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COVID-19 Vaccination Challenges in Developing Countries

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The pandemic of coronavirus disease 2019 (COVID-19) is challenge of the century for humanity. Pre-pandemic normalcy is assumed to never return until a safe and effective vaccine becomes available and a global vaccination campaign is successfully introduced. To tackle the pandemic of Covid-19 safe and effective vaccines has been developed and pharmaceutical companies Pfizer/BioNTech, Moderna and AstraZeneca started to manufacture the vaccine and make it available in the market. Globally all the countries are in race to secure vaccine access for their populations but it is challenge for developing countries to make vaccine available for the population especially the poor and vulnerable groups. Pakistan is developing country which is facing the double burden of the communicable diseases like malaria, HIV/AIDS, tuberculosis and non-communicable diseases along with financial issues faced by the health system (1, 2).

For stopping the transmission of COVID-19 disease it is the need of the hour that along with all the precautionary measures like social distancing and hand washing the global access to the vaccines must be ensured. Key challenges faced by the developing countries including Pakistan for universal access of vaccine to their populations may include limited vaccine availability due to manufacturing capacity, affordability and vaccine storage or cold chain problems. Poor transport infrastructure and a lack of adequate refrigeration facilities may also hamper the distribution of vaccines. Access for internally displaced people and refugees is another issue. The major barrier for access of vaccine may be the cost in developing nations. The estimated price of Oxford vaccine at maximum of \$3 per dose for Lower and Middle Income Countries (LMICs) and \$4-\$5 elsewhere. Pfizer company has been agreed a cost with the US Administration of \$19.50 a dose. It may become a benchmark for developing nations. Moderna is charging \$32 to \$37 a dose for smaller deals and less for larger orders (3, 4).

The risk of severe morbidity and mortality due to COVID-19 is high among elderly and people with comorbidities like diabetes mellitus, malignancies, Chorionic liver & kidney diseases. The rate of infection is also high among health care providers as they are directly in contact with people suffering from COVID-19 and they can transmit the infection to large number of patients and their attendants admitted or visiting the hospital. For COVID-19 those at higher risk of severe infection (including elderly, individuals with medical conditions that predispose them to severe disease and healthcare providers) should be prioritized for access to vaccine.

Vaccines can lose their effectiveness if they are not kept within a narrow temperature range. Most are heat sensitive: warm temperatures kill the live-attenuated viruses or bacteria within, reducing potency. Many are also freeze-sensitive: extreme cold can corrupt adjuvants added to vaccines to help them work and ultimately reducing their effectiveness. The COVID-19 vaccine made by one of the front-runners in vaccine race (Pfizer) needs to be kept at minus 70 degrees Celsius, which is colder than winter in Antarctica. Moderna vaccine also needs to be frozen too, but only at minus 20 Celsius, more like a regular freezer (5, 6). Since there will be limited vaccine doses will be available in Pakistan initially the immunization managers across the country will need to have plans to distribute all vaccine doses that are available at the recommended temperature to maintain their potency. It will be a big challenge presented by the Pfizer vaccine, which requires these ultra-cold conditions and if not addressed timely it will result in loss of vaccine efficacy and ultimately all the cost and efforts devoted for prevention of disease through vaccination will be useless.

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Correlation between Calcium Phosphorus Product and Mean Arterial Pressure among Hemodialysis Patients with End Stage Renal Disease

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Significance:

The mean arterial pressure serves as an expression of blood pressure in patients on chronic hemodialysis. Serum calcium phosphorus product is considered as a risk factor of vascular calcification that is associated with hypertension in the patients of end stage renal disease. The literature regarding this relationship is inconsistent therefore this study is designed to determine the correlation between calcium phosphorus product and mean arterial pressure among hemodialysis patients with end stage renal disease.

ABSTRACT

Background: The mean arterial pressure serves as an expression of blood pressure in patients on chronic hemodialysis. Serum calcium phosphorus product is considered as a risk factor of vascular calcification that is associated with hypertension in the patients of end stage renal disease. The literature regarding this relationship is inconsistent therefore this study is designed to determine the correlation between calcium phosphorus product and mean arterial pressure among hemodialysis patients with end stage renal disease.

Methods: A total of 110 patients of end stage renal disease on hemodialysis for at least one year, 20 to 60 years of age were included. Patients with primary or tertiary hyperparathyroidism, peripheral vascular disease, malignancy, hypertension secondary to any cause other than kidney disease were excluded. Mean arterial pressure was calculated according to the standard protocol in lying position. Blood samples for estimation of serum calcium and phosphorous were taken and was sent immediately to the laboratory for serum analysis.

Results: Mean age was 44.17 ± 10.94 years. Mean calcium phosphorous product was 46.71 ± 7.36 mg/dl and mean arterial pressure was 103.61 ± 12.77 mmHg. The values of Pearson correlation co-efficient (r) were 0.863 for age group 20 to 40 years and 0.589 for age group 41 to 60 years. This strong positive correlation means that high calcium phosphorous product goes with high mean arterial pressure (and vice versa) for both the age groups.

Conclusion: A strong positive relationship exists between the mean arterial pressure and calcium phosphorous product and is independent of patients' age.

Introduction

Chronic kidney disease (CKD) is a worldwide public health problem. In the United States, chronic kidney disease is the ninth leading cause of death and recently there has been upsurge both in the incidence and prevalence of kidney failure (1). About 90% patients of CKD suffer from hypertension that is a major risk factor for progression towards end stage renal disease (ESRD) (2,3). Oppositely the progressive renal disease may also exacerbate uncontrolled hypertension due to volume expansion and increased systemic vascular resistance (4). The leading cause of mortality in patients with ESRD is cardiovascular disease (5). Compared with the general population, dialysis patients have a 3 to 30 folds increase in mortality, depending on the age group examined (6). Thus, it is of utmost importance to explore the causative agents of hypertension and exterminate them to halt the progression of both renal and cardiovascular ailments. Blood pressure is multi-factorial, and its management is quite a challenge in patients with ESRD. In patients on chronic hemodialysis, hypertension is monitored in terms of Mean Arterial Pressure (MAP) instead of measuring systolic and diastolic blood pressure (7). Serum calcium phosphorus product is considered as an indicator of vascular calcification that aggravates hypertension in the patients of ESRD (8). These calcifications are equal to bone formation resulting from vascular smooth muscle differentiation as evident in patients of CKD and lead to higher mortality attributed to increased left ventricular after-load and disturbed coronary perfusion (9). Jean et al. concluded that vascular calcifications are highly prevalent in hemodialysis patients and not linked to blood pressure (10). However, Adragao et al. conducted a prospective study and concluded that higher vascular calcification scores in dialysis patients were significantly associated with MAP and coronary artery disease (11). In another cross-sectional study conducted by Ashkar, it was cited that calcium phosphorous product (CPP) is positively associated with MAP and unrelated to pulse pressure (12). The inconsistency of the results regarding relationship between CPP and MAP is apparent in the existing literature thus this study is designed to explore further evidence regarding the relationship between CPP and MAP and its dependency upon age.

Materials and Methods

Study was approved by Ethical Review committee of King Fahad Central Hospital, Gizan, Kingdom of Saudi Arabia. Total of 110 volunteer male and female patients with permitted range for age, 20 to 60 years with ESRD were selected by non-probability consecutive sampling at nephrology department of hospital. A detailed informed written consent was obtained from all the patients. Patients either having pre-dialysis glomerular filtration rate less than 15ml per minute or the patients requiring at least two session a week for last one year were declared cases of ESRD. Patients were excluded after being scrutinized for primary or tertiary hyperparathyroidism, diabetic mellitus, peripheral vascular disease, malignancy, calciphylax is and secondary hypertension unrelated to kidney disease.

MAP was determined by taking the resting systolic and diastolic blood pressure of the patients in lying position before and after dialysis. Averages of the pre-dialysis and post-dialysis systolic and diastolic blood pressures were taken as final reading. Mean arterial pressure was calculated using the formula:

$$\text{MAP} = 2/3 (\text{diastolic pressure}) + 1/3 (\text{systolic pressure})$$

Corrected serum calcium levels were used according to serum albumin.

Serum Calcium corrected= serum calcium + 0.8(4 – serum albumin mg/dl).

Serum calcium phosphorous product was calculated by multiplying the corrected serum calcium level in mg/dl with serum level of phosphorous in mg/dl. Blood samples for estimation of serum calcium and phosphorous were taken by using aseptic measures and was sent immediately to the laboratory for serum analysis.

Data was entered and analyzed using SPSS version 25. Numerical variable i.e. age, MAP and CPP were summarized as mean and standard deviation. Pearson correlation coefficient (r) was calculated to measure the correlation between CPP and MAP.

Results:

Age range in this study was from 20 to 60 years with mean age of 44.17 ± 10.94 years. 66 patients (60%) were between 41 to 60 years of age and 44 patients (40%) were between 20 to 40 years of age.

Mean calcium phosphorous product was 46.71 ± 7.36 mmHg and mean arterial pressure was 103.61 ± 12.77 mmHg. The values of Pearson correlation coefficient (r) were 0.863 for age group 20 to 40 years (Figure 1) and 0.589 for age group 41 to 60 years (Figure 2).

Correlation between calcium phosphorous product and mean arterial pressure for both the age groups showed strong positive correlation. This correlation was stronger in age group 20 to 40 years than age group 41 to 60.

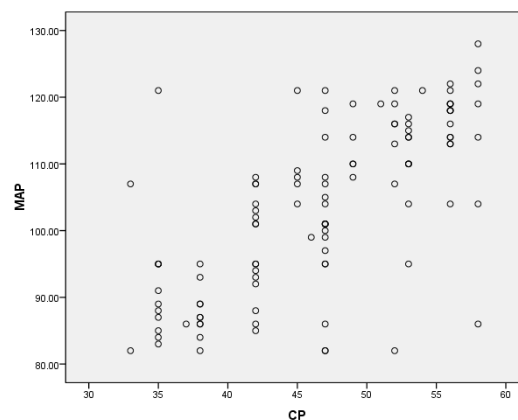


Figure 1: Correlation graph between Calcium phosphorous product and Mean arterial pressure with respect to age 41-60 years (n=66) (r =0.589)

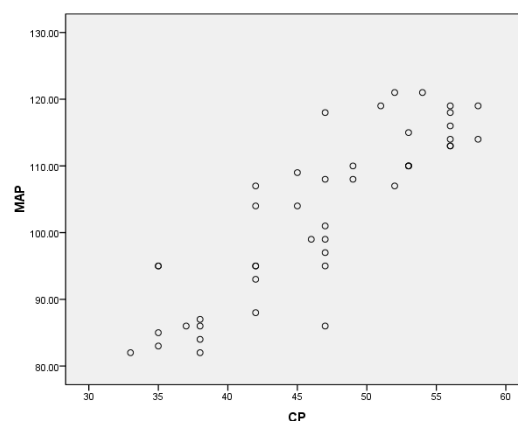


Figure 2: Correlation graph between Calcium phosphorous product and Mean arterial pressure with respect to age 20-40 years (n=44) (r = 0.863)

Discussion

In our study the value of Pearson correlation coefficient (r) is > 1 declaring a strong positive correlation between CPP and MAP thus higher the calcium phosphorous product higher will be the mean arterial pressure (and vice versa).

Our investigation was in agreement with Block et al., who analyzed a random sample of 2669 patients haemodialysed for more than 1 year (mean 4.5 years) and reported that higher the CPP higher is the mortality risk (13). In a cross-sectional study on fifty four hemodialysis patients during a 6-month period, linear regression analysis as applied on the averages of CPP and blood pressures concluded that CPP was significantly associated with pre-dialysis systolic BP and diastolic BP, pre-dialysis MAP, and post-dialysis diastolic BP (12). Strozecki et al., investigated the predisposing factors for cardiac valve calcifications and revealed that no

significant correlations were found with respect to calcium, phosphorus, and calcium-phosphorus product (14). Similarly, Menon et al., concluded in a randomized cohort study of renal disease that serum phosphate levels and CPP were statistically unrelated to cardiovascular disease linked mortality (15).

However Petrovic et al., performed uni-variate regression analysis to confirm that serum phosphate levels and CPP are vital risk factors for the development of aortic valve calcifications (16). In contrast to our study Goodman et al., showed no significant differences in Blood Pressure among patients with or without calcifications (8). Jean et al., also reported similar results in dialysis patients (10). Adragao et al., have publicized that higher vascular calcification scores in dialysis patients were associated with higher mean arterial pressure (11). The total serum calcium x phosphate product is an indicator of the risk of mineral crystallization in soft tissues, (17) which can lead to cutaneous and systemic calciphylaxis, conjunctival precipitation, visceral and in particular, cardiovascular calcification (18). Lundin et al first identified an elevated CPP as a predictor of cardiac mortality along with age at onset of dialysis and sustained hypertension (19). In hemodialysis patients, the pathogenesis of vascular calcification is multifaceted and the process includes certain factors that may promote or inhibit calcification (16). An elevated Ca_xP combination is likely to be a predominant risk factor and Ca alone may also be problematic because, in general, a positive Ca balance may blood pressure and calcium phosphorous product, so maintaining a tight control of calcium phosphorous product will help to manage hypertension by administration of drugs, leading to improved management and decreased the mortality and morbidity associated with hypertension. Promote or accelerate soft-tissue and vascular calcification even in the absence of hypercalcemia (20). On the whole, it is concluded that there is a strong positive relationship between

Conclusion

The study concludes that in patients of ESRD there is a strong positive correlation between the serum calcium phosphorous product and mean arterial pressure in both age groups (20-40years and 41-60 years).

Conflict of interest: Authors do not have any conflict of interest to declare.

Disclosure: None

Human/Animal Rights: No human or animal rights are violated during this study.

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An Institutional Review of Knowledge, Attitudes and Practices of Medical Students Regarding Hepatitis B and C: A Cross-sectional Study

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Significance:

Viral hepatitis is among one of the major health issues of globe. Medical students are high-risk group due to lack of screening and post vaccination screening programs. Several studies have been conducted to assess knowledge, attitude, and practices of healthcare workers regarding hepatitis. There is a need to adapt the knowledge and develop and implement attitude of students towards positive practices. Students and health-care professionals should be screened regularly for hepatitis B and C.

ABSTRACT

Background: Hepatitis is a major health issue. The aim of this study was to assess the knowledge, attitude and practices (KAP) of medical students regarding hepatitis B and C.

Methods: A descriptive cross-sectional study conducted from March, 2018 to May, 2018. 310 medical students from Allama Iqbal Medical College participated. KAP towards Hepatitis B and C was assessed by using a pre-validated questionnaire. Association of gender and year of study was established with KAP of respondents. Also, associations of knowledge with attitude and practices were also established using Chi-square test taking ≤ 0.05 as standard p-value. SPSS version 21.0 was used.

Results: 269 (86.77%) out of 310 distributed questionnaires were received. 116 (43.1%) respondents fell in age group 16-20, 150 (55.8%) in 21-25 years while 3 respondents (1.1%) were 25 year and above. 146 (54.3%) respondents were females and 123 (45.7%) respondents were male. There were 54 (20.1%) respondents from first year, 59 (21.9%) respondents from second year, 53 (19.7%) respondents from third year, 55 (20.4%) respondents from fourth year and 48 (17.8%) respondents from final year. 132 (90.4%) female respondents and 98 (79.7%) male respondents had good knowledge regarding hepatitis B and C. No significant relationship was established between gender of respondents with their attitude and practices. As for relationship of knowledge of respondents with their attitude and practices, no significant association could be established.

Conclusion: Overall, the medical students have adequate knowledge, sensible attitude but unsatisfactory practices in regards to Hepatitis B and C.

Introduction

Viral hepatitis is among one of the major health issues of globe. It is an infectious disease caused by hepatitis virus that effects the liver (1). The Global Hepatitis Report 2017 showed hepatitis as the major public health disorder that caused 1.34 million deaths in 2015, a figure analogous to the yearly deaths caused by Tuberculosis (TB) and Human Immunodeficiency Virus (HIV). 257 million people worldwide harbor Hepatitis B virus (HBV) and 71 million are affected Hepatitis C virus (HCV) (2). With 6% to 6.8% population infected with HCV, Pakistan bears world's highest burden of hepatitis C (3, 4). Hepatitis B exists simultaneously along with hepatitis D in one-third of HBV-infected population of Pakistan (5). 1 in every 40 people die worldwide due to end-stage liver disease. Chronic infections with HBV and HCV are notorious for cirrhosis and liver cancer. Globally 57% cirrhosis and 78% hepatocellular carcinoma (HCC) is attributable to HBV and HCV. Pakistan lies in an area of intermediate endemicity for HCC (6, 7). Modes of transmission in health-care settings worldwide and in Pakistan include low risk perception by hospital workers (8), contaminated needle use, lacking sterilization of medical equipment, drug abuse and unsafe/unscreened blood and blood product transfusion (9,10). Prevention is the key to tackle hepatitis B and C which includes standard Universal precautions (11), prophylactic vaccination and standard treatment (12-14). Medical students are high-risk group (15) due to lack of screening and post vaccination screening programs (16). A number of studies have been conducted to assess knowledge, attitude and practices of healthcare workers regarding hepatitis. Results of a KAP study revealed that only 5 (2 %) students out of a total of 246 had completed the three doses schedule of HBV vaccination, whereas a significant number of students, 66 (26.8 %), had been exposed to blood/body fluid via needle stick injury at least once since they started their training in the health facility (17).

This study aims to determine knowledge, attitude and practices (KAP) of medical students being a high-risk group of Hepatitis B and C, compare KAP differences

regarding Hepatitis B & C among medical students of different years, and to evaluate the vaccination status of medical students.

Materials and Methods

Study Design & Settings: A descriptive cross-sectional study was conducted amongst the medical students of Allama Iqbal Medical College. The institute is a public school of medicine, nursing and allied health sciences located in Lahore, Punjab, Pakistan. Jinnah hospital is attached to the college as a teaching hospital. Verbal consent was taken from all participants.

The study was conducted for period of two months from March, 2018 to May, 2018.

Study Sample: A non-probability convenient sample was drawn from the medical students of Allama Iqbal Medical College, Lahore, Pakistan. 310 questionnaires were distributed among the medical students of all five years from which 269 questionnaires were returned as correctly filled making the sample size (N) as 269. Other questionnaires were discarded on the basis of being incomplete and incorrectly filled.

Inclusion criteria: 1) Students of all five years from MBBS degree program. 2) Vaccinated as well as non-vaccinated students.

Exclusion criteria: 1) Students of allied health sciences. 2) Students of nursing institute. 3) Student who did not give verbal consent. 4) Incomplete/incorrectly filled questionnaires.

Data Collection: A self-administered questionnaire comprising of 20 close-ended type questions was designed. The questions were kept simple and easy to understand. The questionnaire was validated by the facilitators at the Community medicine department of the college. A pilot study to pre-test the questionnaire was conducted and later on some modifications were made in the questionnaire. Data from pilot study was not included in final analysis. 10 to 15 minutes were given to the respondents to fill all the fields of questionnaire. The questionnaire included: demographic data of the respondents such as name (optional), age, year of study, marital status and screening status of hepatitis B and C; 10 questions about the knowledge regarding hepatitis B and C which included basic facts, modes of transmission, complications, treatment and vaccination information; 4 questions about the attitude towards hepatitis B and C; 5 questions about the practices of the medical students regarding hepatitis B and C; 1 question about the vaccination status and the possible reasons for not being vaccinated.

Scoring of Knowledge, Attitudes & Practices: A score of 2 was given to questions answered correctly, 1

for incorrect answers and 0 for questions answered as “don’t know”. The total score of knowledge ranged from 0 to 20. The total score of attitudes ranged from 0 to 8. The total score of practice ranged from 0 to 10. Respondents having score of $\geq 75\%$ (≥ 15) were considered to have good knowledge and $< 75\%$ (< 15) were considered to have poor knowledge. As for attitude, a score of $\geq 75\%$ (≥ 6) was considered as a good attitude score and $< 75\%$ (< 6) was considered as a poor attitude score. Regarding practice, respondents who scored $\geq 75\%$ (≥ 8) were said to have good practices and those who achieved $< 75\%$ (< 8) were said to have poor practices towards hepatitis B and C control and prevention.

Ethical Considerations: Institutional ethical approval was obtained from Institutional Research Ethics committee of Allama Iqbal Medical College prior to the conduct of this study. All subjects were informed regarding the purpose of the study. The confidentiality was assured to all the respondents and verbal consent was taken. Furthermore, a sentence regarding the purpose of the study and consent of the respondent was also mentioned and highlighted on the questionnaire.

Statistical Analysis: SPSS version 21.0 was used to analyze the data. The data was tabulated into frequency tables. Clustered bar graphs and pie charts were used to present important variables. Some crosstabulations were done and Chi-square test was applied. A p value of ≤ 0.05 was set as standard for significance

Results

A total of 310 questionnaires were distributed out of which 269 were received with a response rate of 86.77%. Table 1 shows the demographic data of the respondents. None of the subjects reported with positive Hepatitis B Surface Antigen (HbsAg). 1 (0.4%) respondent had positive hepatitis C screening test result.

Table 1 Demographic Data of Participants (N=269)

VARIABLES	FREQUENCY (N)	PERCENTAGE (%)
AGE GROUP (YEARS)		
16-20	116	43.1
21-25	150	55.8
25 AND ABOVE	3	1.1
GENDER		
FEMALE	146	54.3
MALE	123	45.7
MARITAL STATUS		
UNMARRIED	257	95.5
MARRIED	12	4.5
YEAR OF STUDY		
FIRST YEAR	54	20.1
SECOND YEAR	59	21.9
THIRD YEAR	53	19.7
FOURTH YEAR	55	20.4
FINAL YEAR	48	17.8
HEPATITIS B SCREENING TEST RESULT		
NOT DONE	147	54.6
NEGATIVE	122	45.4
POSITIVE	0	0.0
HEPATITIS C SCREENING TEST RESULT		
NOT DONE	152	56.5
NEGATIVE	116	43.1
POSITIVE	1	0.4

Table 2 shows knowledge of the respondents regarding hepatitis B and C. The study revealed that majority of the respondents 258 out of the total of 269 (95.9%) had heard of hepatitis and 254 (94.4%) were aware of the disease. 254 (94.4%) respondents knew that hepatitis is a viral disease. 250 (92.9%) respondents had knowledge of the cirrhosis and hepatocellular carcinoma caused by hepatitis B and C viruses. Regarding the routes of transmission 261 (97.0%) respondents said that hepatitis

Table 2 Knowledge regarding Hepatitis B and C

Questions	Yes		No		Don't Know	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
Have you ever heard of hepatitis B and C	258	95.9%	11	4.1%	0	0.0%
Are you aware of hepatitis B and C	254	94.4%	15	5.6%	0	0.0%
Do you think of hepatitis B and C as viral diseases	254	94.4%	11	4.1%	4	1.5%
Do you think hepatitis B and C viruses cause liver cancer and cirrhosis (Liver scarring)?	250	92.9%	4	1.5%	15	5.6%
Can hepatitis B and C be transmitted by un-sterilized syringes, needles, surgical instruments, contaminated blood and blood-products?	261	97%	7	2.6%	1	0.4%
Hepatitis B and C cannot be transmitted by contaminated water or food. Do you agree?	138	51.3%	106	39.4%	25	9.3%
Do you think there is any vaccination available for hepatitis B?	216	80.3%	32	11.9%	21	7.8%
Do you think there is any treatment available for hepatitis B?	211	78.4%	35	13%	23	8.6%
There is no vaccination available for hepatitis C. Do you agree?	150	55.8%	74	27.5%	45	16.7%
Do you think there is any treatment available for hepatitis C?	169	62.8%	57	21.2%	43	16%

B and C can be transmitted by un-sterilized syringes, needles, surgical instruments, contaminated blood and blood-products. 106 out of 269 respondents (39.4%) considered contaminated food and water as source of hepatitis infection. 216 (80.3%) respondents knew about the vaccination and 211 (78.4%) respondents knew about the vaccination of hepatitis B. 74 out of 269 respondents (27.5%) said there is vaccination for hepatitis C while 45 (16.7%) respondents said that they had no idea about the vaccination. 150 out of 269 (55.8%) respondents agreed that there is no vaccination for hepatitis C. 169 (62.8%) knew about the treatment of hepatitis C.

