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Editorial

Awareness to Control Dengue Fever

Mohsin Masud Jan
Editor

In early 2019, the World Health Organisation (WHO) included dengue fever among the top 10 global public health threats. "Widespread dengue infections across the world are largely attributable to climate change. Currently, half of the world population residing in 125 countries is at risk.

Many other countries in the region, Pakistan faced a dengue fever upsurge in 2019. The carrier mosquito can't fly more than 100 metres in its lifetime of around 20 days. It is born in houses and lays eggs there or at nearby places.

Dengue mosquito landed in Pakistan in 1994 along with a consignment of tyres. It affected Karachi in 2005 and a major outbreak occurred in 2011 when around 27,000 people were infected with the disease.

Community awareness can create a major obstacle to dengue fever spread can reduces the number of cases.

Dengue fever can lead to a severe flu-like illness. It is caused by four different viruses and spread by Aedes mosquitoes. The symptoms range from mild to severe. Severe symptoms include dengue shock syndrome (DSS) and dengue hemorrhagic fever (DHF).

The course of infection is divided into three phases: febrile, critical and recovery. The febrile phase involves high fever, potentially over 40°C (104 °F), and is associated with generalised pain and a headache; this usually lasts two to seven days. Nausea and vomiting may also occur. Symptoms of dengue fever include severe joint and muscle pain, swollen lymph nodes, headache, fever, exhaustion and rash.

In about 5 percent of people with dengue fever, the disease goes into a critical stage. The critical phase usually lasts for a day or two. During this stage, plasma (the liquid part of blood) can leak out of the body's smallest blood vessels.

The mosquito becomes infected when it takes the blood of a person infected with the virus. After about one week, the mosquito can transmit the virus while biting a healthy person. However, a person infected and suffering from dengue fever can infect other mosquitoes.

Dengue fever cannot spread directly from person to person. Since several viruses can cause dengue fever, someone can get the disease more than once. Dengue fever can be diagnosed by isolation of the virus, by serological tests.

Diagnosis of acute or recent dengue infection can be established by testing serum samples during the first five days of symptoms and/ or early convalescent phase (more than 5 days of symptoms.)

Patients suffering from high fever are often put through a series of tests to detect the cause of fever.

A flat, red rash may appear over most of the body two to five days after the fever starts. A second rash, which looks like the measles, appears later in the disease. Infected people may have increased skin sensitivity and are very uncomfortable.

Some develop dengue hemorrhagic fever after the initial fever declines — a more severe form of the illness that can cause organ damage, severe bleeding, dehydration and even death. But with early treatment, the mortality rate for all dengue fever is currently less than 1 percent.

There is unfortunately no vaccine or cure for dengue fever, so if you think you have it, rest, drink plenty of fluids and take a pain-reliever with acetaminophen and avoid medicines with aspirin, which could worsen bleeding. The symptoms and signs may last about one to two weeks with complete recovery, in most cases, in a few weeks.

Special attention needs to be given to these warning signs as it could lead to severe dengue:

- Severe abdominal pain.
- Persistent vomiting.
- Bleeding gums.
- Vomiting blood.
- Rapid breathing.
- Fatigue/ restlessness

If left untreated, dengue hemorrhagic fever is more likely to progress to dengue shock syndrome. Common symptoms in impending shock include abdominal pain, vomiting, and restlessness. Patients also may have symptoms related to circulatory failure.

Fruits: When not able to eat normal solid food, increase intake of fresh fruits such as banana, apple, pomegranate, citrus and guava. They help replenish minerals and vitamins lost in vomiting or as a result of high fever.

Protein rich food: Milk, egg and other dairy products must be consumed to battle with this virus. Non-vegetarians can go with the fish and chicken in a good quantity once they start recovering from the fever.

Soups: Hot soup intakes will enhance the strength and help fight the joint pain.

The best foods to recover from dengue fever are papaya, broccoli, which is an excellent source of Vitamin K and helps regenerate blood platelets, pomegranate, which is rich in essential nutrients and minerals, and spinach.

Some dengue patients start eating kiwi fruit or juice of papaya leaf or take goat milk. These fruits and milk strengthen the immune system and keep the patient hydrated. But if a dengue patient is having a lot of kiwi, his throat can get sour and develop some problem.

Community awareness is necessary for dengue fever.

Assessment of Skeletal Maturity by Using Mandibular Second Molar Calcification

Nazish Amjad[1], Muhammad Hasnain[1], Shahzonia Tariq[1], Haseeb Alamzeb[1], Mussab Irfan[2] and Afshan Bibi[3]

ABSTRACT

Objective: To correlate the mandibular second molar calcification stages as seen on OPG with CVM stages as seen on lateral cephalogram.
Study Design: Cross-sectional study.
Place and Duration of Study: This study was conducted at the Department of Orthodontics, Dental College HITEC-IMS, Taxilla Cantt from August 2021 to October 2021.
Materials and Methods: OPG and Lateral cephalograms of 100 patients reporting to department of Orthodontics for orthodontic treatment were evaluated and compared. SPSS software was used for statistical analysis. Spearman rank order correlation coefficient was calculated for determining the correlation between the two methods.
Results: A strong correlation (r =0.768) was found between CVM and DI stages. DI stage E was found corresponding to CS 1 and CS 2. Stage F corresponded to CS 2 (50.0%) and CS 3 (42.7%). Stage G corresponded to CS 3, 4 and 5. DI Stage H was found corresponding to CS 5 and CS 6 of the CVMI.
Conclusion: A strong correlation is found between DI stages of mandibular second molar and CVM stages. The mandibular second molar calcification stages can be utilized as a reliable indicator to assess skeletal maturity.

Key Words: DI stages, Orthopantomogram, Growing patients, CVM stages, Lateral cephalogram.

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INTRODUCTION

Successful diagnosis, treatment plan and treatment execution of a growing patient demands a thorough understanding of the concepts of growth and development. Age estimation of the patient plays a pivotal role in the inter-disciplinary treatment of orthodontics, pediatric and restorative dentistry, surgical management and dental implant placement. A variety of biological indicators can be used to study the skeletal maturity of an individual.[1] Teeth represent useful material for age estimation. Tooth calcification is known as a reliable criterion for dental age determination as it relies on distinct features of tooth morphology and it utilizes the ratio of root length and crown height.

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Demirjian et al introduced a method to determine the calcification stages and this method is in common practice these days.[2]
The correlation of tooth calcification stages with the skeletal maturity of an individual has been reported previously.[3–5] Perinetti et al[6] and Sukhia et al[7] have suggested that evaluating the dental maturation is helpful in diagnosing the pre-pubertal growth phase only but Toodehzaeim et al[8] have found it useful in diagnosis of the post-pubertal phase. on the other hand, concluded that tooth mineralization stages are helpful in diagnosis of both pre-pubertal as well as post-pubertal growth stages.[9]
Many studies have used mandibular canines[10], second premolars[11] or third molars[12] and evaluated correlation with skeletal age. On the other hand, literature has shown that mandibular second molar calcification stages are also reliable indicators to assess skeletal maturation.[13] This tooth can be preferred over other teeth as the course of its development is continued during the growth spurt period which is our focus of interest. With maxillary molars, estimation errors occur more frequently due to the overlap with other anatomic structures found in this region. This overlap presents difficulty in observing the maxillary molar roots.[14]

Third molars are also not reliable for age assessment as they are known as the most common congenitally missing teeth.

The rationale of this study was to assess the level of skeletal maturity of an individual by observing the mandibular second molar calcification stages on panoramic radiograph which is one of the most commonly advised radiographs for orthodontic and restorative treatment, by evaluating its correlation with CVM stages as seen on Lateral cephalogram. In this way, one can assess skeletal maturation of patients without exposing the patients to un-necessary radiations in accordance with the ALARA principle.

MATERIALS AND METHODS

After approval from institutional Review Board (IRB), Lateral cephalometric radiograph of each patient reporting to the Orthodontic department for Orthodontic treatment were evaluated for CVM stages by two registrars to overcome observer bias. DI stages of mandibular second molar were evaluated on panoramic radiographs according to the method described by Demirjian et al. All the assessments were verified by a colleague and recorded on a performa**.**

Data Analysis: Statistical analyses were performed using the SPSS version 21.0. Quantitative variables like chronological age were calculated in means and standard deviation. Qualitative variables like gender, CVM stage, and mandibular second molar calcification stage were calculated in frequency and percentages. The relationship between mandibular 2nd molar calcification stage and CVM stage was found by calculating Spearman rank order correlation coefficient. Stratification was used to control the effect of modifiers such as age and gender. Post stratification chi-square was performed.

RESULTS

Total 100 patients with age ranging from 10 to 18 years (mean age 13.24 years) were included in this study. Frequency and percentages of both male and female patients were 50 (50.0%). Table 1 shows age distribution of the patients.

Table No.1: Age distribution of the patients

Age(years)	Frequency	Percentage
10-12	41	41
13-15	49	49
16-18	10	10
Total	100	100.0

Table No. 2: Correlation between CVM and DI stages

		Males		Females		Total	
		CVM Stage	DI Stage	CVM Stage	DI Stage	CVM Stage	DI Stage
Spear-man's Rho	Correlation coefficient	1.000	.821	1.000	.648	1.00	.768
	Sig. (2 tailed)		.000		.000		.000
	N	50	50	50	50	100	100

Table No.3: Association between CVM and second molar calcification stages

CVM Stage	DI stage E	DI stage F	DI stage G	DI stage H	Total
	Frequency(Percentage)				
CS 1	2(40.0%)	3(60.0%)	0(0.0%)	0(0.0%)	5(100.0%)
CS 2	6(30.0%)	10(50.0%)	4(20.0%)	0(0.0%)	20(100.0%)
CS 3	0(0.0%)	6(42.9%)	8(57.1%)	0(0.0%)	14(100.0%)
CS 4	0(0.0%)	4(25.0%)	10(62.5%)	2(12.5%)	16(100.0%)
CS 5	0(0.0%)	1(3.3%)	15(50.0%)	14(46.7%)	30(100.0%)
CS 6	0(0.0%)	0(0.0%)	4(26.7%)	11(73.3%)	15(100.0%)

Table No.4: Calculations of the associations between CVM and second molar calcification stages

		CS1	CS2	CS3	CS4	CS5	CS6	Chi Square
		Frequency(Percentage)						
Males	DI Stage E	2(40.0)	5(33.3)	0(14.3)	0(0.0)	0(0.0)	0(0.0)	64.93
	DI Stage F	3(60.0)	7(46.7)	2(28.6)	1(12.5)	0(0.0)	0(0.0)	
	DI Stage G	0(0.0)	3(20.0)	5(71.4)	6(75.0)	4(36.4)	0(0.0)	
	DI Stage H	0(0.0)	0(0.0)	0(0.0)	1(12.5)	7(63.6)	4(100.0)	
	Total	5(100.0)	15(100.0)	7(100.0)	8(100.0)	11(100.0)	4(100.0)	
Females	DI Stage E	0*	1(20.0)	0(0.0)	0(0.0)	(0.0)	0(0.0)	40.26
	DI Stage F		3(60.0)	4(50.0)	1(14.3)	1(5.3)	0(0.0)	
	DI Stage G		1(20.0)	4(50.0)	5(71.4)	11(57.9)	4(36.4)	
	DI Stage H		0(0.0)	0(0.0)	1(14.3)	7(36.8)	7(63.6)	

	Total		5(100.0)	8(100.0)	7(100.0)	19(100.0)	11(100.0)	
*No female subject was found having CS1.								

A strong correlation (r =0.768) between CVM and DI stages was found as shown in Table 2. A strong correlation (r =0.821) was found in males whereas a moderate correlation (r =0.648) was found in females as shown in Table 3. Table 3 shows the association between CVM and second molar calcification stages. DI stage E was found corresponding to CS 1 and CS 2 which signifies the pre–pubertal period. Stage F correlated with CS 2 (50.0%) and CS 3 (42.7%). Stage G corresponded to CS 3, 4 and 5. Stage H was found corresponding to CS 5 and 6 suggesting insignificant/no remaining growth.

Calculations of the associations between CVM and second molar calcification stages were separately performed for both genders to control the effect of gender (modifier) by stratification as shown in Table 4. Slightly more advanced dental maturation for the same CVM stage was found in males as compared to the females.

DISCUSSION

During a routine dental treatment, dental maturity as a method of growth evaluation offers an advantage of easy assessment. The use of specialized radiographs (hand-wrist radiographs) results in high radiation exposure time and dose which makes their use debatable keeping in view the ALARA principle. The fact that panoramic radiographs are easily available and that dental calcification stages are easy to appreciate makes it practical for resorting to assess skeletal maturity without advising any additional radiograph. Therefore, this study utilized the dental calcification stages described by Demirjian et al. This method involves evaluating the root lengths relative to crown height instead of focusing on their absolute lengths so that the reliability of this assessment is not affected by elongated or foreshortened projections of these teeth.

Correlation of tooth calcification stages with the skeletal maturity is reported to be high in many studies.[2,8,11,15,16–19] On the other hand, Perinitti et al[20] and Saglam et al[21] found low or insignificant correlations. Differences in the methods of evaluation may contribute towards this lack of agreement. Variability in the results may also be caused by age, number and racial background of the subjects which in turn are conditioned by factors such as climatic conditions, ethnicity, nutrition quality, socioeconomic background and level of industrialization.

Mithun et al[15] found a strong correlation (C*=0.851 for males and 0.882 for females) between DI and CVM stages. Results of this study support our findings (r = 0.821 for males) where as in contrast to this study, we found a moderate correlation in females (r= 0.648). DI stage E corresponded to CS 2 indicating pre–pubertal growth stage and DI stage F corresponded to CS 3 showing peak of pubertal growth spurt. DI stages G and H were associated with CS 4, 5 and 6 indicating end of pubertal growth.

In 2020, Toodehzaeim et al[8] found a strong correlation between the two parameters in Iranian population. The correlations were 0.819 for females and 0.805 for males which is comparable to our study. The males were in stage G and females were in stage F during the growth spurt stage. However according to this study, these stages are helpful in identifying the post pubertal growth phase only. Similar studies have been carried out in Pakistan by Kamal[19] and Raza et al[13] and the results in both the studies support our findings.

The findings of Sushil[1] et al and Uysal et al[22] indicated that with respect to the skeletal maturity stages, males tend to be advanced than females in tooth calcification. These findings are also consistent with our results. The results of this study are also in accordance to the previous study done by Surendran et al.[23] Thus DI stages are helpful in assessment of pre-pubertal and post-pubertal growth phases.

The results of this study cannot be generalized because of the small sample size and because of the single-institute nature of study. Moreover, the study did not aim to explore the reasons for the potential association between DI and CVM which remains a gap for future researchers. Although the distribution of sample was not even in different groups of DI and CVM, the valuable lessons learnt from this study might contribute towards minimizing the unwanted radiation exposure to the patients.

CONCLUSION

A strong correlation exists between mandibular second molar DI stages and CVM stages. The skeletal maturity of an individual can be assessed by means of mandibular second molar calcification stages.

Author's Contribution:

Concept & Design of Study:	Nazish Amjad
Drafting:	Muhammad Hasnain, Shahzonia Tariq
Data Analysis:	Haseeb Alamzeb, Mussab Irfan, Afshan Bibi
Revisiting Critically:	Nazish Amjad, Muhammad Hasnain
Final Approval of version:	Nazish Amjad

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Prevalence of Dental Pain During Pregnancy

Dental Pain During Pregnancy

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

ABSTRACT

Objective: The purpose of this study was to find out how often oral pain is during pregnancy.
Study Design: Cross-sectional observational study
Place and Duration of Study: This study was conducted at the Dental OPD of Chiniot General Hospital Korangi Karachi from Nov 2019 to July 2020 for a period of nine months.
Materials and Methods: This study was initially designed to include 150 pregnant females but due to COVID -19 situation and OPDs closure restrict many pregnant females for their dental check-ups and appointments in Dental OPDs. Thus, the data collected of 90 participants including all stages of pregnancy and the analysis was done on the results of 90 participants. Before the commencement of data collection, each participant was given an informed consent.
Results: Among the study participants (n=90) who sought dental care, 64 (71.1%) presented with dental pain while 26(28.9%) presented with periodontal symptoms.
Conclusion: A high prevalence of dental pain was observed among pregnant women and dental caries was the most specific determinant of the dental pain.
Key Words: Dental pain, Pregnancy, Dental caries, Oral hygiene status

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INTRODUCTION

Pregnancy is a period during which a woman is evolving, she undergoes many changes and adjustments in her body. During pregnancy, a female is experiencing hormonal, biochemical, and physiological alterations in the body due to which many systemic changes occur. The oral cavity is also affected like general health conditions during the gestational period and is highly vulnerable for oral mucosal changes that may be responsible for many dental problems. This may cause orofacial pain. When foetal growth reduces the stomach's volumetric capacity in the third trimester, pregnant women frequently increase the frequency and quantity of carbohydrate ingestion. Increased tooth plaque accumulation, acid generation, and dental decay are all linked to these changes.

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Both the general and oral health of pregnant women got affected due to physiological and hormonal fluctuations. Increase in levels of estrogen and progesterone causes dilation and increase permeability of blood vessels, lowering the immune response thus reducing host immunity and cause more vulnerability towards oral infections and inflammation. Increase in progesterone and estrogen may lead to hyperemia, edema, bleeding, and increased risk of bacterial infections in oral tissues. Pregnant women are more prone to gingivitis, tooth mobility, dental caries, and erosion, and should undergo preventative oral health care as a result. Due to episodes of acute oral discomfort, pregnant women commonly seek emergency dental care. Limits and restrictions that patients and providers face during pregnancy influence dental care. Fear and worry about dental treatment, a lack of information about dental disorders, and misunderstandings about the influence of dental therapy on foetal development are all reasons why pregnant women avoid dental care. Furthermore, many dental professionals are unsure if conducting dental treatments on pregnant women is safe . Prenatal dental treatment is not typically recommended by obstetricians. Despite the fact that tooth discomfort and oral health assistance during pregnancy are significant dental outcomes, in dental care populations, their prevalence and relationship to risk factors have not been adequately studied. This descriptive observational study investigated the

prevalence of dental pain during pregnancy, its connection with sociodemographic variables and oral health problems, and prenatal dental treatment history in a population of pregnant women in Karachi.

MATERIALS AND METHODS

An observational cross sectional study was conducted in Chiniot General Hospital Korangi Karachi. Ethical approval from Ethical Review Board Szabist University was obtained and a permission letter was obtained from Chiniot General Hospital Korangi Karachi for conduction of the research, with the aim to determine the prevalence of dental pain and the associating factors including the major determinant responsible for that pain. The sample size was estimated using Open epi sample size calculator by taking statistics for dental pain as 54.9% (1), margin of error as 8% and 95% confidence level. For this study data was obtained from pregnant females reported with dental pain. All pregnant females aged between 18 to 45 years in all stages of pregnancy coming for routine dental consultations in Dental OPD or emergency department were included. 140 to 150 estimated sample size of pregnant females was calculated. The Sampling technique used was Non-Probability Consecutive Sampling Technique. Consecutive sampling is a sampling technique in which every subject meeting the criteria of inclusion is selected until the required sample size is achieved, the reason for selecting this sampling technique is due to limited time period for data collection and the number of pregnant females visiting dental clinic is also very limited, so keeping time interval in mind I chose consecutive sampling and include every pregnant female visiting dental clinic having dental pain and other dental issues that fits in the inclusion criteria of my study. This study was initially designed to include 150 pregnant females but due to COVID-19 situation and OPDs closure restrict many pregnant females for their dental check-ups and appointments in Dental OPDs. Thus, the data collected of 90 participants including all stages of pregnancy and the analysis was done on the results of 90 participants. Before the commencement of data collection, each participant was given an informed consent. The details of the study were explained and they were not forced to participate if not willing to. From all the participants that were approached, only 2 pregnant females reported with dental pain and were known cases of diabetes mellitus and one patient who refused to be the part of study were excluded. The study participants were interviewed and asked questions about the sociodemographic data that includes age, residence, educational status, marital status, income status of family. They were asked about their presenting complains due to which they need to visit dentist. Pregnancy status (Gravida and trimester) were also asked from the patients. Dental examination was done by trained clinical experts in Dental care unit in Chiniot General Hospital Karachi. Patients were examined while seated on dental chair. The oral hygiene status was then evaluated, presence of visible plaque and calculus was also investigated, gingival bleeding on probing was also examined, carries status was also evaluated that how many carious teeth are present, is the same tooth pointed by patient having dental pain is carious or not. Already treated, filled, extracted, RCT treated teeth were also examined, any trauma history, gingival swelling (localized, generalized), extra oral swelling was also investigated.

Data was analysed by using SPSS software version 21.0. Mean of the data was reported for numeric variables. Frequency and percentage were reported for nominal and categorical variables. Fisher exact test was applied to assess the significance among appropriate variables.

RESULTS

All recruited pregnant women agreed to participate in the study (n = 90; 100 % response rate). Most (44.4 %) of the participants were aged 26–30 years and had obtained undergraduate diplomas (32.2%). The majority (73.3%) of respondents were housewives and 64.4% of them belonged to a middle socioeconomic background. Most (40.0%) women were in the second trimester of pregnancy and 35.6% were expecting their first child. Among the study participants who sought dental care, 71.1% presented with dental pain while 28.9% presented with periodontal symptoms. Although majority (88.9%) of the respondents did not have any comorbidities, 10% of the women had pre-existing hypertension. 78.9% of the participants had difficulty visiting the antenatal dental clinic. The study population are shown in table.

Among the 64(71.1%) participants who presented with pain, 38(42.2%) women exclusively complained of dental pain. 33.3% of the complains were of acute illness i.e. duration of symptom was of less than one week. Dental caries, present in 53.4% of the participants, was the most common associating factors with the history of presenting complain followed by gingivitis (27.8%) and 7.8% presented with both aforementioned associations. Within the study group 77(85.6%) of the women had no pregnancy related complications while 13(14.4%) had gestational diabetes. Details regarding the current antenatal dental visit are present in table 3.

When questioned about dental pain during the current pregnancy, 64 women (71.1%) responded that they have dental pain. 52 women (77.6%) stated that the pain started during gestation and 15 women (22.4%)

stated that they had pain before gestation which is exaggerating during pregnancy. Only 37.8% visited a formal dental set up to address their complaints during their previous pregnancies. The most common reason for the visit during ongoing pregnancy and previous pregnancies was dental pain (67.6%) followed by restorative procedure (14.7%), periodontal procedure (8.8%) surgical procedure (5.9%) and general checkup (2.9%) as illustrated in table: 2.

Table No.1: Demographics

Variable	n(%)
Age groups	
<=25 years	18(20.0)
26-30 years	40(44.4)
31-35 years	27(30.0)
>=35 years	5(5.6)
Education level	
Graduate	29(32.2)
Intermediate	15(16.7)
Masters	14(15.6)
Matric	15(16.7)
Middle school	8(8.9)
Uneducated	9(10)
Employment status	
employed	22(24.2)
Housewife	66(73.3)
Student	2(2.2)
Family income(a)	
High	4(4.4)
Low	28(31.1)
Middle	58(64.4)
Parity status	
Primigravida	32(35.6)
Multigravida	58(64.4)
Stage of pregnancy during dental visit	
first trimester	23(25.6)
second trimester	36(40.0)
third trimester	31(34.4)
Comorbids	
None	80(88.9)
hypertension	9(10.0)
Hepatitis C	1(1.1)
Difficulty in dental visit during recent visit	
Yes	71(78.9)
No	19(21.1)

Table No.2: Dental pain history for on-going pregnancy and previous pregnancies.

Dental pain during current pregnancy	
No	23(25.6)
Yes	64(71.1)
When did the pain begin.	
During gestation/Before gestation	
during gestation	52(77.6)
before gestation	15(22.4)
Previous visit to the dentist during pregnancy	
No	56(62.2)
Yes	34(37.8)
Reason for previous visit during pregnancy	
Restorative procedure	5(14.7)
General check up	1(2.9)
Periodontal procedure	3(8.8)
Surgical procedure	2(5.9)
Dental pain	23(67.6)

Table No.3: Presenting Complain

Variable	n(%)
Presenting complain of current visit	
Dental pain	64(71.1)
Periodontal symptoms	26(28.9)
Associated symptoms with dental complain	
limited mouth opening	2(2.7)
Extra oral swelling	17(23.0)
Sensitivity	4(5.4)
Associated symptoms with periodontal complain	
Bleeding gums	32(43.2)
gingival pain	4(5.4)
Halitosis	3(4.1)
Swollen gums	12(16.2)
Duration of presenting complaint	
< 1 week	30(33.3)
1 week	7(7.8)
2 weeks	6(6.7)
3 weeks	2(2.2)
4 weeks	8(8.9)
>4 week	37(41.1)
History of presenting complain	
Restoration dislodgment	2(2.2)
RCT treated tooth	1(1.1)
Impacted tooth	4(4.4)
Gingivitis	25(27.8)
Fixed Prosthesis dislodgment	1(1.1)
Dental Trauma	2(2.2)
Dental Caries and gingivitis	7(7.8)
Dental Caries	48(53.4)
Pregnancy general health complication	
No	77(85.6)
Yes(Gestational Diabetes)	13(14.4)

After obtaining the history from the patient general discussion regarding oral hygiene concluded that 55.6% did not know the importance of oral hygiene. Only 21.1% of the women brushed teeth twice a day (as recommended) while 6.7% never brushed their teeth. Abstinences from betelnut chewing was advised and regarding their current habits 31.1% used betel nut regularly.90% of the respondents had previous good experiences during dental visits and 55.6% felt anxious during dental check-up.

Only 45.6% of the women visited the dentist before pregnancy mostly for restorative procedure (34.2%) followed by periodontal procedure (29.3%) while dental pain before pregnancy was reported as low as 19.5%.

DISCUSSION

Due to many changes in the body, weakness and changed lifestyle pregnant females neglect the routine dental care and oral hygiene maintenance, which my further worsen their oral conditions and results in adverse pregnancy outcomes. Prenatal health care providers must have clear knowledge about oral health care and they must acknowledge the importance of good oral hygiene and good oral health during pregnancy. They must advice dental visits to pregnant females for early diagnosis and treatment strategies in order to improve the Oral Health Related Quality of Life. Several studies have demonstrated the importance of dental care during pregnancy. However, in a newly issued guideline for the implementation of prenatal care, the World Health Organization does not list oral health as a core component. The current study discovered a significant rate of dental pain among pregnant women, emphasising the significance of including oral health care within prenatal treatment. In this study the prevalence of dental pain among pregnant women was high (71.1%). Amongst the 64 (71.1%) participants who presented with pain, 38 (42.2%) women exclusively complained of dental pain, 33.3% of the complains were of acute illness i.e. duration of symptom was of less than one week. 52 women (77.6%) stated that the pain started during gestational period and only 15 women (22.4%) stated that they had pain before gestation which is exaggerating during pregnancy. In a previous study which was conducted by a prenatal oral health program on pregnant women of all stages of pregnancy reported that 54.9 % women had dental pain during pregnancy, 84.9 % women reported that pain was initiated during the gestational period it was never experienced by them before. Some studies reported 25.8 to 44 % pregnant women with dental pain. Dental visits during pregnancy are reported at varying rates among nations, with Germany reporting the highest rate at 49 percent, Kuwait has a 50%, in the United Kingdom, the figure is 61 percent, in the United States, the percentage ranges from 35 to 43 percent and 90 % in Denmark . Despite the fact that dental treatment is offered free of charge to pregnant women in the United Kingdom, 39% of women did not visit a dentist throughout their pregnancy. A Study conducted on general population to evaluate the dental pain or tooth ache prevalence and they reported a range of 7-32 % cases with severe tooth ache. Gingival bleeding , bad oral hygiene , dental caries are all determinants of dental pain , poor oral hygiene and visible plaque may be a contributing factor as dental plaque if not removed properly may cover an activated carious lesion which continue growing thus resulting in dental pain. A previous study by Acharya noticed that painful mouth and difficulty in eating and chewing have worse effects on quality of life of a pregnant female. Pregnant women most commonly became the sufferer of dental pain due to several dental problems occurring during their gestational periods. Due to several reasons pregnant females avoid the utilization of Dental Services like fear and anxiety, low perception about the safety of dental treatments and various other misconceptions. Some women also do not utilize dental services due to family restrictions.

CONCLUSION

Gestational period is a unique period in a woman's life but it may cause many physiological, physical and mental changes in a woman. All these changes and transformations supports the formation and maturation of a new life. This Study is beneficial as it provides a baseline data about high prevalence of dental pain and dental caries among pregnant women which will be helpful in creating awareness and developing educational programs and strategies for expectant mothers.

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Incidence of Erectile Dysfunction in Enlarge Prostate Patients

Shahzad Ali, Naresh Kumar Valecha, Mohammad Mansoor, Saeed Ahmad Khan and Yasir Khan

ABSTRACT

Objective: To determine the frequency of erectile dysfunction in patients with benign prostatic hyperplasia.
Study Design: Descriptive Study
Place and Duration of Study: This study was conducted at the Department of Urology, Jinnah Postgraduate Medical Centre (JPMC), Karachi, Pakistan for a period of six months from April, 2020 to October, 2020.
Materials and Methods: It was possible to include everyone who met the inclusion criteria and visited JPMC Karachi. It was only after an explanation of the study's risks and benefits that informed consent was obtained. Five items were included in the questionnaire. Data was calculated using SPSS version 23.0.
Results: Mean ± SD of age was 54.9±8.4 years. In distribution of obesity, 71 (64%) were obese while 40 (36%) were non-obese. Diabetes mellitus was documented in 43 (38.7%) patients. Erectile dysfunction was documented in 21 (18.9%) patients.
Conclusion: It is to be concluded that erectile dysfunction is fairly common in patients with benign prostatic hyperplasia. Furthermore, our findings outline the need for future research to investigate those factors that could be considered as higher risk of erectile dysfunction

Key Words: Erectile Dysfunction, Benign Prostatic Hyperplasia, Lower Urinary Tract Symptoms

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INTRODUCTION

Sexual health is an integral part of overall health and quality of life. When it comes to erectile dysfunction (ED), it is described as a chronic inability to achieve and maintain an adequate erection for a satisfactory sexual intercourse.[1] If you or your loved one suffers from an eating disorder, you may be at risk for more significant health issues, such as coronary heart disease, which is a forerunner to ED.[2–4]

Benign prostatic hyperplasia (BPH) is defined as benign, noncancerous enlargement of the prostate caused by the growth of new stromal and epithelial cells. One of the most common disease that affects older men aged over 50 years and which leads to the symptoms of the lower urinary tract (LUTS-lower urinary tract symptoms)[5].

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In general, erectile dysfunction and BPH/LUTS both affect quality of life; therefore, preservation of sexual function is important and required sympathetic consideration in management of BPH in male patients.[6]

The development of ED and LUTS as a result of BPH is thought to be caused by a number of common pathogenic processes. An insight of the pathophysiology of these disorders can be gained by studying the pathways that connect chronic inflammation with an imbalance in sex steroid ratio[7-9].

In men, LUTS are frequently caused by BPH and are frequently attributable to histologic BPH. Age, BPE, hypogonadism, sedentary lifestyle, depression, hypertension and cardiovascular disease, hyperlipidemia, diabetes, obesity, and inflammation are all risk factors for LUTS in males[10-13].

The incidence of BPH and ED in older men increases with age[14]. According to the Massac husetts Male Aging Study (MMAS) data, the incidence of ED is 26 newly discovered in 1,000 men annually, and ED was present in all age groups, although there is evident correlation with age[15] Comorbidities such as cardiovascular disease, type 2 diabetes, dyslipidemia, and obesity are highly associated with LUTS/BPH and ED regardless of age[16]. Clinicians dealing patients with BPH and/or ED should have considered possibility that patient may have dyslipidemia, hypertension, metabolic syndrome and other associated conditions.

Since ED and BPH/LUTS are correlated, patient seeking consultation for one condition should also be screened for complaints about other condition, so that

patient management includes all possible associated conditions.

Physicians treating LUTS/BPH should be well aware of adverse effects affecting the sexual life of patients and sexual function should be fully evaluated prior to start of treatment and monitored through out to ensure that choice of treatment is appropriate.

Very scanty local studies are available in our local setup to assess the erectile dysfunction in patients with benign prostatic hyperplasia.

As different diseases have different prevalence in different areas of the world depending on the lifestyle, management, diet, socioeconomic and geographical location. That's why the applicability of international literature is not possible in our population and not be generalized in our population. The subjected results of the study will be shared with urologists to draw the conclusion whether the medical treatment for BPH is justified or not in terms of sexual health of the patient.

MATERIALS AND METHODS

This prospective descriptive study was conducted in department of urology at Jinnah postgraduate medical center, Karachi from April 18, 2020 to October 17, 2020. Men with symptomatic BPH having erectile dysfunction, aged between 50- 70 years were included in this study. Patients who had neurological disorder and did not give consent were excluded from the study. 111 Patients were selected from OPD, by using non-probability consecutive sampling. Informed written consent was taken prior to inclusion by them to be part of study. Initial bio data was recorded on predesigned proforma. Trans-abdominal ultrasound was used to evaluate the size of prostate. LUTS and their severity were recorded according to IPSS scoring system.

To evaluate erectile dysfunction, self- administered questionnaire for International index of Erectile Dysfunction was filled by each participant. The questionnaire consisted history of last 4 weeks, based on five items: 1. confidence in getting erection, 2. frequency of achieving erections hard enough for vaginal penetration, 3. frequency of maintaining erection after penetration, 4. ability to maintain erection to completion of intercourse, 5. How often it was satisfactory whenever you attempted. Each item had maximum score of 5 giving questionnaire a full score of 25. Erectile dysfunction was labelled as positive if the patient had IIEF-5 score of ≤ 21, and above 21 was considered as normal erectile function.

Data was entered and analyzed by using SPSS software version 23.0. Mean ± SD was calculated for age, weight, height and BMI. Frequencies and percentages were computed for obesity, hypertension, diabetes mellitus and outcome variable i.e. erectile dysfunction (yes/no). Post stratification, Chi-square/ Fisher's Exact test as appropriate was applied. A two-sided probability value ≤ 0.05 was considered significant.

RESULTS

Total 111 patients were included in this study, who full filled the criteria of inclusion. Mean age of the patients was 54.9±8.4 years ranging from 50 years to 70 years, while mean BMI was 26.5 + 5.6 kg/m^2. 64% of the patients were obese while 40% were non-obese. DM was present in 38.7% of the patients and HTN in 52.3% patients. Out of 111 patients, 21 patients (18.91%) had erectile dysfunction. Stratification of ED was done with age, DM, obesity and HTN that was statistically insignificant as shown in tables 1,2,3 and 4.

Table No.1: Stratification of Age Group with Erectile Dysfunction (N=111)

Age group [in years]	Erectile dysfunction		P-value
	Yes	No	
45 – 60	14 (12.6%)	70 (63.1%)	0.285
> 60	7 (6.3%)	20 (18.0%)	

Applied Chi-Square test

Table No.2: Stratification of Obesity with Erectile Dysfunction(N=111)

Obesity	Erectile dysfunction		P-value
	Yes	No	
Obese	13 (11.7%)	58 (52.3%)	0.827
Non-obese	8 (7.2%)	32 (28.8%)	

Applied Chi-Square test

Table No. 3: Stratification of Hypertension with Erectile Dysfunction(N=111)

Hypertension	Erectile dysfunction		P-value
	Yes	No	
Hypertensive	10 (9.0%)	48 (43.2%)	0.637
Non-hypertensive	11 (9.9%)	42 (37.8%)	

Applied Chi-Square test

Table No.4: Stratification of Diabetes Mellitus with Erectile Dysfunction (N=111)

Diabetes mellitus	Erectile dysfunction		P-value
	Yes	No	
Diabetic	8 (7.2%)	35 (31.5%)	0.946
Non-diabetic	13 (11.7%)	55 (49.5%)	

Applied Chi-Square test

DISCUSSION

The present study was based on a cross-sectioned outline of men with ages distributed between 50 and 70y, from outpatient department of tertiary care center for the treatment of urological diseases. These men were visited to OPD for lower urinary tract symptoms secondary to BPH.

It has been seen that ED is increasing with increase in age. The ED often is multifactorial, can be organic OR psychogenic in origin. While the etiology of BPH is not exactly determined[17].

Regardless of impact of age, co morbidity, differences in life style, the symptoms of BPH may be related to

ED in elderly men, according to epidemiological studies.[18]

Mechanism of action of α-1 adrenergic receptor is possible connection between these two diseases. The tone of the smooth muscle cells in the prostatic capsule and the neck of the bladder increases via these receptors, just as a penile erection dose. Noradrenaline and androgens causes contraction of smooth muscles, through adrenergic receptors which affect the process of relaxation of same, which would lead to erectile dysfunction.[19]

Although volume of prostate in BPH and its association to ED is indisputable, but precise mechanism is not yet confirmed.[20]

In most men, after age of 40 years, ED and BPH evolve as age related phenomena.[21]

Prevalence of ED in men increases under influence of age, BPH and comorbidities.[22,23] Erectile dysfunction (ED) was shown to be more common in men who had an increase in the severity of their LUTS/BPH. The findings of our study are comparable with different studies conducted by various researchers worldwide, few of which are discussed below.

The mean age noted in our study was 54.9±8.4 years. In the study of Valdivia JG, et al.[24] The mean age was noted as 51±14.7 years. Another study of Reddy SV, et al[25] noted age as 45.67±13.21 years. Ugalde-Resano R, et al[26] stated age as 49.48±14.1 years. In this study, the mean weight was 67.2±9.3 kg whereas mean height was 162.5±12.8 cm. Jimenez-Romero ME, et al[27] noted the mean weight as 78.5 kg and height as 167.5 cm. The mean body mass index was 26.7±5.6 kg/m^2. Ugalde-Resano R, et al[26] noted mean BMI as 28.54±5.6 kg/m^2. The studies of Jimenez-Romero ME, et al[26] and Park DS, et al[28] reported the BMI as 27.31 kg/m^2 and 24.4±2.4 kg/m^2 respectively.

In present study, out of 111 patients, 71 (64%) were obese while 40 (36%) were non-obese while hypertension was noted in 58 (52.3%) patients.

A multinational prospective study of sexual function and the comorbidities noted obesity in 36% and hypertension in 38% cases. Another study of Santos PR, et al[29] noted hypertension in 20 (41.6%) patients. In current study, diabetes mellitus was documented in 43 (38.7%) patients. The prevalence of diabetes in the study of Toluey M, et al[30] was noted as 307 (42.8%). Lakhani MS, et al[31] noted diabetes in 64 (45.1%) patients. In present study, frequency of erectile dysfunction among 111 patients was found to be in 21 (18.9%).

In order to confirm the link between BPH and ED, we feel that further international studies of men with LUTS/ BPH and no chronic illness are required, and that these studies should assess urinary symptoms and erectile function using IPSS and IIEF, respectively.

CONCLUSION

Erectile dysfunction and BPH are both frequent illnesses that have a high prevalence and a considerable negative impact on quality of life. As both conditions have multifactorial and complex etiologies, patients can have maximum benefits with multidisciplinary approach to treat Diabetes, Dyslipidemias, metabolic syndrome and coronary artery diseases. Furthermore, our findings outline the need for future research to investigate those factors that could be considered as higher risk of erectile dysfunction.

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Frequency of Hyperlipidemia in Patients Present with Erectile Dysfunction

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ABSTRACT

Objective: To determine the frequency of hyperlipidemia in patients present with erectile dysfunction (ED) at tertiary care hospital, Karachi.

Study Design: Descriptive Cross-Sectional Study

Place and Duration of Study: This study was conducted at the department of Urology, JPMC, Karachi from January, 2020 to December, 2020 for a period of year.

Materials and Methods: All married male from age 40 to85 years age, who presented in outpatient clinic and fulfilled inclusion criteria were included in the study. Brief history was taken and their erectile dysfunction was assessed by IIEF-5 Questioner. Fasting serum Lipid profile was sent of all the patients and serum TG levels > 150mg/dl were taken as a reference for diagnosing the hyperlipidemia. Associated risk factors for ED such as diabetes mellitus, high blood pressure, Coronary artery disease (CHD) smoking, Triglyceride Level and obesity were noted.

Results: Total 171 married male patients were included in this study with the mean age of 65.45±12.41 years ranging from 45 to 85 years. Their mean SBP and DBP were 153.04±21.26 mmHg & 83.78±13.7 mmHg while their mean BMI was 30.99±7.11 Kg/m^2. Their Serum fasting lipid profile like total Cholesterol, TGL, LDL, HDL, and VLDL was 157.61±48.48, 106.26±38.87, 93.02±36.73, 39.66±13.98 & 24.39±13.34 were noted. CAD was seen in 51 (31%) patients. In 40(23.4%) patients TG levels were found to be higher.

Conclusion: Hyperlipidemia is common in ED patients. These patients have a high risk of later developing CHD. Erectile dysfunction might therefore serve as sentinel event for coronary heart disease. In conclusion, we report a high prevalence of hyperlipidemia in men presenting with ED. The opportunity to screen for, diagnose and treat these and other cardiovascular risk factors at the time of assessment for ED has potential long-term benefits in this group of patients.

Key Words: Erectile dysfunction, Hyperlipidemia

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INTRODUCTION

Erectile dysfunction (ED), also called as insufficient penile erection, is leading sexual disorder in male.[1] ED is defined as inability to achieve or maintain penile erection to have good satisfactory vaginal intercourse.[2] Its prevalence is higher and 40% of the population is affected with ED.[3]It has been observed that it increase with age affecting male> 40 years mainly.[4]

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In reported previous literature, ED was to be higher in United States and Asia when compared to rest of the world.[5] It has been estimated that out of 322 million, about200 million males will suffer from ED only in Asia by 2025.[6,7,8]

This will cause too much burden over the health care system as well as economically. Factors which result in ED may be psychogenic and organic. Rigid erection at any sexual thought night or morning, while unable to attain erection at time of intercourse is purely directs mostly for psychogenic ED (PED). PED mainly present with sudden onset or short course of time while on contrary patient with organic ED (OED) mostly comes with slow and progressive course and long duration.[2] ED is found to be associated with numerous endocrine and metabolic conditions like Type 2 DM, hyperlipidemia, insulin resistance, metabolic syndrome

and testosterone deficiency.[9,10] Patients with ED may have decreased quality of life and high risk of depression and weakened psychological health.[11] ED is now being used as marker for Coronary Artery Disease(CAD).[2] Hyperlipidemia may be caused by excessive use of cholesterol rich diet or any congenital disease(Metabolic error). In literature, it is evident that hyperlipidemia is associated with ED.[12,13] Hyperlipidemia is strongly correlated with ED since for each rise in one mmol/L of serum cholesterol results in decrease in erectile function by 32%.[14] The aim of this study is to determine the frequency of hyperlipidemia in patients with ED in the local population which will help the clinicians in managing the patients with ED having raised serum lipid levels.

MATERIALS AND METHODS

This descriptive cross sectional study was conducted at department of Urology, JPMC, Karachi from 01-01-2020 to 31-12-2020. After taking approval from institutional review board committee. All male patients in between the age of 40 – 85 years, who had ED and having fasting serum Triglyceride level greater than 150 mg/dl were included in present study. Patients who were on psychotic medicine, lipid lowering agents and receiving antibiotics for infection were excluded from the study. Patients who had neurological and endocrinological disorders, alcoholics or drug abusers were also not the part of this study. Patients who were not giving consent were also excluded from the study. Nonprobability consecutive sampling technique used for sampling. Total 171 patients were included in this study who fulfilled the criteria. After written informed consent detailed history was taken from each patient. Their erectile dysfunction assessed by using IIEF-5 scoring system. Fasting serum lipid profiles were sent to the same laboratory. Associated risk factors like Diabetes mellitus (DM) Hypertension (HTN), Body mass index (BMI) and smoking history were also recorded. Data was collected in the prescribed proforma and entered and analyzed by using SPSS version-21. Descriptive statistics were recorded in terms of mean ±s.d of age, BMI, systolic and diastolic blood pressure and fasting lipid profile. Effect modifiers like age, DM, HTN, BMI, smoking and TGL were stratified by using appropriate chi square test and p-value of <0.05 was taken as significant**.**

RESULTS

Total 171 male patients were included in this study. Age of the patients was from 40 to 85 years (mean 63.45± 12.41 years. mean SBP and DBP were 153.04± 21.26 and 83.78 ±13.7 mmHg and mean BMI was 30.99 ± 7.11 kg/m^2. 40 patients were found to have higher TGL greater than 150 mg/dl. In 171 patients with ED, 129 patients had HTN and 90 patients had DM while 27 patients had history of smoking. On work up 35 patients were found to have coronary heart disease. Stratification were done for modifiers factors of age smoking, HTN, DM and CAD to see the effect on the outcome of hyperlipidemia using chi-square test and given in table one. Age and CAD were statically insignificant while DM, HTN and smoking were found to be statistically significant with hyperlipidemia.

