.4	23	0.50	167.25	6.8	105
VUF	1	50.5	24	4.00	169.48	6.9	0
VVF	16	30.3	25	3.56	164.50	6.4	33

UVF: Ureterovaginal Fistula, URVF: Uretherovaginal Fistula, VUF: Vesicouterine Fistula, VVF: Vesicovaginal Fistula

DISCUSSION

Fistula can result from poor labor and delivery care or poor surgical technique, either of the cases are controllable and the important thing is to find ways to avoid such possibilities. Similarly availability of a fully equipped, good staffed and good-quality emergency obstetrical care is significant along with an upgraded contact to family planning consultancy services.[11] The prevalence of fistula patients is quite common and approximately out of 1000 deliveries 3 to 4 vaginal deliveries suffer from it especially in cases where the patient reaches the hospital after a delay.[4,12] Some researchers also wrote about a fistulas caused due to poor medical treatment.[1,13] In our study however majority of cases about 70% were caused due to hysterectomy followed by obstructed labor at 22% while a similar study showed 70% cases due to iatrogenic obstetric to be the main cause.[14] Another study showed obstructed labor in 59.4% with iatrogenic cause in 36.7%.[15]

In our study the most common urogenital fistula was the vesicovaginal fistula i.e. 70% while 22% ureterovaginal fistulae and 4% patients were vesicouterine and 4% uretherovaginal fistula respectively. A similar study conducted of 113 women showed 69.9% Vesicovaginal fistula, 25.7% ureterovaginal fistula, 2.7% vesicouterine fistula and 0.88% urethrovaginal fistula.[15]

Out of the 16 cases of Vesicovaginal Complex fistula, 7 patients were repaired with O Connor technique TPTV with Omental flap and 3 with transvesical and 6 lesser complex fistulas were treated with Transperitoneal transvesical technique. In 5 cases of ureterovaginal fistula; 1 was treated through end-to end anastomosis and 3 ureteric-reimplantation and 1 using Bories Flap while DJ Stent was kept in all patients.Similar study conducted on 26 women, 5 fistulae were treated conservatively, one involved vaginal repair and peritoneal transvesical approach was used in 3 cases while 4 ureteric re-implantation were carried out and 13 patients had trans-vesicle-transperitoneal supra-pubic repair with interposition of J-flap of omentum.16In our study the operation time was 164.39 ±2.47mins while in other literatures it varies from 70 to 280 minutes and they also reported an overall success rate of 86 to 100%[17-19] while in our study the success rate was 95.6%. Improvising the programs for establishing the proper obstetric care centers, provision of trained staff, insuring the timely access of pregnant women, increased literacy and awareness in society will definitely decrease the incidents of obstetric fistula in the developing country like Pakistan.

Being a single center study with a moderate sample size were some of the limitations of this study so our findings cannot be generalized. We also followed patients for a relatively shorter duration. Further studies involving multiple centers and large sample size will further confirm the findings of this research.

CONCLUSION

Hysterectomy and obstructed labor remained the most common cause of urogenital fistula. Surgical treatment to manage urogenital fistula proved effective in our study and it helps in reducing urinary incontinence.

Acknowledgment: The authors would like to thank Muhammad Aamir (Research Consultant, Bahawalpur) for his volunteer support in statistical analysis of this research.

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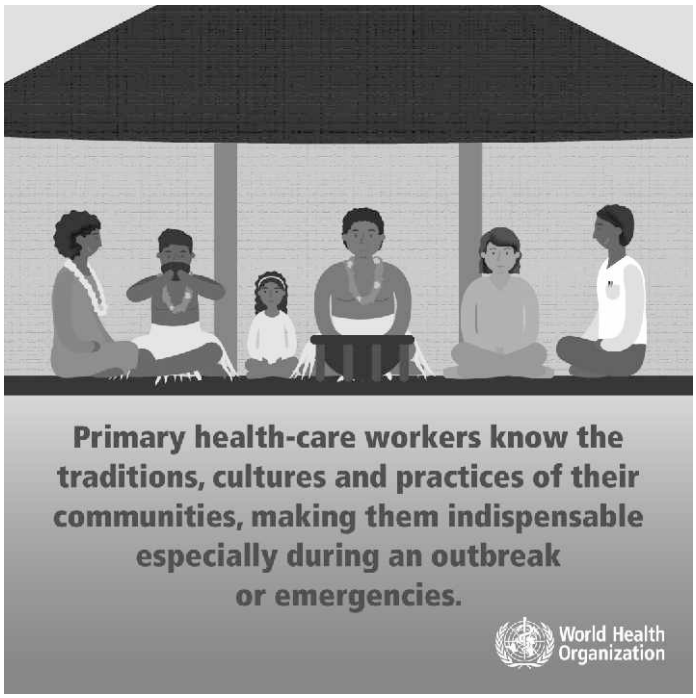

PHYSICAL FITNESS LEVELS IN MEDICAL STUDENTS AND ITS CORRELATION WITH ACADEMIC PERFORMANCE

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How to cite: Hussain SAS, Ashfaq S, Saeed S, Hussain SAS, Farooq M, Salam E, et al. Physical fitness levels in medical students and its correlation with academic performance. JAIMC. 2020; 18(4): 732-37.

Abstract

Background: Long study hours and being cooped up cramming long prose of medical literature basically means that medical students in Pakistan have to sacrifice time which could have been spent on physical activity which equates to poor physical activity.

Objective: The objective of this research is to assess the physical fitness level in medical students and the correlation between physical fitness and the academic performance of students.

Methodology:

Two hundred and fifty medical students were included in the study. Aquestionnaire was given to the participant after briefing them regarding the research topic, objectives and what was required of them. All the data collected was entered in SPSS ver:17. 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 showed that the majority of individuals were of average physical fitness amounting to 172(68.8%). 49(19.6%) individuals had good physical fitness. Of the individuals with poor physical activity 3(10.34%) had poor academic performance.19(11.04%)individuals with average cumulative physical activity had poor academic performance.

Conclusions: The physical fitness of most of the medical students in the study was of an average level. We found that those individuals having average physical fitness were academically superior to those who fell on the extremes of the physical fitness spectrum.

Key words: academic performance, cognition, exercise, medical students

According to the CDC, physical fitness is defined as 'the ability to carry out daily tasks with vigor and alertness, without undue fatigue, and with ample energy to enjoy leisure-time pursuits and respond to emergencies.' The components of fitness that we considered were as follows; cardiopulmonary endurance, muscular endurance, muscular strength, speed, number of sports and number of exercises participated in.

This is a globally pressing issue with physical fitness levels deteriorating and being in an appalling state around the world. Affluent and developed nations are not immune, only 62 % of Scottish people, 66% of English men and 56% of English women claim to meet CMO recommendations.[1] Low physical fitness leads to a myriad of problems inflic-

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Submission Date: 12-08-2020
1st Revision Date: 14-09-2020
Acceptance Date: 22-09-2020

ting both the individual and the nation as a whole. In developed countries, it has led to an array of illnesses and causes 22-23% of CHD,16-17% of the colon cancer, 15% of diabetes,12-13% of strokes and 11% of breast cancer. It has a great toll on the country's economy as well and costs the NHS 94 million pounds annually.[2] Pakistani individuals are even less likely to reach physical activity recommendations as compared to individuals in England. Only 21% of people in America are meeting the guidelines laid done by CDC in their 2008 physical activity guidelines. Lack of physical activity is associated with many adverse effects. Although, widely regarded as separate entities, physical fitness and levels of anxiety and depression are directly related. The physical deterioration manifests as: CVS diseases, Coronary heart disease, overweight or obesity, decrease in skeletal muscle mass, increased blood pressure and increase cholesterol. Such adverse effects prove a hindrance, and as such medical students may suffer from inadequacy both in their scholarly pursuits and other facets of life.

Long study hours and being cooped up cramming long prose of medical literature basically means that medical students in Pakistan have to sacrifice time which could have been spent on physical activity which equates to poor physical activity. No such research was present that focused primarily on this demographic and this section had been largely overlooked, as such we saw it pressing that we put together this article which provides insight to this pressing problem. The objective of this research is to assess the physical fitness level in medical students andthe correlation between physical fitness and the acade-mic performance of students.

METHODOLOGY

ACross Sectional study was conducted at Allama Iqbal Medical College, Lahore during April-May 2017. 250 medical students from Allama Iqbal Medical College, Lahore of 1st year to 5th year were included in the study. A questionnaire was given to the participants after briefing them regarding the research topic, objectives and what was required of them. All the data collected was entered in SPSS ver:17. 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

From the questions asked each option was assigned a score, with the least physically tasking assigned the lowest score (1) and the most physically tasking, the highest score (4). Accordingly the respondents on the basis of their cumulative score were classified into 3 groups which were as follows: poor (0-6), average (6-13) and good (14-24).

From the questions asked regarding academic performance, the least academic were assigned the lowest score[1] and the best academic scores assigned the highest.[5] Accordingly, the respondents on the basis of their cumulative score were classified into 3 groups which were as follows: poor (0-4), average (5-7) and good(8-10). 29(11.6%) individuals had poor physical fitness, 172(68.8%) had average physical fitness and 49(19.6%) individuals had good physical fitness. The individuals with poor cumulative physical activity had 3(10.34%) that had poor academic performance; there were 21(72.41%) with average academic performance and 5(17.24%) had good academic performance. The individuals with average cumulative physical activity had 19(11.04 %) that had poor academic performance; there were 107(62.20%)that had average academic performance and 46(26.74%) had good academic performance. The individuals with good cumulative physical activity had 7(14.29%) that had poor academic performance; there were 37(75.51%) with average academic performance and 5(10.20%) had good academic performance.

Of the 250 individuals, 80 (32%) reported that they did not partake in any form of exercise in a

typical week, 97 (38.8%) reported that they exer-cised 1-3 times a week, 41 (16.4%) reported that they exercised 3-5 times a week, and 32 (12.8%) reported that they exercised more than 5 times a week. When questioned about their cardio-respiratory endurance by virtue of their ability to jog without getting exhausted, 74 (29.6%) reported that they can do so for 1-5 minutes, 74 (29.6%) reported that they can jog for 6-10 minutes without exhaustion, 45(18%) stated that they can jog without exhaustion for 11-15 minutes, and 57 students (22.8%) stated that they perform the stated task for greater than 15 minutes. When assessing muscular endurance we asked the participants how many push-ups they could perform with ease, 124 students (49.6%) stated that they can perform 1-5 pushups with ease, 49 students (19.6%) stated that they can perform 6-10 pushups, 37 students (14.8%) stated that they can perform 11-15 pushups whilst 40 students (16%) stated that they can perform more than 15 pushups with ease. While assessing the muscle strength of the candidates, we asked them about the amount of weight they could lift, the results were as follows: 110 students (44%) could lift 5kg-10kg; 70 students (28%) could lift 11kg-30kg; 44 students (17.6%) could lift 31kg-50kg; 26 students (10.4%) could lift greater than 50kg. On the question of speed evaluation, 29 students (11.6%) stated that they run at a slow pace, 122(48.8%) at a medium pace, 78 (31.2%) at a fast pace, and 21(8.4%) could run at a very fast pace. Of the given options, when asked to identify the sports they partook in,84 individuals (33.6%) said that they had participated in one of the sports mentioned in the options, 36 individuals (14.4%) participated in 2, 24 individuals (9.6%) participated in 3, 13 individuals (5.2%) participated in 4, 6 individuals (2.4) partici-pated in 5, and 1 individual (0.4%) participated in 6, 1 individual (0.4%) reported to have participated in 8 of the mentioned sports, and 4 individuals (1.6%) had participated in all 9 mentioned sports, the remai-ning 81 individuals (32.4%) however, did not parti-cipate at all. When asked regarding their present physical fitness compared to that before medical college we

Table 1: *Socio-Demographic Profile of Medical Students*

Variables	Frequency	Percent %
Frequency of Exercise in a week		
Never	80	32.0
1-3	97	38.8
3-5	41	16.4
>5	32	12.8
Cardiorespiratory endurance		
1-5 min	74	29.6
6-10 min	74	29.6
11-15 min	45	18.0
> 15 min	57	22.8
Muscular endurance		
1-5 pushups	124	49.6
6-10 pushups	49	19.6
11-15 pushups	37	14.8
15< pushups	40	16.0
Muscle Strength		
5-10 kg	110	44.0
11-30 kg	70	28.0
31-50 kg	44	17.6
>50 kg	26	10.4
Speed		
slow pace	29	11.6
medium pace	122	48.8
fast pace	78	31.2
Very fast pace	21	8.4
Participation in sports		
Yes	169	67.6
No	81	32.4
Perceived Physical Fitness		
more fit	122	48.8
less fit	128	51.2
Determine what this change in physical fitness did to their study capabilities		
Diminished	64	25.6
Improved	68	27.2
No change	118	47.2
Percentage in last 5 tests		
<50%	22	8.8
51-60%	92	36.8
61-70%	82	32.8
71-80%	42	16.8
81<%	12	4.8
Percentage in last Professional		
<50%	1	0.4
51-60%	23	9.2
61-70%	92	36.8
71-80%	127	50.8
81<%	7	2.8

surprised to see that the frequencies were cut down the middle with 122(48.8%) considering themselves to be more fit at the time they were questioned and 128(51.2%) considered themselves to be less fit than they previously were. We attempted to determine what this change in physical fitness did to their study capabilities and found that 64(25.6%) considered that their study capabilities had dimi-nished, 68(27.2%) reported that their study capabi-lities had improved and 118(47.2%) had no change in their study capabilities. In an attempt to assess their present academic performance we inquired as to how well they did in their previous professional examination and recent class tests. We found out that 22(8.8%) individuals averaged less that 50% in their last 5 class tests, 92(36.8%) reported that they averaged 50-60% in their last 5 class tests, 82(32.8%) reported that they had an average in the range 61-70% in their last 5 class tests, 42(16.8%) individuals reported to have secured an average of 71-80% in their last 5 class tests and only 12(4.8%) individuals had a score above 80% in their last 5 class tests. When the question about the marks that they attained in their previous professional examination arose, only 1(0.4%) individual reported that he secured less than 50%, 23(9.2%) reported to obtain marks in the 50-60% range, 92(36.8%) reported that they obtained marks in 61-70% range, 127(50.8%) individuals reported that they had secured marks in the 71-80% range and only 7(2.8%) secured marks above 80%.

Table 2: *Comparsion Between Cumulative Physical Activity (CPA) And Cumulative Academic Performance (CAP)*

Cumulative Physical Activity (CPA)	CUMULATIVE ACADEMIC PERFORMANCE (CAP)			Total	
	Poor (0-4)	Average (5-7)	Good (8-10)		X^2=6.664 P=.155
Poor(0-6)	3 (10.3%)	21 (72.4%)	5 (17.2%)	29	
Average (6-13)	19 (11%)	107 (62.2%)	46 (26.7%)	172	
Good (14-24)	7 (14.2%)	37 (75.5%)	5 (10.2%)	49	
Total	29	165	56	250	

DISCUSSION

The complexity of the physical activity and fitness relationship makes it an arduous task to specify possible mechanisms. Generally, physical activity can improve physical fitness particularly when long standing attitudes target increased fitness. The results of a study conducted by The University of Cincinnati,[14] stated that no definite correlation exists between physical activity and the physical fitness of students.

Furthermore, the medical students think highly of their own physical health[14,21]. This is in contrast to what we have recorded during our course of the research, in which we observed that 122(48.8%) considered themselves to be more fit at the time they were before their admission in the medical college, while 128(51.2%) considered themselves to be less fit than they previously were.

In a study conducted by the University of British Columbia on the exercise behavior and attitudes among 4th year medical students,[22] 64% of the 4th year students met the CSEP guidelines of the minimum of exercise required to be classified as moderate to vigorous activity per week, and 73% of the students met the previous standards established in 1998. This is in contrast to what we observed among the 4th year students of AIMC, 29(11.6%) individuals had poor physical fitness, 172(68.8%) had average physical fitness and 49(19.6%) individuals had good physical fitness, from the total of 250 correspondents.

After the analysis of the data collected, we tried to create a correlation between the Cumulative Physical Activity (CPA) and the Cumulative Academic Performance (CAP) (TABLE#23), out of the individuals with poor cumulative physical activity 3(10.34 %) had poor academic performance; there were 21(72.41%) with average academic performance and 5(17.24%) had good academic performance. The individuals with average cumulative physical activity had 19(11.04%) that had poor academic performance; there were 107(62.20%) that had average academic performance and 46(26.74%) had

good academic performance. The individuals with good cumulative physical activity had 7(14.29%) that had poor academic performance; there were 37(75.51%) with average academic performance and 5(10.20%) had good academic performance. We found that those individuals having average physical fitness were academically superior to those who fell on the extremes of the physical fitness spectrum.

Individuals with poor and good physical fitness followed similar trends in relation to academic performance. This is somewhat related to a research conducted the University of Illinois,[23] according to which there was a direct and exponential relationship between academic achievements and total fitness, with results dictating that those with greater physical fitness levels scored better across the board (Total achievements, reading, mathematics).

Another article[24] further corroborates the research conducted by the University of Illinois (previously cited), by proving that there is a positive association between academic achievements in most of the academic subjects and majority of health related physical fitness components.

The discrepancy between our findings and those in the articles cited maybe due to a myriad of reason. First of all, the students who gave better thought to their physical fitness and had a good cumulative physical performance, gave no time to their studies, and hence couldn't perform well. Unfortunately, our study was not able to eliminate the possibility of the student's attitudes towards both physical fitness and academic performance. There were no questions formulated to measure a student's motivation towards their academics or physical fitness. Students who excel in school and immerse themselves in the school experience, maybe more likely to exert more effort on physical fitness and academic tests. Laboratory procedures such as VO2 max remain more valid measures of aerobic fitness. Voluntary participation and the timing at which our research was conducted might have been one of the reasons for the discrepancy in the results. A social desirability bias maybe manifested as a result of self-report surveys. All the participants were from the same medical college, so generalizing the results is not possible. Certain factors that affect physical fitness and may affect academic performance such as smoking, alcohol consumption and other such behaviors were not taken into consideration.

CONCLUSION

The conclusion of my study is:

- The physical fitness of most of the medical students in the study was of an average level.
- We found that those individuals having average physical fitness were academically superior to those who fell on the extremes of the physical fitness spectrum.
- Individuals with poor and good physical fitness followed similar trends in relation to academic performance.

RECOMMENDATIONS

- Medical students should be offered programs that provide an environment to enable them to achieve the recommended amount of PA per week.
- Curriculums should be designed in such a manner that they integrate PA into its core and further propagate the positive message of bringing PA from the Future Doctor to the patient.

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BURNOUT IN JUNIOR DOCTORS AND ITS IMPACT ON PATIENT CARE

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How to cite: Imran N, Najeeb N, Mughal F, Gillani Z, Asif A. Burnout in junior doctors and its impact on patient are. JAIMC. 2020; 18(4): 738-43.

Abstract

Objectives: To determine the prevalence of burnout among junior doctors and how does it affect the patient care.

Methodology: After institutional ethical approval and informed consent, data was collected by a self-administered questionnaire including demographic information, Maslach Burnout Inventory (MBI), measuring ddepersonalization (DP), emotional exhaustion (EE) and personal achievement (PA), and questions about patient care practices and attitudes as well as depression. Statistical analysis was conducted using SPSS 22. Descriptive statistics was done and T-test was applied to determine the significant relationship between burnout and suboptimal patients care practice. P<0.05) was considered as statistically significant.

Results: Two hundred sixty six junior doctors participated in this study with 139 (52.3%) being males. A significant proportion of our participants (58.3%) met the criteria of burnout. No significant differences among gender, age, working position, marital status in our sample. Participants who met the criteria of burnout reported more with sub-optimal patients care practices and attitudes. Indifference towards demise of patients and hectic routine leading to discharging patients quickly were mostly affected by burnout. More than 50% responded yes to statement that they were feeling depressed and bothered by little interest in doing things.

Conclusion: There is urgent need for interventions to address burnout to reduce the adverse impact of burnout on physician personal, professional life as well as on patient care.

Keywords: Burnout; Junior doctor; Patient care; attitudes; practices

After passing the medical school a large proportion of graduates experience a feeling of indisposition when faced with the stressful work environment of a clinical setting which has become a fundamental to this field of science. Juggling the management of critically unwell patients alongside a nerve racking and taxing amount of work. It is expected that some of them will endure mental stress that decreases their utility and gives them a feeling of discontent-ment regarding their personal and professional pre-set goals.[1] The job of a junior doctor is hence, inherently stressful. Combine this with a towering level of responsibilities, unclear role descriptions and a meager freedom of decision making, it is not surpri-sing that the junior doctors are always at the risk of burnout.[2] Pines and Maslach's 3 defines burnout as; ''a syndrome of emotional exhaustion involving the development of a negative self-concept , negative job attitudes and loss of concern and feeling for clients. Burnout is denoted by depersonalization (DP), emotional exhaustion (EE) and a feeling of decreased personal

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Submission Date: 11-08-2020
1st Revision Date: 23-09-2020
Acceptance Date: 28-09-2020

achievements (PA) that causes a certain decline in professional efficacy.[4]

Physician languor is a global problem. The continuous existence and propagation of burnout among junior doctors has been surprisingly increasing with reported prevalence range from 25-76 percent.[5,6] It has been associated with delayed clinical judgements and increasing iatrogenesis.[7] Hence, tackling this problem is of elemental importance, as it not only has declining effects on the quality of life of junior doctors, but also pessimistic for the safety of patients and the results of a hospital stay.[8,9] As McCue[10] puts it, "it is unlikely that optimal medical care can be delivered by unhappy or maladapted physicians". Prompt interception of this issue is essential to save the quality of provided clinical care and the integrity of doctor-patient relationship.

The objective of current study is to document the prevalence of burnout in junior doctors of a tertiary care University teaching Hospital, Lahore and explore its consequences on patients' care.

METHODOLOGY

This cross-sectional descriptive study was conducted in different departments of Mayo Hospital Lahore Pakistan, from February to April, 2020. The sample size of 266 doctors was estimated by using a 95% confidence level, 5% absolute precision with an expected percentage of burnout among doctors as 70%.[11] Participation in this research was voluntary, responses and information obtained were kept confidential.

Inclusion criteria included junior doctors (House officers, Medical officers, Postgraduate residents working in surgery, medicine, allied medicine and allied surgery departments), while doctors who have completed their training or senior doctors were excluded. After institutional ethical approval, informed written consent and confidentiality assurance ,data was collected by a self administered questionnaire. All participants completed demographic information.

Maslach burnout inventory questionnaire (MBI) was utilized to quantify the burnout in junior doctors, (MBI) is an self-examining psychological tool consisting of 22 items linked to occupational burnout with response option from 0 (Never) to 6 (Daily).[4] The MBI computes three facets of burnout: Emotional Exhaustion (9 items), Depersonalization (5 items) and Personal Accomplishment (8items). On the basis of total score in each dimension person is classified to have: Emotional Exhaustion (9 items): Low burnout (0-16) , moderate burnout (17-26) , high burnout (≥27).Depersonalization (5 items) :low burnout (0-7) , moderate burnout (8-12) , high burnout (≥13). Personal Accomplishment (8 items): burnout (≥ 39) , high burnout (0-31). Impact on patient care was calculated by a an appraisal developed and used by Shanafelt et al which was self-administered in nature.[12] This contained eight statements describing practices (five items) and attitudes toward patient medical care (three items). Response options for each question were 1=never; 2 = once a year; 3= several times a year; 4= once a month; 5=once a week.

The last part of the questionnaire included the PRIME-MD questions to assess current depression.[13] It consist of two questions and a positive answer to either of these is defined as current depression. Statistical analysis was conducted using SPSS 22. Descriptive statistics were applied on categorical and numerical variables and data was stratified for gender, marital status, designation and MBI scores. T-test was applied to determine the significant relationship between burnout and suboptimal patients care practice ($p<0.05$).

RESULTS

Total of 266 doctors participated in this study with 139 (52.3%) being males. Majority of our participants were doing housejob or in first and second year of their residency (Table 1). The burnout frequency was calculated by taking into account the cut off values of three subscales of MBI i.e emotional exhaustion EE ≥27, depersonalization DP ≥10

and personal accomplishment PA ≤ 10. We defined burnout as high score in EE and DP. According to our study, 58.3% of our participants met the criteria of burnout. The prevalence varied across all three subscales. The frequency of occurrence of burnout on its three subscales is shown in Table 2. Approximately 75% of participants had high emotional exhaustion and 66% had high depersonalization (Table 2). The T-test revealed no significant differences among gender, age, working position, marital status in our sample.

Participants who met the criteria of burnout reported more with sub-optimal patients care practices and attitudes. The most frequent element on self-reported sub-optimal patient care was, discharging patients due to work load. Indifference towards demise of patients and hectic routine leading to discharging patients quickly were mostly affected by burnout (Table 3). More than 50% responded yes to statement that they were feeling depressed and bothered by little interest in doing things.

Table 1: Demographic Data of the Responding Residents

Variable	Participants n (%)
Total Respondents	266
Age	
21-25	91 (34.2)
26-30	136 (51.2)
31-35	19 (7.2)
36+	16 (6.2)
Gender	
Male	139 (52.3)
Female	127 (47.7)
Marital Status	
Single	163 (61.3)
Married	101 (38)
Other	2 (0.8)
Respondents Level	
House Officer	108 (40.6)
Medical Officer	16 (6)
PG 1	62 (23.3)
PG 2	41 (15.4)
PG 3	23 (8.6)
PG 4	14 (5.3)
Department	
Medicine	78 (29.3)
Medicine Allied	73 (27.5)
Surgery	56 (21.1)
Surgery Allied	59 (22.1)

DISCUSSION

Medical profession is a highly demanding, stressful and taxing field, where the majority of arduous workload falls on the junior doctors in addition to the volatile amalgamation of issues leading to physical as well as emotional burnout and decline in health care provision. Our research helps in finding out the pervasiveness of burnout in junior doctor and its effects on the provision of health care in a tertiary care hospital in a developing country.

Table 2: Frequency and Level of Burnout Subscales (n=266)

Subscale	Frequency n (%)
Emotional exhaustion (nine items, mean score 33.34, SD 10.759)	
Low Burnout (0-16)	22 (8.3)
Moderate Burnout (17-26)	45 (16.9)
High Burnout (⩾27)	199 (74.8)
Depersonalization (five items, mean score 15.19, SD 6.449)	
Low Burnout (0-7)	36 (13.5)
Moderate Burnout (8-12)	54 (20.3)
High Burnout (⩾13)	176 (66.2)
Personal accomplishment (eight items, mean score 33.92, SD 7.319)	
Low Burnout (⩾39)	82 (30.8)
Moderate Burnout (32-38)	96 (36.1)
High Burnout (0-31)	88 (33.1)

The result of our study showed that burnout is prevalent among junior doctors with a frequency of 58.3% , which is comparable to prevalence reported in studies from different parts of the world.[6,11,12,14] Respondents in our study had highest frequency in MBI subscale Emotional Exhaustion (75%) and Depersonalization (66%) while Personal Accomplishment remained unaffected. Similar trend was noted in a study from Saudi Arabia.[11] This can be explained by the fact that being a doctor in traditional societies like Pakistan and Saudi Arabia, is considered a source of pride to the family, and is also

Table 3: *Self-Reported Suboptimal Patient Care Practices and Attitudes*

Variable	Percentage n (%)	Burnout Respondents (%)	Non-Burnout Respondents (%)	p value
Self-reported suboptimal patient care practiced at least monthly				
I found myself discharging patients to make services manageable because the team was too busy	101 (38)	61 (23)	40 (15)	0.026*
I did not fully discuss treatment options or answer the patient's question	70 (26.3)	50 (18.8)	20 (7.5)	0.000**
I made treatment or medication errors that were not the result of a lack of knowledge or inexperience	47 (17.7)	36 (13.5)	11 (4.2)	0.000**
I ordered restraints or medications for an agitated patient without evaluating him or her	48 (18)	40 (15.1)	8 (3.1)	0.000**
I did not perform diagnostic test because of a desire to discharge the patient	45 (17)	40 (15.1)	5 (1.9)	0.000**
Self-reported suboptimal patient care attitudes at least monthly				
I paid little attention to the social or personal impact of an illness on a patient	71 (26.6)	56 (21.1)	15 (5.7)	0.000**
I had little emotional reaction to the death of one of my patient	90 (33.8)	63 (23.7)	27 (10.1)	0.001**
I feel guilty about how I treated a patient inadequately	82 (30.8)	57 (21.4)	25 (9.4)	0.000**

*P.value<.05. **p-value<.001

preferred for marriages; these sociocultural factors may sustain the Personal Accomplishment.[11] Our study didn't show any significant relation between burnout and age which is different from literature in which age was noted to be one of the risk factors.[15,16] Supplemental research is required to pin point the causes of this discovery. Residents of Internal Medicine had most burnout (29%) in our study which is also highlighted as at risk specialty, alongside Gynaecology & Obstetrics and Emergency Medicine.[6] Also of concern was very high proportion of burnout doctors in our study being house officers, emphasizing that well-being measures and self-care need to be emphasized to junior doctors, very early in beginning of practical life.