Table 3 displays the attitude of the respondents towards hepatitis B and C. 242 (90.0%) respondents had the opinion that they are risk of getting hepatitis B or C as medical students. 128 (47.6%) participants were exposed to hepatitis B or C positive patients. Adopting personal protective measures were considered necessary while dealing with hepatitis B or C positive patients by 227 (84.4%) respondents. 34 out 269 (12.6%) respondents have had needle pricks in last one year during their medical wards and patient interaction.

Table 3 Attitude towards Hepatitis B and C

Attitude towards Hepatitis B and C	Yes		No		Don't Know	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
As medical student, do you think you can get hepatitis B or C?	242	90%	11	4.1%	16	5.9%
Have you ever been exposed to a patient who is hepatitis B or C positive?	128	47.6%	120	44.6%	21	7.8%
Do you think whether adopting personal protective measures (like wearing gloves) necessary while dealing with patients suffering from hepatitis B and/or C?	227	84.4%	33	12.3%	9	3.3%
Have you had any needle pricks in last one year during your wards or in any interactions with patients?	34	12.6%	231	85.9%	4	1.5%

Table 4 presents the practices of participants regarding hepatitis B and C. 145 out of 269 respondents (53.9%) have been screened for hepatitis B and C and knew about their present statuses. Out of those who received their vaccinations, 83 (30.9 %) were completely vaccinated and 11 (4.1%) respondents did not receive all the 3 doses of vaccine. Screening before vaccination was done by 34 (12.6%) respondents. 175 (65.1%) respondents did not receive hepatitis B vaccination.

Table 4 Practices related to Hepatitis B and C

Hepatitis B and C Practice items	Frequency (N)	Percentage (%)
Have you ever been screened for hepatitis B and/or C?	Yes	145
	No	124
Do you know your present status (Whether you are positive or negative for HBV or HCV)?	Yes	145
	No	124
If positive, did you take any action on positive HBV or HCV tests?	Yes	1
	No	0
	Not positive	268
If vaccinated did you receive all 3 doses of hepatitis B vaccine?	Yes	83
	No	11
	Never vaccinated	175
Before getting hepatitis B vaccination, did you do screening for Hepatitis B?	Yes	34
	No	60
	Never vaccinated	175

Figure 1 shows the screening statuses of the respondents from first year to final year. Regarding the vaccination status of the respondents, a total of 83 (30.9%) respondents were completely vaccinated and 11(4.1%) did not receive all the three doses. 105 (39.0%) respondents said that they were unaware of the vaccination. 15 (5.6%) respondents believed that vaccination comes with dangerous side-effects. 42 (15.6%) respondents did not get vaccinated because they

had fear of needles. 13 (4.8%) respondents did not receive vaccination because of its cost. Figure 2 shows the reasons given by the respondents for not been vaccinated.

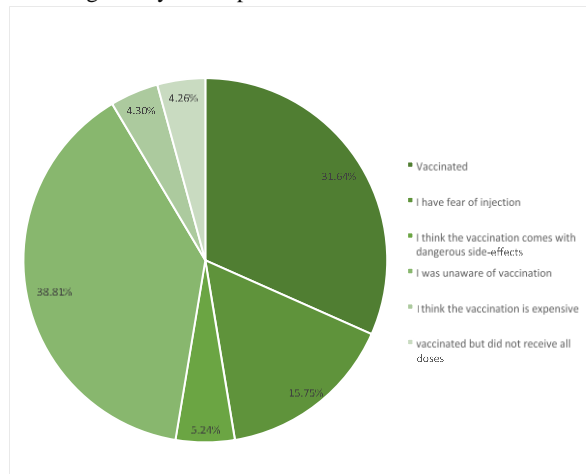


Figure 1 Screening Status of Participants

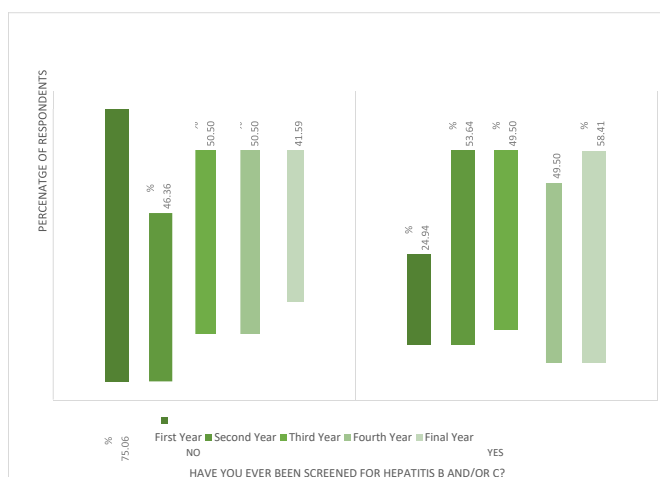


Figure 2 Reasons given by the respondents for not being vaccinated

Table 5 Results of Chi-Square Test

	Gender Based Comparison	Comparison in terms of Year of study
Knowledge	p=0.013	p=0.00
Attitude	p=0.3	p=0.016
Practices	p=0.5	p=0.00

*p value of ≤ 0.05 was set as standard for significance

Among the 132 (90.4%) female and 98(79.7%) male respondents, male subjects had good knowledge regarding hepatitis B and C, no significant relationship was established between gender of respondents with their attitude and practices. Significant differences were found in knowledge, attitude, and practices regarding hepatitis B and C in terms of years of study (Table 5). As for relationship of knowledge of respondents with their

attitude and practices, no significant association was established (p=0.8).

Discussion

Viral hepatitis is an issue of public importance because of global increase in mortality rates due to this. In 2015 1.34 million deaths people died due to hepatitis (2). Pakistan bears high burden of hepatitis B and C and lies in an area of intermediate endemicity for HCC (7). In this study, medical students being a high-risk group were targeted for KAP survey. KAP surveys include assessment of knowledge of respondents, in this case, of medical students regarding their knowledge of the disease, their attitude and way of seeing the disease and their practices of prevention and protection against the disease. As of vaccination, questions were asked to know the status of medical students with regards to pre-vaccination screening and whether vaccination was completed. Medical students were also inquired about their reasons for not being vaccinated. A number of KAP surveys regarding hepatitis B and C have been carried out on medical students in the past (14-24).

In this study, when asked about previous screening 54.6% were never screened for hepatitis B and 56.5% were never screened for hepatitis C. These percentages are higher as compared to results of Olusegun Adekanle et al in 2014 which showed lack of screening awareness among medical students (8). All the respondents demonstrated adequate knowledge regarding hepatitis B and C same as in other researches (18-25). Regarding contaminated food and water as the source of transmission only 51.3% had correct knowledge. As of treatment and vaccination of hepatitis C, respondents had inadequate knowledge. These results were consistent with those of Salwa A. Atlam et al in 2016 and Tazeem Shahbaz et al in 2014 whose studies also show inadequate knowledge of respondents in these fields (18, 22).

More respondents considered that they are at high risk of getting hepatitis by virtue of their work set-up as compared to the study of Tazeem Shahbaz et al in 2014 (18). 33% respondents said adopting personal protective measures while interacting with a hepatitis B or C patient is not necessary. The percentage was almost consistent with study of Benzy Paul et al in 2014 (11). Less number of respondents were exposed to needle pricks as compared to Fazal Rehman Babar’s study conducted in medical students of KCD (Khyber College of Dentistry) and BMC (Bolan Medical College) which showed higher number of needle pricks (20).

Only 30.9% of respondents said they were completely vaccinated. This percentage is much less as compared to studies of Muhammad Asif et al in medical college of Mirpurkhas and Tazeem Shahbaz et al in Lahore Medical

and Dental College (18, 24). Out of the 94 respondents who were vaccinated only 34 did screening before vaccination. The pre-vaccination screening is done so that only those who will benefit, get vaccinated and to avoid false vaccine protection in infected people (8). Despite adequate knowledge, most respondents reasoned I was unaware of vaccination when asked about the cause of not been vaccinated whereas Muhammad Asif et al demonstrated lack of motivation as the reason behind no vaccination at Mirpurkhas medical college (24). Despite more knowledge regarding hepatitis in females, their attitude and practices did not show any significant association which was consistent with study of Nazeer Khan et al (14). Year of study and its association with knowledge, attitude and practices was found significant but no association could be established between knowledge of hepatitis B and C and attitude and practices of medical students which is contrary to study Salwa A. Atlam et al (22). Despite good knowledge, the poor attitude and practices of students were surprising. According to the findings of this study, only good knowledge is not adequate for overcoming high prevalence of hepatitis B and C. Appropriate steps and policies should be made for screening and vaccination especially in medical colleges, because medical students and health-care practitioners are at a risk of contracting this infection. Introduction of hepatitis B vaccination in infancy, resulted in reduction in global HBV prevalence in 2015 (2). Hepatitis B vaccination of those individuals who did not receive it at birth through EPI in Pakistan and preventive measures for hepatitis B and C remain the only ways of overcoming hepatitis and controlling further cases of hepatitis.

Conclusion

Medical Students of Allama Iqbal Medical College had good knowledge and attitude regarding hepatitis B and C but their practices were not satisfactory. Modes of transmission and hepatitis C treatment and vaccination were the areas where students presented insufficient knowledge. There was significant association between gender of respondents and their knowledge. Also, year of study showed significant association with knowledge, attitude and practices of students. However, no significant association could be established between knowledge and attitude and knowledge and practices of medical students. There is a need to adapt the knowledge and develop and implement attitude of students towards positive practices. Students and health-care professionals should be screened regularly for hepatitis B and C.

Conflict of interest: Authors declare no conflict of interest.

Disclosure: None

Human/Animal Rights: No human or animal rights were violated during this study.

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Factors influencing Outcome of Extradural Hematoma in a Tertiary Care Hospital of Dera Ghazi Khan, Pakistan

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Significance:

Pakistan is developing country undergoing major economic and demographic transition coupled with increasing urbanization and motorization. Head injury is among the leading causes of mortality in the country. In young adults head injury is the leading cause of mortality. Some of the factors that increase the risk of road traffic accidents are unsafe traffic environment, poor road infrastructure and encroachments that restrict safe area for pedestrian's lack of safety engineering measures, traffic mix and an increasing number of motorized vehicles. Identifying factors is very crucial for policy making in this particular matter.

ABSTRACT

Background: The outcome for this neurosurgical problem is still far from set target in many developing countries like Pakistan. Major proportion of cases presenting with EDH in hospital still has poor outcome. This poor outcome of EDH is attributed to many factors including weak health systems of most developing countries. Objective of study was to analyze factors influencing outcome among patients of head injury with an extradural hematoma before surgery admitted in neurosurgery department of Dera Ghazi Khan Medical College, Dera Ghazi Khan.

Materials and Methods: This cross-sectional analytical study was conducted in neurosurgery department of Dera Ghazi Khan Medical College from January 2019 to December 2019 after ethical approval. All the patients with extradural hematoma of either gender admitted in the department during the study duration in which surgery was performed to evacuate extradural hematoma were included in the study. Data was collected by using preformed, pretested questionnaire. A vital signs and Glasgow coma scale record was maintained at thirty minutes interval. Computerized tomography was done in every patient. The EDH volume was calculated by using Peterson and Epperson equation $a \times b \times c \times 0.5$. Data was entered and analyzed by using SPSS version 22. Chi square test was applied to observe any statistically significant difference between various strata if existed and p value <0.05 was taken as significant.

Results: Total 237 patients with Extradural Hematoma (EDH) were admitted in neurosurgery department during the study period were included in study. More than half 136 (57.4%) patients were more or equal to the age of 18 years. Majority of the patients 218 (91.9%) in the study

were male. Major cause of extradural hematoma among patients in this study was road traffic accident 154 (64.9%). The outcome of EDH was found to be significantly ($p < 0.001$) associated with age of patients. More than ninety percent of the patients who were directly admitted to tertiary care hospital has good outcome as compared to 109 (60.2%) patients which were referred and difference in outcome was statistically significant ($p < 0.001$). The volume of EDH is not significantly associated with the outcome ($p = 0.090$). The GCS score of the patients at the time of admission is significantly associated with the outcome ($p < 0.001$). Study findings showed that GCS score of the patients at the time of surgery was also found to be significantly associated with outcome of EDH ($p < 0.001$).

Conclusion: There is a strong association of outcome in extradural hematoma with age, gender and GCS of the patient. In higher GCS the outcome was excellent but in low GCS the outcome was poor.

Introduction

Pakistan is developing country undergoing major economic and demographic transition coupled with increasing urbanization and motorization. Head injury is among the leading causes of mortality in the country. In young adults head injury is the leading cause of mortality. Some of the factors that increase the risk of road traffic accidents are unsafe traffic environment, poor road infrastructure and encroachments that restrict safe area for pedestrian's lack of safety engineering measures, traffic mix and an increasing number of motorized vehicles. Unsafe driving behavior and lack of valid driving licenses or fake driving licenses (1, 2). One of the leading causes of death and disability is head injury. Mortality rate after head injury vary from 10-40% and is an index of alertness and efficiency of health care and hospital setup in a country (3-6).

Risk factors of poor outcome in extradural hematoma (EDH) include old age, intradural lesions, temporal location, increased hematoma volume, rapid clinical progression, pupillary abnormalities, increased intracranial pressure (ICP) and low Glasgow coma scale (GCS) (7). Most significant factors associated with unfavorable outcome of EDH are advanced age, lower GCS, and higher EDH volume. Many reports on extradural hematoma have drawn attention to avoidable factors implicated in preoperative deterioration, such as more time spent in transportation to the hospital and late

diagnosis, but less consideration has been given to the specific factors that influence the outcome of patients who arrive comatose in the operating room. EDH still remains a serious neurological condition (8,9,10). Extradural hematomas (EDH) accounts for 2.7-4% of traumatic brain injuries (TBI) and majority of the reported cases are in second or third decade of their life (11,12). Extradural hematoma (EDH) life threatening lesion in neurological surgery was killing at least four of five patients previously but in the modern era of computed brain imaging which is affording prompt, precise diagnosis in the trauma patients, EDH has become one of the disease conditions that may truly be called the delight of a neurosurgeon. Outcome from timely neurosurgical intervention is so fairly assured that a target of zero mortality has been set for it (13-16). Unfortunately, the outcome for this neurosurgical problem is still far from set target in many developing countries like Pakistan. Major proportion of cases presenting with EDH in hospital still has poor outcome. This poor outcome of EDH is attributed to many factors including weak health systems of most developing countries (9). This study was designed to investigate the factors influencing the outcome of EDH among patients admitted in neurosurgery department of Dera Ghazi Khan Medical College, Dera Ghazi Khan, Punjab Pakistan.

Materials and Methods

This cross-sectional analytical study was conducted in neurosurgery department of Dera Ghazi Khan Medical College, Dera Ghazi Khan from January 2019 to December 2019 after ethical approval from hospital ethical committee. All the patients with extradural hematoma of either gender admitted in the department during the study duration in which surgery was performed to evacuate extradural hematoma were included in the study while those with post-operative hematoma were excluded from the study. A detailed history and clinical examination was carried out in every patient. Data was collected by using preformed, pretested questionnaire. A special effort was made to obtain the data regarding mode of injury and means of transportation used to reach the Hospital. The classical signs of extradural hematoma like deterioration of conscious level, pupil size difference and hemiparesis were checked. A vital signs and Glasgow coma scale record was maintained at thirty minutes interval. Computerized tomography was done in every patient. The EDH volume was calculated by using Peterson and Epperson equation $axbxc \times 0.5$, where a, b and c represents diameter of the hematoma in sagittal, axial and coronal planes respectively. Surgery was performed in all the cases with EDH thickness ≥ 1.5 cm, midline shift of equal or more than 5mm and hematoma volume 25 ml or more in supratentorial and 10ml or more

in infratentorial compartment, and in the patients with focal neurological deficits such as limb weakness, unequal pupils, sign of herniation (decerebrate posture) and deterioration of GCS (2 or more points decrease in GCS score from that of admission). Dependent variable of the study was outcome of EDH. The variable was categorized into two groups, good outcome = good recovery and moderate disability, and bad outcome = severe disability, vegetative state and death. The Independent variables were age, gender, type of admission, blood loss and GCS score before surgery.

Data was entered and analyzed by using SPSS version 22. Variables included in the analysis were age, gender, occupation, site of EDH, associated other intracranial or extra cranial injury and severity of injury by using GCS. Chi square test was applied to observe any statistically significant difference between various strata if existed and p value <0.05 was taken as significant.

Results:

Total 237 patients with Extradural Hematoma (EDH) were admitted in neurosurgery department during the study period. More than half 136 (57.4%) patients were more or equal to the age of 18 years. Majority of the patients 218 (91.9%) were male. Only 56 (23.6%) patients with extradural hematoma were directly admitted to teaching hospital and 76.4% were referred to teaching hospital. Major cause of extradural hematoma among patients was road traffic accident 154 (64.9%) followed by assault 47 (19.8%). At the time of admission 174 (73.4%) patients had GCS between 9-15 and before surgery GCS score of 177 (74.7%) patients was between 9-15.

Outcome of EDH in about half of the patients 48 (47.5%) with less than 18 years age was bad while 107 (78.8%) patients with equal to or more than 18 years age is good. Among male patients 153 (70.2%) had good outcome. The outcome of EDH was good among 51 (91.1%) patients who were directly admitted to tertiary care hospital as compared to 109 (60.2%) in referred cases. The cross tabulation of outcome with causes of EDH showed that 119 (77.3%) patients of road traffic accidents had good outcome followed by 25 (53.3%) assault and 16 (44.4%) other causes. The bad outcome of EDH was observed among 11 (22.4%) patients in which volume of extradural hematoma was less than 30 ml. The outcome of EDH was bad among 46 (73.1%) patients in which GCS score at the time of admission was between 3-8 while 141 (81.1%) patients with GCS between 9-15 at the time of admission had good outcome. Similarly 80% patients with GCS score between 3-8 at the time surgery had bad outcome (Table-III).

Table I: Characteristics of the patients with EDH

Variables	Frequency (n)	Percentage (%)
Age		
<18 years	101	42.6%
≥ 18 years	136	57.4%
Gender		
Male	218	91.9%
Female	019	08.1%
Admission		
Direct	056	23.6%
Referral	181	76.4%
Cause of EDH		
Road traffic accident	154	64.9%
Assault	47	19.8%
Others	36	15.3%
Volume of EDH		
< 30 ml	49	20.7%
> 30 ml	188	79.3%
GCS score at the time of admission		
3-8	63	26.6%
9-15	174	73.4%
GCS score before surgery		
3-8	60	25.3%
9-15	177	74.7%

Table II: Location of EDH among patients

Location	Frequency (n)	Percentage (%)
Temporal	98	41.3%
Frontal	51	21.5%
Parietal	42	17.7%
Temporo-parietal	35	14.8%
Occipital	09	03.8%
Posterior Fossa	02	00.9%
Total	237	100%

Discussion

More than half of the patients of EDH with causes other than road traffic accidents and assault had bad outcome. The study findings revealed that volume of EDH is not significantly associated with the outcome (p=0.090) which is comparable with findings of many other studies in which no meaningful relationship between the volume EDH with outcome was noted (17, 18).

The findings of the study showed that GSC score of the patients at the time of admission is significantly associated with the outcome (p<0.001). The similar findings were noted in the study conducted by Ndoumbe A et al. in which GCS score at the time of admission was strongly predictive for good or poor outcome (19). In this study GCS score of the patients at the time of surgery was also found to be significantly associated with outcome of EDH (p<0.001) Which is consistent with the findings of Khan MB et al in which they observed that time since trauma and surgery were directly related to outcomes and

that surgical delay beyond 12 hours resulted in statistically significant worse outcomes (20).

Table III: Characteristics of the patients with EDH and their outcome

Variables	Frequency	Outcome		p value
		Good	Bad	
Age				
<18 years	101	53 (52.5%)	48 (47.5%)	<0.001
≥ 18 years	136	107 (78.8%)	29 (21.2%)	
Gender				
Male	218	153 (70.2%)	65 (39.8%)	0.002
Female	019	07 (36.8%)	12 (63.2%)	
Admission				
Direct	056	51 (91.1%)	05 (8.9%)	<0.001
Referral	181	109 (60.2%)	72 (39.8%)	
Cause of EDH				
Road traffic accident	154	119 (77.3%)	35 (22.7%)	<0.001
Assault	047	25 (53.2%)	22 (46.8%)	
Others	036	16 (44.4%)	20 (55.6%)	
Volume of EDH				
< 30 ml	049	38 (77.6%)	11 (22.4%)	0.090
> 30 ml	188	122 (64.9%)	66 (35.1%)	
GCS score at the time of admission				
3-8	063	17 (26.9%)	46 (73.1%)	<0.001
9-15	174	141 (81.1%)	33 (18.9%)	
GCS before surgery				
3-8	070	14 (20.0%)	56 (80.0%)	<0.001
9-15	167	146 (87.4%)	21 (12.6%)	

Conclusion

There is a strong association of outcome in extradural hematoma with age, gender and GCS of the patient. The outcome of extradural hematoma is affected by GCS at the time of admission. In higher GCS the outcome excellent but in low GCS the outcome is poor.

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Disclosure: None

Human/Animal Rights: No human or animal rights are violated during this study.

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Efficacy of Tranexamic Acid in reducing intra-operative bleeding during tonsillectomy

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Significance:

Tonsillectomy is a very commonly performed procedure. During procedure in the department, no one was given tranexamic acid for the control of bleeding whereas, the literature strongly recommends use of such tranexamic acid for bleeding control. This study was planned to examine the effect of tranexamic acid to reduce the blood loss. If blood loss is minimized through the use of tranexamic acid, then it is used in all tonsillectomy cases.

ABSTRACT

Background: Our study aims to determine the effectiveness of tranexamic acid in decreasing the intraoperative blood loss during tonsillectomy.

Materials and Methods: Study design was randomized double-blind control trial. This study was conducted from 1 November 2017 till 30 June 2019 in the department of ENT unit-II, the civil sandeman provincial teaching hospital Quetta. Ethical approval was taken from Ethical Review Board of the civil Sandeman provincial teaching hospital Quetta. A sample of 100 patients were surveyed, 55 men and 45 woman, 10-30 year age range, 1.2:1 men to female with a mean 20 year age. Patients who met the criteria for inclusion experiencing an elective tonsillectomy were randomly assigned to two groups. Every community has equivalent patients. An injection of 10 mg/kg body weight was given intravenously into group-A 5-10 minutes prior to surgery, and normal saline of the same amount was administered intravenously into group-B. Intraoperative bleeding was measured at Operation Theatre in both groups during surgery. In intraoperative blood loss, the effectiveness of tranexamic acid / placebo was determined by measuring loss of blood computed by Gravimetric method and blood obtained in suction jar by measuring.