Table No.1: Descriptive statistics of lipid profile in patients presenting with erectile dysfunction (n = 171)

Lipid Profile	Mean ± SD	Median	Maximum	Minimum
Total Cholesterol	157.61±48.48	148	332	53
TGL	106.26±38.87	99	327	39
LDL	93.02±36.73	89	252	22
HDL	39.66±13.98	38	106	10
VLDL	24.39±13.34	20	105	8

Table No.2: Comparison of Hyperlipidemia in patients presenting with erectile dysfunction among different study characteristics (n = 171)

Confounding Factors	Hyperlipidemia (TGL)			P-value
	Present n= 40	Absent n= 131	Total n= 171	
Age Groups				
<= 63 Years	22 [12.9%]	66 [38.6%]	88 [51.5%]	**0.609**
>63 Years	18 [10.5%]	65 [38%]	83 [48.5%]	
Total	40 [23.4%]	131 [76.6%]	171 [100%]	
Coronary artery disease (CAD)				
Yes	14 [8.2%]	39 [22.8%]	53 [31%]	0.531
No	26 [15.2%]	92 [53.8%]	118 [69%]	
Total	40 [23.4%]	131 [76.6%]	171 [100%]	
Family of History (CAD)				
Yes	13 [7.6%]	22 [12.9%]	35 [20.5%]	0.031*
No	27 [15.8%]	109 [63.7%]	136 [79.5%]	
Total	40 [23.4%]	131 [76.6%]	171 [100%]	
Diabetic Mellitus (DM)				
Yes	30 [17.5%]	60 [35.1%]	90 [52.6%]	<0.001*
No	10	71	81	

	[5.8%]	[41.5%]	[47.4%]	
Total	40 [23.4%]	131 [76.6%]	171 [100%]	
Hypertension (HTN)				
Yes	37 [21.6%]	92 [53.8%]	129 [75.4%]	0.04*
No	3 [1.8%]	39 [22.8%]	42 [24.6%]	
Total	40 [23.4%]	131 [76.6%]	171 [100%]	
Smoking Status				
Yes	11 [6.4%]	16 [9.4%]	27 [15.8%]	0.020*
No	29 [17%]	115 [67.3%]	144 [84.2%]	
Total	40 [23.4%]	131 [76.6%]	171 [100%]	

*P value is statistically significant

DISCUSSION

Sexual activity is a foremost segment of men's quality life. ED not only affects the sexual performance, along with this it badly affects couple/married relationship, self-confidence and mental health. As discussed earlier, ED can be physiologic (organic) or psychogenic in origin. Psychological disorders like depression, psychological stress and performance anxiety affects erectile function which usually are sudden in onset with short duration, while in organic disorders hormonal, vascular or neurogenic pathologies are responsible for ED. Among the organic disorders, vascular reasons are the most common affecting erectile function such as atherosclerosis of penile arteries. Impaired Endothelial function and peripheral artery is seen in patients with DM, HTN and CAD. Hyperlipidemia is also responsible for ED which is mostly due to hyperlipidemia induced atherosclerotic changes in the penile vessels as seen in patient of DM and HTN, which ultimately causes failure to relax endothelial cell of corvernosa resulting in impaired/ reduced blood flow in the penis. There are number of studies which suggest that hyperlipidemia is responsible for ED while some researchers are of opinion that hyperlipidemia doesn't cause ED. In a study[12], they found hyperlipidemia was present in 16 % of general population and 29 % in patients with ED and same findings were also seen in another international study.[13] Roumeguere et al[15] and Khurana et al[16] found that hyperlipidemia was present in 70.6% and 42% patients respectively with ED. In previous reported studies, it is observed that ED is found to be higher in aging male and consequently affecting their quality of life. There is now consensus on hyperlipidemia induced ED but it is still not clear which lipid value LDL, HDL, TGL or TC is responsible for ED. In one study it was seen that TC & HDL together cause ED in 4 % of the patient while 70.6% of the patients with ED were found to have raised TC in Roumeguere et al[15] study. They retrospectively assessed the male patients who presented in urology department with ED and found that 15% of the patients who were tested for hyperlipidemia had raised serum TC level.[17] While they[18] found that TGL were associated with ED, which is similar in our study but Moustafa et al[19] and Kim[20] results were contrary to our result. In present study, 23.39% of the patient had hyperlipidemia. Our finding of hyperlipidemia in patients with ED are almost consistent with international studies.[12,13] while on the contrary our results are much lower compared to Roumeguere et al[15] and Khurana et al[16] results. In a study, co-morbid like HTN, DM, CAD and smoking were also reported in patients with ED having hyperlipidemia which are consistent with present study except smoking.[17] Researchers have found that ED may be the first presentation and alarm for the CAD[15]similar findings were seen in another study which concluded that ED is correlated with ischemic heart disease as it antecede and point to the ischemic heart disease.[21] This is because both ED and CAD shares the same pathophysiology such as endothelial dysfunction and inflammation. ED is incorporated with increased chances of having ischemic events like myocardial infarction, cerebrovascular events leading to morbidity and mortality [22] Indeed, ED precedes a cardiovascular event by 2–5 years.[23] In one study, it was seen that 19 % patients with ED had found to have silent CAD documented on angiography suggesting cardiovascular evaluation in ED patients.[24] In present study 53 (31%) patients found to have CAD.

Although the contribution of hyperlipidemia in patients of erectile dysfunction (ED) may be slight in patients with multiple risk factors, improving serum cholesterol could help with ED symptoms. Initiating lifestyle changes to improve lipids could simultaneously improve other risk factors for ED such as hypertension, obesity, and blood sugar as well. Erectile dysfunction could be a window of opportunity for diagnostic and treatment of heart disease. There is a dearth of reliable figures for the prevalence of hyperlipidemia in Pakistan. This study will also look at common treatment modalities related to Erectile Dysfunction (ED). This study furthermore will also provide that on the basis of these results, clinicians take account of proper management of hyperlipidemia as a part of the treatment plan for erectile dysfunction.

CONCLUSION

Hyperlipidemia is not uncommon in ED patients. These patients have a high risk of later developing CAD. Erectile dysfunction might therefore serve as sentinel event for coronary heart disease. In conclusion, we report a high prevalence of hyperlipidemia in men presenting with ED. The opportunity to screen,

diagnose and treat these and other cardiovascular risk factors at the time of assessment for ED has potential long-term benefits in this group of patients.

Author's Contribution:

Concept & Design of Study:	Naresh Kumar Valecha,
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Effect of Rosuvastatin Alone and Combination with Omega-3 Fatty Acid on Cholesterol and Fasting Blood Glucose Levels in Hypercholesterolemic and Diabetic Patients

Aziz Ahmed Solangi[1], Gunesh Kumar[2], Naveeta Rathi[1], Nasreen Qazi[1], Muhammad Azhar Mughal[3] and Qamar Zaman[1]

ABSTRACT

Objective: To compare the effect of rosuvastatin and rosuvastatin omega-3 fatty acid on serum cholesterol and fasting blood glucose levels in hypercholesteremic and diabetic patients.

Study Design: Cross-Sectional Study

Place and Duration of Study: This study was conducted at the department of pharmacology and therapeutics with the collaboration of Cardiology OPD and ward LUHMS Jamshoro/Hyderabad for six months from March, 2020 to September, 2020.

Materials and Methods: Serum cholesterol & fasting blood sugar level was done from gel tubes bottles by using serum after centrifugation at 3,500 revolutions per minute for 10 minutes. The data was entered and analyzed using SPSS version 23.0.

Results: In this study total of 240 patients of hypercholesteremia and diabetics were studied. patients were divided into two groups as per treatment. Baseline serum cholesterol and fasting blood sugar were found to be statistically insignificant in both groups. After 30 days' average serum cholesterol was significantly decreased 201.55±28.19 mg/dL in group B, as compared to group A as 230.62±32.74 mg/dL (p-0.001). However, after 30 days' average of FBS was statistically insignificant. After 60 days of treatment, the average serum cholesterol was significantly decreased to 180.17±18.10 mg/dL in group B, as compared to group A as 210.59±25.44 mg/dL (p-0.001). However, after 30 days' average of FBS was decreased but still statistically insignificant according to study groups (p-0.451).

Conclusion: It was concluded that serum cholesterol significantly decreased among the combined treatment group**.** Administration of Omega-3 fatty acids play important role in preventing hyperglycemia among statin treatment patients**.**

Key Words: Serum cholesterol, FBS**,** rosuvastatin, mega-3 fatty acid

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INTRODUCTION

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All across the world, patients with or at risk for cardiovascular disease are prescribed statins (hydroxy-3-methylglutaryl coenzyme A reductase inhibitors) (CVD).[1] Cardiovascular disease (CVD) can be prevented in large part by lowering the level of LDL cholesterol in the blood. "Coronary heart disease risk equivalent": Diabetes is now widely accepted as a risk factor. [2] Individuals with type 2 diabetes are more likely to suffer from dyslipidemia, which has been linked to an increased risk of cardiovascular disease death in these patients (CVD). [2]

Diabetic patients with dyslipidemia are typically treated with statins as the first line of pharmacological intervention.

It is well accepted that statin medication lowers LDL-C levels, although other lipoproteins, such as HDL-C, also have a role.[3] Currently, seven FDA-approved statins are widely used, and each has a unique benefit-risk profile.

According to the American Heart Association (AHA), CVD influences 83.6 million people in the US, accounting for 32.3% of all deaths, and is a major cause of mortality.[4] According to the AHA, 0.0154 billion Americans are affected by atherosclerotic CVD.[4] In the US, CHD, which encompasses CAD, MI, UA, and HF, is the greatest cause of mortality for both females and males.[4] The incidence of CHD is expected to increase by 106 billion dollars in direct healthcare expenditures by 2030.[4] Because greater LDL-c levels have been linked to atherosclerotic CVD in both epidemiologic and experimental investigations, pharmacological methods to reduce risk have centered on LDL-c lowering as a major objective.[4,5] Low HDL-c concentrations have been reported as independent markers of CHD in epidemiologic studies, demonstrating an inverse relationship between CVD and HDL-c.[5] Combining niacin or fibrate with any statin can enhance HDL-c and lower triglycerides more effectively than statin treatment individually.[5] In 2009, the AHRQ published an evidence study contrasting statin intensification with combinations of various lipid-modifying drugs.[5,6] The NCEP's ATP-3 guidelines included recommendations for when to start lipid-lowering medication depending on LDL-c levels and CHD risk factors, as well as LDL-c targets for ideal CHD risk minimization.[6] These studies show that "add-on" combined treatment improves cholesterol outcomes but does not diminish atherosclerosis or lower rates of CVD-associated death, MI, stroke, or revascularization.[6] This research puts into question earlier beliefs that reducing LDL-c or boosting HDL-c is a good predictor of better clinical results, and it emphasizes the necessity of patient-centered health outcomes in assessing the efficacy of lipid-modifying medications.[6,7] Long-term usage of rosuvastatin produces a rise in transaminase (hepatic enzyme), which is destructive to hepatocytes, as well as DM through raising insulin resistance.[8,9]

MATERIALS AND METHODS

This cross-sectional study was performed on 240 patients with a history of hypercholesterolemia in the department of pharmacology and therapeutics with the collaboration of Cardiology OPD and ward LUHMS Jamshoro/Hyderabad for six months from 08-03-2020 to 07-09-2020. Adult patients of either sex, age 30 to 70 years, and diagnosed cases of hypercholesterolemia with diabetes were included while those patients with a history of hepatitis, renal failure, carcinomas, Pregnant and lactating mothers were excluded. All the patients were divided into two equal groups. Group A (n = 120) consisted Rosuvastatin 10 mg O.D and Group B (n = 120) consisted Rosuvastation 10mg 1O.D+Omega-3 fatty acids 500mg 1 O.D. Patients were enrolled through informed consent for participation in my study and admitted with diagnosed cases of hypercholesterolemia and diabetes in cardiac-OPD Department of cardiology LUHMS Jamshoro/ Hyderabad. The sample was labeled by patient's codes & date, then the sample was sent immediately to the DR laboratory.

Serum cholesterol & fasting blood sugar level was done from gel tubes bottles by using serum after centrifugation at 3,500 revolutions per minute for 10 minutes. Tests were performed through Hitachi Cobas C 311 analyzer (for Serum cholesterol and fasting blood sugar).

Statistical analysis:

After the collection of data, the analysis was conducted by using Statistical Package for Social Science (SPSS) software, version 20.0. Frequency and percentage were computed for a qualitative variable like gender. Mean and standard deviation was computed for quantitative variables like age, blood Pressure; serum cholesterol. P-value ≤ 0.05 was considered statistically significant.

RESULTS

In this study total of 240 patients of hypocholesteremia and diabetics were studied. patients were divided into two groups as per treatment. The mean age was 43.33±7.56 years in group A (Rosuvastatin10 mg) and 43.33±7.56 years was in group B (p-0.087) (p-0.087). **Table.1**

Out of 120 patients of group A, 58 were males and 65 were females, while out of 120 patients of group B 62 were males and 55 were females. However, gender comparison among both groups was statistically insignificant (p-0.075). **Table**.1

Out of all patients of group A overweight (25-30 or >30 Kg/m2) patients were 68 and the remaining were seen with normal BMI, while in group B overweight (25-30 or >30 Kg/m2) patients were 72 and 52 were presented with normal BMI. **Table.1**

In this study baseline, average serum cholesterol was 260.22±33.32 mg/dL in group A (Rosuvastatin 10 mg) and 153.19±19.57 mg/dL was in group B (Rosuvastation 10 mg 1 O.D+Omega-3 fatty acids 500mg), the average of serum cholesterol was statistically insignificant as per study group at baseline (p-0.866). Bassline average of FBS was 155.33±20.11 in group A (Rosuvastatin 10 mg) and 153.19±19.57 mg/dL was in group B (Rosuvastation 10mg 1O.D+Omega-3 fatty acids 500mg), these findings of FBS average were also statistically insignificant according to study groups (p-0.472). Table.2

In this study after 30 days' average serum cholesterol was significantly decreased 201.55±28.19 mg/dL in group B (Rosuvastation 10mg 1O.D+Omega-3 fatty acids 500mg), as compared to group A (Rosuvastation 10 mg) as 230.62±32.74 mg/dL (p-0.001). However, after 30 days average of FBS was decreased to 120.33±20.11 in group A (Rosuvastatin10 mg) and 135.19±19.57 mg/dL was in group B (Rosuvastation 10mg 1O.D+Omega-3 fatty acids 500mg), while these findings of FBS average were still statistically insignificant according to study groups (p-0.148). Table 2.

Table No.1: Distribution of patients according to the baseline characteristics between the treatment groups (n=240)

Baseline characteristics	Group A (n=120)	Group (B n=120)	p-value
Age (Mean ±SD)	46.34±6.35	43.33±7.56	0.087
Gender			
Male	58	65	0.64
Female	62	55	
Body Mass Index (Kg/m^2)			
<18 Kg/m2	04	06	0.066
18-25 Kg/m2	48	42	
25-30 or >30 Kg/m2	68	72	

Group A= Rosuvastatin 10 mg O.D
Group B= Rosuvastation 10mg 1 O.D+Omega-3 fatty acids 500 mg 1 O.D

Table No.2: Distribution of patients according to the comparison of mean cholesterol and Fasting Blood Sugar values at baseline, after 30 and 60 days between the treatment groups (n=240)

At baseline	Group A (n=120)	Group (B n=120)	p-value
Fasting blood sugar (baseline)	155.33±20.11 mg/dL	153.19±19.57 mg/dL	0.866
Serum cholesterol (baseline)	260.22±33.32 mg/dL	248.30±40.55 mg/dL	0.472
After 30 days			
Fasting blood sugar	135.19±19.57 mg/dL	120.33±20.11 mg/dL	0.148
Serum cholesterol	230.62±32.74 mg/dL	201.55±28.19 mg/dL	0.001
After 60 days			
Fasting blood sugar	130.55±18.24 mg/dL	118.20±21.44 mg/dL	0.451
Serum cholesterol	210.59±25.4 4 mg/dL	180.17±18.1 0 mg/dL	0.00 1

Results are presented as Mean ± Standard Deviation
* P-value is statistically significant calculated by student's t test
Group A= Rosuvastatin10 mg O.D
Group B= Rosuvastation10mg1O.D+Omega-3 fatty acids 500mg 1 O.D

After 60 days' treatment the average serum cholesterol was significantly decreased as 180.17±18.10 mg/dL in group B (Rosuvastation 10mg 1O.D+Omega-3 fatty acids 500mg), as compared to group A (Rosuvastation 10 mg) as 210.59±25.44 mg/dL (p-0.001). However, after 30 days' average of FBS was decreased to 118.20±21.44 mg/dL in group B (Rosuvastation 10mg 1O.D+Omega-3 fatty acids 500mg), as compared to group A (Rosuvastatin10 mg) as 130.55±18.24 mg/dL, while these findings of FBS average were still statistically insignificant according to study groups (p-0.451). Table 2.

DISCUSSION

In this study total of 240 patients of hypocholesteremia and diabetics were studied. The findings of this study showed that after 30 days' average serum cholesterol was significantly decreased 201.55±28.19 mg/dL in group B (Rosuvastation 10mg 1 O.D+Omega-3 fatty acids 500mg), as compared to group A (Rosuvastatin 10 mg) as 230.62±32.74 mg/dL (p-0.001).

In this study, after 60 days treatment the average serum cholesterol was significantly decreased as 180.17±18.10 mg/dL in group B (Rosuvastation 10mg 1 O.D+Omega-3 fatty acids 500mg), as compared to group A (Rosuvastatin 10 mg) as 210.59±25.44 mg/dL (p-0.001). This was similar to the study of Hisao Ogawa et al.[10] who reported that Low-density lipoprotein cholesterol levels were also decreased at 12 months: −34.79% in the rosuvastatin group and −32.78% in the atorvastatin group.

However, after 30 days' average of FBS was decreased to 118.20±21.44 mg/dL in group B (Rosuvastation 10mg 1 O.D+Omega-3 fatty acids 500mg), as compared to group A (Rosuvastatin 10 mg) as 130.55±18.24 mg/dL, while these findings of FBS average were still statistically insignificant according to study groups (p-0.451). Samir Maruti Adsule et al.[11] found that Rosuvastatin reduced levels of serum cholesterol after a 12-week treatment. The statistical significance of the changes in lipid parameters following treatment was strong (P 0.001). The pilot trial with rosuvastatin undertaken by Gleuck et al. at. The Cholesterol Center, Jewish Hospital, Cincinnati, USA, is in agreement with these finding.[12] A statistically significant difference was detected between atorvastatin and rosuvastatin in the lowering of LDL-C levels after 12 weeks of treatment, according to Hrishikesh

Kashyapa and colleagues.[13] According to the results of this study, diabetic dyslipidemic patients agree with the findings of the ANDROMEDA and URANUS trials, as well as the CORALL and LISTEN studies, which were all conducted on diabetic patients.[10,14–16]

Another study found that both atorvastatin and rosuvastatin increased HDL-C levels significantly after 6 weeks and 12 weeks of medication, however, the difference between the two groups was not statistically significant at 6 weeks. When it came to HDL-C levels at the end of 12 weeks, rosuvastatin had a statistically significant advantage over atorvastatin (11.16 percent vs 7.1 percent). This study's findings are comparable to those of this one. The LISTEN and ASTRO-2 trials on Japanese patients and the investigation by Adsule et al. on Indian volunteers yielded the same results.[10,17,18] It has been found that atorvastatin and rosuvastatin+omega-3 fatty acid have statistically significant effects on HDL-C levels in diabetic dyslipidemic patients, however, there are no significant differences across groups.[14–16]

Results from this study show that both regimens are safe and tolerable, which is consistent with earlier studies.[10,15,16]

An alternative trial in patients with type 2 diabetes mellitus (URANUS) demonstrated no statistically significant differences between rosuvastatin and atorvastatin in terms of HDL-C levels after four weeks of treatment.[19] This finding contrasts with that of Hunninghake et al., who found that rosuvastatin led to greater increases in HDL-C concentration.[20]

Rosuvastatin 10 mg and rosuvastatin+omega-3 fatty acid was found to be comparable in patients with hypercholesterolemia in earlier research.

In three different studies, rosuvastatin 10 mg and rosuvastatin+omega-3 fatty acid was more effective than atorvastatin 10 mg alone a reducing LDL-C after six weeks of treatment in patients with hypercholesterolemia (LDLC 160 and 250 mg/dL [4.1 and 6.5 mmol/L]), CHD and low HDL-C in 461 patients (aged 40–80 years), and type 2 diabetes in 263 patients (45.8 percent vs. 42.6 percent)[21–23], rosuvastatin 10 mg was also considerably more effective than other statins at reducing LDL-C (47.0 percent vs. 43.7 percent, p 0.001) in an 8-week study of 3140 high-risk patients with hypercholesterolemia and CHD, atherosclerosis, type 2 diabetes or a 10-year CHD risk > 20%.[24].

CONCLUSION

As the study concluded the combined therapy of rosuvastatin with Omega-3 fatty acids was found to be effective in the treatment of hypercholesteremia among diabetes patients. Administration of Omega-3 fatty acids play important role in preventing hyperglycemia among statin treatment patients. More large-scale studies are recommended on this subject.

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Knowledge, Attitude and Behavior of Dental and Medical Postgraduates towards Photodynamic Therapy

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ABSTRACT

Objective: To evaluate and compare knowledge, attitude, and behaviors among medical postgraduates (MPG) and dental postgraduates (DPG) regarding Photodynamic therapy (PDT).

Study Design: Cross sectional Survey study

Place and Duration of Study: This study was conducted at the Department of Restorative and Prosthetic Dentistry, College of Dentistry, Dar Al Uloom University, Riyadh, Saudi Arabia from January 2021 to March 2021.

Materials and Methods: A questionnaire registered on www.surveys.google was used. The sample size was 433 participants. Total 387 health professionals responded with 89 % of response rate. Contact details of registered DPG and MPG were requested from the office of Saudi Commission for health Specialist. The questionnaire comprised of four sections. The first section is comprised of socio-demographics. The second domain inquired about knowledge i.e., invasiveness, mechanism of action, and photosensitizers. The third section investigated attitude in clinical practice. Whereas the fourth section of the questionnaire inquired about behavior and willingness to offer PDT as a treatment option. Statistical Package for the Social Sciences was used to analyse data. Descriptive analysis was performed and the result was presented in the form of mean, frequencies, and percentages.

Results: Most MPG displayed adequate knowledge, 80%, 82%, and 79% were aware of the invasiveness, mechanism of action, and role of photosensitizers in PDT respectively. Whereas, DPG displayed inadequate knowledge. Similarly, MPG demonstrated a better attitude towards PDT. A notable result signifies an extraordinary response of MPG for discussing PDT as a treatment alternative with their patients. When inquired about the recommendation of therapeutic benefits of PDT, 65% of MPG and 40% of DPG recommends PDT in their practice. Role to treat cancer and acne was well-known among MPG (90%) whereas dental trainees did not exhibit adequate behavior

Conclusion: DPG showed inadequate knowledge regarding PDT. However, their response presented keenness in acquiring knowledge through training and workshops. On the contrary, MPG exhibited satisfactory knowledge and behavior towards PDT.

Key Words: Photodynamic therapy, Dental postgraduates, medical postgraduates, Knowledge

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INTRODUCTION

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Photodynamic Therapy (PDT) is defined as the light-induced inactivation of unwanted cells. It is also known as phototherapy or photo radiation therapy. It has been practiced in medicine for more than three decades.[1] It is a highly selective and minimally invasive technique to treat malignant and premalignant conditions. Its mechanism of action involves a photoactivatable agent (photosensitizer) activated upon irradiation with the light of a specific wavelength in the presence of oxygen to form reactive oxygen species (ROS).[2] These ROS are responsible for causing oxidation of cellular component

i.e., plasma cell membrane and DNA resulting in cell death. [3,4]

In recent years PDT has emerged as a non – invasive therapeutic modality for the treatment of various diseases.[5,6] Currently the use of PDT has been expanded to several different medical fields i.e., dermatology, ophthalmology, and cosmetic surgery, and their outcomes are reasonably convincing.[7] However, there are certain limitations associated with its use. As visible light can penetrate the tissues not deeper than 5-10 mm, which confines the application of PDT to mainly superficial lesions. In addition, use of PS leads to skin photosensitivity which lasts for weeks which restricts its use as a therapeutic regimen.[8,9]

In dentistry, PDT was initially adopted as a novel disinfection technique. It represents a suitable alternative for treating localized microbial infections. In addition, its role has been lengthened to overcome the antibiotic resistance produced by bacteria.[10] Today, PDT has been widely utilized among different domains of dentistry i.e., periodontology, endodontics, operative, oral medicine, and oral pathology.[11] It is also claimed that over the last few years the use of PDT has been advanced and moved beyond educational centers and specialist care units to general dental practice. Looking towards the future, it is anticipated that PDT will become a vital component of present-day dental practice.[12]

To our knowledge from available indexed literature, it was found that treatment through laser is common nowadays, whereas the application of PDT is limited. In addition, studies related to the assessment of knowledge, attitude, and practice related to PDT among medical and dental professionals are scarce. Therefore, the present study aimed to assess and compare knowledge, attitude, and behaviors among medical postgraduates (MPG) and dental postgraduates (DPG) related to PDT from the different medical and dental tertiary care centers.

MATERIALS AND METHODS

Study design: A descriptive study was designed as a questionnaire-based, cross-sectional analysis to assess and compare the knowledge, attitude, and behaviour regarding PDT among DPG and MPG from different teaching hospitals. STROBES checklist was followed for reporting cross-sectional survey. The total period of the study was 3 months from January 2021 to March 2021

Sample Size calculation: A short-structured questionnaire was administered through online survey forms registered on www.surveys.google. Using power calculation analysis, the sample size was calculated and estimated to be 433 participants with a confidence interval of 95%, 5% margin of error, and 80% power. Raosoft calculator was used in determining the sample size. Participants were approached by sending a link containing a questionnaire along with a consent form on their registered email addresses. Contact details of registered DPG and MPG were requested from the office of Saudi Commission for health Specialist. To improve the response rate reminder weekly emails were sent periodically. A total of 387 participants responded with a response rate of 89%.

Structured questionnaire: A questionnaire was comprised of four sections. The questionnaire was adopted after reviewing a questionnaire from a study by Vohra et al. The research team of statisticians along with authors reviewed the content of each question to make sure that the survey reflected appropriate phrasing and understanding (Cronbach's alpha 0.80). The four domains of the survey comprised of questions related to socio-demographics i.e., age, gender, institute, clinical experience, and year of post-graduation. The second section inquired about the level of knowledge among medical and dental postgraduates in the form of responses yes or no. The third section investigates their behaviour. Whereas the fourth section asked about their attitude and their willingness to learn more about PDT.Statistical Package for the Social Sciences (SPSS Inc., software version 21 Chicago, IL, USA) was used to analyse data. Descriptive analysis was performed and the result were presented in the form of mean, frequencies, and percentages.

RESULTS

Total 433 postgraduates enrolled in medical and dental postgraduate training programe in Saudi Arabia were sent an email with a questionnaire attached but only 387 responded with a response rate of 89%. 200 were males and 187 were females.

The participant's ages ranged from 26 to 33 years, with mean± SD 29.50±1.21. By designation, 51% were dental postgraduate trainees whereas 49% were medical postgraduates. Based on their post-graduation year 49% were junior postgraduates (1-2 years of training) whereas 195 were senior postgraduates (3-4 years of training). Their demographic characteristics are listed in Table 1

Table 2 demonstrates knowledge items with the correct answers. It also represents the percentage of correct responses by medical and dental postgraduates regarding PDT. Most medical postgraduates displayed adequate knowledge related to PDT, and nearly 80%, 82%, and 79% were aware of the invasiveness, mechanism of action, and the role of photosensitizers in PDT respectively. Whereas among dental professional's knowledge seems to be inadequate. 64% of dental professionals were aware of the invasiveness of the procedure whereas their knowledge related to the mechanism of action and use of photosensitizer was insufficient

Table 3, investigated the behaviour of postgraduates towards PDT by inquiring about their behaviour in

clinical practice. When asked about the therapeutic role of PDT i.e., treating ulcers both medical and dental trainees displayed inadequate knowledge. However, its role to treat cancer and acne was well-known by the medical trainees (90%) whereas dental trainees did not exhibit adequate behavior. When inquired about the recommendation of therapeutic benefits of PDT, around 65% of MPG and 40% of DPG recommend PDT in their practice.

Table No.1: Sociodemographic characteristics of medical and dental postgraduates (n =387).

Average age: 29.50±1.21 years
Gender − n (%) Male 200 (52) Female 187 (48)
Designation − n (%) Medical resident 192 (49) Dental residents− 195 (51)
Post-graduation year n (%) 1-2 years junior PG 192 (49) 3+ years senior PG 195 (51)

Table No.2: Response summary of MPG and DPG regarding knowledge items (n=387).

Item	Correct answer	Medical post-graduates %	Dental post-graduates %
Do u think Photodynamic therapy is invasive and painful?	False	80	64
Photodynamic therapy (PDT), also known as photo-radiation therapy, involves the use of a photoactive dye.	True	57	51
PDT is based on the principle that the target cells are destroyed using toxic reactive oxygen species generated upon the interaction of a photosensitizer, light and oxygen.	True	82	55
Photo sensitizers are activated with low level laser between 630 and 700 nm.	True	79	49
PDT affects both surrounding tissues and micro-organisms.	True	55	48

Figure 1, inquired about the attitude of medical and dental postgraduates towards PDT. Medical postgraduates displayed a better attitude towards PDT than dental postgraduates. Around 67% of the medical postgraduates responded that their patient feels contented about knowing PDT as a treatment option whereas only 55% of dental postgraduates responded positively about the response of the patient. Similarly, a significant number of medical postgraduates and dental postgraduates 80% and 61% respectively were interested in gaining clinical expertise through hands-on practice. When questioned about patient's expectations on discussing PDT as a treatment option, a low response rate was noted from both health care professionals. Similarly, a significant number of medical postgraduates (69%) considered discussing PDT with patients as peripheral to medical care. Whereas, only 50% of dental trainees agreed that they discussed PDT with their patients.

Table No.3: Behaviour response summary of dental and medical postgraduates

Item	Correct answer	Medical post-graduates(%)	Dental post-graduates(%)
Do you think PDT has a role to treat oral ulcers?	yes	55	57

Do you think PDT has a role to treat cancer and acne?	yes	90	55
Do you recommend therapeutic choices of PDT to the patient?	yes	65	40
Do you recommend patients to consider PDT in your respective fields?	yes	75	35

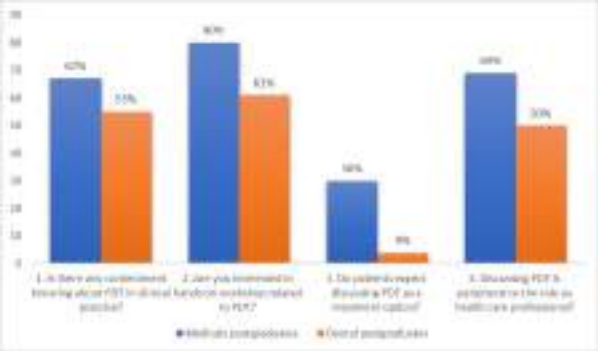

Figure No.1: Attitude towards PDT among medical and dental postgraduates

DISCUSSION

The existing cross-sectional design aims to evaluate and compare the knowledge, attitude, and behaviour among MPG and DPG towards PDT from different universities of Pakistan. To our understanding from available literature, this is a unique survey representing distinctive findings related to PDT among health care professionals. The response rate was calculated to be 89% which was considered to be satisfactory. This method of research design was adopted as cross-sectional surveys are efficient, easy, and rapid. In addition, it gives the researcher an insight into certain behaviour and attitude. It also helps in establishing hypothesis which can be further investigated through interventional study designs.[13]

A questionnaire was designed and generated through online google forms to collect the desired sample. In today's world online surveys or web-based surveys have been considered as an important tool for the collection of data. As the method is convenient, less biased compared to the manual survey. Moreover, it has the advantage of rapid response and less cost compared to the conventional survey.[14]

The present study displayed some interesting outcomes. It was found that medical trainees displayed superior knowledge, attitude, and behaviour than their fellow dentists. Most of the respondents from medical backgrounds showed better understanding and awareness towards the invasiveness of the procedure, mechanism of action, and role of photosensitizer used in PDT. Their familiarity with PDT was also reflected through their attitude and behaviour in clinical practice. Another notable result from the present study signifies an extraordinary response of MPG for discussing PDT as a treatment alternative with their patients. Furthermore, they consider informing patients about different treatment strategies as their peripheral role. Though medical professionals display an adequate amount of knowledge, their attitude towards learning and gaining more information about PDT through attending hands-on workshops was quite overwhelming. This can be explained by the fact that PDT has been practiced in the medical profession for the last 3 decades for treating different diseases.[15] It also reflects a well-designed medical curriculum at undergraduate and postgraduate levels. [16]The finding of the present study is in line with the study conducted by Al Moman *et al*., among medical nurses in Riyadh city, Kingdom of Saudi Arabia. It was found that nurses displayed satisfactory knowledge and modest awareness towards PDT.[17]

In contrast knowledge, attitude, and behavior among dental PGs regarding PDT varies considerably from the medical professionals. Response to the questions exploring knowledge, attitude, and behavior was quite discouraging. Dental practitioners from the present study exhibited inadequate knowledge regarding PDT. The lack of knowledge was also reflected through their attitude and behavior in clinical practice. Most of the dentists did not confer PDT as a treatment option and gave less attention to PDT in their routine dental settings. They also didn't take into consideration their sole obligation to discuss this treatment with patients. Primarily, the reason for this outcome can be linked to PDT being an innovative concept in dentistry.[18] Secondly, high cost and limited expertise to handle the equipment can influence the low acceptability of PDT in their routine dental practice.[16,19] Moreover, in the author's opinion paucity in the dental curriculum can limit its generalizability among practicing dentists. A similar survey conducted by Vohra at el., among dentists of Karachi city displayed adequate amount knowledge as well as positive towards PDT.[20]

CONCLUSION

DPG showed inadequate knowledge regarding PDT. However, their response presented keenness in acquiring knowledge through training and workshops. On the contrary, MPG exhibited satisfactory knowledge and behaviour towards PDT.

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Hepatitis C – Knowledge and Attitude Among Patients Attending OPDs in Tertiary Care Hospital in Karachi: A Patient's Survey

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ABSTRACT

Objective: To assess knowledge and attitude about Hepatitis C among Patients attending tertiary care hospital at Gadap town, Malir Karachi.
Study Design: Cross Sectional Study
Place and Duration of Study: This study was conducted at the Al-Tibri Medical College, Isra university campus at Gadap town, Malir Karachi. Survey was conducted from October 2018 to March 2019.
Materials and Methods: Systematic (Random) Sampling Technique was used. Data was collected by help of a pre-tested semi-structured questionnaire. Data was analyzed by using SPSS version -24.
Results: A total of 259 patients filled/answered the questionnaire, waiting outside of general OPDs to see a doctor. (n=259) Total number of male Patients were n=101 (39%) and females n=158 (61%). The results findings revealed that Out of the 259 participants, 92 (35.5%) showed adequate and satisfied level of knowledge about Hepatitis C. whereas, 167 (64.5%) of the study participants possessed 'in-adequate and poor knowledge' regarding Hepatitis C. Majority (93.4%) of survey participants was not aware of good practice against Hepatitis C and 88.1% of the participants were inadequate knowledge about utilization of healthcare services regarding hepatitis C.
Conclusion: There was a prominent lack of awareness with respect to the HCV infection, its risk factors and prevention among the Gadap town community in Malir Karachi.
Key Words: Hepatitis C, Knowledge, Attitude, Patient, Tertiary care hospital Gadap Town, Karachi

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INTRODUCTION

Hepatitis is an infection of the liver. Hepatitis has many types, but Hepatitis C and B are the most serious as those are viral blood borne infections and are transmitted through unscreened blood transfusions, disinfectants medical equipment, devices and re-utilization of syringes. Vaccine for hepatitis C has yet not discovered. Unscreened blood transfusions and re-use of syringes are one of the main causes of the prevalence of hepatitis C in Pakistan.

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The worldwide commonness of HCV contamination is 2.5 to 3%[1]. Prevalence of hepatitis C differs in nations and locale of world, it is more than 11% in Egypt and considered highest rate of hepatitis in the world[2], it is ranging from 2% to >3% in African countries[3]. Its prevalence in the United State is 1.6% and its prevalence in the European countries is 1 to 2.3%[4]. At present 2%–3% of the world's populace are living with hepatitis C infection[5]. Majority of patients developed liver cirrhosis and hepatocellular carcinoma which is 27% and 25% respectively but this rate is different in different countries, for instance in Japan 90% hepatocellular carcinoma cases are caused by HCV infection[6]. More than 350 thousand people are died due to HCV infection every year in the world[7].

Pakistan is among top ten countries having the highest population in the world; various studies in Pakistan indicates HCV prevalence is between 3.2-14%[8], most HCV prevalence rate is accounted for in Punjab which is 6.7% followed by in Sindh is 5% then in Baluchistan

is 1.5%, and lowest in Khyber Pakhtunkhwa which is 1.1%. More than 10 million individuals in Pakistan are living with HCV contamination[9]. It is affirmed from different studies in Pakistan that prevalence of hepatitis C is >40%[10].

Hepatitis C is very endemic in Pakistan attributed mainly to unsafe injections, as one person in Pakistan averagely takes 13 injections per year[11]. Different survey reports confirmed risk of HCV transmission and relationship between the quantity of frequent and unsafe infusions got in the 6 months preceding the determination of viral hepatitis[12].

It was identified by number of studies that people who were minimum level of education had good sense of risk factors for disease then illiterate persons[13]. Tragically, the education rate of Pakistan is only 43%[14]. Gadap town is most in reverse and least possible created zone of Karachi city, where individuals have minimum approach to medical services.

MATERIALS AND METHODS

The calculated sample size was 259. Patients belong to all communities having age more than 17 years were included voluntarily, who refused to give informed consent, those with mental illness, those who were extremely ill, those who were very old and disabled were excluded from the sample. Data collected by help of a semi-structured pre-tested questionnaire. Before the distribution of the questionnaire, the objective of the study and questions were explained and translated into the local language; and anonymity was assured.

The questionnaire was divided into four parts contain 44 questions. Part one contains questions to assess the socio-demographic characteristics of the respondents. Part two have 20 questions to evaluated knowledge about hepatitis C transmission, its etiology, types, symptoms; age of occurrence of disease, mode of acquisition, possible transmission routes, complications, and treatment. Knowledge was assessed by giving 1 to correct answer and 0 to the wrong answer. Score < 12 were taken as inadequate knowledge of Hepatitis C.

Part three comprised of 9 questions regarding awareness and practices towards hepatitis C. Attitude towards Hepatitis C was evaluated through questions regarding perception about acquiring Hepatitis C infection, treatment, and importance of screening. Practices towards Hepatitis C were explored by asking questions about availability of Hepatitis C vaccination, use of new syringes / razors / blades, and transfusion of contaminated blood and blood products.

The awareness and practices assessed by giving 1 to positive and 0 to negative answer regarding answers pertaining to awareness and practices. The scale classified awareness and practices as good if score > 6 and poor < 5.

Part four contain questions regarding health services utilization which included knowledge about healthcare facility in the area, vaccination status of participant's. A cut-off level of 60% i.e. 5 out of 8 correct responses were labeled as good practices and a score below to 5 were considered as bad and unsafe practices.

A majority of the responses were dichotomous i.e. recorded in 'Yes' or 'No' and 'do not know' in all parts of questionnaire. The collected data was analyzed with help of SPSS.24.0

RESULTS

A total of 259 patients filled/answered the questionnaire (n=259). Total number of male Patients were n=101 (39%) and females n=158 (61%). Most of the Patients were in range of 21 to 45 year of age n=152 (58.7%). As regards educational status of the study participants majority of patients have secondary level education n=132 (51%). Among total number of respondents, 198 (76.4%) were married and 61 (23.6%) were unmarried. 201 (77.6%) out of total number of study participants were unemployed among them 33 (12.7%) were house wives and 23 (8.8%) were students. Among employed study participants 20 (7.7%) were own business, 14 (5.4%) were government/local government employees, 17 (6.5%) were self-employed. Out of 259 research participants, One hundred nine (42.1%) individuals belonged to semi urban area and 89 (34.4%) belonged to urban area, followed by 61 (23.5%) who were from rural area. As regards to ethnic back ground ninety two n=92 (35.5%) were Baluchi speaking, 71 (27.4%) were Urdu speaking, 69 (26.7%) were Sindhi speaking, 13 (5%) and 9 (3.4%) were Punjabi and Pashto speaking respectively (Table I).

Table No.I: Socio-Demographic Characteristics of Study Participants (N = 259)

Variables		Frequency (n)	Percentage (%)
Gender	Male	101	39
	Female	158	61
Age (32.16 ± 8.66)	17 – 26	64	24.7
	27 – 36	122	47.1
	37 - 46	51	19.7
	More than 46	22	8.5
Education	Uneducated	62	23.9
	Primary	40	15.4
	Secondary	132	51.0
	Graduate	25	9.7
Marital Status	Married	198	76.4
	Un-Married	61	23.6
Occupation	Unemployed	201	77.6
	Employed	58	23.4
Residence	Urban	89	34.4
	Semi-urban	109	42.1
	Rural	61	23.5
	Baluchi	92	35.5

Language	Sindhi	69	26.7
	Punjabi	13	5.0
	Pashto	9	3.4
	Urdu	71	27.5
	Speaking Other	5	1.9

Assessment of Knowledge towards Hepatitis C among the study participants: The findings revealed that out of the 259 participants, 92 (35.5%) showed adequate and satisfied level of knowledge about HC. whereas, 167 (64.5%) of the study participants possessed 'in-adequate and poor knowledge'. Most of participants' were unaware of modes of hepatitis C infection, including reuse of syringes (83.0%), blood transfusions (78.3%), use of intravenous drugs of addiction (91.5%), and multiple sexual contact (89.9%). However, most (67.8%) respondents correctly believe that hepatitis C primarily affects the liver.

Participants had good knowledge about affects of hepatitis C regarding age group and cost of treatment. Majority of respondents were considering that hepatitis C is spreading due to contaminated food and physical contact with person suffering from hepatitis C. Nearly half 133 (51.3%) of the study participants knew that jaundice is common symptom of hepatitis C and affect the liver (Fig 1).