Burnout has significant impact on patient care.[12] We also found that high frequency of suboptimal care practiced and attitudes among Burnout doctors. 38% of doctors reported discharging the patients to reduce the workload, out of which 23% met the criteria of burnout. This is despite the fact that our response were based on self-report and biased reporting remains a possibility. According to previous studies done, burnout in physician develop at any stage of training,[17,18] and has been linked to their dissatisfaction[17,19] and turnover.[20] Many researches have been carried out which linked burnout to medical errors. Physicians suffering from burnout syndrome reported more with making errors in their clinical practices. Many patients suffer due to physician burnout around the globe. According to report in BMJ, after heart disease and cancer, medical error is the 3rd leading cause of death. An analysis of 2974 malpractice complaints in Canada found that most were about harms caused by doctor's error.[21] Most common error made by a physician in work place is misdiagnosis which leads to maltreatment or delayed treatment of a patient and missing any co-morbidity. Next one is the medication error, i.e. prescribing wrong drug, giving improper dose or incorrect mode of administration. Physicians having burnout syndrome in our study reported more with maltreatment of patients and medication error.

Burnout can elicit grave personal and professional repercussions if left untreated. Personal impairment can be classified into two groups: Corporeal and Mental. They can appear as symptoms ranging from mild to severe. Burnout leads to

impairment of physician who can complain of feeling weary, drained, fed up, distracted and bad-tempered. It can also increase the possibility of any medical accident. Psychologically, a drained out physician is at a higher risk of elevated stress levels, mood disorders and impulsive behavior. The presence of any of these symptoms can lead to impairment in physicians' personal life and competency at work, which may lead to substance abuse. Doctor are also at increased risk of suicide (28-40 per 100,000) as compare to general population (12.3 per 100,000).[22] Professional consequences of burnout physicians are the failure of interpersonal relationships, more risk of iatrogenesis, medical errors and negligence, decreased patient satisfaction, quality of care provided and results of medical consultations and managements. The most potent indicator of burnout is, behavioral and psychological effect on physician personal and professional life.

CONCLUSION

Hospital management should take definite steps towards addressing the obstacles faced by junior doctors leading to burnout, proposing solu-tions and assessing their effectiveness. Surveys should be conducted timely to measure physical, emotional and mental exhaustion of doctors. The management and seniors collectively can help in reducing the load of administrative duties on an over-worked physician. Working hours should be reduced. Timely breaks and day off should be planned. In addition to this, doctors may engage themselves into relaxing activities like yoga, medi-tation, walk etc. Confidential psychological support services and well- being measures should be supported by Institutions. All these can help doctors well- being and can increase their work output.

Limitations

Our study does have a number of short comings. It is a single institution study. Very few doctors responded from Gynecology and Obstetrics and Emergency departments, the specialties linked with highest burnout risk. We also did not perform a thorough survey regarding depression. Suboptimal care practices and behaviors were self-reported and may not necessarily reflect factual frequency of these attitudes. Despite these limitations, study has thrown light upon the continued high-level presence of burnout among junior doctors in tertiary care hospital settings and urgent need to address it to minimize personal and professional consequences.

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ROLE OF DIRECT ACTING ANTIVIRAL IN ATHEROSCLEROSIS REDUCTION AFTER HCV ERADICATION IN CIRRHOTIC PATIENTS

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How to cite: Maqsood M, Ejaz U, Maqbool KT, Shahzad A, Khalid M, Yameen M. Role of direct acting antiviral in atherosclerosis reduction after HCV eradication in cirrhotic patients. JAIMC. 2020; 18(4): 744-52.

Abstract

Background: Recently after arrival of direct acting antiviral therapy(DAA), it has been documented sustained virological response(SVR) improves mortality in patients with cirrhosis and also improve cardiovascular risk factors but the direct impact of SVR on atherosclerosis is unclear.

Objective: To evaluate role of Direct Acting Antiviral in Atherosclerosis reduction after HCV eradication in cirrhotic patients

Methodology: Total 218 patients consecutively enrolled with HCV related liver fibrosis or compensated cirrhosis from 2016 to 2018 in Lahore General Hospital, Lahore. All patients were treated with directly acting antiviral according to EASL guidelines. All patient's demographic profile, clinical and biochemical parameter at baseline and after 12 month follow up recorded. Inter media thickness(IMT), Carotid thickness (IMT more than 1mm) and carotid plaque (focal lesion more than 1.5mm) at level of common carotid arteries were assessed by Doppler ultrasound at baseline and 12 months after DAA.

Results: Out of 218 patients 56.9% were male, mean age was 61 ± 7.9 years and 71.1% had compensated cirrhosis,22% patients had diabetes mellitus(DM), 42.7% had hypertension(HTN),32.6% were smoker and 14.3% were obese. All patients achieved sustained virological response(SVR). Baseline IMT was 0.89±12, carotid thickness was seen in 40.4% patients and carotid plaque in 43% patients. Post treatment at 12 follow up IMT significantly reduced 0.77 ±0.11, Carotid thickness 17% vs 40.4%. Carotid plaque 32.6% not reduced. No significant changes were seen among cohort of obese patients. All results were confirmed according to sub group and stratified in respect to liver fibrosis and cardiovascular (CV) risk factor.

Conclusion: HCV eradication by DAA significantly reduced atherosclerosis in carotid artery in patients with fibrosis of liver with or without other cardiovascular risk factors. These findings indirectly prove HCV is independent risk factor for atherosclerosis and all patients with cardiovascular events should undergo HCV screening.

Key Words: HCV, DAA, SVR, atherosclerosis

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Submission Date: 27-07-2020
1st Revision Date: 11-09-2020
Acceptance Date: 24-09-2020

Hepatitis C Virus (HCV) is prevalent in Pakistan and 6% population is chronically infected[1] worldwide 1% population is suffering with HCV[2] and it's not only responsible of liver disease but also put a large burden of morbidity and mortality due to systemic and extrahepatic diseases.[3] It's related to numeral of extrahepatic manifestations which are strong indication for treatment regardless of liver disease[4] Younossi et al. published a meta-analysis during which documented HCV infection increases the risk of immune modulation that causes develop-

ment of cryoglobulinemia, B cell lymphoma, insulin resistance and metabolic derangement more frequently as compared to patients without infection[5] These observations are confirmed experimentally as data has confirmed improvement of extrahepatic manifestations after HCV eradication either with direct acting antiviral therapy or interferon (IFN) based regimens.[4] Chronic hepatitis C (CHC) is associated with atherosclerosis of carotid artery[6-8], coronary artery atherosclerosis and myocardial injury.[9-11] It also increases risk of stroke[12], cardiovascular events and cardiovascular related mortality.[13,14] A meta-analysis of HCV and its association with cardiovascular risk documented high mortality.[15] Available data documented that eradication of HCV with interferon and ribavirin reduce cardiovascular risk.[14,16-21]Since the arrival of DAA even with advance fibrosis sustained virological response(SVR) is still 93%[22] Recently, a couple of trials published with encouraging data regarding reduction of atherosclerosis of carotid artery after DAA[23] and conditions promoting atherosclerosis and insulin resistance[24] Since the advent of DAA and its use in HCV infection is safe and effective, high rate of SVR giving the opportunity to evaluate the extra hepatic manifestations related to HCV infection.[25] Limited data is available regarding reduction of atherosclerosis risk in advance disease with fibrosis after DAA in HCV infected patients. On the basis of these observations we assumed that SVR by DAA reduced atherosclerosis related cardiovascular events hence, decreased coronary artery disease and ischemic stroke risk. A retrospective data published by Butt A.A et al. 2019, stated that SVR is associated with reduced cardiovascular risk.[26] It was retrospective data but included 96% male patients that exhibit limit of this study. During this trial we would like to analyze the reduction of atherosclerosis of carotid artery among patients with advance hepatic fibrosis who sustained virological response after DAA. The objective of the study was to evaluate role of Direct Acting Antiviral in Atherosclerosis reduction after HCV eradication in cirrhotic patients

METHODOLOGY

Prospective study conducted in Lahore General Hospital, Lahore Pakistan a tertiary care hospital. All participants were enrolled after informed written consent. Trial was approved from ethical committee of institution. Participants included achieved SVR and post treatment minimum one year. Patient started DAA Dec 2016 and July 2018. All patients consecutively enrolled in study fulfil the inclusion and exclusion criteria. Inclusion criteria included, 1) All Patients had advance fibrosis or compensated cirrhosis secondary to HCV, 2). They received directly acting antiviral therapy (sofosbuvir, daclatasavir and ribavirin). Advance fibrosis was confirmed by the measurement of hepatic stiffness by Fibro Scan (>10 0r <12kPa) or compensated cirrhosis confirmed by esophageal varices. Exclusion criteria,1) decompensated cirrhosis (Child Paugh B, C), 2) Hepatocellular carcinoma,3) Fibrosis other than HCV (Wilson disease, autoimmune hepatitis), 4) Heavy alcohol ingestion(>25G/day), 5) History of immunosuppressant, 6) HIV infection,7) IV drug addict,8) Prior history of stroke or coronary artery disease,9) Patients on statin or antiplatelets.10) Previously had been taken interferon therapy. Control group included those patients who were not on DAA, either waiting for therapy or refused to take.

Demographic profile and relevant clinical data was collected before and after 9 to 12 month of antiviral. BMI more than 30 defined obese, Blood pressure more than 130/85 defined hypertension (HTN), diagnosis of diabetes made on basis of American Diabetes Association, previously diagnosed case of Diabetes current treatment oral Hypoglycemic or insulin noted. At the time of enrollment blood sample (12 hour fasting) collected for, ALT, cholesterol, platelets and blood sugar level. HCV RNA determined by real time PCR.

Carotid atherosclerosis was evaluated before treatment and 9 to 12 months after treatment by an expert radiologist who was unaware of treatment using B-mode high resolution ultrasound with linear probe. Control population who did not receive treat-

ment also undergo Carotid scan. Same ultrasound specialist perform baseline and follow up scan. Carotid arteries of both sides evaluated at level of common, bulb and internal carotid in all patients. The carotid thickening IMT was estimated as the distinction between the intima lumen and media adventitia interface on the common carotid artery, plaque was measured 10 mm below their bifurcation with including 10 mm of bifurcation. For each participant,[3] measurements done in both sides, i.e. anterior, posterior and lateral wall. Maximum reading of IMT was considered. IMT was defines as 1mm or more. Carotid plaque was defined as 1.5mm or more at common carotid artery level. Estimation of IMT is right now utilized as intermediate result in clinical trial. Studies examining reproducibility of IMT estimations announced that fluctuation is most minimal while deciding the mean thickness in the common carotid artery[27] that the reproducibility of IMT estimations in the common carotid artery route is consistent even in patients with increased artery wall thickness[28] and that assessments by individual sonographers in multicenter considers is possible with a good interobserver understanding.[29-32] Regarding the clinical importance of IMT estimations, an expanded IMT is documented indicator of risk estimation coronary artery disease and stroke, the two common risk factor of cardiovascular mortality[32] likewise giving extra prognostic data to that of regular hazard factors]. Right now, an IMT≥1 mm has been related with a higher risk of cardiovascular incidence[33,34]. During this trial we would like analyze the reduction of atherosclerosis of carotid artery among patients with advance hepatic fibrosis who sustained virological response after DAA.

Continuous variable was summarized as mean and SD, categorical variables as frequency. Chi square or student's t test used to analyze where appropriate. Baseline IMT and delta IMT (12 months after treatment by DAA) relationship with biochemical and clinical variables were measured by multiple linear regression models. Multiple logistic regression models were used to measure the relationship between IMT, Carotid plaques laboratory and clinical variable in HCV infected patients where p value less than 0.05. Post treatment biochemical variable analyzed with dependent variable i.e. carotid thickening. Analysis were performed on SPSS Ver:21.0.

RESULTS

Baseline characteristics of 218 patients depicted table 1. Out of 218 patients 56.9% were male and mean age was 61 years. Compensated cirrhosis was 71.1% patients. DM was present in 22 % patients, 14.2% patients had obesity (BMI more than 30) and HTN 42.7% patients. Platelets less than 100000 cmm in 20% patients. All patients were treated with sofosbuvir 400mg plus dacltasavir 60mg and ribavirin for 3 months and sofosbuvir plus dacltasavir for 6 months according to EASL guidelines. All patients achieved SVR.

Mean IMT was 0.89±0.12, Carotid thickening was seen in 40.4% and carotid plaque 43.1%.

Table 1: *Baseline Characteristics (n= 218)*

Age	**61.069± 7.99**
Gender	
Male	124 (56.9%)
Female	94 (43.1%)
Comorbid	
Hypertension	93 (42.7%)
Smoking	71 (32.6%)
Cirrhosis	155 (71.1%)
DM	48 (22%)
ALT	67.8 ±22.03
Blood Glucose	102.63 ±18.46
Cholestrol	164.68 ±27.72
BMI	26.2 ±3.56
Platelet Count	179.94 ±47.4

Values are presented in n(%) and mean ±Standard deviation

Carotid stenosis more than 60 % not seen in any patient. Both carotid thickening and carotid plaque were seen more in older age patients, DM and lower platelet count. When analyzing low platelet with final outcome as carotid plaque p less than 0.003, (OR 1.00, 95%CI 1.00 to 1.01 p=0.002), older age (OR 1.04, 95%CI 1.01 to 1.07, p=.003) confirmed independent risk factor at logistic regression

analysis.

Mean IMT significantly reduced from baseline to follow up at 12 month follow up after eradication

Table 2: *Changes from Baseline to follow up in IMT, Carotid Thickness & Carotid Plaque*

	Baseline	At follow-up	
IMT	0.89± 0.122	0.77± 0.119	
Carotid Thickness	88 (40.4%)	37 (17%)	<0.001
Carotid Plaque	94 (43.1%)	120 (55.3%)	<0.001

P value applied by paired t-test for IMT and chi-squared applied for Carotid thickness and Carotid Plaque

Mean Difference of IMT	P-value
0.12 ±0.05 (CI 95%: 0.11-0.13)	<0.001

P value applied by paired t-test for IMT

Table 3: *Subgroup Analysis - Changes from Baseline to follow up in IMT*

	IMT at Baseline	IMT at follow-up	P-value
<65 (n=112)	0.83 ±0.120	0.711 ±0.098	<0.001
Age ⩾ 65 (n=106)	0.94 ±0.09	0.82 ±0.11	<0.001
BMI ⩽ 30 (n=187)	0.89 ±0.112	0.76 ±0.12	<0.001
BMI>30 (n=31)	0.88 ±0.17	0.84 ±0.08	0.34
Smoking (n=147)	0.9077 ±0.11	0.81 ±0.13	<0.001
No Smoking (n=71)	0.88 ± 0.126	0.75 ±0.10	<0.001
Platelet <100,000 (n=20)	1.017 ±0.01	0.944 ±0.061	<0.001
Platelet >100,000 (n=198)	0.877 ±0.121	0.75 ±0.11	<0.001
No Hypertension (n=125)	0.911 ±0.13	0.78 ±0.11	<0.001
Hypertension (Yes) (n=93)	0.86 ±0.96	0.75 ±0.12	<0.001
No Diabetes (n=170)	0.87 ±0.12	0.76 ±0.10	<0.001
Diabetic Patient (n=48)	0.94 ±0.14	0.82 ±0.154	<0.001
Cirrhosis (No) (n=63)	0.934 ±0.125	0.82 ±0.13	<0.001
Cirrhosis (Yes) (n=155)	0.87 ±0.12	0.75 ±0.11	<0.001

P value applied by paired t-test for IMT

of HCV by DAA (from 0.89±0.122 to 0.77±0.11 p= 0.001), Carotid thickening also reduced from 40.7 % to 17 %, p<0.001. Carotid plaque didn't improve observed in 43.1% patients before therapy and 55.5% at 12 month follow up. We also observed blood glucose level reduction 102.6±18.46 to 90±18 p=0.001, ALT level 67.8±22.03 to 35.2± 21 p=0.01 and BMI 26.2±3.56 to 26.9±3.4 p=0.5 didn't change. Cholesterol level paradoxically increased from baseline to follow up (164.3 ± 27 to 175 p = 0.01). Trend of increasing cholesterol observed in both cirrhotic (155 ± 30 to 170 ± 28, p = 0.001), and non-cirrhotic (163 ± 29 to 178 ± 31, p = 0.01) patients. Platelet count increased from baseline to follow up (179.9 ± 47 to 192 ± 52, p = 0.01). Improvement of blood glucose was seen in both diabetic (133 ±19 to 95±29, p 0.001) and non-diabetic (97 ± 16 to 85.3 ± 18, p=0. 005), some patients requirement of insulin and oral Hypoglycemic also reduced. According to these results IMT and carotid thickening was confirmed when stratified according to risk factors and liver fibrosis and disease severity. IMT and carotid thickening improved in all group of patients younger or adult more than 65 years, smoker nonsmoker, with and without HTN, non-obese, diabetic and non-diabetic and with and without increased cholesterol. All results were shown table 2. Results were similar according to liver disease and fibrosis. Only obese patient didn't show improvement in IMT but thus group was very small.

DISCUSSION

To date available data suggested HCV infection increased risk of cardiovascular disease and atherosclerosis. It had been documented SVR achieved either spontaneously or after interferon based therapy It improved cardiovascular risk in compensated cirrhosis with advance fibrosis and decreased carotid thickening.[6-9,11-14,35] All risk factors and cirrhosis when individually stratified confirm the development of atherosclerosis. We found SVR with antiviral significantly reduced atherosclerosis and cardiovascular events[10,17,19-21] so far few trials available during which documented DAA in HCV infected patients decreased cardiovascular events. Naho et al. documented HCV virus eradication by direct antiviral follow over the period of 5 years observed reduction of major extra hepatic complications cardiovascular outcome and also reduced mortality in patient with compensated cirrhosis with Child Pugh A classification. But in this study there's no discrimination between acting antiviral therapy or interferon therapy. These observations were similar to our results[19] Singer et al. which was unpublished trial documented SVR reduce cerebrovascular and cardiovascular diseases after adjustment of risk factor age, gender, Hypertension, DM and co-morbidities. This was

retrospective study[21] During this current trial HCV infected cohort included 40% population Age above 65 year and significant study population had cardiovascular risk factors. As already documented platelet and age were risk factor for atherosclerosis[8] we found carotid thickness atherosclerosis improved with or without risk factor of cardiovascular diseases like DM, hypertension, smoking platelet count and old age. we didn't find improvement of carotid atherosclerosis among patients with obesity. Adinofli et al. recently published a data, during this trial 48% patients were male, BMI 25.9, diabetes 18%, 44% hypertension, 13% patients had over 200 mg cholesterol. In this trial mentioned that cardiovascular risk reduced 2 to 3.5 time after HCV eradication by DAA as compare to untreated patients. The risk of cardiovascular events reduced irrespective of liver fibrosis. According to this study cardiovascular risk reduced 43% after DAA and 22% after IFN therapy, hence eradication of HCV not only improved liver disease but also decreases morbidity due to cardiovascular events i.e. Coronary artery disease, stroke or TIA. Moreover, CV risk decreased 56 to 75-year population and every 55 cases one case reduced if 10000 HCV infected cases treated by DAA. Data also proved that HCV infection indirectly related to cardiovascular diseases independently as other risk factors i.e. HTN, DM, smoking, obesity and male gender. Some risk factors especially pro atherogenic risk factors BMI and cholesterol increased, in addition to growing age but despite of all, overall reduction of CV risk observed average 68%. Long term follow up may cancel the beneficial effect of HCV eradication in term if CV risk reduction actors because of above mentioned risk factors. It is necessary to warn the patients after SVR not gain the weight and frequently check lipid profile, as both are the modifiable risk factor.[36] These results and outcome were almost like our results. Pro atherogenic risk factors were improved after DAA and data also suggested some inflammatory marker and cytokine improved after eradication of HCV[37] SVR achieved patients insulin resistance significantly improved and documented 76% reduction of insulin resistance[24] and improve glucose metabolism. It had been also documented risk of DM reduced after achieving SVR by DAA.[38]

HCV patients treated with Interferon and achieved SVR had documented significant reduction of risk of coronary artery disease and stroke.[16,17] In a prospective trial mentioned by Gargnani et al. HCV eradication by DAA or interferon based therapy reduced cardiovascular events. This trial done in Cumulative fashion not assessed the therapeutic dose[39]. In our trial prospectively DAA evaluated. Petta et al published a data in which documented role of DAA in HCV infected patients in atherosclerosis reduction. Petta et al documented atherosclerosis more prevalent among patients of HCV who have cardio metabolic risk factor especially DM and hypertension. In this trial half of cohort was more than 65 years, 2/3 patients were compensated cirrhosis and advance fibrosis. In study population significant proportion of patients were positive with cardiovascular risk factors, DM 20% patients, HTN 42%, smoking 34%, obesity 14% and hypocholesteremia 23In this study evaluated the impact of eradication of HCV by DAA on carotid atherosclerosis and stratified the risk factors of cardiovascular diseases. DAA significantly improve IMT and carotid thickening in all patients with or without risk factors, but SVR had no effect on carotid plaque. SVR after DAA independently had impact on atherosclerosis regardless of fibrosis vs cirrhosis or lower vs higher platelets counts. Only small group of patients with obesity didn't improve atherosclerosis and carotid thickness. Regarding glucose metabolism, mean glucose also decreased in serum but cholesterol level elevated.[23] These observations were similar to our results. Previously published data on cohort of HCV patients also consisted with these findings who were treated with interferon or DAA[40-43] and this mechanism explained as HCV had interaction at cellular level and impaired glucose and lipid metabolism[44]. IMT improved after eradication but we didn't found any relation of HCV infection with

carotid plaque. The rationale behind this might be short term effect of inflammatory and fibrogenic mediators related to HCV infection more sensitive in short term in IMT as compared to stable plaque.in fact HCV increase cardiovascular risk by increasing insulin resistance[45], by activating systemic inflammatory response via TH1 and NK mediated response[46] increased TNF and IL 6[47,48], decreased adiponectin [49] and HCV infection directly damage endothelium.[50,51] However, we could not exclude SVR effect on carotid plaque long term follow up. Our trial did not evaluate the mechanism involved in reduction of cardiovascular risk after SVR by DAA. Trial documented that it improved atherosclerosis and proatherogenic metabolic, immunologic and inflammatory pathways and therefore it reduced cardiovascular incidence.[24,37,52] Most likely inflammation may be a purposed mechanism. Our data, although small sample suggested significant reduction of IMT and carotid thickness. In the same line a trial published suggesting that an anti-inflammatory treatment cankinumab, colchicine or flu vaccine significantly reduce cardiovascular risk and support this postulated mechanism of inflammation.[53-55]

In our study there was some limitation, it had been single center trial consisting of small sample size. All patients had right of treatment as consistent with WHO goal till 2030 eradication of HCV, there were a limited number of controls. We followed up to 1 year after treatment hence, long run data of cardiovascular events after HCV eradication was lacking.

CONCLUSION

In conclusion data from our study showed that SVR by DAA significantly reduced atherosclerosis. Since 2015 it had been documented 71 million people throughout worldwide suffering with HCV and it has been mentioned that 1.5 million disability adjusted life years (DALY) from cardiovascular diseases are to be related to HCV infection.[56] These results indirectly proved that HCV is an independent risk factor of atherosclerosis and all patients should be screened with any atherosclerosis related event i.e. stroke or coronary artery disease.

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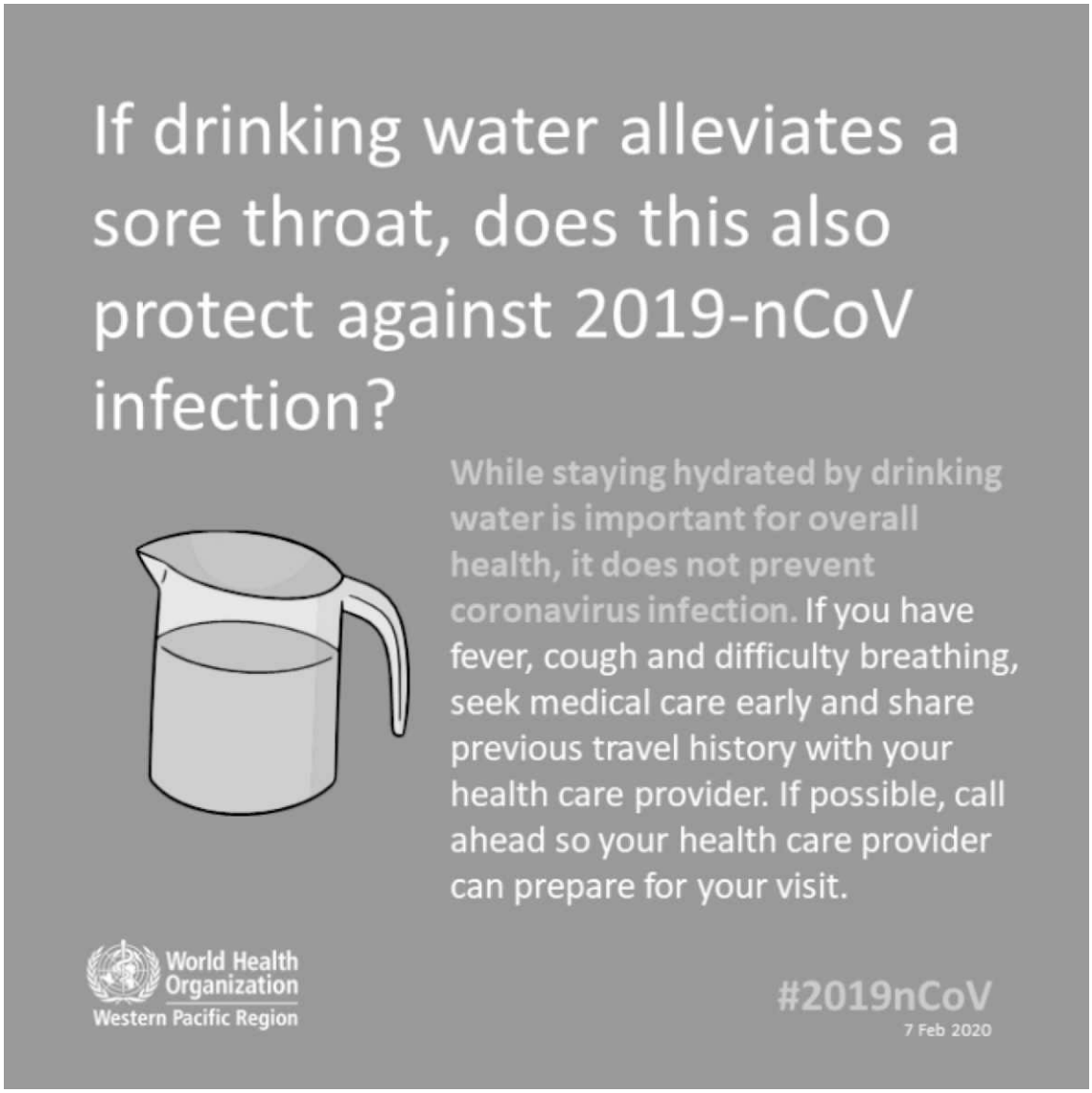

ROLE OF ENFORCEMENT OF TRAFFIC LAWS IN PREVENTION OF ROAD TRAFFIC ACCIDENTS IN LAHORE: A COMPARATIVE CROSS-SECTIONAL STUDY

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How to cite: Salman F, Asif S, Atiq S, Salman S, Gillani SYR, Naseer R. Role of enforcement of traffic laws in prevention of road traffic accidents in Lahore: a comparative cross-sectional study. JAIMC. 2020; 18(4): 753-58.