Results: In Group-A and Group-B patients, there was a significant difference in intra-operative loss of blood during tonsillectomy. In group A, intra-operatively, there was overall blood loss of 1404 ml and the average blood loss was 33ml. During surgery in group-B the blood loss was 3132 ml, and the average loss of blood was 62-64ml. As a result, group B was more intraoperative bleeding and consumed more time compared to group A.

Conclusion: Study group patients receiving preoperative intravenous tranexamic acid have less intraoperative loss of blood and less time consuming than placebo patients who have not obtained tranexamic acid intravenous.

Introduction

Tonsillectomy is the surgical procedure in which the palatine tonsils are completely removed (1). Reduction of tonsils has also been done since antiquity (derived by, tonsa, Latin for "oar"). It's the most frequently done operation in otorhinolaryngology these days. Beside other indications, the most common indication is recurrent tonsillitis (chronic tonsillitis). It is usually performed above 4 years and below 42 years of age. It is done under general anesthesia. There are different methods of tonsillectomy but the most common one is the dissection and snare method. Each method has their advantages and disadvantages. The most common complication of tonsillectomy is hemorrhage because of its rich blood supply (2). Massive hemorrhage during tonsillectomy is life threatening emergency (3). Hemorrhage after tonsillectomy has a possibility of complications due to obstruction of the airway, trauma and eventually death unless identified early or intra-operatively (4). Thus, most essential part of tonsillectomy after removal is complete control of hemorrhage. Excessive intraoperative hemorrhage may need blood transfusion which further increase the risk of early and late post tonsillectomy morbidity and mortality including increased hospital stay and cost (5,6,7). Intraoperative bleeding also increases morbidity and mortality of patients due to other reasons. Thus it is necessary to avoid the morbidity and mortality due hemorrhage. So, careful homeostasis is required. Early methods for controlling bleeding are pressure and caustic agents, later on ligation by catgut, silk, noosties and packing of tonsillar fossa became popular. Negus forceps control the hemorrhage by homeostasis during tonsillectomy effectively and hemorrhage declines although types of complications remain the same (8). Tranexamic acid results in the reduction in loss of blood during traditional snare and dissection methods (9,10). Antifibrinolytic drugs are being employed which minimize blood loss by inhibiting fibrinolysis and consequently the need for blood transfusion. This further decreases the morbidity and mortality in patients. Aprotinin, Epsilon- Amino caproic acid and tranexamic acid are the anti-fibrinolytic drugs. Tranexamic acid is an alternative for synthetic lysine. It has an antifibrinolytic effect on plasminogen derivatives through reverse blockage of the lysine binding site. This prevents plasminogen convergent into fibrin plasmin surface (11). This has been accessible since last 40 years and has only

recently been developed as a prescription tool for blood loss reduction during surgery (12,13). It is now used worldwide because of its proven role in reducing and prevention of hemorrhage during tonsillectomy (14). It is effective and cheap (15). Intravenous injection of tranexamic acid was used widely (7) and successfully in different surgeries like cardiac, orthopedic, cesarean section and prostate (16). It was also used topically throughout dental and oral surgeries as mouth wash (17). Tranexamic acid has been used initially in patients undergoing adenoidectomy (18). Tranexamic acid has few side effects including headache, dizziness, and vomiting. The rationale of our study is to know the efficacy of intraoperative injection of tranexamic acid in reducing bleeding during tonsillectomy.

Tonsillectomy is a very commonly performed procedure. During the procedure in the department no one was given tranexamic acid for the control of bleeding whereas, the literature strongly recommends use of such tranexamic acid for bleeding control. This study was planned to examine the effect of tranexamic acid to reduce the blood loss. If blood loss is minimized through the use of tranexamic acid, then it can be used in all tonsillectomy cases. Current study aimed to determine the effectiveness of tranexamic acid in decreasing the intraoperative blood loss during tonsillectomy.

Materials and Methods

This double-blind random controlled trial was done from 1 November 2017 till 30 June 2019 in the department of ENT unit-II, Quetta Civil Provincial Teaching Hospital. Ethical approval was taken from Ethical Review Board of the civil Sandeman provincial teaching hospital Quetta. Based on history, clinical examinations, and investigations, 100 patients were diagnosed with recurrent tonsillitis (Chronic Tonsillitis). Consecutive patients having recurrent tonsillitis, aged 10-30 years in which 55 sufferers were men and 45 sufferers were women with such a male-to - female ratio of 1.2:1 were included. Patients underwent elective tonsillectomy by dissection and snare method under general anesthesia. Patients with acute throat infection or infection in other region of body and of any co-morbidity were excluded.

With the help of table of random numbers, all patients were randomly assigned to one of two groups, 50 patients across each group. Tranexamic acid with 10 mg/kg body weight was given intravenously 5-10 minutes prior to commencement of surgery in group-A and the patients receiving 5-10 mg of normal saline were labeled as group-B. The operator was blinded of the intravenous injection given either tranexamic acid or normal saline according to group allocated. Patients were observed by pulse, blood pressure, respiratory rate and evidence of fresh bleeding during and on completion of surgery and

thorough surgical homeostasis were ensured. Blood loss was calculated by gravimetric method and in suction jar. The calorimetric method of measuring blood content in used gauze pieces is a much more correct approach. The gravimetric estimation method was shown to fit well with the calorimetric process and is thus reasonably reliable to be used to measure intraoperative loss of blood (19). In order to measure blood as in suction jar, the amount of fluid in the suction was started pouring into a measuring cylinder and the amount of fluid present even before treatment was subtracted. The lower edge of a liquid level meniscus was considered for readings after the foam had settled. Across all weightings an HMT Company electronic measurement scale with ISI signs has been used. This has a sensitivity of 2 gm, with just low and high capacities of 10 gm and 6 kg. Until keeping on the surgical tray, gauze parts were measured to be used for operation. Post-surgery weighed again all soiled gauze parts and untouched gauze parts and the distinction was taken as the quantity of bleeding with a transformation of 1 gm=1 ml of blood (20). Its amount of blood loss evaluated in Group-A was compared to group-B level of blood loss. Therefore, the effectiveness of tranexamic acid and placebo in terms of the amount of intraoperative blood loss was determined. To test the hypothesis that intraoperative bleeding was less in group-A than in group-B, the frequencies of more or less intra-operative bleeding were calculated. Using SPSS version 20.0 data were entered and analyzed. Mean and standard age deviations were calculated for all patients. The ratio of men to women was determined. Frequencies of sometimes intraoperative bleeding were calculated during tonsillectomy and compared by applying T- test. The p-value was considered significant at 0.05 or less than 0.05.

Results:

Tests of all 100 patients who had undergone dissection and snare process tonsillectomy were done from November 2017 till June 2019. There were 55 patients male and 45 patients had men-to - woman ratio of 1.2:1 with 10-30 years of age and 20 years of average age. Many of the patients have had chronic tonsillitis. Intravenously tranexamic acid of 10 mg/kg body weight was administered to 50 group-A patients 5-10 minutes before start of surgery and normal saline of same amount was administered intravenously to the next 50 group-B patients. Intraoperative bleeding was significantly different between group-A (research group) and group-B (placebo).

In group-A there was total blood loss of 1404 ml intra-operatively and mean blood loss was 33.08 ml. In group-B patient there was total blood loss of 3132 ml during surgery and mean blood loss was 62.64 ml. This shows

that the intra-operative blood loss was 44.8% less in group-A patient. Group-A patients also take less time for surgery.

Frequencies of more or reduction of intraoperative blood loss throughout tonsillectomy were compared in both groups through the application of t-test. The obtained p-value has been less than 0.05. Thus, intraoperative bleeding was less in group-A Patients who has received tranexamic acid injection intra-operatively as compare to group-B patients which has received the same amount of normal saline.

Table 1: In group-A and group-B patients with p-value shows total and mean blood loss

GROUP	TOTAL BLOOD LOSS	MEAN BLOOD LOSS	P value
Study group	1404ml	33.05ml	0.32 2362
Controlled group	3132ml	62.64ml	

Study Group: 1404 ml p-value (right-tailed) = 0.32, p-value (two-tailed) = ± 0.49

Controlled Group: 3132 ml p-value (right-tailed) = 0.32, p-value (two-tailed) = ± 0.49

Discussion

Tonsillectomy remains one of the basic surgical procedures in otorhinolaryngology. The problems encountered during surgical procedure remained the same, however, the tranexamic acid has been widely used in a number of other procedures to minimize bleeding, demonstrating its effectiveness in reducing surgical bleeding. Such include prostatectomy (21) (a 52.94 per cent reduction in bleeding during surgery); caesarean section (22-23) (Showed reduction of 43.08% of bleeding during surgery), orthopedic surgery (24-25) (Showed reduction of 39.8% of bleeding during surgery) and cardiac surgery (26-27) (showed reduction of 45.32% of bleeding during surgery).

Castelli and Vogt, in their study, noted a 28 per cent (10) reduction in blood loss. Review study of older studies to tonsillectomies on the use of tranexamic acid demonstrated a significant loss of blood (28).

These all studies and numbers demonstrated the effectiveness of tranexamic acid throughout surgery in lowering intraoperative blood loss. In our study, the rate of bleeding reduction during tonsillectomy was 45.8% near George A, Kumar R's study and Kumar S showing 44.45 per cent reduction in intraoperative blood loss in patients receiving tranexamic acid intramuscular injections (29). No side effect of the tranexamic acid was mentioned in studies. In addition to surgery, tranexamic acid was also used with great success to reduce bleeding in non-operative certain situations, including epistaxis, topmost GIT bleeding, and menorrhagia, that also showed

significant decrease in bleeding through the use of tranexamic acid. In spite of the enormous evidence in support of tranexamic acid success in preventing bleeding throughout tonsillectomy, studies have been conducted in which tranexamic acid has not proved to be useful, this could be due to tranexamic acid which may not have an effect on blood vessels bleeding and is more successful in managing capillary oozing(29). That's why in certain patients who underwent, in spite of giving tranexamic acid intra-operative intravenous injection does not reduce intra-operative bleeding.

Conclusion

Tonsillectomy is the basic and usual procedure of ENT surgery. Blood loss due to tonsillectomy still remains a significant cause of morbidity and mortality, despite advances in tools and techniques. Procoagulants like tranexamic acid have been used successfully in controlling intra-operative bleeding during tonsillectomy. This reduction in bleeding further decreases the need of blood transfusion and consequently the early and late morbidity and mortality of patient, without any side effect. Patients of group-A (study group) receiving intravenous tranexamic acid also take less time for surgery.

Conflict of interest: Authors do not have any conflict of interest to declare.

Disclosure: None

Human/Animal Rights: No human or animal rights are violated during this study.

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Current Screening Strategy Poses Risk of Spreading of Hepatitis C Virus Infection

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Significance:

Compulsory screening of blood and blood items before transfusion, legitimate disinfection of dental and surgical instruments, and suitable transfer of contaminated stuff and dispensable syringes are among the issues that should be addressed by using of combo testing or antigen testing that can reduce the transmission of viral infections through transfusions. These procedures can significantly reduce the false positive reports of HCV during the window period, which is reported to be as long as 17 days by using fourth generation of ELISA.

ABSTRACT

Background: Hepatitis C virus is one of the significant causes of morbidity and mortality in the World. Surprisingly, despite national screening campaigns, new cases of HCV are still on the rise.

Methods: A total of 5914 healthy blood donors was included in this study after informed consent. Anti-HCV ELISA was used to check presence of antigen in participant's plasma using Monlisa HCV Antigen-Antibody Ultra kit. Final confirmation was done by using real time PCR considered as a gold standard.

Results: 0.5% of anti-HCV ELISA negative samples showed presence of antigen in plasma, when checked through core Ag detection method.

Conclusion: Our result suggested that HCV core antigen detection and/or combo testing are far safer screening methods for the detection of HCV and the use of these methods can avoid/reduce further spread of this deadly disease.

Introduction

Hepatitis is a common disease occurring worldwide and is a significant cause of illnesses and deaths (1). According to the World Health Organization, approximately 3% of the world population are infected with hepatitis C virus (HCV) with an increase of 3-4 million cases every year. Round about 65-85% of hepatitis C patients develop chronic hepatitis C further leading to hepatocellular carcinoma and death (2, 3). Awareness in the public regarding the transmission and prevention of HCV infection, provision of safe blood and blood products and accessibility to cost effective HCV antiviral drugs have considerably reduced the HCV prevalence in the developed countries. However, in many developing countries lack of knowledge about transmission and prevention of HCV, insufficient

facilities to screen blood and blood products, and unavailability/unaffordability to effective HCV therapies are the major factors which are responsible for inevitable rise in HCV infection (4, 5). Pakistan is amongst one of the countries that have very high rate of HCV patients both acute and chronic. There are about 10 million people with HCV in Pakistan. Published literatures showed that the prevalence of HCV infection is approximately 4% in Pakistan (6, 7). Recent studies illustrated that 90% of HCV positive patients were not aware of the infection (8, 9). It has been shown that prevalence of HCV increases with age and the reason can be because of exposure to risk factors.

Earlier in 1992, blood transfusions were considered as one of the major route of transmission of HCV owing to approximately 15-20 % of the total transmitted cases (10, 11). By changing the rule from paying the blood donors to just all volunteer has decreased the post-transfusion hepatitis to 10%, which was further reduced to 1 per million transfusions due to pre-transfusion blood screening for different infectious agents including HCV. The few cases that still occur is due to blood transfusions from newly infected patients that are in the window period i.e. antibodies are still not developed. This window period can be as long as 6-8 weeks (12). Moreover, early diagnosis of HCV among immunocompromised and hemodialysis patients is more difficult, where antibody respond late and take more time to develop.

In order to detect the false negative reporting, especially during the window period, we planned this study to evaluate the efficiency of the screening method (Ab detection based) commonly used in most of the blood banks within the country. We found that 0.5 % cases out of the healthy donors were found positive when analyzed by commercially available methods targeting either Antigen or antigen/antibody both.

Materials and Methods

Five thousand nine hundred and fourteen donors from the blood banks of different health centers and hospitals of Punjab province of Pakistan were included in the present study. Complete history was taken from each blood donor through pre-designed tested questionnaire, which was approved by institutional ethical committee. Blood donors with the ages ranging between 20-60 years and body weights of more than 50 kg were included in this study. Donors with the history of hepatitis, current or recent systemic disease, drug abuse, recent surgery or

transfusion of blood or blood product within last 12 months were excluded from this study. Written informed consent was acquired from each participants. All the research work carried out was in compliance with Helsinki's declaration.

Screening of Blood groups and different infectious agents: Blood groups of all the subjects were checked by slide and tile method using the readily present agents. Screening of hepatitis B virus (HBV) and immune deficiency virus (HIV) was performed by using ABBOTT PRISM® kits according to the manufacture protocol.

Screening of the subjects for HCV: All the subjects were initially screened with commercially available assay for the detection of antibodies against HCV (anti-HCV Ab) i.e., ARCHITECT Anti-HCV. Then, all the plasma was further analyzed by two other commercially available kits targeting either only the core antigen using Abbott Architect HCV Chemiluminescent Microparticle Immunoassay (CMIA) or both antigen and antibody using anti-HCV Monalisa® HCV Antigen-Antibody Ultra (Bio-Rad Laboratories Limited, Marnes La Coquette, France). These entire tests were performed as per the manufacturer's protocol.

Real-time PCR for HCV RNA detection: We used RT-PCR as gold standard for the HCV detection in this study. Briefly, the HCV RNA was extracted via Fovergen kit and HCV RNA was amplified using commercially available AmpliSens HCV PCR kit and CFX Bio-Rad real time PCR according to the manufacturer protocol.

Statistical Analysis: All the data are expressed in percentages. The statistical analysis was performed using SPSS version 20 for analyzing percentages of different blood groups.

Results

Demographic analysis of the studied population: Out of 5914 blood donors, 5840 (98.74%) were male and 74 (1.25%) were female. The age-wise distribution among male and female is shown in (Table 1 and 2).

After checking for the prevalence of HCV among different blood group, we found higher prevalence of HCV subjects with A +ve and B+ve blood groups in both female and male, respectively (Figure 1).

Screening results of other infectious agents

All the subjects were analyzed for HBV and HIV, out of these subjects it was not found any positive case for HIV, even then 70 (1.18%) subjects were positive with hepatitis B virus (HbsAg). The Blood group distribution between males and females in HBV infected individuals is shown in Figure 3. Higher prevalence of HBV was found among the subjects with A+ve blood group (Figure 2).

Table 1: Gender wise distribution of Blood Donors According to age group

Male donors distribution		
Age group	No. of donors	Percentage
18-30	4246	71.79%
31-40	1162	19.64%
41-50	234	3.95%
51-60	94	1.58%
Female donors distribution		
18-30	56	75.6%
31-40	16	21.6%
41-50	2	2.7%
51-60	0	0

Table 2: Distribution of Anti HCV positive cases in Different Districts of Pakistan

Districts	Prevalence of HCV	Districts	Prevalence of HCV
Khaniwal	14.28%	Pattoki	6.97%
Nankana	11.94%	Sargodha	6.66%
Faisalabad	11.76%	Gujranwala	5.88%
Kasoor	9.94%	Sialkoat	5.26%
Bahawalpur	9.09%	Multan	4.34%
Okara	8.74%	Lahore	3.42%
Shiekhupura	8.41%	Sahiwal	2.53%
Pakpatan	7.89%		

Screening results of HCV through three different methods:

All the blood donors included in this study were checked for HCV using three different commercially available kits. Out of 5914 subjects, 292 were found positive for the presence of anti-HCV antibodies in their plasma. Surprisingly, the other two methods, either targeting only HCV core Ag or both HCV core Ag and Ab (combo testing) showed 30 more positive cases in addition to the previously reported 292 positive cases analyzed through anti-HCV detection method. So, total number of 322 (292+30) were assigned as HCV affected individuals and were confirmed by RT-PCR.

Confirmation of HCV through RT-PCR: To confirm our results, we used RT-PCR against HCV as gold standard. All the included subjects were finally analyzed through RT-PCR and found that out of 5914 subjects, 322 (292+30) were confirmed for the presence of viral RNA in their plasma.

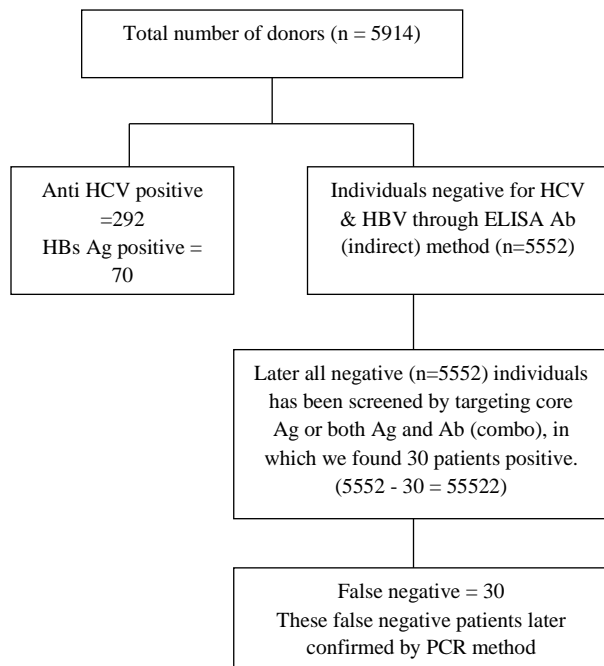


Figure 1. Schematic representation of the study

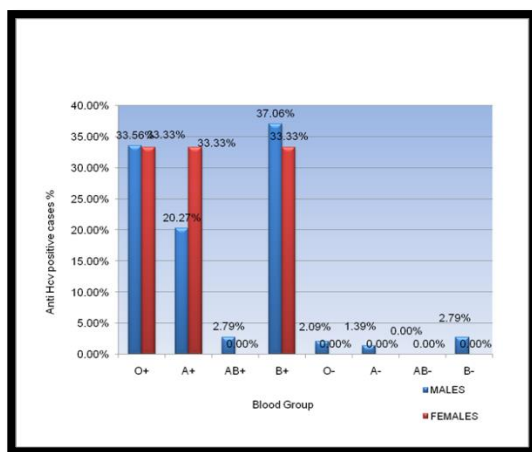


Figure 02. Distribution of Anti HCV Positive case with Blood Groups and Sex

Incidence of HCV positive cases in different districts of Pakistan:

The distribution of HCV positive cases among different districts was also checked as shown in Figure 4. It was found that prevalence of HCV was 3.42% in Lahore (lowest), 9.94% in Kasur, 8.74% in Okara, 8.41% in Shaikhupura, 5.88% in Gujranwala, 2.53% in Sahiwal, 6.97% in Pattoki, 7.89% in Pakpatan, 11.76% in Faisalabad, 11.94% in Nankana, 6.66% in Sargodha, 5.26% in Sialkot, 14.28% in Khanewal (highest), 9.09% in Bahawalpur, 4.34% in Multan. Prevalence of anti HCV positive cases was highest in Khanewal District.

Discussion

We reported that when compared with the universally accepted HCV detection method (RT PCR), the most common method currently in-use (Anti-HCV Ab detection) all across Pakistan and in many other countries of the world as well failed to report all the HCV positive cases. When we compared these results with two other commercially available kits, we found that both the kits were able to detect those false negative samples and showed similar sensitivity and specificity compared to the gold standard (PCR).

There are approximately half million people affected by HCV in the globe and the number is still rising at an astounding rate mostly in the developing countries (12, 13). In Pakistan the number of HCV patients is quickly increasing and it is reported that there are 9 million carriers of HCV (14). In 2008, approximately 91.8 million total blood donations are collected. Blood transfusions increase the risk of getting transfusion-transmissible infections (TTI) such as HCV, HIV, HBV, syphilis and other less common infections such as malaria, toxoplasmosis, and brucellosis etc (15). EIAs are commonly used to detect anti-HCV antibodies for screening of HCV in these donated blood all around the world. New assays that either combines the detection of anti-HCV Ab, and/or antigen be used to lower the transmission rate (16). These methods are of great importance to medical institutes as it can prevent infections, protect doctor-patient relationship, lower the exposure of medical staff to the viral infections more efficiently and also good for early detection and diagnosis of infections (17). Our data showed higher number of male blood donors as compared to females. This was majorly due to physiological gender differences among females as well as other social and economic burdens faced by them. Previous study has also reported that most of voluntary donors were males 96.96% with respect to 3.41% females which is similar to the present study with higher number of young blood donor (18).

We found that the incidence of HCV was 5.4% (322), HBsAg was 1.18% (70) and not a single positive case of anti-HIV was observed in healthy blood donors. Another study conducted in the same province previously reported the incidence rate of HCV has risen significantly during the same time period, even in the presence of better screening methods, treatment and awareness (19). Most frequent incidence of HCV positive cases was seen in Khanewal 14.28%. This may be due to low literacy level, poor hygienic conditions and socioeconomic status in this area. On the contrary, the prevalence in Lahore was the lowest due to better level of awareness, health care facilities and access to treatment.

We strongly recommend that these new assay/method, may be implemented as soon as possible to decrease the accidental spread of HCV. Compulsory screening of blood and blood items before transfusion, legitimate disinfection of dental and surgical instruments, and suitable transfer of contaminated stuff and dispensable syringes are among the issues that should be addressed by using of combo testing or antigen testing that can reduce the transmission of viral infections through transfusions. These procedures can significantly reduce the false positive reports of HCV during the window period, which is reported to be as long as 17 days by using fourth generation of ELISA.