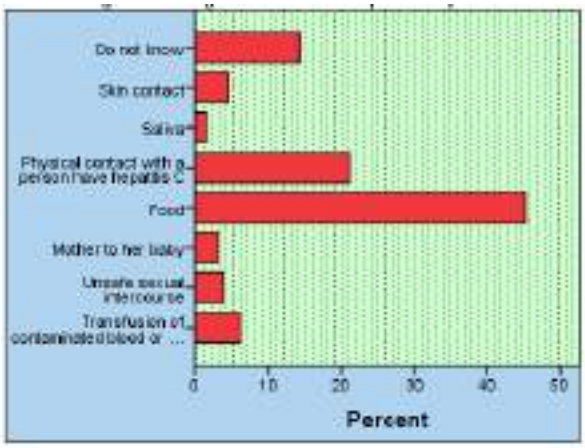

Figure No.1: Knowledge about mode of Hepatitis C spread

Assessment of Awareness and Practice towards Hepatitis C Prevention: Majority of the respondents, 234 (90.4%) not tested to Hepatitis C and said that they have no any knowledge about hepatitis C vaccine. Nearly all 252 (97.3%) of participants did not instruct barber to change the razor before shaving or before piercing needles in ear or nose and 148 (57.1%) of participants never asked for a new syringe when needed. Only 9 (3.5%) respondents using antiseptic solutions to clean sharp needles and instruments and only 23 (8.9%) knew that HCV positive person cannot donate blood.

Comparisons of Socio-Demographic Characteristics with Knowledge, Awareness, Practice and health care services Scores utilization: With Pearson's correlation analysis gender and occupation showed good association with adequate knowledge whereas age and ethnicity was found to be positively associated with adequate knowledge and good awareness and practice pertaining to hepatitis C respectively. Table 2.

Utilization Health Care Services towards Hepatitis C Prevention: 189 (72.9%) participants were not sure that Hepatitis C is preventable or not but 35% participants were positive that it can be prevented through health education, media and seminars. Almost all 255 (98.5%) neither attended and 246 (95.0%) never heard any health education campaign against hepatitis C. Out of 259 participants only 16 (6.2%) vaccinated, 122 (47.1%) were not vaccinated due to different reasons. (Fig 2)

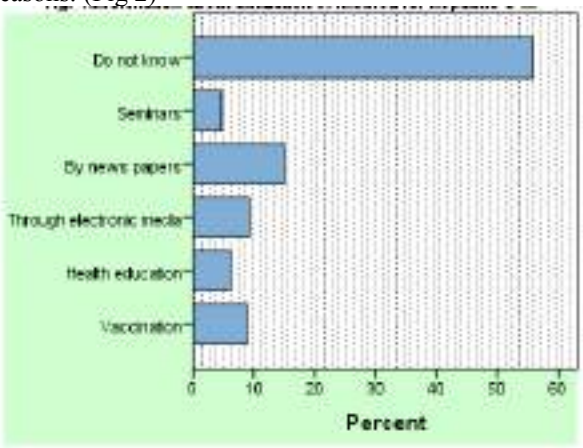

Figure No.2: Information about utilization of method for hepatitis C.

Univariate analysis of age and occupation depicted those participants of age group between 17 – 26 years were 34% hardly have adequate knowledge (OR = 0.66, 95% CI 0.36 – 2.02) and age group between 27 – 36 years was not statistically significantly associated with adequate knowledge towards Hepatitis C. However, significant association was observed for relationship of occupation with adequate knowledge when compared to unemployed participants, employed participants were around two times more likely (OR = 0.14, p-value 0.03, and 95% CI 0.07–0.78) to have appropriate knowledge (OR = 0.14, p-value 0.03 and 95% CI 0.07–0.78). Similarly, the effect of age was not statistically significantly associated with positive attitude towards Hepatitis C. Association of gender, marital status and ethnicity on practices towards Hepatitis C on univariate analysis elucidated that 60% males hardly acquired adequate awareness and practice (OR = 0.40, 95% CI 0.18 – 0.90) in comparison to females. Who were employed were 74% less likely to have good awareness and practices (OR = 0.26, 95% CI 0.15 – 1.91), towards Hepatitis C in contrast to the unemployed respondents.

Correlation between Awareness and Practice of the study participants: Significant positive but weak

linear correlations between awareness and practice were discovered in this study (r = 0.183, p = 0.003). The findings support the hypothesis that there is a link between awareness and practice and the use of healthcare services. In this study, the association is weak. Good awareness and knowledge, it is determined, can lead to good practices.

Table No.2: Study Participants Overall Scores comparison of Knowledge, Awareness, Practice and Utilization Healthcare Services of Study Participants

	Total Score	Median (IQR)	Adequate Knowledge	In-adequate Knowledge
Knowledge regarding Hepatitis C (8.56 ± 3.71)	19	8(5)	N (%)	N (%)
			92 (35.5)	167 (64.5)
Awareness and Practices Regarding Hepatitis C (3.59 ± 2.58)	10	5(3)	Good awareness & Practice	Bad awareness & Practice
			17 (6.6)	242 (93.4)
Utilization of Health care Services regarding Hepatitis C (2.37 ± 2.79)	8	4(1)	Adequate Knowledge	In-adequate Knowledge
			31 (11.9)	228 (88.1)

Table No.3: Correlation of Age & Education with Adequate Knowledge regarding Hepatitis C

Characteristics	Total	Adequate Knowledge N (%)	In-adequate Knowledge N (%)	Adjusted OR (95% CI) *	p-value
Age (year)					
17 – 26	64	29 (45.3)	35 (54.7)	0.54 (0.23 – 1.56)	0.02
27 – 36	122	36 (29.5)	86 (70.5)	1	-
37 - 46	51	19 (37.2)	32 (62.8)	0.73 (0.32 – 2.15)	0.16
More than 46	22	8 (36.4)	14 (63.6)	0.75 (0.33 – 2.26)	0.18
Education					
Uneducated	62	11 (17.7)	51 (82.3)	0.20 (0.09 – 0.51)	0.04
Primary	40	13 (32.5)	27 (67.5)	0.78 (0.43 – 2.27)	0.20
Secondary	132	52 (39.4)	80 (60.6)	0.59 (0.33 – 1.75)	0.15
Graduate	25	16 (64.0)	9 (36.0)	0.26 (0.12 – 0.65)	0.06

DISCUSSION

Results of the study showed there are significant gaps and lack in knowledge, awareness and practice towards hepatitis C. The mean awareness and practice score was 3.59±2.58 showed poor knowledge to hepatitis C among the study participants. Knowledge regarding Hepatitis C was explored through questions related to its types, modes of transmission by using contaminated material such as razors / blades / syringes / tooth brush and also about its complications related to liver, availability of vaccine and cost of treatment and was thus found grossly unsatisfactory among the residents of Gadap Town, Karachi. These findings are consistent with other study conducted in Karachi, which found that respondents had little knowledge about hepatitis C infection[15]. Similar studies were carried out in Pakistan and various countries of world among different targeted populations, almost all studies have reported poor knowledge, negative attitudes and bad practices towards Hepatitis C in the communities, these finding are in line with our present study findings[16].

The present study disclosed surprising results. Literacy rate of research participants is though reasonably high i.e. 60.7% but low level of awareness and practices about Hepatitis C reflects standard of education in rural and semi-urban areas of city.

Regarding considerable gaps in knowledge more than two third of survey participants had no idea what causes Hepatitis C or how it spreads, this is also accordance to the studies of other researchers conducted earlier[17]. About 66% of respondents knew that Hepatitis C could develop liver disease/ cancer, as well as harm other organs. More than 70% of the study participants in our study revealed that Hepatitis C is curable or they were not firm about that. Thus this misconception of study participants leads them to harmful practices. Our study results also indicated overall lack of awareness of study participants towards use of new syringes / needles / blades and safe transfusion of blood. Barbers in Pakistan have been known source of spread of HCV as stated by Janjua and Nizami[18].

In addition, about 27% of the survey respondents revealed to believe that HCV patient could donate blood. Whereas; half of them were not sure about it,

therefore clearly reflects their poor awareness towards infection control practices.

Considering the healthcare services utilization pattern in Gadap town, more than 50% of the study participants believed that hepatitis C is preventable and can be prevented through health education and mass media campaign.

In this study, 93.8% of respondents had not received any vaccination against any type of hepatitis. This is less than the 87.8% immunization rate found in a research conducted in Mirpur Khas Sindh[19].

Thus it is confirmed that individuals, who were weak in knowledge, were more likely to show negative attitudes to those who were knowledgeable.

CONCLUSION

This study discovered that in the community there is little awareness of Hepatitis C, its risks, modes of transmission, and prophylaxis. Require an immediate need to conduct countrywide health education programs to raise the awareness of HCV transmission in the Pakistani population exists. Another vital issue questioned about the overview group practice and attitude about this life threatening infection and the requirement of further HCV awareness.

Author's Contribution:

Concept & Design of Study:	Riaz Ahmed Bhutto
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Nursing Profession - Public Image at Private Tertiary Care Hospital of Karachi

Nursing Profession - Public Image

Irfan Ali[1], Riaz Ahmed Bhutto[2], Sultan Muhammad[1], Wakeel Ahmed[1], Anjum Saeed[3] and Saifullah Saddiqui[1]

ABSTRACT

Objective: To explore the public image toward nursing as a profession at private tertiary care hospital of Karachi, Pakistan.
Study Design: Cross sectional study
Place and Duration of Study: This study was conducted at the Jinnah Medical College Hospital, Karachi, from November 2020 to February 2021.
Materials and Methods: Data was collected by well-designed questionnaires by non-probability consecutive sampling technique from general public coming in hospital except medical staff. Data was evaluated using SPSS version 25.
Results: 101 participants took part in the study. About 70% participants think that nursing is a respectful profession. 100% participants believe that nurses play vital role for the caring of the patients. 88.5% participants answered that in future, nursing profession will be well developing in Pakistan. 92.5% participants believe that nurses work for the humanity. 50% participants believe that nurses work independently without doctors.
Conclusion: People perception of nursing are strongly influenced by nursing care that they receive. Majority of the participants gave the positive remarks about nursing image and profession.
Key Words: Nursing profession, Public image, Tertiary care hospital, Karachi, Pakistan

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INTRODUCTION

Nursing is an important component of healthcare delivery system of a country. Nursing profession face a global difficulty with its image and prestige, as well as its role description. The "character of an object or individual as seen by the public" is defined as "image." A simple definition about nursing image defined by Kalisch and Kalisch is, "The sum of people's views, thoughts, and impressions of nurses and nursing,"[1]. The communication of nurse to his family, friends and public define the nursing profession, which has an impact on nursing's image. Nurses remain invisible in health care; their competence, ability, sense and knowledge are simply a reflection, not actuality, as the word 'image' implies[2].

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Empiric affirmation from both developed and a developing country reveals that nursing's low or negative image is a persistent problem[3]. The nature of nursing job, which entails “man-of-all-work” and close touch with the human being, has also been cited as one of the elements that negatively impacts nursing image throughout the world[4]. Thousands of European women felt driven by God to care for the ill in the 19th century. Women in the nursing orders of sisterhoods that appeared at right time did amazing things in the name of divine: they travelled internationally organizing groups of immigrant and native girls and women, they constructed and ran big hospitals, even health center networks, and that they constructed schools, orphanages, and different vital social establishments for the poor[5]. Nursing was considered as an inferior occupation before 18th century b/c it was thought that nursing is a profession/occupation for prostitutes, widows and women for poor families. It was considered that for nursing employment there was no need for study or intelligence. In 19th century, Florence Nightingale, the lady of the lamp struggled to improve nursing profession as a respectful and acceptable profession in the society.

In Western countries nursing's image has been extensively researched, but it has not been fully analyzed in Pakistan. Nursing is mostly a female profession in Pakistan, and the low position of women

in Pakistani society has a considerable impact on the profession's image. The current state of nursing is regarded to be caused by a number of economic, socio-cultural and political reasons, including a negative perception of the nursing profession in the country[6]. Nursing's negative image in Pakistan appears to have an impact on the talent and commitment of individuals who enter and stay in the profession. Nurses are often regarded by the general public as good people who care for human being. Nursing has ranked first in the yearly list of profession assessed for honesty and ethic norms for the past 11 years, with 81 percent of respondents in concert. This high level of trust has been a continuous outcome in the poll year after year[7]. The statue of nursing also impact on entering the profession but also it continues to work in it. When medical domination is combined with the ideals of a male-dominated country like Pakistan, it becomes even more ubiquitous. Due to the reversed ratio of nurses to doctors at government hospitals, nurses' activities are often limited, and many regular nursing tasks, such as monitoring vital signs and dressing wounds, are undertaken by doctors. Nurses are often in charge of dispensing medications, carrying out doctor's orders, and performing clerical duties. Because of the scarcity of fundamental health-care resources, what nurses learn in school may not be implemented in their work environments[8]. Nurses' and nursing as a profession's image is critical in the recruitment and retention of workers in the healthcare industry[9]. Nurses are the backbone of the healthcare sector and are essential in the delivery of high-quality care to all citizens of a country[10]. As a result, the nursing profession's image should be raised by careful structuring of nursing curricula in order to be a magnet for recruiting a large number of male students to enter the field and to retain professionalism in nursing practice. Despite significant advancements in the nursing field, nurses still confront numerous problems in terms of maintaining a professional image. Nursing has been regarded an important profession but society gave poor value to it because it is female dominant profession, society gave more value and dignity to male dominant profession, however the image of past perception of nursing has been changed and researcher have proved that this is a positive change about the impression of nursing. The purpose of this study was to look at people's perspectives of the nursing profession in Pakistan.

MATERIALS AND METHODS

This is cross sectional study. Data was collected from 101 subjects from both genders having more than 18 years of age, any educational level and occupation, including those who were admitted.in hospital and their attendants at private tertiary care hospital at Karachi, from November 2020 to February 2021. The respondents were selected by convenient sampling technique. The study received ethical approval from the University's Ethical Review Committee. The subjects gave their written informed permission. The information was gathered using a predetermined set of questions that had two parts: demographic information and participant perceptions. Male and female have equal chance to participate in our study. Medical staff and participants who refuse to take part in study were excluded from study. Statistical Package for the Social Sciences (SPSS) version 25.0 was used to analyze the information.

RESULTS

Total 101 individuals answered/filled the questionnaire (n=101) with a response rate of 99%. Number of male respondents were n=61 (61%) and females n=39 (39%). Majority of respondents were in range of 20 to 46 year of age n=72 (72%). Mostly they had secondary level education n=59 (59%), n=76 (76%) were married, n-91 (91%) were government, private or self-employed. Forty nine n=49 (49%) individuals belonged urban area and fifty one n=51 (51%) belonged to semi-urban area.
When the participants were asked about whether females are dominant in nursing profession, majority of (82%) participants viewed that nursing is not female dominant profession compared to (18%) participants who said yes nursing is a female dominant profession. This clears that male are also getting equal rights in nursing profession. In response to question is nursing a respectful profession; 70% participants agreed, while 30% had opinion that this profession is not respectful profession, Nursing is generally regarded as a respectable career that works to maintain an individual's health.

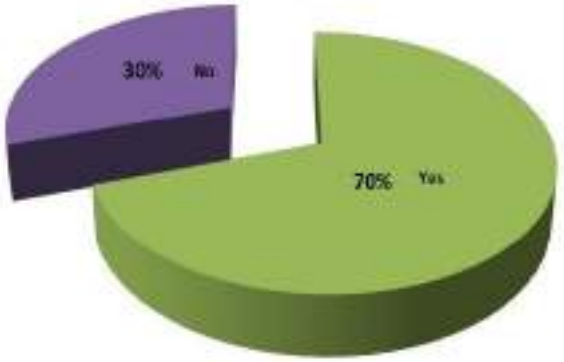

Figure No.1: Is nursing is a respectful profession?

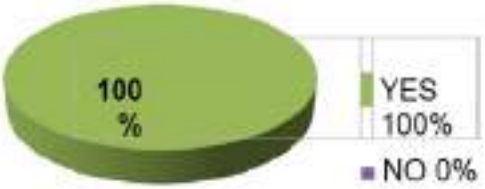

Figure No.2: Is there any contribution of nurses in the care for patient recovery?

100% respondents agreed that nurses are take care and contributing in the patient recovery it shows that people accepting this contribution of nurses.

Mismatch between desired and actual role in practice has a great impact in professional recognition. 95% of participants considered that nurses are well educated, only 4% responded thought that nurses not educated. Thus concept related to previous literature review has been changed and nurses are considered educated by today's society. Study revealed 64% participants equally treated nursing and medical student, it shows that both profession are treated equally. Pakistan is among few countries in the world where the nurse-to-doctor ratio is 1:6. Because of this nurse-to-doctors inverse ratio in government hospitals, nurses' roles are typically limited, and many routine nursing activities, for example vital sign monitoring and wound care, are undertaken by doctors. Nurses are typically in charge of dispensing medications, carrying out doctor's orders, and performing clerical duties which are contrary to their training and education. Regarding negative behavior when they are dealing with patients and their family members, 35% respondent agreed to it. This is due to age, education, social, professional experience and occupational factors. Instead of being highly trained and educated, the nursing profession is limited to bedside care, drug administration, and other related tasks. Nursing is also portrayed as subservient to doctors. Image of nursing can be enhanced by emotional strength, patience and knowledge. Many of nursing functions are still invisible.

Question about can media play any role for the betterment of nursing profession, 59% of participants strongly agreed while 35% were disagreed and 6% had no idea about it. 50% participants agreed nurses can handle patients if they are experienced without physician assistance. The unfavorable perception of nursing among doctors, on the other hand, has detrimental implications. "Job happiness is highly determined by how much respect you obtain from your colleagues as well as the common people of a society," Larocque (2003) asserted. Unfortunately, many doctors do not regard nurses as coworkers, resulting in a negative impact on the nursing profession.

When participant asked do nurses work collaboratively with each other, 87.5% responded in "yes" and 12.5% participants responded in "no". The perception about nursing communication with patient and public, 93% responded that nurses communicating in good way, only 7% respondent disagreed. Nursing is viewed as a humanitarian service profession by 92% of research participants, while it is viewed as a source of income by 6%. 88% percent of respondents believe the nursing profession will develop in the future. When asked if nurses are better at caring for patients than doctors, 75% said yes, while 2% said both are necessary.

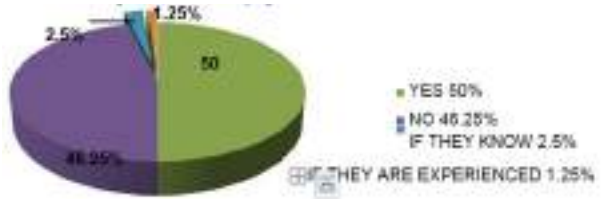

Figure No.3: Do you think that nurses can work independently in dealing with patient without any assistance of physician?

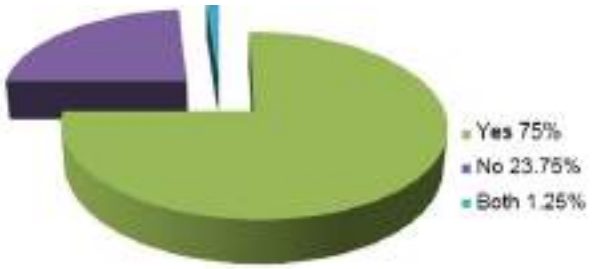

Figure No.4: Do you think that nurses can take care of the patients better than doctors?

DISCUSSION

The majority of the study participants had a favourable opinion of nursing profession. Because this study was conducted in a private hospital, attendants in private hospitals had higher positive impressions; this could be due to the fact that nurses at private hospitals have more roles and duties in patient care. These findings are equivalent to those of an Indian study[11,12]. Nurses, according to Waters (2010), are the backbone of the healthcare system and are essential in providing high-quality treatment to all citizens of a country. A study shows that nurses feel proud that they are competent health professionals with great responsibilities, felt respected and trusted professionals. Mismatch between desired and actual role in practice has a great impact in professional recognition nursing professionals are pushing more to medical roles that causes ignoring of fundamental role of nursing care. Approximately half of the participants in this research saw nurses as assisting doctors in delivering care to their patients. According to number of studies, doctors are more inclined to regard nurses as subordinate to doctors and to solely follow the doctor's orders. According to a British Journal, "The Government will not financially recognize the nursing profession unless its representative take on more responsibility, delegate their conventional practice, and comply more and more medical roles in order to assist the government in relation to the current shortage of doctors,"[13]. The nursing profession was viewed positively by people with no education or a low degree of education than by those with a greater level of education. Nursing proved to have a low perception in terms of occupational dispersion. Where the ratio of skilled nurses to patients is dwindling and a variety of healthcare aides have taken over much of the basic job

of nurses at the bedside. The nurse-to-patient ratio was favourably connected with the image of nursing among patients unified by hospital. Personal interactions with nurses generally form the basis of public perceptions of nursing and nurses, which can lead to a restricted opinion of a nurse based on only a brief personal experience. The majority of participants in our study believed that nurses did not require power to make decisions. Nursing is undeniably a career in which autonomy and accountability are vital aspects. In terms of the nursing profession's desirability, the common people's responses were somewhat supportive of wanting their "daughters and sisters to be nurses." Nursing is not often regarded as a desirable career in Pakistani society.[14-16]

CONCLUSION

The finding gave positive idea about image of nursing in Pakistan that nurses are educated, respectful, and responsible and a part in the recovery of patients, moreover nurses live in peaceful manner and are caring for the patient without presence of doctor and patient's family. The majority of the study participants had a favourable opinion of nursing. The availability of nurses and the quality of nursing care they get have a significant impact on people's perceptions of nursing profession. As a result, the availability of skilled nurses has a direct impact on the image of nurses. People in Pakistan have a low knowledge of nursing profession, which necessitates significant marketing techniques to boost the profession's image.

Author's Contribution:

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Prevalence of Oral Cancer and its Associated Risk Factors among Oral Cancer Patients Presenting at HBS Dental and General Hospital, Islamabad

Oral Cancer and its Associated Risk Factors

Sobia Siddique[1], Shahida Maqbool[2], Syeda Kinza Asghar[3], Sumera Ijaz[4], Hafsa Niaz[2] and Sana Naeem[1]

ABSTRACT

Objective: To determine the prevalence of oral cancer and to find out the various risk factors associated with oral cancer.

Study Design: Descriptive cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Oral Pathology and Oral Medicine, HBS Medical and Dental College Islamabad from November 2018 to September 2021 for a period of 03 years.

Materials and Methods: Five hundred and forty-three patients diagnosed with oral cancer were enrolled. Daily and monthly outpatient statistics was also recorded for the study period.

Results: The mean age was 54.58±0.50 years. Among patients with different types of habits, 323 (73.2%) patients were tobacco chewers, there were 60 (13.6%) smokers, 32 (7.3%) pan chewers without tobacco, 17 (3.9%) smokers and tobacco-chewers, 2 (0.5%) alcoholics and 7 (1.5%) patients had multiple habits (alcohol use along with smoking and or tobacco chewing). In total, maximum number of patients belonged to carcinoma of buccal mucosa219 (40.4%) followed by cancer of tongue96 (17.7%), carcinoma of gingivo-buccal sulcus49 (9%), carcinoma of alveolar ridge or gingival 41 (7.5%), carcinoma of retromolar area33 (6.1%), carcinoma of palate31 (5.7%), carcinoma of floor of mouth 21 (3.8%) and carcinoma of lip21 (3.8%). On the whole, maximum number of patients belonged to stage IV oral cancer in 249 (45.9%) followed by stage III in 182 (33.5%), stage II in 92 (16.9%) and stage I oral cancer in 20 (3.7%).

Conclusion: This study gives different grades of oral squamous cell carcinomas well as frequency and site of involvement. Oral cancer developed at a younger age with higher prevalence of female. It has been observed that the risk factors like habits and oral cancer have significant associations.

Key Words: Oral cancer, Risk factors, Tobacco, Prevalence, Prevention

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INTRODUCTION

In oral cancer, the tongue, buccal mucosa, lips and remaining part of the oral cavity are included however, the major salivary glands are not included. Till now oral cancer is remained as a fatal disease, also the most disfiguring and devastating among all malignancies. Globally, it is considered for higher rate of mortality and morbidity particularly in countries which are under developed.[1,2] Every year almost 400,000 expected new cases of oral cancer are diagnosed worldwide, two-third of which are found in countries of continent Asia including Pakistan, Bangladesh, Indonesia, Sri Lanka and India.[3] Oral cancer is the frequent malignancy and more than 25% of oral cancer cases are observed in the countries which are at a high risk.[4] Its prevalence is directly proportional to the age and maximum in age >60 years, although its incidence is also increasing in younger people of 40 year age.[5]

Oral squamous cell carcinoma is very common malignancy consisting of about 90% of all malignancies of oral cavity.[6] Most of the oropharyngeal cancers are oral squamous in nature comprising 90% to 94% of the oral cancer.[7] There are different forms of presentation and several clinical features of oral squamous cell

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carcinoma. After tumor's surgical resection the life quality of the patient suffering from cancer is very poor because of esthetic and functional reasons. If the patient of oral cancer is diagnosed earlier then the patients have chances of good prognosis. The oral pathologist is the first one who observe the patients having oral cancer therefore the dentist must be aware of oral cancer.[8,9]

The oral cancer has risk factors including betel quid chewing, use of alcoholic beverages, chronic inflammation and heavy consumption of tobacco. In recent decades incidence of oropharyngeal cancer and HPV-associated oral cancer has been increased mostly found in younger people.[10,11]

As the prevalence of oral cancer changes by anatomical site, age, treatment and geographical site. So, from each geographical site collection of descriptive data of oral cancer is important to assess the problem. The objective of this study was to determine the prevalence of oral cancer and its associated risk factors among oral cancer patients.

MATERIALS AND METHODS

This descriptive cross-sectional study was conducted at Department of Oral Pathology and Oral Medicine of HBS Medical and Dental College Islamabad from 1st November 2018 to 1st September 2021. Ethical committee approval was obtained from the Institutional Ethics Committee. A total of 543 patients diagnosed with oral cancer were included in this study as per inclusion criteria. Patients with other oral malignancies and oral pathologies were excluded from the study. Information was also collected concerning the personal habits like smoking, use of various forms of smokeless tobacco and alcohol. Data about the duration of onset of symptoms, family history was also recorded. Regarding family history, only history of cancer in the patients' family with respect to patients' parents or siblings was recorded. It was recorded as present or absent.

The anatomic site of cancer, type, its histologic differentiation, regional lymph node involvement and its staging were also recorded. Squamous cell carcinoma cases on the basis of histologically divided in 3 grades: Grade I include well differentiated, Grade II moderately differentiated & Grade III poorly differentiated as per criteria of WHO. The clinical staging of the tumor was corded was mentioned. The staging based on TNM grades was broadly divided into Stage I (TIN o), Stage II (T-No), Stage III ($TIN_{1,2}$) and Stage IV ($T4N_{1.2.3}$ or M_1). Data was entered and analyzed using SPSS-20.

RESULTS

Most of the patients 148 (27.2%) were in the 60-69 year group, followed by those belonging to the age group 40-49 years140 (25.8%) and 50-59 years137 (25.2%), 70-79 years58 (10.7%), 30-39 years38 (7%), 80 years or more12 (2.2%) and less than 29 years age group10 (1.9%). The mean age of the patients was 54.58±0.50 years with an age range of 22 to 93 years. There were 334 (61.5%) females and 219 (38.5%) males. Among the total patients (543), there were 441 (80.2%) with habits and 102 (19.8%) free from habits and the difference was statistically significant ($p<0.0001$). Among patients with different types of habits (441), 323 (73.2%) patients were tobacco chewers, there were 60 (13.6%) smokers, 32 (7.3%) pan chewers without tobacco, 17 (3.9%) smokers and tobacco-chewers, 02 (0.5%) alcoholics and 07 (1.5%) patients had multiple habits (alcohol use along with smoking and or tobacco chewing). Proportion of patients with history of smokeless tobacco use-323 (73.2%) were significantly higher ($p<0.001$) compared to those with other types of habits (Tables 1-2).

Among patients with habits (441), majority of patients184 (41.5%) had practiced the habits for a period of 20-29 years followed by 10-19 year duration group 132 (30%), less than 10 year duration group 71 (16.1%), 30-39 year duration group 48 11%) and more than 39 year duration group6 (1.4%). The mean duration of habit was 23.25 years (Table 3).

Table No. 1: Comparison of gender according to age

Age (years)	Gender		Total
	Male	Female	
≤29	**6 (60%)**	**4 (40%)**	10 (1.9%)
30-39	**17 (44.7%)**	**21 (55.3%)**	38 (7%)
40-49	**56 (40%)**	**84 (60%)**	140 (25.8%)
50-59	**55 (40.1%)**	**82 (59.9%)**	137 (25.2%)
60-69	**55 (37.2%)**	**93 (62.8%)**	148 (27.2%)
70-79	**19 (32.8%)**	**39 (67.2%)**	58 (10.7%)
80^+	**1 (8.3%)**	**11 (91.7%)**	12 (2.2%)
Total	**209 (38.5%)**	**334 (61.5%)**	543 (100%)

Table No.2: Comparison of gender according to marital status

Marital status	Gender		Total
	Male	Female	
Married	**204(38.1%)**	**331 (61.9%)**	535 (98.5%)
Unmarried	**5 (62.5%)**	**3 (37.5%)**	8 (1.5%)
Total	**209 (38.5%)**	**334 (61.5%)**	543 (100%)

Table No.3: Comparison of gender according habits

Habits	Gender		Total
	Male	Female	
With habits	**170 (38.5%)**	**271 (61.5%)**	441(80.2%)
Free from habits	**39 (38.2%)**	**63 (61.8%)**	102 (19.8%)
Total	**209 (38.5%)**	**334 (61.5%)**	543 (100%)

All the histologically confirmed oral cancer patients belonged to squamous cell carcinoma type. In total, maximum number of patients belonged to

carcinoma of buccal mucosa 219 (40.4%) followed by cancer of tongue 96 (17.7%), carcinoma of gingivo-buccal sulcus49 (9%), carcinoma of alveolar ridge or gingival 41 (7.5%), carcinoma of retromolar area 33 (6.1%), carcinoma of palate 31 (5.7%), carcinoma of floor of mouth 21 (3.8%) and carcinoma of lip 21 (3.8%). There were 32 (5.9%) patients with oral cancer involving multiple sites. Majority of the patients had well differentiated squamous cell carcinoma 272 (50.6%) followed by moderately differentiated 144 (26.5%) and poorly differentiated squamous cell carcinoma 124 (22.9%).

Table No.4: Distribution of patients consistent with types of habits according to gender

Habits	Gender		Total
	Male	Female	
Smoking	**60 (100%)**	**-**	60 (13.6%)
Pan chewing without tobacco	**5 (15.6%)**	**27 (84.4%)**	32 (7.3%)
Smokeless tobacco	**79 (24.5%)**	**244 (75.5%)**	323(73.2%)
Smoking &tobacco chewing	**17 (100%)**	**-**	17 (3.9%)
Alcohol use	**2 (100%)**	**-**	2 (0.5%)
Multiple habits	**7 (100%)**	**-**	7 (1.5%)
Total	**170 (38.5%)**	**271 (61.5%)**	441 (100%)

Table No.5: Distribution of patients according to duration of reporting first signs of oral cancer among gender

Duration	Gender		Total
	Male	Female	
<15 days	**1 (50%)**	**1 (50%)**	2 (0.4%)
15 days-1 month	**47 (33.3%)**	**94 (66.7%)**	141 (26%)
1-3 months	**96 (38.1%)**	**156 (61.9%)**	252 (46.4%)
4-6 months	**41 (42.7%)**	**55 (57.3%)**	96 (17.7%)
7 months-1 year	**16 (42.1%)**	**22 (57.9%)**	38 (7%)
>1 year	**8 (57.1%)**	**6 (42.9%)**	14 (2.5%)
Total	**209 (38.5%)**	**334 (61.5%)**	543 (100%)

Table No.6: Distribution of patients according to site of carcinoma and sex

Site of carcinoma	Gender		Total
	Male	Female	
Buccal mucosa	**59 (26.9%)**	**160(73.1%)**	219 (40.4%)
Tongue	**63 (65.6%)**	**33 (34.4%)**	96 (17.7%)
Gingivo-Buccal sulcus	**14 (28.6%)**	**35 (71.4%)**	49 (9%)
Alveolar ridge/Gingiva	**11 (26.8%)**	**30 (73.2%)**	41 (7.5%)
Retromolar area	**10 (30.3%)**	**23 (69.7%)**	33 (6.1%)
Palate	**21 (67.7%)**	**10 (32.3%)**	31 (5.7%)
Floor of mouth	**17 (81%)**	**4 (19%)**	21 (3.8%)
Lip	**4 (19%)**	**17 (81%)**	21 (3.8%)
Multiple sites	**10 (31.4%)**	**22 (68.6%)**	32 (5.9%)
Total	**209 (38.5%)**	**334 (61.5%)**	543 (100%)

Table No.7: Distribution of patients according to histological differentiation of squamous cell carcinoma

Differentiation	Gender		Total
	Male	Female	
Well	110 (40%)	165 (60%)	275 (50.6%)
Moderate	52 (36.1%)	92 (63.9%)	144 (26.5%)
Poor	47 (37.4%)	77 (62.6%)	124 (22.9%)
Total	209 (38.5%)	334 (61.5%)	543 (100%)

Table No.8: Distribution of patients according to lymph node metastasis and sex

Metastasis	Gender		Total
	Male	Female	
Present	162 (37.9%)	266 (62.1%)	428 (78.8%)
Absent	47 (30.3%)	68 (69.7%)	155 (21.1%)
Total	209 (38.5%)	334 (61.5%)	543 (100%)

Table No.9: Distribution of patients according to staging of oral cancer and sex

Stage of carcinoma	Gender		Total
	Male	Female	
I	**11 (55%)**	**9 (45%)**	20 (3.7%)
II	**34 (37%)**	**58 (63%)**	92 (16.9%)
III	**74 (40.7%)**	**108 (59.3%)**	182 (33.5%)
IV	**90 (36.1%)**	**159 (63.9%)**	249 (45.9%)
Total	**209 (38.5%)**	**334 (61.5%)**	543 (100%)

On the whole, most of the patients had lymph node metastasis 428 (78.8%) at the time of diagnosis and 155 (21.1%) patients had no lymph node metastasis. Proportion of females was higher compared to males in both the groups. On the whole, maximum number of patients belonged to stage IV oral cancer in 249 (45.9%) followed by stage III in 182 (33.5%), stage II in 92 (16.9%) and stage I oral cancer in 20 (3.7%) [Tables 4-9].

DISCUSSION

There were 61% males and 39% females with mean of 48.52±5.24 years. The distribution of gender is in line with African and Pakistani population, although the male predominance was noted equal to 4:3:1 in larger

sample conducted at multicenter.[12,13] It has been considered worldwide that the prevalence of oral cancer is associated with increasing age. Patients having 40 to 49 years of age have maximum risk of oral cancre.[12] Our study have mean age of 55 years, these finding are comparable with the results of multi-center study conducted in Yemen and Pakistan.[14,15]

Among the total patients, 80.2% of them had habits and 19.8% of them were habit free and the difference was statistically significant ($p<0.0001$). This is in line with the studies by Gupta et al.[16,17] from India about the upper gastrointestinal tract indicated that the extrapolation of risk of cancer in general population on the basis of total risk score of smoking, chewing tobacco, drinking and habits of other morbid lifestyle has a high level of prognostic validity and power.

In our study patients with habits, 73.2% chewed tobacco, 13.6% were smokers, 3.9% patients with both smoking and tobacco chewing habits and 1.5% with multiple habits indicating that 92.2% of the patients used tobacco in some form. There were 7.3% patients who chewed pan without tobacco. Among these groups of patients, proportion of patients with tobacco chewing habit (smokeless tobacco) were significantly higher ($p<0.001$) compared to patients with other types of habits. This finding is in line with the annual reports of Muwonge et al[18] and Petti et al.[19] In our study, all the histologically confirmed oral cancer patients included in the study belonged to squamous cell carcinoma type. On the whole, maximum number of patients (40.4%) belonged to carcinoma of buccal mucosa followed by carcinoma of tongue (17.5%), carcinoma of gingivo-buccal sulcus (9%), carcinoma of alveolar ridge (7.5%) and the least common was carcinoma of floor of the mouth (3.8%) and carcinoma of lip (3.8%). There were 5.9% of patients with oral cancer involving multiple sites. In various population and geographical location the site of involvement varies in oral cancer. 50% cases of oral cancer floor of the mouth and the tongue has been observed in patients enrolled from Western societies, but the labial/buccal mucosa, gums, plate were minimally involved.[20]

Siddiqi et al[21] reported that relative risk (RR) for mouth cancer (lip, tongue and oral cavity) was 3.43 in users of SLT/chewers. Mostly, tongue is observed the most common site of involvement for oral cancer due to drinking alcohol and smoking in excessive amount.[22]

Overall, almost 50.6% patients (grade I) had well differentiated squamous cell carcinoma, (grade II) moderately differentiated 26.5% and (grade III) poorly differentiatedsquamous cell carcinoma to be 22.9% patients. Son et al[23] reported that mostly patients had grade-I squamous cell carcinoma.

Most of the patients (78.8%) had lymph node metastasis at the time of diagnosis compared to 21.1% patients who had no lymph node metastasis. This is in line with the study of Sankarnarayanan1 (74% had lymph node metastasis at initial visit) and the same author reported that data from other studies in major hospitals in India show 60%-80% lymph node metastasis and only 10-15% having localised cancers. Quadri et al[24] and Hung et al[25] in their studies had 54% patients having lymph node metastasis.

CONCLUSION

This study gives different grades of oral squamous cell carcinoma as well as frequency and site of involvement. Oral cancer developed at a younger age with higher prevalence of female. It has been observed that the risk factors like habits and oral cancer have significant associations. The oral health practitioners should be actively involved in conducting and implementing several strategies of prevention in this cancer prone region.

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Final Approval of version:	Sobia Siddique

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

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Comparing the Effects of Rosuvastatin and Silymarin on Lipid Levels as Monotherapy or Combination Therapy for the Treatment of Hyperlipidemia

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ABSTRACT

Objective: To evaluate the effects of silymarin alone or in combination with rosuvastatin on elevated total cholesterol, Triglycerides, high levels of Low Density lipoproteins and low levels of High Density Lipoproteins.
Study Design: Randomized open clinical trial study
Place and Duration of Study: This study was conducted at the National Medical Center, Karachi from October 2020 to March 2021 for a period of six months.
Materials and Methods: 90 Hyperlipidemic males and females age group 40≥ and ≤75 years were allocated into three groups of 30 subjects each by computer allocated balloting randomization. The Group A subjects were given Tablet Rosuvastatin 10mg OD alone. The Group B subjects were given Tablet Rosuvastatin 10mg OD and Tablet Silymarin 200mg 1× BD. The Group C subjects were advised Tablet Silymarin 200mg 1×BD alone for the period of 3 months. Baseline investigations FLP, LFTS and CPK were done at week 0 and at week 12. There were total three visits of patients, at week 0, at week 6 and at the end of week 12.
Results: Rosuvastatin and Silymarin are consistent in decreasing the lipid levels at week 12 when compared with the baseline. Silymarin also shows good result in decreasing liver enzymes and CPK levels significantly.
Conclusion: Silymarin shows great potential in decreasing lipid levels of the blood when used alone and in combination with rosuvastatin. It has also shown great results in decreasing liver enzymes when used alone or in combination with rosuvastatin. The results of this study can further be evaluated with bigger sample size.
Key Words: Hyperlipidemia, Triglycerides, Low Density Lipoproteins, High Density Lipoproteins, Rosuvastatin, Silymarin

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INTRODUCTION

Hyperlipidemia is an umbrella term that deals with various genetic or acquired disorders characterized by elevated serum levels of lipoproteins mainly very low-density lipoprotein, low density lipoprotein and Low levels of high-density lipoprotein[1]. It is also associated with elevated levels of triglycerides, cholesterol and cholesterol esters.

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Increase in cholesterol levels and triglyceride level leads to atherosclerosis which is intimal thickening, lipid accumulation and calcification in the arteries causing endothelial dysfunction and can result in cardiovascular diseases[2]. Rosuvastatin, a HMG CoA reductase inhibitors have been approved as a first line Drug for Hyperlipidemia and significantly decrease high levels of cholesterol, TG and LDL[3]. Statins are usually well tolerated but it has certain adverse effects including gastrointestinal tract disorders, musculoskeletal pain, infections related to respiratory tract, headaches and lack of adherence give rise to depleted outcomes which causes shift towards the alternative therapies[4,5].

Silymarin, a traditional herbal remedy obtained from the seed of silybum marianum also known as milk thistle plant. It belongs to the largest family of kingdom plant Asteraceae and is epidemic in the Mediterranean and North African regions but can be also be found in

North West areas of Pakistan[6] and all the temperate areas around the globe. It is a complex mixture having an empirical formula $C_{25}H_{22}O_{10}$[7] and is composed of ample flavonolignans, out of them silibinin is the most essential component and composed of two diastereomers silibinin A and silibinin B thought to be responsible for the biological activity of silymarin[8]. Other flavonoligams includes silibinin, isosilibinin, silydianin, silychristin, isosilychristin, silimonin[9]. Besides Flavonolignans it also contains several flavonoids which includes taxifolin, quercetin, dihydrokaempferol, kaempferol, apigenin, naringin, eriodyctiol, and chrysoeriol. Silymarin has been used as a remedy since ancient times. For about 2000 years, its been used as an herbal medicine for many types of hepatic and gallbladder disorders of acute and chronic nature[10]. Silymarin can have a major role in decreasing lipid profile in patients of hyperlipidemia[11] as it is affiliated with alteration of membrane lipid by interfering with the secretion and uptake of lipoproteins Various studies show beneficial effects on LDL cholesterol. It is said that that it can be used alone or in combination with other anti-hyperlipidemic drugs to reduce the levels of TC, TG, LDL and increases the levels of HDL cholesterol in the blood[12].

MATERIALS AND METHODS

It is a randomized open clinical trial that was conducted in 130 males and females ≥ 40 and ≤75 years of age diagnosed with hyperlipidemia with fasting lipid profile TC ≥ 200, LDL ≥ 100 mg/dl, Triglycerides ≥ 150 and BMI ≥28 associated with either Diabetes, Hypertension, Hypothyroidism or Ischemic heart disease were inducted in the study after a written informed consent. Patients with age < 40 and >75 years, having myopathies, having raised CPK levels, BMI < 28, pregnant woman and lactating mothers were excluded from the study. Recruitment of patient was done from OPD of National Medical Center. Out of these 130 patients only 90 patients completed the study which were allocated into three groups of 30 patients each by a computer allocated balloting randomization. The Group A subjects were given Tablet rosuvastatin 10mg OD alone. The Group B subjects were given Tablet Rosuvastatin 10mg OD and Tablet Silymarin 200mg 1× BD. The Group C subjects were advised Tablet Silymarin 200mg 1×BD alone for the period of 3 months. Baseline investigations FLP, LFTS and CPK were done at week 0 and at week 12. There were total three visits of patients, at week 0, at week 6 and at the end of week 12. At week 0 patients were asked to read consent form and sign it, they were assessed for anthropometric measurements, evaluation form was filled with personal and laboratory data and were advised to take low carbohydrate and low fat diet. At week 6 the patients were called to check for any adverse symptoms and check their compliance and after 12 weeks patients were called along with the laboratory investigation reports. At this time their anthropometric measurements were also checked and documented.

RESULTS

90 patients of Hyperlipidemia completed the study and divided equally into three groups Group A, Group B and Group C. The mean age of the patients included in the study was 50.61±8.150. The population of female was more as compared to males and majority of them were married.

Anthropometric measurements: Weight, height, waist and hip circumference were noted at 0 week and at 12th week. BMI and Waist Hip ratio was calculated. The mean BMI of the patients was found to be 34.1±7.71 and mean waist ratio was found to be 0.93 for all 90 patients.

Laboratory Findings

Lipid profile: The paired analysis between day 0 and day 90 of all 3 groups for the lipid profile parameters was done which includes total cholesterol, triglycerides, high density lipoprotein cholesterol and low-density lipoprotein cholesterol was performed by Paired Students t test.

Total cholesterol: The levels of total cholesterol were recorded at week 0 and at week 12. The results for Group A, B and C is significant having p value less than 0.001.

Triglycerides: The levels of triglycerides were recorded at week 0 and at week 12. The results for Group B and C is significant having p value less than 0.001 while p value for group C is 0.038 which is non-significant.

Low density lipoprotein cholesterol: The comparison between day 0 and day 90 of LDL levels between 3 groups and the results were significant for all three groups having p value less than 0.001.