Abstract

Background: Enforcement can be an important tool to control accidents and reduce both morbidity & mortality. Recently Enforcement in form of helmet/seat belt rule, speed cameras, E-challan has been introduced in city of Lahore.

Objective: To determine the effect of enforcement of traffic laws in prevention of road traffic accidents in Lahore.

Methodology: This is a comparative cross-sectional study conducted in the city of Lahore. Data was collected from Rescue 1122 at a single time for two periods before Enforcement from 24-9-2017 to 11-2-2018 (Group A) and after Enforcement from 24-9-2018 to 11-2-2019 (Group B) through record based consecutive sampling. Data was analyzed and compared using software Epi info.

Results: Total number of RTAs before Enforcement was 27,413 while after Enforcement from was 30,562, a net increase in accidents. Most of the victims above 80% in both groups were male and most accidents occurred between 21-40 years of age. However, deaths in Group A were 197 while they were significantly reduced in Group B to 100, also the proportion of Alive and Stable victims increased from 47.3% (Group A) to 59.8% in Group B. As regards the compliance to Enforcement, over speeding proportion was high whereas one wheeling proportion was low in Group B compared to Group A.

Conclusion: Enforcement of traffic laws resulted in marked reduction of one wheeling, severity of injury and number of deaths.

Keywords: RTAs, Enforcement, Outcome of Injuries, Compliance, E-Challan.

Road Traffic Accidents (RTAs) are one of the health issues that utilize a major portion of emergency medical services worldwide. An estimated 1.35 million people die annually of RTAs and a major portion of this occur in developing countries largely borne by pedestrians, cyclists and motorcyclists.[1] Pakistan being a developing country also faces the world's ninth leading cause of death (RTAs), and according to a report 25,781 people died in year 2013 in the country.[2]

There are various risk factors leading to RTAs and traffic violations is among them. According to a study in United States, the key to traffic violations lie in the simple principle known as the[3] Es namely Education, Enforcement and Engineering/ Infrastructure of roads. Lack of any of these three contributes to road violations and crashes. Law enforcement solely has a greater influence in controlling traffic violations and simultaneously RTAs.[3] The various traffic violations common among drivers are over speeding, ignoring traffic signs, overloading, mobile use, not wearing seatbelt,

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Submission Date: 10-08-2020
1st Revision Date: 14-09-2020
Acceptance Date: 21-09-2020

driving without license and in many cases the vehicles are not even roadworthy.[4]

Law enforcement through both conventional and modern techniques is becoming a good way of controlling traffic violations. The use of speed cameras and E-challan system are the innovations being used presently in the developed world to control violations and road crashes. In a study conducted on effectiveness of speed cameras, results showed that there was a reduction of 10% to 40% in road collision average being 25.9% across camera sites[5]. While the E-challan system will not only reduce the efforts of traffic police and help them focus other violations but it also has the potential to automate many more violations.[6]

In Pakistan as well, traffic law enforcement is a big concern especially in part of the traffic warden as he is at times immobile and cannot pursue and apprehend the offender who decides not to stop[3]. Steps have been taken by the government to address this concern and the first automatic E-challan system started working at 90 spots of Lahore[7] along with the strict implementation of helmet rule for motorcyclists. Speed cameras at 10 main roads of the city have also been displayed to check for over speeding. The purpose of this study was to determine the effect of enforcement of traffic laws in prevention of road traffic accidents in Lahore. As a general rule it was expected that people will be more careful and number of road traffic accidents were supposed to reduce in addition to reduced injuries in accidents. Current study was an effort to determine the effects of these enforcements on the general trend of RTAs so that officials can be made aware of their benefits, and these can be further extended to other parts of the city and simultaneously to other cities of the country for the benefit of the public.

METHODOLOGY

This was a comparative cross-sectional study conducted in the city of Lahore on RTAs. Data of RTAs was obtained after prior permission from Rescue 1122. Data was collected at a single time from 1122 records through record based consecutive sampling for two periods, Group A (containing data before Enforcement from 24-9-2017 to 11-2-2018) and Group B (containing data after Enforcement from 24-9-2018 to 11-2-2019). Comparison of the same dates of different years was made to avoid any seasonal variation in road traffic. Accidents occurring on the road, received first aid by 1122, are on record of 1122 were considered RTAs. Enforcement of Traffic Laws included strict check on Wearing Helmet or Seat belt, Meeting the Speed limit on the Roads & E challan in addition to previously present Laws. Effect in prevention was determined by number and outcome of accidents. Subjects with Incomplete data were excluded from the study. The two groups were then analyzed and compared using software epi info. Frequency and percentages were calculated for age, gender, affecters (Pedestrians, Passengers, Drivers, and Underage drivers), status of the subject (Alive & Stable, Alive & Unstable, Dead), vehicle type(Bike, Car, truck, rickshaw, bus, van, tractor Trolley or other Vehicles) Injury Type (Spinal Injury, Head Injury, Single Fracture, Multiple Fracture or Minor injury) and cause of accident (over-speeding, carelessness, wrong-turn, U-turn, one-wheeling, tyre burst or others. Chi square test was applied to see the difference for before and after comparison. P value less than 0.05 was considered significant.

RESULTS

Total number of Road Traffic Accidents from 24-09-2017 to 11-02-2018 (before Enforcement of traffic laws, Group A) was 27413 with total victims 27052 whereas from 24-09-2018 to 11-02-2019 (after Enforcement of traffic laws, Group B) the number of RTAs was 30562 with total victims 31165 which shows an increase in the number of accidents and number of victims.(figure 1)

In Group A 82.86% were male and 17.13% were female whereas in group B 81.05% were male and 18.95% were females. Age was stratified in groups as shown in table1.

Those who got injured in RTAs were pedestrians, passengers, drivers & under age drivers. Number and percentages are given in table 1. When chi square test was applied significant difference was observed among the two groups. (Table 2)

When status of the subject who had RTA was observed there was a marked reduction in the number of the deaths from 197 to 100 and the number of unstable patients reduced from 52% to 40%. Results were statistically significant p=0.00 (Table 2)

While observing the causes of RTA between both groups statistically significant difference was noted. Over-speed frequency was high in group B whereas one wheeling frequency was effectively low when compared with group A. figure2

Table 1: Differences in Group A & B (Descriptive)

Variable	Categories	Before (Group A)		After (Group B)	
		No.	%	No.	%
Gender	Male	22417	82.86	25259	81.05
	Female	4635	17.13	5906	18.95
Age	Age1to10yrs	1055	3.89	1232	3.95
	Age11to20yrs	4751	17.56	4400	14.11
	Age21to30yrs	7147	26.41	6816	21.87
	Age31to40yrs	5242	19.37	6599	21.17
	Age41to50yrs	3983	14.72	5434	17.43
	Age51to60yrs	2952	10.91	4229	13.56
	Age.above60yrs	1922	7.10	2455	7.87
Affecters'	Pedestrians	5161	18.05	6729	20.26
	Passengers	4305	15.05	5410	16.29
	Drivers	17586	61.51	19026	57.30
	Underage drivers	1537	5.37	2039	6.14
Status of the subjects	Alive & Stable	12784	47.25	18631	59.78
	Alive & Unstable	14071	52.01	12434	39.89
	Dead	197	0.72	100	0.32
Vehicle Type	Bike	16025	58.49	18185	59.06
	Car	2121	7.74	2414	7.84
	Truck	816	2.97	1083	3.51
	Rickshaw	4437	16.19	4753	15.43
	Bus	433	1.58	577	1.87
	Van	2063	7.53	2231	7.24
	Tractor Trolley	30	0.109	419	1.36
	Other Vehicles	1471	5.36	1124	3.65
Injury Type	Spinal Injury	521	1.92	725	2.32
	Head Injury	2938	10.86	3254	10.44
	Single Fracture	2824	10.43	3149	10.10
	Multiple Fracture	1660	6.13	1977	6.34
	Minor	19109	70.63	22060	70.78
Cause	Over speeding	8513	31.05	10190	33.34
	Carelessness	6853	24.99	7628	24.95
	Wrong. Turn	5276	19.24	5650	18.48
	U-turn	4631	16.89	5016	16.41
	One. Wheeling	48	0.17	2	0.006
	Tyre Burst	567	2.06	338	1.10
	Others	1525	5.56	1738	5.68

Table 2: Differences in Group A & B (analytical)

Variables	Categories	BEFORE Group A	AFTER Group B	Chi square (p value)
Gender	Male	22417	25259	32.25 (0.00)
	Female	4635	5906	
Affecters'	Pedestrian	5161	6729	48.43 (0.00)
	Passengers/Drivers	23428	26475	
Over-speeding	Yes	8513	10190	34.60 (0.00)
	No	18900	20372	
One Wheeling	Yes	48	2	47.65 (0.00)
	No	27365	30560	
Vehicle Type	Car/Bike	18146	20599	2.96 (0.085)
	Others	9250	10187	
Injury Type	Spinal Injury	521	725	15.87 (0.003)
	Head Injury	2938	3254	
	Single Fracture	2824	3149	
	Multiple Fracture	1660	1977	
	Minor	19109	22060	
Death	Dead	197	100	47.35 (0.00)
	Alive	26855	31065	

DISCUSSION

The purpose of this study was to have an idea about the effectiveness of recently introduced Enforcement of traffic laws implemented in the form of wearing Helmet/seatbelt, speed camera and E-challan on the roads of Lahore. For this purpose, data was collected for two periods before and after Enforcement from 1122 records after prior consent. Group A (before Enforcement) consisted of data of road traffic accidents occurring from 24-9-2017 to 11-2-2018 while Group B (after Enforcement) consisted of data of road traffic accidents occurring from 24-9-2018 to 11-2 2019. Same periods and equal number of days before and after Enforcement

were taken to avoid the monthly variations occurring in trends of RTAs, as proposed by a study in India that accidents are relatively higher in extreme weather[8], so that a true comparison can be made between the two groups.

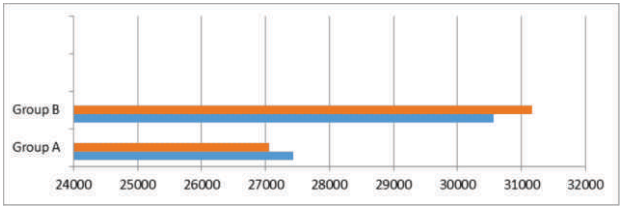

Figure 1: *Number of accidents & Victims*

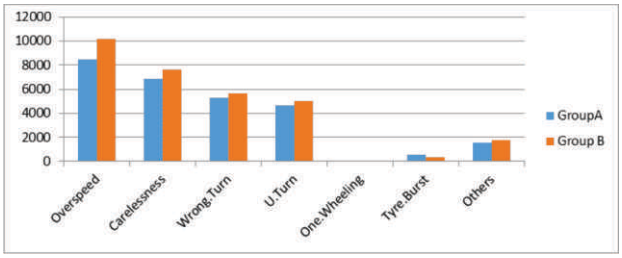

Figure 2: *Cause of accidents*

Comparison of the victims of RTAs between the two groups showed that there is a significant decrease in the severity of crashes. Deaths in Group A which were 197 before Enforcement reduced to 100 afterwards in Group B, about 49% decrease. This significant decrease in deaths renders to Enforcement, particularly of Helmet rule. Wearing of helmet decreases chances of having head injuries which is a major cause of death in RTAs. A study on autopsies of victims of accidents stated that about 42% of deaths occurred due to head injuries.[9] A systematic review of universal Helmet laws in USA showed not only an increase in helmet use but also a decrease in total deaths by 32%.[10] Similarly, "Alive and Stable" victims which were about 47% in Group A increased to 59.7% in Group B showing an improvement in outcome of injuries. A retrospective nationwide study in Korea showed that proportion of clinically important injury was high in no seatbelt group compared to seatbelt group.[11] Thus wearing of seatbelt, which is a part of enforcement resulted in less severe accidents. The proportion of "Live and Unstable" victims decreased in Group B to 39.8% from 52% in Group A, again showing a positive impact of Enforcement. The above results are in consistence with a cross-sectional study of Enforcement in about 10 countries which concluded that effective implementation of traffic laws reduce traffic fatalities in low-income countries.[12]

However, there was a net increase in the incidents of RTAs in Group B compared to Group A, about 10% increase. This is in contrast to most studies where increase in traffic law Enforcement reduced accidents. A study in USA suggests that only the increase in traffic citations reduced crashes significantly[13]. But the increase in case of present study can probably be assigned to an increase in the number of vehicles in the city. According to Punjab Excise Department, 100,000 new cars are added annually in the province,[14] a bulk of it being added in Lahore's traffic. A detailed study has also suggested that increased traffic volume results in increased number of accidents.[15]

This study also covers data regarding compliance of drivers to Enforcement. There were slight reductions in proportions of one wheeling, carelessness, wrong turn in Group B compared to Group A. Though the reduction was not much high but it still presented a change of trend among road occupants towards following of traffic rules. Recently, a similar study conducted regarding law enforcements in Spain in form of license and strict penal code showed compliance among drivers.[16] Our results however showed an increase in trend of over speeding in Group B compared to Group A by about 3%. These results are different to what was being expected. However, this non-compliance to speed cameras may be due to the reason that these speed cameras are considered a threat within a range of distance, beyond that range violations cannot be ruled out. As shown by a detailed study across Britain, effects of stationary speed cameras are only localized up to 500m of their sites of installation and beyond that collisions do increase.[17] Our study did not contain data regarding site of accidents so it might be possible that accidents occurred due to over speeding

beyond that range of compliance to Enforcement of speed cameras. Another explanation may be strict check through cameras which was not previously there, so may be more cases are recorded by now.

The risk factors of RTAs remained same between the two groups with slight variations in their proportions. In both groups male victims predominated being greater than 80% similar results were found in previous studies for example study of RTAs in Western Utter Pradesh showed 89% male[18] victims of accidents. Most of the accidents occurred between 21-40 years of age, same was seen in a study of Nepal where 50% accidents occurred between these ages[19]. Largely the victims of RTAs in the two groups were either Drivers or pedestrians. Previous study also shows that most of the victims of RTAs are usually drivers followed by pedestrians.[20] Among vehicles motor bikes were a major risk factor of road crashes similar to a study in which motorcycle accidents were 37% being a large contributor to RTAs.[21]

Overall the results show that there in an impact of Enforcement in changing the trends of RTAs particularly with respect to severity of crashes which were markedly reduced and the compliance to traffic laws which though not being much significant still showed slight improvement. According to the recent report of Punjab Safe City Authority, E- challan system has helped reduce fatal crashes by 70% during the first year.[22] Studies have shown that Enforcement not only decreases the incidents of RTAs but also there is a positive shift in behavior of vehicle occupants towards compliance to traffic laws. Hence, Enforcement of traffic laws should not be neglected while making policies to control RTAs and authorities should focus on effective Enforcement and technology should also be used for this purpose.

Limitations: Data was obtained through record based consecutive sampling, and only those factors related to trends of RTAs about which data was available were studied. Many other factors affecting the trends of RTAs about which data was not available could not be assessed. It was grouped data and data of individuals was not available to us.

Also the Enforcement was not fully applied in some parts of the city, whereas the data represented the city as a whole so there is a strong chance that most of the RTAs occurred in those parts of the city where Enforcement was ineffective.

CONCLUSION

Enforcement of traffic laws resulted in marked reduction of one wheeling, severity of injury and number of deaths.

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RETROSPECTIVE ANALYSIS OF OSTEOARTICULAR TUBERCULOSIS FROM A TERTIARY CARE HOSPITAL IN LAHORE

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How to cite: Bilal M, Liaqat R, Hashmi GM, Basit MS, Hameed M, Karamat A. Retrospective analysis of osteoarticular tuberculosis from a tertiary care hospital in Lahore. JAIMC. 2020; 18(4): 759-63.

Abstract

Background: Pakistan is one of the countries with high burden of tuberculosis, with a prevalence of 181/100,000. Musculoskeletal TB represents 1-3% of all the cases of TB. It was previously considered as a rare extra pulmonary manifestation of tuberculosis (EPTB), accounting for only 10-18% of all extra pulmonary cases, but the recent studies have reported it be the most common site of extra pulmonary involvement. The objective of this study was to measure the magnitude of problem through reliable reproducible data representative of our population and compare it with national and regional studies.

Methodology: This is a retrospective study of 5 years duration in one of the largest TB referral facility in Lahore. Review of these data was performed to analyze the incidence of Osteoarticular TB in our catchment area.

Results: Total number of new cases of Extrapulmonary Tuberculosis (EPTB) was 7800 (19%). Out of these EPTB patients, osteoarticular TB was diagnosed in 356(4.6%) patients. In this study majority of the patient population was females (56%) who needed hospitalization. While in outdoor capacity majority of the patients were males (54%). The most commonly affected site of infection is the spine 80% followed by the hip, knee, and ankle/foot (10%–13% each). In our hospitals, all new registered patients are referred to their respective specialties.

Conclusion: Osteoarticular TB cases are managed by orthopedic specialists, in line with WHO guidelines and TB DOTS program. This course has successfully led to decrease in mortality and incidence of newly diagnoses TB cases but Pakistan is still among top 5 countries with high burden of TB and still a lot of work needs to be done.

Keywords: Osteoarticular TB, spinal, hip and knee TB, EPTB

Worldwide, 9 million new tuberculosis (TB) cases are annually reported.[1] Tuberculosis is still a serious health problem in the developing countries, which accounts for 95% of worldwide TB cases and 99% of worldwide TB mortality.[2] Pakistan is one of the countries with high burden of tuberculosis, with a prevalence of 181/100,000. Musculoskeletal TB represents 1-3% of all the cases of TB. It was previously considered as a rare extra pulmonary manifestation of tuberculosis (EPTB), accounting for only 10-18% of all extra pulmonary cases, but the recent studies have reported it to represent 27- 35% of all extra pulmonary cases and also the most common site of extra pulmonary involvement.[3] EPTB reports in Pakistan range from a quarter of all TB patients, presenting to a hospital in Rawalpindi, to a third of TB patients visiting General Practitioner (GP) clinics in Karachi and the frequency of EPTB cases by site has been reported highest in lymph nodes (35.6%), and spine (26.3%), followed by Central Nervous System (CNS) (18%), abdomen (18%), extra spinal skeletal system (18%), pericar-

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Submission Date: 12-08-2020
1st Revision Date: 14-09-2020
Acceptance Date: 18-09-2020

dium (3%), breast (3%), pleura (2%) and others.[2] The spine is involved in 50% cases while rest 50 % cases are of extra spinal osteoarticular TB. Signs and symptoms of osteoarticular tuberculosis are frequently nonspecific which overlaps with several infectious and non-infectious diseases such as rheumatoid arthritis, septic arthritis, chronic osteomyelitis and metastasis. The latency period of these bacteria can persist up to several years after the initial infection and majority of patients do not show concurrent pulmonary disease. Hence, the disease is difficult to diagnose and it may damage the joints or cause spinal cord compression resulting in paralysis.[4] Therefore, it is very important to maintain a high degree of clinical suspicion. Though the diagnosis in endemic areas can be made on clinical and radiological examination; however, the tissue diagnosis is mandatory. If diagnosed and treated early approximately 90-95% of patients would achieve healing with near normal function.[5]

The numbers of tuberculous cases is continuing to grow in Pakistan due to population growth and overcrowding, poor socioeconomic conditions and inadequate treatment. Many cases of osteoarticular tuberculosis presenting to clinicians, either remain undiagnosed or are diagnosed late, therefore, bone and joint destruction is advanced. The diagnosis of TB arthritis is often delayed due to lack of awareness, insidious onset, lack of characteristic early radiographic findings and often lack of constitutional or pulmonary involvement. Intense current and previous efforts into diagnostic, therapeutic, and preventive interventions have focused on pulmonary TB in adults, but TB arthritis has been relatively neglected. We will collect and analyze the demographic, clinical, and radiological and laboratory data of patients with tuberculous osteoarticular involvement presented here to not only highlight this disease but also to provide a reliable representative data. Awareness of these features help clinicians in early diagnosis and management of the disease.

Osteoarticular Tuberculosis: tuberculosis invol-ving any bone in limbs, pelvic and shoulder girdle and axial skeleton excluding skull, and maxillofacial bones.

The objective of this study was to measure the magnitude of problem through reliable reproducible data representative of our population and compare it with national and regional studies.

METHODOLOGY

This is a retrospective study of 5 years duration in one of the largest TB referral facility in Lahore with cases received from all across Punjab. The following information was recorded on the designated proforma: demographic characteristics including age, gender, site, laboratory test results including erythrocyte sedimentation rate (ESR), gene Xpert, results of histological and bacteriological culture reports if performed.

All patients diagnosed with osteoarticular TB in our institution are managed by multidisciplinary team including orthopedic surgeon, respiratory physicians, dedicated Histopathologist and physiotherapist with an interest in TB patients' rehabilitation. TB is a notifiable disease and data regarding diagnosis, anatomical site, ethnicity, treatment, drug resistance and outcome were recorded for all patients (irrespective of site)

Review of these data was performed to analyze the incidence of Osteoarticular TB in our catchment area. Results were evaluated and compared to previously reported data for purposes of discussion. All newly diagnosed cases of Osteoarticular TB were included in the study. Cases with a history of recurrent disease and MDR were excluded from the study.

RESULTS

We recorded 5 years data of new cases of TB registered during 2014-2018 at Gulab Devi Hospital Lahore. Total number of new cases of Extrapulmonary Tuberculosis (EPTB) were 7800 (19%). Out of these EPTB patients, osteoarticular TB was diagnosed in 356(4.6%) patients. Out of these 356 patients, 205 (57.6%) cases were recorded in Indoor facility and 151 (42.4%) cases were seen in outdoor facility.

Incidence of new cases was variable during the years and may be due to inconsistencies in the data collection table 1. Highest number of Osteoarticular TB was recorded in 2016 (n=65). Age range is

consistent throughout the years with an average age of 36 year, minimum age reported was 15 and maximum age reported was 75. Incidence of osteoarticular TB was higher in female (55%) and male (44%). Table 1

Regarding the site of osteoarticular TB, among indoor patients (n=205), most common site is Spine 178 cases (86.5%) followed by Hip joint 6 cases (3%), Elbow joint 3 cases (1.5%) and knee joint 2cases (1%). Unfortunately 16 cases (8%) had no site recorded in the files Figure 1. Incidence of osteoarticular TB was higher in female (55%) and male (44%).Table 1

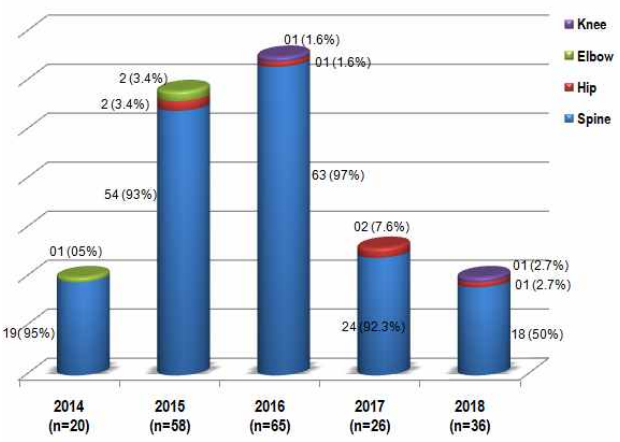

Figure1: *Frequency Distribution of Osteoarticular Tuberculosis in Various Sites in Indoor Patients 2014-2018*

Among the outdoor patients (n=151), spine remains the most common site 132 cases (87.4%), elbow joint 7cases (4.6%), Knee Joint 6 cases (4%), Hip Joint 3cases (2%) and Ankle Joint 3 cases (2%) Figure 2. Incidence of osteoarticular TB was higher in male 82 cases (54%) and female 69cases (46%). Table 2

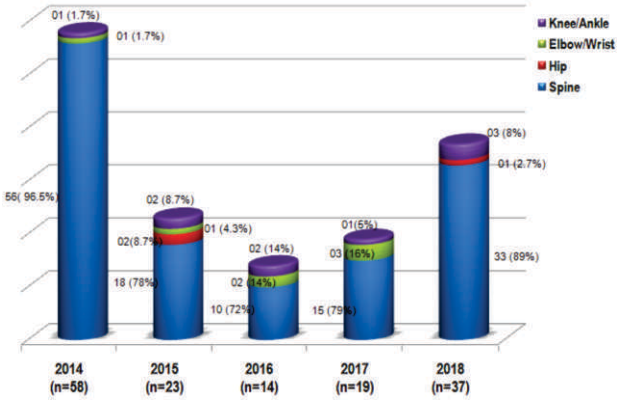

Figure 2: *Frequency Distribution of Osteoarti-cular Tuberculosis in Various Sites in Outdoor Patients 2014-2018*

DISCUSSION

Our study focused on the analysis of osteoarticular cases among new TB patients registered at our centre. The rate of extrapulmonary TB (EPTB) worldwide is increasing as reported in recent studies.[3-5] Young patients, females, and people of African or Asian origin seem to have a higher risk of developing EPTB.[6,7] Our study reveals the EPTB frequency at 19% out of which 4.5% had osteoarticular TB. Other

Table 1: *Demographic Profile of Patients Presented Indoor since 2014-2018*

	2014 (n=20)	**2015** (n=58)	**2016** (n=65)	**2017** (n=26)	**2018** (n=36)	**2014-18 (N = 205)**
Age (Average)	34	35	37	34	34	Mean Age
Range	15-70	15-70	15-75	15-70	15-74	34.8±1.8 Years
Gender n (%)						
Male	07 (35%)	26 (45%)	27 (42%)	14 (54%)	17 (47%)	**91 (44%)**
Female	13 (65%)	32 (55%)	38 (58%)	12 (46%)	19 (53%)	**114 (56%)**

Table 2: *Demographic Profile of Patients Presented to OPD Since 2014-18*

	2014 (n=58)	**2015** (n=23)	**2016** (n=14)	**2017** (n=19)	**2018** (n=37)	**2014-18 (N = 151)**
Age (Average)	36	37	37	38	40	Mean Age
Range	16-60	19-72	15-68	19-74	15-75	37.6±2.6 Years
Gender n (%)						
Male	26 (45%)	10 (43%)	13 (93%)	12 (63%)	21 (57%)	**82 (54%)**
Female	32 (55%)	13 (57%)	01 (07%)	07 (37%)	16 (43%)	**69 (46%)**

studies have shown a range from 10%–25% involvement of musculoskeletal systems,[1,8] leading to an estimated global prevalence of 19–38 million cases.[9] The reported peak age of adult patients with musculoskeletal TB ranges from 45 to 60 years.[7] Although some studies report a bimodal age distribution.[10] In this study majority of the patient population was females (56%) who needed hospitalization. While in outdoor capacity majority of the patients were males (54%). This is in line with other studies.[4,8]

The most commonly affected site of infection is the spine 80% followed by the hip, knee, and ankle/foot (10%–13% each).[7] In pediatric population, large joints are most commonly involved according to one study.[11] According to European surveillance data, host related factors play a role in the distribution of site and is useful in diagnosis. Indian subcontinent have strong predilection for osteoarticular TB.[12] According to one study, 53% published literature also focussed on diagnosis and treatment of TB spine[13]. Among spine, thoracic region takes up 50% cases, followed by Lumbar and cervical regions.[14,15] Our study has data limitations and we could not elaborate on most commonly affected area of spine.