Conclusion

Continuous improvement in blood screening, use of sensitive assays and donor requirements led to safer blood transfusions than before. The government drug enforcement agencies may make a policy to use antigen testing or the combo testing rather than only antibody testing (ELISA) to avoid false positive HCV results due late immune response and accidental transmission of HCV among healthy populations.

Conflict of interest: Authors do not have any conflict of interest to declare.

Disclosure: None

Human/Animal Rights: No human or animal rights are violated during this study.

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Effect of Gestational Diabetes on Serum Leptin during Pregnancy and Postpartum Period

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Significance:

Pregnancy is associated with leptin resistance as leptin mRNA receptor is found to decrease during pregnancy. During early pregnancy, increase in Serum leptin, is found to be associated with the increased risk of Gestational diabetes in later pregnancy. A vicious cycle develops between insulin and leptin as increase in insulin level in pregnancy stimulates adipose tissue to produce serum leptin which in turn promotes secretion of cytokines i.e. IL-6 & TNF- α leading to inflammation and further increase in serum leptin. These cytokines increase the insulin resistance, resulting in hyperinsulinemia which results in hyperleptinemia. This study was planned to find correlation b/w GDM and serum leptin levels among Pakistani women as limited research data is available.

ABSTRACT

Background: Gestational diabetes mellitus (GDM) is associated with marked increase in insulin resistance. The objective of study is to determine the relation of gestational diabetes with serum leptin and serum insulin levels during pregnancy and postpartum period.

Methods: This case control study conducted on total ninety samples that include cases and controls taken after 24 weeks of gestation. The case sample included 40 pregnant women with GDM and 10 women with GDM at postpartum stage. The control sample included 30 normal pregnant women with no GDM and 10 normal women at postpartum. Fasting serum leptin and fasting serum insulin were measured by ELISA. HOMA index was calculated by fasting serum insulin and fasting blood glucose.

Results: Serum leptin (30.89 ± 1.35), serum insulin (27.67 ± 1.32) and HOMA index (8.33 ± 0.53) significantly high in gestational diabetic women than normal pregnant ($p < 0.05$) during pregnancy. However, after delivery of fetus, serum leptin, serum insulin and HOMA index in gestational diabetics significantly decreased compared to during gestation period. Hence a positive correlation of GDM was determined against serum leptin and HOMA index.

Conclusion: Serum leptin level is raised in GDM which has a positive correlation with insulin resistance. This study finds that the serum leptin levels may use as a marker to early screen and diagnose Gestational diabetes.

Introduction

Pregnancy is associated with a series of physiological changes that include increased food intake, accumulation of body fat and progressively raised insulin resistance (1). During the first trimester of pregnancy, there is an increase in the insulin secretion and maternal fat cells while insulin sensitivity either remains unchanged or increases. However, from mid trimester onwards, insulin sensitivity decreases. So, for maintenance of euglycemic state, a 2-fold increase in insulin secretion is required. Any abnormality in the physiological pregnancy that can't compensate the insulin necessity will contribute to the complications like gestational diabetes (2). The pathogenesis of GDM is related to either insufficient insulin production against the demand during pregnancy or the raised-up insulin resistance (3). Food intake stimulates leptin production but in the presence of resistance it fails to induce satiety. Serum leptin deficiency or leptin resistance both promote food intake leading to obesity (4).

The expression of the placental leptin and increased adipose tissue coincide with the raised maternal serum leptin levels. Hence, the maternal serum leptin levels attain peak level till the 28th week of gestation then gradually decreases and after the delivery becomes normal due to expulsion of placenta (5). Leptin increases the body's insulin sensitivity through the regulation of insulin-mediated glucose metabolism by skeletal muscles and by hepatic regulation of gluconeogenesis (6,7).

Pregnancy is associated with leptin resistance as leptin mRNA receptor is found to decrease during pregnancy. During early pregnancy, increase in Serum leptin, is found to be associated with the increased risk of Gestational diabetes in later pregnancy (8). A vicious cycle develops between insulin and leptin as increase in insulin level in pregnancy stimulates adipose tissue to produce serum leptin which in turn promotes secretion of cytokines i.e. IL-6 & TNF- α leading to inflammation and further increase in serum leptin. These cytokines increase the insulin resistance, resulting in hyper-insulinemia which results in hyperleptinemia (9).

This study was planned to find correlation between GDM and serum leptin levels among Pakistani women as limited research data is available.

Materials and Methods:

This case-control study was approved by Ethical Committee of University of Lahore Teaching Hospital,

Lahore. The case sample included 40 pregnant women with GDM and 10 women with GDM at postpartum stage. The control sample included 30 normal pregnant women with no GDM and 10 normal women at postpartum. An informed, written consent was taken from each participant of study. The maternal blood samples were collected from all the participants after taking a detailed history regarding bio data, address, age, Gestation age, parity, gravida, previous history of the GDM, family history of Diabetes, sibling history of diabetes, drug history and past history of chronic illness. The general physical examination included measurement of weight, height, body mass index and blood pressure.

The Case participants involved in the research were pregnant women aged between 18 to 40 years with the Gestational diabetes, after 24-28 week of gestation. GDM was confirmed by oral glucose tolerance test (OGTT). The Control participants include normal healthy pregnant women. Cases and control included in study during postpartum period were taken 4 weeks after delivery of fetus. All the women with the known history of metabolic disorders, diabetes mellitus and preeclampsia or any other complication of pregnancy were excluded from the study. At the 24- 28th week of the gestation, a standard 2hour OGTT was performed. After screening of pregnant women with glucose challenge test, the subject asked for overnight fast of 8 - 14 hours (drink only water), the subject was offered 75 g oral glucose in 250 – 300 ml water over five minutes. Fasting, after 1 hour and after 2 hours, blood sample was taken. Gestational Age was estimated by last menstrual period date and confirmed by ultrasound. After confirmation of case and control by OGTT, maternal fasting plasma samples were collected in the volume of 6 ml tubes. These samples were span 3000 rpm for 15 minutes by centrifuge machine and then sera separated into appropriate tubes and frozen at -20°C until analysis were done. At time of procedure, the samples thawed by keeping them at the room temperature and serum leptin and serum insulin were measured by ELISA. The homeostasis model assessment index-insulin resistance (HOMA-IR), the important determinant of insulin resistance, measured by an equation:

$$HOMA\ Index = \frac{[fasting\ insulin\ (\mu IU/ml) \times fasting\ glucose\ (mmol/L)]}{22.5}$$

HOMA index less than 3 is considered normal, person with no insulin resistance. The value than 3 more is associated with insulin resistance (10).

The data was analyzed by using SPSS 21. For the continuous variables we used mean and the standard error of mean. Categorical data was expressed as numbers (n) and percentages (%). For the comparison of serum leptin, serum insulin and HOMA index in cases and controls during pregnancy, ANOVA was performed. Paired t-test was performed to analyze serum leptin, serum insulin and

HOMA index of cases and controls during pregnancy and postpartum period. The p-value less than 0.05 was considered statistically significant.

Results:

Mean Age \pm standard deviation (years) of the cases with Gestational diabetes was 25.28 \pm 0.72 and among the control group it was 23.76 \pm 0.83. Basal metabolic index (BMI) (Kg/m²) of gestational diabetics (26.95 \pm 0.88) is greater than that of the controls(20.59 \pm 0.34).

Gestational diabetics showed OGTT fasting (6.74mmol/L \pm 0.12), OGTT after 1 hours (12.56mmol/L \pm 0.14), OGTT after 2 hours (10.04mmol/L \pm 0.12), Serum insulin (27.48mIU/L \pm 0.49), HOMA index (8.26 \pm 0.23) and Serum Leptin (31.08ng/ml \pm 0.70) significantly higher than that of control i.e. 4.46 \pm 0.09, 8.48 \pm 0.16, 6.74 \pm 0.14, 14.63 \pm 0.37, 2.90 \pm 0.09 and 11.48 \pm 0.16 respectively.

Table I shows comparison of cases during pregnancy with Gestational diabetes and during postpartum period, done by paired t test. Results showed significant decrease (p < 0.05) in serum Insulin, serum leptin and HOMA index from pregnancy to postpartum period.

Table II showed correlation of blood glucose against HOMA index and serum leptin. Results showed a positive significant correlation of blood glucose with HOMA

Table I: Serum insulin, HOMA Index and serum Leptin of Gestational Diabetic women during pregnancy and Postpartum Period

Tests	Cases (during pregnancy)	Cases (after delivery)	P value
Serum Insulin (mIU/L)	27.67 \pm 1.32	19.56 \pm 0.65	< 0.05
HOMA Index	8.33 \pm 0.53	3.56 \pm 0.29	< 0.05
Serum Leptin (ng/ml)	30.89 \pm 1.35	17.89 \pm 1.40	< 0.05

P value < 0.05 is significant

Data expressed as mean \pm standard error of mean.

index. Blood glucose level also represents a significant positive correlation with serum leptin.

Discussion

Our results have depicted that the pregnant ladies with GDM have significantly higher serum leptin level, serum insulin level and the HOMA index. After delivery, leptin levels decrease in both cases and controls, but cases have higher serum leptin level than control, which is above normal. The accumulation of adipose tissue, hyperinsulinemia and insulin resistance, as seen in pregnancy

are the possible contributing factors for this leptin rise. (11) The desensitizing effect of anti-insulin hormones i.e. human placental lactogen, prolactin, glucocorticoid and progesterone contribute in insulin resistance and thus hyperinsulinemia, which further cause hyperleptinemia by stimulating adipose tissue. (12) As leptin secreted by placenta during pregnancy, other than adipose tissue, an obvious decrease in serum leptin after delivery reflect the role of placenta in contribution of hyperleptinemia. (13) Our study results are consistent with Qui et al., who conducted a cohort study and revealed that b/w the serum leptin levels and GDM exists a positive correlation that is independent of BMI and other risk factors¹⁴. Saini and colleagues also conducted a case control study and revealed that a positive correlation exists b/w serum leptin and GDM but they found negative correlation b/w adiponectin and GDM. (15) In our study, significantly higher BMI among the ladies with GDM is an indirect evidence that higher adipose tissue is an influential factor for insulin resistance and GDM.

Our results are supported by Mazor et al., who worked in an animal model and explained that the obesity promotes leptin resistance by activating hypothalamic matrix metalloproteinase-2 which blocks its peripheral receptors and halts its functioning. (1)

The relation of leptin and insulin resistance is evidenced by some researchers. Serum insulin and HOMA index shows positive correlation with serum leptin. (10) A study recruits 36 patients with diabetes and impaired glucose tolerance during pregnancy and 24 normal pregnant with normal glucose tolerance found raised level of serum insulin and serum leptin in Gestational diabetics, concluded positive relation between serum leptin and insulin level. (16)

Our study results mainly suggest contribution of adipose tissue and placenta in leptin release. The role of placenta in leptin secretion leads to hyperleptinemia and promotes leptin resistance which further cause hyperinsulinemia and then insulin resistance. Leptin mainly contribute in insulin resistance in gestational diabetics. (17)

TABLE II: PEARSON CORRELATION RESULTS				
	HOMA INDEX		Serum Leptin	
	r	p	r	p
Blood Glucose	0.786**	0.000	0.360*	0.022
r represents correlation. p value represents significance. ** Correlation is significant at the 0.01 level (2-tailed) * Correlation is significant at the 0.05 level (2-tailed)				

Conclusion

This study has determined serum leptin level is raised during pregnancy and the contributory factors are placenta and adipose tissue. This raised serum leptin concentration leads to insulin resistance (HOMA index) and subsequently serum insulin levels raise but the gestational diabetes progresses. As serum leptin shows positive association with insulin resistance, hence our future recommendation is to use serum leptin as a marker to early screening and diagnosis of gestational diabetes. This will help in combating GDM associated maternal and fetal complications.

Conflict of interest: Authors do not have any conflict of interest to declare.

Disclosure: None

Human/Animal Rights: No human or animal rights are violated during this study.

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A critical analysis of individual patient factors in gaining access to healthcare

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Significance:

Impartial access to health care is the right of every human being. Even though it is the first priority of every doctor to provide the best care to their patients, often times, patients do not have equal access to health care. This research was conducted to evaluate such parameters which affected patients' experience with the healthcare system. This research would serve as the guiding principles that the doctors can adopt to remove such prejudices from their practice.

Abstract

Background: Pakistan is one of the largest host of refugees. People in Pakistan have bad access to healthcare not only due to bad facilities but also due to discrimination based on their personal characteristics and possessions. The behavior not only damages the dignity of the people being targeted but also creates hindrances in further seeking professional medical help and follow-ups thus deteriorating the health status of the community as a whole. Health providers possess a moral commitment to encourage dignity and treat their patients without any kind of discrimination in their behavior. Patient experiences of discrimination result in delay in seeking healthcare, they do not stick to advice of professionals and ultimately poor health. The objective of this study is to identify sources of discrimination and its effects on patients' health status and their level of satisfaction.

Methods: This descriptive study took place in Outdoor Patient Department, Mayo Hospital, Lahore. 170 patients were selected from all the patients coming to OPD with equal male to female ratio. Each patient was given a questionnaire containing relevant questions to know whether they faced any sort of discriminatory behavior or not.

Results: 66% females and 49% males of the study sample experienced discrimination at some stage of their hospital visit.

Conclusion: Our study concluded that females experienced more discrimination than males. Therefore, gender is the most important factor when it comes to discriminatory experiences. Moreover, people with the higher income had fewer incidents of discrimination than their counterparts.

Introduction

In Pakistan, the system of health has basically been originated from the health system of British before the Independence of subcontinent. It consists of primary, secondary and tertiary healthcare that is gradually evolving with time. Discrimination means the prejudice or partiality those different categories of people face. Discriminatory behavior based on people's socioeconomic status, their sexual identities and various racial, religious or ethnic backgrounds is a ground reality globally. In a research conducted about discriminatory experiences on African American it was found that 63% felt discriminatory behavior in accessing to healthcare due to their colour and race and 58.9% felt distinctive behavior due to their low socioeconomic rank. (1) Often a visible contrast in health laws of a country and provision of health care facilities is observed. (2) Discriminatory behavior is faced by different category of people and the numbers vary in different settings. It was revealed that more than 10 percent of patients suffered some sort of distinctive behaviour in their stay at hospital, the common patient factors were age, language, nationality, these factors being negatively perceived. Skin color, sexual orientation, and income based discrimination were relatively uncommon. Any type of discrimination was associated with lesser satisfaction of the patient as compared to patients facing no discrimination. (5)

A country must possess a health system that protects the integrity and physical dignity of each individual. The individual physical dignity and integrity is recognized in international law. (3) Health providers possess a moral commitment to encourage dignity and treat their patients without any kind of discrimination in their behavior. (4) Patient experiences of discrimination result in delay in seeking healthcare, they do not stick to advice of professionals and ultimately poor health. (5) Pakistan is one of the largest host of refugees. People in Pakistan have bad access to healthcare not only due to bad facilities but also due to discrimination based on their personal characteristics and possessions. Refugees also suffer from discrimination in host country. Findings from both Canada and Sweden show decline in their health status after settling in host country. (6) Because of discrimination there is underutilization of health care consequently increase in morbidity and mortality. (7) Maintaining and assuring patients dignity must be a top priority of healthcare providers. The ideology of dignity

is clarified by its characteristics. In interviews with 102 patients Matiti (2002) 11 classes of attributes were found i.e. ,confidentiality, control, involvement in care , need for information, privacy , form of address, nurse patient communication, Independence, form of address, choice, decency, and respect. (8)

The behavior not only damages the dignity of the people being targeted but also creates hindrances in further seeking professional medical help, follow-ups and hence the deteriorating health status of the community as a whole. So, in order to prevent and rectify the problems mentioned previously and for effective steps to be taken and policies are made, there is a need for identification of the reasons that lead to a discriminatory behavior towards the general while accessing healthcare.

The main aim of our study is to improve the healthcare utilization by assessing discriminatory culture in public health care system. The objective is to identify sources of discrimination and its effect on patients' health status and patients' level of satisfaction.

Materials and Methods

The design of our research is "Descriptive Survey". The study was conducted at Outdoor Patient Department, Mayo Hospital, Lahore. The duration of our study was 9 months from January 2019 to September 2019. The sample size of 170 patients is estimated by using 95% confidence level, 5% absolute precision with expected %age as 12.6%. The sampling technique used is Non-probability Convenient sampling. All the patients over 18 years of age coming to the Outdoor Patients Department for checkup or follow-up were included in our study. Data was collected through a pretested questionnaire. Questions were selected from Picker patient experience-15. Questions were selected according to our social settings by research team and were translated both in English and Urdu and any ambiguous question that could be misinterpreted was rephrased. Every participant was given appropriate time to complete the questionnaire and research team helped the participants in understanding the questionnaire. Data was collected using the questionnaires and was entered in SPSS-26. The variables were created related to the data which included gender, socioeconomic status, religion and discrimination out of which nominal measurements were used for gender while the other variables were measured on a scale where certain values obtained from the bio-data of patients were added for analysis. Tests of Association and Descriptive statistical analysis was performed on the data and frequency tables were obtained for each variable which reported the relative distribution of each variable separately. Graphical analysis was also performed using bar-graphs to obtain the visual correlation of different

variables. Chi-Square test was performed to find out the significance of the difference between expected and observed data. The p value <0.05 was the standard set for considering the statistical significance. Cross-tabulations were structured for each variable with discrimination separately and the p value for gender was 0.03.

Results:

The analysis revealed that out of one-seventy patients 77 (45.3%) faced discriminatory behavior from the healthcare staff while the other 93 (54.7%) did not report any sort of discriminatory experiences. Gender based discrimination was the highest compared to others while patients reporting discrimination because of language or religion were rare. Discrimination was reported more frequently by women than by men, not only by younger patients but also by the very old. 56 (66%) females experienced discriminatory behavior from the healthcare staff compared to 42 (49%) males. Cross-tabs also showed a significant relationship between discrimination and gender with p value <0.05 on chi-square test since the number of females who reported discrimination was significantly greater than the expected count. Discrimination based on religious beliefs was not significant at all. One possibility of that maybe the unavailability of religious diversity in the data set. No relationship could be established between religion and discrimination.

Discrimination based on socioeconomic status was also present to some extent. 35 (20.5%) were those with income between ten and fifteen thousand rupees per month, 47 (27.6%) were those with income between fifteen and twenty thousand rupees per month, 24 (14%) had income between fifteen and twenty thousand rupees and only 5 (3%) were those with income greater than twenty thousand rupees per month. But no statistical relationship could be established using chi-square test.

Experiencing discrimination from any cause was associated with higher problem scores on the questionnaire compared with no or fewer experiences of discrimination. People with experiences of discrimination in the past were also less likely to reconsider the idea of revisiting the hospitals.

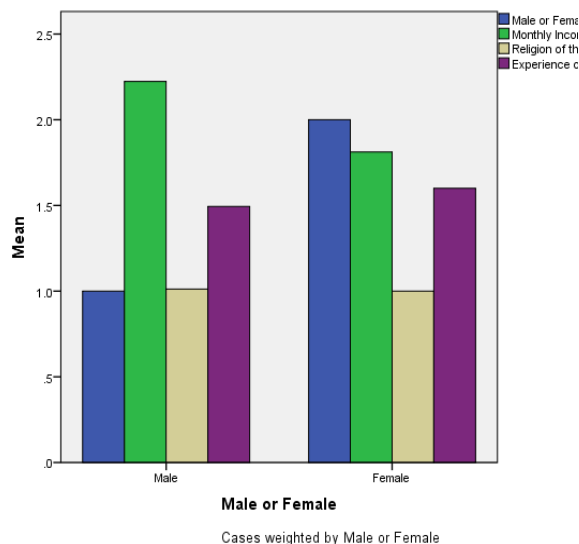


Figure 1- Bar graph plotting means of different variables weighed by Gender

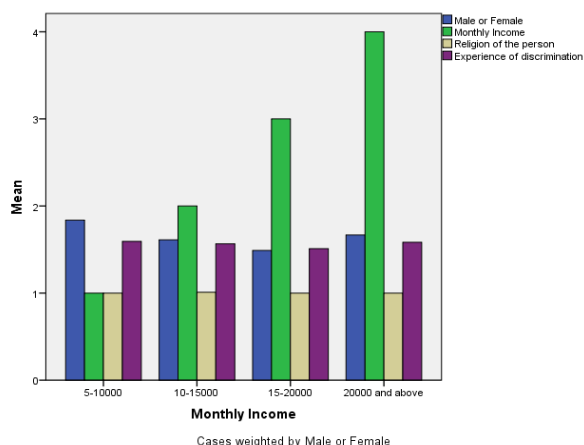


Figure 2- Bar graph representing the association of variables weighed by Monthly Income.

Discussion

Prevalence Our study was focused on the patients visiting the tertiary care hospitals for checkup and analyzed different possible causes of discrimination that included socioeconomic status, gender and religion. Regarding socioeconomic status our data suggests that higher family income decreases likelihood of individuals reporting perception of discrimination in healthcare. Consequently, people with lower family incomes had to face some discrimination while accessing healthcare. However, gender was the most significant source of discriminatory experiences as females had to face more discrimination compared to males. Religion was not found to be related to discrimination possibly because of lack of diversity in the data set so there is a need for the conductance of

further studies regarding that variable with more diversity in the sample.

According to UNDP’s human development report (1996) gender equality measures (GEM) for South Asia shows the lowest value (0.235) among all the regions of the world. Furthermore, as per gender development index (GDI) Pakistan has been rated the poorest (0.179) among south Asian countries, where the average index is 0.226. (10)

All this data strengthens our research finding that female gender suffers from discrimination while seeking healthcare opportunities. However, the magnitude of discrimination based on gender was quite low in our study which makes us think that there must be some other factor responsible for discrimination in healthcare access.

Pakistan’s population is increasing exponentially which obviously demands a widened and more equipped public healthcare system to cope with the medical necessities of the people. The WHO reports the density of physicians (per 10,000 populations) to be 7.8%. (11) These statistics clearly indicate that resources and consumers are not balanced to an appreciable extent. Therefore, a small portion of socially privileged individuals have easy access to healthcare. This is in line with our finding that socio-economic status is an important factor while assessing discriminatory experiences in patients. This is consistent with previous research that indicates that those with multiple disadvantaged status experience more discrimination than those with privileged social status. (12, 13, 14, 15, 16)

A research conducted in USA indicated that African Americans and Hispanics believed they would’ve received better medical care if they were different race while this was not the problem in case of White Americans. (9) We also considered the racial factor while investigating discrimination in healthcare access in our study but no significant data was found in this regard.

Members of different socioeconomic classes were more likely to perceive discrimination when in worse health. Therefore, it is important to check "frustration effect" i.e. when individual feels poorly there is tendency to feel that health professionals are not attentive towards them. (9) This feeling of frustration may lead to perception of discrimination even among high income group members and those with other social advantages. However, our study could not check this effect.

Together, these findings underscore the significance of clinical quality of clinical encounters and the need to appreciate patients' past as well as present experiences with inequality. Taking in consideration the results of this study, healthcare providers must ensure that no patient is treated differently because of his/ her gender so the generalized health of the community is improved.

Conclusion

Discriminatory behavior was observed especially in case of females and low-income level individuals. So, gender and socioeconomic status are the two factors that impact patients' overall experiences while utilizing the healthcare facilities. We could not access racially and religiously diverse data because of lack of availability of the diversity in our data set or study settings. A larger sample size or different study settings may be needed for that purpose.

Conflict of interest: Authors do not have any conflict of interest to declare.

Disclosure: None

Human/Animal Rights: No human or animal rights are violated during this study.