High density lipoprotein cholesterol: HDL levels were marked at day 0 and at day 90 of the study. The results for group A and B were non-significant having p values 0.857 and 0.684 respectively. Group C showed highly significant results having p value less than 0.001.

Liver function tests: The comparison between day 0 and day 90 of the treatment group for liver function tests which include SGPT and SGOT was done by paired student T test.

Serum Glutamic Pyruvic Transaminase: SGPT was done to assess the liver function and also to see the effects of drugs. All three groups showed significant result having p value 0.025, 0.005 and < 0.001 for group A, B and C respectively.

Serum Glutamic-Oxaloacetic Transaminase: SGOT levels were marked at day 0 and at day 90 of the study All three groups showed significant results having p values < 0.001, 0.026 and < 0.001 for group A, B and C respectively.

Creatine Phosphokinase: CPK levels were marked at day 0 and at day 90 of the study. The results for group

A was 0.054 which is non-significant and got significant results for group B and C having p values 0.012 and <.001 respectively. (Table 1 to 3 & Figure 1).

Table No.1: Association of Clinical variables at the time of admission among different groups

Variables		Group		
		Group A (Rosuvastatin	Group B (Rosuvastatin+Silymarin)	Group C (Silymarin)
Age(years)	40-51	14(46.7%)	17(56.7%)	23(76.7%)
	52-63	10(33.3%)	10(33.3%)	7(23.7%)
	64-75	6(20%)	3(10%)	0(%)
Gender	Female	18(60%)	19(63.3%)	19(63.3%)
	Male	12(40%)	11(36.7%)	11(36.7%)
BMI	Baseline	35.647±12.28	33.704±4.88	32.943±1.82
	3 Months	33.297±3.65	33.237±4.82	32.407±1.77
Waist Hip Ratio	Baseline	0.9330± 0.038	0.9347±0.046	0.9393±0.016
	3 Months	0.9343±0.030	0.9410±0.028	0.9433±0.016
Marital Status	Married	29(96.7%)	28(93.3%)	30(100%)
	Unmarried	1(3.3%)	2(6.7%)	0(%)
Diabetes	Yes	23(76.7%)	23(76.7%)	29(96.7%)
	No	7(23.3%)	7(23.3%)	1(3.3%)
Hypertension	Yes	15(50%)	15(50%)	14(46.7%)
	No	15(50%)	15(50%)	16(53.3%)
Hypothyroidism	Yes	3(10%)	2(6.7%)	0(%()
	No	27(90%)	28(93.3%)	30(100%)
IHD	Yes	2(6.7%)	2(6.7%)	3(10%)
	No	28(93.3%)	28(93.3%)	27(90%)

Table No.2: Group variables

	Group	Variables	Mean±STD	P-value
Group A (n=30)	Baseline	Pre TC mg/dl	220.17±37.929	
	3 months	Post TCmg/dl	180.23±27.656	<.001*
	Baseline	Pre TG mg/dl	194.47±63.35	
	3 months	Post TG mg/dl	163.17±56.37	0.038*
	Baseline	Pre LDL mg/dl	120.83±35.276	
	3months	Post LDL mg/dl	98.40±16.188	<.001*
	Baseline	Pre HDL mg/dl	37.80±8.536	
	3 months	Post HDL mg/dl	37.90±7.915	0.857
Group B(n=30)	Baseline	Pre TC mg/dl	215.33±50.174	
	3 months	Post TCmg/dl	181.07±40.299	<.001*
	Baseline	Pre TG mg/dl	191.87±73.629	
	3 months	Post TG mg/dl	154.83±60.428	<.001*
	Baseline	Pre LDL mg/dl	122.03±27.456	
	3 months	Post LDL mg/dl	101.17±21.651	<.001*
	Baseline	Pre HDL mg/dl	39.03±20.280	
	3 months	Post HDL mg/dl	37.67±6.440	0.684
Group C(n=30)	Baseline	Pre TC mg/dl	243.97±33.970	
	3 months	Post TC mg/dl	212.63±28.847	<.001*
	Baseline	Pre TG mg/dl	170.07±12.682	
	3 months	Post TG mg/dl	155.73±11.246	<.001*
	Baseline	Pre LDL mg/dl	112.03±13.142	
	3 months	Post LDL mg/dl	100.90±11.093	<.001*
	Baseline	Pre HDL mg/dl	35.03±4.375	
	3 months	Post HDL mg/dl	37.03±4.473	<.001*

Table No.3: Effect on Liver Function Test and CPK

Group	Variables	Mean±STD	P-value

Group A (n=30)			
Baseline	Pre SGPT mg/dl	26.30±14.898	
3 months	Post SGPTmg/dl	22.27±7.051	0.025
Baseline	Pre SGOT mg/dl	27.37±7.083	
3 months	Post SGOT mg/dl	25.53±6.415	<.001*
Baseline	Pre CPK units/L	51.57±24.54	0.054
3 months	Post CPK units/L	46.67±16.01	
GroupB(n=30)			
Baseline	Pre SGPT mg/dl	32.67±15.979	
3 months	Post SGPTmg/dl	27.63±12.0	0.005
Baseline	Pre SGOT mg/dl	31.30±12.669	
3 months	Post SGOTmg/dl	28.57±12.065	0.026
Baseline	Pre CPK units/L	53.77±29.84	
3 months	Post CPK units/L	50.10±27.93	0.012*
Group C(n=30)			
Baseline	Pre SGPT mg/dl	46.10±21.07	
3 months	Post SGPTmg/dl	38.20±13.535	<.001*
Baseline	Pre SGOT mg/dl	34.50±6.458	
3 months	Post SGOTmg/dl	32.07±5.919	<.001*
Baseline	Pre CPK units/L	36.40±14.03	
3 months	Post CPK units/L	34.90±13.51	<.001*

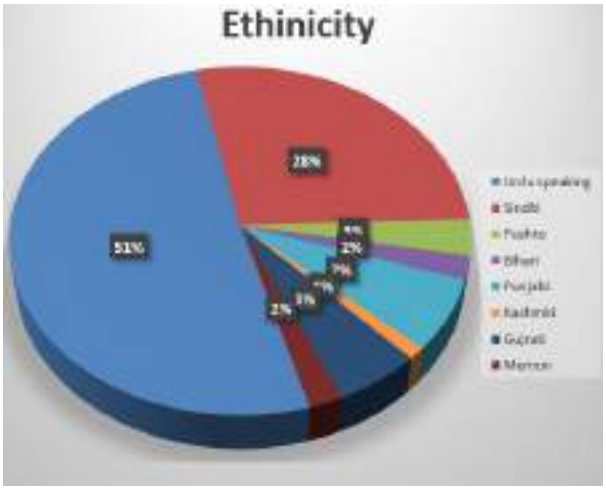

Figure No.1: Ethnicity of study population

DISCUSSION

This study was conducted to evaluate the effects of Rosuvastatin and Silymarin on blood levels of total Cholesterol, Triglycerides, LDL and HDL in hyperlipidemic patients and also focuses on the effect of these drugs on liver enzymes and CPK levels. As Rosuvastatin has established role in decreasing lipid levels but in this trial Silymarin has proved itself in decreasing lipid levels comparative to Rosuvastatin.

Decrease in Levels of Lipid profile in Rosuvastatin group is consistent with Liu which states decrease in levels of total cholesterol by 26% with the use of Rosuvastatin 10mg for 4 weeks and 31% reduction when given for 8 weeks with the sample size of 64 patients[13] and also Bostan which states the reduction in the levels of total cholesterol along with the reduction in levels of LDL, Apo E protein and Homocysteine. It has a sample size of 100 patients and they were given Tablet Rosuvastatin 20 mg for 6 months[14].

Decrease in Levels of Lipid profile in Rosuvastatin and Silymarin group is consistent with Abdul conducted the study on Silymarin and lovastatin with 45 patients altogether which was done to evaluate the effects of Silymarin on hyperlipidemia with different etiologies and gives significant result which shows the synergistic effect of Silymarin with statins in lowering down cholesterol levels[12].

Decrease in Levels of Lipid profile in Silymarin group is consistent with Hayder who conducted the study with 20 patients divided into 2 groups giving 600mg sugar as placebo and 600mg Silymarin for the period of 2 weeks[15] and also with Nauman who conducted a study to evaluate the effect of Silymarin 200mg BD on Type 1 diabetic patients who have poor control over insulin. This study along with other benefits also gives significant results in lowering TC levels compared with control group after 60 days. These results are consistent with the results of this study[16].

SGPT and SGOT were done to assess the liver function and also to see the effects of drugs. Rosuvastatin significantly decreases SGPT and SGOT levels which was significant with Nakahara[17]. Combination of Rosuvastatin and Silymarin also significantly decreases the liver enzymes which was consistent with Abdul[12]. Silymarin Group showed significant result in decreasing liver enzymes which was consistent with

studies conducted by Hussein[18], Wah Kheong[19] and Ghalandari[20].

CONCLUSION

Natural products such as Silymarin when given in a dose of 200 mg BD for the period of 3 months can be a good alternative to high dose statins in order to decrease lipid profile as a monotherapy along with decreasing SGPT and SGOT levels and also as combination therapy to avoid high doses of statins and provide good control on increased lipid levels specially in patients associated with co morbidities like Diabetes, Hypertension, Hypothyroidism and Ischemic heart disease. It is considered as a safe drug as there was no adverse effect associated with its use in our study.

Recommendations: Silymarin has vast range of therapeutic uses. Many trials can be done with a bigger sample size to evaluate its effect on lipids with different statins and other lipid lowering drugs, its role in glycemic control, hepatic protection, different liver diseases, in different poisoning cases, as a chemotherapeutic agent and also as anti-neurodegenerative agent.

Author's Contribution:

Concept & Design of Study:	Muhammad Ali Zubair
Drafting:	Mehwish Mansoor, Talea Hoor
Data Analysis:	Hina Amjad, Muhammad Sajid Abbas Jaffri, Muhammad Ajmal Tahir
Revisiting Critically:	Muhammad Ali Zubair, Mehwish Mansoor
Final Approval of version:	Muhammad Ali Zubair

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Incidence and Presentation of Ectopic Pregnancy

Nasreen Sultana Kakar, Rohana Salam, Zubia Bugti, Rizwana Naz, Naila Ehsan and Samia Saifullah

ABSTRACT

Objective: To determine the incidence and presentation of ectopic pregnancy presented at Gynecology Unit 1, Civil Hospital Quetta.
Study Design: Descriptive study
Place and Duration of Study: This study was conducted at the at the Department of Obstetrics and Gynecology, Civil Hospital Quetta for a period of one year from January, 2019 to December, 2019.
Materials and Methods: A total of 24 patients with ectopic pregnancy were reported during this time period. All 24 patients were informed and included in the study with their willful consent to participate.
Results: Patients had a mean standard deviation age of 29 ± 5.12 years. The youngest patient in the group being of age 22, and the eldest included was of age 38. Out of these 24 patients, 23 (95.8%) were ruptured ectopic while one (4.2%) was unruptured. 10 patients (41.7%) had right sided ectopic pregnancy and 14 patients (58.3%) had left sided ectopic pregnancy. All 24 patients were presented with vaginal bleeding, pelvic pain, abdominal pain, and amenorrhea. Out of these, 14 were also presented with shock.
Conclusion: Considering the risk factors and clinical presentation, early diagnosis of ectopic pregnancy can help reduce the mortality and morbidity rate.

Key Words: Incidence, Ectopic Pregnancy

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INTRODUCTION

Ectopic pregnancy is a gynecological emergency defined as the implant of a fertilized ovum besides the typical uterine cavity [(1)]. While it is common for such pregnancies to occur in the fallopian tube, they may also be observed in the cervix, ovaries or the abdomen. A study suggests that 1-2% of all pregnancies may end up in this complication of ectopic pregnancy, and contributes greatly to the morbidity of the patient [(2)]. It claims the life of about 10-15 women each year and no appreciable decrease in the morbidity or mortality rate has been observed in the past few decades. Although most ectopic pregnancies are tubal, about 10% of ectopic pregnancies may be non-tubal. A study states that non-tubal ectopic pregnancies result in higher morbidity and mortality rate as a result of their late presentation and challenging diagnosis[(3)].

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This complication is more common in the developing countries. Not only does an ectopic pregnancy threaten the life of a woman, its late and ineffective treatment may also result in having an adverse impact of the fertility by damaging vital reproductive organs such as the ovaries, fallopian tube or even the uterus [(4)].
Various factors have contributed to the incidence and prevalence of ectopic pregnancies over the years. A study suggests that pelvic inflammatory diseases are the most common cause of ectopic pregnancy however; various other factors also contribute to its occurrence[(5)]. Pregnant women who present themselves in the emergency with complaints of vaginal bleeding and/or abdominal/pelvic ache are often examined as suspects of ectopic pregnancy [(6)]. A pelvic ultrasound is usually required to evaluate the patient's situation. With a sound knowledge of laboratory tests, sonographic procedures and imaging characteristics related to ectopic pregnancy, an ectopic pregnancy could be identified with ease [(7)].

MATERIALS AND METHODS

This study was conducted at the Department of Obstetrics and Gynecology, Civil Hospital Quetta for a period of one year from January, 2019 to December, 2019.A total of 24 patience with ectopic pregnancy were reported during this time period. All 24 patients were informed and included in the study with their willful consent to participate.

RESULTS

Patients had a mean standard deviation age of 29 ± 5.12 years. The youngest patient in the group being of age 22, and the eldest included was of age 38. Out of these 24 patients, 23 (95.8%) were ruptured ectopic while one (4.2%) was unruptured. 10 patients (41.7%) had right sided ectopic pregnancy and 14 patients (58.3%) had left sided ectopic pregnancy. All 24 patients were presented with vaginal bleeding, pelvic pain, abdominal pain, and amenorrhea. Out of these, 14 were also presented with shock.

Table No.1: Patients detail regarding Clinical presentation

Clinical Presentation	Number of patients (percentage)
Vaginal bleeding/brown discharge	24 (100%)
Abdominal pain	24(100%)
Pelvic pain	24 (100%)
Amenorrhea	24 (100%)
Shock	14 (58.3%)

Table No.2: Ectopic Pregnancies detail

Ruptured ectopic pregnancies	95.8%
Unruptured ectopic pregnancies	4.2%
Left-sided ectopic pregnancies	58.3%
Right-sided ectopic pregnancies	41.7%

DISCUSSION

Ectopic pregnancy is one of the leading causes of morbidity and mortality in women particularly during their first trimester of pregnancy. Mortality rate for EP is about ten times greater than that of vaginal birth and five times greater than that of induced abortion. Not only does it pose a serious threat to the woman's life, it also highly reduced the chances of future pregnancies and takes an enormous toll on the mother's mental and physical health [8] [9]. It is important to identify the risk factors associated with ectopic pregnancy as well as know their presentation and appropriate management to ensure a reduced mortality and morbidity rate. An extensive study conducted in the United States shows that the incidence of ectopic pregnancy in the US has increased over the years, where the incidence was 11.0% in 2006 and rose to 13.7 in 2013 in every 1000 pregnancies. Women of all ages were concluded to be prone to this increase in incidence [10]. A Nigerian study suggests that incidence of ectopic pregnancy was 8.3% from a total of 2067 gynecological admissions. The mean age of females in this study was 29 ± 5 years, similar to that of our study here. The percentage for ruptured pregnancies was observed to be 98.3%, comparable to that of our 95.8% incidence [11]. Another study reports that incidence of ectopic pregnancy was 12.5% in United Kingdom per 1000 deliveries, 3.12% in India and 0.6% in Pakistan [12].

Various risk factors contribute to the prevalence of ectopic pregnancy in women. Majority of the literature reviewed for this study in regard to risk factors suggested that pelvic inflammatory disease accounts as a major risk factor of ectopic pregnancy [1, 2, 4, 5, 13, 14]. Pelvic inflammatory diseases cause scarring, this in turn turns out to interfere with the capture and movement of the egg. It also interferes with the movement of the spermatozoa, increasing the chances of an ectopic pregnancy. It also contributes to the delayed diagnosis of ectopic pregnancy as well as delayed treatment for acute pelvic infection [14].

Another study suggests a connection between ectopic pregnancy and single women. It reasons that multiple sex partners contribute to the prevalence of STDs and PIDs, which in turn are strongly related to ectopic pregnancies. Age was also stated to be a risk factor in the study as it suggests that early debut of intercourse (age 15-19) raises the probabilities of an ectopic pregnancy. The age group 25-29 was less prone to ectopic pregnancy by a percentage of nearly 65% [15].

Assisted reproductive technology is gaining popularity as a treatment for infertility. However, this comes with an increased frequency of ectopic pregnancies. Tubal inflammation is one of the most prominent risk factors of ectopic pregnancy. Since most patients that seek IVF treatment have tubal infertility, the rate of ectopic pregnancy in patients seeking assisted reproductive technology is higher than theoretically expected [16]. Another study suggests that treatment for infertility accounts for 31.5% of ectopic pregnancies, making it a major risk factor [18].

Smoking is yet another risk factor strongly related with ectopic pregnancy. An extensive study including 41,440 pregnancies concluded that currently smoking women had a 73% higher chance of having an ectopic pregnancy as compared to a woman who had never smoked. An ex-smoker had a lower chance than a current smoker did however; they were still at a solid 22% higher risk of ectopic pregnancy. A clear relation between duration of smoking was not observed, both a light and relatively new smoker and a smoker of 15+ years were at a high risk of EP [17].

It is also found that there is a strong correlation between previous tubal surgical procedures and ectopic pregnancies. A tubal damage can increase the chances of ectopic pregnancy to up to three times. Endometriosis is considered as another prominent risk factor of ectopic pregnancy and is said to increase the incidence of EP in women. Previous history of ectopic pregnancy also puts the patient at a higher risk of further ectopic pregnancies in the future [2].

Clinical presentation helps categories a patient for a certain complication and so it is important to discuss the clinical presentation for ectopic pregnancy for timely diagnosis. A study suggests that in addition to the potential risk factors, presentation with amenorrhea, vaginal bleeding and abdominal pain were observed in 27.7% of the cases. Since this indication is rather low, the study suggested early and regular ultrasound

inspection for timely diagnosis[18]. A study by Cozlea et al found out that amenorrhea was observed in all patients, 98.75% of which was observed before the 14th week of gestation while 1.25% was observed after the 14th week. 80% of the patients came in with vaginal bleeding while it was absent in 20% of the patients. About 60% ectopic pregnancies in this study were right sided as opposed to our study of greater incidence of left sided EP [(19)].

CONCLUSION

Ectopic pregnancy is one of highest contributors to maternal and fetal morbidity and mortality rate. Our study included 24 patients of ectopic pregnancy, most of which were presented with vaginal bleeding, amenorrhea, abdominal pain, pelvic pain and some were in shock. Most of them were left sided ectopic pregnancies and all except one were ruptured. Considering the risk factors and clinical presentation, early diagnosis of ectopic pregnancy can help reduce the mortality and morbidity rate.

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Diagnostic Accuracy of Ultrasonography (USG) in Diagnosing Carpal Tunnel Syndrome (CTS) Taking Nerve Conduction Studies (NCS) as Gold Standard

Muhammad Wazir Ali Khan and Hafiz Muhammad Zeeshan

ABSTRACT

Objective: To evaluate the diagnostic potential of ultrasound taking nerve conduction study as the gold standard in patients with clinical and electro diagnostic evidence of CTS.

Study Design: Analytical Validation Study

Place and Duration of Study: This study was conducted at the department of Neurology Sh Zayed Medical College/Hospital, Rahim Yar Khan for a period of six months from March to August 2021.

Materials and Methods: 80 patients were enrolled after fulfilling the selection criteria. A total of 160 hands were tested. USG and NCS studies were performed. Cross sectional area of the carpal tunnel was calculated and the results were analyzed for sensitivity and specificity, positive predictive value and negative predictive values and diagnostic accuracy.

Results: Of the 80 patients and 160 hands tested, 8 patients were male and 72 were females. On NCS, 142 hands (89%) were tested positive for CTS and 18 hands (11%) were tested negative. On ultrasonography, 128 hands (80%) had CSA of more than 8.5mm^2, and 32 hands (20%) less than 8.5mm^2. Sensitivity of USG was 91% with 90% specificity. Diagnostic accuracy was 88% for USG to diagnose CTS. The results were significant with a p-value 0.0005 (.05).

Conclusion: Ultrasound is comparable to NCS in diagnosing CTS. It is cheap, readily available and does not require much technical expertise and equipment.

Key Words: Carpal Tunnel Syndrome (CTS), Nerve conduction studies (NCS), Cross sectional area (CSA), Ultrasonography (USG)

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INTRODUCTION

Carpal tunnel syndrome (CTS) is the most common symptomatic compressive neuropathy at the wrist. Median nerve is entrapped at the carpal tunnel.[1]. It has a prevalence of 2.7 to 5.8% in the adult population[2] and is more common among adult women (9%) than men (0.6%)[3].

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Typical symptoms include numbness, tingling or pain in the lateral two-thirds of the hand in the distribution of the median nerve. Symptoms are more severe at night and often patients are awakened from sleep. Patients may experience radicular pain in the arm, forearm and hand. Weakness may be noted in hand grip and opposition of the thumb[4].

The abnormally high pressure or injury may cause CTS. Although, many cases are idiopathic but also associated with smoking, pregnancy, overuse of hands and wrist, wrist injury, obesity, hypothyroidism, diabetes, renal failure, rheumatoid arthritis and osteoarthritis, etc.[5] It was estimated that between 400,000 and 500,000 cases of CTS require operative treatment annually in the States.[6] Similarly, surgical decompression is done in UK for 43 to 74 per 100,000 per year[7]. Several clinical

examination tests help in the diagnosis of CTS but none of these tests are diagnostic on their own. The tests commonly used are Tinel's test, Phalen's Test and reverse phalen test. Nerve conduction studies are considered the gold standard test. However, they are also associated with false positive and false negative results[8]. Comparison of ultrasound and nerve conduction studies for the diagnosis of carpal tunnel requires a reference standard for the diagnosis of CTS. In a meta-analysis, similar diagnostic accuracy between USG and CTS was found. [9] Median nerve compression at the carpal tunnel results in nerve swelling proximal and distal to the tunnel. The CSA of the median nerve at the tunnel inlet is measured on ultrasound, cutoff values of CSA are used to determine whether the test is positive or negative [10]. The CSA of median nerve at the distal wrist crease varies among different reports [11]. It has ranged from 7.2 to 9.8 mm^2 in various reports. The median nerve CSA range for diagnosing CTS is from 9 to 15 mm^2. These values have a sensitivity and specificity from 70 to 88% and 57 to 97%, respectively[12,13].

In our region, as we have very limited resources, especially the electrophysiological test availability, affordability and expertise is the concern, we designed this study to look for better, cheaper, comparable and easily available alternatives for early diagnosis of carpal tunnel syndrome. Also, very little work is done on this topic in our region.

MATERIALS AND METHODS

Study Design: It is a cross sectional diagnostic study conducted at Sheikh Zayed Hospital, Rahim Yar Khan. The study duration was six months. The sample size was 80 patients, with a total 160 hands tested. The sampling technique used was non-probability purposive sampling.

Selection Criteria: Inclusion criteria: Patients with a CTS-6 score of ≥12 points (Appendix 1). Patients from both genders and all ages and those who agree to participate in this study

Exclusion criteria:

· All patients with history of trauma

· All patients with a history of wrist surgery, wrist trauma or congenital deformity.

. All pregnant females.

· All patients with history of post stroke contractures

· All patients who received steroid injections.

. All patients diagnosed with polyneuropathy, radiculopathy or mononeuritis.

Data Collection: Permission taken from the ethical review committee and informed consent taken from all the participants. High probability cases or the suspected cases were defined by using CTS-6 criteria. The CTS-6 is a clinical model that estimates the clinical diagnostic possibility of CTS. A total of six criteria are used for the clinical diagnosis using CTS-6 score. A score of ≥ 12 is considered for labelling patients with high probability of having CTS. We tested our hypothesis that "Ultrasonography is comparable to nerve conduction studies in diagnosing carpal tunnel syndrome".

Demographic details of the patients like age, gender, duration of symptoms, CTS 6 score were recorded using questionnaires. All patients underwent standard USG and NCS procedures for diagnosis of CTS. The data analysis was done using SPSS.

Ultrasound: All USG examinations were performed by the radiologist expert in musculoskeletal US, at Sheikh Zayed medical college/hospital, Rahim Yar Khan, on the same equipment, with high resolution and broadband linear transducers. The US examination was done on both hands with the forearm in a supine position, keeping the wrists in neutral position. The cross-sectional area (CSA) at the proximal "in let"of the carpal tunnel is directly measured. A cutoff value ≥8.5 mm^2 at the carpal tunnel inlet, considered to confirm diagnosis of CTS using USG.

Nerve Conduction Studies: For electro diagnostic study (EDX) we used the Neuropack EMG-EP measuring device. Device model is MEB-9200K, 2003; Nihon Kohden Corporation, Tokyo, Japan. Reference values of Dumitru and Zawarts were used[14]. The EDX studies were performed by only one neurologist with 12 years of experience. The skin and room temperatures were maintained around 32°C and at 25°C, respectively. Both the hands were tested, whether symptomatic or not. The nerve conduction studies were done by recording median and ulnar sensory peak latencies, median nerve conduction velocities, and median distal motor latencies (DML) in both hands. Standard parameters of median and ulnar nerve stimulation and surface recordings were used. The EDX parameters considered for diagnosing CTS were: a) more than 0.4 ms difference between the median and ulnar sensory peak latencies. b) a median distal motor latency (DML) of more than 4.0 ms.[15]

Data Analysis: Data analysis done using Statistical Package for Social Sciences (SPSS) version 25. For numeric data, mean and standard deviation were calculated. For categorical data, frequency and percentage were measured. Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of Ultrasonography (USG) was determined. Keeping NCS taken as the gold standard, the two by two tables used for the USG findings to find the sensitivity and specificity, positive predictive value, negative predictive value, and diagnostic accuracy of ultrasonography in accurately diagnosing CTS. Chi square test done to find the significance of USG findings. The level of significance was 0.05. The ROC curve is drawn for true positives and true negatives.

Area under the curve (AUC) depicts the diagnostic accuracy of USG in diagnosing carpal tunnel syndrome.

RESULTS

Of the 80 patients and 160 hands tested, 8 patients were male and 72 were females. Mean age of the patients was 37.6 ± 9.1 years (24–55 years) and the gender ratio was 1:9 [M:F]. On NCS, 142 hands (89%) were tested positive for CTS and 18 hands (11%) were tested negative. (Table 1). On ultrasonography, 128 hands (80%) had CSA of more than 8.5mm^2, and 32 hands (20%) less than 8.5mm^2.(Table 2). Sensitivity of USG was 91% with 90% specificity. Diagnostic accuracy was 88% for USG to diagnose CTS. Chi square test for significance was done for the same samples undergoing the two tests. (Table 3). The results were significant with a p-value 0.0005 (.05). Of the female patients, 91.5% have positive nerve conduction studies and 75.6% females have positive results on USG. 75% of males have positive nerve conduction studies and 44% have positive USG. The ROC curve drawn for sensitivity and 1-specificity, shows that more than 80% of patients were successfully detected as having CTS on USG. It indicates that the test is a good test to diagnose CTS.

Table No.1: Nerve Conduction Studies Results n=160

	Positive	Negative
Male	12	4
Female	130	14
Sub Total	142	18
Total	160	

Table No.2: Wrist Ultrasonography Results N=160

	Positive (CSA >8.5)	Negative (CSA <8.5)
Male	7	9
Female	121	23
Sub Total	128	32
Total	160	

Table No.3: Outcome parameters of USG

Sensitivity	91%
Specificity	90.00%
PPV	98.40%
NPV	60%
Accuracy	88%

DISCUSSION

The diagnosis of CTS is based primarily on typical clinical signs and symptoms and confirmed by nerve conduction studies. Median nerve ultrasonography has been considered a potential diagnostic tool in diagnosing CTS[8]. The CSA measurement at the carpal tunnel inlet is most frequently used for the diagnosis of CTS by ultrasound[16]. In our study, we used inlet CSA of the median nerve of symptomatic high probability cases of CTS.

In our study, of the 80 patients and 160 hands tested, 8 patients were male and 72 were females. Mean age of the patients was 37.6 ± 9.1 years (24–55 years) and the gender ratio was 1:9 [M:F]. On NCS, 142 hands (89%) were tested positive for CTS and 18 hands (11%) were tested negative. On ultrasonography, 128 hands (80%) had CSA of more than 8.5mm^2, and 32 hands (20%) less than 8.5mm^2. Sensitivity of USG was 91% with 90% specificity. Diagnostic accuracy was 88% for USG to diagnose CTS. The results were significant with a p-value 0.0005 (.05). In our study women were much higher in number than men. The factors underlying increased incidence include hormonal factors, higher frequency of musculoskeletal problems. CTS in women causes swelling and increased pressure on the median nerve. Similar to other studies, the women in the middle age group are frequently affected [17]. Most of the study participants were household women, who are engaged in daily chores like washing clothes and other cleaning tasks. All these increase the risk of developing CTS by causing frictional inflammation and tendon pressure[18].

Although electrodiagnostic studies are more accurate in diagnosis of CTS, USG can identify the underlying pathology causing CTS, anatomical variants or space occupying pathology[19].

Median nerve CSA values were 11.64 mm^2 for mild, 13.74 mm^2 for moderate, and 16.80 mm^2 for severe CTS in a meta-analysis of 16 studies[20]. In compression neuropathies, peripheral nerve CSA is an important USG finding.

Our study clearly shows that USG is comparable to NCS in the diagnosis of CTS. Inlet CSA is a valuable measurement, can be done at low cost and with less technical expertise. Women, due to their physiological make up, are more likely to develop CTS. Routine household activities are important contributory factors.

Our study has certain limitations, it uses a cut-off value of ≤ 8.5 and also uses single criteria to confirm CTS diagnosis. It does not take into account the severity or grading of CTS and compare it with the CSA values. This can help in further classifying the USG values for higher and severer grades of CTS on USG. Also the sample size can be increased and a case control study can be done to compare the asymptomatic control group to sampled group for comparison of CSA values in symptomatic and asymptomatic groups.

CONCLUSION

Ultrasonography is comparable to nerve conduction studies for the early diagnosis of CTS. It can effectively exclude the secondary causes of CTS. It is cheap, readily available and does not require much technical expertise and equipment.

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Fosfomycin an Old Drug with A New Role in E.Coli Associated Urinary Tract Infections

Shandana Altaf[1], Ahmad Zeb Khan[2], Farman Ullah[2], Irfan Mirza[2], Sayed Anwar Hussain[3] and Mufti Baleegh-ur-raheem Mahmood[2]

ABSTRACT

Objective: To know the impact of Fosfomycin an Old Drug with A New Role in E.Coli Associated Urinary Tract Infections.

Study Design: Descriptive Study

Place and Duration of Study: This study was conducted at the department of Nephrology Khyber Teaching Hospital, Peshawar from July 2020 to June 2021 for a period of one year.

Materials and Methods: Urine Culture Sensitivity of patients with UTI was assessed and E. Coli sensitivity pattern was studied.

Results: Over all sensitivity of E. coli to Fosfomycin was 84.31% in the studied population. According to gender distribution of the cohort the sensitivity to Fosfomycin was 83.33% in male patients and 84.84% in the female patients. To compare the sensitivity of Fosfomycin versus other antibiotics in UTI, we found that Fosfomycin was showing sensitivity against E. coli related UTI of 84.31% compared to that Ciprofloxacin 20.58%, Trimethoprim sulphamethoxazole 17.64% and Amoxicillin-clavulanic acid 13.72%.

Conclusion: This study shows that in the presence of mounting antibiotics resistance, Fosfomycin is a safe and suitable alternative in the treatment of UTI caused by MDR pathogens like E. Coli which otherwise do not respond to other antibiotics.

Key Words: UTI, E. Coli, Fosfomycin

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INTRODUCTION

Urinary tract infections (UTI) are among the commonest types of bacterial infections worldwide. More than 10 million out patients visit and 2 million emergency room visit occurs annually in USA due to UTIs [1,2]

Antimicrobial resistance is increasing worldwide, leading to infections that are difficult to treat and are associated with higher morbidity and mortality. The treatment of UTI with these resistant organisms is a challenge for the practicing Physicians and Nephrologists.

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The misuse and over use of these antibiotics have led to the emergence of resistant strains of bacteria specially the Escherichia Coli (E, Coli) which is the most common pathogen isolated from urine cultures world over. There are few new antibiotics on the horizon and those that have been approved recently are mostly for intravenous use, therefore older 'forgotten' drugs are being re-explored for the treatment of UTI and cystitis[3,4,5,6]

Fosfomycin is a broad spectrum bactericidal antibiotic and an acceptable alternative drug in such cases is available in oral form, is well tolerated and has low resistance rates in E. Coli based UTI, having little interaction with other drugs.[7] Based on the efficacy, safety and well tolerability, the 2011 Infections Disease Society of America (IDSA) and FDA clinical practice guidelines endorsed Fosfomycin as a first line treatment for uncomplicated UTI and cystitis.[8,9,10,11]

This drug was used for a long time in the past for treatment of UTI, but gradually lost its favor due to emergence of newer antibiotics in the market. However, with the emergence of resistance to different antibiotics such as B Lactam antibiotics, quinolones and aminoglycosides worldwide, Fosfomycin is again emerging as a viable alternative option.[12,13] Data from

Spain showed the overall resistance level to all types of Escherichia Coli (E, Coli) isolated (ESBL producing and ESBL non-producing) to Fosfomycin remained significantly low at 2.9% in 2019. Similarly, data from Poland showed the overall susceptibility of E. Coli isolates to Fosfomycin were 62.2% in complicated UTIs and 77.6% in uncomplicated UTIs. [14,15,16] Similarly another study at Dutch hospitals showed resistance rates of 14% for ciprofloxacin, 23% for trimethoprim-sulphamethoxazole and 36% for amoxicillin-clavulanic acid with higher resistance rates in patients having UTI due to E. Coli uropathogens.[17]

Fosfomycin disodium is very hydrophilic agent therefore only 3% of drug is bound to protein in serum and this permits favorable tissue availability. Also, the low molecular weight favors higher diffusibility as well.[18,19] Approximately 93% of administered dose undergoes the glomerular filtration in the kidney and is excreted unchanged in urine.[20] A small number of adverse effects, like nausea, vomiting abdominal colic, diarrhea and dyspepsia have been reported following oral usage.[21] In preventing different stages of cell wall synthesis Fosfomycin may have synergistic effect with B Lactam antibiotics because Fosfomycin prevents the first stage of cell wall synthesis, while B-Lactam antibiotics inhibits the final phase of it.[22]

Therefore, this old forgotten drug is now emerging again for the treatment of E. coli associated UTIs and cystitis. It also has a unique property of not sharing any structural similarity and lack of cross-resistance with other antibiotics.[23]

MATERIALS AND METHODS

This is a descriptive study conducted over a period of one year from July 2020 to June 2021 in the department of Nephrology Khyber Teaching Hospital, Peshawar. The study was approved by the institutional ethical committee.

Urine sample of patients received in Out Patient Department of Nephrology, with signs and symptoms of UTI, were send for culture & sensitivity in the above-mentioned period. Urine sample received in the Microbiology Laboratory from these patients were plated by semi-quantitative culture method on blood agar and MacConkey's agar and incubated at 37oC overnight. The isolates obtained from the samples with significant bacteremia with the background of relevant supportive clinical features of UTI were processed further. The bacterial species identification was performed by standard biochemical methods.[24]

Inclusion criteria used to define patients with UTI caused by E. Coli were:

1. Signs and symptoms of UTI (for example dysuria, urgency, suprapubic tenderness, fever and hematuria or pyuria.)
2. Urine culture positive for E. Coli $>10^5$ colony forming units/ml in a clean-catch, midstream urine sample.
3. In vitro susceptibility of E. Coli to Fosfomycin as determined by the agar-dilution method and according to European committee on antimicrobial susceptibility testing (EUCAST) criteria.

RESULTS

Out of 102 patients studied during this period 36 (35.29%) were male and 66 (64.70%) were female patients, with male to female ratio of 1:1.8 (Table 1).

Patient age was in the range of 12 years to 80 years with mean of 54 years.

Over all sensitivity of E. Coli to Fosfomycin was 86 out of 102 (84.31%) in the studied population. (Table 2).

According to gender distribution of the cohort the sensitivity to Fosfomycin was 30/36 (83.33%) in male patients and 56/66 (84.84%) in the female patients (Table 3).

Regarding age wise distribution of culture positive UTI 9/102 (8.82%) were less than 25 years of age, 52/102 (50.90%) were in the age range of 25-50 years and 56/102 (54.90%) were above 50 years of age (Table 4).

In the Fosfomycin sensitivity spectrum we found that 9/9 (100%) patients were sensitive in the age group of less than 25 years, while 33/52 (63.46%) were in the age group of 25-50 years and remaining 44/56 (78.57%) were patients above 50 years of age (Table 5).

To compare the sensitivity of E. Coli to Fosfomycin versus other antibiotics commonly used in the community, we found that Fosfomycin was showing sensitivity in 86/102 (84.31%) as mentioned earlier and compared to that Ciprofloxacin 21/102 (20.58%), Trimethoprim-sulphamethoxazole 18/102 (17.64%) and Amoxicillin-clavulanic acid 14/102 (13.72%) showed low level of sensitivity against the E. Coli in urine culture (Table 6).

Table No.1: UTI Occurance in Different Gender

Characteristic	No	Percentage
All patients	102	100%
Male	36	35.29%
Female	66	64.70%

Table No.2: Total Positivity Ratio

Positive cultures	Negative cultures
86 (84.31%)	16 (15.68%)

Table No.3: Gender Distribution among Positive Cases

Characteristics	Positive cultures	Negative cultures	Total
Male	30	6	36 (83.33%)

Female	56	10	66 (84.84%)

Table No.4: Age Wise Distribution of Culture Positive UTI

Age range	No	Percentage
Less than 25 years	9/102	8.82%
25-50 years	38/102	37.25%
More than 50 years	56/102	54.90%

Table No.5: Sensitivity in Different Age Groups

Age range	Total patients	Positive cultures	Percentage
Less than 25 years	9	9	100%
25-50 years	52	33	63.46%
More than 50 years	56	44	78.57%

Table No.6: Sensitivity Pattern Against E. Coli in Different Antibiotics

Drugs	Positivity against E. Coli	Percentage
Fofomycin	86/102	84.31%
Ciprofoxacin	21/102	20.58%
Trimethoprim sulphamethoxazole	18/102	17.64%
Amoxicillin clvulanic acid	14/102	13.72%

DISCUSSION

Our study showed that urinary tract infections (UTI) in females were 64.70% as compared to males 35.29%. Usually, 60% of all females will develop UTI in their life time. In our study it was shown that 54% of patients with UTI were above 50 years of age compared to 37% patients having UTI in the age group of 25-50 years. The Fosfomycin sensitivity ratio in E. Coli related UTI was found to be more than 84% which was significantly better than most of the commonly used drugs. In the positive cohort of almost 100% cases in younger age group of less than 25 years showed sensitivity to Fosfomycin, while 78% of patients above 50 years of age were sensitive to Fosfomycin against E. Coli related UTI.

The overall sensitivity of Fosfomycin against E. Coli was 84% in our study and it was also compared to the other commonly prescribed antibiotics. The sensitivity of ciprofloxacin against E. Coli was only 20%, trimethoprim-sulphamethoxazole was 17% and amoxicillin-clavulanic acid was only 13% which showed significant resistance against this commonly found uropathogen. Ciprofloxacin is still mostly prescribed in OPDs for the treatment of UTIs, along with significant number patients getting the other two antibiotics as mentioned above. This overuse has led to the emergence of significant resistance to these commonly prescribed drugs.

Fosfomycin demonstrated potent in-vitro activity against E. Coli along with other common uropathogens.[24] Antimicrobial resistances to Fosfomycin is rare in E. Coli (1-3%) as compared to fluroquinolones and trimethoprim-sulphamethoxazole (>20%) [25]. This finding is in keeping with our study pattern of sensitivity against this old but re-emerging drug.

In our study we have shown high amount of resistance to the other commonly prescribed antibiotics against frequently occurring uropathogen like E. Coli. This is similar to what has been described by different researchers in various studies [17,26-28]. Various studies from our neighboring country India has also revealed similar pattern of resistance [29,30]. The data from our study regarding high Fosfomycin sensitivity against E. Coli has also been demonstrated in different studies worldwide [28-30]. For example, Gupta et al showed 52.6% of isolates from UTI were ESBL producer and all of these strains were susceptible to Fosfomycin [31]. Similarly, according to Rejendran et al, Fosfomycin was the only antibiotic that effectively inhibited most strains of E. Coli including MDR strains [32]. In another study by Karlowsky et al, they have reported significant susceptibility against E. Coli collected from 2010 to 2013 as part of Canadian National Surveillance Study CANWARD [33].

Due to its good renal excretion, Fosfomycin concentration in urine is very high which enhances its ability to break up the biofilms due to catheters. This was determined by Gopichand et al in their study and they have concluded that Fosfomycin could inhibit biofilm formation [34]. Regarding tolerability, different clinical trial has shown well tolerability and good compliance of this orally effective drug [35-37].

As an oral antibiotic with fewer side effects, and a broader spectrum of antibacterial activity that includes different strains of E. Coli, Fosfomycin has the potential to improve patients' quality of life while minimizing health care cost and easily availability.

CONCLUSION

This study shows that in the presence of mounting antibiotics resistance, Fosfomycin is a safe and suitable alternative in the treatment of UTI caused by MDR pathogens like E. Coli which otherwise do not respond to most of the available antibiotics.

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Exploring Anthropometrics, Body Composition and Antioxidant Capacity in Prediabetic Population with and without Family History of Diabetes

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ABSTRACT

Objective: To explore the anthropometric measurements, body composition, individual and total antioxidant capacity in prediabetic Pakistani population with and without family history of diabetes.
Study Design: Experimental study
Place and Duration of Study: This study was conducted at the department of Physiology, Institute of Basic Medical Sciences, Khyber Medical University, Peshawar, Pakistan between February 2019 to January 2020.
Materials and Methods: Prediabetics (n=50), 18 to 35years age group, were included in the study, 25 participants in positive and negative family history of diabetes. All those participants with HbA1c in the limit of 5.7– 6.4%, and fasting blood glucose (FBG) between 100 to 126 mg/dL were included the study. The anthropometric measurements including body weight, height, waist and hip circumference, waist hip ratio, BMI, fat mass and body fat% were measured. The fasting blood samples were examined for total and individual antioxidant capacity by sandwich Enzyme Linked Immunosorbent Assay (ELISA).
Results: The weight, waist and hip circumference, waist/hip ratio, body mass index, fat mass and body fat% were different in family history positive and negative groups. The mean levels of superoxide dismutase, glutathione peroxidase, Uric acid ($p < 0.006$), Vitamin C, nitric oxide ($p = 0.022$) and total antioxidant capacity were higher in negative compared to positive family history group.
Conclusion: The anthropometric measurements, individual and total antioxidant capacity were different in prediabetic population with positive and negative family history of diabetes.

Key Words: Prediabetes, family history, anthropometry, body composition and antioxidant capacity

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INTRODUCTION

Prediabetes (PD) is a state of hyperglycemia defined by glycemic indices below the level for diabetes[1]. Prediabetes prevalence is on the rise globally and it has been estimated that more than 470 million population will develop PD by the year 2030[1,2]. The prevalence of PD is quite high in Pakistan.

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A survey done in 2018, 14% population had PD in Pakistan being higher in urban population in comparison to rural[3]. The prevalence of type 2 diabetes mellitus (T2DM) across Pakistan was 16.98% and prediabetes was 10.91% across Pakistan according to a survey done by Aamir et al., 2018[1]. Family history (FH) of diabetes especially first-degree relatives (parents and siblings), obesity, sedentary lifestyle, and dyslipidemia are a risk factors for PD and diabetes.