In our hospitals, all new registered patients are referred to their respective specialties. Osteoarticular TB cases are managed by orthopedic specialists, in line with WHO guidelines and TB DOTS program. This course has successfully led to decrease in mortality and incidence of newly diagnoses TB cases[17,18,19] but Pakistan is still among top 5 countries with high burden of TB and still a lot of work needs to be done. Increasing the diagnostic and therapeutic capacity with improved community base strategies is the way forward to control this disease.[20,21,22,23] Our study has limitation in data collection and we aim to improve the process of structured data collec-tion to achieve detailed insight into the analysis of osteoarticular TB.

CONCLUSION

The study gives a glimpse into the demography and anatomy of Osteoarticular TB. Further studies are needed for detailed insight in to variability of yearly data and explain differences observed between reported numbers and site of involvement. Osteoarticular TB is a significant part of overall burden of TB disease and from a public health perspective; it should be addressed on priority bases to avoid long term disability and morbidity associated with it.

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KNOWLEDGE, ATTITUDE AND PRACTICES OF PEOPLE TOWARDS COVID- 19 INFECTION IN PAKISTAN – A KAP SURVEY

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How to cite: Tashfeen A, Khan B. Knowledge, attitude and practices of people towards covid-19 infection in Pakistan. JAIMC. 2020; 18 (4): 764-70.

Abstract

Background: During the current pandemic, Social Media was a viable option of information transfer with clarity and logical flow of information that was easy to follow. The objective of this study was to determine the knowledge, attitudes and practices of people in Pakistan towards COVID 19 through a KAP survey.

Methodology: A cross-sectional, online survey was performed among Pakistani residents aged above 20 years. A pre-validated online questionnaire on COVID-19 (Google form) was distributed through various messenger groups and social media in the authors' network. The questionnaire comprised of 35 close-ended questions, which were further divided into four domains namely demography, knowledge, attitudes and practices towards the COVID-19 pandemic. Survey questionnaire were sent to many groups comprising of 150 contacts out of which 114 responses were received. Data was collected and simplified by calculating percentages of the answers through SPSS 20.

Results: More than half of the participants (53.5%) had excellent knowledge about COVID-19 and the other half (46.5%) had fair knowledge with no one having poor knowledge. Majority of the participants had either excellent attitude (43%) or fair attitude (54.4%) and only a few participants showed poor attitude.

Conclusion: The overall answers of the respondents represented good knowledge, attitude and practice towards Covid-19. Various Social media sources can further clarify the misconceptions about COVID-19 and improve the knowledge, attitude, and practices among public.

Key words: symptoms, transmission, timeline, research, treatment

COVID-19 or coronavirus disease is caused by a novel coronavirus – the SARS-CoV-2 virus. The disease causes a range of symptoms such as fatigue, cough, fever, chills, body aches, headache, shortness of breath, runny nose, sore throat, nausea and diarrhoea.[1] COVID-19 is transmitted primarily through droplet infection, and so can be transmitted person-to-person via coughing or sneezing. The droplets can also contaminate surfaces for time periods ranging from hours to days, depending on the surface and the environment. This can infect another person when their hands come into contact with such surfaces and then touch their mucous membranes i.e. mouth, nose or eyes. One other hypothesized mode of transmission is through aerosols, which may cause droplets to remain suspended in the air.[2] Due to person-to-person contact and droplet infection being the main mode of transmission, the main precaution is to maintain a considerable distance not only from each other but also (at least six feet) between patient and contacts (within the household and even outside the house as well). In addition, it is advised to frequently wash hands, avoid touching the face, wear a mask, avoid contact with contaminated surfaces and disinfect frequently touched surfaces. If tested positive or experiencing signs and symptoms, the best precaution to take is to isolate oneself and advise people you have been in contact with to self-quarantine.[3]

The first case of COVID-19 appeared in Wuhan, China in 2019 and was first reported to the World Health Organization (WHO) as a viral pneu-

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Submission Date: 21-09-2020
1st Revision Date: 29-09-2020
Acceptance Date: 30-09-2020

monia of unknown origin on 31st December 2019. The disease was confirmed to be caused by a novel coronavirus on the 9th of January 2020 and was declared a pandemic by WHO on 11th March 2020.[4]

As of August 2020, no vaccine trial has been successful for mass production. Also no specific treatment regime could be developed for COVID-19 yet. However, there have been many clinical trials investigating antiviral drugs developed for other diseases as a treatment for COVID-19. So far, the drugs Dexamethasone and Remdesivir have shown some promising results.[5]

The most widely used test for coronavirus is an RT-PCR test, which detects whether RNA genetic material from the virus if in saliva or nasal fluids[6]. Testing is particularly important as it allows for local pandemic control via contact tracing, whether through a Bluetooth app or manually. In addition, Awareness Programs by local government and knowledge through Social Media platforms is also important as it allows for recognition of disease process and its prevention. The current study was planned to find the knowledge, attitude and practices of people regarding COVID-19. The data from this study will help the healthcare providers in devising strategies for prevention and control of epidemic.

METHODOLOGY

Local population, more than 20 years of age, belonging to the educated class, having access to Social Media and willing to participate were eligible for this survey. People who already were infected with COVID-19 were excluded from this study.

This was a cross-sectional survey, which was conducted for 15 days from 1st to 15th August 2020.

A convenient, non-probability sampling technique was employed. Due to regional pockets of smart lockdown and to refrain from social contact in the study period, it was difficult to have community sampling, so we chose a Google form for an online survey to collect the data. Respondents' willingness to participate in the study by clicking on the Google form will be taken as consent.

A questionnaire with a total of 35 questions on COVID-19 (KAP Survey) was circulated on Whats-App to the authors' contacts. The survey questionnaire was divided into four domains to collect data. These were Demography (age, gender), Knowledge (Q1 - Q16), Attitude (Q17 - Q23) and Practices (Q24 - Q35) towards COVID-19 pandemic. Each correct answer carried one mark and wrong option was scored as zero. Knowledge was labeled as excellent, fair or poor if the participant had a score of >13, 9-12, or <8 out of total 16 questions, respectively. Attitude was considered excellent, fair or poor on a score of >6, 3-5 or <2 out of total 7 questions, respectively. Practices were marked as yes/no options.

The data was collected by circulating the questionnaire online to contacts by providing a shareable link in various messenger groups on WhatsApp. The participants were aware that if they wanted to and consented to participating in the survey, they would have to complete the full survey and their responses would not be submitted without the full completion of the survey.

Data was entered and analyzed through SPSS version 20. Descriptive statistics were calculated. Frequency and percentages were calculated for gender, age groups and each of the outcome variables i.e. Knowledge (excellent, fair, poor), Attitude (excellent, fair, poor) and various practices.

RESULTS

Questionnaire was received from 114 participants out of 150 (response rate 76 %). The questions in the survey were subdivided into four domains, with each including questions in the order of their appearance in the proforma. These domains were Demography, Knowledge, Attitude and Practices.

The Demographic Domain had questions regar-ding age and gender. There were 73.7 % females and 26.3% males. Majority (35.1%) of the respondents were in the age bracket of 31-40 years followed by 41-50 years (24.6%), 21-30 years (21.9%) and so on (Table-1).

Within the Knowledge Domain 16 question

were asked (Q1-Q16). More than half of the participants (53.5%) had excellent knowledge about COVID-19 and the other half (46.5%) had fair knowledge with no one having poor knowledge.The Attitude Domain had questions 7 questions (Q 17-Q23). Majority of the participants had either excellent attitude (43%) or fair attitude (54.4%) and only a few participants showed poor attitude (2.6%) (Table-2)

Table 1: Demographic Characteristics Of Study Participants (N = 114)

Characteristc		Frequency (n)	Percentage (%)
Gender	Male	30	26.3 %
	Female	84	73.7 %
Age Groups	≤ 20 years	4	3.5 %
	21 - 30 years	25	21.9 %
	31 - 40 years	40	35.1 %
	41 - 50 years	28	24.6 %
	51 - 60 years	15	13.2 %
	> 60 years	2	1.8 %

The Practice Domain (Q24- Q35) comprised of questions regarding staying at home, respiratory hygiene, social distancing, regular hand wash, sanitizing suspected areas of infection, avoiding handshake and touching the mouth, nose, and eyes.

The questions in the Practice Domain were particularly crucial as personal responsibility is especially important with this pandemic, specifically due to the widespread nature of the disease, high rate of infectiousness and relatively long average incubation period of 5-14 days.

Table 2: Knowledge And Attitude Of Participants Regarding Covid-19 (N = 114)

Characteristc		Frequency (n)	Percentage (%)
Knowledge	Excellent knowledge	61	53.5 %
	Fair Knowledge	53	46.5 %
	Poor Knowledge	0	0 %
Attitude	Excellent attitude	49	43.0 %
	Fair Attitude	62	54.4 %
	Poor attitude	3	2.6 %

In our study, participants had a fair idea of safe practices to avoid spread of COVID-19. This may be due to great efforts by the government in sensitizing the population through TV, radio newspapers and other sources of information transfer to create awareness. In this regard, our study showed that most popular medium of information was internet/ social media 57.9% followed by TV/Radio 27.2%. Majority participants (95.6%) said that they wear a mask in public and 99.1% were not in favor of wearing it at home. Guiding family for adopting preventive measures was quite common (91.2%). A focus on having a healthy lifestyle to improve their immunity was reported by 90.4% and 62.3% of them admitted to taking supplements for boosting immunity. A large proportion (93%) claimed to observe Government instructions, however, only 21.1% got themselves tested for COVID-19 during this pandemic (Table-3).

Frequent hand-washing has been described as one of the most effective measures by the experts for prevention of transmission of infection. In our study, 38.6% people reported to wash their hands every two hours, 24.6% every one hour and 15.8% every four hours.

When asked about keeping distance in the public places, 45.6% claimed that they try to keep a distance of 6 feet, 26.3% 2 feet, and 22.8% 3 feet and 4.4% do not worry social distancing. Keeping oneself informed about the current and new research is considered necessary during this pandemic and more than half (53.5%) of the participants in our study reported that they update their knowledge almost daily. However, 31.6% reported to update only once a week, 4.4% on every second day and 9.6% did not feel the need for it.When asked about socializing practices, 30.7% told that they socialize only in emergency, 24.6% did not socialize at all, 16.7% socialized weekly, 9.6% fortnightly, 7.9% once a day, 7% monthly and 3.5%every second day. The questions regarding practices of participants in preventing COVID-19 infection are given in table 3.

Table 3: Practices Of Study Participants Regarding Covid-19 Prevention (N = 114)

Sr. No	Practice	Response	Frequency (n)	Percentage (%)
1.	Do you wear a mask at home?	Yes	1	0.9%
		No	113	99.1 %
2.	Do you wear a mask at public places?	Yes	109	95.6 %
		No	5	4.4 %
3.	Do you guide your family for preventive measures against COVID-19?	Yes	104	91.2 %
		No	10	8.8 %
4.	Have you focused on having a healthy lifestyle for boosting your immunity?	Yes	103	90.4 %
		No	11	9.6 %
5.	Are you taking any supplements for boosting your immunity?	Yes	71	62.3 %
		No	43	37.7 %
6.	Did you get yourself tested for COVID-19?	Yes	24	21.1 %
		No	90	78.9 %
7.	Are you observing Government instructions regarding COVID-19?	Yes	106	93.0 %
		No	8	7.0 %

DISCUSSION

The study was done to evaluate the knowledge, attitude and practices towards COVID-19 pandemic among literate class, who were well-versed with social media.[7]

In the Demographic Domain, majority of the respondents were females (73.7 %).

35.1 % were in the age bracket of 31-40 years and 24.6% in 41-50 years, indicating that majority were in their middle ages and belonging to literate class of urban population. More or less the same findings were also observed in the studies done in China and Iran.[8,9]

Regarding the Knowledge Domain, around 53.5% of the respondents had excellent awareness of its mode of spread, incubation period, response to infection, signs and symptoms (fever, cough and fatigue more than having no symptoms), difference from other flu like conditions, diagnostic test and availability of treatment ,which is a good rate of knowledge for basic scientific facts around COVID-19. Knowledge about the pandemic in our respondents was less as compared to the previous studies conducted in China and Iran where the overall correct rate of knowledge towards COVID-19 is 90% which may be due to the fact that they were hit by pandemic earlier and the studies were conducted during the main outbreak of the disease when people were already well aware about the infection.[8,9] Almost all the respondents understood that the spread of Covid-19 can be reduced by practicing social distancing, 78.8% understood that Covid-19 is transmitted through personal contact and about 99% understood high risk groups. This suggests good knowledge about the disease, which was also observed in an Iranian study (85%). This is important as it means there is an understanding of prevention and control of the disease process.[10]

Regarding the Attitude Domain, 43% respondents were in Excellent and 54.4% were in the Fair category. Pandemic was worrisome to them, not only for themselves but also for their near and dear ones. They were well aware that the elderly, smoking, those with co-morbid conditions and health professionals were more prone to infection. This suggests a crucial understanding about at-risk individuals in the population. More or less the same was also observed in a study by Zhong in China.[8,10]

85-96% respondents were of the view that it was their moral duty to inform the state and 93% thought it was important to support government in their efforts to control pandemic, suggesting a sense of unity and support for the country and its efforts during the pandemic. Regarding closure of schools 24 % were not sure, 52% were in favor and 20% against it. 45% were in favor to impose curfew and

23% thought otherwise. This suggests a somewhat divided opinion on government sanctions.

There was a strong agreement that Governments and Healthcare professionals need to stay informed and in control of the virus in order to create awareness and control the disease process. For instance, 84.1% and 92.1% of participants were worried that they or their family members would get the virus respectively. In a Chinese survey, most participants remained optimistic, however, our survey didn't assess optimism in the same way, as in attitudes regarding the future of the pandemic (whether it will be successfully overcome) were not assessed[8]. 60.8% of participants had a moderate attitude towards the virus in Iran, suggesting slight variations across countries[9]. In Pakistan, only 52.6% believed information available to the public about the virus was sufficient, with 31.6% believing it wasn't and 15.8% being unsure. In Iran only 2.2% believed awareness in society was sufficient and 50.1% believed it was insufficient[9]. The initiatives taken by the state (country wide smart lockdown, closure of educational institutions, restriction on public gathering and marriage congregations, SOP's for public places / public exposure and compulsory wearing of masks) was due to the information via TV, Radio and social media and to some extent by sign posting at public facilities and banners on the roads. Hence, clearly government initiatives and awareness programs have been effective and of use. This may be due to the judicious use of electronic media by the State and good knowledge of the respondents (internet /social media 71% and TV/ Radio 40%). These practices are nearly the same as those observed in a study conducted in Iran (89%).[9] A right attitude can encourage good practices among the public. To improve this, adequate monitoring of social media platforms to confirm and improve the quality of information delivered to the people is of prime importance.[11] In our study, more than half (57.6%) of the respondents had shown a right attitude towards COVID-19, which is not good enough percentage considering the gravity of the situation and to inculcate healthy practices to reduce the burden of the disease (spread and prevalence). There was a need to sensitize the public about COVID-19 facts, which were recommended by the World Health Organization.[12]

Regarding the Practice Domain, 88.1% of the participants had a fair idea about the preventive measures. Main source of information was Broadcast services (57%), which proved helpful for respondents to adapt to the rapidly evolving scenarios. Social media was perceived as a potential tool for information transfer when resources were limited and there were time constraints in which bulk of information was to be dispersed.[13]

However, the percentage was lower as compared to Chinese residents.[8]

Majority (95.6%) of the respondents were of the view of wearing a mask in public and were not in favor of wearing it at home (99.1%). In China, 98.0% of participants in that survey wore a mask, suggesting a similar rate of adherence to Pakistan.[9] Most of the participants were aware of preventive practices (78% knew about washing hands every 30 minutes and 100% every 8 hours). Washing hands only/ washing hands for 20 seconds and sanitizing every 2 hours was also endorsed by 95.6% of the respondents.[14,15] 91.2 % were in favor of preventive measures like keeping some safe distance in public, avoiding hand shake or hugging each other, no socializing or socializing only in emergency and lockdown. 90.4 % of the respondents were in favor of boosting immunity to combat COVID-19 infection and 62.3 % suggested taking supplements for the purpose.[14,15] Overall the respondents were keen on following the Government instructions regarding COVID – 19.[12]

CONCLUSION

When analyzing the overall answers, the respondents seem to represent good knowledge, attitude and practice towards Covid-19. The results have revealed the areas in which participants are in agreement on a number of aspects. They were a diverse group of lite-

rate individuals and thus major stake holders. Current awareness programs are effective as educated class has sufficient knowledge, is adhering to government guidelines and their general attitude towards current pandemic is that of concern. They will act as Role Models for those who are less educated and do not have access to social media.

Limitations of the Study

It was impossible to involve participants from all tiers of the society due to social restraints and limited sample size. Therefore, caution should be used to attempt to generalize the results beyond the participants of this study.

Acknowledgments

The authors thank all the participants who took time out for this study. The authors also thank those who provided statistical, technical and intellectual support.

Conflict of Interest

The ideas presented in this article are solely of the authors and are in no direct conflict to any individual or institution.

Financial Support

None to declare

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MICROBIOLOGY AND SELECTION OF EMPIRIC ANTIBIOTIC THERAPY OF URINARY TRACT INFECTIONS AT A TERTIARY CARE FACILITY IN LAHORE

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How to cite: Shafi ST, Rasheed J, Usama M, Farooq O. Microbiology and selection of empiric antibiotic therapy of urinary tract infections at a tertiary care facility in Lahore. JAIMC. 2020; 18(4):771-781.

Abstract

Background: Urinary tract infections are one of the most common medical conditions that affect people around the globe. The main aim of this study was to analyze the resistance and sensitivity patterns of different antimicrobials and Uropathogens associated with severe UTIs. In light of this data, clinicians at our local hospital improvised the choice for empirical antibiotic against UTIs.

Methods: This cross sectional study included data of 81 hospital admitted patients with UTI. Urine culture and drug sensitivity reports were retrieved and data analysis was done to find out empirical antibiotic choice. The data has been collected from hospital records after taking appropriate consent and permission. Further analysis was done following the new guidelines regarding empirical antibiotic choice. Data analysis was done by Statistical Package for the Social Sciences (SPSS) version 22.0 and expressed as frequency and percentages.

Results: E.coli was found to be the most common (57.14%) uropathogen responsible for UTIs. Among all the causative organisms , (64.28%) were found to be ESBLs. (73%) of organisms showed MDR and (17.8%) depicted XDR characteristics against antimicrobials. New broad spectrum antibioctics like Carbapenems, Aminoglycosides and Colistin were among the most sensitive drugs. After updating local guidelines, empirical antibiotic accuracy for suspected UTI patients was improved from 28% to 64%.

Conclusion: The study showed that newer broad spectrum antibiotics are more sensitive against common Uropathogens.

Key words: Urinary tract infection, ESBL's , Empirical antibiotic, MDR, XDR, Sensitivity and resistance pattern.

Urinary tract infections (UTIs) are a major public health problem and it is estimated that around 150 million people are affected by this infection every year worldwide.[1] It is one of the most common bacterial infections around the globe which are caused by both gram-negative and gram-positive bacteria. Urinary tract infections have become difficult to treat over the passage of time owing to the rise in the antimicrobial resistant strains of the uropathogens. This escalating trend of MDR (multi-drug resistant) and XDR (extended-drug resistant) strains of the uropathogens has resulted in high recurrence rates of these infections among the masses.[20,21] Consequently, putting health care systems under immense pressure with a threat of an ever increasing economic burden along with poor quality of life. Common symptoms of UTIs include pain or burning while urinating, a persistent urge to urinate and passing frequent and small amounts of urine.

Urinary tract infections can be clinically classified into un-complicated and complicated infections. Uncomplicated UTIs mainly affect indivi-

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Submission Date: 17-09-2020
1st Revision Date: 23-09-2020
Acceptance Date: 26-09-2020

duals who are otherwise healthy and have no associated anatomical or neurological abnormalities[2,3]. These uncomplicated infections are further categorized into lower UTIs known as cystitis and upper UTIs known as pyelonephritis[2,4]. Complicated UTIs are defined as UTIs associated with factors which can compromise the urinary tract, including urinary obstruction and retention caused by a foreign body (calculi), neurological disease, renal failure and renal transplant, immunosuppression, pregnancy, indwelling catheters or other drainage devices.[6,7]

There are different risk factors which are associated with multi drug resistant UTIs, including a prior hospital admission with UTI, recent broad spectrum antimicrobial use and travel to MDR prevalent regions. The other risk factors include diabetes, obesity, female gender, sexual activity, vaginal infection, and genetic susceptibility.[4,5] Risk factors for developing a CAUTI (Catheter-associated UTIs) include prolonged catheterization, female gender, older age and diabetes.[8]

Extended-spectrum β-lactamases (ESBLs) are a heterogeneous group of enzymes responsible for the resistance of enterobacteriaceae to extended-spectrum β-lactam antibiotics.[9] ESBL were first recognized in Germany in 1983.[10] It is imperative to mention that a large number of patients infected with ESBL-producing organisms have been exposed to hospital intensive care units[11,12]. Multiple studies show that ESBL-producing Enterobacteriaceae are common in community-based settings.[13,14,15] E.coli is one of the most prevalent ESBL producing organism in community based settings. Furthermore, foreign travel may be a major risk factor for developing community-onset ESBL-producing E. coli infections.[16]

The main aim of this study was to check the overall prevalence and patterns of drug resistance of different uropathogens, specifically in relation to the ESBL linked UTI's, in our local hospital. This data interpretation was aimed at carrying out a clinical audit whereby it was intended to course-correct the choice of empirical antibiotic used to treat UTIs.

METHODOLOGY

This cross sectional study included the data of 56 hospital admitted patients suffering from urinary tract infections over a period of 1 year (july-2019 to aug-2020). Initially urine culture and drug sensitivity reports were retrieved from hospital laboratory and corresponding patient files were also collected to check the empirical antibiotic started for each patient. Prevalence of different UTI causing gram negative organisms along with the frequency of different empirical antibiotics used for treating these infections were also observed. Overall sensitivity and resistance patterns of various antibiotic classes were also studied.

Organisms were classified according to their resistance patterns to different antibiotics which resulted in various categories like 'MDR' (Resistant to at least 1 drug in 3 antibiotic categories), 'XDR' (Sensitive to 1 or 2 antibiotic classes), 'No Resistance' and 'Others' (resistance to one or two classes). Three different categories of enzyme producing gram negative organism were common in this data namely ESBL (extended spectrum beta lactamases, carbapenamase producing and no beta lactamase producing organisms. ESBL group shows resistance towards penicillins, cephalosporins and aztreonam but sensitive to beta lactamase inhibitors like clavunate, sulbactam, tazobactam. They are also sensitive to carbapenems and maybe sensitive to other classes of antibiotics. Carbapenamase producing bacteria which are resistant to a broad category of beta lactam antibiotics including carbapenems. The detection of extended-spectrum beta-lactamases (ESBL) production was carried out using the cephalosporin/clavulanic acid combination discs method according to the guidelines set by CLSI (clinical laboratory standard institute).

As part of clinical audit and quality improvement, clinicians at our local hospital were presented with the initial data and they were educated about different drugs sensitivities and resistance patterns. In light of this data, local hospital guidelines were updated in order to help clinicians with making

better choices when starting empirical antibiotics for UTI patient.

Data analysis was done by Statistical Package for the Social Sciences (SPSS) version 22.0. Categorical variables were recorded using frequencies and percentages whereas the continuous variable like age was analyzed using mean and standard deviation. In addition to this, we used pie charts and bar charts to depict the associations, make comparisons and check different factors implicated in UTI.

To see the effect of age, sex, diabetes, chronic kidney disease and ICU admission on the odds of ESBL, binary logistic analysis was carried out. Five separate bivariate logistic regression analysis were carried out by entering each predictor variable with dependant variable. The results were summarized in a single table in view of brevity Table-1.

RESULTS

Initial data of 56 hospital admitted patients suffering from UTIs was analyzed. E.coli was the most common organism responsible for UTIs with 57.14% while Klebsiella ,Pseudomonas Aeruginosa, Proteus mirabilis, Citrobacter contributed 21.42%, 16.07%, 3.57%, 1.78% of the total infections respectively (See fig- 1). A multitude of empirical antibiotics were used to treat UTIs at the local hospital with Carbapenems and cephalosporins as the most common choice whereas other classes of drugs like fluoroquinolones, aminoglycosides, piperacillin + tazobactam, cefoperazone + sulbactam were used in the remaining patients. However, in approximately 12% of the patients no empirical antibiotic was given (See fig-4). There was a wide pattern of drug resistance observed in our urine culture reports. Only a few drugs like Colistin, Carbapenems and aminoglycosides had good sensitivity patterns as compared to other classes of antibiotics (See fig-5).

Organisms were classified according to their resistance patterns to different antibiotics which resulted in various categories like 'MDR', 'XDR' , 'No Resistance' and 'Others' having individual frequencies of 73% ,17.80% ,5.35% and 4% respectively (See fig- 2). In addition to this, organisms were also differentiated based on their enzyme production capabilities that formed sub groups like ESBL (extended spectrum beta lactamases), Carbapenamase producing G.N.O and No beta lactam producing G.N.O contributing 64.28%, 14.28% and 12.50% respectively (See fig- 3).

Diabetes Mellitus and ICU admission were significantly associated with diagnosis of ESBL gram negative bacterial UTI in a multivariate logistic regression model as shown in Table-1.

As part of clinical audit and quality improvement project, initial data was also analyzed to check the percentage of patients who were started with accurate (sensitive) empirical antibiotics for UTI management. From sept-19 to aug-20 only 28% of the patients were started with sensitive antibiotics. However, empirical antibiotic accuracy was re-analyzed after educating clinicians and updating local guidelines and it increased to 64% (16 out of 25 patients) during the period from sept-20 to oct-20 (See fig- 6).

Table 1: *Binary Logistic Regression of Predictor variables with ESBL*

Variables		OR	95% CI	*p*-value
Age		1.00	0.95 – 1.06	0.99
Sex				
	Male	1		
	Female	2.14	0.59 – 7.84	0.25
Diabetes				
	No	1		
	Yes	14.90	3.71 – 59.49	*< 0.001*
Chronic Kidney Disease				
	No	1		
	Yes	1.90	0.45 – 7.98	0.39
ICU admission				
	No	1		
	Yes	11.70	3.19 – 42.69	*< 0.001*

OR = Odds Ratio; CI = Confidence Interval

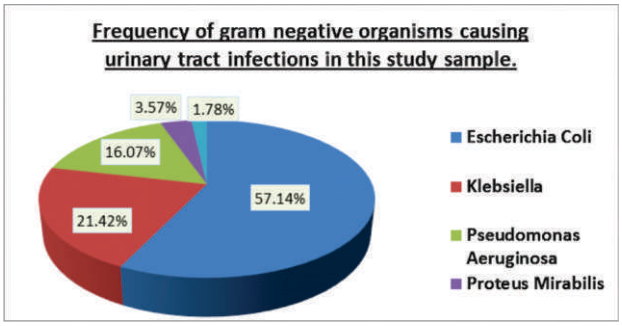

Figure 1: *Pie chart depicting the Percentages of different Gram Negative Organisms iImplicated in Urinary Tract infections in this Study. E.coli was the*

most Common Organism Responsible for this Infection.