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Protective Effects of Omega-3 Fatty Acids on Energy Drink Induced Ovarian Cytotoxicity in Adult Female Albino Rats: A Randomized Controlled Trial

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Keywords: Caffeine; Carbonated Beverages; Cytotoxicity, Cytotoxins, Docosahexaenoic Acids, Eicosapentaenoic Acid, Energy drinks, Infertility, Omega-3, Ovarian Diseases

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Significance:

The widespread use of energy drinks and similar caffeine containing beverages has increased exponentially all over the world, mainly due to their marked advertisements. These beverages are emerging as a major health risk due to lack of awareness in the general population about their adverse health risks. It was uncertain if the energy drinks can be responsible for decreased fertility by damaging the gonadal organs. This study provides an estimate of the prevalence of ovarian tissue damage caused by using energy drinks.

ABSTRACT

Background: Energy drinks (EDs) are commonly used to prevent fatigue, enhance physical, and cognitive performance. Its administration induces toxic effects in body. Omega-3 is an antioxidant and anti-inflammatory agent that helps in proper functioning of immune system. Objectives of this study were to evaluate the morphological effects of fish oil omega 3 fatty acids (Eicosapentaenoic acid / Docosahexaenoic acid) on energy drink induced ovarian cytotoxicity in adult female albino rats.

Methods: The study was conducted at animal house, Anatomy department, Postgraduate Medical Institute, Lahore from January to march 2019. ARRIVE guidelines were followed for conduct of animal study. Ethical approval was obtained from PGMI, Lahore and Advanced Studies and Research Board of University of Health Sciences, Lahore. The study comprised 36 adult female albino rats divided into 3 groups i.e., control, energy drink and omega 3 treated. Rats were sacrificed, ovaries extracted, and sections were stained with H&E and PAS. SPSS version 21.0 were used.

Results: Statistically significant difference was present in gross parameters between the control and experimental groups. Energy drink administration caused a decrease in diameter of mature graafian follicle and diameter of the oocyte. Disruption in basement membrane was more pronounced in Energy drink treated group.

Conclusion: Energy drinks were found to cause cytotoxic effects on ovarian and oocyte morphology, ultimately leading to infertility. Omega 3 reduces the extent of damage caused by the intake of energy drinks.

Introduction

Changed pace of life, pervasive haste and the need of being available twenty-four hours a day cause an increasing number of population to access a group of beverages called the caffeinated energy drinks (EDs) (1). The term "energy drink" (ED) refers to beverages believed to reduce fatigue, increase a person's physical performance, enhance personality and improve individual's cognitive performance. EDs are most widely used by college students, athletes, night drivers (2). The uprising of energy drinks has highlighted both their popularity and controversy, comparing their advertised benefits of enhanced alertness, cognition and energy as compared to the possibly critical health risks (3). The first beverage of this type was introduced in the market in Austria in 1987 and ten years later similar beverages were introduced in the United States of America that comprised of high caffeine and taurine concentrations (2). EDs are widely available in markets now under different brand names. Power horse, Red Bull, code red and monster are few names among some of the popularly used energy drinks with an annual worldwide business of several billions (1).

ED's have gained a widespread popularity since their first appearance all around the globe. The manufacturers attribute these enhanced effects to the unique mixture of the ingredients including caffeine, taurine and glucuronolactone (4). Apart from active ingredients energy drinks also contain guarana extract, ginseng, additional amino acids, vitamins including niacin, pantothenic acid, B6, B12, acidity regulators (sodium bicarbonate, magnesium carbonate) and carbohydrates to complete the list of supposedly helpful ingredients (5). ED brands available commercially have high caffeine content leading to insomnia, anxiety, headache and tachycardia (6). ED's contain extra caffeine through extracts like guarana, kola nut, yerba mate, and cocoa. These additives increase the total caffeine content and efficacy of ED (7). The high sugar content is known to contribute to obesity (8). Body weight gain with use of ED is due to the higher rate of catabolism and leads to a higher rate of lipid storage in the adipose tissue (9). Adverse cytotoxic effects of ED have been evaluated extensively. EDs lead to Hydropic changes in epithelium, intertubular hemorrhage and inflammatory changes in renal tubules (10). Pancreatic cells of rats administered

ED displayed significant necrotic changes, vacuolization and nuclear karyolysis along with congested blood vessels and perivascular infiltration. ED treated rats showed marked gastric ulcers, glandular atrophy and vascular congestion and damage to the physiological barrier between gastric lumen and underlying mucosa (11). The effects of ED on the reproductive system have been documented in a lesser number. The results of another animal study clearly revealed that maternal consumption of high dose caffeine during gestation and lactation significantly decreased weight of the ovary and number of primordial follicles. It also reduced fertility and reproductive competence in the Wistar rat's offspring (12).

Omega-3 fatty acids are a group of polyunsaturated fatty acids (PUFA) (13). In our study we used fish oil Omega-3 and looked for possible helpful effects of fish oil omega-3, Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). These two Omega-3 fatty acids cause significant biochemical and physiological changes in the human body (14). The Food and Drug Administration (FDA) has recommended that a maximum adults dose of 3 grams per day of combined DHA and EPA can be safely consumed (15). The most extensively available dietary source of EPA and DHA is fish oil extracted from herring, mackerel, salmon, anchovies and sardines (16). Omega-3 PUFAs are believed to decrease the synthesis of different inflammatory cytokines, including tumor necrosis factor alpha, interleukin-1, and interleukin-6 (17). EPA helps in proper functioning of inflammatory systems. Prostaglandins effecting as anti-inflammatory action are made directly from EPA. It lowers risk of unnecessary inflammation and inflammation related diseases (16). Recommendations also have been made for DHA intake for pregnant women, females hoping to conceive, nursing mothers, infants, and vegetarians/vegan (18). The Omega-3 is major constituent of oocyte cell membrane (17).

The mean diameters of the ovarian mature graafian follicle were increased in dairy cows fed on a diet rich in omega-3. It reduced Prostaglandin F2a (PGF2) synthesis which improves embryo survival. Omega-3 enriched diet during late gestation results in longer gestational period in humans (19). After artificial insemination, dairy cows that were fed on a diet higher in Omega-3 showed a higher pregnancy rate and pregnancy losses were significantly reduced (20). Supplementation with omega-3 caused prolonged gestation length followed by an improved birth weight and better rate of neonatal survival. There is also an improvement of milk composition of cows due to PUFA supplementation (21). Endogenous n-3 PUFA's have proved to be a significant energy source to the

oocytes and early developing embryos. They improve oocyte development by influencing the fatty acid composition of oocyte lipids, and by modifying the prostaglandins and other metabolites' concentrations in the follicular medium in the surrounding of the oocyte (20).

Atrophic and cystic degeneration of ovaries lead to infertility which is a global health issue. The study was conducted to evaluate the cytotoxic effects of ED and to establish the possible ability of Omega-3 to protect ovarian tissue from ED induced oxidative stress. This explains importance of omega-3's important reproductive role by maintaining ovarian follicular integrity. This study was conducted after the observation regarding increasing use of energy drinks in our community, especially by the young population including students. There have been many researches regarding harmful health effects of these beverages but the author observed that toxic effects of these drinks are still not researched extensively in the field of reproductive health.

Materials and Methods

Study Design & Settings: Open-Label Randomized Control Trial conducted at Experimental Research Laboratory, Anatomy department, Postgraduate Medical Institute (PGMI) Lahore. The study protocol and procedures were approved by the Ethical Committee of PGMI, Lahore and Advanced Studies and Research Board of University of Health Sciences, Lahore. ARRIVE guidelines were followed for conduct of research on lab animals.

Subjects: 36 adult female albino rats of Wister strain weighing 130 – 180 grams and achieving sexual maturity at 55-60 days were obtained from animal house of PGMI. Animals were weighed and examined thoroughly for any gross morbidity. They were individually kept in climate-controlled conditions of temperature $22 \pm 0.5^\circ\text{C}$, humidity (50%±10%), and 12 hours light / dark cycles and were provided standard rat food and water ad libitum. Rats were kept for a week for acclimatization.

Randomization & Masking: Rats were distributed into three equal groups (A, B & C) using random number generator. The participants and investigators were not blinded to the intervention being administered. Group A was Control group while the other two groups (B & C) were experimental groups. The therapeutic reagents used were energy drink and Omega-3. The doses and their duration of administration were selected according to protocol of previously conducted study (11).

Procedures: The control group (A) was given distilled water orally for 30 days. Energy drink treated group (B) was given ED 10 ml /kg body weight (equivalent to approximately 7.5 ml/rat) once a day for 30 days. Energy

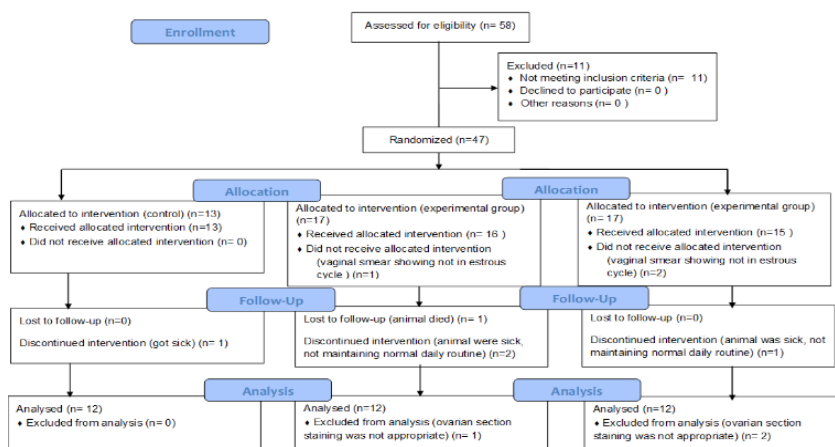


Figure 1 CONSORT Flow Diagram

drink and Omega-3 treated group (C) was given ED 10 ml/kg body weight (equivalent to 7.5 ml/rat) daily along with Omega-3 at a dose of 300 mg/Kg body weight once a day for 30 days (Table 1). Drugs were administered orally by gavage method. The exact dose of energy drink and omega 3 was adjusted according to the exact weight of individual animal and was given through gavage needle. Rats were weighed 24 hours after administration of last dose and were sacrificed under deep anaesthesia. Ovaries (right and left) were dissected out. Weight of both ovaries was recorded carefully on electronic weighing scale. Volume of organ was obtained by immersing organ in water in a calibrated test tube. The difference between two readings of the level of water was calculated as volume of ovary. All the animals were euthanized by decapitation. Their bodies were disposed-off by burying in burial ground at PGMI, Lahore.

Outcomes (Histological Analysis)

Ovaries were washed with normal saline and fixed in 10 ml of neutral 10% buffered formalin. Automatic tissue processor was used for tissue processing and then embedded in paraffin. 3 – 4 µm thick serial paraffin sections were obtained from the paraffin blocks and stained with standard hematoxylin and eosin (H&E) and PAS reagent for the histopathological examination. Slides were examined under light microscope (ACCU-SCOPE 3000-LED Microscope) at 10X and 40X magnifications. Diameter of mature Graafian follicle (µm) and oocyte of Graafian follicle (µm) were calculated by using ocular

Table 1 Experimental grouping of animals, their doses and duration

Groups	Number of animals (n)	Intervention and dosage	Duration
A Control Group	12	food and water <i>ad libitum</i>	30 consecutive days
B Energy Drinks treated group	12	ED10 ml/kg body weight (equivalent to 7.5 ml/rat) by gavage method	30 consecutive days
C Energy Drinks + OMEGA-3 treated group	12	ED10 ml/kg body weight (equal to 7.5 ml/rat) daily along with omega 3 at a dose of 300 mg/Kg body weight (0.5-0.4 ml/rat) orally by gavage method	30 consecutive days

micrometer. For measuring diameters, two measurements were taken. The second measurement was obtained by placing micrometer at a right angle from the midpoint of the first measurement. Average was taken and documented. Follicular diameters were calculated from the outermost wall of the thecal layer, if present. In case of absence of thecal layer, the diameter was measured from the outermost layer of granulosa cells. The diameter of oocyte was measured including the zona pellucida, when present (22). Basement membrane was assessed for intact and disrupted state in PAS stained slides.

Statistical Analysis: Data was analyzed using SPSS 21.0. Normality of data was checked with Shapiro Wilk Test. Mean ± SD was calculated for quantitative variables. One-way ANOVA was applied to determine the mean difference among the groups. Post Hoc Tukey Test was applied for multiple comparisons. Chi square was used to observe association among qualitative variables. A p-value ≤ 0.05 was considered as statistically significant.

Sample Size of the study was calculated as 36 using the following formula:

$$n = \frac{Z_{\beta}^2 [p_1(1 - p_1) + p_2(1 - p_2)]}{(p_2 - p_1)^2}$$

Where p1 is the anticipated proportions of regular menstruation in Omega 3 group, p2 is the anticipated proportions of regular menstruation in control group and Z β² is the desired power of study.

Results:

Effects of ED on body weight: At the start of the experiment the mean body weight of animals in all groups was not significantly different (p-value = 0.699) whereas there was a statistically significant difference in mean body weights among groups at the end of the experiment (p < 0.001). (Figure 2)

For multiple comparisons, post hoc Tukey test showed that final weight gain in group B and C were significantly higher as compared to control group. (Table 2)

The comparison of mean paired ovarian weight and volume in all groups was significantly significant (p < 0.001) (Figure 3).

Table 2 Pair wise comparison of final body weight among groups

S.No.	Groups	Multiple Comparison		Mean Difference (I-J)	Std. Error	p-value
		I	J			
1	A	B	C	-29.0000	4.0507	.000*
		C	-21.0000	4.0507	.000*	
2	B	C	8.0000	4.0507	.134	

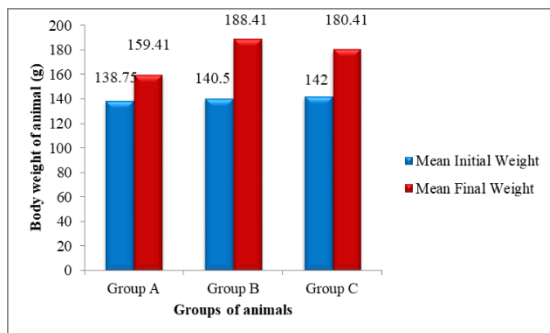


Figure 2 Comparison of initial and final weight amongst animals of group A and B

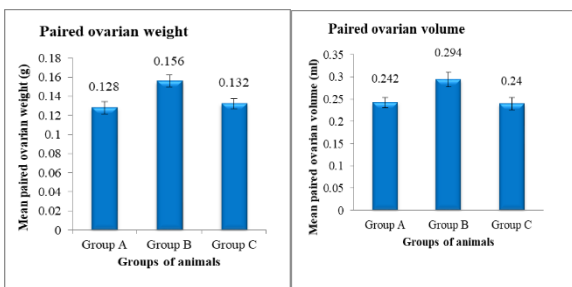


Figure 3 Bar charts showing comparison of paired ovarian weight and volume (ml) among groups A, B and C. Error bars indicating ± SEM.

Effect of ED and omega 3 on weight and volume of ovaries: Post hoc Tukey test showed that paired ovarian weight and volume in groups B was significantly higher as compared to control and ED + Omega-3 treated group. (Table 3).

Table 3 Pair wise comparison of paired ovarian weight (g) among groups

Multiple Comparison						
Parameter	S. No.	Groups I	Groups J	Mean Difference(I-J)	Std. Error	p-value
Mean paired ovarian weight (g)	1	A	B	-0.02841	.00853	0.006*
			C	.03842	.00853	0.886
	2	B	C	.05217	.00853	0.019*
Mean paired ovarian volume (ml)	1	A	B	-0.0519	.01989	0.035*
			C	0.0025	.01989	0.991
	2	B	C	0.0544	.01989	0.026*

Effect of ED and Omega-3 on diameter of Graafian follicle: The mean diameters (µm) of Graafian follicle in all groups were calculated by micrometry at 10X magnification. The mean diameter of Graafian follicle in all groups were significantly different (p-value = 0.001) (Figure 4)

For multiple comparisons, post hoc Tukey test was used which showed that diameter of Graafian follicle in group B (Figure 6) was significantly lower as compared to

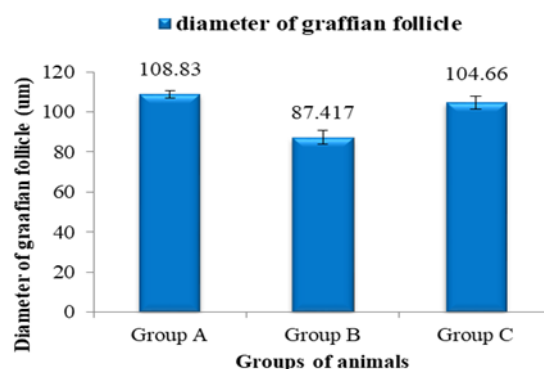


Figure 4 Bar chart showing comparison of mean diameter of Graafian follicle (um) of ovaries among groups A, B and C. Error bars indicating ± SEM

remaining all groups. However, no significant difference was found in the diameter of Graafian follicle among groups A (Figure 6) and C (Figure 6) (Table 4).

Effect of ED and Omega 3 on Diameter of Oocyte of Graafian follicle: The mean diameters (µm) of Oocyte of Graafian follicle in all groups were recorded during micrometry at 40 X magnification. Mean diameter of Oocyte of Graafian follicle in all groups were significantly different (p-value < 0.001) (Figure 5).

Table 4 Pair wise comparison of mean diameter (µm) of Graafian follicle among groups

Multiple Comparison						
	S. No.	Groups I	Groups J	Mean Difference (I-J)	Std. Error	p-value
Mean Diameter (µm) of Graafian Follicle	1	A	B	21.416	4.173	0.000*
			C	4.166	4.173	0.483
	2	B	C	-17.250	4.173	0.001*

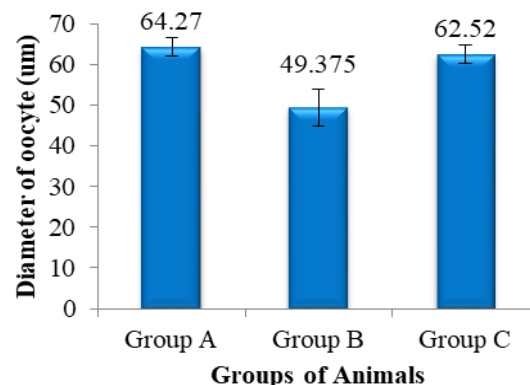


Figure 5 Bar chart showing comparison of mean diameter of oocyte (um) of ovaries among groups A, B and C. Error bars indicating ± SEM

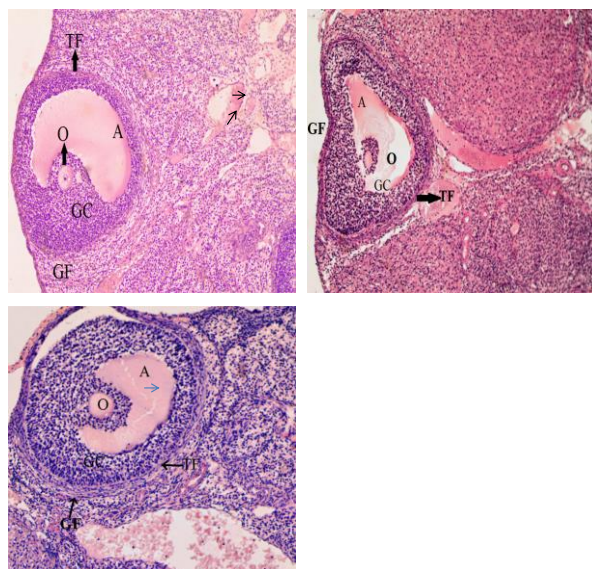


Figure 6 Photomicrograph of ovarian section of group (A) mature Graafian follicle (GF) showing normal oocyte (O) with normal eccentric nucleus surrounded by many layers of polyhedral granulosa cells (GC). Theca folliculi (TF) containing polyhedral theca interna cells. In comparison group (B) showed degenerated Graafian follicle (GF) with shrunken oocyte (O) surrounded by degenerating layers of granulosa cells (GC). Theca follicular (TF) cells show vacuolization. Group (C) showing a mature regenerating graafian follicle (GF) with oocyte (O), antrum (A) and surrounded by many layers of granulosa cells (GC). H&E. X10

For multiple comparisons, post hoc Tukey test was used which showed that diameter of Oocyte of Graafian follicle in group B (Figure 6) was significantly lower as compared to remaining all groups. However, no significant difference was found in the diameter of Oocyte of Graafian follicle among groups A (Figure 6) and C (Figure 6) (Table 5).

Basement membrane of Graafian follicle: Graafian follicle of Control group (A) showed magenta coloured intact basement membrane (a distinct boundary between zona granulosa and theca folliculi) with PAS stain. There was no abnormal or disrupted basement membrane seen in group A (Figure 7). All the rats showed normal zona pallucida (surrounding membrane of oocyte). In group B, all rats had disruption of basement membranes of mature

Table 5: Pair wise comparison of Mean Diameter (µm) of Oocyte of Graafian follicle among groups

	Multiple Comparison					
	S. No.	Groups	Groups	Mean Difference	Std. Error	p-value
		I	J	(I-J)		
Mean Diameter (µm) of Oocyte of Graafian Follicle	1	A	B	14.895	4.452	0.006*
			C	1.750	4.452	0.919
	2	B	C	-13.145	4.452	0.015*

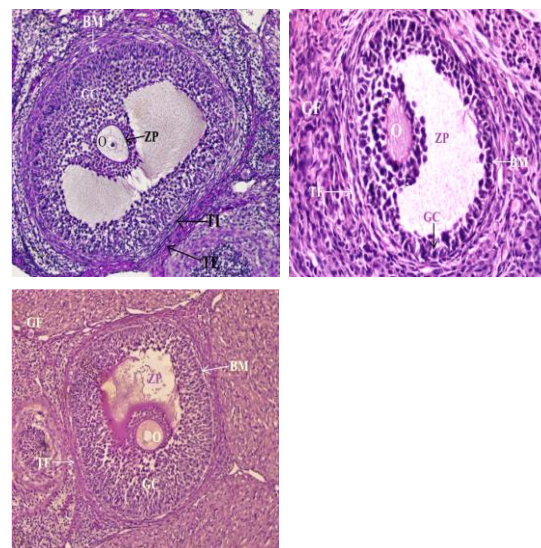


Figure 7: Photomicrograph of an ovarian section from control group (A) showing Graafian follicle (GF) containing oocyte (O) with intact zona pallucida (ZP) surrounded by layers of granulosa cells (GC) with intact magenta colored basement membrane (BM). Theca folliculi containing polyhedral theca interna cells (TI) and vascular theca externa having fusiform fibroblast nuclei (TE). In comparison group (B) showing Graafian follicle (GF) containing degenerated oocyte (O) and degenerated zona pallucida (ZP). Oocyte is surrounded by degenerated granulosa cells (GC) with discontinuous magenta colored basement membrane (BM). Theca folliculi (TF) containing vacuolated theca interna cells. Group (C) shows Graafian follicle (GF) containing oocyte (O) with intact zona pallucida (ZP). Granulosa cells (GC) have intact magenta colored basement membrane (BM). Theca folliculi (TF) containing polyhedral theca interna cells. PAS stain X.40.

graafian folliculi. Zona pallucida was also disrupted in all the animals of group B (Figure 7). In group C, only 3 (25%) rats had disrupted basement membrane of Graafian follicle (Figure 7). Chi square test showed that there was an association between disruption of basement membrane of mature Graafian follicle and groups (Table 6)

Discussion

The adverse effects of ED are largely ascribed to its caffeine content and the possible adverse reactions due to the combined enhanced effects of its various components causing a pro-oxidant environment (23). Omega-3 was used to assess its protective role as it acts in preventing

Table 6 Distribution of basement membrane of Graafian follicle among groups

Rats	Basement membrane		Percentage disruption	P value
	Intact	Disrupted		
Group A	11	01	8.3%	<0.001*
Group B	00	12	100%	
Group C	09	03	25%	

oxidative stress and production of numerous physiological anti-inflammatory mediators (24).