Prediabetes is associated with β cell dysfunction, insulin resistance, increased lipolysis, inflammation, micro and macrovascular complications[4]. The individuals with hyperglycemia in prediabetic stage develop diabetes that is more problematic and difficult to manage[5]. The dyslipidemia, obesity, sedentary lifestyle and low total antioxidant capacity, was reported in prediabetics compared to those with normal glucose level[6].

In addition, individuals who have diabetes have higher serum uric acid concentration than non-diabetic population[7]. Oxidative stress due to high blood glucose level occurs in PD and diabetes and influences the antioxidant capacity[8]. The antioxidant capacity may be affected, and compromised defense can lead to tissue

injury. The antioxidants can be categorized in two categories; enzymatic and non-enzymatic that can neutralize the reactive oxygen species (ROS). The enzymatic antioxidants include 'superoxide dismutase (SOD) and glutathione peroxidase (GPx)', while the non-enzymatic classification have nitric oxide (NO), uric acid (UA), and vitamins like C and E[9].

At present there are no concrete clinical guidelines for management of PD. It is the need of the day to explore the differences in anthropometrics, body composition and antioxidant capacity of the groups with positive FH of diabetes or no FH at baseline for better understanding of the pathophysiological processes and design programs for lifestyle modifications to prevent the development of prediabetes.

MATERIALS AND METHODS

It was an experimental study with purposive sampling. Anthropometric parameters, diabetic profile, and antioxidant capacity was compared between positive and negative FH groups in Pakistani prediabetic population. All the participants, 18 to 35 years of age (n=50); with FH of T2DM in first degree relatives were included in the study. All lab work was carried out from 1st February 2019 to 4th January 2020 in the Department of Physiology, Institute of Basic Medical Sciences, Khyber Medical University, Peshawar, Pakistan. Ethical approval was obtained from the Ethical review committee of Khyber Medical University under DIR/KMU-EB/BP/000580 dated 09/04/2019 and all the experimental work and procedures were done in accord with the Declaration of Helsinki 1964. Prediabetic volunteers were excluded from the study who had history of smoking, sleep disorders, acute or chronic health problems and on antioxidant supplementation. Recruited participants had FBG between 100 -125 mg/dL and HbA1c between 5.7 - 6.4% in accordance with the guidelines of American Diabetes Association[10]. Informed consent was obtained from each participant.

The sample size was calculated using G Power 3.1.9.2. TAC values from Rodriguez et al., 2017 Mohieldein et al., 2015, were used for sample size calculation[11]. The power of 0.95 and $\alpha = 0.05$, the calculated sample size was 26 in the first study and sample size 10 in the second study respectively [6]. We recruited 50 prediabetic participants in the study, 25 with positive FH and 25 with negative FH of diabetes. Their anthropometric measurements and body composition using Xiaomi Mi Scale were determined. Blood samples were taken in fasting state after 48h restriction of high antioxidant diet and analysis was done for diabetic profile and antioxidant capacity by Sandwich ELISA. The antioxidants examined were superoxide dismutase (SOD), glutathione peroxidase (GPx), nitric oxide (NO) Vitamin C, with assay kits from Bioassay Technology Laboratory, Shanghai, China. Uric acid was measured by DIALAB Production, Austria and total antioxidant capacity measured by Ferric Reducing Antioxidant Power Assay (FRAP) using Colorimetric Assay kit by Elabscience USA.

RESULTS

The results were compared between the two FH groups: positive and negative. Positive FH group had a higher weight, body mass index (BMI), waist and hip circumference, body fat, fat mass and lean mass.

Table No.1: *Anthropometric measurements in positive and Negative Family history groups in Prediabetic Population.*

Group Statistics	Family Hx Positive Mean ± SD	Family Hx Negative Mean ± SD	P value
Age (y)	30 ± 4.7	28 ± 5	0.157
Ht (cm)	162 ± 9	167 ± 7	0.030
Wt (kg)	76 ± 15	73 ± 13	0.354
WC (cm)	96 ± 12	91.8 ± 10	0.05
HC (cm)	105 ± 10	100 ± 6.7	0.042
BMI (%)	29 ± 5	26 ± 3.29	0.007
BF (%)	36 ± 7	27.7 ± 6.1	0.001
FM (kg)	26 ± 9	20.21 ± 5.94	0.006
LM (kg)	47.5 ± 12	52.4 ± 9.6	0.118
FBG (mg/dL)	110 ± 7	110 ± 6.4	0.884
HbA1c (%)	6 ± 0.25	6 ± 0.23	0.954
Insulin (µIU/ml)	20 ± 12.4	14 ± 9.5	0.057
Insulin Resistance	5.48 ± 3.5	3.78 ± 2.6	0.059

Ht = height, Wt = weight, WC = waist circumference, HC = hip circumference, WHR = waist-hip ratio, BMI = body mass index, BF = body fat, FM = fat mass, LM = lean mass, FBG = fasting blood glucose, HbA1c = glycated hemoglobin. Independent t test was applied. $P \leq 0.05$ was considered as statistically significant.

Table No.2: *Antioxidant level in Prediabetics with Positive and Negative Family History of Diabetes.*

Antioxidants	Family Hx Positive Mean ± SD	Family Hx Negative Mean ± SD	P value
SOD U/ml	176 ± 105	229 ± 153	0.168
GPx ng/ml	49.6 ± 45	53.6 ± 45	0.761
UA mg/dL	4.5 ± 1	5 ± 0.8	0.006
VitC ng/ml	71 ± 75.5	96 ± 84.5	0.284
NO mIU/ml	168 ± 136	289.2 ± 210	0.022
TAC µg/ml	0.76 ± 0.2	0.79 ± 0.16	0.559

SOD = superoxide dismutase, GPx = glutathione peroxidase, NO = nitric oxide, VitC = Vitamin C, UA = uric acid and TAC = total antioxidant capacity. Independent sample t test was applied. P $\leq$ 0.05 was considered as statistically significant.

A statistically significant difference between the two groups was observed with BMI, hip circumference, body fat and fat mass. The mean FBG, HbA1c, insulin level and insulin resistance were also greater in positive FH group in comparison to no FH of diabetes as in Table 1. The antioxidants SOD, GPx, uric acid, Vit C, nitric oxide, and TAC were greater in negative FH group showing a much better antioxidant defense in those with no FH of diabetes. Uric acid and nitric oxide levels showed statistically significant difference between the two groups being higher in negative family history group as in table 2.

DISCUSSION

The prediabetic participants with FH of diabetes had higher anthropometric measurements and lower antioxidant levels in comparison to those with no FH of diabetes. FBG and HbA1c levels in the two groups in our population were similar in both prediabetic groups. The mean BMI, weight, WC, HC, fat mass and body fat was higher in positive FH group in comparison to negative FH group, but statistically significant increase was observed only for BMI, WC, HC, body fat%, fat mass between participants with positive and negative FH. Participants with positive FH were shorter, older, and heavier and exhibited more features of android obesity as shown in table 1. These differences in body composition based on family history are supported by Wang et al., 2020[12]. Similarly, another study reported individuals with family history of diabetes with greater body fat% and lower lean mass than control supporting our findings[13]. FH of diabetes has evolved as a risk factor for diabetes and can be attributed to genetic component and environmental factors[14,2]. Prediabetes has a causal relationship with obesity, physical inactivity and diminished total antioxidant capacity as compared to normoglycemic individuals and is consistent with our findings[11]. The cardinal signs of T2DM are insulin resistance and malfunction of the beta cells of pancreas[15,16]. This is consistent with our findings: greater insulin resistance in positive FH group of diabetes.

Literature search shows limited work done on redox status in prediabetic population and the conclusions reached so far are controversial. The pathogenesis of PD and diabetes with deranged FBG involves oxidative stress. ROS generated during this leads to cellular injury and are detoxified by the antioxidants[17]. TAC reflects the endogenous and exogenous antioxidants in plasma and is represented by uric acid, ascorbic acid, and proteins[18]. A study done in elderly prediabetic population showed diminished SOD and TAC levels compared to control group and is consistent with our findings[18]. Serum uric acid levels were found to be lower in prediabetic population than normal[19]. In addition, lower uric acid level was observed in prediabetics with positive family history in our study population. Uric acid, an important antioxidant in plasma, shields against ROS[20]. It can therefore be postulated that lower uric acid levels in PD can be because of high oxidative stress and family history of diabetes is a risk factor for T2DM[21]. Vitamin C and nitric oxide levels were also found to be lower in diabetic population as compared to normoglycemic population consistent with our findings[22,23]. Moreover, it has been determined that siblings of diabetics have elevated insulin levels and are predisposed to develop PD and diabetes if not aware of it, so early screening and prevention is recommended[23]. Furthermore, first degree relatives of patients with DM demonstrated a greater risk of developing PD coupled with malfunction of endothelium and beta cells, IR and abnormal glucose metabolism[24].

CONCLUSION

The results of the study show higher weight, waist, hip circumference, BMI, and lower individual and total antioxidant capacity in prediabetic positive family history group than in prediabetic population with no family history of diabetes. So, it is concluded that family history is a risk factor for the development of prediabetes and diabetes mellitus.

Recommendations: Screening of population should be done for prediabetes and diabetes. Antioxidant supplements should be taken by individual with prediabetes especially those with family history of diabetes.

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The Role of Thrombectomy in the Management of Deep Vein Thrombosis

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ABSTRACT

Objective: To investigate the long-term effects of surgical thrombectomy of iliofemoral deep vein thrombosis (DVT) with regards to the occurrence of post-thrombotic syndrome (PTS) and post-surgery venous hemodynamics concerning venous insufficiency and venous obstruction.

Study Design: A retrospective observational study

Place and Duration of Study: This study was conducted at the surgical department of Doctors Hospital & Medical Centre Lahore from May 2019 to May 2021 for a period of 02 years.

Materials and Methods: A total of 50 patients who underwent surgical thrombectomy were included in the study. Among these patients, 35 patients were diagnosed with iliofemoral DVT. 20 patients were evaluated after an average follow-up of 2 years by a comprehensive duplex mapping. CEAP and Villalta scale was used to assess and test the severity of PTS. Digital photoplethysmography (PPG) and venous occlusion plethysmography (VOP) were used to calculate venous hemodynamics.

Results: After the 2-year follow-up, the primary patency rate of the iliofemoral venous segment was 85%. Venous reflux was observed in 45% of patients in the study. 55% of patients were diagnosed with mild or moderate post-thrombotic syndrome. However, no patient developed severe PTS or active ulceration. The average venous flow volume in the operated femoral was 63.2ml/100ml per minute which was notably less than controlled contralateral legs without surgery ($p<0.05$). The average venous refilling time (VRT) was 15.5 seconds which was significantly more than that of non-operative legs ($p<0.05$).

Conclusion: The results of the study indicate good long-term results and excellent patency rates after surgical thrombectomy of iliofemoral veins.

Key Words: Thrombectomy, deep venous thrombectomy, iliofemoral veins

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INTRODUCTION

Deep vein thrombosis (DVT) is a common complication affecting every 300 in 100000 patient's annually[1]. The affected patients report pulmonary embolism as the earliest critical complication whereas post-thrombotic syndrome (PTS) or chronic thromboembolic pulmonary hypertension (CTEPH) is among the serious long-term consequences [2]. Venous claudication and venous ulcers are the most noticeable symptoms of extreme PTS which significantly affects the quality of life [3]. Iliofemoral DVT is the major cause behind the development of severe levels of PTS[4,5].

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Therefore, it is recommended to remove the thrombus as early as possible. Currently, the thrombus is either removed through endovenous methods or surgical interventions[6]. Particularly, the younger patients diagnosed with acute, symptomatic iliofemoral DVT and having a thrombus of age <14 days are suggested to immediately undergo thrombus removal treatment[7]. As first-line therapy, endovascular and pharmacological treatment is suggestive for the patients[6]. However, according to a study, at a certain point, physicomechanical catheter-directed thrombolysis becomes non-beneficial and no significant results are produced when contrasted with anticoagulation alone for the prevention of PTS [8]. This could be due to the inclusion of femoropopliteal along with iliofemoral DVT patients in this trial. In this regard, another related study confirmed that pharmacological catheter-directed thrombolysis benefits only the population with an iliofemoral DVT [9]. However, surgical thrombectomy of iliofemoral DVT has widely been demonstrated as a successful management strategy for PTS [9]. Different imaging technologies duplex ultrasound mapping, air plethysmography, occlusion plethysmography, and

photoplethysmography are available for venous disease diagnosis and for determining the outcomes of surgery[11]. However, despite these wide-ranging techniques, only limited data is available regarding post-surgery hemodynamic effects. Therefore, the following study was designed to investigate the long-term effects of surgical thrombectomy of iliofemoral deep vein thrombosis (DVT) with regards to the occurrence of post-thrombotic syndrome (PTS) and post-surgery venous hemodynamics concerning venous insufficiency and venous obstruction.

MATERIALS AND METHODS

A retrospective observational study was conducted from 15th May 2019 to 15th May 2021 at the surgical department of Doctors Hospital & Medical Centre Lahore. Patients aged over 18 years, diagnosed with iliofemoral DVT, and treated through venous thrombectomy were included in the study. Whereas, patients with septic thrombosis, pregnancy-related DVT, phlegmasia cerulae dolens, atresia of deep veins, or patients in whom mechanical injury such as catheter-related DVT results in iliofemoral DVT was excluded from the study. Although 35 patients, data obtained from the hospital registry of last 3 years, complied with the criteria but the follow-up data of only 20 patients was evaluated as the remaining were either lost or died during the study or had missing data. These 20 patients had iliofemoral DVT, diagnosed through duplex ultrasound. Among them, 11 had had ascending DVT extending from the lower leg to the region surrounding the iliofemoral vein. 5 patients had inferior caval vein involvement while 7 had descending DVT of the iliofemoral vein. However, femoral veins in all these cases were free of thrombus. All patients underwent venous thrombectomy through a standardized procedure. Before the conduction of follow-up, all patients were informed of the purpose of the study, and their consent was sought. Similarly, ethical approval was taken from the ethical committee of the hospital. Included patients were followed for a mean period of 18 months (minimum 16 months, maximum 22 months). PTS was evaluated by the CEAP (Clinical-Etiological-Anatomical-Pathophysiological) score and Villalta score. Moreover, duplex sonography of fibular veins, posterior and anterior tibial veins, popliteal veins, femoral vein, deep femoral vein, external iliac vein, and inferior caval vein was also performed. In addition, small and large saphenous veins were also investigated. The scan was performed by an independent investigator. Duplex scans of femoral vein, external iliac, and inferior caval vein were conducted while patients were placed in a supine position where all other scans were performed in a standing position. Moreover, air plethysmography and photoplethysmography were conducted as already explained [11]. The most significant character of photoplethysmography is the "venous refilling time", an indicator of venous reflux. A value of less than 25s is considered pathological. Similarly, venous occlusion plethysmography measures venous outflow volume which indicates iliofemoral obstruction in which the outflow is less than 40-80ml/min[4].

SPSS (version 18) is used for statistical analysis. Data were expressed as frequency and percentages. The student's t-test was used for assessing the statistical significance of the treatment. A p-value of <0.05 was considered statistically significant.

RESULTS

Among the study population, 12 (60%) were male while 8 (40%) were female. The mean age at follow-up was 53 years ± 3.5 years. 7 right and 13 left legs were treated. At the time of surgery, the average thrombus age was 4.1 days. The patients' data showed that the mean surgery time was 120 minutes. Post-operatively no patient had reported bleeding while only 2% had postoperative seroma and 5% had postsurgical wound infection.

On post-operational evaluation, 3 patients were found to have "incomplete" venous recanalization thus had residual thrombus. 3 patients had post-surgical occlusion of the iliac or femoral vein during the follow-up of 2 years. Thus patency rate was 85%. 5 (25%) patients had postthrombotic alteration such as structural or septum irregularities in vein walls. In terms of reflux, 1 (5%) patients had iliac vein reflux and 6 (30%) had reflux in the deep femoral veins. The majority of patients reported reflux in the popliteal vein. Whereas, regarding superficial veins, 3 (15%) patients demonstrated reflux in large saphenous veins and 1 with incomplete insufficiency of the large saphenous veins was found. Lastly, only 1(5%) patient was found to have reflux in the lesser saphenous vein.

No patient had an active ulcer at the end of the follow-up. 1 (5%) was found to have healed ulcer on the treated leg (C5). According to CEAP classification, 8 patients were classified under C0, 5 with C1, and 1 with apparent varicose veins (C2). Similarly, 2 patients were having pretibial edema (C3), and 3 demonstrated skin changes (C4) (Table I).

Table II presents the categorization of patients according to the Villalta score. It was seen that the majority of patients (55%) had mild or moderate PTS and no case with severe PTS was found.

Photoplethysmography and venous occlusion plethysmography were performed on all patients on both legs. As per the results of the former imaging studies, the average venous refilling time (VRT) was 15.5 - 10.2 sec of the treated legs. 5 patients had severe reflux with VRT less than 10 s. A significant difference was found in VRTs when compared treated legs were compared with untreated legs. Whereas, according to

venous occlusion plethysmography, the average venous outflow volume of all treated legs was 63.2ml/100ml per minute - 25.2. Among the evaluated patients, 4 patients had abnormal venous outflow values of <40 ml/100ml/min. In comparison, the average outflow volume of the untreated legs was 78 ml/100ml per min 30.6 ($p<0.05$) (Table 3).

Table No.1: CEAP Classification

C0	C1	C2	C3	C4	C5	C6
8 (40%)	5 (25%)	1 (5%)	2 (10%)	3 (15%)	1 (5%)	0 (0%)

Table No.2: Villata score

Villalta < 5 (no PTS)	Villalta 5–9 (mild PTS)	Villalta 10–14 (les s severe PTS)	Villalta > 15 (critical PTS)
9 (45%)	10 (50%)	1 (5%)	0(0%)

Table No.3: Hemodynamic outcomes

	treated legs	untreated legs	P-value
Average venous outflow (ml/100ml/min)	63.2-25.2	78 - 30.6	<0.05
Average venous refilling time (seconds)	15.5 - 10.2	26.2 - 8.5	<0.05

DISCUSSION

The above study found a patency rate of 85% which is comparable to already established literature. However, the follow-up time of our study is shorter when compared with the related studies. Plate et al conducted a 10-year long study on patients who underwent surgical thrombectomy and reported a patency rate of 83% [12]. Similarly, Hopler et al concluded 74% and 84% as primary and secondary patency rates, respectively, following a follow-up time of around 64 months [13]. Wagenhauster conducted a study of almost similar periods and reported a patency rate of 89% [14]. Despite such a good patency rate, 3 patients were found to have occlusion iliac or femoral vein which shows an occlusion rate of 15% and indicates that even after successful treatment, the veins still have the potential to remain patent. A similar study, however, reported a lesser occlusion rate of 8.3% [14].

Our study found that almost 50% suffered reflux in deep veins. Plate et al concluded 78% and 33% reflux rate in popliteal and femoral veins following surgical thrombectomy [12]. Our study found a significant difference in terms of VRT between formerly treated and untreated legs. However, it is generally expected that venous reflex should be significantly decreased after surgical thrombectomy when compared with anticoagulation treatment alone [15]. The venous outflow was expected higher in untreated legs compared to treated legs. However, the average venous outflow of 63ml/100ml/min found of treated legs is a physiological value. Similar results were reported by Plate et al [12].

According to CEAP classification, 1 patient had a C5 grade. The same results were reported by Wagenhauser et al who conducted a cohort study on 26 patients [13]. In our study it was found that 45% of patients had no PTS, the majority of patients (55%) had mild or moderate PTS and no case with severe PTS was found. This is with previously reported results where 80% of patients had no PTS [14]. 55% of patients in our study had PTS, considering Villalta score >5. The majority of the patients had mild PTS. It is predicted that early treatments strategies to remove PTS reduce the severe PTS forms [3].

According to the American venous forum guidelines, endovenous techniques are suggested as 1st line therapy [7]. However, they are contradicted in pregnancy, any scenario of internal bleeding, intracranial surgery, or any other cardiovascular events, and trauma. Given that, surgical thrombectomy is favorable in these situations.

The study is limited in terms of limited sample size, shorter follow-up period, and the lack of comparison with the endovenous group.

CONCLUSION

The results of the study indicate good long-term results and excellent patency rates after surgical thrombectomy of iliofemoral veins.

Author's Contribution:

Concept & Design of Study:	Ilyas Sadiq
Drafting:	Muhammad Nasir, Farhan Iftikhar
Data Analysis:	Farhan Iftikhar Muhammad Nasir
Revisiting Critically:	Ilyas Sadiq, Muhammad Nasir
Final Approval of version:	Ilyas Sadiq

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

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Non-HDL Cholesterol as a Predictor of Cardiovascular Disease in Type 2 Diabetes

Hafiz Abdul Kabir and Kashif Ali Hashmi

ABSTRACT

Objective: To analyze the role of non-HDL-Cholesterol as an indicator for the development of CVD in Pakistan's population with type 2 diabetes mellitus (T2DM).

Study Design: Cross-sectional analytical study

Place and Duration of Study: This study was conducted at the department of Cardiology diabetic Centre at Ch. Pervaiz Elahi Institute of Cardiology Multan from June 2020 to June 2021 for a period of one year.

Materials and Methods: The study included 90 subjects, 50 cardio paths with T2DM and 40 control. Standard enzymatic procedures were used to establish biochemical balance. A questionnaire was used as a means of collecting information about pathologies.

Results: The logistic model showed two levels of non-HDL-C: 130 mg/dl < non-HDL-C ≤ 160 mg/ dl (OR = .12, P=.002, 95% CI = .02-0.48) and 160 mg/dl < non-HDL-C ≤ 190 mg/dl (OR = 5.03, P =.036, 95% CI = 1.2-22.88) and smoking (OR= 19.28, P = .00295% CI = 3.38-109.64), inbreeding (OR = 3.66, P = .032,95% CI = 1.13-11.86) and 2 age groups 60-70 years (OR = 2.37, P<0.05,95% CI = 1.33-4.3) and those of 70 years or above (OR = 2.27, P<0.0595% CI = 1.18-4.28).

Conclusion: Non-HDL-C is a potential risk factor for the development of CVD in patients with T2DM in Pakistan.

Key Words: Non-HDL cholesterol, T2DM, cardiovascular diseases

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INTRODUCTION

One of the main causes of death in diabetic patients is cardiovascular complications. The risk of cardiovascular complications is two to more times more in type 2 diabetics as compared to people without diabetes [1]. According to various studies value of non-HDL cholesterol (non-HDL-C) is an predictor for cardiovascular problems in various communities[2]. In the American ethnic population affected by diabetes non-HDL-C is one of the various risk factors of Cardiovascular disease (CVD)[3]. In diabetics, non-HDL-C is a more valuable indicator for CVD as compared to triglycerides or low-density lipoprotein cholesterol (LDL-C), as it is strongly related to atherogenic lipoprotein[4].

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In diabetes, lipid abnormality is commonly characterized by low HDL cholesterol level, increase in triglyceride level, and increased occurrence of small dense particles of LDL[5]. During the disease composition of LDL changes because of which becomes very atherogenic [6]. When the level of triglycerides becomes higher than 100 mg/deciliter, particles of minute dense atherogenic LDL become predominant. In a prospective study conducted on the ethnic diabetic community (Indian community in the USA) which is at high risk of cardiovascular disease, it was established that non-HDL cholesterol has an important predictive value for clinical parameters[7]. Thus, non-HDL-C is a reproducible and simple index for assessing cardiovascular risk, its indicative value is equal, if not more as compared to, LDL cholesterol. This study aims to conduct multivariate analysis to access the role of non-HDL cholesterol in CVD in the diabetic population in Pakistan.

MATERIALS AND METHODS

A cross-sectional comparative study was conducted at the Diabetic Center of Cardiology at Ch.Pervaiz Elahi Institute of Cardiology Multan for 1 year from 22nd June 2020 to 22nd June 2021. The study included 90 subjects, controls (40), and cardio paths with T2DM (50). Both

male and female patients, diagnosed with diabetic heart disease were included in the study. Whereas, control were healthy subjects who visited the hospital for temporary illness. All patients were informed of the study objective and consent was taken. Participants of the study were excluded if they had refused to give their consent. Similarly, ethical approval was taken from the ethical committee of the hospital. For every control and case subject following were noted: name, age, diabetes, knowledge of CVD, height, weight, blood glucose levels, and family history of diabetes, total cholesterol, LDL-C, HDL-C, triglycerides, creatinine, and urea. Cultural and genealogical data of parents of each control and diabetic subject, socio-professional status, and educational level were also considered. Diagnosis of diabetic condition was based on World health organization (WHO) criteria 1985: moderate fasting hyperglycemia designated to fasting sugar levels between 1.1-1.25 g/l whereas diabetes is attributed to patients with fasting glucose levels exceeding from 1.26 g/l. Moreover, BMI was measured by dividing weight in kilogram by square of height in meters. After a fasting condition of minimum 10 hours, 5 ml venous blood was collected for biochemical analysis in a heparin tube. Blood glucose, urea, triglycerides, and total cholesterol were analyzed through standardized enzymes measuring protocols. The non-HDL-C was measured using the formula:

Non-HDL-C = total cholesterol - HDL-C

Minitab 16 software was used to process data. A predictive model of CVD related with T2DM was determined through a binary logistic regression study[8]. The forecast capacity of the logistic model was determined by calculating the area under the curve (AUC) and plotting receiving operating characteristics (ROC) curve. P-value < 0.05 for any variable was considered statistically significant.

RESULTS

According to the Table 1, level 0 represents a non-HDL-C level below 130 mg/dl. If this is considered in logistic model, level 1 subjects (130 mg/dl < non-HDL-C ≤ 160 mg/ dl) indicates that risk of exposure toT2DM and CVD is lowered when contrasted with patients with non-HDL-C below 130 mg/dl (OR = .12; P=.002, 95% CI = 0.02-0.48). On the other hand, those with higher non-HDL-C levels (160 mg/dl < non-HDL-C ≤ 190 mg/dl) are at 5 times greater risk of T2DM and CVD (OR = 5.03; P =.036, 95% CI = 1.2-22.88) as compared to subjects with non-HDL-C level 1 (130 mg/dl < non-HDL-C≤ 160 mg/dl).

About smoking, smokers are at 19 times higher risk of T2DM and CVD as compared to non- smokers (OR= 19.28; P = .002, 95% CI = 3.38-109.64).

About inbreeding, result (OR = 3.66; P = .032, 95% CI = 1.13-11.86) indicate the risk of CVD and T2DM is three and a half times more in those with related parents as compared to those from non-breeding ones.

Those aging from 60-70 years are also used in our model, such subjects are at two times higher risk of CVD and T2DM as compared to those less than younger subjects (OR = 2.37; P<0.01 95% CI = 1.33-4.3).

Nevertheless, the probability of occurrence of T2DM in those above 70 years (OR = 2.27; P<0.05, 95% CI = 1.18-4.28) is two times higher than in those with age between 60 to70 years.

Table 2 represents that adequacy tests by using the deviance method, the Pearson method, Brown methods (symmetrical alternative and general alternative), and Hosmer-Lemeshow method accepts the model with P value more than 0.05.

Table 3 indicates the predictive value of the used model. The percentage of matching pairs is very high (82%). Moreover, the results of table of discordant and matching pairs were shown by Tau-aof Kendall, Gamma of Goodman-Kruskal, and D of Somers. The measurement is usually ranged in between 0-1. The highest value indicates a significant predictive value of the model. The first 2 measurements of .72 and .78 indicate a very significant predictive capability. Similarly, the Kendall Tau-a suggests a considerable predictive capability.

Table No.1: Logistic regression model results

Predictors	Coefficient	Z (Wald)	P-Value	OR	CI (95%)
Constants	-1.10267	-1.61	.008		
Non-HDL-C 1	-2.2052	-1.99	.002	.12	.02-.48
Non-HDL-C 2	1.61404	1.10	.036	5.03	1.2-22.88
Smoking	2.95859	3.35	.002	19.28	3.38-109.64
Consanguinity	1.2945	2.16	.032	3.66	1.13-11.86
Age (60-70 years)	.85685	2.92	.005	2.37	1.33-4.3
Age (> 70 years)	.814497	2.48	.012	2.27	1.18-4.28

Table No.2: Adjustment Adequacy Tests

Methods	K-squire	DF	P-value
Pearson	8718	18	.94
Some of the difference squares	10.6654	18	.87
Hosmer-Lemeshow	.4183	6	.99
Brown:			
General alternative	.4394	3	.80
Symmetrical alternative	.0264	2	.872

DF: degree of freedom

The ROC curve associated the rate of false-positive (FPR) to that of true positive (TPR) through a graph. Generally, p (w) is compared to a threshold S= 0.5 for drawing a prediction. Therefore, the confusion matrix is constructed and the 2 indicators discussed above are extracted.

For every configuration, the confusion matrix was constructed and TPR and FPR were calculated.

The value of the area under curve was .89, thus the model adopted in subjects with CVD and T2DM was found to be quite predictive (Fig I).

Table No.3: The measure of association (between probability previsions and response variables)

Pairs	Number	%tage	Measure recapitulative	
Concordant	2098	83	D of Sommers	.72
Discordant	277	9.9	Gamma of Goodman-Kruskal	.78
Ex aequo	182	7.1	Tau-a of Kendall	.33
Total	2557	100		

DISCUSSION

In diabetic patients with cardiovascular complications, results reveal that risk of the relation between CVD and type 2 diabetes mellitus (T2DM) in both genders is associated with both levels of non-HDL-C (130 mg/dl < non-HDL-C160 mg/dl and 160 mg/ dl < non-HDL-C190 mg/dl), inbreeding, smoking, individuals aging between 60 and 70 years and above. In this study, the potential of association between CVD and T2DM is less in cases having a non-HDL-C level between 130 mg/ dl and 160 mg/dl as compared to the one with non-HDL-C levels less than 130 mg/dl.

While there is five times more risk of this association in subjects having a non-HDL-C value between 160-190 mg/dl than those with the non-HDL-C value between 130 mg/dl-160 mg/dl. Multiple researches reveal that in both diabetics and non-diabetics non-HDL-C is associated with cardiovascular complications. A study shows that diabetic patients with non-HDL-C levels> 130 mg/dl are more exposed to pre-process myocardial injury than those having non-HDL-C < 100 mg/dl[9].

It is also observed that diabetic patients with non-HDL-C levels in between 111.9-134.7 mg/dl are at greater risk of coronary heart disease (with CI =1.09-1.39, HR=1.23) than those with non-HDL-C level less than 11.97mg/dl [10]. A Chinese cohort study with 27020 participants revealed that in individuals with a non-HDL-C more than 190 mg/dl, there is an elevated risk of CVD (with CI =1.50-2.47, HR=1.93) when contrasted with those having non-HDL-C level less than 130 mg/dl who are further categorized based on diabetic status: greater risk of CVD in diabetes patients (CI=1.50-1.42, HR=1.22) as compared to non-diabetics (CI=1.04-1.19, HR=1.11)[11].

In another study, out of 25639 subjects about 2066 developed cardiovascular disease. The risk of development of cardiovascular complications increased with increase in non-HDL-C, when compared to normal non-HDL-C level subjects[12]. Likewise, there is 3 times greater risk of development of CVD (CI=1.58-6.21, HR=3.13) in subjects with non-HDL-C level more than 180 m/dl compared to those with non-HDL-C level less than 100 mg/dl [13].

Considering smoking as a variable, according to our logistic model there is 19 times more risk of the relation between CVD and T2DM in the smoker as compared to a nonsmoker, and our results match with those of Kitamura[14]. Whereas, another study concluded that there is no relation between various levels of non-HDL-C and smoking, as the P-value of .84 was found[11].

There is a lack of careful research on inbreeding and the role of non-HDL-C in CVD and in T2DM. In this study, this factor is used to access its involvement. This model demonstrates that there is three and a half times more risk of association between two diseases because of inbreeding. This is in line with the potent correlation found between cardiovascular profile and inbreeding in 587 patients[15]. Age factor is also used in this model. Results reveal that subjects under 60 are less exposed to both these diseases as compared to those aged 60 and 70, who have two times higher risk of developing these. Those over 70 also have two times higher risk of developing these diseases. A Chinese study containing a sample of 351 patients with heart disease showed the average age to be 58.6 ± 10 years16, which approaches the age of developing T2DM and CVD found in our study.

CONCLUSION

Non-HDL-C carries a potential risk for exposure to CVD in T2DM in Pakistan. Other significantly associated factors studies are age, inbreeding, and smoking.

Author's Contribution:

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Revisiting Critically:	Hafiz Abdul Kabir, Kashif Ali Hashmi
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Assessment of Adverse Pregnancy Outcomes in Women with Uterine Fibroids at a Tertiary Hospital

Pregnancy Outcomes with Uterine Fibroids

Malik Mudasir Hassan, Kamran Naseem and Tanzeela Akram

ABSTRACT

Objective: To assess the pregnancy outcomes among women with uterine fibroids.
Study Design: A prospective observational study
Place and Duration of Study: This study was conducted at the Gynecology & Radiology department of Bahawal Victoria Hospital Bahawalpur from May 2020 to May 2021 for a period of one year.
Materials and Methods: The study included pregnant women with uterine fibroids. Each woman underwent a detailed clinical examination and routine laboratory testing at each antenatal visit. Moreover, fetal health was also assessed regularly through ultrasonography. Parameters including maternal age, size and number of fibroids, obstetric complications, parity, and delivery mode were observed.
Results: A total of 60 pregnant women with uterine fibroids were included in the study. The participants had a mean age of 31.56±4.3 years. Primigravida was reported in 25.03% of women while multigravida in 74.97%. 75% of women had spontaneous conception and 25% utilized different treatments for conception. Only 23.2% of women delivered through normal route and C-section was performed in 76.98% of women. 8% of women had a miscarriage, 12% had a postpartum hemorrhage, and only 3% had placenta previa associated antepartum bleeding. 15.4% had premature delivery while 75.2% completed the normal gestation period. Multiple fibroids and intramural location posed a high risk of C-section than single fibroids or sub-serosal fibroids.
Conclusion: Uterine fibroids can cause severe pregnancy outcomes. Therefore, it is advised to evaluate the complications regularly during the antenatal period and manage them effectively to avoid adverse obstetric outcomes.

Key Words: Uterine fibroids, obstetric outcomes, pregnancy

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INTRODUCTION

Uterine fibroids are one of the most prevalent benign tumors reported in the female reproductive system[1]. However, the burden of the disease remains underestimated as the majority of fibroids are asymptomatic [2]. The data suggest that 1% to 10.7% of pregnant women report the presence of uterine fibroids [3,4] while the incidence rate is constantly on the rise due to delayed childbearing age [5].

Despite the acknowledged increase in prevalence, the association between uterine fibroids and worse obstetric outcomes couldn't be established.

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The already established has reported the relation of uterine fibroids with many pregnancy complications including puerperal infection, dysfunctional labor, premature membrane rupture, preterm birth, fetal malpresentation, antepartum hemorrhage, placental abruption, spontaneous abortion, postpartum hemorrhage, and cesarean sections [6,7,8]. The study, therefore, aimed to assess the pregnancy outcomes among women with uterine fibroids.

MATERIALS AND METHODS

A prospective observational study was conducted at the gynecology & radiology department of Bahawal Victoria Hospital Bahawalpur for 1 year from 20th May2020 to 20th May 2021. Women regularly visited the gynecology department and had ultrasonography (USG) confirmed uterine fibroids were consecutively enrolled in the study. Keeping 95% confidence interval and 80% power of the study, 60 patients were included in the study. The women with previous caesarian section, prior surgery, chronic diseases such as

hypertension and diabetes, and those with uterine malformation were excluded from the study. All participants were informed of the study's objectives and consent was obtained. Ethical approval was sought from the ethical committee of the hospital.

Patients' data registry was assessed to obtain their history whereas data acquired from clinical examination and diagnostic investigations were recorded side-by-side. Fibroids were diagnosed in the 1st-trimester scan. USG was performed at successive antenatal visits to assess fetal health and variation in fibroid size or any related complication. The following variables were analyzed during the study: maternal age, parity, gravidity, gestational age, size and number of fibroids, and obstetric complications.

SPSS (version 18.0) was used for statistical analysis. Quantitative data were presented as mean along with standard deviation whereas qualitative as frequency and percentages. Chi-square and student's t-test were used for comparison of sub-classes of quantitative and qualitative study data, respectively. P-value<0.05 was considered statistically significant.

RESULTS

A total of 60 pregnant women with uterine fibroids were enrolled in the study. The enrolled women had a mean age of 31.56±4.3. 35 (58.3%) women were reported to have single fibroids while multiple fibroids were found in 25 (41.6%) women. 49 (81.6%) women had intramural fibroids while subserosal were found in 19 (31.6%) women. 15 (25.03%) women were Primigravida and 45 (74.97%) were multigravid. 45 (75%) women reported having spontaneous conception while the remaining 15 patients acquired medical assistance for fertility (Table I).

Table II presents the observed obstetrics outcomes among evaluated women. 6 (10%) had threatened abortion, 5 (8%) had a miscarriage, 9(15.4%) had a preterm abortion, 2 (3%) had an antepartum hemorrhage. The majority of women had full-term delivery (92%) whereas 46 (76.98%) had to undergo a caesarian section. Post-partum hemorrhage was reported in 7 (12%) women.

Table III shows the association between obstetric outcomes and fibroid number. The route of delivery was significantly different between the women with a single fibroid compared to the one with multiple fibroids. 8 (13.3%) women with single fibroids had a vaginal route of delivery while only 1 (1.6%) with multiple fibroids (p=0.02). Whereas, 27 out of 35 patients with single fibroids had cesarian section compared to those with 24 out of 25 multiple fibroids patients (p=0.01). There was no significant difference between the two sub-classes in terms of other complications (Table III).

Table IV shows the association between obstetric outcomes and fibroid location. Similar to the association with fibroid number, fibroid location significantly affects the route of delivery. Majority of women with subserosal fibroids (18.3%) delivered through the vaginal route compared to women with intramural fibroids (5%) (p=0.04%).

Table No.1: Clinical characteristics of patients

Variables	Data
Age, years (mean ± SD)	31.56±4.3
Gravidity (N,%)	
Primigravida	15 (25.03%)
Multigravida	45 (74.97%)
Spontaneous conception	45(75%)
Assisted conception	15 (25%)

Table No.2: Obstetric outcomes among patients

Outcomes	Data (N, %)
Threatened abortion	6 (10%)
Miscarriage	5 (8%)
Preterm delivery	9(15.4%)
Antepartum hemorrhage	2 (3%)
Abruption	3 (4.2)
Placenta Previa	2 (3%)
Full-term delivery	51 (92%)
Vaginal delivery	14 (23.2%)
Cesarean delivery	46 (76.98%)
Postpartum hemorrhage	7 (12%)

Table No.3: Association between obstetric outcomes and fibroid number

Variables	Single (N=35)	Multiple (N=25)	P-value
Placental abruption	1 (1.66%)	2 (3.33%)	0.73
Placenta previa	-	2 (3.33%)	0.23
Preterm delivery	4 (6.66%)	5 (8.33%)	0.51
Vaginal delivery	8 (13.3%)	1 (1.66%)	0.02
Cesarean delivery	27 (77.1%)	24 (40%)	0.01
Postpartum hemorrhage	3 (5%)	4 (6.66%)	0.8

Table No.4: Association between obstetric outcomes and fibroid location

Variables	Subserosal (N=19)	Intramural (N=49)	P-value
Placental abruption	1 (1.66%)	2 (3.33%)	0.89
Placenta previa	-	2 (3.33%)	0.3
Preterm delivery	3 (5%)	6 (10%)	0.52
Vaginal delivery	11 (18.3%)	3 (5%)	0.004
Cesarean	8 (13.3%)	46 (76.6%)	0.001

delivery			
Postpartum hemorrhage	3 (5%)	4 (6.6%)	0.9

Consequently, the majority of the later class went through the cesarian section (76.6%). Whereas, no significant difference was found in terms of the incidence of other complications between the two groups (Table IV).

DISCUSSION

The study aimed to evaluate the obstetric outcomes of uterine fibroids. The enrolled women had a mean age of 31.56±4.3, similar to the ones reported in earlier studies such as by Egbe et al.[9] This indicates the higher association of uterine fibroids with advancing gestation age. Similarly, increased gravidity and incidence of fibroids are found to be correlated in our study which is supported by findings of Sheiner et al[10]. Our study reported that 12% of women had postpartum hemorrhage (PPH). A closely similar incidence of PPH in women with uterine fibroids was observed by Parazzini et al[11] and Febo et al[12]. However, few studies have reported contradictory results and found no relation between uterine fibroids and risk of PPH such as the study by Coronado et al [13].

In our study, it was found out that uterine fibroids impede the normal mode of delivery (vaginal route). In compliance with this, Qidwai et al[7] and Stouts et al[6] also reported a higher CS rate in pregnant women with uterine fibroids. However, contradictory results, where no association between fibroids and CS was found, are also established in the literature[14].

We also established an association between several fibroids and obstetric complications. It was found that several fibroids increase the risk of caesarian delivery. Similar results were found by Qidwai et al[7]; however, despite the increased incidence of CS in women with more fibroids, the enhanced risk was not statistically significant. However, Lam et al[15] and Ciavattini et al[16] have observed a significant association between CS and preterm delivery. CS delivery was also significantly associated with intramural fibroid location as found by Zhao et al[17]. However, contrary results were found by Sale et al [11].

The study was found to be limited in terms of study size, limited postpartum follow-up, and lack of control group comparison.

CONCLUSION

Uterine fibroids can cause severe pregnancy outcomes. Therefore, it is advised to evaluate the complications regularly during the antenatal period and manage them effectively to avoid adverse obstetric outcomes.

Author's Contribution:

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Final Approval of version: Malik Mudasir Hassan

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

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Perioperative Outcome of Carotid Endarterectomy with Regional Anesthesia

Muhammad Nasir, Ilyas Sadiq and Farhan Iftikhar

ABSTRACT

Objective: To assess the effect of regional anesthesia in patients treated with carotid endarterectomy.
Study Design: A retrospective study
Place and Duration of Study: This study was conducted at the surgical ward of Doctors Hospital & Medical Centre Lahore from August 2018 to August 2021 for a period of 03 years.
Materials and Methods: A total of 150 patients undergoing carotid endarterectomy were included in the study and data was collected. Patients were administered with combined deep and superficial cervical plexus block. Remifentanil (0.025-0.05 mg/kg/min) was given to the patients during the procedure to make them comfortable, responsive and ensure their corporation. General anesthesia was only administered if the patient refused to consent to regional anesthesia or in case of any other complications. The main goal of the study was the occurrence of conversion from regional to general anesthesia during surgery.
Results: Out of 150 patients, regional anesthesia was opted for 148 patients, while 2 patients were administered general anesthesia. In 1 patient, conversion from regional to general anesthesia took place as the patient was irritated. A shunt was introduced in 20 (13.3%) patients due to loss of consciousness of patients during the carotid clamping. Complications occurred in 1 patient (0.6%) due to neurological deterioration and 1 intraoperative acute myocardial infarction (0.6%). No intra-operative death occurred. 1 patient (0.6%) died during his hospital stay. 2 patients (1.3%) suffered a major stroke and 1 patient (0.6%) suffered a minor stroke. The total rate of stroke and death was 2.6% (4 patients).
Conclusion: The in-hospital mortality under regional anesthesia in patients undergoing carotid endarterectomy is very low and requires very little conversion to general anesthesia. Hence regional anesthesia is regarded safe during carotid endarterectomy.

Key Words: Carotid endarterectomy, regional anesthesia, perioperative outcomes

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INTRODUCTION

Carotid stenosis patients are often at high risk of stroke. However, this risk is reduced effectively by surgical carotid endarterectomy[1,2]. When compared with endovascular carotid stenting, surgical carotid endarterectomy has significantly reduced the risk of perioperative and long-term minor stroke. The two procedures had comparable outcomes with regard to major stroke and long-term functioning[3].
During carotid endarterectomy, regional anesthesia and general anesthesia are administered to the patients but both these options have some degree of risk and cannot be regarded as perfectly safe.