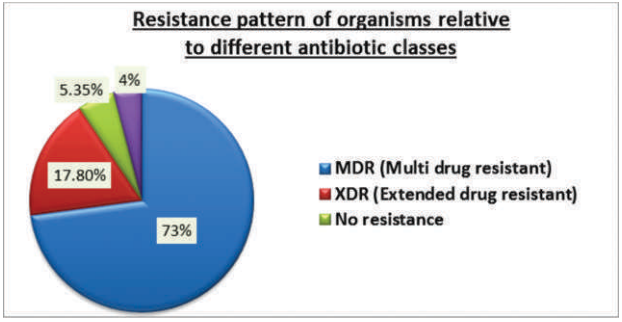

Figure 2: *Resistance pattern based on resistance to number of classes of antibiotics. It includes Multi Drug Resistance (resistance to 3 or more classes), Extended Drug Resistance (sensitive to only one or two classes), No Resistance, Others (resistance to one or two classes).*

MDR: *Resistant to at least 1 drug in 3 antibiotic categories*

XDR *: Sensitive to 1 or 2 antibiotic classes*

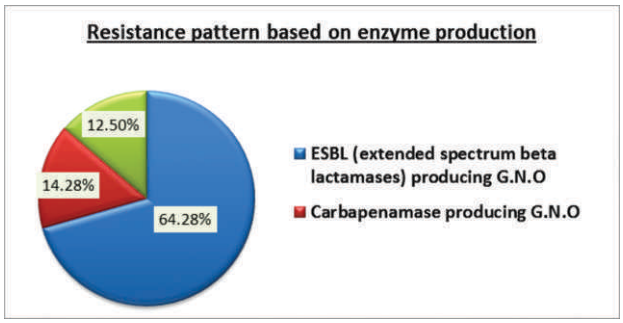

Figure 3: *Resistance pattern based on Enzyme Production. It Includes ESBL (Extended Spectrum beta lactamases) producing gram negative organisms, Carbapenamase Producing gram Negative Organisms and No beta Lactamase Producing gram Negative oOrganisms.*

ESBL: *Gram negative bacteria resistant to penicllins, cephalosporins and aztrionam but sensitive to beta lactamase inhibitors like clavunate, sulbactam, tazobactam. There are also sensitive to carbapenems and maybe sensitive to other classes of antibiotics.*

CARBAPENAMASE: *Carbapenamase producing bacteria which are resistant to a broad category of beta lactam antibiotics including carbapenems.*

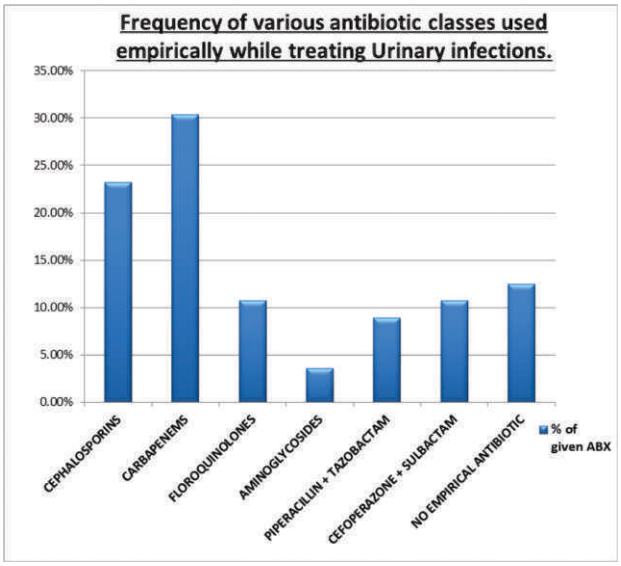

Figure 4: *Bar chart showing Frequency of different classes of Antibiotics used Empirically before the availability of urine culture results. Based on these culture reports, the empirical antibiotic was found to be correct in 28.5% of patients in the study sample.*

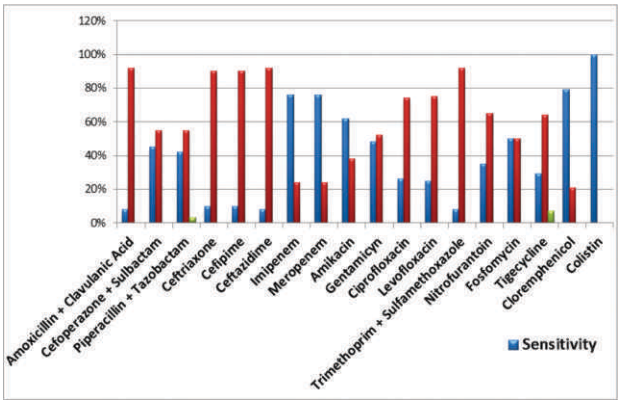

Figure 5: *The Bar Chart displays Comparative Percentages of different Classes of Antibiotics used to treat urinary tract infections in the hospital. There is a marked emergence of resistance patterns of different antibiotic groups.*

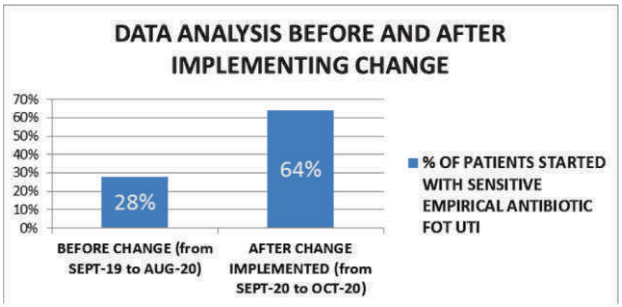

Figure 6: *This Bar Chart shows the Marked*

Increase in Percentage of Patients Getting Accurate/ Sensitive Empirical antibiotic for UTI Management, before and After Sharing Culture and Sensitivity Data with Doctors at Hospital

DISCUSSION

The aim of this study was to evaluate the frequencies of common uropathogens and their associated drug sensitivities and resistance patterns to different classes of antimicrobials. It was intended to use the results of these factors to modify the empirical antibiotic regime for treating UTIs at our local hospital. Uropathogens were studied according to their resistance patterns like MDR, XDR and NO resistance organisms. Similarly, enzyme production abilities also classified uropathogens into ESBL (extended spectrum beta lactamases), Carbapenamases and NO beta lactam respectively.

In this study, only gram negative organism associated UTIs were considered. We observed that E.coli was the most common uropathogen, implicated in 57.14% of the in-patient department UTIs, followed by Klebsiella being responsible for 24.41% of the infections (See fig-1). This trend is comparable worldwide. Similar results were observed in a study conducted in Punjab, Pakistan in 2015 where urine culture isolates showed 62% of E.coli linked urinary tract infections.[17] A study conducted at a teaching hospital in Nepal in 2017 had similar results with E.coli being the most predominant organism for UTIs causing 68.4% of the total infections over a one year period.[18]

In our study sample 64.28 % of the uropathogens were labeled as ESBL (See fig-3). The ESBL group was further studied and it was found that E.coli was the most common organism (61.11 %) which was followed by Klebsiella (25 %). Almost a mirror image of these numbers was observed in a study conducted over uropathogens in Punjab, Pakistan (2015) where the percentage of the ESBL-producing organisms was 65.9% and E.coli was the most common (66.8%) among ESBL category.[17] A study done in Nepal in 2017 showed 38.9% ESBL in their sample.[18] Another comparable stats can be seen in a study done in Netherlands (2014) where E.coli was most common (47%).[19]

An important take away from this study was to observe the drug resistant patterns among the uropathogens. As shown in (fig-2), our sample had 73 % MDR organisms and 17.89% XDR organisms. This increasing trend of resistance has been seen in recent studies like the one done in Pakistan (2009) – (MDR: 83% and XDR : 29.3%).[20] And another research done in Iran during 2013 showed MDR equal to 68% of total sample.[21]

One of the most crucial aspect of this study was to find out the sensitivity and resistance patterns of different antibiotic classes against different uropathogens. Our data analysis showed drugs that had the highest resistance patterns included Amoxicillin+ Clavulanic Acid , Trimethoprim-SMX and Ceftazidime (92%), Ceftriaxone and Cefipime (90%), Ciprfloxacin and Levofloxacin (75%) and Nitrofurantoin (65%). On the other hand, list of drugs with highest sensitivity patterns comprised of Carbapenems (76%), Amikacin (62%) and Colistin (100%) (See fig-5). Similiar trend of rising drug resistance in classes like penicillins, cephalosporins, TMP-SMX, ceftraixone, flouroquinolones and a high sensitivity pattern to drugs like carbapenems and aminoglycosides, is seen in recent studies conducted in (Iran in 2013),[21] (Nepal in 2012)[22], (Hungary from 2004 to 2015).[23]

Several risk factors were seen to be linked with severe UTIs like old age, female gender, diabetics, intensive care admission, sexual activity, vaginal infection, and genetic susceptibility. In our study, there was a significant association of diabetes and critical ICU admitted patients with severe UTI. The p-value was found to be (< 0.001) for both of these risk factors (See table - 1). As compared to this, a study performed in India in 2017 depicted a similar significance for diabetes linking with UTIs, having a p-value (< 0.011).[25]

It is evident that pathogens have become more and more resistant with each passing decade. There are a number of factors which are supposed to

contribute to this pattern. Bacteria encounter a myriad of potentially growth-compromising conditions which force them to adapt to the changes. These factors are called 'Stresses' which cause the bacteria to produce a protective response and enhance the survivability chances of the organism. One important factor is that, antimicrobials themselves in the process of cellular activity cause cellular adaptive responsive to develop in that organism. Cellular responses to nutrient limitation (nutrient stress), oxidative stress, cell envelope damage (envelope stress), antimicrobial exposure and other growth-compromising stresses, have all been linked to the development of antimicrobial resistance in Gram-negative bacteria. Therefore, apart from environmental changes, over exposure to antimicrobials over a period of time can cause antimicrobial resistance in pathogens.[24]

The initial data from patient file records showed the frequency of different empirical antibiotics used for treating suspected UTI patients. Over a period of 1 year, carbapenems, cephalosporins and aminoglycosides were used empirically in 31%, 24% and 4% of the suspected patients respectively. Around 12% of the cases, no antibiotic could be started empirically (See fig-4). In our initial data analysis, it showed that only 28% of the patients were given the correct empirical antibiotics according to their culture and drug sensitivity reports. Clinicians were presented with this data and they were educated regarding different sensitivity and resistance patterns. This resulted in modifying the local hospital guideline for empirical antibiotic regime for UTI. Further analysis spanning over a couple of months was conducted. The data from the patient records was re-analyzed, which showed that during this period 64% of the patients were given the correct empirical antibiotic which matched their sensitivity reports (See fig-6).

It is evident that pathogens possess the ability of evolving resistance at an exponential rate. Basic science mechanisms of these evolving resistance patterns should be studied and local level researches should be conducted to develop a better understanding. Using this information better antibiotic choices can be made. In our country, many newer broad spectrum antibiotics to treat MDR and XDR are not available. Efforts should be made for the development and provision of these highly sensitive antibiotics for treating severe UTIs. Such developments would lead to better clinical outcomes in terms of lower risk of relapse and lower mortality. Practitioners in the clinical settings should be educated regarding the impending evolution of resistance patterns in pathogens. Different clinical trials should also be performed to help study the role of various emerging antibiotics which have better sensitivity patterns. This would further help us choose the best antibiotic among the available choices.

CONCLUSION

The main aim of this study was to check the prevalence of different Uropathogens and their associated sensitivities and resistance patterns to different antimicrobial classes. The results showed that apart from a few newer broad spectrum antimicrobials, there is an increasing trend of drug resistance. These results were used to educate clinicians and update empirical antibiotics guidelines at our local hospital. However, there is much need to carry out further studies and clinical trials at local, regional and national level to further evaluate the evolving resistance patterns and to study the reasons behind it.

Limitations of Study

Limitations of this study include that it is a single center, cross sectional study done at a single point of time. It has a small sample size of 81 hospital admitted patients. Several risk factors linked with UTIs were studied but other factors like prior hospitalization, previous history of UTI, recent use of broad spectrum antimicrobials were not included. The detection of extended-spectrum beta-lactamases (ESBL) production was carried out using the cephalosporin/clavulanic acid combination discs method according to the guidelines set by CLSI (clinical laboratory standard institute) but the

Minimum Inhibitory Concentrations (MIC) was not done.

Acknowledgment

This research was fully supported by Farooq Hospital West Wood Lahore. Authors are highly thankful to Dr.Omair Farooq (Medical Director) for providing the patient records and lab data.

Conflict of Interest

None to declare

Financial Disclosure:

None to disclose.

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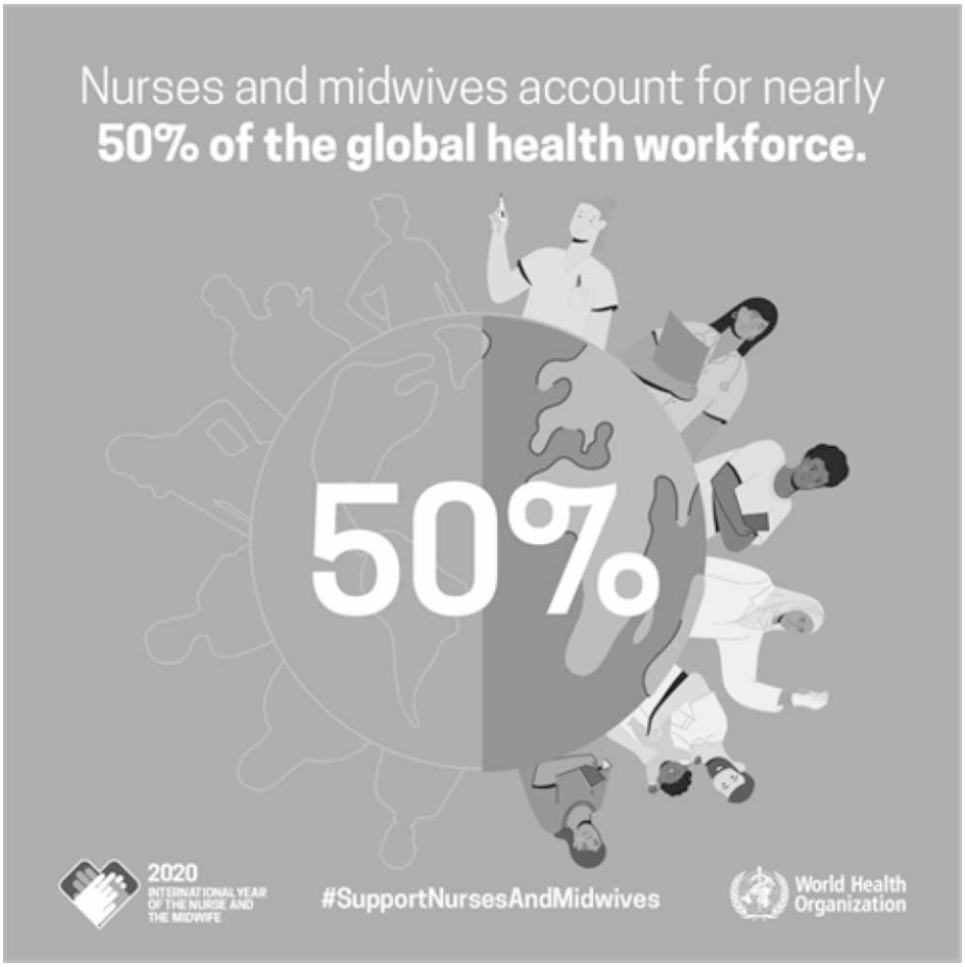

MODIFIED RADICAL MASTECTOMY WITH AND WITHOUT DRAINS -- A RANDOMISED CONTROL TRIAL

Kiran Siddiqui,[1] Naila Jabbar[2]

How to cite: Siddiqui K, Jabbar N. Modified radical mastectomy with and without drains – a randomized control trial. JAIMC. 2020; 18(4): 779-84.

Abstract

Background: Seroma is a collection of serous fluid in the dead space of post mastectomy skin flaps , axilla or breast following modified radical mastectomy (MRM) or breast conserving surgery (BCS) that can lead to significant morbidity such as wound haematoma, delayed wound healing, wound infection, wound dehiscence, prolonged hospitalization, delayed recovery and initiation of adjuvant therapy. Routine drain placement after breast cancer surgery is standard practice. Anchoring the axillary and mastectomy flaps to the underlying chest wall with sutures has been advocated as a means of avoiding drainage following breast surgery. This study compares outcomes following flap fixation vs routine drain placement as well as considers the economic implications of each technique.

Methodology: Data on seroma formation and wound complications following mastectomy and axillary clearance were recorded prospectively. Patients underwent either routine drain placement or flap anchoring by applying multiple rows of subcutaneous sutures without drainage. Equipment and surgical bed costs were also calculated .

Results: Data was available for 56 patients. 27 patients in group A (SD) underwent routine drainage while 29 in group B (FA) underwent flap anchorage without drainage . There were statistically significant lower rates of seroma formation, flap necrosis and wound infection in group B patients as compared to group A. The length of hospital stay was also shorter in group B (1.26 days vs 3.19 days respectively) compared to group A with 7 patients requiring repeated hospital admissions for the management of one or more complications while the rate of readmissions in group B was zero. Flap suturing equated to considerable financial savings.

Conclusion : Flap anchorage technique presents a viable alternative to drain placement with lower rates of seroma formation and other complications and can also lead to considerable economic savings.

Key Words: Seroma, Flap fixation, Flap anchoring, Breast cancer

Seroma is a collection of serous fluid in the dead space of post mastectomy skin flap, axilla or breast following modified radical mastectomy (MRM) or breast conserving surgery (BCS).[1] However there is inconsistency in the definition of seroma across published works. This presumed complication , albeit usually of minor consequences may prolong recovery, length of hospital stay and over stretch the health budget. The reported incidence of seroma formation varies widely between 15 and 18 percent.[2] There are several factors implicated in seroma formation like the extent of lymph node clearance, number of positive nodes, the use of post-operative radiation and whether intraoperative lymphatic channel ligation was done or not. But opinions differ as to their original role[2,3]. The main pathophysiology of seroma is still poorly understood and remains controversial. The optimal ways to reduce the incidence of seroma formation are unknown.

Seroma accumulation elevates the flaps from the chest wall and axilla thereby hampering their adherence to the tissue bed. It can thus lead to significant morbidity such as wound haematoma, delayed wound healing, wound infection, wound dehi-

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Submission Date: 28-08-2020
1st Revision Date: 26-09-2020
Acceptance Date: 30-09-2020

scence, prolonged hospitalization, delayed recovery and initiation of adjuvant therapy.[4]

There are several techniques in practice that have been reported to prevent or reduce seroma formation but no single method has been shown to be consistently and reliably effective. They can be discussed as (i) surgical techniques, (ii) the use of sealants and sclerotherapy, (iii) compression dressing, (iv) the use of drains, (v) shoulder exercise (delayed versus early) and (vi) the role of octeriotide.[5]

Use of suction drainage in the management of mastectomy patients has been found in various studies superior to other methods of fluid evacuation to minimize the dead space.[6] The mechanism posed is that the suction helps skin flaps to adhere to the chest wall and axilla sealing off all the leaking lymphatics.[7,8] This reduces the incidence of post – operative seroma, hematoma formation and flap necrosis, which are recognized complications of modified radical mastectomy.[7,8] When no post-operative suction drains were used, the incidence of seromas was found to be unacceptably high in various studies.[9] Prolonged drainage on the other hand, may increase the hospital stay and increase the risk of infection by allowing retrograde migration of bacteria.[9] Indiscriminate or premature withdrawl of post-operative drains, irrespective of the amount of fluid drained may be accompanied by an increase in the incidence of axillary seromas.[9-11] If kept for longer periods it has been observed the drain itself might contribute to increased drainage and the risk of infection in addition to the increased hospital stay resulting in wasteful utilization of the hospital resources. The use of drains is therefore a two edged sword . The present randomized controlled trial was thus carried out to compare outcomes after modified radical mastectomy (MRM) with and without drainage, using flap suturing technique at the pectoral area.

METHODOLOGY

Sixty female patients undergoing modified radical mastectomy with level 2 axillary dissection in our unit from July 2015 to December 2019 were inclu-ded in the study and were randomly allocated into one of the two groups (Group A= Suction drainage (SD), Group B = Flap anchorage (FA). Four patients were excluded from the study because primary clo-sure of the mastectomy flaps was not possible due to the large defect created by resection of bulky tumors. In these cases latissimus dorsi myocutaneous flap reconstruction was done. The procedures were per-formed by consultant surgeons .

All mastectomies were performed by scalpels and scissors in order to minimize tissue trauma. The axillary contents were also removed by sharp instruments. Electrocautery was not used. Meticulous haemostasis was secured. Only a single Redivac suction drain was placed beneath the mastectomy flaps and axilla in group A (SD) which was removed around the fourth or fifth post-operative day when the drainage was less than 50 ml per day. Size of tube drains and negative suction pressures applied were kept constant in all cases. Volume of contents in the drain bottles was noted daily.

In group B (FA) the mastectomy flaps were anchored to the underlying muscles by applying multiple rows of continuous vicryl 2/0 (Ethicon) sutures for obliteration of the dead space (pictures 1,2 and 3). Interstitch distance was about 7-8 mm and the distance between the rows around 1-1.5 cm. Three to four rows of sutures were usually sufficient for each flap depending upon its size. Care was taken not to include the long thoracic nerve in the suture bite when anchoring the axillary flaps.

Pressure bandages were not applied to any patient in either of the two groups. All patients were given three doses of intravenous 3rd generation cephalosporin's post-operatively.

Patients were discharged when they were comfortable. Those in group A went home with a drain in place after getting clear verbal and written instructions about care of the drain.

First follow up for all patients was scheduled on

5th post-operative day. Viability of flaps, seroma formation (ultrasound examination) and signs of wound infection were looked for. Drains were removed in group A patients if the output was less than 50ml per day. If more than that, subsequent visits were planned accordingly. Those with uneventful recovery were scheduled for 2nd follow up on 10th post-operative day for removal of skin sutures and again ultrasonography was done to assess for the presence and volume of seroma formation if any, which was then aspirated if the quantity was more than 100 ml. Any infections if found were managed accordingly. 3rd and 4th follow ups were done in 3rd and 4th post-operative weeks in which ipsilateral arm mobility was encouraged, wound examination and ultrasonography were also done. After complete wound healing patients were referred to oncologist for adjuvant therapy.

RESULTS

Data presented is of 56 patients, twenty seven in group A and twenty nine in group B. If we look at the results (table 1) we find that 16 patients in group A (56%) developed seroma while 6 patients (22.2%) developed flap necrosis. None of the patients in group B developed flap necrosis (p value < 0.007) and only 2 patients developed seroma formation (p value <0.001) which was less than 100 ml in both the patients and was detected on ultrasonology .

The average length of hospital stay (LOS) in group A being 3.19 days (p value <0.000) and in group B, 1.26 days, another statistically significant finding as shown in table 2.

7 patients (25.9%) in group A underwent repeated hospital admissions because of development of one or more complications listed above but none in group B required a readmission.(p value<0.003)

Table 1: *Complications*

	GROUP A n= 27	GROUP B n=29	P value
Seroma formation	16 (59.3%)	2 (6.9%)	<0.001
Flap necrosis	6(22.2%)	0	<0.007
Wound infection	10(37%)	1(3.4%)	<0.001

Table 2: *Hospital Stay and Readmissions*

	GROUP A n= 27	GROUP B n=29	P value
Average length of hospital stay (LOS)	3.19 days	1.26 days	<0.000[a]
Readmissions	7 (25%)	0	<0.003[b]

a Mann-Whitney test
b Fisher`s exact test

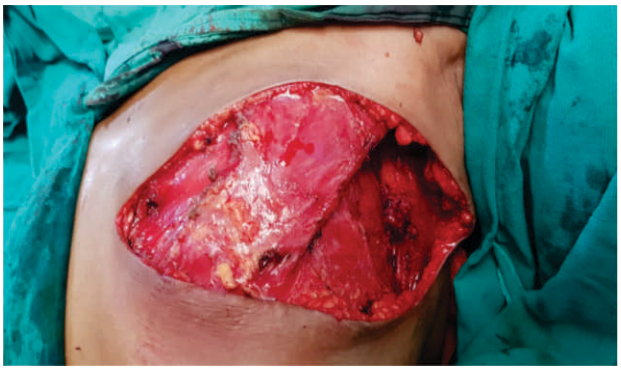
Table 3: *Cost Analysis*

Single surgical bed/24 hours	PKR 10,000 US$ 64*
Total cost per 100 patients having routine drainage	PKR 3,400,000 US$ 21,795*
Total cost per 100 patients having flap anchorage	PKR 1,350,000 US$ 8,654*
Total savings achieved using flap anchorage technique per 100 patients	PKR 2,050,000 US$ 13,141*

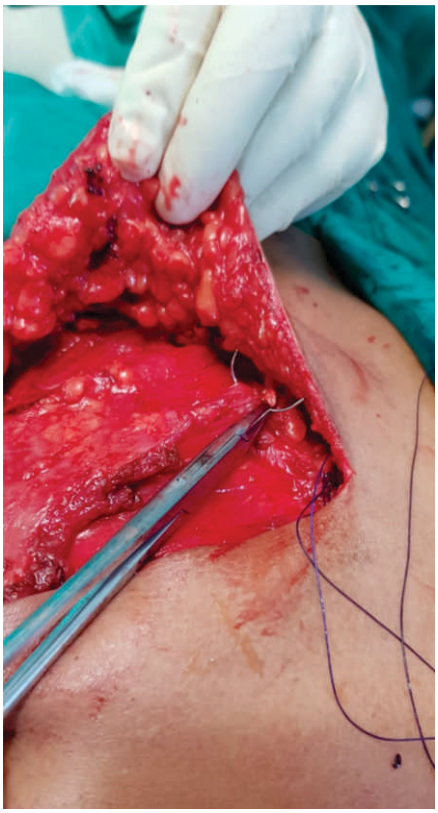
*approximately

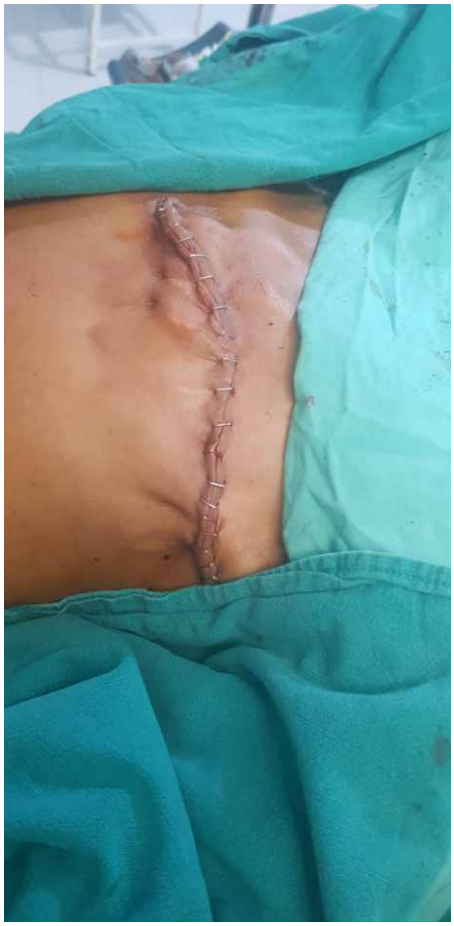
In our hospital, the estimated cost of a single surgical bed is PKR 10,000 per day (table 3). This includes medical, nursing and pathology costs as well as building, construction and medical equipment.

The surgical items required for doing mastectomies with drainage cost approximately PKR 4000 while mastectomies with flap anchorage cost around PKR 3500 per patient. These cost estimates donot take into account the amount of money that the patients and their families have to spend on food, transportation, accommodation etc. each day during their stay in hospital nor do they take into account the economic implications of productivity loss because



of prolonged absence from work .





DISCUSSION

Seroma formation is the most frequently observed early complication after breast and axillary surgery. The use of closed suction drainage is a common practice that has been shown to reduce the incidence of seroma formation.[6-11] These drains are usually removed once the lymph production falls to 35 to 50 ml per 24 hours, a level generally reached between 3 to 17 days after surgery.[6] The length of post-operative axillary drainage is the major cause of morbidity after axillary dissection as the patients are usually discharged only once the drains are removed. The patients with suction drain in situ are normally managed in the hospital (although some authors advocate discharge with the drain in situ).[18] Migration of bacteria along these drains has also been observed which increases the risk of infection if the drains stay in situ for a long time.[12] Early or premature removal however has been found to be associated with unacceptably high incidence of seroma formation and its continuation until fluid discharge is acceptably low, leads to a prolong stay in the hospital, which has a bearing on the cost of surgical management of breast cancer.[6,16-18]

Shortening the hospital stay has been shown to be an effective way of reducing the cost of surgery for breast cancer and axillary drains are the main obstacle in achieving it.[6,13-15] To reduce the hospital stay after MRM, early discharge with the drains in situ has been reported but discharging patients with drains in situ has an inherent difficulty faced by the patients in the management of drains besides higher incidence of wound infection and lower levels of patient satisfaction.[18,19] The other disadvantages are discomfort for the patients, with difficulties in undressing, lying down or using the toilet. It may be feasible with patients of higher culture and social standing but not all the patients have the required background or adequate assistance to help them manage their drains.