Present study showed a gradual normal increase in body weight of control group. A statistically significant percentage weight gain in ED treated and ED plus omega-3 treated groups was observed. This increase final weight gain is due to high catabolism rate induced by the glucose component of the ED. High components of sugars in the ED leads to increased availability of insulin in body that cause an increased rate of lipid storage in the adipose tissues. Results were similar to previous published work (25, 26). Contradictory reports showed the animals given energy drinks added diet had a decreased body weight gain (27).

Increase in mean paired ovarian weight and volume of rats treated with ED was in agreement with previous data (26) showing a significant increase in brain weight of adult rats treated with ED for 30 days. Increase in the weight and volume of the organ resulted due to the swellings of the ovarian tissue based on the cytotoxic effects of the ED on the cells of the ovary. A cytotoxic edema result in the swelling of the tissue. This caused degeneration of the follicles and formation of cystic structures resulting in increased net organ weight and volume. Rats who were caffeine fed for 4 weeks showed an increase in their testicular weight relative to the body weights (28, 29). In contrast to this research reported that the consumption of a higher caffeine dose caused a significant decrease in ovarian weight (12).

Ovarian weight of ED plus omega-3 treated rats was near to the control group, thus proving that the anti-inflammatory effects of omega 3 reduced the ovarian tissue damage and prevented edema of the ovaries. This is in accordance with published work (30) showing that ovarian weights of dairy cows after treatment with omega-3 remained same as that of the control group.

Diameter of the graafian follicle and oocyte as measured by the ocular micrometer was markedly decreased in ED treated group. It was in consensus with previous study, (12) demonstrating that caffeine ingestion causes a decrease in number of cells and cellular death by interfering with follicular cell division. High dose caffeine consumption caused reduction of the seminiferous tubules' diameter due to caffeine induced inhibition of seminiferous cords (28). Similar observation was made on testis of male rats after 40 days of caffeine intake (29).

Omega-3 maintained the oocyte and follicular diameter by decreasing inflammatory vulnerability and suppressing cytokine production. Studies showed that the use of omega-3 supplements in dairy cows for 15 days duration caused an increased number of ovarian follicles

and an increase in their mean diameters, mostly due the anti-inflammatory effects of omega-3 (31).

PAS-stained ovarian sections of rats administered with ED demonstrated a weak to mild PAS-positive reaction. The Graafian follicles demonstrated disrupted (45%) or discontinuous basement membrane (55%). PAS-stained ovarian sections of rats treated with ED plus Omega-3 demonstrated a moderate PAS-positive reaction with intact basement membrane. This confirms role of omega-3 in maintaining basement membrane integrity for survival of ovarian follicle and increasing their number. Omega-3 supplementation positively influences phospholipid fatty acid composition of ovarian follicular and cumulus cells, maintaining the integrity of oocyte membranes, thus improving the oocyte number and quality (32). The cows fed with PUFA n-3 supplemented diet for 15 days had better membrane integrity and oocyte structure than control (31). Contradictory reports showed adverse effects on the morphological appearance and membrane integrity of embryos fertilized from oocytes after exposure to an environment high in polyunsaturated fatty acids (33).

Conclusion

In this study it was observed that the Omega-3 fatty acids have succeeded, to certain extent, in protecting the ovaries from the deteriorating effects of the ED induced histopathological changes. In short, the current study demonstrated that ED induce ovarian cytotoxicity whereas; Omega-3 can significantly attenuate these adverse effects. The possible mechanism of ED harmful effect is the induction of oxidative stress in the tissue, and the anti-oxidant and anti-inflammatory property of Omega-3 could be a possible protective mechanism. From the foregoing results, it is clear that omega-3 fatty acids being anti-oxidant and anti-inflammatory have maintained ovarian tissue architecture, remodeled basement membranes and significantly reduced degeneration of graafian follicles by counter balancing ED induced oxidative stress. Hence it can be recommended as a protective agent against ED induced ovarian damage due to easy, rapid and safe dietary administration, especially with the increasing use of ED among students and athletes.

Conflict of interest: Authors declare no conflict of interest.

Disclosure: None

Human/Animal Rights: No human or animal rights were violated during this study.

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Determination of Blood Flow in Superficial Arteries of Human Face using Doppler Ultrasonography in Young Adults

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Significance:

Human face is highly vascular region and vascularity to the skin and other organs is an important indicator of health and disease. Change in blood flow maybe affected in various pathologies. Blood flow in superficial arteries of face has not yet been described, therefore this study was designed to establish baseline blood flow values in arteries of face.

Abstract

Background: Human face is highly vascular region and vascularity to the skin and other organs is an important indicator of health and disease. Change in blood flow is affected by aging, diabetes, high blood triglycerides, cigarette smoking etc. With so many factors that can alter blood flow in the skin, normal blood flow is important to know for comparison to diseased state. Blood flow in superficial arteries of face has not yet been described, therefore this study was designed to establish baseline blood flow values in arteries of face.

Materials and Methods: Blood flow of right and left side was assessed at level of facial and infraorbital artery. Categorical variables were presented in form of frequency and percentages was done by using Mann-Whitney U. Wilcoxon Signed Ranks test was used to compare left and right facial and infra orbital arteries.

Results: Peak systolic velocity of right and left facial artery had a significant difference having right side mean of 67.02 ± 12.48 and left side mean as 72.67 ± 11.69 . Facial artery diameter of right and left side also had significant difference with mean of 0.14 ± 0.02 and 0.15 ± 0.02 respectively.

Conclusion: No difference was found between vascularity in male & female and left or right side. The study might be useful to establish normal baseline values of various parameters on both sides of face in male and female adults. This study may become important reference for future studies measuring blood flow and even progression of vascular diseases may be assessed by indexes developed on the basis of these studies.

Introduction

Human face is highly vascular region and is the key for maintenance of healthy tissue conditions. (1) The blood flow to the skin and other organs is an important indicator of health and disease. Change in blood flow is affected by

aging, diabetes, high blood triglycerides, cigarette smoking, and other contributors to inflammation. (2-3) Compromised vascularity may lead to alterations in bone strength and remodeling capacity. (4-5) Mandibular and maxillary hypo perfusion and ischemia are particular important problems in the elderly patients and in those undergoing radiotherapy. (4) It is important to know blood flow in health and diseased state, as there are so many factors that can alter blood flow. This vascular flow measurement may also help in facial reconstruction after trauma or during surgery. (6)

Face is mainly supplied by branches of external carotid artery, and small area of nose and forehead is supplied by branch arising from branch of internal carotid artery. Major arterial supply of the facial skin is the facial artery and gets contribution from maxillary artery. (7) Facial artery arises from the external carotid artery just above the tip of greater cornu of hyoid bone, follows the inferior border and enters the face. It provides blood to the muscles of the facial expression. The infraorbital artery branches off the maxillary artery, emerges through the infraorbital foramen, supplies the maxilla, teeth, lower eyelid, nose and upper lip. (8) Mental artery is the terminal branch of the inferior alveolar artery, this artery emerges from the mental foramen to supply facial muscles and skin of the chin. (9)

The facial blood flow can be measured by various invasive and non-invasive methods. These methods include venous occlusion plethysmography, doppler ultrasound, laser doppler blood flow, thermistor, hertzman photoelectric plethysmography and radioactive isotopes. (10) Doppler ultrasound is common, non-invasive and radiation free technique for measuring blood flow in vasculature. (11)

Limited literature is available, it's important to know the blood, ethnic variation. Facial blood flow in superficial arteries has not yet been described and presently ultrasound is the technique to measure blood flow in the skin non-invasively and hence selected to be used on volunteers in present study.

Materials and Methods

After the approval of the study for ethical considerations from the Institutional Review Board of Fatima Memorial Hospital-College of Medicine and Dentistry, this cross sectional study was conducted in the Radiology and Oral Biology department on 50 (25 males and 25 females) dental technologists or dental students of age range 18-30

years. Individuals having history of trauma on face, muscular hypertrophy, facial asymmetry, temporomandibular joint disorder and any inflammatory diseases were excluded from the study.

A notice for volunteer recruitment was displayed on notice boards of the college, stating study title along with the purpose of the study (annexure-I). The individuals who were willing to participate were explained the procedure and informed consent was obtained (annexure-II). Demographic data was noted (name, age and gender). A thorough history was taken and volunteer with above mentioned problem were excluded from the study. A consent form for inclusion into study was filled and an appointment were arranged at Radiology department to where an ultrasound of face was arranged.

Facial and infraorbital arteries (right and left sides) were analyzed by using Color Doppler Ultrasound with linear probe of frequency 7-10 Hz transducer, Model Voluson S6. Facial artery was analyzed by placing the transducer with a thin layer of gel at the intersection border of mandible with the anterior border of the masseter muscle. Infraorbital artery was studied below the infraorbital margin. Data regarding arteries diameter, peak systolic and end diastolic velocity, resistance index and pulsatility index were collected. Demographic information was also recorded.

Data was entered and analyzed in SPSS version 25. Descriptive analysis was performed on all of the variables. Categorical variables were presented in the form of frequency and percentages. Normality was assessed by using Kolmogorov Simonov's test. Comparison between left and right facial and infraorbital

arteries was done by using Wilcoxon Signed Ranks test. Data was stratified according to gender and Mann Whitney U test was performed post stratification. P-value less than 0.05 was considered significant.

Results:

In this study 50 volunteers participated with the mean age of 23.70 ± 3.77 years, mean height of 65.36 ± 3.83 [AK1] inches and mean weight of 65.99 ± 12.27 kg. In which half of the participants were female with mean age of 22.88 ± 3.43 years, mean height of 63.43 ± 2.58 inches and mean weight of 60.96 ± 9.83 kg. Half of them were male with mean age of 24.52 ± 3.97 years, mean height of 67.29 ± 3.95 inches and mean weight of 71.01 ± 12.59 kg.

In overall volunteers there were 48 right handed and two were left handed males. Left and right facial artery was present in all individuals while there was only one female in which infraorbital artery of both sides were not found. All other male and female individuals were able to provide peak systolic velocity, diastolic velocity, systolic diastolic index, resistance index, pulsatility index and diameters of right and left side parameters.

Table. 1 shows the descriptive statistics of vascular status of facial artery. No significant difference between right and left facial arteries was seen except peak systolic velocity and diameter of facial artery. peak systolic velocity showed a significant difference having right side mean of 67.02 ± 12.48 and left side mean as 72.67 ± 11.69 (p-value = 0.049). The diameter of facial artery of right and left side also had a significant difference with mean of 0.14 ± 0.02 and 0.15 ± 0.02 respectively (p-value = 0.001).

Table 1: Descriptive statistics of vascular status of facial artery

Facial artery	Left	Confidence interval	Right	Confidence interval	P-value
facial peak systolic velocity	67.02 ± 12.48	63.47-70.57	72.67 ± 11.69	69.34-75.99	0.049
	67.02(15.75)		72.62(16.56)		
facial diastolic velocity	14.64 ± 5.97	12.95-16.34	14.52 ± 4.89	13.13-15.9	0.912
	13.82(9.34)		13.17(7.20)		
facial systolic diastolic index	5.38 ± 1.64	4.92-5.85	5.12 ± 1.19	4.7-5.46	0.091
	4.99(2.33)		5.05(1.72)		
facial resistance index	0.79 ± 0.05	0.78-0.814	0.78 ± 0.10	0.756-0.814	0.955
	0.800(0.09)		0.80(0.08)		
facial pulsatility index	2.20 ± 0.59	2.03-2.37	2.24 ± 0.55	2.08-2.39	0.883
	2.05(1)		2.09(1)		
facial diameter	0.14 ± 0.02	0.133-0.147	0.15 ± 0.02	0.148-0.163	0.001
	0.14(0.02)		0.16(0.04)		

Table 2: Descriptive statistics of vascular status of infraorbital artery

Infra orbital artery	Left	Confidence Interval	Right	Confidence Interval	P-value
IO peak systolic velocity	28.05±7.98	25.57-30.32	31.18±12.60	27.75-34.61	0.197
	27.50(8.89)		30.41(16.31)		
IO diastolic velocity	5.63±2.60	4.89-6.37	5.50±2.43	4.79-6.17	0.643
	5.52(2.67)		5.38(2.93)		
IO systolic diastolic index	5.37±1.90	4.83-5.19	5.39±1.44	4.98-5.80	0.821
	4.86(2.32)		5.37(1.80)		
IO resistance index	0.080±0.08	0.77-0.82	0.08±0.07	0.786-0.82	0.357
	0.78(0.12)		0.81(0.09)		
IO pulsatility index	2.32±0.74	2.11-2.53	2.12±0.66	1.95-2.30	0.388
	2.22(0.99)		2.13(0.73)		
IO diameter	0.05±0.17	0.048-0.058	0.06±0.02	0.053-0.068	0.176
	0.05(0.02)		0.05(0.04)		

Table. 2 shows the descriptive statistics of vascular status of IO artery. There was no significant difference between

right and left IO arteries. IO peak systolic velocity of 28.05±7.98 for right and 31.18±12.60 for left (p= 0.197).

Table 3: Gender wise comparison of facial artery

Facial artery	Gender				P-value
	Male	Confidence Interval	Female	Confidence Interval	
facial peak systolic velocity left	67.67+14.31	61.7-73.5	66.37+10.605	61.99-70.77	.691
	67.02(13.49)		67.02(15.52)		
facial peak systolic velocity right	74.45+12.42	69.32-79.58	70.89+10.88	66.40-75.38	.327
	72.67(16.37)		68.27(15.76)		
facial diastolic velocity left	15.36+6.58	12.64-18.07	13.92+5.33	11.74-16.14	0.977
	14.65(10.57)		13.05(7.24)		
facial diastolic velocity right	14.71+4.95	12.66-16.75	14.34+4.93	12.30-16.38	0.977
	13.12(9.61)		13.23(5.15)		
facial systolic diastolic index left	5.40+1.72	4.68-6.11	5.37+1.59	4.72-6.03	0.907
	5.14(2.92)		4.95(1.88)		
facial systolic diastolic index right	5.14+1.25	4.62-5.65	5.11+1.15	4.64-5.59	0.907
	5.13(1.74)		4.92(1.61)		
facial resistance index left	0.79+0.066	0.76-0.81	0.80+0.04	0.78-0.82	0.566
	0.78(0.13)		0.80(0.06)		
facial resistance index right	0.79+0.06	0.77-0.82	0.77+0.13	0.71-0.82	0.808
	0.80(0.09)		0.81(0.08)		
facial pulsatility index left	2.22+0.689	1.94-2.51	2.18+0.49	1.98-2.38	0.861
	2.05(1)		2.04(0)		
facial pulsatility index right	2.26+ 0.60	2.02-2.51	2.21+0.51	1.99-2.42	0.823
	2.17(1)		2.08(1)		
facial diameter left	0.14+0.021	0.14-0.15	0.13+0.13	0.12-0.14	0.08
	0.15(0.02)		0.13(0.04)		
facial diameter right	0.16+0.02	0.14-0.17	0.15+0.02	0.14-0.16	0.230
	0.16(0.03)		0.15(0.03)		

Table. 3 and 4 show gender wise comparison of facial and infra orbital arteries. Mean \pm SD for facial and infra orbital arteries are presented in this table. Pulsatility index of infra orbital artery of right side was significantly different for male and females with mean of 2.29 \pm 0.68 and 1.96 \pm 0.52 respectively (p =0.047).

Table 4: Gender wise comparison of infra orbital artery

Infra orbital artery	Gender				P-value
	Male	Confidence Interval	Female	Confidence Interval	
IO peak systolic velocity left	28.06+8.11	25.25-31.95	27.49+7.98	24.20-30.79	0.303
	27.50(7.48)		25.83(10.66)		
IO peak systolic velocity right	32.90+11.03	28.35-37.46	29.46+13.03	24.08-34.83	0.19
	31.18(14.84)		29.69(10.45)		
IO diastolic velocity left	6.06+2.74	4.93-7.19	5.19+2.49	4.19-6.20	0.377
	5.52(3.42)		5.52(1.99)		
IO diastolic velocity right	5.64+2.66	4.54-6.73	5.33+2.22	4.41-6.24	0.484
	5.42(3.12)		4.81(2.86)		
IO systolic diastolic index left	5.16+1.56	4.51-5.80	5.58+2.21	4.66-6.49	0.823
	4.99(2.69)		4.86(2.26)		
IO systolic diastolic index right	5.54+1.45	4.94-6.13	5.24+1.45	4.64-5.84	0.466
	5.39(1.95)		5.23(1.72)		
IO resistance index left	0.79+0.09	0.75-0.82	0.18+0.08	0.77-0.84	0.431
	0.78(0.13)		0.79(0.10)		
IO resistance index right	0.81+0.07	0.78-0.84	0.80+0.07	0.77-0.83	0.922
	0.81(0.09)		0.81(0.07)		
IO pulsatility index left	2.30+0.74	1.99-2.60	2.34+0.57	2.02-2.65	0.0869
	2.18(1.09)		2.269(0.9)		
IO pulsatility index right	2.29+0.68	2.01-2.57	1.96+0.52	1.74-2.17	0.047
	2.35(1.01)		2.09(0.48)		
IO diameter left	0.05+0.17	0.04-0.06	0.05+0.18	0.04-0.06	0.62
	0.05(0.02)		0.05(0.02)		
IO diameter right	0.05+0.02	0.047-0.066	0.06+0.13	0.05-0.07	0.322
	0.05(0.04)		0.05(0.03)		

Discussion

The blood supply of region is important for the health of tissues. Therefore, it is important to know the characteristic of the vascularity of a particular area. Doppler ultrasound aids in analyzing total blood flow characteristics

Doppler ultrasound aids in analyzing total blood flow characteristics. In this study we demonstrated characteristics map of facial areas using facial ultrasound. To our knowledge, there is no published data available yet which can provide baseline values regarding vascularization of face in young adults. Nagase et al

analysed on Doppler ultrasound the facial artery next to mandibular base, the mean diameter of about (0.27 cm) 2.7mm. (12) In another study, the diameter of same artery had a mean of (0.21) 2.14mm. In our study the mean diameter of right and left facial artery is found to be 0.16 cm and 0.15 cm respectively. No statistically difference was found among this parameter in males and females. Zhai YP et al (13) found similar results that there was no significant difference in all measured values of indexes of right and left side.

Jacobovicz et al reinforced the use of Resistance index as this parameter gives estimation of peripheral resistance of

blood flow enabling hemodynamic analysis. [14] Tucunduva observed in his study the average value of RI was 0.81 ± 0.05 mm.15 In our study it was 0.78 ± 0.01 mm for right side and 0.79 ± 0.05 mm for left side and no statistically difference was between male and female in this index. Tucunduva found Peak Systolic Velocity to be 45.31mm, whereas in our study it was 67.67 ± 11.69 mm on right side and 63.47 ± 12.48 mm on left side. [15]

In our study infraorbital artery showed an average diameter of 0.05 ± 0.17 mm on right side and 0.06 ± 0.02 mm on left side, this parameter as observed by Tucunduva found an average diameter of about 0.01 mm (SD 0.24). [15] Peak systolic velocity of the same artery on right and left side was found to be 28.05 ± 7.98 mm and 31.18 ± 12.60 mm respectively, Tucunduva study found it be 15.55mm (SD 13.06).

In our study one female individual infraorbital artery of both sides were not found. This can be explained by the fact given by Ericiti et al that in 75% of cases infraorbital was located on the line which is connecting the lateral palpebral commissure lateral to the ala of the nose and remaining 25% of the are located outside this triangle. [16]

Conclusion

This study show that investigated parameters show no difference between male & female and left or right side. The study might be useful to establish normal baseline values of various parameters on both sides of face in male and female adults. This study may become important reference for future studies measuring blood flow and even progression of vascular diseases may be assessed by indexes developed in the basis of these studies. This knowledge will be helpful not only for dentists but for plastic surgeons and other physicians as well for preoperative planning and intraoperative management. Limitation of the study was the non-availability of intra oral US probe, which preclude other measurements.

Conflict of interest: Authors do not have any conflict of interest to declare.

Disclosure: None

Human/Animal Rights: No human or animal rights are violated during this study.

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Diagnostic Accuracy of Gray Scale Ultrasonography versus Color Doppler in Suspected Cases of Acute Appendicitis

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Significance:

A common surgical emergency is acute appendicitis. Various diagnostic tools are available to diagnosis acute appendicitis. Radiological investigations play an important role in making accurate and early diagnosis and thus preventing morbidity associated with the disease.

Abstract

Background: A common surgical emergency is acute appendicitis. Various diagnostic tools are available to diagnosis acute appendicitis. Radiological investigations play an important role in making accurate and early diagnosis and thus preventing morbidity associated with the disease. To determine the diagnostic accuracy of gray scale ultrasonography versus color Doppler in suspected cases of acute appendicitis.

Materials and Methods: The study was carried in the department of Radiology of Mayo Hospital, Lahore. A total of 75 patients were enrolled of age 18-40 years, both genders who were suspected cases of acute appendicitis. All patients underwent baseline investigations along with gray scale ultrasonography and color Doppler. All patients were subjected to surgery to confirm the diagnosis and findings were subjected to statistical analysis.

Results: The mean age of the patients was 23.25 ± 10.55 and mean transverse diameter of appendix was 8.37 ± 3.39 . There were 62.7% males and 37.3% females. Findings of gray scale ultrasonography and color Doppler were then correlated with surgical findings to calculate the diagnostic accuracy of these modalities. The results revealed that gray scale ultrasonography sensitivity, specificity, positive predictive value, negative predictive value and accuracy was 92.7%, 94.32%, 95%, 91.4% and 93.3% respectively, whereas color Doppler had sensitivity, specificity, positive predictive value, negative predictive value and accuracy of 97.7%, 93.9%, 95.3%, 97% and 96% respectively. Diagnostic accuracy of both modalities together was 98.6%.

Conclusion: Color Doppler has better diagnostic accuracy than gray scale ultrasonography for diagnosis of acute appendicitis and the combination of both modalities yields diagnostic accuracy that is similar to gold standard.

Introduction

Among surgical problems that are of acute nature, the commonest one is acute appendicitis (1). Despite the fact that a lot of advancements have been made in the modalities that can be used for diagnosis, yet it poses great clinical challenge to the surgeons while deciding clinically about its presence in around 30-40% cases (1). This uncertainty in diagnosis leads to negative appendectomy in 15-30% cases and raises the chances of morbidity and mortality (2). It is still not possible to make the diagnosis of acute appendicitis accurately owing to different atypical presentations clinically, which are frequently encountered as multiple inflammatory as well as non-inflammatory conditions mimic the scenario of this pathology clinically (3). Common mistakes in diagnosing such patients are made in females who are of reproductive age and in patients who are at extremes of ages (4).

Severe outcomes can be anticipated in scenarios where the diagnosis of acute appendicitis is missed, these included perforation of appendix, peritonitis, and abscess formation leading to increased rate of mortality by up to 10% (5). There are 12% chances of missing an acute appendicitis (6).

Despite the fact that a lot of improvements have been made in establishing diagnosis and making decision regarding treatment of acute appendicitis with the help of clinical and laboratory techniques as well as by utilizing different scoring methods, still the decision to operate a patient for acute appendicitis still puzzles the surgeons a lot (7).