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One of the major drawbacks of regional anesthesia is that it requires immediate conversion to general anesthesia. This conversion poses risk to the patient and causes hemodynamic instability. Very little has been done to investigate this conversion and its causes, therefore, we have studied it in our study. The goal of our study is to assess the effect of regional anesthesia in patients treated with carotid endarterectomy.

MATERIALS AND METHODS

A retrospective study was conducted from 3rd August 2018 to 3rd August 2021 at the surgical ward of Doctors Hospital & Medical Centre Lahore. A total of 150 patients undergoing carotid endarterectomy were part of the study and data was collected. All the patients agreed to participate in the study and Ethical Committee also approved the study. The patients who were also undergoing bypass surgery and percutaneous transluminal angioplasty (PTA) were excluded from the study.

The severity of carotid stenosis was categorized using the European Carotid Surgery Trial (ECST)[4]. In symptomatic patients, ipsilateral severe (70%-99%) or moderate (50%-69%) carotid stenosis was an indication for surgery and in asymptomatic patients, if there was a high incidence for stroke, there was a need for surgery[5, 6].

Preoperative anticoagulation therapy was often replaced by perioperative "Heparin Bridge" depending upon patient's attributes and probability of any thromboembolic events. The patients were also administered heparin the night before surgery. All the patients who had unpaired coagulation profiles and received dual antiplatelet therapy were administered superficial plexus block. Patients were administered with combined deep and superficial cervical plexus block or superficial plexus block alone as per the anesthesiologist's recommendation.

Endovenous midazolam (0.2 mg/kg) was administrated and cervical plexus block was performed pre-surgery. While administering regional anesthesia during surgery, pulse oximetry, pulse, intra-arterial blood pressure, and 5-lead ECG was also recorded.

We used the anesthetic technique as used in literature[7, 8]. We performed a superficial cervical plexus block by subcutaneously injecting ropivacaine 0.75% in the posterior triangle. Similarly, we performed a deep cervical plexus block after a negative aspiration blood test by injecting 4 or 5 mL of 0.75% ropivacaine thrice at the level of the transverse processes of the higher cervical vertebrae (C2, C3, C4). A maximum of 1.5mg/kg ropivacaine was permitted to be injected. Lidocaine 1% (4 mg/kg maximum) was administered subcutaneously for wound infiltration. For pain management during the surgery, lidocaine (1%) was administered. Remifentanil (0.025-0.05 mg/kg/min) was given to the patients during the procedure to make them comfortable, responsive and ensure their corporation and blood pressure was controlled by continuous titration of endovenous infusion of nitroglycerin. If necessary, clonidine or urapidil was injected. Midazolam or fentanyl was also injected during the procedure on occasion. Conversion to general anesthesia was only done if any complication like allergy to regional anesthesia, an infection at the site of the block, or if the patient refused to opt for regional anesthesia.

Systemic heparinization (50 IU/kg) was used with an activated clotting time target greater than 200 seconds and at the end of the procedure, 5mg protamine was injected. If the carotid cross-clamping test showed neurologic deterioration, a shunt was placed.

The primary endpoint was the rate of conversion of regional to general anesthesia during the surgery. The data was recorded for the rate of myocardial infarction, ICU admission, irregular heartbeat, need for re-operation. Secondary endpoints were the mortality rate and frequency of the major heart and neurological events (minor and major strokes and mini-stroke).

Minor stroke was a condition whose onset of symptoms lasted up to 24 hrs. Major stroke was a non-disabling stroke that showed neurological symptoms at hospital discharge. Minor stroke was a stroke with mild symptoms that lasted between 24 hours and hospital discharge.

Statistical analysis: Study population and risk of complications were described by descriptive statistics. The occurrence events and risk ration along with 95% CI was documented. Data was calculated in mean and numbers and percentages, standard deviation, or median and interquartile range. Comparison of groups was done by performing Fisher's exact test, t-test, or complement c2 serum test. If P was less than 0.05, it was regarded as statistically significant. GraphPad Prism version 6.00 for Mac OS X was used to analyze all study data.

RESULTS

Results from 152 endarterectomies in 150 patients were included in this study. Table I shows patients' demographic data. 148 patients (98.6%) received regional anesthesia and 2 patients (1.3%) were administered general anesthesia. In 1 patient (0.6%), conversion from regional to general anesthesia took place as the patient was irritated. A shunt was introduced in this patient. So, the rate of conversion from regional anesthesia to general anesthesia was 0.6% (1 of 150) (95% confidence interval, 0.14-0.59). The patients who were administered regional anesthesia and those who received general anesthesia did not differ with regard to demographic and clinical characteristics before surgery.

Table No.1: Patients' Demographics Data

Demographic characteristics	
Age, years	69.5±700
Male	93 (62%)
Medical history	
Hypertension	110 (73.3%)
Dyslipidemia	65 (43.3%)
History of neurological events	34 (22.6%)
Stroke	13 (8.6%)
TIA	8 (5.3%)
Syncope	4 (2.6%)
Amaurosis	3 (2%)
Vertigo	4 (2.6%)
Other neurological symptoms	2 (1.3%)
Type 2 diabetes mellitus	30 (20%)
Smoking history	27 (18%)
Renal insufficiency	22 (14.6%)
Chronic obstructive pulmonary disease	8 (5.3%)
Acute myocardial infarction	15 (10%)
PBCI or CABG	30 (20%)

Four surgeons performed the surgeries. The surgery time of general anesthesia patients was more than regional anesthesia patients (76.5 ± 18.7 vs 164± 15.8 minutes, p<0.01). A shunt was introduced in 20 (13.3%) patients receiving regional anesthesia due to loss of consciousness of patients during the carotid clamping but only one was converted to general anesthesia. No intra-operative death occurred.

Post-surgery complications were only observed in 1 patient (0.6%) who suffered a heart attack during surgery and cardiogenic shock after the procedure and required Percutaneous coronary intervention immediately after surgery, admission in the ICU, intra-aortic balloon pump, inotropes, and ventilator. Three days after the surgery, he underwent revision surgery for bleeding. After 20 days, he suffered a transient ischemic attack and pneumonia. After a month, he showed no symptoms and was hence, discharged.

1 patient underwent re-operation due to acute neurologic deterioration post-surgery. 1 patient (0.6%) died during his hospital stay.

Table No.2: Postoperative complications

Combined stroke and death	4 (2.65)
Reoperation	2 (1.3%)
Bleeding	1 (0.6%)
Neurological events	1 (0.6%)
Admission to ICU	1 (0.6%)
From the OR	1 (0.6%)
From the ward	-
Major stroke	2 (1.3%)
Ischemic	1 (0.6%)
Hemorrhagic	1 (0.6%)
Minor stroke	1 (0.6%)
TIA	-
Myocardial infarction	1 (06%)
Renal artery thrombosis	-
Surgery time, minutes	65 ±17
Hospital stay, days	4.54 ±1.98
In-hospital mortality	1 (0.6%)
Caused by a major stroke	1 (0.6%)
Caused by myocardial infarction	-

DISCUSSION

Among the 150 study patients, only 1 patient (0.6%) required conversion from regional anesthesia to general anesthesia, which is less than the rate in previous studies.

According to research, patients convert to general anesthesia due to adverse events in surgery and complications caused by regional anesthesia. Most of the patients convert due to failure of local anesthesia which makes the patients uncomfortable and restless, pain, claustrophobia, local anesthetics toxicity, blockage of airway because of cervical hematoma, accidental injection of local anesthetics in the subarachnoid region, and vocal fold paralysis leading to respiratory distress[9, 10]. On the other hand, during surgery, patients are mostly converted to general anesthesia due to syncope at carotid clamping and problems caused by shunt placement (reduced perfusion, gas or plaque embolization, physical injury during shunt insertion or removal)[11, 12].

In the present study, the patient converted to general anesthesia due to discomfort and irritation due to failure of local anesthesia or claustrophobia. Block failure was also observed in other researches[9, 13, 14].

No intraoperative and only one postoperative death was reported in our study and this mortality rate is significantly less than previous research. Also, with regard to in-hospital outcomes, the mortality rate in our population was significantly lower than the mortality rate reported in other studies. This low mortality rate has been explained in other studies[15].

The incidence of stroke in our study was lower than in the literature[16, 17]. Additionally, the cardiovascular events after the surgery in our study comply with other studies[14, 16].

Our study can help surgeons administer cervical locoregional anesthesia especially cervical superficial plexus block more effectively with fewer adverse effects.

CONCLUSION

As indicated by the results of the study, the in-hospital mortality under regional anesthesia in patients undergoing carotid endarterectomy is very low and requires very little conversion to general anesthesia. Hence regional anesthesia is regarded safe during carotid endarterectomy.

Limitations: We did not record pain and discomfort data from patients undergoing carotid endarterectomy under regional anesthesia. We also did not record differences in clinical outcome, anesthesia administered during surgery, and surgery duration for surgery patients who were administered superficial or combined deep-superficial cervical plexus block. No data of preoperative medication and their effect was collected. Our study may not be suitable for centers that do not prefer regional anesthesia for carotid endarterectomy.

Author's Contribution:

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Comparison of Moderate Blockage of Left Main Stem (LMS) Assessment on Catheter Angiography Versus Coronary Computed Tomographic Angiography

Muhammad Zubair, Muhammad Ramzan, Muhammad Asif Zarif and Tariq Mehmood Khan

ABSTRACT

Objective: To assess the diagnostic ability of non-invasive computed tomographic angiography (CTA) against invasive catheter angiography (ICA) in patients with moderate left main stem (LMS) (40-49%).

Study Design: Prospective Comparative Study

Place and Duration of Study: This study was conducted at the cardiology department of Ch. Pervaiz Elahi Institute of Cardiology Multan for one year from July 2020 to July 2021.

Materials and Methods: Computed tomography angiography (CTA) and invasive catheter angiography (ICA) were performed in 45 coronary lesions with moderate severity. Percent diameter stenosis (%DS) and Minimal lumen diameter (MLD) were assessed by ICA and CTA. Inducible ischemia was determined by fractional flow reserve (FFR) value less than 0.80. The diagnostic value of the two methods was compared.

Results: 8 (20%) lesions had FFR ≤0.80. Mean CTA MLD was found to be lower than mean ICA MLA (1.3 ± 0.5 vs. 1.5 ± 0.5 mm, $P < 0.001$). Similarly, mean CTA %DS was higher than ICA %DS (53.5% ± 14% vs. 49.8% ± 11.8%, $P < 0.001$). These findings remained independent of the location of the lesion, its severity, and its plaque nature. In terms of ischemia prediction, diagnostic value of CTA %DS was less than that of ICA %DS ($P = 0.04$).

Conclusion: Invasive and non-invasive methods vary by diagnostic criteria in terms of the detection of ischemia-producing coronary stenosis. Compared with ICA, CTA overestimates lesion severity and has a lesser diagnostic capacity to assess ischemia.

Key Words: Coronary stenosis, coronary lesions, computed tomography angiography, invasive catheter angiography, LMS

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INTRODUCTION

Invasive coronary angiography (ICA) is considered a gold standard for the accurate estimation of coronary artery disease. However, the more advanced coronary computed tomographic angiography (CCTA) technology has allowed anatomical assessment of the coronary arteries through a non-invasive protocol [1]. Since CCTA has now been increasingly utilized for research and clinical purposes, it seems critical to assess the association between the parameters obtained from ICA and CCTA.

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Fractional flow reserve (FFR) is defined as an invasive psychological index to predict the existence of severe coronary stenosis that is capable to generate ischemia [2]. Literature has frequently recommended the adoption of FFR-directed percutaneous coronary intervention protocol [3, 4]. Computation of FFR is now perceived as the most reliable invasive strategy to evaluate the severity of coronary stenosis. The existing studies reported the inability of anatomical criteria to effectively predict ischemia-generating coronary stenosis [5, 6]. However, to the best of our knowledge, no study has so far been conducted in Pakistan that compared the diagnostic accuracy of ICA to that CCTA in different lesion subsets. Thus, this study was designed to evaluate the diagnostic ability of non-invasive computed tomography angiography (CTA) against invasive catheter angiography (ICA) in patients with moderate left main stem.

MATERIALS AND METHODS

A prospective comparative study was conducted from 14th July 2020 to 14th July 2021 at the cardiology department of Ch.Pervaiz Elahi Institute of Cardiology Multan. Patients who had undergone ICA and FFR measurement from moderate left main stem (LMS) (visually 40-49%) in major coronary arteries and had CCTA within three months before ICA were included in the study. During the consecutive enrollment, patients diagnosed with the acute coronary syndrome; visible thrombosis in target vessel; lesion length greater than 40 mm; additional stenosis (greater than 30%) in the target vessel; left ventricular ejection fraction less than 40%; the existence of collateral vessel; myocardial heart disease, and idiopathic CCTA were excluded from the study. The participants were informed of the study's objective and consent was sought. The study was initiated after the approval of the ethical review board of the hospital.

CCTA was performed according to the guidelines published by the Society of Cardiovascular Computed Tomography (SCCT) [7]. Patients with heart rates greater than 65bpm were administered metoprolol orally and 0.2 mg nitroglycerin was given sublingually just before the scan. CCTA results were analyzed by two independent CT-reader who were kept blinded to the study's objective. Each of them analyzed each segment for minimal lumen diameter (MLD), plague characteristics, and % diameter stenosis (%DS). All the measurements were computed by analyzing minimal slice thickness [8]. Whereas long-axis views were used for % DS assessment as described in earlier studies [8]. Plagues were classified as calcified and non-calcified plaques.

For CA, 5- to 7- catheter was used to engage the targeted coronary artery. 100 to 200ug of nitroglycerin was administered followed by the acquisition of angiographic images. Measurement of FFR was carried out through .014-inch pressure sensor-tipped was as already explained [9]. Hyperemic state was achieved either through an intravenous infusion (145ug/kg/min) of adenosine or intracoronary bolus infusion (40ug in the right coronary artery and 80ug in the left coronary artery). Myocardial ischemia was diagnosed with an FFR value of ≤0.80 [9]. The quantitative analysis of CA was carried by an independent experienced observer who was unaware of CCTA findings and FFR value. Guide catheter was used for calibration and a reference for measurement of lesion length, MLD, and reference diameter. Lesion location was assessed by following the American Heart Association classification [10]. Lastly, % DS was calculated.

SPSS (version 18.0) was used for statistical analysis. Categorical variables were presented as percentages while continuous variables were presented as mean with corresponding standard deviations. Continuous variables of two techniques were compared through student's t-test. Similarly, paired t-test was used to compare the angiographic parameters of the two techniques. Whereas, the difference in categorical variables was assessed through *the* χ^2 test. The diagnostic value of CCTA and ICA in assessing myocardial ischemia (FFR ≤0.8) was evaluated by the "area under the curve" (AUC) calculated through the "receiver operating characteristic (ROC) curve" analysis. DeLong method was used to compare AUCs. The best correlation value (BCV) was computed through the highest sum of specificity and sensitivity. Association between FFR and ICA and CCTA parameters was determined through Pearson's correlation coefficients. A P-value less than 0.05 for any variable was considered statistically significant.

RESULTS

A total of 30 patients with 45 lesions were consecutively included in the study. Table I and II present baseline characteristics of patients and their angiographic parameters. Mean FFR for all analyzed lesions was .83± .08 and 8 lesions (17.7%) had FFR ≤of 0.8. The majority of lesions with FFR ≤0.8 were found in the left anterior descending coronary artery compared to those with FFR greater than 0.8 that were majorly located in non-LAD lesions. Both ICA and CCTA exhibited smaller lumen and higher plaque deposition in the coronary lesions having FFR ≤ 0.80 than those with FFR> 0.80 (Table II).

The mean MLD measured by ICA was larger than that of CCTA (1.51±0.5 vs 1.28 ± 0.5, p<0.001). This trend remained the same regardless of plague characteristics, lesion severity, and lesion location (Table III). Positive correlation was found between ICA MLD and CCTA MLD (r = .448, P < .01) and ICA %DS and CCTA %DS (r = .443, P < 0.001). ICA MLD and CCTA MLD and ICA %DS and CCTA %DS had a 95% limit of agreement between the corresponding values with the following ranges: −1.2 to 0.8 mm and −23.3% to 32.6%, respectively. (Table III).

Table No.I: Baseline Data of the Participants (N=30)

Variables	Data
Age, years	59.8 ± 7.6
Male	19 (63.3%)
Risk factors	
Hypertension	22 (73.3%)
Diabetes mellitus	12 (40%)
Hyperlipidemia	16 (53.3%)
Clinical diagnosis	
Stable angina	10 (33.3%)
Silent ischemia	4 (13%)
Prior myocardial infarction	2 (7%)
Prior revascularization	7 (23.3)
Left ventricular ejection fraction, %	64.7 ± 7.5

A weak negative association was found between FFR CCTA %DS (r= -.25, p<.0001) whereas a weak positive association existed between FFR and ICA %DS (r= -.55, p<.01) Table IV. The functional significance of FFR≤0.80 was assessed through calculation of BCVs that was 53.5% for CCTA %DS and 49.8% for ICA %DS. The diagnostic value of BCV for the prediction of ischemia existence was 59.9% for CCTA %DS and 67.2% for ICA% DS. Comparison of AUCs showed the significantly lower diagnostic value of CCTA %DS than ICA %DS (AUC area difference=.106, P=.002).

Table No.2: Angiographic and CCTA findings of the analyzed lesions

Parameters	All participants	FFR ≤0.8	FFR >0.8	P-value
N	30	8	22	
FFR	.83 ± 0.05	.76 ± .08	.88 ± 0.04	<.001
LAD lesion (*n*, %)	17	5 (62.5%)	12 (54.5%)	
Proximal lesion (*n*, %)	23	7 (87.5%)	16 (72.7%)	
Angiographic parameters				
Minimal lumen diameter (mm)	1.45 ± 0.3	1.3 ± .4	1.8 ± .5	<.01
Reference diameter (mm)	3.3 ± .5	2.9 ± .3	3.1 ± .3	.013
% diameter stenosis (%)	49.2 ± 11.8	57.6 ± 9.8	45.1 ± 11.1	<.01
Length of lesion (mm)	15.7 ± 8.7	16.6 ± 9.4	16.8 ± 8.9	0.88
CCTA parameters				
Minimal lumen diameter (mm)	1.29 ± .45	1.10 ± .5	1.3 ± .32	<0.01
Reference diameter (mm)	3.0 ± .4	2.7 ± .3	3.1 ± .2	0.03
% diameter stenosis (%)	53.5 ± 13.1	58.1 ± 12.5	51.2 ± 12.1	0.002
Lesion length (mm)	31.2 ± 11.2	28.9 ± 13.6	31.2 ± 11.1	0.54

LAD: Left anterior descending coronary artery

Table No.3: Comparison between ICA and CCTA parameters according to different lesion subsets

	CCTA MLD	ICA MLD	*P*-value
N=30	1.3 ± 0.5	1.5 ± 0.5	<.001
Lesion location			
LAD	1.28 ± .5	1.51 ± .5	<.0001
Non-LAD	1.41 ± 0.4	1.59 ± 0.6	0.0001
Reference vessel size by ICA (mm)			
≥3.0	1.32 ± .4	1.71 ± .6	.0001
<3.0	1.22 ± 0.3	1.45 ± .5	0.003
Calcified vs. Non-calcified plaque by CCTA			
Calcified	1.31 ± .5	1.50 ± .3	.002
Non-calcified	1.27 ± 0.4	1.51 ± 0.6	<0.001

LAD: Left anterior descending coronary artery

Table No.4: Association between FFR and ICA and CCTA parameters

Parameters	*N* (FFR ≤0.8)	Correlation (*r*)	
		CCTA %DS	ICA %DS
All participants	30 (22)	−0.25	−0.55
Lesion location			
LAD	17 (12)	−0.25	−0.54
Non-LAD	13 (10)	−0.31	−.57
Reference vessel size as per ICA (mm)			
≥3.0	18 (7)	−0.28	−.58
<3.0	12 (15)	−0.25	−0.56
Lesion length as per ICA (mm)			
≥20	7 (8)	−0.21	−0.55
<20	23 (14)	−0.29	−0.53
Calcified vs. non-calcified plaque as per CCTA			
Calcified	10 (7)	−0.265	−0.45
Non-calcified	20 (13)	−0.256	−0.59

DISCUSSION

This study reported: CCTA overestimated the stenosis severity as compared to ICA; CCTA findings had a weaker association with FFR than that of ICA parameters; this trend remained the same irrespective of the lesion characteristics, and CCTA has limited capacity in diagnosing ischemia-producing stenosis as compared to ICA. Although CCTA is capable enough to provide critical diagnostic information for the assessment of coronary artery disease, the existing literature has given contrasting judgments on the degree of agreement between ICA and CCTA parameters [11, 12]. We included the patients with intermediate stenosis (40-49%) who often pose challenges in deciding the need for revascularization. Majority of the lesion (76.6%) were clinically significant as there were found in the proximal site of prominent coronary arteries. In such significant lesions, CCTA parameters overestimated the severity of lesions when compared with ICA. Mean values of CCTA MLD and ICA MLD demonstrated a difference of 0.2 mm. It is important to understand this difference is clinically important particularly when a patient's assessment is made through two different imaging modalities. Previous related studies reported the inefficacy of CCTA in

predicting the clinical significance of coronary stenosis [5, 13, 14]. However, these studies were limited in terms of patient selections-those with intermediate stenosis.

Our study also reported a weak correlation of CCTA parameters with FFR regardless of the lesion characteristic as compared to the other modality. Moreover, the diagnostic value of CCTA %DS in predicting the significance of stenosis was less than ICA %DS. This justifies the higher BCA of CCTA %DS than ICA %DS (53.5% vs 49.8%). The functional inferiority could be due to the current temporal and spatial resolution of CCTA. This limitation, however, can be addressed by the utilization of novel techniques[15, 16]. CT-derived non-invasive FFR has been found to have the superior diagnostic capacity to CCTA %DS (84.3 vs. 58.5%) through computational fluid dynamics technology[16]. Since the technology allows three-dimensional analysis of coronary geometry, better estimation of lesion severity is predicted that too with the non-invasive technique [16]. However, based on these results it is anticipated that any new technology dependent on CCTA will be limited in diagnosis the severity of coronary stenosis.

However, this study is limited in several aspects. Firstly, the smaller study size with limited analyzed lesions might affect the accuracy of the study. Secondly, the exclusive inclusion of patients with intermediate stenosis might introduce selection bias. Lastly, the study hasn't provided the any findings related to clinical outcomes. Therefore, further studies are required to evaluate the clinical effects of the difference between invasive ICA and non-invasive CCTA.

CONCLUSION

Invasive and non-invasive methods vary by diagnostic criteria in terms of the detection of ischemia-producing coronary stenosis. Compared with ICA, CTA overestimates lesion severity and has a lesser diagnostic capacity to assess ischemia.

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Diagnostic Accuracy of Strain Ultrasound Elastography in Differentiating Benign and Malignant Thyroid Nodules, Taking Histopathology as the Gold Standard

Malik Mudasir Hassan[1], Kamran Naseem[1], Tanzeela Akram[2], Aqsa Ashraf Bukhari[3] and Ifrah Zafar[3]

ABSTRACT

Objective: To evaluate the diagnostic accuracy of strain Ultrasound elastography in differentiating malignant and benign thyroid nodules.

Study Design: A descriptive cross-sectional study

Place and Duration of Study: This study was conducted at the Radiology department of Bahawal Victoria Hospital Bahawalpur from Feb 2020 to Feb 2021 for a period of one year.

Materials and Methods: A total of 80 patients with palpable thyroid nodules were included after passing through selection criteria. Strain ultrasound elastography was done to distinguish benign and malignant lesions in all patients. The findings were compared with the results of histopathology testing.

Results: The mean age of participants was 46.5± 6.21 years. Out of 80 patients, 43 (53.7%) were male and 37 (46.2%) were female. Mean disease duration was 8.71± 4.52 months and mean nodular size was 4.38±1.50 cm. The strain USG confirmed positivity for malignancy in 40 cases while the other 40 were regarded negative for any malignancy. In comparison with histopathology findings, 3 were found to be false-positive and 2 were false negative. On adjusting the confounding variables, strain USG was found to be 95% sensitive, 90.5% specific, had PPV of 90.8%, NPV of 94.1%, and was 93% accurate in terms of differentiating benign from malignant thyroid tumors on comparison with histopathology.

Conclusion: Strain ultrasound elastography is a non-invasive technique with a considerable diagnostic accuracy of differentiating benign and malignant thyroid nodules when compared with gold-standard histopathology.

Key Words: Ultrasound Strain elastography, thyroid nodules, histopathology, malignancy

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INTRODUCTION

Around 33% of individuals aged between 18-65 years are diagnosed with thyroid nodules while the incidence is as high as 50% in individuals older than 65 years [1] Although most of thyroid nodules are benign in nature , 5-15% are reported to be malignant [2] Generally the status of the thyroid gland and presence of nodules is assessed through ultrasound which is then followed by estimation of thyroid-stimulating hormone and anti-thyroid antibodies to identify the underlying causes of benign nodules like Hashimoto's thyroiditis.[2]

Similarly, calcitonin is measured to detect medullary thyroid cancer. Lastly, a fine needle aspiration cytology is conducted to make a definite diagnosis.

Although ultrasound (US) accurately reports thyroid nodules, it is limited in terms of differentiating benign from malignant nodules[3]. The sensitivity and specificity of US in defining thyroid nodules range from 52-97% and 26.6-83%, respectively [4]. American thyroid association guidelines state that the US is not

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sufficiently sensitive or specific to diagnose all types of malignant nodules [5]. Recently elastography is utilized as a novel technique to evaluate thyroid nodules which compare elasticity of nodules [6]. Clinically, two types of Elastography: Shear and strain are in practice [7]. Among them, strain elastography assesses two characters of elasticity: Firstly, colors within and surrounding the nodules are assessed, and secondly compares the region of interest with the surrounding reference area. Later, the strain ratio is calculated. A raised strain ratio strongly predicts malignancy [8]. According to a study, strain elastography found malignant thyroid tumors in 40.65% of the suspected population [9]. Another study reported 100% sensitivity and 80.2% of specificity of strain elastography in differentiating benign from malignant thyroid nodules [10]. However, the literature is divided while describing the efficiency of strain ultrasound elastography in differentiating benign from the malignant thyroid nodule. Moreover, local data is scarce on this subject. Therefore, the study was designed to evaluate the diagnostic accuracy of strain US elastography in differentiating malignant and benign thyroid nodules. Moreover, a biopsy is believed as the gold standard in diagnostic testing of thyroid nodules but given its invasive nature, there is a need to introduce a non-invasive accurate technique for detecting the nature of thyroid nodules. Therefore, the results of our will significantly assist clinicians in choosing the correct treatment plan.

MATERIALS AND METHODS

A cross-sectional descriptive study was conducted at the radiology department of Bahawal Victoria Hospital Bahawalpur from 17th February 2020 to 17th February 2021. The study considered all the patients aged between 30-70 years, with clinically noticeable thyroid nodules and who had been diagnosed with the disease since the diagnosis of the disease. Where the participants with a record of thyroid surgery and histopathologically confirmed cases of thyroid cancer were excluded from the study. All the enrolled were asked for informed consent while ethical approval was sought from the ethical committee of the hospital. The qualified participants were enrolled through a non-probability consecutive sampling technique. Afterward, all patients underwent strain ultrasound elastography through a high-resolution unit, carrying a linear array probe. The evaluation of benign and malignant tumors was based on pre-operational definitions of two types of tumors. The findings of strain US elastography were then compared with results of histopathology testing, conducted side-by-side. Besides, baseline data included age, gender, size of the nodule, and disease duration.

SPSS (version 18.0) was used for statistical evaluation. All continuous variables were presented as mean along with standard deviation whereas categorical variables were as frequency and percentage. Considering histopathology as the gold standard, specificity, sensitivity, diagnostic accuracy, negative predictive value (NPV), and positive predictive value (PPV) of strain ultrasound elastography in terms of its differentiating capacity was calculated. The effect of confounding variables was controlled through stratification.

RESULTS

A total of 80 patients were included in the study. The mean age of participants was 46.5± 6.21 years. Out of 80 patients, 43 (53.7%) were male and 37 (46.2%) were female. Mean disease duration was 8.71± 4.52 months and mean nodular size was 4.38±1.50 cm. Table 1 states that strain USG confirmed positivity for malignancy in 40 cases while the other 40 were regarded negative for any malignancy. In comparison with histopathology findings, 3 were found to be false-positive and 2 were false negative (Table I).

On adjusting the confounding variables, strain USG was found to be 95% sensitive, 90.5% specific, had PPV of 90.8%, NPV of 94.1%, and was 93% accurate in terms of differentiating benign from malignant thyroid tumors on comparison with histopathology.

Table II and III present the diagnostic data after stratifying it according to disease duration and size of the nodule, respectively.

Table No.1: Diagnostic accuracy of strain accuracy as compared to histopathology

	Positive cases as per histopathology	**Negative cases as per histopathology**	**P-value**
Positive cases as per strain USG	37 (true positive)	3 (false positive)	.001
Negative cases as per strain USG	2 (false negative)	38 (true negative)	.01

Table No.2: Stratification of findings as per disease duration and diagnostic characteristics of strain USG

	Positive cases as per histopathology	**Negative cases as per histopathology**						**P-value**
Disease duration ≤12 months			**Sensitivity** 94.9%	**Specificity** 90%	**PPV** 90.1%	**NPV** 94.7%	**Diagnostic accuracy** 92%	

Positive cases as per strain USG	27	2						0.01
Negative cases as per strain USG	2	30						0.01
Disease duration>12 months			**Sensitivity 100%**	**Specificity 91%**	**PPV 90.8%**	**NPV 100%**	**Diagnostic accuracy 98%**	
Positive cases as per strain USG	10	1						0.02
Negative cases as per strain USG	-	8						0.01

Table No.3: Stratification of findings as per the size of nodule and diagnostic characteristics of strain USG

	Positive cases as per histopathology	**Negative cases as per histopathology**						**P-value**
Size of module < 5cm			**Sensitivity** 90.6%	**Specificity** 89%	**PPV** 88%	**NPV** 91.9%	**Diagnostic accuracy** 92%	
Positive cases as per strain USG	22	2						0.01
Negative cases as per strain USG	2	26						0.01
Size of module > 5cm			**Sensitivity** 100%	**Specificity** 92%	**PPV** 94.5%	**NPV** 100%	**Diagnostic accuracy** 97%	
Positive cases as per strain USG	15	1						0.01
Negative cases as per strain USG	-	12						0.01

DISCUSSION

Thyroid nodules are prevalent worldwide; however, the prevalence rate varies in different populations and according to the method used. For instance, the prevalence is reported to be 2 to 6% by palpation, 19-35% by the US, and up to 65% according to autopsy reports [11]. Undoubtedly, palpation plays a significant role during physical examination but the US is mandatory for an accurate diagnosis regarding the presence of disorder [11]. However, it is also true that histology testing's are required to distinguish between benign and malignant nodules. In cases of non-diagnostic cytology, high-resolution thyroid ultrasonography and real-time elastography are employed for conclusive findings [12]. Elastography is a novel diagnostic method that compares tissue elasticity to evaluate nodules [13].

Our study was based on strain ultrasound elastography. The results found that USG confirmed positivity for malignancy in 40 cases while the other 40 were regarded negative for any malignancy. In comparison with histopathology findings, 3 were found to be false-positive and 2 were false negative. Moreover, strain USG was found to be 95% sensitive, 90.5% specific, had PPV of 90.8%, NPV of 94.1%, and was 93% accurate in terms of differentiating benign from malignant thyroid tumors on comparison with histopathology. In contrast to the 50% positivity rate in our study, another study reported a 40.65 % diagnosis rate of strain ultrasound elastography and specificity and sensitivity of 93% and 88%, respectively, in the differentiation of malignant and benign thyroid lesions[9]. Another study reported 100% and 80.2% sensitivity and specificity of strain elastography (SE), respectively, in differentiating benign and malignant nodules [10].

However, few studies have also disregarded strain elastography in distinguishing malignant lesions. For instance, Moon et al. Evaluated 703 thyroid nodules by SE and reported inferior sensitivity (65.4%) and NPV (79.1%). Therefore, the study didn't recommend SE as an accurate diagnostic modality [14]. Similarly, in 2012, another study evaluated 237 thyroid nodules and

concluded lower efficiency of ultrasound elastography when compared with US gray-scale [15].

However, in 2013, another study used a four-grade elasticity score to evaluate 912 nodules and found a PPV of 36.1% which was insignificantly raised than micro calcification (35.9%) but significantly higher than isthmus location (16.9%) and hypo echogenicity (13.6%). Whereas, the NPV of 92.75 was higher than the compared predictors of malignancy. The results of this study are noticeable since it evaluated the highest number of nodules that have ever been systematically assessed through SE and the study also had no selection bias [16].

Another aspect was discussed by Ko et al. who reported that findings of SE done by experienced physicians had higher specificity in terms of distinguishing benign lesions from malignant lesions as compared to inexperienced physicians [17]. In another, the highest Cohen's kappa coefficient was reported for the strain ratio (0.95) and the lowest coefficient for the echogenicity score (0.83) [18].

Asari et al. explained that the underlying principle of real-time USE stating that softer tissue parts are more vulnerable to deformation than harder parts under stress. Thus, allowing a relatively accurate assessment of tissue diameter than the conventional US. The authors reported 94%, 81%, 55.2%, and 98.2% sensitivity, specificity, PPV, and NPV, respectively, of the USE [19].

The present study was limited in terms of a smaller sample size and study design. Therefore, longer studies with a larger sample size are advised to compare other aspects of USE with the gold standard.

CONCLUSION

Strain ultrasound elastography is a non-invasive technique with a considerable diagnostic accuracy of differentiating benign and malignant thyroid nodules when compared with gold-standard histopathology.

Author's Contribution:

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Data Analysis:	Aqsa Ashraf Bukhari, Ifrah Zafar
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Study of Ureteric Stones Complications (Preterm Delivery & Urinary Tract Infection) During Last Trimester of Pregnancy

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ABSTRACT

Objective: The study was conducted to assess the ureteric stone complications (urinary tract infection & preterm delivery) particularly during the last trimester of pregnancy.

Study Design: A retrospective cohort study

Place and Duration of Study: This study was conducted at the Urology & Gynecology & Obstetrics Department of Mukhtar A Sheikh Hospital Multan from March 2020 to March 2021 for a period of one year.

Materials and Methods: Total 400 pregnant women with no ureteric stones and 35 pregnant women with ureteric stones were included in the study. The inclusion criteria were the women who delivered a live and singleton infant and were presented with ureteric stones in the last trimester. The exclusion criteria were to exclude the women whose time of discharge at birth and gestational age at delivery were found to be inconsistent. Written permission to conduct the study was obtained from the Institutional Review Board and Ethical Committee. The data retrieved included the demographic variables, history of the patient, gestational age, outcomes, and all the associated risks of ureteric stone on preterm delivery. Besides this, the percentage analysis of the frequency of urinary tract infection (UTI) before delivery was also calculated in both groups.

Results: The mean ages of the pregnant women presented with and without ureteric stones were 25 and 27 years respectively with a standard deviation of ±4.3 & ±5.2. It was observed that 12% (4) of the pregnant women with ureteric stone delivered preterm infants while only 5% (20) of the pregnant women without ureteric stone delivered preterm infants ($p<0.001$). Preterm PROM occurred in 3.4% (14) and 10% (3) of pregnant women that presented without ureteric stones & with ureteric stones respectively. A statistically significant difference was seen in the frequency of UTI in both groups with 5% (20) and 25% (9) pregnant women presenting with UTI among the ones with no ureteric stones and with ureteric stones respectively.

Conclusion: The study concluded that there is a comparatively high risk of preterm delivery and urinary tract infection in women who present with complain of ureteric stone in the last trimester of their pregnancy.

Key Words: ureteric stones, preterm delivery, urinary tract infection

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INTRODUCTION

Ureteric stone in pregnancy is a well-known and major health concern. It is frequently associated with non-obstetrical abdominal pain resulting in hospital admission.

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The incidence of ureteric calculi during pregnancy varies in the range of 1/200 to 1/2000 . However, these values are not different from the incidence reported in other women. It has been observed that multiparous women are more frequently affected as compared to primiparous women. Most of the cases are reported from the women during the second or third trimester of their pregnancy. Smooth muscle relaxant, dilatation of urinary tract due to ureteric obstruction in the presence of a gravid uterus, the effect of progesterone & infection all predisposes to the formation of ureteric calculi during pregnancy. Consequently, it leads to hydronephrosis in 90% & 67% of the pregnant females on the right and left side respectively. These normal physiological & anatomical changes not only result in stasis and calculi formation but also makes it difficult to diagnose the underlying condition. The stones are composed of calcium phosphate and are more

commonly present in ureters than in the renal pelvis. The physiological dilatation of the collecting system favors the migration of renal stones into the ureter .

It is so necessary to treat ureteric stones as they can have a serious impact on the health of the mother & fetus. Up to 40% of women can suffer from preterm labor & delivery due to early rupture of membranes. It can also result in "complications like obstructive uropathy, hypertension, higher incidence of cesarean section, gestational diabetes mellitus, recurrent abortions and pre-eclampsia" . In such situations, it gets difficult to diagnose ureteric calculi accurately. The typical clinical presentation of ureteric stone in pregnant females includes hematuria, fever, colicky pain radiating to the labial region, and tenderness. These signs and symptoms are sometimes misleading and get diagnosed "as diverticulitis, appendicitis, and placental abruption". One of the reasons for misdiagnosis is the limited use of radiological techniques during pregnancy. Only ultrasonography is considered as a diagnostic test for ureteric calculi due to the lack of ionizing radiation .

A retrospective cohort study design was utilized in the current research article to analyze the effect of ureteric stone on preterm delivery particularly in the female who presented with this condition in the last trimester.

MATERIALS AND METHODS

A retrospective cohort study design was used. The data of the women who were admitted during the prenatal or intrapartum period with complain of ureteric stones was retrieved. The cases included were admitted to the hospital during one year. The inclusion criteria were the women who delivered a live and singleton infant and were presented with ureteric stones in the last trimester. The exclusion criteria were to exclude the women whose time of discharge at birth and gestational age at delivery were found to be inconsistent. For comparative analysis, the data of the healthy women with no complaint of ureteric stones and who also delivered a live singleton infant during the same period (years) was retrieved. Written permission to conduct the study was obtained from the Institutional Review Board and Ethical Committee.

The data retrieved included the demographic variables, history of the patient, gestational age, outcomes, and all the associated risks of ureteric stone on preterm delivery. Gestational age was determined by record of ultrasonography reports & by date of last menstrual period taken from details provided in the patient's history.

The gestational age of fewer than 37 weeks was categorized as preterm birth and less than 32 weeks as extreme premature birth. The infants born with less than 2500 grams were considered infants with low birth weight. The number of infants that died within one year was also noted. The incidence of premature rupture of membrane at 12 – 24 hours before the onset of labor & the one that happened before 37th week of gestation were also included in the study. Besides this, the percentage analysis of the frequency of urinary tract infection (UTI) before delivery was also calculated in both groups.

Data Analysis: The retrieved data was organized and analyzed by using the Standard package for the Social Sciences (SPSS version 25). Demographic variables and associated health complications were expressed using mean & standard deviation. The relative risk associated with birth outcomes due to ureteric stones was expressed using percentage analysis. A Chi-square test was used to obtain a p-value. P-value <0.001 was considered significant.

RESULTS

35 pregnant women presented with ureteric stones & 400 were admitted with no complaint of ureteric stones. All these women delivered a single live infant. Demographic variables of women admitted with and without ureteric stones are provided in Table I. The mean ages of the pregnant women presented with and without ureteric stones were 25 and 27 years respectively with a standard deviation of ±4.3 & ±5.2. Among 400 pregnant women (without ureteric stones) 40.7% (162) were primiparous while 59.2% (237) were multiparous. Among 35 pregnant women (with ureteric stones) 35.7% (12) were primiparous while 64.2% (22) were multiparous. There was a statistically significant difference between the mean age & parity of the group of women who presented with and without ureteric stones. Other noticeable health complications in study participants included renal disorder & hypertension. 8.93% (3) pregnant women with ureteric stone also had underlying renal disorder while 0.41% (2) pregnant women who presented with no complaint of ureteric stone had the renal disorder. Hypertension was observed in the 1.1% (4.4) & 5.7% (2) group of pregnant women with and without ureteric stones respectively.

It was observed that 12% (241) of the pregnant women with ureteric stone delivered preterm infants while only 5% (214) of the pregnant women without ureteric stone delivered preterm infants ($p<0.001$).

Preterm PROM occurred in 3.4% (14) and 10% (3) of pregnant women that presented without ureteric stones & with ureteric stones respectively. 2% (8) & 3% (1) infants had low birth weight while 1% (41) and 3% (61) infant deaths were reported in pregnant women that presented without ureteric stones & with ureteric stones respectively. A statistically significant difference was seen in the frequency of UTI in both groups with 5% (20) and 25% (9) pregnant women presenting with UTI among the ones with no ureteric stones and with ureteric stones respectively.

Table No.1: Demographic variables of pregnant women admitted with & without complaint of ureteric stones

Variables	Without Ureteric stones n=400	With ureteric stones n=35	P value
Age Mean SD	 25 ±4.3	 27 ±5.2	 <0.001 <0.001
Parity Primiparous Multiparous	 162 (40.7%) 237 (59.2%)	 12 (35.7%) 22 (64.2%)	<0.001
Renal disorder Hypertension	2 (0.41%) 4.4 (1.1%)	3 (8.93%) 2 (5.7%)	<0.001 <0.001

Table No.2: Birth outcomes and potential risk factors for preterm delivery

Birth outcomes	Without ureteric stones	With ureteric stones	P value
Preterm delivery			
< 37 weeks	16 (4%)	8% (3)	<0.001
< 32 weeks	4 (1%)	4% (1)	<0.001
Preterm PROM	14 (3.4%)	10% (3)	<0.001
Low birth weight	8 (2%)	3% (1)	>0.001
Infant death	4 (1%)	4% (2)	>0.001
UTI before delivery	20 (5%)	25% (9)	>0.001

DISCUSSION

Ureteric stones affect approximately 1 in 714 pregnant women. In this study . Our study reports the increased risk of preterm labor and urinary tract infection in pregnant women who presented with ureteric stones. The study included the participants who presented with ureteric stones in their last trimester. Previous studies also show that most cases of ureteric stones are usually admitted in the last trimester of pregnancy. The occurrence of UTI is an indicator of preterm labor . When antepartum ureteric stones are treated conservatively, it results in a significantly higher risk of urinary tract infection at delivery as compared to women with no complaint of ureteric stones. However, the women who require intervention at the time of delivery are also at increased risk of UTI, bacteriuria & infection .

The other complication associated with ureteric stones that has gained much attention in the literature is the induction of preterm labor . A case series in past reported induction of preterm labor in 66% of patients who presented with renal stones . Similarly, another study found out that many complications can occur in cases of antepartum stone admission . Furthermore, a comparative study with randomly selected women concluded that there is an 80% increased risk of preterm delivery in pregnant women who receive management therapy for renal stones .

Ureteric stones are not associated with perinatal complications. However in our study, we reported that there is a noticeable difference in the number of spontaneous and induced labor in pregnant women with and without ureteric stones.

"Another study performed by Lewis and colleagues observed 7% risk of preterm labor for women with antepartum symptomatic stones compared to 3% of control subjects and an elevated but not statistically significant incidence of premature delivery" . Although some retrospective reviews showed a minimum of 0.08% preterm deliveries in patients suffering from renal stones during their pregnancy. This study however reported an increased rate of obstetric complications associated with the group of pregnant women presenting with antepartum stones .

Hereby our study results are in accordance with most of the previous studies. We reported the adverse birth outcomes, the associated risk of preterm labor, and the frequency of UTI in women who presented with ureteric stones in the last trimester of their pregnancy.

CONCLUSION

The study concluded that there is a comparatively high risk of preterm delivery and urinary tract infection in women who present with complain of ureteric stone in the last trimester of their pregnancy.