In a developing country where the patients are poor, uneducated, coming from far and remote areas with limited medical facilities there is an added

difficulty in management of the drains away from the hospital.

There is therefore a considerable cohort of patients for whom early discharge with drains in situ is not appropriate or who suffer increased anxiety as a result. Breast units all over the world continue to search for alternate solutions to the challenge of seroma prevention and prolonged hospital stay.

Skin flap fixation to reduce dead space may be as effective as routine drainage at lowering seroma rates as is evident from many clinical trials. Halsted[20] first described flap fixation in 1913 and others have since described techniques of anchoring flaps to close dead space. In 1993, a randomised controlled trial (RCT) by Coveney et al.[21] demonstrated that fixation of the skin flaps using multiple tacking sutures to close the dead space reduced seroma formation in patients undergoing mastectomy. Subsequently, an RCT by Purushotham et al.[22] demonstrated that mastectomy without drainage does not increase seroma formation when this technique is applied. Other studies have found similar results, but the use of routine drainage has remained standard practice in most specialist units.[23,24]

In an attempt to reduce costs and expedite early hospital discharge whilst maintaining a high-quality service, we compared rates of seroma formation, wound complications and LOS following either routine drain placement or flap fixation and examined the financial implications of each technique.

Our results show strong evidence in favour of flap anchorage technique. None of the patients in group B(FA) developed flap necrosis ($p< 0.007$) and only one developed wound infection ($p< 0.001$) while only 2 patients (6.9%) developed seroma formation ($p < 0.001$) which was less than 100 ml and detected on ultrasonology. This is in contrast to group A (SD) in which 16 (59.3%) patients developed clinically significant seroma requiring repeated aspirations and 6 patients (22.2%) developed flap necrosis. The number of patients developing wound infection was 10(37%). This increased the average length of hospital stay in group A compared to group B (3.19 vs 1.26 days respectively) $p < 0.000$ with seven patients (25%) requiring repeated hospital admissions for the management of one or more complications in group A and none in group B ($p<0.003$).

The financial implications of the two procedures are tremendous as shown in table 3. The total cost of doing mastectomies with drain per 100 patients, with each patient spending on the average three days in the hospital, is approximately thirty four lakh rupees (US$ 21,795) while that of doing mastectomies with flap anchorage technique, whereupon the patient remains admitted for only twenty four hours or so, is around thirteen lakhs and fifty thousand rupees per 100 patients (US$ 8,654) . The amount of money that can be saved with switching to the flap anchorage technique is atleast twenty lakh and fifty thousand rupees per 100 patients (US$ 13,141). This amounts to considerable financial savings without causing any adverse effects on patients outcome. The resources thus saved , in an economically constrained country, can be put to other areas of patient care , treatment and research.

CONCLUSION

In this study, flap anchorage without drainage resulted in a significantly shorter hospital stay without any increase in the incidence of seroma formation or wound infection. We suggest that the policy of routine drainage, as practiced by most of our surgeons, should be reviewed. Flap fixation is a viable alternative to routine drain placement and could lead to considerable financial savings, which if considered at national level, potentially summate to saving of several million rupees .

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BREAST CONSERVING THERAPY WITH SENTINEL LYMPH NODE BIOPSY IN A TERTIARY CARE HOSPITAL

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How to cite: Siddiqui K, Tariq S, Abbas, T. Breast conserving therapy with sentinel lymph node biopsy in a tertiary care hospital. JAIMC. 2020; 18(4): 785-91.

Abstract

Background: Breast conserving surgery (BCS) with sentinel lymph node biopsy (SLN) is a standard, safe and preferred therapeutic procedure in early detected breast cancers because it provides the same level of overall survival as mastectomy. Yet in many develeoping Asian countries including Pakistan this procedure is not popular. We have shared our early experience on a small cohort of patients with encouraging results as well as looked into the reasons surgeons are reluctant to take up this procedure and suggested solutions as well.

Objective: To evaluate outcome of breast conservation therapy with sentinel lymph node biopsy in a tertiary care setting.

Results: Thirty-seven patients underwent Breast conserving therapy with sentinel lymph node biopsy over a period of 3 years. Mean age was 32.5years (range 20-70yrs) . 31patients (83.7%) had symptomatic breast cancer, while 6 patients (16.2%) had screen detected malignancy. Sixteen patients had stage I disease while twenty-one had stage II disease. Among 37 patients with breast cancer, 17(45.9%) were classified as T I while 20(54.1%) had T2 disease. Twenty-three patients (62.1%) were found to be node positive on frozen section and underwent level 2 axilary clearance while fourteen (37.9%) were nodes negative.

Conclusion: Breast conservation surgery is safe ,effective and cosmetically superior procedure providing greater patient satisfaction and comparable outcomes.

Key words: Breast cancer, Breast conservation therapy, Sentinel lymph node sampling

According to the figures published by Global Cancer Observatory 2018, breast cancer has the highest age standardized incidence (34.4%) and second highest mortality rate (19.6%) with 911014 (22.3%) newly diagnosed cases reported in Asia. It is probably one of the most researched cancers all over the world with tremendous changes and refinements in every aspect of its treatment witnessed over past few decades. But when it comes to surgical options, we find that unlike Western hemisphere, breast conservative therapy (BCT) is unpopular in Asian countries. In Western countries, BCT rates are often reported to be in excess of 60% (Table 1).[1-4] This is in contrast to Asian communities where the average reported rates of BCT are considerably lower.[5-11] This discrepancy between BCT Vs Mastectomy rates in Western and Asian communities has been attributed to many factors which we will discuss in our study as well as share our own experience of performing BCT with sentinel lymph node biopsy in a small cohort of 37 patients with encouraging results.

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Submission Date: 30-08-2020
1st Revision Date: 27-09-2020
Acceptance Date: 30-09-2020

METHODOLOGY

A study was conducted at Surgical Unit I between Jan 2015 to Dec 2019. Prospective data of 37 patients fulfilling the inclusion criteria (women with stage I and II disease, upto 70 years of age with no contraindications to chest wall irradiation therapy and BCS, and committed to completion of adjuvant therapy) were included in the study. The treatment of each patient was tailored according to wishes of the patient and recommendations of tumor board which comprised of specialist surgeon, pathologist, radio-

logist, medical oncologist and radiotherapist. Detailed multiple counselling sessions were done with patients and their families.

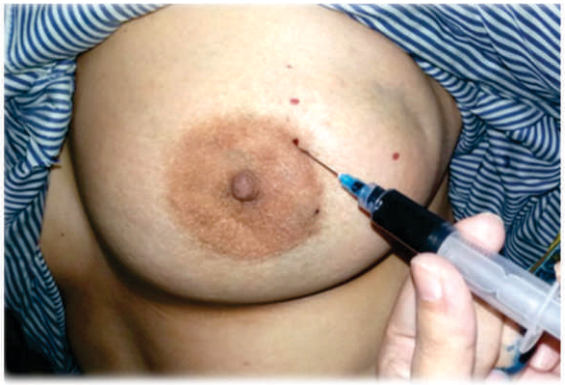

Figure 1: *Blue Dye being Injected*

All patients underwent breast conservation surgery. Lumpectomy with 1 cm tumour free margin was carried out. For sentinel lymph node biopsy 4-6 ml methylene blue dye was injected in the intradermal sub areolar region of the breast having malignancy approximately 4 -6 hours before surgery (figure 1). First 2-4 lymph nodes identified during dissection because of colour staining (figure 2) were sent for intra operative frozen section analysis alongwith breast lump to assess margin status (in all patients of BCT to lower re- excision rates).

Successful BCT was defined by pathological clear margins and completion of recommended adjuvant therapy. After completion of treatment, patients were followed up three monthly for first two years and then six monthly. At each follow up detailed history and clinical examination was done alongwith symptoms directed investigations. Post BCT mammo-gram was obtained annually after

Table 1: *Comparison of Published Data for BCT Rates*

Author	Centre/Country/Study Period	n	Characteristics	% BCT
International/Western				
Agarwal et al.. 2014	SEER database (1998-2008)	132 149	Tumour <*A*cm. 5.3 lymph node +	70%
McGuire et al., 2009	Moffitt Cancer Centre, FI., USA (1994-2007)	5865	Stage 0-IV	63.70%
Lee et al., 2009	University of Michigan Medical Centre, Michigan, USA (2003-2005)	993	Tis-T4	63%
Garcia-Etienne et al, 2012	EUSOMA (2003-2010)	15,369	Stages 0,1, II (stage III.T3/T4 excluded)	73.30%
Local				
Chuwa et al.. 2009	National Cancer Centre Singapore (2002-2003)	767	Symptomatic Screen detected Stage 0-IV	28.20% 45.20% 31.50%
Wang et al., 2011	Changi General Hospital. Singapore (2002-2008)	761	Symptomatic Screen detected Stage 0-IV	18.50% 40.20% 23.30%
Chang et al., 2011	National University Hospital. Singapore (1990-2007)	2449	Stage 0-IV	29.20%
Woon and Chan. 2005	Tan Tock Seng Hospital. Singapore (2000 -2002)	389	Stage I JIB (T1-T2)	39.10%
Regional (South Asia/East Asia)				
Yip et al.,2009	University of Malaya Medical Centre (2001-2005)	953	T1.T2	29.70%
Yau et al., 2009	Pamela Y. Nethersole Eastern Hospital. Hong Kong (1994-2007)	2375	TI.T2	30%
Gadgil et al., 2012	Bhabha Atomic Research Centre Hospital, Mumbai (2005-2010)	99	T1-T4	42.20%
Jung et al., 2011	Korean Breast Cancer Society database (2008)	13.908	Stage 0 J	58%
Current Study	MammoCare, Singapore (2009-2011)	116 45 161	Symptomatic Screen detected Stage 0-IV	81.80% 95.60% 85.70%

*BCT: Breast conservation treatment: SEER: Surveillance. Epidemiology and End-Result; FL: Florida, USA: United States of America

completion of radiotherapy. Women receiving tamoxifen were referred for annual gynaecological examinations.

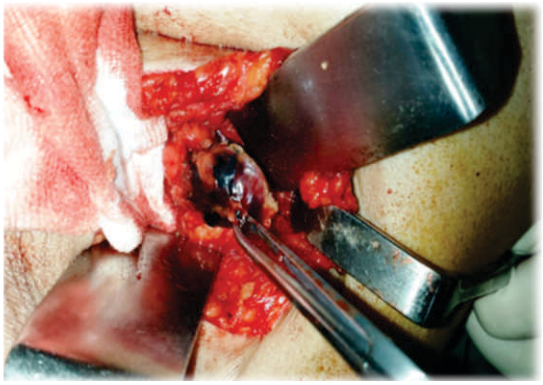

Figure 2: *Stained Sentinel Lymph Node*

RESULTS

Thirty-seven patients underwent Breast Conserving Therapy with sentinel lymph node biopsy over a period of 3 years. Mean age was 32.5 years (range 20-70yrs). Relevant demographic and tumour characteristics are provided in Table 2. Twenty five patients (67.5%) were pre-menopausal, four (10.8 %) peri-menopausal and eight (21.6%) were post-menopausal. Thirty-one patients (83.7%) had symptomatic breast cancer, and six (16.2%) had screen detected malignancy. All patients had infiltrating ductal carcinoma. Of the thirty seven patients with breast cancer, seventeen (45.9%) were classified as T1 and twenty (54.1 %) as T2 . Ten (27%) patients had a grade 3 tumour, nineteen (51.3%) had grade 2 and eight (21.6%) were grade 1. BCT with sentinel lymph nodes biopsy was successfully carried out in all 37 patients with 0% mortality and a median follow-up of 18months (range 12-36). 2 patients (5.4%) had surgical site infection which was managed conservatively (Table 3).

Table 2: *Demographic and Clinicopathological Profile of Subjects*

Variables n= 37	Frequency	Percentages
Age (years) Mean = 32.5		
20 – 45	21	56.7
46 – 70	16	43.2
Menstrual status		
Pre-menopausal	25	67.5
Peri –menopausal	4	10.8
Post-menopausal	8	21.6
Mode of Presentation		
Symptomatic tumours	31	83.7
Detected on screening	6	16.2

Table 3: *NPI status of Patients*

Variables n =37	Frequency	Percentages
Tumor size at presentation Mean =**3.3cm**		
T1	17	45.9
T2	20	54.1
Tumor Grading		
I	8	21.6
II	19	51.3
III	10	27.0
Lymph node as frozen section report		
Positive	23	62.1
Negative	14	37.9

DISCUSSION

For about three decades, BCT and mastectomy have been considered to provide equivalent survival for women with breast cancer.[12] There is now recent data to suggest that BCT may confer a higher breast cancer-specific survival rate compared with mastectomy.[4] Although the reasons behind this observation have yet to be clearly elucidated, this new information elevates the role of BCT in women with early breast cancer. Thus, a low rate of BCT, as seen in Asian populations, may not offer optimum survival. Most series of surgical treatment of breast cancer in Asian countries report BCT rates lower than 55%. Table 1 lists BCT rates from different regions. Mac Bride et al has recently published a non-systematic review paper highlighting factors associated with therapy choice.[13] They identified some key factors in literature including role of surgeon, patient's beliefs and access to radiation facility. To this list we will like to add another factor and that is underutili-zation of available resources. Many tertiary centres and a large number of surgical specialists in our country are underutilizing the procedure of BCT which is considered a resource intense treatment that can only be offered to a small number of patients at centres with high expertise and state of the art facilities.

We faced similar apprehensions but then we decided to make use of what was easily available around us. For sentinel lymph node biopsy, instead of patent blue dye or radioisotopes we used methylene blue which is easily available. To decrease false negative results, we sampled at least 4 lymph nodes in each axilla. A few laboratories have started offering frozen section facilities at subsidized rates and we have been sending our patients on table sentinel lymph node samples and lumpectomy specimens to them. If more and more surgeons start practising BCT and utilizing this facility, we are sure that the number of laboratories offering frozen section facilities will increase.

In physician related factors, we found data supporting female gender, higher case number, training and individual surgeon practises being associated with increased BCT rates.[14-19] Hersmen et al conducted a large SEER database review with over 56,000 patients; this study looked at the most surgeon-related characteristics. They found increased BCT rates associated with multiple characteristics including being US-trained (OR, 1.12; 95% CI, 1.03-1.22), performing > 10 BCT procedures (OR, 1.29, 95% CI, 1.21-1.38), year of graduation after 1975 (OR, 1.16; 95% CI, 1.08-1.25), and the most influential being female gender (OR, 1.40; 95% CI, 1.25-1.55).[14] A much smaller survey of Colorado women by Cyran et al also found female physician gender associated with increased BCT rates (OR, 3.8; 95% CI, 1.21-14.4).[19]

When patients are diagnosed with breast cancer they obtain support and advice from multiple sources esp.when making decisions regarding type of breast surgery. The surgeon's recommendations or preference for a particular type of procedure is frequently cited an important factor in this decision-makingprocess. But medical decision-making has evolved over the last several decades from one based on paternalism, in which the physician decided on the best course of treatment according to his/her view of what was in the best interest of the patient, to one focused on patient autonomy, in which the informed patient makes decisions about accepting or declining treatment options based on his/her own values and priorities. In modern medical ethics, shared decision-making has been proposed as the ideal model for medical decision-making that both acknowledges patient autonomy and the role of the physician in providing expert medical opinion[20,21]. This model is particularly suited to treatment decisions in the management of the primary tumor in breast cancer, as the patient may face several surgical treatment options that result in equivalent oncologic outcomes. Now the question arises as how to empower the patient to play a more proactive role in choosing the treatment that best suits them. For this we think adopting a multidisciplinary treatment approach can be very useful.

The use of multidisciplinary treatment teams/ tumor boards is becoming quite common in the management of breast cancer patients, especially at larger, academic institutions where breast cancer specialists are available in multiple disciplines. One of the benefits of a multidisciplinary approach is that patients understand all the components of their breast cancer treatment prior to starting treatment, and this increased knowledge may have an impact on treatment decisions regarding surgery for breast cancer. In a study of elderly women aged ≥ 65 years with local or regional breast cancer treated from 1994 to 1995, those patients who had a consultation with a radiation oncologist preoperatively were 6.7 times more likely to have BCS compared to those who did not ($P \leq 0.001$).[22]

Our unit has been conducting tumor boards regularly for past two years. The board is held fortnightly and all new cases of different malignancies admitted in the ward are discussed thoroughly. The treatment of patients is then tailored according to their wishes and recommendations of board which comprises of specialis surgeon, pathologist, radiologist, medical oncologist and radiotherapist. We strongly recommend that all tertiary care hospitals must establish multidisciplinary boards in their instituitions to optimise patient management and satis-

faction.

Another important factor related to surgeons is training. All surgeons practising breast cancer surgery should get trained in breast oncoplastic surgery as well. In modern science women with smaller volume breasts cannot be denied BCT. For such women, there are manoeuvres that can be applied to achieve higher BCT rates (23-27) Adjuvant radiotherapy is considered part and parcel of BCT. Treatment requires daily appointments for 4-6 weeks. Potential financial, family and overall life impact may be more for those living far from treatment locations. Both Celaya et al and Boscoe et al[28,29] conducted US-based studies that found individuals living farther from radiation treatment centers were less likely to undergo BCT. Celeya et al found that women living < 20 miles from a radiation treatment facility were at a decreased likelihood of undergoing BCT compared with women living at 20 to 40 miles (OR, 0.65; 95% CI, 0.53-0.79) and > 60 miles (OR, 0.31; 95% CI, 0.15-0.65).27 Boscoe et al reported that the likelihood of mastectomy increased monotonically with increasing distances to both the nearest surgical and radiation treatment centres. For distance to a radiation treatment centre, the highest increase was found at 75 to 100 km (OR, 1.43; 95% CI, 1.23-1.65). Therefore, Limited access to a radiation facility for adjuvant radiotherapy is a major factor inhibiting surgeons performing BCT in a community.

After 40 years of improving, increasing and extending adjuvant breast cancer therapies, there are increasing concerns about over treatment, with TIME magazine featuring this controversy on their October 2015 front cover. This editorial discusses the rationale and design of a new study, PRIME-TIME, which investigates the omission of radiotherapy after breast-conserving surgery (BCS) in patients at very low risk of recurrence by using biomarkers. It is expected IHC4 +C will prove an effective yet inexpensive method for risk stratification that can be adopted as part of standard of care.[30]

Till such time when this revolutionary treatment guideline can be adopted, we could facilitate patients receiving radiotherapy by administering accelerated partial breast irradiation(APBI)instead of whole breast irradiation (WBI). Recent data published by Strnad et al clearly demonstrates the non-inferiority of partial irradiation approach over whole breast irradiation.[31] One of the main benefits of APBI is that it reduces total treatment time from 3-6 weeks to less than a week which improves patient's satisfaction, overall quality of life, decreases toxicity to surrounding organs and tissues. APBI is also more cost effective.[32]

Meta-analysis of various studies has shown that overall main themes influencing women's choice of mastectomy were; mastectomy being more reassuring options, avoiding radiation and more expedient treatment. The main themes influencing women choice of BCT were; body image concerns and feminity, physician recommendations, long term survival being equivalent and less surgery being involved. Schou et al found individuals rating 'fear of cancer recurrence' highly correlated with choice of mastectomy (rs = 0.43; P = .000).[33] Both Temple et al (P = .001)[(17)] and Molenaar et al (P < .001)[34] found that women who underwent mastectomy rated fear of cancer recurrence significantly higher compared with women who underwent BCT. Lee et al found those rating 'removing your entire breast to gain peace of mind' were significantly more likely to undergo mastectomy as well (OR, 1.88; 95% CI, 1.60-2.20)[35] In a qualitative study, Caldon et al reported 'most reassuring treatment' as the primary reason women chose mastectomy, further stating that 'many choosing mastectomy said this option reduced their anxiety about the completeness of cancer excision.[36]

CONCLUSION

We have shared our initial experience of BCT with sentinel lymph node biopsy in a tertiary care hospital on a small cohort of patients with encouraging results. We have also highlighted and discussed the plausable contributing factors which are responsible for relatively lower rates of BCT vs mastecto-

my in our community and how we overcame those hurdles by making the best use of resources available in our setup.

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OUTCOME OF PATIENTS ON DIALYSIS INFECTED WITH COVID-19

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How to cite: Cheema SS, Habib H, Saleem M, Akhtar M, Cheema S. Outcome of patients on dialysis infected with COVID-19. JAIMC. 2020; 18(4): 792-95.

Abstract

Background: There is a lack of evidence about the optimal management of novel coronavirus disease 2019 (COVID-19), and even less data is available in patients on maintenance hemodialysis therapy than the general population who are at higher risk of worse outcome due to multiple comorbidities. So, this study was conducted with an objective to assess the outcome and its determinants among dialysis patients infected with COVID-19.

Methodology: About 80 patients who were already on maintenance hemodialysis in different tertiary care hospitals of Lahore were enrolled in this study after they contracted COVID-19 during 1st April 2020 to15th August 2020. A well designed questionnaire based on study variables was used and information regarding gender, age, duration of dialysis, need for mechanical ventilation comorbidities like diabetes, hypertension, ischemic heart disease and COPD was noted. Outcome of patients (recovery/death) were also recorded and data was analyzed using SPSS version 24.0

Results: Out of these 80 hemodialysis patients infected with COVID-19, 51(63.7%) were male and 29(36.3%) were female. Mean age of patients was 54.16±12.5 years while mean duration of dialysis was 4.02±3.04 years. About 75(93.8%) patients had at-least one comorbidity while 49 (61.3%) patients were diabetics,72(90%) patients were hypertensive,36(45%) patients had ischemic heart disease/Congestive heart failure and 3(3.8%) patients had chronic obstructive lung disease. It was seen that 54(67.5%) patients survived COVID-19 infection, 23 (28.7%) patients needed mechanical ventilation while 26(32.5%) patient died out of 80 patients enrolled in this study. Cross-tabulation was done between age, gender, duration of dialysis and co-morbidities with clinical outcome and chi square test/fischer exact test was applied. It was seen that only duration of dialysis was significantly associated with mortality (p-value = 0.045).

Conclusion: Dialysis patients infected with COVID-19 have far high mortality.

Key Words: Dialysis, COVID-19

Coronaviruses are important pathogens for humans and animals causing a spectrum of illnesses. A novel coronavirus identified in November 2019 caused pneumonia in people of Wuhan, a city of Hubei province in China. In February 2020, World Health Organization labelled the disease COVID-19 meaning coronavirus disease 2019.[1] The virus that causes COVID-19 is designated as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); formerly, it was referred to as 2019-nCoV. Although, SARS-CoV-2 mainly causes pneumonia but virtually it can affect any organ system like heart, nervous system,[2] digestive tract, blood and kidneys.[3] COVID-19 was declared a global pandemic on March 11, 2020, by the World Health Organization (WHO).[4] COVID-19 has affected huge number of people, causing up to 979,160 deaths till 24th

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Submission Date: 10-09-2020
1st Revision Date: 17-09-2020
Acceptance Date: 20-09-2020

September 2020.[5]

People with certain comorbidities like Ischemic heart disease, Diabetes Mellitus, hypertension, lung diseases and other chronic diseases are more prone to death after acquiring COVID-19[6]. End stage renal disease patients on maintenance dialysis are also at higher risk of fatality due to multiple risk factors[7]. Many comorbidities like Diabetes, hypertension, ischemic heart disease along with frequent hospital visits make end stage renal disease patients more susceptible to have severe COVID-19 disease and increased mortality.

A study was conducted in New York USA, showing mortality of 28% in end stage renal disease patients infected with COVID-19[7]. However, no data is available on this in our population of ESRD who suffered covid-19.As data is emerging day by day regarding COVID-19, this study was designed to determine the exact outcome of dialysis patients infected with COVID-19 and the role of comorbidities as predictive factors for outcome to help in evidence based management of these patients.

METHODOLOGY

This was cross sectional study including 80 end stage renal disease patients on maintenance hemodialysis for at least 3 months, reported to be infected with COVID-19 after confirmation with PCR, from different tertiary care hospitals (Jinnah hospital Lahore, Bahria international hospital Lahore, Fatima memorial hospital Lahore and National hospital Lahore) after taking an informed consent. Data was collected between 1st April 2020 to 15th August 2020, using questionnaire based on demographic profile and study variables after informed consent. All the patients were followed up to assess the outcomes as recovered, needed mechanical ventilation or expired due to COVID-19. Data was analyzed using SPSS version 24.0. Confidentiality of data was ensured.

RESULTS

Out of these 80 hemodialysis patients infected with COVID-19, 51(63.7%) were male and 29(36.3 %) were female. Mean age of patients was 54.16 ± 12.5 years while mean duration of dialysis was 4.02 ± 3.04 years. About 75(93.8%) patients had at-least one comorbidity while 49 (61.3%) patients were diabetics,72(90%) patients were hypertensive, 36(45%) patients had ischemic heart disease/ Congestive heart failure and 3(3.8%) patients had chronic obstructive lung disease. It was seen that 54(67.5%) patients survived COVID-19 infection, 23 (28.7%) patients needed mechanical ventilation while 26(32.5%) patient died out of 80 patients enrolled in this study as shown in table no. 1 and figure no. 1. Crosstabulation was done between age,

Table 1: *Characteristics of Patients*

Patient characteristics	Frequency	Percentage %
Age		
<40 years	11	13.8
41-55 years	33	41.3
>56 years	36	45
Gender		
Male	51	63.8
Female	29	36.3
Duration of Dialysis		
<5 years	65	81.3
5-10 years	10	12.5
>10 years	5	6.3
Mechanical Ventilation Needed:		
Yes	23	28.8
No	57	71.3
Expired (cause of Death is COVID-19)		
Yes	26	32.5
NO	54	67.5
Co-morbidities		
Yes	75	93.8
NO	5	6.3
COPD		
Yes	3	3.8
No	77	96.3
IHD/CHF		
Yes	36	45.0
No	44	55.0
DM		
Yes	49	61.3
No	31	38.8
HTN		
Yes	72	90.0
No	8	10.0

Table 2: Relationship of risk factors with Outcome

Risk Factors	Outcome		p-value
	Recovered	Expired	
Age of Patient			
<40 years	8	3	0.809
41 - 55 years	23	10	
> 56 years	23	13	
Duration on Dialysis (yrs)			
< 5 years	40	25	0.045
5 - 10 years	10	0	
> 10 years	4	1	
Co-morbidities			
Yes	50	25	0.538
No	4	1	
COPD			
Yes	0	3	0.11
NO	54	23	
IHD/CHF			
Yes	22	14	0.270
NO	32	12	
DM			
Yes	30	19	0.132
NO	24	7	
HTN			
Yes	50	22	0.265
NO	4	4	

gender, duration of dialysis and co-morbidities with clinical outcome and chi square test was applied. It was seen that only duration of dialysis was significantly associated with mortality (p-value = 0.045) as shown in table no. 2.

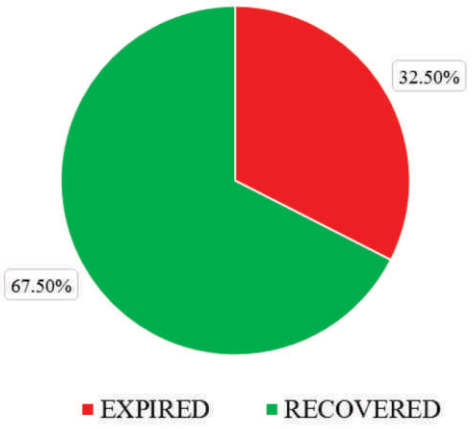

Fig. 1: *Mortality of ESRD Patients Infected with COVID-19*

DISCUSSION

End stage renal disease patients are more prone to fatality as these patients have uremic milieu which impairs primary host defense mechanisms.[8] Apart from cardiovascular disease, infections are leading cause of death in end stage renal disease patients.[9] Initial studies reported increased fatality in patients of COVID-19 with underlying comorbidities, such as hypertension and diabetes mellitus, which are more prevalent in the ESRD patient.[7] Moreover, it is seen that besides these comorbidities, End stage renal disease patients have frequent hospital visits and intermingling with other patients during waiting time making them more susceptible for acquiring infection.