Imaging plays an important part making diagnosis of acute appendicitis as well as complications arising from it and also helps in providing alternate diagnosis where necessary (8). The main radiological modality used for establishing diagnosis of acute appendicitis is ultrasonography. Graded compression ultrasonography (USG) is an inexpensive, fast and noninvasive method with an accuracy rate of 71%–90% for the diagnosis of acute appendicitis (9). Still few cases are missed due to various reasons like obesity, severe guarding and excessive bowel gases (10). Moreover, lack of proper infrastructure (poor quality ultrasound machine) and sufficient time to patient care can lead to less detection of appendicitis by ultrasound (11).

Another imaging modality that has gained attention in recent years is the Color Doppler which can detect appendiceal wall hyperemia, thus helping in differentiating an enlarged appendix from acute

appendicitis and gangrenous appendicitis. It has been shown to have a higher diagnostic accuracy compared to conventional gray scale ultrasound. In a study by Joseph, H.T. et al, it was found that the diagnostic accuracy of color Doppler was 97.08% compared to ultrasound that was 95.09% in detecting acute appendicitis (12).

A lot of international research has been carried out on the diagnostic accuracy of ultrasonography and Color Doppler. However, no such study has been carried out in Pakistan. So the purpose of current study was to assess the diagnostic accuracy of graded compression ultrasonography and color Doppler in suspected patients of acute appendicitis keeping surgical notes (operative findings) as gold standard. This study will help in yielding more accurate diagnosis and thereby benefiting the affected patients as well as reducing workload of hospitals by reducing the number of negative appendectomies, and to recommend imaging modality that can be used as first-line for diagnosing acute appendicitis. Accurate early diagnosis of appendicitis can decrease its complications and minimize the mortality, morbidity and costs.

Materials and Methods

Participants: The study was carried out in the Radiology Department of Mayo Hospital, Lahore from 1st January 2020 till 30th September, 2020. A total of 75 patients, aged 18 to 40 years of both genders were included in the study who were diagnosed as having suspected acute appendicitis were included i.e. who presented with right lower abdominal pain along with any one or more of these symptoms i.e. nausea/vomiting, decreased appetite, guarding and tenderness of the right iliac fossa. Patients who were non-cooperative, pregnant females, or patients who presented with adnexal mass or a history of renal stones were excluded from the study.

Study Design: It was a cross sectional comparative study. After taking informed consent and approval from the ethical review board of the hospital, all eligible participants were enquired about their symptoms and were examined thoroughly. Baseline investigations such as CBC, serum electrolytes, RFTs, LFTs, CRP was carried out. Findings were noted down on a predesigned performa. IV line was secured in all patients. Patients were then subjected to gray scale ultrasonography followed by Color Doppler to look for acute appendicitis and findings of both modalities were noted down. On gray scale ultrasonography, appendicitis was labeled if the transverse diameter was >6mm of an incompressible, tubular structure which was filled with fluid and was blind ended. Those with a diameter between 4-6mm were labeled as suspected acute appendicitis. On color Doppler, if the surrounding walls of appendix were hyperemic, it was labeled as appendicitis.

After radiological evaluation, all patients were evaluated for anesthesia fitness that was carried out by the anesthesia team and was followed by surgical intervention for suspected acute appendicitis. Findings of the surgical intervention were noted down and were compared with those of ultrasonography and color Doppler and were subjected to statistical analysis.

Statistical Analysis: The data was analyzed through SPSS version 24.0. Quantitative measures such as age, transverse diameter were presented as mean and standard deviation. Qualitative variables such as gender, presenting symptoms (nausea, vomiting, rebound tenderness, anorexia, fever), visualization of appendix, transverse diameter, compressibility, abnormal appendiceal wall signature, appendicolith, echogenic surrounding mesentery, free fluid presence, mesenteric lymph nodes involvement, hyperemia and its type, ultrasound findings, color Doppler findings and findings of surgical intervention were presented as frequency and percentages. 2*2 table was made to determine the diagnostic accuracy of gray scale ultrasonography and color Doppler in diagnosing acute appendicitis keeping surgical intervention findings as gold standard. Sensitivity, specificity, positive predictive value and negative predictive value were calculated.

Results:

75 patients were enrolled in the study. The mean age of the patients was 23.25 years with a standard deviation of 10.55 and the mean transverse diameter of appendix on ultrasonography was 8.37 with a standard deviation of 3.39 (table 1). There were 47 (62.7%) males and 28 (37.3%) females. Among males, 36% had appendicitis and in females 21.3% had appendicitis. 21.3% patients were of lower class, 34.7% belonged to lower middle class and 44% were of middle class. The frequency of presenting symptoms and other qualitative variables is mentioned in table 2.

Findings of gray scale ultrasonography and color Doppler were then correlated with surgical findings to calculate the diagnostic accuracy of these modalities. The results revealed that gray scale ultrasonography had a sensitivity of 92.7%, specificity of 94.32%, positive predictive value of 95%, negative predictive value of 91.4% and accuracy of 93.3%, whereas color Doppler had a sensitivity 97.7%, specificity 94%, positive predictive value 95.3%, negative predictive value 97% and accuracy of 96%. The results also revealed that the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of gray scale ultrasonography combined with color Doppler was 97.7%, 96.9%, 98%, 97% and 98.6% respectively.

Table 1: Showing Mean and Standard Deviation of Quantitative Variables

QUANTITATIVE VARIABLES	N=75, MEAN±SD
Age	23.25±10.55
Transverse diameter of Appendix	8.37±3.39

Table 2: Showing Frequency and Percentages of Qualitative Variables

QUALITATIVE VARIABLES	N=75 (100%)
GENDER:	
Male	47 (62.7%)
Female	28 (37.3%)
SOCIOECONOMIC STATUS:	
Lower Class	16 (21.3%)
Lower Middle Class	26 (34.7%)
Middle Class	33 (44%)
PRESENTING COMPLAINTS:	
Nausea	69 (92%)
Vomiting	69 (92%)
Rebound Tenderness	58 (77.3%)
Anorexia	45 (60%)
Fever	74 (98.7%)
GRAY SCALE ULTRASONOGRAPHIC FINDINGS:	
Visualization Of Appendix	74 (98.7%)
Transverse Diameter >6mm	37 (49.3%)
Non-compressible Appendix	37 (49.3%)
Abnormal Appendicular Wall Signature	40 (53.3%)
Appendicolith	4 (5.3%)
Free Fluid	11 (14.7%)
Mesenteric Lymph Nodes	10 (13.3%)
Probe Tenderness	29 (38.7%)
COLOR DOPPLER FINDINGS:	
Hyperemia	41 (54.7%)
Type of hyperemia:	
Curvilinear/diffuse	34 (45.3%)
punctate	9 (9.4%)
APPENDICITIS DIAGNOSIS:	
On Gray Scale Ultrasound	37 (49.3%)
Color Doppler	43 (57.3%)

Discussion

A major bulk of emergencies related to abdominal surgeries are formed by cases of acute appendicitis (1). Despite higher prevalence, acute appendicitis always puts the judgment made by surgeon on clinical grounds to an

actual test at an early stage different modalities are used for making early diagnosis of this condition (2). The most effective methods of diagnosing are total leucocyte count, C-reactive protein, ultrasound and CT abdomen (4). However, none has proven to be perfect and all these modalities have certain pros and cons. Suggestions have been given that utilizing different diagnostic tools in combination can help in getting better results diagnostically (7).

The current study revealed that color Doppler has a higher sensitivity and diagnostic accuracy compared to gray scale ultrasonography when used alone for the diagnosis of acute appendicitis. However, when both of these imaging modalities were combined, the overall sensitivity, specificity, PPV, NPV and diagnostic accuracy was increased more that was almost like the gold standard. Transverse diameter > 6mm and non-compressible appendix were significant findings associated with acute appendicitis on gray scale ultrasonography and hyperemia was significantly correlated with acute appendicitis on color Doppler.

In view of diagnostic accuracy, a study was conducted by Gaitini, D. et al in 2018 (25), who conducted a study to evaluate the diagnostic accuracy of color Doppler and contrast enhanced CT scan for diagnosing acute appendicitis. The results revealed that color Doppler Sonography and CT correctly diagnosed acute appendicitis in 66 of 75 patients and in 38 of 39 patients, respectively, and correctly denied acute appendicitis in 312 of 326 and in 92 of 92 patients. Sonography was inconclusive in 17 of 418 cases and CT, in one of 132 cases. Sonography and CT allowed alternative diagnoses in 82 and 42 patients, respectively. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for color Doppler sonography were 74.2%, 97%, 88%, 93%, and 92%, respectively, and for CT, 100%, 98.9%, 97.4%, 100%, and 99% (25). The authors concluded that color Doppler ultrasonography had a good diagnostic yield for diagnosing acute appendicitis. Transverse diameter of appendix of >6 mm and non-compressibility was significantly associated with positive diagnosis (25). Similar results have been shown by current study with diagnostic accuracy of gray scale ultrasonography as 93.3%. Current study also revealed that transverse diameter >6mm and non-compressibility were associated significantly with the diagnosis of acute appendicitis on gray scale ultrasonography.

In another study by Joseph, H.T., 2020, 102 patients with acute appendicitis were evaluated by ultrasound and color Doppler, keeping histo-pathological findings as gold standard. The sensitivity was high of color Doppler than that of ultrasound, where as they were equal in terms of specificity. Color Doppler had an accuracy of 97.08% and

ultrasound had an accuracy of 95.09% (12). Similar results were shown by current study. The current study also revealed that color Doppler had superior sensitivity and accuracy than ultrasound, however, specificity of both was equal.

Thus, addition of color Doppler to routine ultrasound can enhance the diagnostic yield in acute appendicitis. Our study had certain limitations. Firstly, it was conducted in a single center so the results cannot be generalized. Secondly, the sample size was sample, so the results cannot be taken as representation of whole population. Thirdly, there was selection bias, as color Doppler could only be used when appendix was visualized by gray scale ultrasound. Lastly, healthy individuals were not assessed, as only those who were suspected to have acute appendicitis were enrolled.

Conclusion

The study concluded that color Doppler have a better overall sensitivity and diagnostic accuracy compared to gray scale ultrasound alone. However, when both were combined the diagnostic yield was near accurate to the findings of gold standard and thus can help in identification of complicated cases of acute appendicitis by providing early, accurate diagnosis and enabling in making better decisions about further management of such cases.

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Disclosure: None

Human/Animal Rights: No human or animal rights are violated during this study.

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Determinants of Patient Care and Satisfaction in Pakistan- A Scoping Review

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Significance:

Patient satisfaction with healthcare services in Pakistan is widely understudied. The objectives of this scoping review are to highlight the determinants of patient care and satisfaction in public and private sectors. As per the World Health Organization, quality of care comprises of six dimensions where the case must be effective, efficient, accessible, patient-centered, equitable, and safe. Gaps in service provision must be addressed by healthcare managers, policymakers, and physicians in Pakistan.

ABSTRACT

Background: Pakistan established the Punjab healthcare commission to improve patient care catering to professional accountability in the public and private sectors. As per the World Health Organization, quality of care comprises of six dimensions where the care must be effective, efficient, accessible, patient-centered, equitable, and safe.

Objectives: The objectives are to determine if patients are satisfied with the quality of services in public and private sectors, or if any neglect was present.

Methods: The literature on patient care and satisfaction was compiled using a scoping review methodology. PubMed, CINAHL Plus, and Scopus were used to collate information. Duplicates were removed using Endnote X9.

Results: Of the 467 abstracts and titles that were screened for relevance, 74 were considered for full-text review and potential inclusion in the scoping review. Out of 16 included studies, 7 (43.8%) of the included studies originated from Pakistan. The characteristics of included studies such as quality of care and patient satisfaction are tabulated.

Conclusion: Current literature does not provide quality- and satisfaction- focused studies, and has methodological discrepancies. It is required that the medical profession adopt a sense of self-monitoring. Gaps in service provision must be addressed by healthcare managers, policymakers, and physicians in Pakistan.

Introduction

The goal of providing health care facilities to patients is to deliver high-quality patient-centered care. The

Institute of Medicine (IOM) prioritizes patient care and safety and identifies its importance in healthcare facilities (1). As per IOM patient care is "Providing care that is respectful of, and responsive to, individual patient preferences, needs and values, and ensuring that patient values guide all clinical decisions" (1). It is imperative to note that a healthcare construct is a multidimensional approach, which makes it delineate specific factors like patient visits and the series of outcomes (2, 3). Quality care is defined as "the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge." Specifically, patient satisfaction measures qualitative outcomes such as patient retention, medical malpractice, and also clinical outcomes. This also affects the patient-centric delivery of quality care, and the efficiency of services. Often, patient satisfaction is considered as a proxy, however, it is a useful indicator to measure the success of doctors and hospitals in developing countries such as Pakistan. Satisfaction may be defined as the extent to which the individuals' experiences compare with expectations. The World Health Organization suggests (WHO) states that the quality of care may be divided into six dimensions of quality of care described as 1) efficient, 2) effective, 3) accessible, 4) patient centered, 5) safe, and 6) equitable

The provincial government established the Punjab Healthcare Commission (PHC) for this purpose in 2010 with objectives to enhance patient satisfaction levels and complaints that catered to professional accountability (4). This also sheds light on awareness among tertiary healthcare establishments and patients about responsibilities and rights. Healthcare is a central concern in a developing country like Pakistan, with concerns by practitioners, government officials, and researchers. Patient Satisfaction has three hierarchies (3). The first includes satisfaction with healthcare delivery, referring to the service or clinic, accessibility issues, patient-clinician communication, and the quality of facilities being provided. The second relates to treatment, for example, exercise or dietary recommendations. The third is satisfaction with medications, with a focus placed solely on the quality of pharmacological interventions and prescriptions. Patient care and satisfaction are both considered

important in literature due to the relevance and difficulty of measurement. In the light of available data, a systematic literature review is conducted related to the quality of medical, physical, mental, and emotional care to patients along with satisfaction levels.

Materials and Methods

Research questions: The review questions were:

1. Are patients satisfied with the quality of services provided in public and/or private sectors?
2. Is patient neglect during service provision prevalent across hospitals?
3. Are patients satisfied with the data regarding treatment and care, availability of hospital personnel, and communication and medications?

Eligibility criteria: There were no time or language restrictions to the included publications. This review included papers from inception to September 2019. To ensure that a wide spectrum of literature was included in the scoping review, there were no restrictions on the type of studies included in the review. Additional eligibility criteria are listed below as Population, Concept, and Context (PCC).

Population: The review targeted children and adults, where children were defined as 18 or under. These could be from any sociodemographic background in the emergency, outpatient, or inpatient departments.

Concept: The concept of satisfaction with the quality of health care delivery, satisfaction with the treatment, and satisfaction with the medication was encompassed in this review. All those studies that did not address either one of the three patient satisfaction hierarchies were omitted.

Context: The studies were conducted or based in LMICs or HICs with the higher value provided to Pakistan. Papers involving various settings or study designs were eligible for inclusion.

Search strategy: The search strategy of the review as finalized based on active discussions by investigators (ZS and AS). Key concepts are listed in Table 1. The strategy was utilized to search the following databases: PubMed, CINAHL Plus, and Scopus. An additional manual search was conducted to obtain national studies. The databases permitted good coverage of primary or secondary publications with a public health focus. The search of all databases was conducted from February 2019 until September 2019. Grey literature was searched using a combination of keywords as defined in Supplementary Table 1 (S1). WHO and non-government websites were searched with guidelines published by Punjab Healthcare Commission (PHC), Pakistan. Due to the surplus in articles found, the reference list of select articles was used for searching

relevant studies (umbrella review).

Study selection and citation management: All retrieved articles from database searches were stored and exported to EndNote X9 reference manager. Post duplication removal by two reviewers (ZS and AS), the title and abstract screening of publications was conducted. In the next step, all three reviewers conducted full-text reviews of studies. Any uncertainty was resolved via consensus.

Data extraction and collation: After the customized data was extracted and developed by two reviewers (ZS and AS) using a shared spreadsheet, manual data extraction was conducted to identify materials for tabulation. A pilot extraction was conducted for 5 randomly selected studies, and the process was used for all included studies. Extracted data included the following: number, author (year), title, design, findings, and country. The following methods were used to present results for this scoping review. First, the PRISMA flow diagram is presented to describe the study selection processes. Second, tables are presented of extracted data for eligible studies. Third, a literature review of all included studies sorted by the study is written concerning the review questions. As there were a moderate number of studies, they were categorized on a study-by-study basis.

Results:

Of the 467 abstracts and titles that were screened for relevance, 74 were considered for full-text review and potential inclusion in the scoping review. A larger proportion of the studies originated from Pakistan (43.8%). The characteristics of included studies are presented in Table 1.

Discussion

In Pakistan, various determinants may contribute to poor patient care and satisfaction outcomes. These factors present challenges for low- and middle- income countries (LMICs) due to limited resources. Previous literature highlights the types and frequency of these variables presenting in Southeast Asia and worldwide. Low resource countries like Pakistan have limited assessments for quality of care in the public and private sectors. Patient satisfaction ought to be understood in the context of social and cultural barriers to develop appropriate intervention and data collection techniques in Pakistan. The review builds on national health policies while aiming to improve patient outcomes. Shaikh reasons that actual assessment of the health care systems lies with the provision of patient care and not mere indicators of morbidity and mortality (5).

No	Author (year)	Title	Design	Findings	Country
1	Shaikh, 2005	Quality of health care: an absolute necessity for patient satisfaction	Points of View	Quality improvement is imperative to develop healthcare systems in Pakistan	Pakistan
2	Freitas <i>et al.</i> , 2014	Quality of nursing care and satisfaction of patients attended at a teaching hospital	Cross-sectional	Institutes must monitor evaluation systems for care quality to attend to patients' expectations	Brazil
3	Sultana <i>et al.</i> , 2016	Level of Satisfaction of Admitted Patients	Observational, Cross-sectional	Patients were reasonably satisfied with health services except for hygiene standards and medication prices	Pakistan
4	Naseer <i>et al.</i> , 2012	Determinants of patient's satisfaction with health care system in Pakistan: a critical review	Review	Attention to patients' expectations, perceptions, and responsiveness of healthcare systems is important	Pakistan
5	Glickman <i>et al.</i> , 2010	Patient Satisfaction and Its Relationship With Clinical Quality and Inpatient Mortality in Acute Myocardial Infarction	Observational, prospective cohort	High patient satisfaction is linked to strict guideline adherence, with improvement in the quality of acute MI care	United States
6	Fenton <i>et al.</i> , 2012	The cost of satisfaction: a national study of patient satisfaction, health care utilization, expenditures, and mortality	Observational, prospective cohort	Higher patient satisfaction was associated with first inpatient departments, second greater total expenditures, and third higher mortality	United States
7	Algwaiz <i>et al.</i> , 2012	Violence exposure among health care professionals in Saudi public hospitals. A preliminary investigation	Observational, Cross-sectional	Nurses and physicians are at a high risk of violence, requiring preventive measures to make hospitals safer	Saudi Arabia
8	Mukhtar <i>et al.</i> , 2013	Patient satisfaction; OPD services in a Tertiary Care Hospital of Lahore	Observational, Cross-sectional	While patients were satisfied with outpatient services, studies must be conducted in primary and secondary care facilities, and regular feedback must be imbibed in Pakistan's system	Pakistan
9	Kruszecka-Krówka <i>et al.</i> , 2019	Determinants of Parental Satisfaction with Nursing Care in Paediatric Wards—A Preliminary Report	Observational, Cross-sectional	Parental satisfaction with nursing care is determined by the age of the child, mode of admission, and educational level of respondents	Poland

10	Javed <i>et al.</i> , 2019	Patients' satisfaction and public and private sectors' health care service quality in Pakistan: Application of grey decision analysis approaches	Observational, Cross-sectional	Using analytical methods, and noting the five dimensions of health care quality, patients are more likely to be satisfied with private health care facilities	Pakistan
11	Hussain <i>et al.</i> , 2019	What Factors Affect Patient Satisfaction in Public Sector Hospitals: Evidence from an Emerging Economy	Observational, Cross-sectional	Significant communication gaps exist in the doctor-patient setting, and Pakistan's healthcare system is deprived of physical facilities and adequate services	Pakistan
12	Al-Abri <i>et al.</i> , 2014	Patient Satisfaction Survey as a Tool Towards Quality Improvement	Review	While patient satisfaction surveys are an established yardstick for quality improvement plans, they must be more extensively used for developing improvement plans	Oman
13	Harrison <i>et al.</i> , 2015	Patient safety and quality of care in developing countries in Southeast Asia: a systematic literature review	Review	Southeast Asia requires large-scale prevalence studies to identify root problems of safety and quality	Australia
14	Hussain <i>et al.</i> , 2014	Inpatient satisfaction at tertiary care public hospitals of a metropolitan city of Pakistan.	Observational, Cross-sectional	Patients were relatively satisfied with the quality of care, but the subpar hospital environment and sanitation was a major concern	Pakistan
15	Papastavrou <i>et al.</i> , 2014	Linking patient satisfaction with nursing care: the case of care rationing - a correlational study	Observational, descriptive, correlational	The rationing of nursing care is a problematic area, which requires considerable policy development	Cyprus
16	Eyasu <i>et al.</i> , 2016	Adult Patients' Satisfaction with Inpatient Nursing Care and Associated Factors in an Ethiopian Referral Hospital, Northeast, Ethiopia	Observational, Cross-sectional	The low patient satisfaction index requires in-service training programs for nurses with special emphasis placed on improving communication skills	Ethiopia

Despite the huge health infrastructure, primary health care centers only attract 21% of patients while 77% of them rely on private facilities (5). This major influx in private care centers is predominantly because of decreased waiting time, flexible open hours, all-time availability of health care staff, and better confidentiality in diseases considered taboo.

A world health report notes, health care quality is enmeshed in the triad of acuity, good budget, and social acceptability (5). This raises concerns for the medical fraternity especially in healthcare facilities of developing countries like Pakistan ultimately requiring regular scrutiny and feedback. The attitudes of healthcare providers must ideally be centered on feedback from their clients. The atmosphere of the health care setting should not be intimidating but ought to encourage the patient to communicate problems (5). Confidence to female clientele in Pakistan can be instilled by addressing customized needs in privacy. Such measures will not only improve inpatient care satisfaction but also lead to the prosperity of Pakistan as a whole.

An observational study by Freitas including 275 patients at a teaching hospital in Brazil in 2014 assessed the quality of nursing care and satisfaction of patients, using the concomitant application of three instruments, which targeted sociodemographic characteristics, and an interview script on nursing care. It comprised of 9 items and 40 sub-items with yes or no questions, and a Brazilian patient satisfaction instrument called ISP containing 3 domains and constructed in a 5 point Likert scale respectively (6). The study effectively used the Cronbach alpha coefficient, adding them in a software Microsoft excel 2010, using scores of 4 or greater as satisfactory, setting significance value at or below 0.05 and analyzing by positivity, median value, and spearman's coefficients (6). It concluded that only two parameters were voted safe: hygiene and physical comfort; nutrition and hydration. The rest was declared unsatisfactory (6). However, the parameters of confidentiality, professionalism, technicality, and education suggested patients were satisfied. Thus, a continuum of evaluation system brimming with patient feedback periodically is essential for high-quality care in Pakistan.