Author's Contribution:

Concept & Design of Study:	Waqas Khan
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The Frequency of Hyperuricemia in Patients with Congestive Heart Failure

Imran Khan[1], Umair Ali[2], Tanveer Ahmad[1], Yasir Arafat[1], Hidayatullah[3] and Shoaib Subhan[4]

ABSTRACT

Objective: To find the frequency of hyperuricemia in patients with congestive heart failure.
Study Design: Cross sectional study
Place and Duration of Study: This study was conducted at the Department of cardiology, Department of cardiology Qazi Hussain Ahmed Medical Institute Nowshera from 21st October, 2019 to 20th April, 2020.
Materials and Methods: About 145 patients presenting with heart failure and raised uric acid level, with age more than 18 years and less than 60 years of either gender were studied. Serum uric acid level was measured in a specialized lab. Chi square test was applied with $p < 0.05$ as significant value.
Results: Out of these 145 patients, 87 patients (60%) were male. "Among these 145 CHF patients, 93 patients (64.14%) were found to be hyperuricemic". Out of these 93 hyperuricemic patients, 82.8% in hyperuricemic patients or 53.1% in total patients were males. "About 38 patients (40.86%) were in NYHA Class II, 25 patients (26.88%) were in NYHA Class III and 30 patients (52.25%) were in NYHA Class IV."
Conclusion: Raised serum uric acid level is associated with bad prognosis in patients with Heart Failure especially in male population.

Key Words: Congestive Heart Failure (CHF), Hyperuricemia, serum uric acid (SUA), New York Health Association (NYHA).

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INTRODUCTION

Heart failure is a one of the costly, commonly found and potentially fatal condition.[1] About 2% of adults have heart failure all over the world specially patients with age of more than 65 which increases the risk to 6–10%.[2,3]

There are a number of risk factors for heart failure with hyperurecemia being one of them. A Japanese study concluded that the prevalence of hyperuricemia increased during the 10-year follow-up. It was found to be more in men of age 65 years and even 4 times more in young males as compared to females.

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Hyperuricemia is an abnormally high level of uric acid in the blood. Uric acid level of 360 µmol/l (6 mg/dl) for women and 400 µmol/l (7.2mg/dl) for men is considered normal, depending on individual lab ranges.[4]

Raised serum uric acid is one of the most predictive factor for mortality in heart failure patients and also causes raised levels of cardiovascular diseases in patients specially with diabetes. If the patient has hypertension in addition to hyperuricemia, then the risk increases to 3- to 5-fold times. LIFE study in patients with hypertension and left ventricular hypertrophy suggested, a treatment-induced decrease in serum uric acid decreasing cardiovascular risk.

Franse et al, in his study showed a relationship between serum uric acid levels, diuretic treatment and the risk of cardiovascular diseases in the Systolic Hypertension in the Elderly Trial (SHEP).[5]

The aim of this study was to determine the frequencies of hyperurecemia and its effect in patients with congestive cardiac failure.

MATERIALS AND METHODS

This study was conducted at Cardiology unit, Qazi Hussain Ahmed Medical Institute Nowshera**.** Duration of the study was 6 months from 21st October, 2019 upto 20th April, 2020 and the study design was cross sectional (descriptive) study. Sample size was calculated using WHO sample size calculator with 95% confidence interval and 5% margin of error. Non probability consecutive sampling technique was used. Patients with age more than 18 years and less than 60 years of either gender, presenting to Cardiology Unit, with heart failure symptoms were included in the study.
A level of more than 7.2mg/dl for adult males & older women while level of more than 6mg/dl for young women was considered as hyperurecemia. Patients already on drugs which can increase serum uric acid level, with malignancies and other conditions with rapid cell turnovers were excluded. This study was approved by hospital ethical and research committee.
Patients were subjected to history and examination. "Heart Failure severity was assessed using New York Health Association (NYHA) classification." A 5 cc of blood was taken from all the patients and was sent to hospital laboratory on the same day.
Data collected was entered in SPSS 21. "Mean ± SD was calculated for continuous variable like age and serum uric acid levels and categorical variable like gender was expressed as frequencies and percentages". Chi square test was applied with $P < 0.05$ as significant value.

RESULTS

About 145 patients with signs and symptoms of Heart Failure were included. Out of these, 87 patients (60%) were males. About 93 patients (64.14%) were found hyperuricemic as shown in table 1. Among these 93 hyperuricemic patients, 77 patients were male , while in normourecemic patients 10 were males and 42 were female (table 1). Among these 145 CHF patients, patients with age between 18 to 40 years were 7 (4.83%), between 41 to 50 years were 41 (28.27%) while between 51 to 60 years were 97 (66.90%). Mean age was 57± 2.73 years.(table 2) In total 93 Hyperuricemic patients, those between age group of 18 to 40 years were 3 (3.22%), between 41 to 51 years were 21 (22.58%) while between 51 to 60 years were 69 (74.19%). The mean age was 55 ± 3.58 years. (Table 3). About 78 patients (53.79%) were in 'NYHA Class II', 35 patients (24.14%) in 'NYHA Class III' while 32 patients (22.07%) were in 'NYHA Class 4' (table 4). Only 2 patients (1.38%) with serum uric acid (SUA) below 6 mg/dl were in NYHA IV compared to 24 patients (16.54%) whose SUA was above 8 mg/dl. Mean uric acid (SUA) levels are 7.7 ± 2.17 md/dl. (table 5)

Table No. 1: Stratification of CHF patients with respect to hyperuricemia and gender: (N=145)

Gender	Hyperuricemic		Normouricemics		Total	
	No.	**%Age**	**No.**	**%Age**	**No.**	**%Age**
Male	77	53.11	10	6.89	87	60
Female	16	11.03	42	28.96	58	40
TOTAL	93	64.14	52	35.86	145	100

Table No. 2: Stratification of CHF patients with respect to age: N=145

Age (years)	Frequency	Percentage
18 - 40	7	4.83
41 - 50	41	28.27
51 - 60	97	66.90
total	145	100

Mean age was 57 years with SD ± 2.73.

Table No. 3: Stratification of hyperuricemia with respect to age: (N=93)

Age (years)	Frequency	Percentage	
		In hyperuricemic	In total
18 – 40	3	3.22	2.07
41 – 50	21	22.58	14.48
51 – 60	69	74.19	47.58
TOTAL	93	100	64.14

Mean age was 55 years with SD ± 3.58.

Table No 4: Severity Distribution of Congestive Heart Failure Patients:(N=145)

Severity	Frequency	Percentage
NYHA Class II	78	53.79
NYHA Class III	35	24.14
NYHA Class IV	32	22.07
Total	145	100

NYHA= New York Heart Association

Table No. 5: Serum uric acid levels and severity of congestive heart failure: N=145

SUA (mg/dl)	NYHA II		NYHA III		NYHA IV		Total		P value
	No.	%Age	No.	%Age	No.	%Age	No.	%Age	
<6	40	27.59	10	6.89	2	1.38	52	35.86	0.12
6 - 8	30	20.69	12	8.27	6	4.14	48	33.10	0.06
8.1 - 12	8	5.51	11	7.59	14	9.65	33	22.76	0.002
>12	0	0	2	1.38	10	6.89	12	8.27	0.001

TOTAL	78	53.79	35	24.14	32	22.07	145	100	

NYHA= New York Heart Association

DISCUSSION

Heart Failure is not just a hemodynamic disorder but it also causes the activation of neuroendocrine and immune system, causing further damage. Long-term course of heart failure, not only involves the heart and muscles but it also causes its effect on peripheral tissues and organs due to reduced blood supply, increasing to the disease burden. The heart failure pathophysiology involves metabolic disturbances, cellular hypoxia as well as hormonal abnormalities.[6] "Increased UA levels have been reported in heart failure patients and recent clinical data supports the possibility that UA adds important prognostic information alone and in combination with other measures of cardiac function and patient functional status in this group."[7] Some of the studies have reported hyperuricemia, an increased risk of all cause mortality in heart failure patients. In a meta-analysis of patients with Heart Failure, it was also found that high UA levels is one of the leading cause of all-cause mortality .[7] "Our findings are consistent with previous observations which found hyperuricemia was common in patients with HF." "Higher uric acid level was independently associated with long term adverse outcomes in these patients".[8]

In patients with HF, hyperurecemia was found irrespective of their use of diuretics , renal issues and other factors.[9] UA levels were previously been correlated with LV functions in heart failure patients.[8] Anker et al. demonstrated relationship between serum UA levels and prognosis in patients with systolic dysfunction. This study also reported hyperuricemia as a cause of exercise intolerance. [9]

"In our study, UA was found to be higher among symptomatic Heart Failure patients as compared to asymptomatic patients". "About 25.51% of the hyperuricemic patients were in NYHA III and NYHA IV whose UA level was more than 8 mg/dl as compared to 12.41% hyperuricemic patients with UA less than 8 mg/dl with mean UA levels was significantly higher in higher NYHA class". This finding can be used as a biomarker for the prognosis in HF patients. Uric acid level is correlated ejection fraction as evident by the study. "Therefore, we believe UA levels may be useful to assess the extent of LV remodeling".

Hypertension, renal dysfunction, and coronary artery disease is directly related to serum uric acis level. The lower the level the better the prognosis.[11] This may be a cause of hypertension in heart failure patients and its prognostic effect on the patients as it was observed in our study. [12]

The significance of our observation lies in its use for developing a risk prediction rule for heart failure, however literature has conflicting evidence regarding use of uric acid as a mortality predictor [12].

"Randomized controlled studies have also been unclear about the putative benefit of allopurinol or its metabolite oxypurinol on established heart failure. Although La Plata study showed improvement in left ventricular ejection fraction with the use of allopurinol."[13]

CONCLUSION

Serum uric acid is strongly related to exacerbation of chronic heart failure in cardiac patients. It can be used as one of the prognostic factor for asymptomatic as well as from symptomatic patients of CHF.

Author's Contribution:

Concept & Design of Study:	Imran Khan
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Matter of Time: Early Versus Late Percutaneous Coronary Intervention in Acute Coronary Syndrome

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ABSTRACT

Objective: To find the outcomes of patients undergoing early versus late percutaneous coronary intervention after Acute Myocardial Infarction.

Study Design: Cross sectional Study

Place and Duration of Study: This study was conducted at Cardiology Unit of Qazi Hussain Ahmed Medical Institute, Nowshera from January 2021 to June 2021 for a period of six months.

Materials and Methods: Study included 200 patients including 120 males. Mean age was 55±5.60 years. Patients presented with acute myocardial infarction, undergoing percutaneous coronary intervention were included. Patients were divided into two groups on the basis of time to intervention. Group 1 comprised of patients in which intervention was done in 24hr to 72 hrs, while Group 2 consisted of patients with intervention done after 7 days of presentation. Patients were then followed to look for primary outcomes like Myocardial infarction (STEMI, NSTEMI), cardiac death and angina in 6 months. Student t test and Chi Square used for analysis.

Results: About 58.60% patients presented with STEMI while 41.40 % with NSTEMI. Group 1 consisted of 90 patients and Group 2 consisted of 110 patients. Mean EF of patients was 43.8±9%. Mean stent diameter was significantly smaller in group 1 (2.7±0.31 vs. 3.2±0.41 mm, p=0.04) while stent length was more in Group 2 (p=0.05). In total 12.5% patients had primary adverse events with cardiac mortality of 2.5%. On compilation, 13.33% of patients in the Group 1 and 15.45 % of patients in Group 2 suffered from primary adverse outcomes (p=0.11). Mortality rate was found not much different between the 2 groups (p=0.14).

Conclusion: Percutaneous coronary intervention has no doubt greater benefit in patients with acute myocardial infarction but timings of intervention after 24hr of presentation especially in stable patients does not differ much.

Key Words: Percutaneous Coronary Intervention (PCI), ST Elevation Myocardial Infarction (STEMI), Non ST Elevation Myocardial Infarction (NSTEMI), Recurrent Angina (RA)

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INTRODUCTION

Coronary intervention (PCI) as a treatment for ST-segment–elevation myocardial infarction (STEMI) reduces mortality compared to other strategies like fibrinolysis.[1,2]

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With the passage of time a number of technical and pharmacological advances have evolved. These advancements have resulted in improvement in cardiac patients with complex coronary disease[3].

It remains controversial about PCI resulting in reducing mortality in other forms of coronary artery disease (CAD) like stable ischemic heart disease. There are some patients undergoing successful primary PCI but still having residual coronary lesions. Some of the patients suffer an acute coronary syndrome without ST-segment elevation (NSTEMI). Some patients suffer from acute myocardial infarction (MI) but without immediate revascularization, however this category of patients is less frequently encountered. Another category of patients is those who are diagnosed as stable CAD.[4]

Although PCI is indicated urgently for ACS patients but most of the intervention is done for stable CAD [5]. Numerous clinical trials have investigated the merits of medical therapy vs PCI in stable CAD[6-8].Some authors have defined stable CAD as unrevascularized post-MI state but recent studies have changed this concept. This became controversial after publication of trials like the COMPLETE trial (PCI for multi-vessel disease following STEMI) and ISCHEMIA trial, (PCI for stable CAD).[9]

The results of COURAGE have defined the "role of PCI in stable CAD more precisely"[10]. This trial suggested that intervention in combination with medical therapy has no significant effect in stable ACS patients [12]. Although a recent Japanese study on stable angina pectoris concluded PCI superiority to medical therapy alone [13].

Therefore, we aim at determining the outcomes in patients having early intervention as compared to late intervention presented with acute coronary syndrome and are clinically stable**.**

MATERIALS AND METHODS

This was a prospective observational study conducted at Cardiology Unit, Lady Reading Hospital Peshawar. Between 1st January 2021 to 30th June, 2021, consecutive patients of acute coronary syndrome (STEMI, NSTEMI and Unstable Angina) aged between 30-70 years, undergoing PCI, presenting to cardiology unit, were enrolled. The study was approved by the hospital ethical committee. Informed consent was taken from the patients before enrollment.

Study subjects with prior MI with complications like cardiogenic shock, cardiomyopathies, prior revascularization were excluded. Patients with valvular and congenital heart disease, deranged RFTS (serum creatinine >2mg/dl) and bleeding issues were also excluded. Study subjects were divided into two groups onthe basis of time to intervention. Group I comprised of patients in which intervention was done in 24hr to 7 days, while Group 2 consisted of patients in whom intervention was done after a month.

Patients characteristics, risk factors, and Echo details were recorded. Coronary angiography was performed from right femoral as well as radial approach. All patients were given standard loading doses of dual antiplatelet therapy(DAPT) before procedure as well afterwards. Patients were then followed up for 6 months to look for primary outcomes like Major Myocardial infarction (STEMI, NSTEMI), cardiac death and angina.

Data was analyzed on SPSS version 17 (SPSS Inc., Chicago, IL, USA). Quantitative variables like stent length were expressed as Mean±SD while qualitative variables like age and gender were expressed as numbers and percentages (%). For quantitative data we used Student t test while Chi square test was used for qualitative variables. P ≤0.05 was considered statistically significant.

RESULTS

A total of 200 patients were included with 120 male patients. Mean age was 55±5.60 years (range 30 -70 years). About 58.60% patients presented to the department with STEMI while 41.40 % patients were diagnosed with NSTEMI. Among STEMI patients about 70% of the patients had anterior wall while 30% had inferior wall Myocardial infarction. Group 1 consisted of 90 patients and Group 2 consisted of 110 patients. Among the patients 62% were hypertensive, 57% were diabetics and 50% were smokers (Table 1). The mean value of left ventricular (LV) ejection fraction (EF) of patients was 43.8±9%.

Different stent parameters were also considered. Mean stent diameter was significantly smaller in Group 1 (p=0.04) while stent length was more in Group 2 as compared to Group 1 (p=0.05). No significant difference was found between the groups in terms of angiographic and procedural success as shown in table 2.

Table No.1: Demographic variables of study population (n=200)

Variables	Number (n)	Percentage (%)
Age	55±5.6 years (range 30 -70 years	
Males	120	60%
Females	80	40%
STEMI	110	54.6%
NSTEMI	52	26.3%
USA	38	19.1%
EF	43.8±9	
Hypertension	124	62%
Diabetes	114	57%
Smokers	100	50%

STEMI: ST Eleveation Myocardial Infarction, NSTEMI : Non ST Eleveation Myocardial Infarction, USA : Unstable Angina, EF: Ejection Fraction

Table No.2: Angiographic Variables observed in study (n=200)

Variables	Group 1(n=90)	Group 2 (n=110)	p value
Number of vessels			
1	60	70	
2	18	20	0.38
3	12	20	
Length of stents			
<20	50	35	0.05
>20	40	70	
Diameter of	2.5+	3.2+ 0.61	0.04

stents	0.41		

The different outcomes of the patients at 6 months follow up are shown in table 3. In total 25 (12.5%) patients had primary adverse events [STEMI = 08 (4.0%) NSTEMI= 04 (2.0 %), Recurrent Angina = 13 (6.5%)]. About 5 (2.5%) patients died.

In group 1, STEMI, NSTEMI and Recurrent angina was found in 03, 02 and 05 patients respectively. Similarly, in group 2, 05 patients presented with STEMI, 02 patients with NSTEMI while 07 patients presented with recurrent angina.

Cardiovascular death was recorded in 2 patients in group 1 and 3 patients in group 2 respectively (Table 3)

On compilation, 13.33% of patients in the Group 1 and 15.45 % of patients in Group 2 suffered from primary adverse outcomes (p=0.11). Similarly, mortality rate was not much different between the 2 groups (p=0.14) as shown in table 4.

Table No.3: Outcomes at 6 months post procedure

Variables	Group 1 (n=90)		Group 2 (n=110)	
	number	percent	number	percent
stemi	03	3.33	05	4.54
nstemi	02	2.22	02	1.81
angina	05	5.55	07	6.36
death	01	1.11	03	1.81

Table No.4: Post Procedure Outcomes at 6 months between groups (n=200)

Variables	Group 1 (n=90)	Group 2 (n=110)	p value
ACS	11.11	12.72	0.11
Death	1.11	1.81	0.14

DISCUSSION

Our study revealed that the overall death post PCI in ACS group was 2.8% which is much less as compared to a study where it was 16% in unstable CAD subsets, although it reduced all-cause mortality in study population.[4] In another study there was no major impact on MI and cardiac death in stable CAD just like in our study (p=0.14). Similar results were also shown in other 2 large studies named COMPLETE trial (multi-vessel disease in STEMI) and the ISCHEMIA trial (stable CAD). PCI has established benefit in mortality over fibrinolysis, in patients with STEMI. The utility of PCI in stable CAD is however controversial. [9]

A patient discharged post STEMI would be considered to have stable CAD, just as in our study group.[13] In accordance with our study in another study they also went for late post MI intervention showing similar results of complications as in early intervention group .[4] However urgent angiography would be considered in un-revascularized post-MI patient if indicated. "Moreover data suggests that PCI does not reduce overall mortality, cardio vascular mortality or MI in patients with stable CAD".[4] From previous data it is clear that the un-revascularized post-MI patients such as unstable coronary artery disease (CAD) as well as multi-vessel disease following STEMI were managed with fibrinolysis in routine without undergoing angiography. But our study suggests that PCI has more benefit as compared to fibrinolysis.[14]

The data from the ISCHEMIA trial, showed that there was "no difference in all-cause mortality", "cardiovascular mortality" or "MI between the early and late intervention just like in our study".[9]

In near future PCI might be accepted as the preferred procedure toreduce mortality .[15] However, for stable CAD, there is lack of evidence about its favorable effect on "all cause mortality", as well as on cardiovascular mortality and re infarction. Like our study another data showed that the difference between early vs late intervention was not much different in case of major MI and cardiovascular death[15]

One of the study having 8912 patients requiring PCI for stable CAD, included symptomatic patients on anti-anginals, patients with single vessel disease, had a success rate of 97% with reduction in mortality. PCI is being performed in patients with co morbidities and complex coronary anatomy with marked reduction of MACE approximately from the last 27 years. [16] In our study frequency of diabetes mellitus, hypertension, and smoking was high.

The courage trial has shown some efficacy of PCI in relieving ischemic symptoms with improved outcomes in patients with stable CAD, previously in ACIP study[17]. The reduction in the use of nitrates and calcium channel blockers has been found although the use of beta-blockers has increased in recent times. These reflects the trends in medical therapy for stable CAD.[17]

CONCLUSION

Although it is evident from international data that PCI has greater benefit in ACS patients but the benefit of early interventions as compared to late intervention in avoiding adverse events like re MI, cardiac death and angina does not differ much.

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Concept & Design of Study:	Iqtidar Ud Din
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The Presentation and Management of Differentiated Carcinomas Thyroid

Gul Sher Khan[1], Muhammad Amir[2], Asif Mehmood[1] and Nazli Gul[4]

ABSTRACT

Objective: Differentiated carcinomas of thyroid (DTC) are very common endocrine tumours with excellent prognosis and this study is aimed to highlight the presentation, management and outcome of the DTCs.

Study Design: A retrospective study

Place and Duration of Study: This study was conducted at the Surgical department of Khalifa Gul Nawaz Teaching Hospital Bannu in collaboration with the BINOR (Bannu Institute of Nuclear Medicine oncology and Radio-therapy situated in the vicinity of KGN MTI) from March 2014- March 2017 and was compiled in July 2021, after a follow up period of five years.

Materials and Methods: A total of 300 patients of DTC, including 210 (70%) female and 90 (30%) male with nodular disease of thyroid (DTC) were included in this study. Age ranged from 18-85 years with a mean age of 45 years.

Results: Out of the 300 patients with DTC, 190 were of papillary carcinoma, 90 with follicular carcinoma and 20 of mixed variety. 60 patients had lobectomy and out of these, 40 cases had completion thyroidectomy. 200 patients had total thyroidectomy and the remaining 40 cases having ipsilateral lymph nodes positive, had total thyroidectomy along with modified radical neck dissection. 130 (43%) patients had radioactive iodine therapy (in BINOR) 6-8 weeks after total thyroidectomy. 75 cases (25%) had regional and distant metastases. Altogether 7 patients died of the disease at the end of 5 years follow up. The mortality rate was 2.3%.

Conclusion: Fine needle aspiration cytology (FNAC) is a gold standard, safe, inexpensive and reliable method of confirming the diagnosis of DTC. Management of DTC requires a multidisciplinary approach consisting of thyroid specialist surgeon, pathologist and specialist in radiation oncology and nuclear medicine. Surgery is the first line treatment while radioactive iodine therapy, TSH suppression, regular physical examination and imaging investigations like ultra-sound (US), CT scan and radioactive iodine scanning of the patients, periodic thyroglobulin detection are the good strategies regarding the management of the DTC.

Key Words: Differentiated Thyroid Carcinoma (DTC), fine needle aspiration cytology (FNAC), thyroid nodule, thyroid lobectomy, total thyroidectomy, thyroglobulin (Tg), radioactive iodine (RAI), surveillance and thyroid stimulating hormone.

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INTRODUCTION

Papillary and follicular carcinomas are the differentiated thyroid cancer. DTC are the most common endocrine tumoures.

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The incidence of these tumours has been increasing for the last few decades but the mortality remains the same[1], which is due to the increase in the number of small /occult or in situ cases diagnosis. These small cases do not contribute to mortality. Increase detection is due to improved pathological sectioning and the incidental detection of clinically occult foci on imaging performed for some other purpose [2,3]. The survival rate of DTC is excellent so the management should have an initial oncoligical surgical resection, providing follow up, radioactive iodine therapy, thyroid stimulating hormone (TSH) suppression and close surveillance.

Papillary carcinoma is the most common accounting to 60-80% and follicular carcinoma 10-15%[4]. Follicular carcinoma is lethal than papillary due to its vascular spread and have distant metastases. While papillary carcinoma has lymphatic spread and have locoregional recurrences. Two papers published by US and Germen thyroid group confirmed that the incidence of follicular carcinoma is high in the region with iodine

deficiency[5,6]. Radioactive iodine is no longer recommended for the treatment of low risk patients with DTC. The prognosis of Papillary thyroid carcinoma (PTC) is generally good, about 10% of patients would finally die of the disease and an even a high proportion would suffer the morbidity of recurrence [7,8]. In papillary thyroid carcinoma (PTC), there is usually a history of ionizing radiation exposure for benign or malignant disease in childhood or adult, nuclear fallout or nuclear energy accidents. DTC constitute 2% of all the body cancer [9]. Regarding the distribution of the disease, 2/3rd cases are found in women and 1/3rd in men [10].

The age, sex, size of the tumour, extra thyroidal spread and completeness of resection have been found to effect the prognosis[11]. Despite of the best practice, recurrence rate are reported from 8-23%[12,13]. Cervical metastases occur in 35-80% cases of Differentiated papillary carcinoma[14]. These metastases do not adversely affect the survival rather they increase the locoregional recurrences and reoperation rate [15].

Patients with recurrence disease undergo salvage surgery and radioactive iodine therapy. The mortality with recurrence has been reported as 40-50% and these patients with recurrence having an increase risk of multiple recurrences. The risk for distant metastases is 10-15% for follicular thyroid carcinoma.

MATERIALS AND METHODS

This is a retrospective study from the medical record review of 300 patients with DTC admitted to the surgical department of Khalifa Gul Nawaz Teaching Hospital Bannu, was conducted from March 2014-March 2017 and compiled in July 2021, after a follow up period of 5 years.

In this study, the record regarding the patients demography i.e. the age, sex, diagnosis and size of the tumour, solitary or multifocal, stage of the tumour, extra thyroidal spread, information about the site of recurrence (locoregional, distant or unspecified), mode of detection (clinical, FNAC, imaging, thyroglobulin estimation) and treatment (surgery/radioactive iodine^{131} therapy) for the primary disease and recurrence. Extent of the primary disease was retrospectively staged according to the current American Joint Committee on cancer (AJCC). Treatment success was ascertained on the basis of undetectable thyroglobulin estimation and or normalization of imaging modalities including iodine^{131} scanning, ultrasonography and CT scanning.

Follow up was counted from completion of treatment to the last known recurrence at the end of 5 years surveillance. Outcome was written as alive with no disease, alive with disease and died of the disease.

Demographic data of 300 patients treated for well differentiated thyroid carcinoma.

- Age - - - - - - - - - - - - - - 45 (18-85) years.
- ≤45years - - - - - - - - - - - - -190 patients.
- > 45yrs - - - - - - - - - - - - - -110 patients.
- Sex F/M- - - - - - - - - - - - - - - 210/90.

Histological diagnosis

- Follicular carcinoma - - - - - - - 90 cases.
- Papillary carcinoma - - - - - - - 190 cases.
- Mixed type - - - - - - - - - - - - - -20 cases.

Tumour size - - - - - - - - - - - - - - - - - - 2.5(1-6)cm.

Multifocal -45.

Extra thyroidal spread - - - - - - - - - - - - - - - - 40.

AJCC staging;

- I ----------120.
- II ---------- 95.
- III ----------60.
- IV ----------25.

Surgery;

- Lobectomy ---------- 60.
- Completion thyroidectomy ---------- 40.
- Total thyroidectomy ---------- 200.
- Total thyroidectomy with neck dissection ----------40.

Radioactive iodine^{131} treatment ---130 (43%) cases.

Recurrences ---------- 75 (25%) cases.

Outcome;

- Alive without disease - - - - - - - 228.
- Alive with disease - - - - - - - - - - 65.
- Dead of the disease - - - - - - - - -- - 7.

All the patients in stage I were alive and free from the disease at the end of 5 year follow up. From stage II out of 95 patients, 70 patients were alive and free from the disease. 25 patients were alive and with recurrences. In stage III, 2 patients expired due to the disease, 20 patients were alive but with recurrences and 38 patients were alive without the disease. In stage IV there were 5 expiries and all the rest of 20 patients had multiple recurrences at the end of 5 year follow up.

STATISTICAL DATA: Cancer specific survival was calculated for each stage of the disease using Kaplan Meier`s curves and the difference between the stages and or risk groups was compared by the "log rank test. The hazard risk and confidence intervals were calculated for cancer specific mortality and morbidity using Cox proportional models. The relative significance of each staging system was estimated by calculating P value. $P < 0.05$ indicates statistical significance. Statistical analysis was performed using SPSS for window 11 computer software.

RESULTS

A total of 300 patients with DTC, including male 90 (30%) & female 210 (70%), age ranging from 18-85 years with a mean age of 45 years were included in the study.

The differentiated carcinoma thyroid (DTC) included, papillary carcinoma 190 cases, follicular 90 cases and mixed type 20 cases. Out of the 190 papillary carcinoma cases, 30 cases were of micro-carcinoma

(≤ 1cm size) on histopathology of the resected specimen.

On TNM staging the number of cases were;

Stage 1 ---------- 120 (40%).
Stage II ---------- 95 (32%).
Stage III ---------- 60 (20%).
Stage IV ----------25 (8.3%).

The initial management;

1. Lobectomy ----------60 (20%).
2. Completion thyroidectomy ---------- 40.
3. Total thyroidectomy ----------200 (66.7%).
4. Total thyroidectomy with ipsilateral cervical lymph node dissection-----40 (13.3%).

Follow up and surveillance of the patients;

Complete follow up data were available from the patient's record. The median follow up was for 58 months (range 56-60 months). All the patients after surgery were followed with in the first 4-6 weeks to decide on the further management. The further visits were scheduled as 1 visit after every three months in the first year, every 6 months for the next 3 years and annually after that. During each visit physical examination, chest X-rays, ultra-sound or CT-scan, periodic estimation of thyroglobulin levels, having being done, seen. Distant metastasis were diagnosed on the basis of histology, radiology and radioactive iodine scanning.

Adjuvant radioactive iodine^{131} therapy was given to 130 (43%) patients (in BINOR) 6-8 weeks after surgery. 75 (25%) patients develop recurrences (50 female & 25 male) at the end of 5 years follow up.

Recurrences from the tumour stages were;

Stage II ---------- 10.
Stage III ---------- 40.
Stage IV ---------- 25.

Regarding the site of recurrences;

1. Regional ---------- 55.
2. Distal metastasis ----------15.
3. Unspecified ---------- -----5.

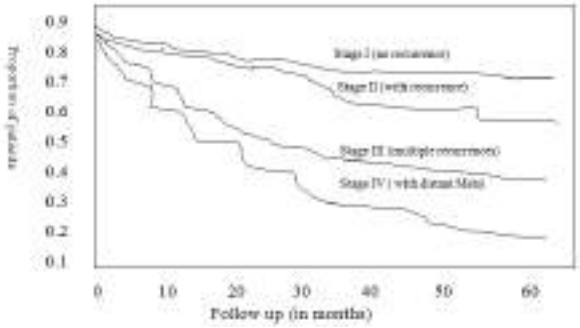

Figure No.1: Disease specific survival for patients in stages I-IV

Locoregional recurrences were seen in the cervical lymph nodes in cases of papillary carcinoma and distant metastases were seen in; clavicle, sternum, ribs, skull, lung fields, vertebra and long bones of the limbs in cases of follicular carcinoma.

The recurrences were treated by salvage therapy including further surgery, radioactive iodine therapy and external beam radiotherapy in some cases.

Morbidity: The results of present study were quite hopeful. Initial cure was obtained in almost in 75% (225) of the cases with a recurrence rate of 25% (75) patients.

Mortality: There were 7 cancer related deaths (2 from stage III and 5 from stage IV) with a mortality rate of 2.3%. Regarding survival at the end of 5 years follow up, the stage wise figures were as follow;

Stage I ---------- 98.6%.
Stage II - - - - - - - - - - - -98%.
Stage III ---------- 96%.
Stage IV - - - - - - - - - - - 80%.

Hospital stay was 4-7 days with a mean of 5.5 days.

DISCUSSION

This study clears a number of important facts regarding the differentiated thyroid carcinomas. Papillary carcinoma is commoner than the follicular carcinoma in our locality. The same distribution ratio prevails in USA and UK. Our study showed that there were more deaths due to follicular carcinoma than the papillary due to its vascular spread. The median age at the initial diagnosis was 45 years and the male/female ratio 30%/70%, are comparable to that in Europe and USA.

Most tumours were present in the stage I (40%) which is due to increased early diagnosis and improved pathological techniques. The same is the situation internationally.

The stage wise survival rates in our study were closely approximating the international values.

In the recent years, papillary micro-carcinoma have been increasingly diagnosed and treated in various parts of the world [16,17]. Clinically occult tumours are mostly incidental and indolent in behavior while patients with clinically overt micro-carcinomas have a more aggressive behavior and type of presentation. Cervical metastases represent the most common focus for recurrent disease [18], and that cervical mets do not affect the survival[19]. Cervical ultra-sound and thyroglobulin levels are commonly used for long term surveillance of PTC and are the sensitive markers for recurrent disease[20]. Fine needle aspiration cytology (FNAC) is the gold standard for the initial evaluation of nodular disease of thyroid.

The most significant factors for the development of recurrences were male sex, advanced age and stage of the disease, the size of the tumour and the extra thyroidal spread. Male sex and age >45 years, an aggressive combination therapy consisting of surgery and radioactive iodine was used. PTC was associated with a good disease specific outcome in 60-80% of cases. In our study initial cure was obtained in most of

the patients with recurrence in only 25% cases at the end of 5 years follow up. In this study a significant better survival was observed in young female, papillary tumours and patients without distant metastases. Patients with surgery and early radioiodine therapy had a statistically significant survival versus patients with surgery and a delayed radioactive iodine therapy ($p < 0.001$). Morbidity has been reported as from 15-30% while in our study it was 25%.

In this study patients with one or more of the following risk factors were considered for radioactive iodine therapy and surgery. The risk factors were tumour size ≥ 2 cm, age >45 years, extra thyroidal spread, macroscopic post-operative residual disease in the neck and distant metastasis. For detection of mets whole body scan with iodine was performed 6-8 weeks after surgery.

Surgery was the first line treatment. Patients underwent lobectomy, completion thyroidectomy, total thyroidectomy and total thyroidectomy with lymph node dissection neck. Lobectomies were performed in some favorable cases e.g. young age, micro papillary carcinoma and minimally invasive follicular carcinoma with indolent histologies. Some cases of Lobectomies were converted to completion thyroidectomy on the basis e.g. multi-focality on the histology of resected specimen, unfavorable histology, old age and male sex. Total thyroidectomy was performed on large tumour (size >2cm) and multi-nodular thyroid disease. While total thyroidectomy with cervical lymph nodes dissection was performed in cases of positive cervical lymph nodes. Routine palpation and sampling/clearance of the lymph nodes in the central compartments neck (group VI cervical lymph nodes) was done in cases of total thyroidectomy.

Early detection of the disease by estimation of thyroglobulin and iodine scanning are prognosticaly good as the disease is picked up in the early stages. Unspecified recurrences were those cases of total thyroidectomies where the Tg levels were high but on imaging or scanning no mets were detectable.

The cases of recurrences were subjected to salvage surgery, radioactive iodine and external beam radiotherapy in a few cases.

CONCLUSION

There is a progressively an increasing trend in the DTC incidence. Follicular carcinoma is lethal than papillary carcinoma due to its vascular spread. A multidisciplinary approach is needed in the management of DTC. Surgery is the first line treatment modality. Presently there is an increase in the detection of early stage DTCs. whatever is the size, stage, sex and grade of the DTC, prognosis is a good in young patients i.e. between 21and 45 years. Management of DTC includes surgery, radioactive iodine therapy, TSH suppression and periodic estimation of thyroglobulin level.

Author's Contribution:

Concept & Design of Study:	Gul Sher Khan
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Data Analysis:	Asif Mehmood, Nazli Gul
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Lithium Induced Male Reproductive Organ Injury in Albino Rats

Lithium Induced Male Reproductive Organ Injury in Albino Rats

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

ABSTRACT

Objective: Metal ingestion causes degenerative injury to seminiferous tubules and antipsychotics drugs like Lithium brings deleterious changes to seminiferous tubules in this study the diameter of seminiferous tubules was measured and documented.

Study Design: Experimental study

Place and Duration of Study: This study was conducted at the Anatomy department and Animal house of Basic Medical Sciences Institute from May, 2013 to June, 2013 for a period of 02 months.

Materials and Methods: Three months of age weighing 270 -290 grams were chosen for this study and distributed into two equal groups A and B. Group A served as control, received only laboratory diet group B received Table Lithium Carbonate 20 mg/kg body weight for four weeks. At end of the study period the dissection of lower abdomen was carried out and testis were removed and the diameter of seminiferous tubules in both groups were measured and documented.

Results: The total number of albino rats selected for this study was twenty. The results showed a highly significantly increased diameter of seminiferous tubules P value <.001 in Group A animals as compared to group B animals and a highly significantly decreased P value < .001 diameter of seminiferous tubules in Group B Animals as compared to Group A rodents.

Conclusion: Lithium carbonate causes highly significant decreased thickness of seminiferous tubules.

Key Words: Antipsychotic drugs, seminiferous tubules, deleterious effects

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INTRODUCTION

Male reproductive organs being the testis are two in number [1] one on each side. Each testis is present in the scrotal sac. Each testis has coiled seminiferous tubules[2] which are responsible for the production of sperms.[3]

It has been documented that seminiferous tubular, diameter [4,5] ranges between 200-300 µm. Toxins, [6] Heavy soft metals like lead [7] and lightweight alkali metals like Lithium[8] decreases spermatocytes and diameter of testicular tubules. Many deleterious effects of lithium are documented on various organs like Central nervous system, Kidneys, Thyroid, and Parathyroid also, the damaging effects of Lithium on testis have been documented by Saad et al[9] 2017 they in their research found that Lithium causes, decreased diameter of seminiferous tubules.

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Still there is decrement of literature on the damaging effects of lithium on testis and seminiferous tubules; we conducted this study so as to bring to light the damaging effects of the drug on seminiferous tubules.

MATERIALS AND METHODS

Our experimental study was designed and conducted at Anatomy department Basic Medical Sciences Institute Jinnah Post graduate Medical Centre Karachi from fifth May to 5th June 2013. Total twenty Albino rats of three months of age and weight ranging between 270 -290 Grams were taken from the Animal House of Basic Medical Science Institute, Jinnah Postgraduate Medical Centre, and Karachi. They were kept under observation for seven days prior to the commencement of the study.

The animals were divided into two groups A, B each comprising 10 rats:

Group A: served as control

Group B: received. Lithium Carbonate of 20 mg[10] /g /day

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The albino rats were kept under laboratory favourable environment, at animal house, water and food supplied ad libitum. At the end of the period of treatment, rats were sacrificed under light Ether[11] anesthesia. A midline abdominal incision [12] extending up to the skin of scrotum, all coverings of scrotum were dissected and both testes were identified and removed. Testis after cutting them longitudinally were fixed in Bouins fluid for 24 hours[13]. After fixation of the tissue it was passed in ascending grades of alcohol and placed in paraffin blocks. Almost five micron thick sections of testis were taken in both groups. The level of significance (P) was calculated by the help of student's t-distribution table. The highly significance level was considered as p<.001 All the calculations were done utilizing, SPSS version 2007.

RESULTS

The total number of albino rats selected for this study was twenty.

The results showed a highly significantly increased diameter of seminiferous tubules P value <.001 in Group A animals as compared to group B animals and a highly significantly decreased P value < .001 diameter of seminiferous tubules in Group B Animals as compared to Group A rodents.

Group A contained ten rodents and Group B comprised of ten rats. Five micron thick Haematoxylin and Eosin stained sections of Testis were visualized which showed seminiferous tubules. They are lined by a complex seminiferous epithelium. The section on microscopy of Group A (Control group) Showed Modified Stratified Columnar epithelium present on a continuous basal lamina. The Germinal epithelium was showed several types of germ cells. There was a highly significantly increase mean thickness of seminiferous tubule of control group A at four weeks which was 276.02±05µm. There was no pyknosis of nuclei, also Apoptosis of germinal cells was absent

Group B five micron thick Haematoxylin and sections Eosin stained sections of seminiferous tubules showed Damaged and apoptotic germinal cells and a highly significantly decreased diameter of seminiferous tubule which was 167.05±.55µm. There was marked vacoulation with in seminiferous tubules. The seminiferous tubules had a distorted appearance and were empty spaces due to germinal cell death within the seminiferous tubules.

Table No.1: Mean Diameter in µM of the Thickness of Seminiferous Tubules JN Different Groups of Albino Rats

Groups	Treatment Received	Sub-Groups	4th Weeks	P-Value A vs. B
A (n=10)	Control	A	276.020±.5 µm	P<.001
B (n=10)	Lithium Carbonate	B	167.05±0.55 µm	

DISCUSSION

Lithium the Typical Antipsychotic[14] and atypical antipsychotics like olanzapine[15] causes germinal cell death due to oxidative stress. It is observed that medicinal literature is deficient on the adverse effects of Antipsychotics like Lithium carbonate on diameter.

For the above same reason, we concluded our study and documented the decrement of seminiferous tubular diameter after ingestion of Lithium Carbonate.

This study documented changes of distortion and degeneration of the diameter of seminiferous tubules due to harmful effects

Heavy Metals like Cadmium[16], Mercury. Arsenic, Lead causes sperm cell death due to release of reactive oxygen species. The ROS causes increased oxidative stress, lipid peroxidation and DNA damage resulting in cell death and due to germinal cell loss, there was decline in the diameter of the seminiferous tubules. The same results of depletion of germinal epithelium and diminished seminiferous tubular diameter was documented in this research and this may be due to the reason that the drug Lithium carbonate caused release of Reactive oxygen species which resulted in sperm cell.

The above results of oxidative stress causing damage to seminiferous tubules were also found by Ghazal, Nabiuni and Elaheh[17].They reported a highly significant reduction in seminiferous tubular diameter. Our results in accordance with them this may be due to the fact that Lithium causes release of Reactive oxygen species which results in DNA damage causing cell death and apoptosis which is visualized as increased space between the germinal cells.

CONCLUSION

This is study concluded that Lithium carbonate reduces the diameter of seminiferous tubule. It is suggested that, the results should be considered when prescribing lithium to male patients who may lead to infertility.

Author's Contribution:

Concept & Design of Study:	Tazeen Kohari
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Data Analysis:	Faryal Azhar, Usama Faruqui
Revisiting Critically:	Tazeen Kohari
Final Approval of version:	Tazeen Kohari

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

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Prevalence and Associated Risk Factors of Intestinal Parasitic Infections in Children at Slum Area of Karachi

Intestinal Parasitic Infections in Children

Naveed Mansoori[1], Syed Ishtiaq Ahmed Fatmi[2], Noor-us Sabah[1] and Syed Muhammad Mubeen[1]

ABSTRACT

Objective: To determine the prevalence and associated factors for intestinal parasitic infections in children aged 5 to 15 in Khuda Ki Basti, Karachi, Pakistan.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at Community Health Sciences, Hamdard College of Medicine & Dentistry, Hamdard University, Karachi from May, 2018 to August, 2018 for a period of four months.

Materials and Methods: Two hundred eight children aged 5 to 15 years were randomly selected after permission from the Institutional ethics review committee. The stool specimens were collected and taken to the laboratory. SPSS version 23.0 was used for data entry and analysis. Frequency and percentages were calculated for description variables.

Results: Stool examination was carried out for 208 children. Four intestinal parasites were identified with an overall prevalence of 38 (18.27%). The most prevalent intestinal parasite found was Entamoeba histolytica (10.10%) then Ascaris lumbricoides (03.36%), Giardia lamblia (03.36%) and H. nana (01.44%).

Conclusion: The overall prevalence of parasite infections was low in this study due to good hygienic practices, such as a significant number of children wash their hands before eating and a large number of children wash their hands after using the toilet.

Key Words: Parasitic infections, Children, Hygienic practices, slum area of Karachi

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INTRODUCTION

In both, industrialised and developing countries, intestinal parasite infections remain are still a major public health concern. All of these illnesses are widely recognised to be endemic in areas with poor sanitation and crowded living conditions and they are linked to the community's water supply, age, and socioeconomic status .[1] Intestinal parasite infections are widespread worldwide, affecting an estimated 3.5 billion people. They are responsible for clinical morbidity in approximately 450 million people.