Thus it is first multi-centric study in Pakistan that was designed to assess outcome of COVID-19 in patients of end stage renal disease and impact of risk factors like age, duration of dialysis, Diabetes, hypertension, ischemic heart disease and chronic obstructive lung disease on patient's prognosis. In our study 80 ESRD patients with COVID-19 were included from different tertiary care hospitals. Mean age of patients in this study was 54.12 years which is in-contrast to 64.5years reported by another study in New York[7] and this difference might be attributed to the fact that probably Asian patients develops ESRD at a younger age.[10] This difference in the age of onset might also be the reason for similar difference noted in the mean duration of dialysis as 4.02 years and 3.2 years in current study and the New York study respectively.[7] About 90% patients were Hypertensive and 61.3% were diabetics which are consistent with the findings of the study conducted by Molly et al[7]. However, inconsistency was seen in the frequency of ischemic heart disease (IHD) among ESRD patients as they reported a prevalence of 55% of IHD as compared to 45% seen in our population. This difference is likely due to relatively elder population of US had more chances of getting ischemic heart disease.

Mortality was seen in 32.5% of the patients of ESRD who suffered from COVID-19 in our study

and duration of dialysis was significantly associated with mortality. This is a bit higher as compared to mortality reported in New York study as 28% and Probably longer duration of dialysis explains little bit higher mortality in our study population as the average duration of dialysis was also higher in the current study as compared to the New York study. Studies conducted in Spain assessing outcome of COVID-19 in 36 ESRD patients on hemodialysis showed mortality of 30.5%[11] while another study done in Bresica[12] showed 29 % of ESRD patients infected with COVID-19 died which also support our results.

Main limitations of our study were relatively smaller study population and lab parameters like inflammatory markers i.e CRP, Ferritin, D-dimers have not been assessed to establish relationship with fatality.

CONCLUSION

High mortality among End stage renal disease patients emphasizes the need for strict infection control measures in dialysis centers as well as at their residences.

Centers for Disease Control and Prevention (CDC), interim guidance for infection prevention, and control recommendations for patients with suspected or confirmed COVID-19 in outpatient Hemodialysis facilities, should be followed in all the dialysis and health care centers to decrease the risk of exposure to COVID-19 and protecting lives of these patients for better outcomes.

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PREVALENCE OF COVID-19 IN ASYMPTOMATIC ESRD PATIENTS ON MAINTENANCE HEMODIALYSIS & DIALYSIS STAFF DURING CORONAVIRUS PEAK IN PAKISTAN

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How to cite: Cheema SS, Habib H, Cheema S. Prevalence of COVID-19 in asymptomatic ESRD patients on maintenance hemodialysis and dialysis staff during coronavirus peak in Pakistan. JAIMC. 2020; 18(4): 796-800.

Abstract

The outbreak of coronavirus disease 2019 (COVID-19) has become a global pandemic and posing a serious threat to hemodialysis staff and patients. The prevalence of COVID-19caused by SARS-CoV-2 in asymptomatic ESRD patients on maintenance hemodialysis (MHD) and dialysis staff is unknown. **Objectives:** Hemodialysis patients and staff are a fragile population in a mandatory congregate setting. The purpose of this study is to determine the prevalence of COVID-19 in two hemodialysis units of Jinnah Hospital, Lahore.

Methods: In this cross-sectional study, 198 asymptomatic ESRD patients on maintenance hemodialysis and 83 dialysis staff members were tested for COVID-19. They were tested using qualitative RT-PCR on nasopharyngeal swabs taken from 18th June to 23rd June 2020.

Results: Forty five out of 198 (22.7%) dialysis patients and 10 out of 83 (12%) dialysis staff members were tested positive for COVID-19. Cummulative prevalence of patients and staff was 19.5% (55/281).The mortality rate was 6.6% (3/45) among patients infected with COVID-19.

Conclusion: It was concluded that prevalence of COVID-19 is high in dialysis staff and asymptomatic hemodialysis patients in Lahore, Pakistan.

Key Words: COVID-19, ESRD, MHD, Dialysis

Starting in December 2019, Coronavirus disease (COVID-19) is a newly discovered highly contagious disease caused by SARS-CoV-2 virus, involving upper and lower respiratory tracts and may be complicated to pneumonia and acute respiratory distress syndrome. It may affect other organ systems such as the cardiovascular, gastrointestinal tract, genitourinary tract, blood, and central nervous system.[1] The rapidly spreading outbreak, which first emerged in Wuhan, Hubei Province in China, was declared a global pandemic on March 11, 2020, by the World Health Organization (WHO). The magnitude of disease spread is increasing day by day and authentic statistics are available from different sources.[2]Maintenance hemodialysis (MHD) patients are highly vulnerable for capturing infection and deve-loping its complications.[3] Many risk factors such as old age, Diabetes Mellitus, hypertension, ischemic heart disease, chronic lung diseases, and other immunocompromised conditions make this popula-tion group more vulnerable for COVID-19 infection. This vulnerability is further enhanced by their fre-quent hospital visits and close proximity toother hemodialysis patients.

Burden of COVID-19 is increasing rapidly in general population of Pakistan as recent data is suggesting that current confirmed cases of COVID-19 are 15,759 out of 144365 tested people with prevalence of 60 cases per one million population till 30th April 2020.[4] As of April 28, 2020, COVID-19 has been confirmed in over 3 million individuals worldwide and resulted in 212,000 deaths.[2] As the disease is spreading rapidly in the community, it is necessary to test all the asympto-matic patients in nursing homes and other congre-gate living situations.[5] This would be helpful in controlling the

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Submission Date: 10-09-2020
1st Revision Date: 24-09-2020
Acceptance Date: 29-09-2020

transmission of SARS-CoV-2 infec-tion in health care providers and other patients.

METHODOLOGY

It was a cross-sectional study including 198 asymptomatic ESRD patients on maintenance hemodialysis and 83 dialysis facility staff members. The study was conducted on dialysis patients and staff of two dialysis centers of Jinnah hospital, Lahore. They were tested using qualitative COVID-19 Real Time (RT)-PCR on nasopharyngeal swabs taken from 18th June to 23rd June 2020.This test has been performed on VERSANT K PCR (SIEMENS) Fully Automated PCR System (Extraction Siemens-Amplification Anatolia) at AQ Khan PCR Lab of Jinnah Hospital, Lahore.

RESULTS

Total 198 asymptomatic ESRD patients on maintenance hemodialysis were tested out of which 128(63.4%) were male and 70(36.5%) were female. Meanage of patients was 50 years. Out of 198 asymptomatic hemodialysis patients, 45 patients (22.7%) were tested Positivefor SARS-CoV-2 infection. Mortalityrate was 6.6% (3/45) among infected and no patient from COVID-19 negative group has died during this period.

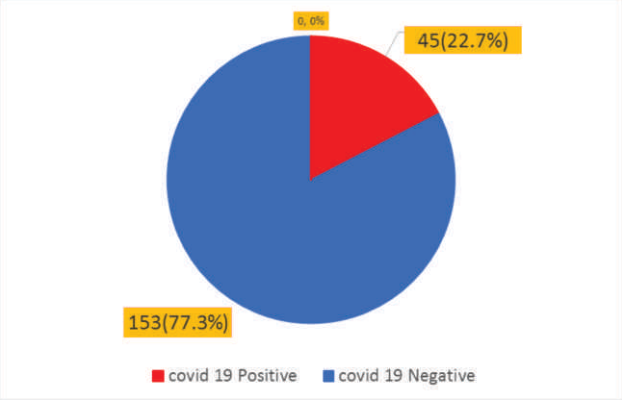

Figure 1: *Frequency of SARS-CoV-2 Infection among Asymptomatic Hemodialysis Patients is 22.7% (45 out of 198)*

Prior to screening of patients, all dialysis staff members were also tested for SARS-CoV-2 infection, from 18th June to 23rd June 2020. All 83 dialysis staff members (including doctors, nurses and paramedical staff) were tested. Ten (12%) out of 83 facility staff members were tested positive. Positive individuals included 03 staff nurses and 07 ward boys.

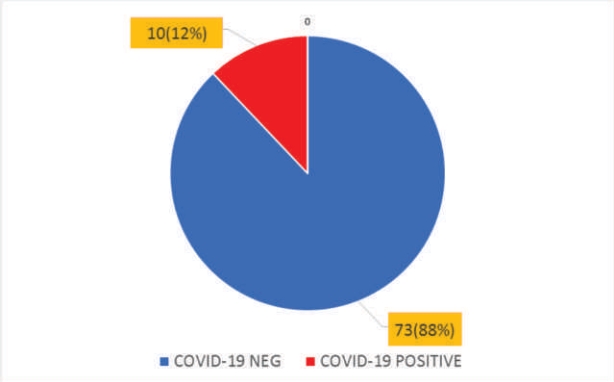

Figure 2: *Frequency of SARS-CoV-2 Infection among Asymptomatic Hemodialysis Facility Staff is 12%. (10 out of 83)*

Table 1:

	COVID-19 NEGATIVE	COVID-19 POSITIVE	TOTAL
Esrd patients on mhd	153(77.27%)	45(22.7%)	198
Dialysis unit staff	73 (88%)	10 (12%)	83
Grand total	226(98.32%)	55(19.5%)	281

The combined result of both dialysis staff and ESRD patients on hemodialysis showed 55 (1.67%) out of 299 were tested positive for COVID-19.

DISCUSSION

This cross sectional study showed high prevalence (hemodialysis patients: 22.7% & staff: 12%) of COVID 19 in asymptomatic hemodialysis population and dialysis staff. This is similar to the prevalence of 16.1% (37/233) in hemodialysis patients and 12.1% (4/33) in staff6, reported from Wuhan China. These positive COVID-19 cases were much less in April when we tested the same cohort since COVID-19 outbreak in Pakistan had still not peaked at that time. In April, The reported prevalence was 0.92% and 3.6% among dialysis patients and staff respectively. This was also seen when the epidemic emerged in the HD center of Renmin Hospital, Wuhan University. The first case was diagnosed on

January 14, 2020 and cases initially increased till epidemic's extinction on February 17, 20206. The patients and HD staff were quarantined in our dedicated COVID-19 ward. The patients are getting their routine dialysis in COVID-19 ward. If we had not tested all the patients and our staff we would have never known about these positive cases and they might have become the source of a wide spread outbreak in our dialysis unit. This is the first single center study of prevalence of COVID-19 in hemodialysis patients and staff of a tertiary care center in Pakistan.

In April, We started screening when one of our 'ward boy' was tested positive. He was asymptomatic but his test was done since he had contact with one of the ICU patient on ventilator who was positive for COVID-19. We, in phase 1, did COVID 19 RT-PCR on all the dialysis staff including nurses, ward boys/girls, doctors and other employees. A total of 83 tests were done and one nurse and one laundryman were found positive. The nurse also works at a private hospital and lives in a hostel. But we were not sure if she contracted this from the patients or staff at the dialysis center, from her hostel, or from the private hospital. All of her contacts have been advised to be tested. The laundryman was not a dialysis center employee but he would collect and deliver laundry privately for our dialysis center. We were worried that the ward boy, laundryman, or nurse might have spread or become the source of outbreak in our dialysis center. So, in phase 2, we decided to test our whole dialysis patient population rather than the potential contacts of these positive cases. Thus overall 216 nasopharyngeal swabs at the bed side of dialysis patients were collected. RT-PCR for COVID-19 were carried out at AQ Khan PCR lab of Jinnah Hospital Lahore. In June, when COVID-19 had peaked in Pakistan we tested all patients and staff again. Most of them were asymptomatic and some had mild symptoms like fever, sore throat and cough. The results reflect a significant increase in frequency and prevalence. Moreover, three of our dialysis patients had died after requiring mechanical ventilation. One of our patient who had expired developed hemorrhagic stroke as well.

It has been shown that HD patients and staff are distinct group of individuals that are more susceptible to contract COVID-19. Measures to prevent, protect, screen and isolation are essential in the management of an epidemic and should be taken at the beginning of an outbreak.[6] We had only 2 patients who tested positive for COVID-19. This low prevalence could have been secondary to strict 'WHO, CDC and NKF precautions' we have implemented at our dialysis center. We have had no shortage of protective equipment and all doctors and dialysis staff were using it as per protocol and were following standard donning and doffing procedures. Recently we have significantly decreased HCV seroconversion by strict implemen-tation of all the CDC precautions and that might have helped us in COVID 19. Moreover, our dialysis stations are separated by glass walls into separate cubicles which might have also prevented the cross contamination.

Limited data is available on screening in asymptomatic patients for COVID-19 infection but these asymptomatic patients can be a source of infection to other hemodialysis patients. In the city of Wuhan, There were 7184 patients on dialysis in 61 different hemodialysis centers. At only one center in Renmin Hospital, Wuhan University, 37 out of 230 patients on HD and 4 of 33 staff members developed COVID-19 infection between January 14 and Feb-ruary 17, 20206. The death rate was assessed and it was found out that 6 of 7 patients on HD who have died had COVID-19 infection. However, the cause of death was considered to be due to cardiovascular causes and not directly due to the COVID-19 infec-tion. Patients on HD with COVID-19 were found to have less lymphopenia, lower serum levels of inflammatory cytokines, and milder clinical disease than other patients with COVID-19 infection.

One of the limitations of our study is low sensitivity of current gold standard in testing for COVID-19 (RT-PCR detection of SARS-CoV-2) from naso-

pharyngeal swabs. There is a possibility that a few positive cases might have been missed because of the low sensitivity of the test. One or more negative results do not rule out the possibility of SARS-CoV-2 infection. Factors responsible for false negative results in an infected individual are Poor quality of specimen with small amount nasal secretions or if the specimen was collected late or very early in infection and some technical reasons related to test.

Official guidance from the Centers for Disease Control and Prevention (CDC) can be freely accessed at the CDC7 and American Society of Nephrology[8] websites. Some of the recommendations for appropriate prevention and control of COVID-19 infection in outpatient Hemodialysis facilities has been advised during this interim period: Education of patients and medical staff about hand hygiene, coughing etiquette and Use of PPE. The staff should be prepared so that they can advise patients to call ahead if they feel sick and to implement triage protocol. Moreover proper management of patients and staff with symptoms or illness should be done in timely manner. Patients and staff should be advised about usage of face masks, isolation in separate rooms, and separation by 6 feet in all directions, routine cleaning and disinfection procedures, resource utilization by keeping track of PPE inventory, preserving PPE and the efficient use of human resources.[7]

On March 10, 2020 the CDC advised that hemodialysis could be performed on clinically stable patients in the outpatient dialysis setting[7], and, on March 26, 2020, the End-Stage Renal Disease Networks broadcast that "COVID (+) patients who are stable need outpatient dialysis," emphasizing the critical importance of limiting hospital use to those who truly require hospitalization.[9]

Currently 3 of our staff members and 2 of our hemodialysis patients, who have been quarantined, are clinically stable and to-date remain asymptomatic. This is in contrast to recent case report of 5 cases of COVID-19 in hemodialysis center of china where fever, diarrhea and fatigue were the main symptoms[10]. As suggested by Weiner DE et al.,[11] We should continue implementing rigorous screening programs at hemodialysis facilities to identify potential cases; reducing crowding in waiting rooms; disinfecting items not typically addressed, such as hand rails on scales, waiting room seats, door knobs, and elevator buttons; and designating hemodialysis patients who are symptomatic as persons under investigation (PUIs), who are tested for COVID-19 and treated with enhanced precautions.

We should continue to follow the strict precautions and official guidance from the Centers for Disease Control and Prevention (CDC), for patients with suspected or confirmed COVID-19 in outpatient Hemodialysis facilities.[7] Lockdown relaxation, carelessness in taking preventive and control measures and the decision to allow congregational prayers during the month of Ramadan might become a major source of COVID-19 transmission in Pakistan. Given limited resources one might argue to screen only symptomatic patients but we strongly recommend, if possible, to screen all the patients and staff in a dialysis facility to prevent spread of infection to others from asymptomatic individuals. May God protect our doctors, health care providers, patients and all the mankind!

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CONTRACEPTIVE PRACTICES IN PATIENTS WITH CARDIAC ABNORMALITIES

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How to cite: Iqbal N, Latif L, Salam N, Nisar M. Contraceptive practices in patients with cardiac abnormalities. JAIMC. 2020; 18(4): 801-6.

Abstract

During pregnancy in order to meet the metabolic demand of growing fetus and mother numerous alterations occur in cardiovascular system during pregnancy. There is an increase in blood volume and decrease in systemic resistance resulting in increase cardiac rate and output. Contraceptive practices are very important in women having cardiac abnormalities to prevent pre and post- partum complication. It also helps in keeping desired spacing, planned pregnancy and to some extent prevent transmission of few hereditary condition to the developing fetus e.g., dilated, hypertrophic cardiomyopathy and Marfan syndrome. World Health Organization (WHO) has formulated suggestions on the use of contraceptive methods.

Key words: Cardiac Lesion, Contraceptive Practices

During pregnancy in order to meet the metabolic demand of growing fetus and mother numerous alterations occur in cardiovascular system. There is an increase in blood volume and decrease in systemic resistance resulting increase cardiac rate and output.[1] These accommodative alterations help the developing fetus; but in women with cardiac lesions decompensation may occur. In developed countries still the cardiac disease is an indirect cause of maternal morbidity and mortality.[2,3,4] Contraceptive practices are utmost important in women having cardiac lesions to prevent pre and post-partum complication, it also help to keep desired spacing, planned pregnancy and to some extent prevent transmission of few hereditary condition to the developing fetus e.g., dilated, hypertrophic cardiomyopathy and Marfan syndrome.[5,6,7] There is no ideal method of contraception avail in market that is 100% effective for women having pre-exiting cardiac lesions, so more emphasis should be given on proper counselling regarding family planning.[8] While prescribing contraceptive method both pros and cons must be discussed in detailed with the couple. World Health Organization (WHO) has promulgated suggestions on the refuge of contraceptive methods and classified into four classes contingent on the cardiac lesion and preferred method (WHO Medical Eligibility Criteria).[9] Contraindications of contraception are graded onWHOMEC scale 1 - 4. In WHOMEC – 1 scale there is no limitation to the choice of contraception, whereas in WHOMEC-4 health hazard are enhanced.[10] The WHOMEC accepted by the "Faculty of Sexual and Reproductive Healthcare (FSRH) of the Royal College of Obstetrician and Gynecologist (RCOG)" to create the "UK Medical Eligibility Criteria for Contraceptive Use (UKMEC)".[11] The UKMEC scale 1- 4 is precisely like the WHOMEC, however counseling vary towards every contraceptive methods. In category-4, woman with cardiac lesions develop pulmonary hypertension, they cannot tolerate physiological changes during pregnancy and in labour. The Maternal fatality in females with pulmonary hypertension is markedly reduced from 56% to 17% due to advance management.[12,13] Table-l highlight the WHOMEC/ UKMEC classification and rendition of eligibility on medical grounds for contraceptive methods. Table-II highlight the classification for the hazard of contraception and pregnancy with cardiac

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Submission Date: 17-07-2020
1st Revision Date: 14-08-2020
2nd Revision Date: 19-09-2020
Acceptance Date: 20-09-2020

Table 1: *Whomec/Ukmem Classification Medical Eligibility for Contraceptives*

Whomec/ Ukmec Class	Eligibility for Contraceptives with Medical Conditions	"ABCD" Classification
1	No limitation of use	**A**lways Useable
2	Benefits are usually more than empirical or evidence peril	**B**roadly Useable
3	Empirical or evidential perils are usually more than benefits	**C**aution/ **C**ounseling
4	Intolerable health hazards	**D**o not use

Table 2: *Risk of Contraception & Pregnancy in Cardiac Lesions*

Whomec/ Ukmec Class	Risk related with Contraceptive Method and in Medical Conditions[9]	Risk related in Pregnancy with Cardiac Lesions[11]
1	Condition without limitation, Always useable	No increased risk to Maternal Morbidity/Mortality
2	Condition when benefits are more than peril. Usually useable	Little increase of Maternal Morbidity/ Mortality
3	Condition when perils are more than benefits	Significantly increased risk of Maternal Morbidity/ Mortality
4	Condition where an intolerable health hazard	Pregnancy is contraindicated

Table 3: *Recommended Contraceptive Methods:*

Contraception	Advantages	Contraindication	Recommendation
Progestogen only Pills, Injection, Implants, IUS	Menstrual irregularity, or cessation. No more risk of thrombosis	Bosentan use, Severe needle phobia Risk of vasovagal response	Usually recommended in women with cardiac lesions
Combined Pills, Transdermal patch, Vaginal ring	Regular Menstruation , Improve Acne	BMI>35,Smoker>35, Risk for thrombosis IHD, CHD, Heart Failure, Arrhythmia	Usually avoided in women with cardiac lesions
Intrauterine Cu-T, Mirena	Effective 3-5 years	Risk of vasovagal response	Usually recommended in women with cardiac lesions
Condoms, Male/Female, Cervical Cap / Diaphragm	Hormone free, Protection from STD	NONE	Use as adjunct contraceptive in women with cardiac lesions
Sterilization	Hormone free Permanent	Unable for operation Risk of psychosis	Vasectomy
Natural Methods	Hormone free		Not suitable for women with cardiac lesion.

lesions. Table-III outlines the recommended contraceptive practices. The purpose of this review is to appraise currently available contraceptive practicesin women with cardiac lesions.

A wide range of contraceptive agents are available in the market but while prescribing to a woman with cardiac lesion it should be tailored keeping following points:

- Choice of the women
- Hypertensive, Thrombotic risks of estrogen comprising contraceptives
- Drug interaction, degree of efficacy and non-contraceptive benefits of the method
- Vagal stimulation, infection, bleeding and anesthesia riskswith insertion of IUCD.

Combined Hormonal Contraceptives

These contain both estradiol and progestogen, inhibit ovulation and said to be an effective contraceptive. The main three varieties are

- Combined oral contraceptive pills (COC)
- Combined transdermal patch
- Combined vaginal ring

The COC pills commonly used contraceptive practice in the world, one pill is taken per day consecutively 21 days and then next 7 days no pill is taken, in order to have good compliance placebo could be added during pill free days[14]. The benefits of COC are, menstrual regularity, improve dysmenorrhea, menorrhagia, acne and premenstrual syndrome[15]. The combined transdermal patch is used per week for 3 week to the skin and then one week patch free, withdrawal bleed will occur in patch free days. The systemic side effects with transdermal patch are more (nausea, vomiting, breast tenderness, dysmenorrhea) than COC pills and vaginal ring. The combined vaginal ring is placed in the vagina for 21 days followed by 7 days interval, withdrawal bleeding will occur, adverse effect are vaginitis and discharge.[16]

Adverse Effects of Combined Contraceptives

Thromboembolic phenomena with combined contraceptives are enhanced if risk factors like obesity, smoking, hypertension and diabetes are present so contraindicated in females with own / family history of arterial or venous thrombosis[17]. In pregnancy & postpartum the hazard of thrombo-embolism is quite high (UKMEC- 4)[18]. COC pills are safe for the breast feeding women. Women having structural heart lesions either arterial or ventricular septal defect, extreme care should be taken because it may predispose embolidurin reverse shunting.[19] Incidence of stroke and myocardial infarction is more common in women with cardiomyopathy or chronic heart failure and on COC pills.[20] In women there is a prolongation of QT interval after puberty due to endogenous estrogen and is a great single risk factor of the first cardiac issue during reproductive years such as arrhythmia.[21] It has been observed that premature ventricular contractions are more dominant in women who are using COC pills, the progestogen would be helpful by shorting the action potential.[22]

Progestogen Hormone Contraceptives

These types of preparations contain only progestogen, they prevent conception by thickening of cervical mucus therefor sperm penetration is precluded. Some new preparation act by suppression of ovulation. The preparations are

- Progestogen – only Pills (POPs)
- Injectables – Depot medroxyprogesterone acetate (DMPA)
  – Norethisterone enanthate (NET-EN)
- Subcutaneous Progestogen Implant – Implanon (Etonogestrel)
- Levonorgestrel Intrauterine System – Mirena (LNG-IUS)

Progestogen only contraceptive practices are much safer for women with Cardiac lesion such as severe cardiovascular or pulmonary artery disease because these are not link up with thromboembolic phenomena[23]. The POPs are taken daily with no pill free interval. Desogestrel 75 mg is a newer POPs that causes anovulation and mimic with COC. Injectable progestogens are given deep intramuscular (DMPA) into the gluteus, or deltoid, effective for 12 weeks. Its long term use may produce hypo-estrogenic status that is significant for women with risk of ischemic heart disease.[24] They can be recommended in women taking anticoagulant, major demerit of injectable progesterone as compared to POP or implant is because of its irremovability. Subcutaneous Progestogen Implant is effective for three years, inserted on the medial aspect upper arm under the skin of the non-dominant side. It is recommended in Cardiac women taking anticoagulants provided their INR is within normal range.[19] Intrauterine system (Mirena) is an excellent contraceptive for women with cardiac lesion except with pulmonary vascular disease or a single ventricle. The incidence of bradycardia is greater with IUS insertion as compare to CU-T, this may be due to its large size.[25]

Adverse Effects of Progestogen Contraceptives

The main problems with progestogen–only contraceptives are irregular vaginal bleeding, decreased contraceptive efficacy if used with bosenton that is an enzyme inducer.[26] These contraceptives may interact with warfarin metabolism, simple ovarian cyst can develop. Injectable contraceptive also colligate deformation of lipid profile[27] and there is a temporary loss of bone mineral density.[28] Temporary adverse effects are headache, mood changes, weight gain, breast tenderness and acne.

Intrauterine Contraceptive

Intrauterine contraceptive devices are very effective for women with cardiac lesions these are

- Cu-T (IUD)
- Mirena (LNG-IUS) Levonorgestrel

Intrauterine contraceptive is a T-shaped plastic device containing either copper or progestogen. The copper ions bring modifications in the endometrium, endo-cervix and make them hostile to the ascending sperm there by prevent fertilization. The release of copper causes inflammatory reaction which is spermicidal.[29] The copper secretion also reduces the ability of oocyte to become fertilized, and then

implanted to the endometrium.[30] The Copper IUD is effective 99% and pregnancy risk is less than 0.8%.[31] Mirena is one of the ideal contraceptive for women having cardiac lesions, it releases 20 micro-gram/day levonorgestrel into the uterine cavity and make it hostile for fertilize ovum. Its efficacy is 99.8%.[31] Both IUD are effective for five years, can be inserted 5th or 6thday of menses, safe for women on antico-agulants and risk assessment should be done before insertion.

Adverse Effects of Intrauterine Contraceptives

The incidence of expulsion is reported 1 in 20 women & most frequent is in firstthree months of insertion especially following menses, FSRH guide-lines advise follow up of women after periods is mandatory.[32] According to FSRH the risk of perfora-tion with CU-T and Mirena is 1-2 per 1000 women[32], still there is 6-times more hazard of perforation of the uterus with Mirena if inserted 48 hours to 4 weeks postpartum.[33] Insertion of IUD is associated with cross-contamination of vaginal infection. Generally the risk is low < 1% and can occur in first 20 days after insertion, Mirena is much superior as compare to copper device because continuous release of pro-gesterone enhance the barrier role of the cervical mucus, and prophylactic antibiotics has no added benefits[34]. According to FSRH recommendation that women with history of prior endocarditis or replace-ment of prosthetic valve must have prophylactic intravenous antibiotics to prevent infection.[19] The risk of ectopic pregnancy is 0.2/1000 with copper-T(IUD) and Mirena 1/1000, these are quite low as compare to other contraceptive practices 3-4.5/ 100035. Copper IUD is associated with menorrhagia, poly-menorrhagia and dysmenorrhoea.[36] Intrauterine devices for contraception is contraindicated in UKMEC-4, women with pulmonary vascular lesion and with Fontan circulation.