There are various parameters, which may be considered for measuring patient satisfaction. Studies originating from Bangladesh and Malaysia show that the attitude of healthcare providers and the unavailability of free drugs respectively are important determinants of patient satisfaction. Surveys conducted in Swat and Benazir Bhutto Hospital have shown that the majority of patients are dissatisfied with the staff and that the

quality of hospital care is measured inefficiently (7). An observational study at the Holy Family Hospital Rawalpindi, from May to June 2013 addresses these concerns (7). In the study, a non-structured questionnaire using 12 variables was used to guide the interviewers who received formal training. Verbal consent was taken and confidentiality was maintained using the patient-interviewer relationship. The results showed that 81.53% of patients were satisfied based on the 170 patient study-sample. Overall, the study found that 15.84% of patients were dissatisfied necessitating further investigation of the root cause in Pakistan. The observational study found there was a moderately high level of satisfaction at Holy Family Hospital where the key traits measured included hygiene and medication (7). The study was an imperative one as it analyzed subjective key deficiencies in the healthcare system in Pakistan.

A critical review published in 2012 unfolds the determinants of patient satisfaction within the health care system in Pakistan." (8). The delivery of care by healthcare workers and patient satisfaction were notably central factors in the review (8). While literature pertaining to this area is limited in developing countries in Asia, *Mailha et al.* use various databases like Medscape, PakMedinet, and PubMed to ensure that a wide range of data is included. The study consists of 21 articles and selected variables include the overlap of patient satisfaction and healthcare services (8). The study listed age, literacy, gender, and social class as characteristics influencing the patient satisfaction level in Pakistan. Key findings of the study focus on autonomy, privacy, decision-making, communication, hygiene, and sanitation. The review prompted call-to-action by suggesting to calibrate patient expectations with the responsiveness of the healthcare system. While the concept has not gained peak attention in Pakistan, healthcare organizations and workers must assess patient satisfaction as a measurement for the quality of care (8).

Patients are found to be more satisfied with healthcare services if the healthcare workers are aware of respect of dignity, autonomy, and attentive to meeting expectations. However, social class, age, education, gender, may influence patient expectations or ethnicity, which are significant predictors in patient satisfaction surveys (8). Psychological factors including patient perceptions are potentially neglected determinants in Pakistan (8). Private health care centers are more responsive to certain patient perceptions, albeit, exceptions exist (8). The way forward is by introducing interventions at the individual, hospital, and healthcare policymaker level by 1) introducing the concept of care

quality among HCWs, 2) increasing the staff's competence and motivation by regularly conducting seminars or re-training modules, 3) gradually improve patient trust and satisfaction by incorporating essential verbal or written surveys and feedback forms. A practical option is to instill the concept of interpersonal communication skills to Pakistani HCWs.

A survey measured the influence of clinician behaviors on the satisfaction of the patient. Based on the results of 6,467 patients, proper guidance was one of the main enlisted factors improving recovery and decreasing the mortality rate. Another dataset collected from a sample of 36,428 patients suggested that satisfaction towards care could yield opposite results (9). High levels of patient satisfaction were linked to morbidity than mortality (10, 11). The violence faced by HCWs may lead to psychological problems for them due to underlying weakness in doctor-patient relationships. A study found that 77% of HCWs in Pakistan face either physical or verbal abuse. Specifically, 74% of the clinicians were subjected to verbal abuse (12). In addition to Pakistan, similar issues were reported in two hospitals from Saudi Arabia in 2011 where 67.4% HCWs (most commonly nurses) faced verbal abuse (12). A survey from Kuwait shows that 86% of doctors suffered verbal insults, 28% were physically attacked, and 7% had serious injuries. Results from a survey carried out in Australia showed that 58% of respondents were verbally insulted and 18% experienced property damage (12).

Mukhtar et al. find factors affecting patient satisfaction to be provider-related and Patient-related (13). Patient satisfaction is a multi-disciplinary concept, with determinants including interpersonal communication skills, physician's proficiency, access to care, the behavior of staff, infrastructure, and the basic provision of facilities (13). The emphasis on patient satisfaction is linked to improved compliance and timely care provision by HCWs. An observational study conducted in the emergency department of a tertiary hospital in Pakistan notes the demographic history and questionnaire responses. Of the 250 participants, the 2013 study found that 94% of patients were satisfied with healthcare services. Overall, patients stated that the health facility was clean and adequately ventilated; they would re-visit the hospital in the future (13). Future studies must assess these links in primary and secondary health care facilities, and obtain regular feedback from patients (13).

In a modern healthcare system, the provision of quality health care is correlated with the satisfaction of the patients (14). A 2019 observational study in pediatric wards at two children hospitals in Krakow assessed

various determinants of parental satisfaction with nursing care (14). Participants were divided into groups based on developmental ages. A standardized questionnaire-EMPHATIC was used (14). Five major criteria for satisfaction evaluation included Information, Care and Treatment, Availability, Parental participation, and Professionalism approach. The study followed the principles of Helsinki's Declaration. The authors found that the mean score of satisfaction was high i.e. 4.19 points. The highest score was found for availability and the lowest for care and treatment and parental participation (14). Lower levels of satisfaction were seen in parents of children with emergency admissions, those with a post-trauma condition, and the highly educated group (14). While the study was preliminary due to limited subjects, the implications for Pakistan may be to assess satisfaction assessing emotional state qualitatively.

In a 2019 study, *Javed et al.* find a relationship between patient satisfaction and five health dimensions (15). The area of study was public and private health care centers in Lahore and Rawalpindi, Pakistan. Data was collected through SERVQUAL instruments. Deng's GRA, absolute GRA, and second synthetic GRA models were used. The constructs of the SERVQUAL model where tangibility, reliability, responsiveness, assurance, and empathy. According to Grey Relational Analysis models, *Javed et al.* observed that reliability and responsiveness strongly indicated the satisfaction levels of patients (15). The respondents were both inpatients and outpatients. Hurwickz's criterion suggests that satisfaction with private health care centers is the result of perceived service quality, while quality is a result of a comparison of expectations with performances. The limitations of the study relate to the selected model, which was unable to evaluate all factors about care provision.

Patient satisfaction is one of the two central components of quality of care including 1) understanding expectations and providing services, and 2) respecting the patient (16). In a 2019 study, Hussain et al. identify that the identification of patient satisfaction may improve certain areas of care provision in public sector hospitals. However, the quality of service delivery is rarely assessed. The study demonstrates the performance of public healthcare centers in Pakistan by interacting with physical services (environmental and tangible), pharmacy and laboratory services, and doctor-patient communication. Primary data was collected from 554 participants using random sampling methods. Using multiple regression analysis, the results revealed that pharmacy and laboratory services had positive effects. The study suggests that communication

gaps exist in the doctor-patient setting. The healthcare system in Pakistan is deprived of physical facilities, which requires further improvements.

Al-Abri et al. investigate published literature from 1997 to 2012, and explore various contributing factors to patient satisfaction (17). The 2013 study evaluates the outcomes of 29 texts in the past 15 years using the snowball search method (17). Although quality outcome indicators are not well-defined or conceptualized, standardized tools ought to be developed to understand the determinants affecting patient satisfaction levels (17). Various studies examine the correlation between demographic factors, level of education, and patient satisfaction; the strongest driver of overall patient satisfaction is ease to access to care (17). The most common problems experienced by patients are related to the living arrangements and amenities. Harrison reviewed 33 texts on patient safety and quality of care in developing countries like Southeast Asia published between 1991 to 2014 (18). WHO's definition of patient safety and quality of care was used (18). Four inter-related quality and safety concerns were identified in Southeast Asia including healthcare delivery, risk of patient infection, medication use, and errors. The quality and provision of perinatal and maternal care with the quality of healthcare provision was reviewed. Of thirty-one, 12 articles were concerned with nosocomial infections which were common post invasive procedures, hospital stay over 6 days, high body temperature, ICU admission status, or antibiotic use (18). The over-prescribing of antibiotics was identified in three studies falling under medication error. Errors were found due to incomplete prescriptions, but pharmaceutical and dispensing errors were also evident. The reviewed studies of maternal and perinatal care suggest that particular problems are the risk of infection and difficulty managing Emergency Obstetric Care (EmOC) or birth complications requiring intervention (18).

Satisfaction is an essential target for clinical practice in the public health sector, mainly due to neglect by policymakers. In a similar study, *Hussain et al.* determine inpatient satisfaction regarding service quality provision in public-sector hospitals in Karachi, Pakistan (19). The 2014 study covered a non-representative population in family physician clinics and Out-Patient Departments (19). By employing a cross-sectional method under IRB approval of Dow University, a questionnaire that covered demographic details (gender, age, income level, residence, admission duration) with a 5 point Likert scale questions targeting satisfaction with the administration, staff, and doctors

(19). With a sample size of 664, *Hussain et al.* used SPSS 20 and set the alpha reliability at 0.7 (19). The results suggested that 67% of patients agreed that doctors were updated on checking them with patient care. 58.3% were not pleased with the sanitation measures in the hospital (19). *Hussain et al.* found that 63.7% of patients were satisfied with the staff (19). The study provided further evidence that public health hospitals have not focused on improving environmental, communicational, and medical services (19). Linking patient care and satisfaction to bedside treatment is still required in a developing country. Comparing this with a country like Saudi Arabia where 99% of patients confirm that they are satisfied with the quality of care all critical factors from the study must be utilized to improve the departmental conditions of public healthcare hospitals.

Papastavrou et al. link patient satisfaction with nursing care and measure the effect of a lack of resources (20). The study explores nurse-reported nursing care, the threshold of patient satisfaction across rationing levels. The study confirms that the Organization for Economic Cooperation and Developments (OECD) expenditure is a ticket to growth. WHO recognizes nursing care as a cost and not revenue. Previously published literature consists of the relationship between nursing perceptions and the quality of care in the work environment where improved environments lead to increased ratings by nurses and patients. *Papastavrou et al.* carry out the correlational, descriptive, and explorative design in five acute care hospitals with 352 participants (20). Alpha value was set at 0.05, and patients completed the patient satisfaction scale. Other scales include the BERNCA scale, and the Revised Professional Practice Environment Scale (20). The results after adjusted regression models showed that patients with the lowest rationing level showed low patient satisfaction as well. *Papastavrou et al.* conducted a primal study to examine patient satisfaction as a direct outcome of the rationing of nursing care with multidimensional satisfaction measuring instruments. The findings of the study include a negative relationship between satisfaction and care rationing from technical and interpersonal aspects of care that necessitates further exploration of patient/carer relationships (20). The study concluded that multiple policy considerations, patient safety, nursing care-rationing requirements ought to be recognized (20). This paves the pathway to the allocation and distribution of resources among patients. A new questionnaire may be devised for the Pakistani population to note clinical, economic, or other provider-defined criteria (21).

Conclusion

There are limited published studies that cover patient care and satisfaction with implications for Pakistan. Current literature does not provide quality- and satisfaction- focused studies and has methodological discrepancies. Critical gaps exist for pre, and post-admission care in indoor healthcare facilities, wherein no accounting or monitoring system is found. It is required that the medical profession adopt a sense of self-monitoring. An assessment of patient satisfaction levels across patient profile characteristics along with contextual specifications about patient-doctor interaction must be evaluated. The review discussed WHO's Quality of Care factors (i.e. effectivity of treatment/education measures, the efficiency of care, accessibility to services, acceptable/patient-centered nature of care, equitability and safety) related to patient care and satisfaction within the healthcare system of Pakistan. Gaps in service provision must be addressed by healthcare managers, policymakers, and physicians in Pakistan.

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Supplementary Material

Supplementary Table (S1)	
No	Search string
1	((((((((((("Patient"[Title] OR "Satisfaction"[Title]) OR "Quality"[Title]) OR "Healthcare"[Title]) OR "nursing care"[Title]) OR "level of satisfaction"[Title]) AND "Pakistan"[Title]) OR "clinical quality"[Title]) OR "expenditures"[Title]) OR "parental satisfaction"[Title]) OR "service quality"[Title]) OR "satisfaction survey"[Title]) OR "southeast asia"[Title]) OR "inpatient satisfaction"[Title])
2	((((((("patient s"[All Fields] OR "patients"[MeSH Terms]) OR "patients"[All Fields]) OR "patient"[All Fields]) OR "patients s"[All Fields]) AND (((("personal satisfaction"[MeSH Terms] OR ("personal"[All Fields] AND "satisfaction"[All Fields])) OR "personal satisfaction"[All Fields]) OR "satisfaction"[All Fields]) OR "satisfactions"[All Fields])) AND (((("service"[All Fields] OR "service s"[All Fields]) OR "serviced"[All Fields]) OR "services"[All Fields]) OR "services s"[All Fields]) OR "servicing"[All Fields])) AND "care"[All Fields]) OR (("pakistan"[MeSH Terms] OR "pakistan"[All Fields]) OR "pakistan s"[All Fields])
3	((("patient care"[MeSH Terms] OR ("patient"[All Fields] AND "care"[All Fields])) OR "patient care"[All Fields]) AND (((("personal satisfaction"[MeSH Terms] OR ("personal"[All Fields] AND "satisfaction"[All Fields])) OR "personal satisfaction"[All Fields]) OR "satisfaction"[All Fields]) OR "satisfactions"[All Fields])) AND (("pakistan"[MeSH Terms] OR "pakistan"[All Fields]) OR "pakistan s"[All Fields])



COVID-19 and Primary Percutaneous Coronary Intervention (PCI): Delayed Presentations and Outcomes for STEMI care

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Significance:

Primary percutaneous coronary intervention (PCI) is the recommended therapy for acute myocardial infarction. The COVID-19 pandemic has altered the course of STEMI care. In this brief communication, we discuss delayed presentations and outcomes during acute coronary syndrome from Emergency Medical Services (EMS) to stenting.

Abstract

Primary percutaneous coronary intervention (PPCI) is a non-surgical procedure that requires catheterization to improve blood flow to the heart and is the recommended therapy for Acute Myocardial Infarction (AMI). The ongoing COVID-19 pandemic has altered the course of reperfusion therapy for patients with ST-elevation myocardial infarction (STEMI). It is imperative to emphasize the awareness of timely PCI and the effects it has on improving patient outcomes. Based on the consensus statement by the American College of Cardiology (ACC), American College for Emergency Physicians (ACEP), and the Society for Cardiovascular Angiography and Interventions (SCAI), it is critical to inform the public to call the emergency medical system for AMI symptoms and obtain the appropriate level of care. Ultimately, COVID-19 has posed unprecedented challenges to public health. The immediate threat is linked to morbidity and mortality related to the infection, and the masked threat is the waning attention and resources utilized for the care of other diseases. First medical contact is the main time target and reducing treatment delays improving patient outcomes in AMI patients with STEMI should be the next immediate objective in healthcare systems worldwide.

Introduction

Primary percutaneous coronary intervention (PPCI) is a non-surgical procedure that requires catheterization to improve blood flow to the heart and is the recommended therapy for Acute Myocardial Infarction (AMI). The ongoing Coronavirus 2019 (COVID-19) pandemic situation has altered the course of reperfusion therapy for patients with ST-elevation myocardial infarction (STEMI) (1). At this critical time, it is essential to

emphasize the awareness of timely PCI, and effects on improving patient outcomes.

Brief Communication

Tam *et al* explore the impact of the outbreak of COVID-19 on STEMI systems of care in Hong Kong, China (2). The target is made on reducing first medical contact as opposed to reducing the door to balloon time and standard quality indicators. While their study is preliminary it has implications for hospitals targeting STEMI care. The single care center in Hong Kong included seven patients with PCI-treated STEMI who were COVID-19 negative. Six of these patients presented during office hours and one presented during non-office hours. STEMI care was compared to patients treated from February 1, 2018, until January 21, 2019, comprising 108 patients before the pandemic (2). Three outcomes were defined that included firstly, patients who reported for chest discomfort from onset to the first medical contact. Secondly, the patients' arrival at the emergency department for wire crossing during PPCI. Third, the arrival and the catheterization laboratory for wire crossing.

For 17 days, they noted the changes in the time component of STEMI management before and after the COVID-19 outbreak. The patient time lag was the largest, over 235 hours, from the onset of symptoms to first medical contact. The delay in PCI during the COVID-19 outbreak stems from a reluctance to go to the hospital. Aligned with the findings of the study, patients with STEMI chose not to seek medical care. Public health emergencies can lead to lapses in patient presentations (1,2). Additional precautions that are taken by catheterization laboratories in screening travel history, chest X-ray, symptomatology and wearing protective gear, lead to delays in diagnosis and late transfer to healthcare centers (2). For patients that were treated during the pandemic, the time of arrival at the department to device and catheterization laboratory to device was delayed as compared to patients who were treated before the outbreak. The most relevant findings from the hospital in Hong Kong include the desire to seek help by seven STEMI patients. Delays in arrival and treatment at health facilities lead to negative health outcomes. While the COVID-19 pandemic is a central factor contributing to delays, other causes may relate to cultural and educational, and severity perception of disease (3).

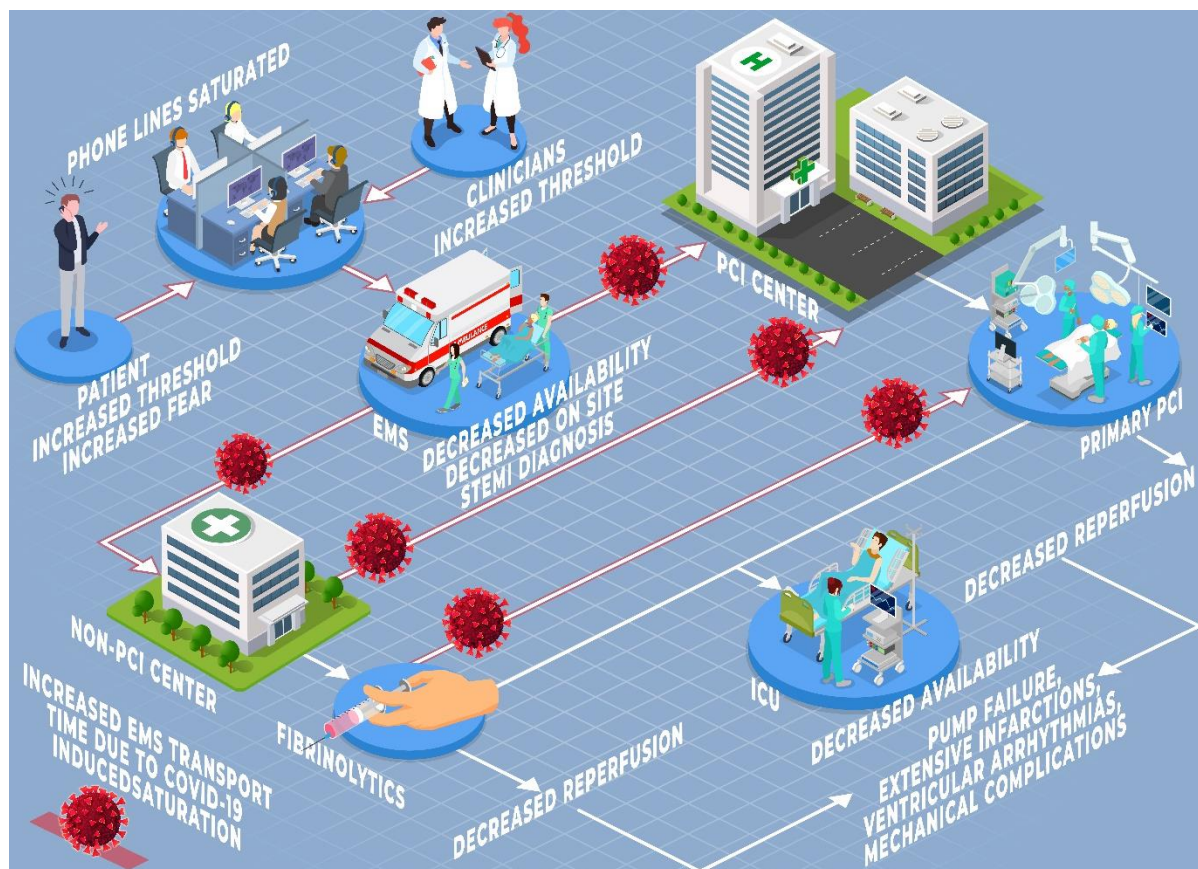


Figure. Primary Percutaneous Coronary Intervention (PCI) and coronavirus disease (2019): Delays in catheterization during acute coronary syndrome from Emergency Medical Services (EMS) to stenting.

PCCI is the current standard of care for patients who present to PCI centers, within the 90 minutes of first medical contact. Jie Zeng, Huang, and Pan reported a balanced protocol from Sichuan Provincial People's Hospital in a letter to *Intensive Care Medicine* (4). To bolster awareness of balancing AMI among patients affected by the epidemic, it is essential that they choose the nearest center that offers PPCI. The report highlights the importance of avoiding public transportation and adopting principles of maximum protection (4). Further, patients with AMI with fever and respiratory symptoms ought to visit the fever outpatient clinic. Once an epidemiological history is obtained, the patient is admitted to the isolation ward for the rapid nucleic acid test. This is a leading cause of delay for times of STEMI emergency reperfusion. A modulation of US intervention care is essential for catheterization laboratory protocols (4,5). Based on Sichuan's experiences, a protocol may be adopted for patients who are at high risk or confirmed cases of COVID-19 to visit the laboratory on a case-by-case basis. STEMI rates have reduced during the COVID-19

pandemic, partly due to the lack of access to emergency departments or risking hospital exposure (5,6). The hindrances to PCI are tripartite. First, patients presenting to hospitals without PCI-capacity are subjected to delays for PPCI or refusal. Second, patients presenting directly to hospitals with PCI-capacity in ambulances are not receiving benefits of prehospital cardiac catheterization laboratory activation. Third, evaluations by the emergency departments are prolonged due to additional screening for COVID-19 as the presentations may confound with the interpretation of ST-segment elevation. Delays in catheterization curing acute coronary syndrome are noted from Emergency Medical Services (EMS) to the stenting process (Figure).

Based on the consensus statement by the American College of Cardiology (ACC), American College for Emergency Physicians (ACEP), and the Society for Cardiovascular Angiography and Interventions (SCAI), it is critical to inform the public to call the emergency medical system for AMI symptoms and obtain the appropriate level of care (7). The use of PCI in STEMI patients must be continued to avoid reperfusion therapy.

Before transferal to a PCI center, it is essential that the established COVID-19 infection be discussed. The statement notes that fibrinolysis is to be carried within 30 minutes of diagnosis and a transfer to rescue PCI is made when necessary (7). The use of a pharmacoinvasive approach may be considered only if PPCI is not feasible.

Conclusion

COVID-19 has posed unprecedented challenges to public health; the immediate threat is linked to morbidity and mortality related to the infection, and the masked threat is the waning attention and resources utilized for the care of other diseases. Pertaining to STEMI care, first medical contact is essential to ensure quality metrics for delivery of care and targeting clinical decisions, and not merely the in-hospital door to balloon time. While a focus on using prehospital time metrics is essential, a rigorous study of quality measures in-hospital processes is recommended (2,5). The best outcomes are linked to ensuring that the first medical contact and treatment delay is shortened. This may help in improving cases with delayed presentations, positively impacting case-by-case outcomes, and increasing awareness of current therapies in practice. The present work highlights that time is critical in the treatment of STEMI during the COVID-19 outbreak, particularly in high-risk patients as they may have poor outcomes. There are methodologies to expedite this process and ensure timely presentation and positive outcomes. Offering reperfusion therapies and PPCI is required but does not cover for external factors disrupting the patients' admission workflow. First medical contact is the main time target, and reducing treatment delays improving patient outcomes in AMI patients with

STEMI should be the next immediate objective in healthcare systems worldwide.

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