Barrier Methods

Barrier methods consists of condoms, male and female, cervical cap, and diaphragm effective in women with cardiac lesion because they are free from hormones and additional benefits of condoms are, protection from sexually transmitted disease[37]. Prior to sex, the cervical cap or diaphragm are placed over the cervix along with some spermicide to provide additional protection. No barrier method is contraindicated in women with cardiac lesion but because of its high failure rate it should be combined with other contraceptive method.

Adverse Effects of Barrier Methods

Barrier methods are linked up with higher percentage of failure. In male condoms the reported failure rate is 18%, with female 22% in the first year of using, higher rate with female condoms is because it can slip easily[31,38]. With cervical cap or diaphragm in spite of spermicidal usage failure rate is 12%.[31] Non-latex quality condoms are high rate of failure than latex quality condoms.[37]

Sterilization / Vasectomy

The permanent way of contraception is called Sterilization in female (occlusion of fallopian tubes) and Vasectomy in males (occlusion of Vas defe-rence). Women with UKMEC 3 or 4 class it is fruitful to advice sterilization, but it may lead significant psychological impact on women's relations with her partner. Sterilization is effective in 99.5% whereas Mirena is effective in 99.8%[31]. Vasectomy is the safest contraceptive method and more effective than sterilization because of low failure rate 0.15%[39]. According to NICE guidelines hysteroscopic steriliz-ation is better than laparoscopic in women with Cardiac lesion.[40]

Emergency Contraception

Emergency contraception are essential for women with unprotected intercourse against unwan-ted pregnancy, especially with serious Cardiac lesion. According to NICE guidelines two oral contraceptive pills are recommended, Levonorges-trel (POP) and Ulipristal acetate (Oral Synthetic Selective Progesterone Receptor Modulator). The mechanism of EC is inhibition of ovulation, the Levonorgestrel must be taken in first 72 hours and Ulipristal in first 120 hours of sex done without protection. The failure rate of levonorgestrel is1.7-

2.6%[41]. Copper IUD is also said to be an emergency contraceptive, effective over 99% and can be inserted within 5 days after unprotected sex[42]. It prevent fertilization and implantation in to the endometrium.

Natural Methods

There are certain natural methods of contraception such as rhythm and withdrawal, 100% free of side effects but still not recommended in women with cardiac lesion because of high incidence of failure 24% and 22% respectively.[31]

Termination of Pregnancy

Termination of pregnancy is recommended when continuing is going to threaten the life of women[43]. There are two ways to perform TOP, Medical or Surgical. Medical TOP can be executed irrespective duration of pregnancy but Surgical TOP up-to 14 weeks of gestation only[43].

CONCLUSION

Pre pregnancy counseling is Mandatory for all women of reproductive age having Cardiac Lesion. The choice contraception should be appropriately tailored from the available published guidelines[8,10] to each individual. In some women contraceptive practices are safe than pregnancy and this issue must be discussed in detail. The combined contraceptive pills is contraindicated in some cardiac lesion but Progestogen only pills is safe in almost all cardiac disease. Subcutaneous Implant are quite safe because of its easy insertion and a few side effects. Mirena (LNG-IUS) is a preferable contraceptive in women with cardiac lesion due to 99.8% efficacy. Emergency contraception should be recommended when unwanted pregnancy make women's life at risk after unprotected sex.

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HYDROGEN SULPHIDE GAS POISONING LEADING TO PERMANENT NEUROLOGICAL DEFICITS

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How to cite: Siddiqui MH, Rana MA, Elahi R, Tariq S, Zartash S, Pervaiz R. Hydrogen sulphide gas poisoning leading to permanent neurological deficit. JAIMC. 2020; 18(4): 807-9.

Abstract

Hydrogen sulphide gas is the second major cause of toxin related death, after carbon monoxide at the workplace. When exposed to higher concentrations of hydrogen sulphide, acute exposure mainly involves central nervous system and lungs causing symptoms as dizziness, headache, poor coordination, sudden loss of consciousness & pulmonary oedema. We present two cases of hydrogen sulphide poisoning presented in the medical emergency. We have discussed different modes of damage caused by the gas, clinical features of the poisoning and the steps involved in the management of these cases.

Hydrogen sulphide also known as sewer gas, swamp gas, tank damp and manure gas is a colorless, flammable and highly toxic gaswith characteristic rotten egg smell and can be detected as low as 0.5bbp. [1,2,6]

This gas has a very strong odor but is known to cause olfactory fatigue. There are many case reports of hydrogen sulphide exposure in petroleum and agriculture industry but very few with sewer gas exposure having permanent neurological deficits[1,2].

In this case report, we present two cases who presented to the emergency with hydrogen sulphide poisoning. We discuss different modes of damage caused by the gas, clinical features of the poisoning and the steps in the management of such cases.

Table 1: Frequency of Allergies in a Sample of 300 Medical Students in Lahore, Pakistan, in 2014

ABGs	pH	PaCO2	PaO2	Sat O2	BE
Post intubation	7.38	21.6	79.1	92.8	-11.7
15 min after ventilation	7.38	25.2	96.5	96.5	-11.5

Case 1

A 50 years old male brought into the emergency room by a private ambulance. The man was attempting to clear some blockage in the sewerage system and after opening the lid a smell of rotten egg was reported, immediately after which the patient lost consciousness and fell in to the sewer. He recovered after 15 minutes with a Glasgow Coma Scale of 8/15. Patient was intubated and ventilated in the ER. His arterial blood gases showed.

Patient was shifted to ICU with FiO_2 of 1litre and SpO_2 of 96%. Clinical examination was unremarkable except GCS of 8 (E4M3V1) and on ventilator with bilaterally dilated pupil with sluggish response. Whole body CT scan was unremarkable and a repeat CT scan of brain after 24 hours also turned out to be unremark-able. In the next 13 days, patient's neurological status did not improve and finally tracheostomy was done for him. Meanwhile CSF examination & MRI brain also turned out to be normal. EEG showed generalized low amplitude beta waves and excessive theta waves which was in

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Submission Date: 07-08-2020
1st Revision Date: 11-09-2020
Acceptance Date: 16-09-2020

favor of mild to moderate degree of encephalopathy. Post tracheostomy, patient wasweaned off from the mechanical ventilator and started breathing

pH	$PaCO_2$	PO_2	HCO_3	BE
7.35	34	60	19	-7.6

spontaneously with no improvement in GCS.

Case 2

A 50 years old male, known case of bronchial asthma, admitted to ICU, through emergency, with history of inhalation of H_2S gas when he opened a sewer lid to look inside. Patient was reported to collapse immediately, while a rotten egg smell was reported by bystanders. In the emergency room, his GCS was 5/15 (intubated and ventilated immediately), temperature 38C, pulse 98/min and B.P 140/90 mmHg. His ABGS at that time showed

On examination, he was cyanosed with bilateral dilated pupils with sluggish reaction to light along with few bilateral coarse crepitations in chest. Rest of examination was unremarkable. CT chest showed evidence of pneumonitis while CT brain and CSF analysis was unremarkable. MRI brain showed hypoxic brain injury. After 3 weeks, tracheostomy was done for the patient and he was weaned off from ventilation. Though the patient was breathing spontaneously, his maximum improvement of GCS was spontaneous eye opening and abnormal flexion to pain.

DISCUSSION

Hydrogen sulphide gas is the second leading cause of toxin related death (after carbon monoxide) in the workplace.[4] When exposed to higher concentrations, acute exposure mainly involves CNS and lungs causing symptoms as dizziness, headache, poor coordination, sudden loss of consciousness & pulmonary oedema.[13] With transient exposure, recovery is rapid and complete, while prolonged exposure leads to fatal outcomes or permanent sequelae.

Exposure to hydrogen sulphide is mainly via inhalation. Once absorbed, it is evenly distributed throughout the body. Sulphur is highly irritating to the airways and causes symptoms ranging from rhinorrhea to hemoptysis.[13] The gas also causes leucopenia and cardiac injuries with strong insult leading to elevated cardiac enzymes.[6]

Hydrogen sulphide is a mitochondrial toxin[5], inhibits cytochrome oxidase (terminal enzyme of respiratory electron transport chain) more potently than cyanide, leading to histotoxichypoxia. A phenomenon referred to as Knock Down[2,3] occurs after short exposure to a very high concentrations of hydrogen sulphide gas and was reported in oil field workers as sudden loss of consciousness with amnesia, followed by immediate full recovery most likely due to direct toxic effects of gas on brain.[2,3]

In few cases, acute, nonfatal exposure causes permanent neurological sequelae.[1] Scientific evidence suggests that this is due to hypoxia secondary to respiratory insufficiency (due to pulmonary edema and H_2S induced paralysis of respiratory center of brain) rather than direct toxic effect on brain.[10] Neurological high dependency areas of brain are more susceptible to the toxin and result in spasticity, tremors, ataxia, prolonged coma and convulsions. Persistent vegetative state and pseudobulbar palsy in other reports with permanent retrograde amnesia, executive functional deficits, slowing in central information and planning deficits are also documented.[13,12,7,9]

Cognitive and behavioral deficitsare more common than motor deficits. Some researchers believe that few reports of permanent neurological sequelae are due to lack of detailed neuropsychological testing and long term followup.[2,3,11]

There have been few reports of neurological sequelae with detailed neuroimaging. MRI findings in our case report (greenish discoloration of cerebral cortices and basal ganglia) suggest hypoxic brain damage similar to those in functional neuroimaging studies, showing greater or more prolonged exposure.[7,9,12,13] Pathologically anoxic injuries can be classified as hypoxic hypoxia (decreased partial pressure of blood oxygen) and histotoxic hypoxia

(tissue inability to utilize oxygen) due to toxins. Our patients most likely suffered from hypoxic insult or both.

Our patients' MRI findings were similar to cortical laminar necrosis represented in hypoxic brain damage, whereas HIE is associated with extensive lesions throughout the cerebral cortex. High oxygen dependent areas of brain (basal ganglia and cortices) are more prone to hypoxic insult.

In managing these patients, ABC i.e., airway, breathing and circulation remains the most important of all steps as seen in other poisonings as well. Supportive care of the patient comes after that e.g., rehydration, nursing and nutrition care, care of bowels and bladder, prevention of bed/pressure sores and treatment of accompanying infection if any. Victims have been reported to survive without sequelae with supportive therapy alone. There are few reports suggesting that early administration of hyperbaric oxygen, amyl nitrite and sodium nitrite as antidotes may be beneficial.[8]

Some case reports and few animal studies suggest possible use of therapeutic red cells' exchange in management of H_2S poisoning.

Prevention and limiting exposure to the gas proves to be of utmost value for workers who are at risk. The use of gas alarms and portable meters should be emphasized.

CONCLUSION

We presented two cases of accidental exposure to hydrogen sulphide leading to acute and permanent neurological deficits. Immediate rescue from the affected zone, pre hospital management including administrating amyl nitrites as antidotes and general supportive care and the hospital admission in the intensive care for further management are the hallmarks in the management of hydrogen sulphide gas poisoning.

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ACUTE DEMYELINATING ENCEPHALOMYELITIS AS FIRST PRESENTATION OF ACUTE HIV SYNDROME

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How to cite: Siddiqui MH, Rana MA, Elahi R, Tariq S, Zartash S, Aamir A. Acute demyelinating encephalomyelitis as a first presentation of acute HIV syndrome. JAIMC. 2020; 18(4): 810-14.

Abstract

Acute disseminated encephalomyelitis (ADEM) is an autoimmune demyelinating disease of the central nervous system precipitated by infection or vaccination. The triggering element may be viral or bacterial. Clinical features depend on the inflamed area of CNS (brain & spinal cord). ADEM is considered in patients presenting with acute multifocal neurological signs and symptoms, with the history of preceding illness.

Magnetic Resonance Imaging (MRI) isthe useful diagnostic test. Immune suppression isthe goal of treatment while intravenous immunoglobulins and plasmapheresis can be used if steroids fail. We report an unusual case who presented initially as acute HIV syndrome with neutropenia, then developed neurological signs and symptoms of Guillain Barre Syndrome (GBS) but on investigations proved to be a case of acute demyelinating encephalomyelitis and showed complete recovery once intravenous immunoglobulins were initiated.

The case report describes clinical features of ADEM, its diagnosis, its relationship with acute HIV syndrome and treatment modalities and emphasizes upon the importance of keeping the index of suspicion wide for any patient admitted with post infectious neurological deficits especially if the presentation is multifocal. Timely diagnosis and intervention is the key to successful management of such cases.

Key Words: Acute disseminated encephalomyelitis, ADEM, Autoimmune demyelination, HIV, Acute HIV syndrome

Acute disseminated or demyelinating encephalomyelitis (ADEM) is an autoimmune demyelinating disease of central nervous system. ADEM is an uncommon illness, and the precise incidence is unknown.[1] Commonly triggered by infections or sometimes by immunizations,[2] ADEM is caused by an inflammation of the brain and spinal cord. Its progression is rapid and it typically follows monophasic course, but chance of recurrence and risk for permanent damage is also present in some patients.

We hereby report a case of ADEM admitted to ICU with unusual presentation.

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Submission Date: 02-08-2020
1st Revision Date: 20-08-2020
Acceptance Date: 10-09-2020

CASE

A 27 years old male patient presented with fever and sore throat for three weeks. He gave history of unprotected sexual contact one month ago. He had seen many physicians by the time he presented to ER and had been prescribed multiple antibiotics. Apart from high grade fever 39.4 C and tachycardia of 122 beats per minute, rest of examination was normal. His first set of labs was striking with Hb15.1g%, WBCs 1.5 with lymphocytes count of 0.4 only. Urine analysis revealed heavy proteinuria, pyuria, hematuria and granular casts. Nephrologist had the opinion of acute interstitial nephritis secondary to antibio-

tics. From Emergency, he was admitted for observation and treatment of febrile neutropenia and acute HIV was the working diagnosis. HIV1 Western Blot was negative but HIV2 EIA was positive which was later confirmed with HIV2 Western Blot. After five days of staying in the observation room, he complained to have double vision, back pain, giddiness and limbs weakness. Examination revealed internuclear ophthalmoplegia, quadriparesis with power in both upper and lower limbs with diminished reflexes. Lumbar puncture was carried out considering GBS and CSF analysis showed lymphocyte pleocytosis, raised proteins (156 mg/dl) and absent oligoclonal bands. His neurological status worsened and he became unconscious following an episode of seizures. He was intubated and transferred to ICU and intravenous immuno-globulins (IVIG) were started. At that time, the provisional diagnosis was Guillain Barre syndrome with Miller fisher syndrome element. His nerve conduction studies and electromyography turned out to be normal. At this stage, his MRI brain and cervical cord was carried out and it showed features of acute disseminated demyelinating encephalomyelitis. See figures 1, 2 and 3. Course of IVIG was continued for five days. The patient showed remarkable improvement by the end of IVIG course and at the end of second week of hospitalization(four days after finishing course of IVIG) he was extubated with no residual neurological deficit. His kidney functions improved by the end of third week when he was discharged from hospital in a stable state. Unfortunately, he didn't show up forfollow up, so a follow up MRI could not be done.

The case is interesting in this regard that it started as a case of febrile neutropenia and HIV, then was suspected to have developed GBS but eventually turned out to be post infectious acute demyelinating encephalomyelitis with acute HIV syndrome and showed a rapid improvement on administration of IVIG.

DISCUSSION

Acute demyelinating encephalomyelitis is an immune-mediated inflammatory disease of central nervous system that is stimulated by viral or bacterial infection usually gastroenteritis or upper respiratory tract infection. However, an underlying pathogen is not always identified.[2,3] A small number of cases with ADEM following immunization has also been reported.[4]

It is considered that ADEM results from an autoimmune response to specific myelin proteins and lipids such as basic protein, proteolipid protein, myelin oligodendryocyte protein because they have structural similarity and are attacked by IgG Autoantibodies

The consequence of inflammatory cascade causes increased vascular permeability and congestion in the CNS which results in clinical features of ADEM.[5,6]

CLINICAL FEATURES

After a preceding illness and a period of few days (to 2 months) the patient may present with multifocal neurological manifestations like headache, fever, nausea, vomiting and altered mental status ranging from irritability, confusion and psychosis, to somnolence and coma.[9]

Multiple motor features are seen and may involve weakness of a single limb (monoparesis) or mayresult in paraparesis or even quadriparesis. Sensory deficits are frequently seen and brainstem involvement can result in external ophthalmoplegia, dysphagia and dysarthria. Additional signs and symptoms may include meningism, ataxia, aphasia, optic neuritis (sometimes bilateral), nystagmus, extrapyramidal movement disorders, urinary retention, seizures, and increased intracranial pressure.[9,10]

Variants of ADEM have been recognized and include acute hemorrhagic encephalomyelitis (AHEM) which is more fulminant than ADEMand presents with features of meningitis, headache, seizures, multifocal neurologic signs, asymmetrical neurologic deficits, and rapid progression to coma.[10]

Sometimes AHEM includes hemorrhagic necrosis of white and gray matter, and is called acute

necrotizing hemorrhagic leukoencephalitis (ANHLE).

Other forms may have clinical or subclinical evidence of peripheral nervous system involvement.[12]

DIAGNOSIS

There is no specific criteria to diagnose ADEM. It is usually considered when patients present with acute multifocal neurologic signs and symptoms, with history of preceding illness or immunization. A wide range of neurological conditions are enlisted in differential diagnoses like Brain Tumor, Multiple Sclerosis, Vasculitis, sarcoidosis, Lyme's disease, Progressive multifocal leukoencephalopathy and infectious meningoencephalitis.

Following modalities are used to help ascertain the diagnosis.

MRI SCANNING

Although an urgent CT Brain is usually done to establish the cause of acute neurological deterioration but Megnatic Resonance Imaging (MRI scan) is considered as the most important tool of diagnosis. On MRI, supratentorial or infratentorial demyelinating lesions are present and destructive "blackhole" lesions are absent on Tl-weighted images, which suggest prior episodes of inflammationor demyelination.[13-17]

CEREBROSPINAL FLUID ANALYSIS

In ADEM, Cerebrospinal fluid (CSF) findings vary significantly[9,17]. Abnormalities (found in 50 to 80%) are nonspecific and include a lymphocytic pleocytosis, usually with a CSF white blood cell count of <100 cells/ml, and a mildly elevated CSF protein of <70 mg/dl, although higher white cell counts have been reported. Oligoclonal bands may be present in 20 to 65 percent of patients with ADEM.

OTHER INVESTIGATIONS

Other investigations like evoked potentials and EEG, are usually nonspecific and depend on the localization of CNS lesions; hence, these studies do not often contribute to the diagnosis.

Similarly, EEG shows bilateral slow activity, which is nonspecific and non-localizing.[17]

TREATMENT

Empirical treatment with antiviral (acyclovir) and antibiotic should be startedand continued until an infectious disease process is excluded. Immunosuppression is the mainstay of the treatment for ADEM and can be achieved by high dose intravenous steroids, Intravenous immunoglobulins (IVIG) and therapeutic plasma exchange (TPE).

HIGH-DOSE INTRAVENOUS GLUCOCORTICOIDS

Methylprednisolone intravenous infusion (20-30 mg/kg/day or 500 mg daily) for five day or up to 1000 mg for three days followed by tapering dose of oral glucocorticoids for four to six weeks is recommended.[9,12]

INTRAVENOUS IMMUNE GLOBULINS

Intravenous immune globulin (IVIG) can be used if the response to glucocorticoidsis poor. In one report, three patients with classic ADEM who failed to respond with glucocorticoids were managed with intravenous IVIG (dose: 0.4g/ kg/ day for five days).[18]

THERAPEUTIC PLASMA EXCHANGE (TPE or PLASMAPHARESIS)

Limited data is available about use of Therapeutic Plasma exchange but it has also been used for ADEM in adults who have failed to respond with glucocorticoids. One retrospective cohort study of plasma exchange for all demyelinating diseases, including 10 patients with ADEM showed that male patients preserved reflexes on examination, and early plasmapheresis showed improved outcome.[18]

CYCLOPHOSPHAMIDE

Cyclophosphamide (1 gm) given intravenously has also been used in poor responders to glucocorticoids. Repeat dosing may be necessary to achieve maximum benefit.[19-21]

PROGNOSIS

Prognosis is favorable and most patients improve with treatment, and spontaneous recovery has occurred in patients with mild symptoms. Complete recovery has been reported in 10 to 46 percent of adults. Cognitive impairment, mostly affecting attention and concentration, has persisted in some. Death may occur, especially in those with fulminant disease, with mortality rates of 4 to 12 percent reported in larger modern series. This will be interesting to note that although traditionally considered to be a monophasic illness, there are cases of adults with relapsing ADEM. In such recurrences, the symptoms often localize to the originally affected CNS site. In fact, new clinical symptoms may localize to a previously silent lesion on neuroimaging. Relapses may also present as cognitive difficulties or neuropsychiatric disease, such as depression or psychosis. Recurrent ADEM frequently responds to glucocorticoid treatment.[20-22]

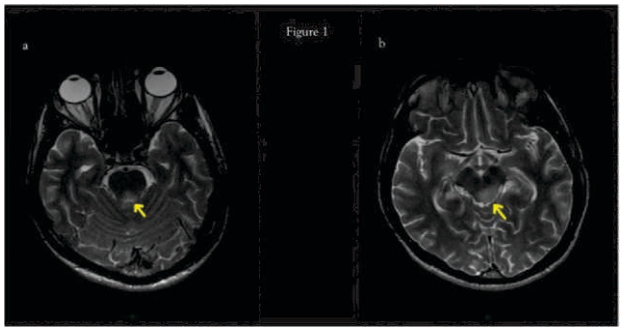

Figure 1: MRI Brain

Abnormal high signal intensities in T2 sequence are seen involve in the posterior pons (a) and posterior midbrain (b) marked by yellow arrow.

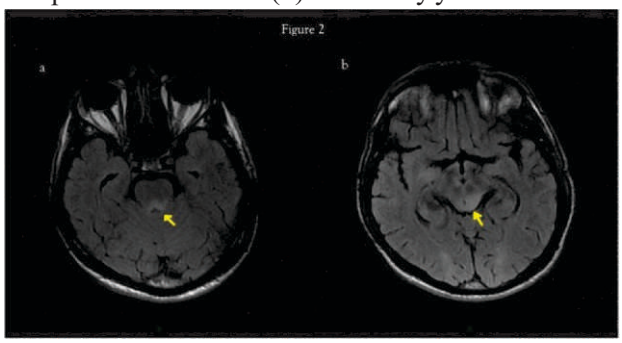

Figure 2: MRI Brain

Abnormal signals in FLAIR sequence in axial section of midbrain (a) and pons (b) (yellow arrow)

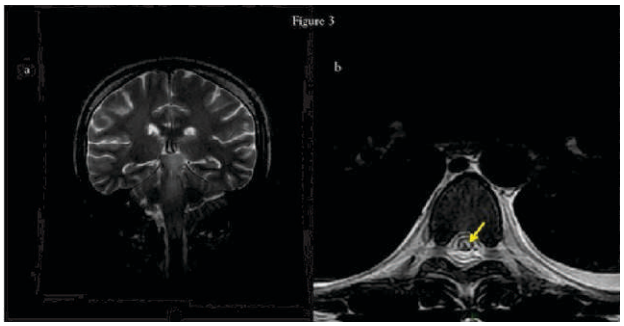

Figure 3: MRI Cervical Spine

T2 high signal intensities lesions involving the long segments of spinal cord coronal section (a) and axial section (b) marked by yellow arrow.

ACKNOWLEDGMENT

We are grateful to Dr. Rizwan Elahi, Consultant Physician and Nephrologist at Madina Munawar, Saudi Arabia for reviewing literature and sorting out latest updates in the management of acute demyelinating encephalomyelitis, which helped us in writing this case report.

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SYSTEMIC EFFECTS OF COVID-19

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How to cite: Khalid MF. Systemic effects of covid-19. JAIMC. 2020; 18(4): 815-17.

Abstract

Background: After the first case report of novel coronavirus from Wuhan (China) in December 2019,[1] and its declaration as a pandemic by WHO on 11 March, 2020, [2] it has become the first priority of the healthcare professionals worldwide. With more than 46.4 million reported cases and more than 1.2 million deaths worldwide (as of 1st November, 2020),[3] COVID-19 has occupied the first place in global health agenda. Being an airborne disease, the most well-renown effects of COVID-19 are on the respiratory system but are not confined to this organ system only. The systemic inflammation of COVID-19 is the pathogenic basis of systemic effects of this virus. The pathologic signs and symptoms of this disease on various organ systems are due to the direct effects of the virus or inflammatory mediators especially IL1, IL6, and TNF-alpha.[4]

Respiratory Manifestations

These are the symptoms which caused most of the evident signs and symptoms in the patients since COVID-19 itself is an airborne disease.[4] According to Guan et al. the most common symptoms were fever, productive cough (in about 67% of the patients) and dyspnea in increasing order of incidence.[5]While another study,[6] showed that prevalent respiratory signs were cough (63%), sputum production (28%) and shortness of breath. The most severe clinical presentation requiring urgenthealthcare attention are respiratory distress or respiratory failure.[7]The patterns on chest imaging findings were ground-glass opacity (61%) pulmonary consolidation or exudation (37%), unilateral pneumonia (19%), and bilateral pneumonia in 69%.[6] Patients already suffering from other respiratory complications or chronic respiratory disorders (COPDs) have been reported to face more perilous symptoms as compared to patients without COPD.[8]

Cardiovascular Manifestations

The second most common organ system affected by COVID-19 is the cardiovascular system.[4] Various studies showed the people having risk factors for other cardiovascular diseases to be more prone to face the serious complications of COVID-19. These factors include: age > 60 years, obesity, hypertension, and diabetes mellitus.[5] The CVS complicationsrelated to COVID-19 which may require immediate medical attention include myocarditis, heart failure, cardiac arrhythmias (*torsades de pointes)*, and acute coronary syndrome as direct consequences of systemic inflammation.[4]

Neurological Symptoms

Various neurological symptoms varying from central to peripheral origin, and mild to moderate intensity have been reported in patients with asymptomatic COVID-19 infection and those with the serious variant of the disease. These include nonspecific abnormalities such as malaise, dizziness, headache, and loss of smell and taste, encephalopathy and encephalitis, ischemic stroke, acute disseminated encephalomyelitis, acute necrotizing hemorrhagic encephalopathy, Guillain-Barre syndrome.[9]

Renal Indications

According to another article,[10] COVID-19 infection can cause multiplerenal complications via differentmechanisms. These may include direct cytokine lesion, cardio renal syndrome

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Submission Date: 16-09-2020
1st Revision Date: 20-09-2020
Acceptance Date: 24-09-2020

Organ System	Clinical manifestations	Pathological findings/mechanisms
Urinary system	• Acute kidney injury • Isolated urine abnormalities (proteinuria, hematuria)	Viral-induced kidney inflammation
Hematopoietic system	Signs of anemia.	• Viral-induced hyper inflammation • Spleen enlargement/atrophy • Diffused lymphoid tissue atrophy • Immune reaction in response to the infectious process (for leukocytosis and neutrophilia) • Virus-induced apoptosis, increased lymphocyte activation, and inhibition of lymphocyte proliferation (for lymphopenia) • Platelet consumption (for thrombocytopenia)
Gastrointestinal tract	• Diarrhea • Vomiting • Abdominal pain	• Alteration of intestinal permeability with resultant malabsorption • Viral binding on ACE2 cholangiocytes (for liver dysfunction)
Musculoskeletal system	• Muscle pain • Muscle weakness • Joint pain	• Cytokine-mediated sensitization of sensitive receptors on the muscular fibers (for muscle weakness and pain)

type 1, renal medullary hypoxia, renal compartment syndrome, renal tubular toxicity,renal hypoperfusion, septic acute kidney injury (septic AKI).[10]

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