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Developing countries are said to be the most affected with school-aged children accounting for, the vast majority of cases.[2] The distribution of these parasite illnesses is influenced by a variety of factors. These include socio-demographic factors associated with poverty, such as a lack of access to proper sanitation, potable water, and healthcare, as well as the current climatic and environmental circumstances. School-aged children are one of the groups most vulnerable to parasite infections of the intestine. Parasites have a wide range of negative impacts on schoolchildren, which is disturbing. These infections have a negative impact on children's survival, hunger, growth and physical fitness, school attendance, and cognitive function .[3]

Parasitic infection is a major cause of childhood malnutrition, anaemia, stunted physical and mental growth, psychosocial issues, recurring gastrointestinal and upper respiratory tract infection, and hence contributes to high morbidity and death in children. Despite improving socioeconomic situations and higher living standards, it remains a public health issue in advanced countries, such as the United States.[4] The reason that helminthic infestation is a global public health problem and because clinician have generally ignored it since, while worms can cause significant clinical problems. Patients rarely report to health

centers due to the sluggish progression of the signs and symptoms.[5] Intestinal parasite infections are more common in school children aged 5 to 14 years. They account for 12% of the total disease burden in children.[6] Due to the high incidence and major unfavourable consequences of intestinal parasite infection in children, several studies have been undertaken in many cities across Pakistan, however a severe deficiency was felt for a recent study in Karachi.[7-9] Hence, the objective of the present study is to determine the prevalence of intestinal parasite infections and its associated factors in children aged 5 to 15 years old in 'Khuda Ki Basti', a semi-urban slum settlement in Karachi, Pakistan.

MATERIALS AND METHODS

A cross-sectional study was undertaken among children living in Khuda ki Basti, a semi-urban slum settlement in Karachi. After approval from ethical review committee of Hamdard University, from May, 2018 to August, 2018 for a period of four months, two hundred and eight children aged between 5 to 15 years were selected randomly. Pre-tested questionnaire was used for the collection of data from the parents of study participants. A clean, dry, screw-capped and appropriately labelled plastic container was delivered to parents of 208 children for sample collection. Informed consent was acquired from parents for sample collection. Labels with code number, name, age and sex sufficed to identify the specimens. The container was sent the day before and the participants were instructed to defecate in it the next morning. It was to be avoided by not diluting it with the urine or water. It was ensured that the study individuals were not taking any medication such as antibiotics, anthelminthics, anti-diarrheal agents, antacids or hypertonic salts. A total of 208 stool samples were collected and transferred to the laboratory. SPSS version 23.0 was used for data entry and analysis. Frequencies and percentages were calculated for descriptive variables.

RESULTS

Frequency distribution of socioeconomic demographic variables were studied in a total of 208 children of which 76 were between 5 to 6 years, 86 between 6 to 10 years and 46 were more than 10 years of age. Out of 208 children, 106 were males and 102 females. Out of total, 150 were school going children. Majority of the children 160 (77%) belongs to poor families, 26 (12.5%) children from economically good families and 22 (10.5%) children had very good financial background. Assessment of educational status of the mothers showed that 66 (31.7%) mothers were illiterate & among the literate group, 128 (61.5%) matriculate and 14 (6.7%) mothers were educated till graduate level.

Stool examination was carried out in 208 samples. Four intestinal parasites were identified with an overall prevalence of 38 (18.27%). The most prevalent intestinal parasite found was Entamoeba histolytica (10.10%) then Ascaris lumbricoides (3.36%), Giardia lamblia (3.36%) and H. nana (1.44%). (Table 1)

Frequency of the risk factors like hand washing before eating, soap for hand washing, washing hand after using toilet, practice of finger nail trim and boiled water for drinking purpose were determined among the all children. (Table 2)

Table No.1: Laboratory Results

Parasite	Total Partici-pants	Stool D/R Performed	Positive Results	%age
Entamoeba histolytica	208	208	21	10.10%
Ascaris lumbricoides	208	208	7	3.36%
H. nana	208	208	3	1.44%
Giardia lamblia	208	208	7	3.36%

Table No. 2: Frequency of Risk Factors Among Children

Risk factors		Frequency	%tage
Hand washing before eating	Yes	186	89.40
	No	22	10.60
Soap for hand washing	Yes	128	61.50
	No	80	38.50
Washing hand after using toilet	Yes	184	88.50
	No	24	11.50
Practice of fingernail trim	Yes	126	60.60
	No	82	39.40
Boiled water for drinking purpose	Yes	74	35.60
	No	134	64.40

DISCUSSION

The overall prevalence of parasitic infections in this study was 18.27%. Entamoeba histolytica (10%) is the most common intestinal parasite in our study. Other parasites in our study include Giardia lamblia (3.36%), H. nana (1.44%), Ascaris lumbricoides (3.36%).

The observed prevalence of intestinal parasites of 22 (18.33%) was in line with the Okyay's study (13.80% & 22.40%) in western city of Turkey.[10] It was lower as compared with reports of other similar studies, 79.9% in North Gondar[11], 91.2% in Jimma[12], 63.8% in Egypt[13] and in Gondar (34.2%).[14]

According to the present study, the prevalence of the parasite Entamoeba histolytica was highest (10% among children). This prevalence was low in comparison to the prevalence reported by Gopi Chand et al. (30.76%)[15] and Adepeju et al (67.60)[16] and is most

likely due to good hygiene practices among children of this slum area of the Karachi.

The frequency of the parasitic infection caused by Ascaris lumbricoides was 3.36%. This incidence was consistent with the 3.4% and 3.9 % prevalence reported in India[17] and Rome respectively [18]. However, the prevalence was significantly low than in studies conducted by Gondar et al [11] (48%) and in another study in Northern Ethiopia, it was found to be 83.4%.[19]

The prevalence of Giardia lamblia was found to be 3.36%, which is low when compared to a study conducted in Pakistan's district Mianwali[20] in Punjab province, where 37.7% of stool samples tested positive for Giardia lamblia. This disparity could be explained by the fact that in this study sample 89.40% children washed their hands before eating and 88.50% washed their hands after using toilet.

H nana parasitic infection was detected in 1.44% stool samples, which is relatively low when compared to other research. A study conducted in Pakistan found 31.0% prevalence which might be attributable to the current study's participants' good hygienic status when compared to prior studies.[20]

In underdeveloped nations, exceptionally high prevalence have been observed; for example, in a study from rural southern India, the overall period prevalence of intestinal parasites was 97.4%/month.[21] Another study in Sierra Leona reported 73.5%prevalence rate. [22] The higher rates in these communities could be linked to lack of hygiene.

CONCLUSION

Our targeted community has a lower prevalence of parasite infection. This lower prevalence of parasite infestation reflects improved living condition and cleanliness. Over the last few years, the combined efforts of Pakistan's health care workers' authorities in the fight against parasites have resulted in a significant drop in the prevalence of parasitic infestation.

The young children who were found to be positive had a propensity of going outside, playing on the dirt, and eating without washing their hands, which contributes to their high prevalence. Poor sanitation, open field defecation, unclean stagnant water, and a low economic level are the key risk factors for high prevalence.

Author's Contribution:

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

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Radiological Perspective of Covid-19 Pneumonia in Tertiary Care Hospital, Karachi

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ABSTRACT

Objective: To evaluate the radiographic patterns in COVID associated pneumonia in a tertiary care hospital of Karachi.

Study Design: Analytic study

Place and Duration of Study: This study was conducted in specifically designed COVID wards and HDU in Dow University Hospital, Karachi between 1st June 2020 to 15th July 2020, by reviewing the admission records of COVID diagnosed patients.

Materials and Methods: A total of 150 patients presented with pulmonary symptoms were evaluated for chest radiographs.

Results: Out of 150 COVID detected patients, 80 were males (53.33%) and 70(46.66%) were females with a mean age of 51.14±15.96 years. Frequent radiographic patterns were diffuse infiltrates occupying more than half lung field 56(37.33%), diffuse infiltrates less than half of lung field 45 patients (30%), lobar pneumonia in 9(6%) and cardiomegaly with basal infiltrates were observed in 7 patients (4.6%). Dominant symptoms were shortness of breath on exertion 105 patients (70%), fever 60(40%). The most common signs observed were hyperventilation 105(70%) and crepitation's 30(20%). The most common comorbidities observed in the study were Uncontrolled Diabetes 114(74%), Hypertension 76(50.6%), and ischemic heart disease 52(34.66%).

Conclusion: The majority of COVID detected with pneumonia were male, common radiographic patterns were pulmonary infiltrates. Lobar pneumonia and pleural effusion were rare findings and typically seen in severe disease where patients need mechanical ventilation.

Key Words: Pneumonia, COVID-19, coronavirus infections, clinical features, radiographic features.

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INTRODUCTION

The Covid-19 infection came out as global plunder at the end of 2019 emerging from the city of Wuhan from China.[1,2] WHO officially announced it as a pandemic on 11 March 2020 spreading with a furious pace involving six continents across the world.[3] The clinical spectrum of Covid infection comprises multisystem involvement including CNS, GIT but predominantly involving the respiratory tract.[4]

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The primary symptomatology associated with Covid-19 infection include fever, dry cough, sore throat, fatigue and Pneumonia. Sometimes patients present with gastrocintestinal symptoms for example diarrhea and abdominal pain. Advanced cases of COVID 19 disease can be complicated as ARDS, septic shock, metabolic acidosis, and coagulopathies[5] In some cases thromboembolic phenomenien is also noted. This thromboembolic phenomenon can present as blockage of majaor blood vessels of vital organs, which can leads to Myocardial Infarction, Acute kidney injury or Cerebro vascular accidents.

Most patients with covid-19 infection have a mild upper respiratory tract infection and do not progress to pneumonia.

The chest radiograph may be normal in up to 63% of people with covid-19 pneumonia, particularly in the early stages.

The standard diagnostic tool for confirmation of infection recommended by WHO is the reverse transcription-polymerase chain reaction RT-PCR. However, the contribution of imaging studies is under

constant evolution both in terms of chest x-ray and CT scan.[6] Most recently, chest x-ray has been recognized as a first-line imaging technique by Italian Society of Radiology (SIRM) while chest CT reserve for identification of Covid-19 in selected cases.[7-9] A normal chest radiograph does not completely exclude the covid-19 pneumonia. Not a single feature of covid-19 infection on a chest radiograph is specific or diagnostic, but a combination of multifocal lung changes for example ground glass opacities or typical consolidation, which are most commonly seen bilaterally, may be the diagnostic feature.

Similar to bacterial pneumonias, covid-19 pneumonia can cause increase in density of the lungs unilateral or bilateral. This may be easily seen as opacities in the lungs on chest X rays, but the intensity of this opacity is depends on the severity of the disease. It conceals the lung markings that can be normally seen in chest x-rays; though, this may be deferred in appearing or may be absent.

Peripheral, coarse, horizontal white lines, bands, or reticular changes which can be defined, as linear opacities can also be seen in combination with ground glass opacities.

After the lung markings are partly masked by the increased whiteness, a ground glass pattern (ground glass opacity) forms on xrays. This can be a subtle and might need confirmation with a consultant radiologist. Once the lung markings are totally vanished due to the whiteness, it is called as consolidation (this is frequently seen in severe COVID-19 disease).

The British Society of Thoracic Imaging said that there is “no role for computed tomography imaging in the diagnosis of covid-19 unless the patient is seriously ill (NEWS score >3) OR if PCR is unavailable” and the American Society of Thoracic Radiology (STR) declares that “routine screening computed tomography for the identification of covid-19 pneumonia is currently not recommended by most radiology societies.”

However, it is interesting to note that CT is more reliable as compared to chest x-ray in term of sensitivity (97-98%).[10-12] But at the same time, difficulties encountered while performing a CT scan (like radiation exposure and repeated standard disinfection of equipment and lack of availability) has opened and pivoted way for a chest radiograph to be considered as the most widely utilized radiological tool. In addition to that, cross infectivity can be minimized to a major extent with the utilization of portable x-ray units on account of reduced patient mobilization and quick availability of results.[7-9]

Furthermore, radiological changes in Covid pneumonia can present with a variable spectrum such as peripheral (unilateral, bilateral) or diffuse involvement preferably involving middle and lower zones.[13,14] In particular, the most repeatedly observed manifestation in Covid pneumonia include ground-glass opacities, unilateral or bilateral lobar consolidations, peripheral infiltrates and diffuse opacities while the least noticed x-ray changes are cavitation, pneumothorax, and pleural effusion.[14,15]

The present study is designed to understand different x-ray changes associated with Covid-19 which will not only help in early identification of cases in whom the RT-PCR is false negative but will also contribute towards the timely management, ultimately results in a better outcome.

MATERIALS AND METHODS

We conducted this observational, retrospective and descriptive study, in the department of Covid specified wards and HDU at Dow University Hospital, Karachi. The study conducted between 1st June 2020 to 15th July 2020, by reviewing the record of 150 COVID-19 diagnosed patients admitted with their documented signs, symptoms, and investigations including chest radiographs. Data entered in a prescribed proforma and then evaluated with 150 patients have a correlation between their symptoms, signs, blood CBC, acute phase reactant, and ABG’s with chest radiographs. All of them were on conventional therapy comprising of antibiotics, anticoagulation, and methylprednisolone, with patients refractory to, were offered treatment with antiviral (remdesivir), IL-6 inhibitors (tocilizumab), or convalescent plasma therapy. Two consultants analyzed the radiographic patterns, symptoms, and signs assessed. The results were analyzed by SPSS version 19 with descriptive statistics.

RESULTS

Table No.1: Radiographic patterns

S. No.	Radiographic patterns	Number of patients	%age
1	Pulmonary infiltrates>half of lung field	56	37.33
2	Pulmonary infiltrates less than half of lung field	45	30
3	Lobar pneumonia	9	6
4	Normal x ray	10	6.66
5	Infiltrate’swith cardiomegaly	7	4.66
6	Reticulonoular shadow	3	2
7	Infiltrates in hemi thorax	2	2
8	Infiltrates with pleural effusion	2	2
9	Collapse of lung	1	0.66
10	Apical infiltrates	0	
11	Cavitatory lesions	0	

A total of 150 patients were admitted during the study period from 1st June till 15th July 2020. Majority were males (N= 80, 53.33%) while rest were females (N=70, 46.66%). The mean age was 51.14±15.96 years (Range: 7-84 years). Radiographic patterns are described in Table 1.

Frequent radiographic patterns were diffuse infiltrates occupying more than half lung field 56(37.33%) (figure 1), diffuse infiltrates less than half of lung field 45 patients (30%) (figure 3), lobar pneumonia in 9(6%) (figure2) and cardiomegaly with basal infiltrates were observed in 7 patients (4.6%). Dominant symptoms were shortness of breath on exertion 105 patients (70%), fever 60(40%). The most common signs observed were Hyperventilation 105(70%) and crepitation's 30(20%). The most common comorbidities observed were Uncontrolled Diabetes 114(74%), Hypertension 76(50.6%), and ischemic heart disease 52(34.66%).

Figure No.1: Common Radiological patterns bilateral diffuse lung infiltrates

Figure No.2: Lobar pneumonia

Figure No.3: Diffuse bilateral infiltrates

DISCUSSION

Patients with COVID-19 infection can be present with fever, cough, and dyspnea. Though lethargy is common as in most of the viral infections but rhinorrhea, sore throat, and diarrhea are not common. Various reports have stated that initial imaging might show normal findings in 15% of individuals, so a normal chest imaging examination does not exclude the infection.[5]

A case series retrospective study of 64 patients admitted with covid-19 infection in Hong Kong indicate that 31% (20 patients) had normal chest xrays on admission. Out of those 35% (n=7) developed typical radiological changes on follow-up x rays. This study also proposed that peak radiological changes on chest radiography are seen between days 10 to 12 after onset of the symptoms.

A study published in Lancet described the clinical manifestations of corona virus disease in 41 patients.[16] showed abnormal chest imaging findings were observed in almost all the patients, with 40 having bilateral disease at initial imaging. In our study about 90 % of patients had pulmonary disease with the majority of them had pulmonary infiltrations bilaterally and only 2 patients have unilateral lung involvement. In this study, 30% of patients had more than half of the lung field involvement while only 6% of patients had pneumonic consolidation.

With reference to five case series studies, [17,18,19] and some case reports 20 have investigated the radiological features of COVID-19 infection. Pneumonia associated with COVID-19 disease has nonspecific and sometimes vague radiographic features. The typical findings include multifocal bilateral pulmonary infiltrations with patchy consolidations, prominent peripherally subpleural distribution, and preferred posterior part or lower lobe predilection.[14] We observe similar findings in our patients with predominant bilateral infiltrates (Figures-1).

Similar to our findings a quantitative meta-analysis of 2847 patients in China and Australia and a multinational descriptive study of 39 reports of 127 patients, found that covid- changes are frequently bilateral on chest 95% confidence interval 58.6 to 87.1) an

glass opaqueness in 68.5% of cases (95% CI 51.8 to 85.2), though, those data are collective so it is very difficult to associate the radiological features to the duration and severity of the disease.

In a case series of 1099 admitted patients through laboratory established covid-19 infection from all over the China, of those 274 patients who had chest x rays on admission 162 (59.1%) showed clear cut abnormalities, most frequently "bilateral patchy opacities" (n=100, 36.5%). Out of 1099 patients 975 had computed tomography done but it remained unclear that how many of the chest xrays were false negatives for covid 19 infecton.

Bilateral consolidation can be seen in severely ill patients, this usually merged to form a single massive consolidation with pleural effusion, known as "White Lung".[21,22] This massive consolidation is seen only in 7 of our patients, so it indicates that massive consolidation is not a common complication in our region.

Pleural effusion, lung cavitation, lymphadenopathy, and calcification are rarely reported.[23] Similarly, these complications were hardly seen in our studied patients. Pericardial effusion is rare to identify in COVID-19 patients, with an incidence of approximately 5%, which may indicate the occurrence of severe inflammation.[24] Pericardial effusion and cardiomegaly were not seen in our study group.

CONCLUSION

The imaging features in COVID-19 are inconstant. There is a significant overlap with those of other pathologies, namely Pleural Effusion, Cardiomegaly, cavitary lesions, and collapse of the lungs. Evidence suggests that chest imaging mainly x-rays will show abnormality in about 85% of patients, with 75% of patients having bilateral lung involvement which manifests as subpleural and peripheral areas of pulmonary infiltrates and consolidation. The outcome of the disease couldn't be predicted by seeing the Chest x-ray alone.

Author's Contribution:

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Clinical Findings & MR Features in CNS Tuberculosis. A Tertiary Care Hospital Study

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ABSTRACT

Objective: To know the clinical findings & MR features in CNS Tuberculosis. A tertiary care hospital study.
Study Design: cross-sectional study
Place and Duration of Study: This study was conducted at the Neurology department of Jinnah Postgraduate Medical Centre, Neurology Department DUHS and Medicine Department of Mohtarma Benazir Bhutto Medical College, Karachi from January 2018 to December 2019 for a period of 02 years.
Materials and Methods: The research was done on 89 serially registered patients of CNS tuberculosis selectively intracranial pathology in the said institutions. Enrolled subjects were between the age 15 to 52 years suggestive of cerebral tuberculosis with MRI evidence were involved and data was analyzed using the SPSS 25 software.
Results: The mean age of subjects was ± SD 31.42 ± 10.84 years while the mean presenting symptoms duration was found 11.46 with SD ± 6.39. Percentage of male patients was 59.6 and Female patients were 40.4 Percent. 37.1% patients have positive family history of tuberculosis. 23.6% subjects have diabetes in their family. The most common presenting symptom was fever 82%, while headache was the second most common features that is 79.8%, neck stiffness was found in 76.4 percent, 68.5% had disturbed conscious level and hemiplegia was seen in 44.9%. Diverse MRI appearances for example enhancement of Basal cistern was found in 20.2 percent, enhancement of meninges in 66.3%, 29.2% have non obstructive hydrocephalus, tuberculomas were found in 67.4 percent patients and last but not the least 25.8 percent subjects have ischemic infarcts. About 14.6 percent patients have mixed MRI appearances a like tuberculomas with meningeal enhancement, basal cistern enhancement with tuberculoma in 9% patients. 12.4 percent patients have cerebral ischemia with tuberculomas. 5.6% patients have typical infarcts with enhanced meninges and ring enhanced tuberculomas.
Conclusion: In our study tuberculomas was on the top in MRI findings second most common was meningeal enhancement. Hydrocephalus was on third. So, it is concluded the patients should be referred promptly to tertiary care hospital for better diagnosis of difficult neurological case.

Key Words: CNS Tuberculosis; Cerebral TB; Tuberculoma, Meningitis

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INTRODUCTION

Cerebral tuberculosis is reflected as a serious community health issue.

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The main objective of our study was to document the CNS especially the cerebral TB manifestation and MRI findings.

Mycobacterium tuberculosis is a serious public health problem in under developed countries and still many peoples are affected by this disease. According to the recent WHO report tuberculosis was 10 million population till 2017 and about 1.6 million people died because of it[1]. According to National TB Control Program (NTP) of Pakistan around 413,450 tuberculosis patients found in Pakistan per year. The incidence is 231/100,000 people, with the prevalence of 630,000 cases (at 364/100,000 people). The mortality rate is about 60,000 (34/100,000 people).[2] Pulmonary Tuberculosis is on the top, but the disease burden is additionally augmented by extra pulmonary TB, including CNS TB. The mortality rate is very high in extra pulmonary TB especially in the CNS disease.[3]

CNS tuberculosis is more common in immuno compromised patients including elderly population and patient with diabetes and HIV.[4] Furthermore Alcoholism, malignancy, prolonged use of steroids, and immunosuppressant medications are the other risk factors for tuberculosis.[5]

CNS manifestations of TB can be parenchymal or meningeal disease. Most common is meningeal involvement followed by enhancing Tuberculomas usually multiple. Cerebritis and Abscess formation can also occur. Contrast enhanced MRI is the investigation of choice for CNS TB along with CSF analysis.[6, 7] The prognosis of disease is mainly depending on prompt diagnosis and early treatment of CNS TB.[8]

MATERIALS AND METHODS

The research was done on 89 serially registered patients of CNS tuberculosis selectively intracranial pathology at the Departments of Neurology, Dow University of Health Sciences, Jinnah Postgraduate Medical Centre and SGLGH, Karachi, from January 2018 to December 2019. The patients were included in the study who satisfy the inclusion criteria for example age and Radiological findigs[18], clinical signs and symptoms of intracranial tuberculosis subacute to chronic in nature. Claustrophobic patients and patients with metal in body like prothesis were excluded.

Criteria for the diagnosis of cerebral tuberculosis mostly based on a typical history of TB or past history, along with characteristic CNS symptoms and signs beside fever and headache, those include typical focal neurological deficits, sign of meningeal irritation, and/or seizures. GeneXpert and CSF culture and MRI findings of meningeal enhancement, ring enhanced lesions and hydrocephalus. CSF ADA level helps us in dubious cases.

Data Collection Procedure: Admitted patients who met our inclusion criteria were registered. Informed consent was acquired from all the subjects. The respondents were curtain about the privacy of their data. Patients were referred to Department of Radiology of DUHS and JPMC for the MRI brain with Gadolinium contrast. MRI results were assessed by the Neuro-Radiologists having more than 12 years of experience. The radiologists were blinded from the purpose of the research.

Data Analysis: Data was analyzed by using 25th version of SPSS. Mean and standard deviation were used to assess Descriptive statistics of age and duration. Percentages and Frequency were mentioned for categorical variables for example hydrocephalus, meningeal enhancement, effect modifiers for example gender, age, Family history and duration of symptoms typical of tuberculosis were controlled via stratification. Fisher exact test and Chi-square were applied when needed and p-value of ≤0.05 was taken as noteworthy.

RESULTS

The mean standard deviation of age was 31.42 ± 10.84 years in patient from 15 to 52 years old. These patients have typical symptoms of disease for 2 to 4 weeks and the mean duration was 11.46 days with 6.39 Standard Deviation (Table 1). When we looked at gender distribution it was found that the male patients were 59.6% (n=53) whereas females were 40.4% (n=36). Positive family history was found in 37.1% of patients whereas 23.6% patients have Diabetes Mellitus in family. When we look into the diverse MRI appearances of CNS tuberculosis it was found that meningeal enhancement seen in 66.3% (n=59), basal cistern enhancement was present in 20.2% (n=18), hydrocephalus was found 29.2% (n=26), 67.4% have tuberculomas (n=60) whereas ischemic infarction was noted in 25.8% (n=23) subjects (Figure 1).

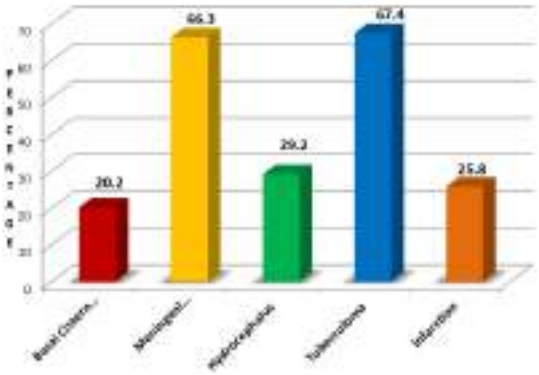

Figure No.1: MRI Manifestations in intracranial TB

Additionally, it was observed that only meningeal enhancement was seen in 15.7% patients. Ring enhancing tuberculomas with meningeal enhancement was seen in 14.6% cases, 12.4% have multiple tuberculomas. Meningeal with basal cistern enhanced MRI along with typical multiple Tuberculoma were seen in only 9% cases. Infarction was present in 12.4% cases, whereas tuberculoma, Ischemic infarction and meningeal enhancement in combination were found in 5.6% patients. Only 9 percent patient have infarction alone (Table 2).

About 33% of patients (n=30) registered through our outpatient clinics have history of only 1 week. Around 35 cases came between the duration of 8-14 days. History of 2 to 3 weeks was found in 18 patients. Six patients came in between 22-28 days whereas only 2 cases were brought in ER after a history of a month (30 days or later) (Figure 2).

Stratification of age, gender, symptoms duration and Tuberculosis in Family was done for assessment and adjustment of result related to MRI findings of CNS Tuberculosis (Table 3). Ring enhancing multiple Tuberculomas were spotted less in females (45%) than males (55%). Age was also an effect modifier for Basal meningeal enhancement, but it is more common in

young age between 15-25 years. Only 11.1% have basal cistern enhancement in age group between 36-45 years. History of diabetes mellitus in family did not have an augmented effect on any of MRI appearances (meningeal enhancement, basal cistern enhancement, Tuberculoma, hydrocephalus or cerebro-vascular lesions).

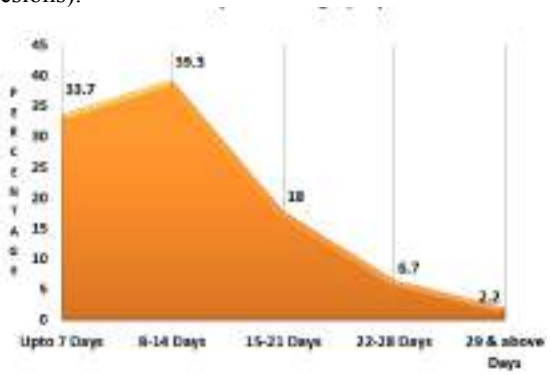

Figure No.2: Duration of presenting symptions

Table No.1: Demographic data of the study population (n=89)

Characteristics	Frequency	
Age (Years)	31.42 ± 10.84 (Range: 15-52 years)	
Duration of Symptoms (Days)	11.46 ± 6.39 (Range: 15-30 days)	
Gender	**Males**: 53 (59.6%)	**Females**: 36 (40.4%)
Family history	**Tuberculosis**: 33 (37.1%)	**Diabetes**: 21 (23.6%)
Age category (Years)	15-25	33 (37.1%)
	26-35	21 (23.6%)
	36-45	21 (23.6%)
	46 & Above	14 (15.7%)
Clinical features	**Fever**	73 (82.0%)
	Headache	71 (79.8%)
	Neck Stiffness	68 (76.4%)
	Altered Consciousness	61 (68.5%)
	Paresis	40 (44.9%)

Table No.2: Combinations of MRI manifestations in patients of Intracranial TB

MRI manifestations	Frequency (n)	Percentage (%)
Meningeal Enhancement alone	14	15.7
Meningeal Enhancement & Tuberculoma	13	14.6
Tuberculoma alone	11	12.4
Tuberculoma, Meningeal, Basal Cistern Enhancement & Hydrocephalus	8	9
Infarction alone	7	7.9
Meningeal Enhancement with Tuberculoma & Infarction	5	5.6
Meningeal Enhancement with Hydrocephalus	4	4.5
Tuberculoma with Hydrocephalus	4	4.5
Tuberculoma, Meningeal & Basal Cistern Enhancement	4	4.5
Basal Cistern Enhancement & Tuberculoma with Infarction	2	2.2
Meningeal & Basal Cistern Enhancement	2	2.2
Tuberculoma, Infarction, Basal Cistern Enhancement & Hydrocephalus	1	1.1

Table No.3: Effect of gender, age, duration of disease and family history of T.B and diabetes on frequency of different patterns of MRI manifestations

Patterns	Basal cistern Enhancement (n=18)	Meningeal Enhancement (n=59)	Hydrocephalus (n=26)	Infarction (n=23)	Tuberculoma (n=60)
Gender					
Males (n=53)	3 (16.7%)	34 (57.6%)	14 (53.8%)	12 (52.2%)	33 (55.0%)
Females (n= 36)	15 (83.33%)	25 (42.4%)	12 (46.2%)	11 (47.8%)	27 (45.0%)
p-value	**<0.001****	**0.388**	**0.319**	**0.276**	**0.152**
Age categories (in years)					
15-25 (n=33)	10 (55.6%)	21 (35.6%)	10 (38.5%)	3 (13.0%)	26 (43.3%)
26-35 (n=21)	2 (11.1%)	12 (20.3%)	4 (15.4%)	7 (30.4%)	11 (18.3%)
36-45 (n=21)	2 (11.1%)	14 (23.7%)	7 (26.9%)	10 (43.5%)	14 (23.3%)
46 above (n=14)	4 (22.2%)	12 (20.3%)	5 (19.2%)	3 (13.0%)	9 (15.0%)
p-value	**0.129**	**0.309**	**0.676**	**0.010***	**0.241**

Duration of disease (in days)					
≤7 (n=30)	5 (27.8%)	14 (23.7%)	8 (30.8%)	8 (34.8%)	21 (35.0%)
8-14 (n=35)	8 (44.4%)	28 (47.5%)	7 (26.9%)	8 (34.8%)	21 (35.0%)
15-21 (n=16)	4 (22.2%)	10 (16.9%)	6 (23.1%)	3 (13.0%)	12 (20.0%)
22-28 (n=6)	1 (5.6%)	5 (8.5%)	4 (15.4%)	3 (13.0%)	4 (6.7%)
≥29 (n=2)	0 (0.0%)	2 (3.4%)	1 (3.8%)	1 (4.3%)	2 (3.3%)
p-value	**0.816**	**0.030***	**0.048***	**0.600**	**0.973**
Family history of Tuberculosis (T.B) and Diabetes Mellitus (DM)					
T.B present (n=33)	12 (66.7%)	21 (35.6%)	14 (53.8%)	8 (34.8%)	24 (40.0%)
T.B absent (n=56)	6 (33.3%)	38 (64.4%)	12 (46.2%)	15 (65.2%)	36 (60.0%)
p-value	**0.005***	**0.428**	**0.032***	**0.499**	**0.281**
DM present (n=21)	3 (16.7%)	14 (23.7%)	8 (30.8%)	5 (21.7%)	14 (23.3%)
DM absent (n=68)	15 (83.3%)	45 (76.3%)	18 (69.2%)	18 (78.3%)	46 (76.7%)
p-value	**0.438**	**0.594**	**0.224**	**0.527**	**0.566**

All p-values are computed through chi-square test and Fisher's Exact test as indicated, with ≤0.05 is considered significant (represented by *) & ≤0.001 is considered highly significant (represented by **).

DISCUSSION

Extrapulmonary tuberculosis can damage and major vital organ of the body but tuberculosis of central nervous system is the most devastating among the others because of significantly high mortality or the patient can developed permanent neurological deficit.[9] About 6-12% cases of extrapulmonary tuberculosis are related to central nervous system, which are about 2-3 % of entire cases of Mycobacterium Tubeculosis.[9] Tuberculosis of the central nervous system, is secondary to granulomatous inflammation of meninges, brain parenchyma or vertebral column and spinal cord secondary to Mycobacterium species.

Gene Xpert testing, Culture of mycobacterium and ADA are some specific tests done on the sample taken from Cerebrospinal fluid, but result of all these tests took quite a lot of time so management might be delayed. Alternatively, MRI imaging of the brain are spinal cord provide time saving are faster result with better image resolution of brain parenchyma and soft tissues than CT scans, therefore smoothing the process of speedy diagnosis and early treatment. MRI imaging is superior to CT scan as better soft tissues exposure and for lesions of posterior fossa. Through MRI brain we can easily judge the stage of disease either early disease or late with complications. In our study the mean age of patients was 33.5 ± 18.5 SD years the subjects were in between 15 to 52 years age group. The majority of the case are in their twenties as we found in the study of Wasay M. et-al.[10] Gender seemed to be major modifier in our research as male to female ratio was 6:4. The stratified analysis showed female subjects have more basal cistern enhancement than males. Tuberculomas were on the top in MRI findings noticed in male patients (55%) which is about 10% more when compare with female cases (P-value of 0.151). Fever was the topmost clinical feature in 82%, followed by neck stiffness seen in 76.4% of cases indicative of meningeal inflammation. Headache, impaired consciousness and limb weakness were found in 79.8%, 68.5%, and 44.9% cases correspondingly. In our study none of the patient presented with seizures. A variety of MRI features were noted, which varied from a single lesion to multiple lesions. Tuberculomas with meningeal enhancement were found in 67.4% and 66.3% cases respectively, whereas hydrocephalous seen in 29% cases. Infarction was found in 25.8% of patients followed by basal cistern enhancement in 20.2% patients. The one of the major complication of hydrocephalus in CNS TB is secondary to inflammation and obstruction of the basal subarachnoid cisterns granulomatous infection, or by blockade of third ventricle by tuberculomas.[11] Even a small tuberculoma varies from 0.5 to 2.0 mm in size is sufficient to block the aqueduct of third verticle.[12] In our study it was found that the size of largest tuberculoma was 4.0mm. In our study 26 patients (29.2%), have hydrocephalus and from those, 19 patients went into neurosurgery procedure for VP shunt. We found that frequency of hydrocephalus directly corresponded to stage of illness as stated by Bhargava S, et al.[13] So it is essential for the physician from rural areas or primary health care to recognize the alarming clinical features of CNS TB and promptly refer them to tertiary care unit for imaging and better management.

Some patients have multiple lesions that is meningeal enhancement with multiple tuberculomas were seen in 14.6% cases, basal cistern and meningeal inflammations were seen in only 2.2% cases. Whereas basal cistern and meningeal inflammation with tuberculoma, were noticed in 4.5% patients and tuberculoma with hydrocephalus, and inflammation of meninges were diagnosed in 9% patients. These findings are indicative of predominance of tuberculoma and meningeal inflammation were the frequent MRI manifestations. In various previous researches, these findings slightly differ from our result.[10,14,15,16,17]The

additional MRI appearances in second or third stage of the disease were meningeal inflammation as noted by (P-value = 0.030 & 0.048 respectively). In addition to the obstructive hydrocephalus secondary to tuberculoma or inflammation, additional alarming complication was ischemic infarction mostly in "TB zone" the area of the brain especially the thalamus and the area supplied by the medial lenticulostriate arteries. The infarcts are mostly ischemic and usually in stage 3 of illness. In many studies 21% to 38% patients with CNS TB have infarcts, similar findings were found in our study.[18] In our study it was found that about 25% patients have MRI proof of ischemic infarction and signs of acute infarct were seen in about 44.9% patients.

CONCLUSION

In our study tuberculomas was on the top in MRI findings, the second most common was meningeal enhancement. Hydrocephalus was on third. So, it is concluded the patients should be referred promptly to tertiary care hospital for better diagnosis of difficult neurological case.

Unfortunately, patients were referred to us from the peripheral areas after they developed neurological complications. The morbidity and mortality can be straightforwardly controlled by correct early diagnosis and management.

Author's Contribution:

Concept & Design of Study:	Naeemullah Bullo
Drafting:	Dileep Kumar, Jawwad us Salam
Data Analysis:	Munir Hussain Siddiqui, Babar Bashir Iftekhar Ahmed
Revisiting Critically:	Naeemullah Bullo, Dileep Kumar
Final Approval of version:	Naeemullah Bullo

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

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Association of Vitamin D Deficiency with Acute Respiratory Tract Infection in Children of Peshawar

Amin Ullah[1], Rakshanda Kokab[1], Asmat Ullah Khan[3], Hakim Zada[4], Abdul Qadir Khan[5] and Sara Ziaullah[2]

ABSTRACT

Objective: To identify the association of vitamin D levels on incidence of respiratory tract infection in children of Peshawar.

Study Design: Observational study

Place and Duration of Study: This study was conducted at the Paediatric Units of Mercy Teaching Hospital and Kuwait Teaching Hospital, Peshawar from 1st January 2020 to 31st July 2020.

Materials and Methods: One hundred and ninety nine children were enrolled. All male and female children in current study were between 0 weeks to 5 years. The medical history of all participants was recorded in self-made questionnaire and blood sample was collected to identify the vitamin D levels. Participant had genetic inheriditry disease such as X linked rickets, hypophosphatemia rickets were excluded.

Results: The baseline mean vitamin levels in healthy children were high 15±7 ng/mL than respiratory tract infected participants 5±3 ng/mL. 49% children were males and 52% were females. The vitamin D level was shown association with upper, lower and recurrent lower respiratory tract infections by showing $p<0.05$. The most commonly found symptom was common cold, and pneumonia in upper, lower, and recurrent lower respiratory tract infection, respectively whereas, insignificant findings were observed between vitamin D with age and gender by showing $p>0.05$.

Conclusion: Vitamin D shown association with the incidence of respiratory in children of Peshawar.

Key Words: Vitamin D Deficiency, Acute respiratory tract, Children, Infection

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INTRODUCTION

Respiratory tract infections are most prevalent other infectious illnesses in young age children globally.[1] The deficiency in Vitamin D, steroid hormone, levelis one of the possible factor to develop respiratory tract infections. Vitamin D plays key role in the synthesis of peptide cathelicidin in respiratory tract epithelium layer. This acts against microbial activity and subsequently decline disease severity. Moreover, it prevents replication of influenza virus.[2,3]

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The activated for of vitamin D, vitamin D(1,25 $(OH)_2D$), increases human immunity. Esposito et al[4] suggested that the physiological level of vitamin D may be an advantageous and economical cheap method to protect against respiratory infections in humans. Grant et al[5] conducted a randomized controlled study in the population of New Zealand and found that providing Vitamin D3 supplements in infants greatly reduce visits to primary health care units for acute respiratory infection in young age children. Nonetheless, Xiao et al[6] meta-analyzed 7 clinical trials of "British Journal of Nutrition" and found non-supportive evidences of vitamin D supplementation againstthe prevention of respiratory infections in early childhood, however, the use of these supplementation possible advantageous in children diagnosed with asthma. Moreover, growing piece of evidences concluded the use of these supplementation during pregnancy decreases respiratory infections in young infants.[7,8]

In Pakistan, vitamin D deficiency is prevalent due to inadequate diet and sun exposure of mothers during pregnancy and malnutrition in early age children. Kazi

et al[9] performed study in Lahore, Pakistan, and found that 83 percent of recurrent in pulmonary infected children were vitamin D deficient. Moreover, Haider et al[10] conducted the study at department of paediatric medicine at National Institute of Child Health hospital, Karachi and found the revealed that 74% of severe pneumonia infected patients had nutritional rickets.

Taken all together, the high prevalence of respiratory tract infections increases the focus of attention to identify the vitamin D status in young age children having respiratory tract infections in Peshawar. This will give us an estimation of the magnitude of this problem in our local paediatric population. This will be beneficial because vitamin D deficiency is a preventable condition which can be easily treated with supplementation. Thus knowledge of the vitamin D status in children having respiratory infections will help prevent and treat this condition in our local population.

MATERIALS AND METHODS

The present descriptive study was conducted in Paediatrics units of Mercy Teaching Hospital and Kuwait Teaching Hospital, Peshawar from 1st January 2020 to 31st July 2020 and 199 enrolled children. The enrolled children were < 5 years of both sex, while children diagnosed with inherediitory disease causing vitamin D deficiency (X linked rickets, hypophos-phatemic rickets, etc) were excluded. Initially, ethical approval of the study was taken from prime foundation Pakistan, institutional review board, Peshawar and necessary details of the study was provided to the patents before taking consent.

The demographic profile, history of the patient was collected via self-made questionnaire whereas serum 25-OH-vitamin D levels were identified. The patient considered as vitamin deficient at 25-OH-vitamin D levels < 10 ng/ml (25 nmol/l). The data of vitamin D level were classified as vitamin D normal and vitamin D deficient. Statistical analysis was done by using SPSS-23 by considering $p<0.05$.

RESULTS

There were 49% males and 52% were females. The baseline mean vitamin level in normal and respiratory tract infected participants was 15±7 and 5±3 unit. The respiratory infections were found associated with vitamin D deficiency. The increase infection was also shown in lower respiratory tract in vitamin D deficient children. Moreover, the recurrent lower respiratory tract was also significantly associated with vitamin D deficiency by showing $P<0.001$. Comparatively, upper respiratory infection was shown decrease incidence but associated highly deficient children (Fig.1, Tables 1-3). The commonly found symptom in upper respiratory infection was common cold in vitamin D deficient children. Secondly, nasal obstruction and sore throat were found while pharyngitis, tonsillitis, otitis media, sinusitis and laryngitis were found minimum prevalence, but they were associated with vitamin deficiency (Fig. 1, Tables 1-2).

Beside upper respiratory tract symptoms, the high incidence of lower tract was pneumonia in deficient children, which was associated with vitamin D decrease level. Furthermore, tuberculosis and bronchiolitis were the next in the high prevalence and significantly associated with vitamin D deficiency.

Table No.1: Association between respiratory tract infections with vitamin D levels in children

Variable	Normal vitamin D (Yes)	Vitamin D deficient (No)	p-value
Respiratory tract infection (%)	41	94	<0.001
Upper respiratory tract infection (%)	16	22	<0.001
Lower respiratory tract infection (%)	23	44	<0.01
Recurrent lower respiratory tract infection (%)	2	26	<0.001

Table No.2: Upper Respiratory tract infection in children

Upper respiratory tract infection	Normal vitamin D (Yes)	Vitamin D deficient (No)	p-value
Nasal obstruction (%)	14	31	<0.001
Sore throat (%)	28	34	<0.001
Tonsillitis (%)	0	5	<0.001
Pharyngitis (%)	0	11	<0.001
Laryngitis (%)	0	14	<0.001
Sinusitis (%)	0	20	<0.001
Otitis media (%)	0	14	<0.001
Common cold (%)	57	68	>0.01

Table No.3: Lower and recurrent Lower Respiratory tract infection in children

Variable	Normal vitamin D (Yes)	Vitamin D deficient (No)	p-value
Lower respiratory tract infection			
Bronchiolitis (n)	3	10	<0.001
Pneumonia (n)	6	48	<0.001
Tuberculosis (n)	1	12	<0.001
Recurrent lower respiratory tract infection			
Bronchiolitis (n)	1	5	<0.001
Pneumonias (n)	0	14	<0.001
Tuberculosis (n)	0	4	<0.001

Moreover, in recurrent lower respiratory infection, bronchiolitis, tuberculosis and pneumonia and were identified. The significantly highest prevalence of pneumonia was found in lower respiratory tract infection, and this was associated with vitamin D level. Moreover, tuberculosis and bronchiolitis were shown moderate incidence but associated with vitamin D deficiency (Fig. 1, Tables 1, 3).

Moreover, the findings shown insignificant infection rate with age. There was no association were found between vitamin D levels with gender and age of participants by showing p-value > 0.05 (Fig. 2).

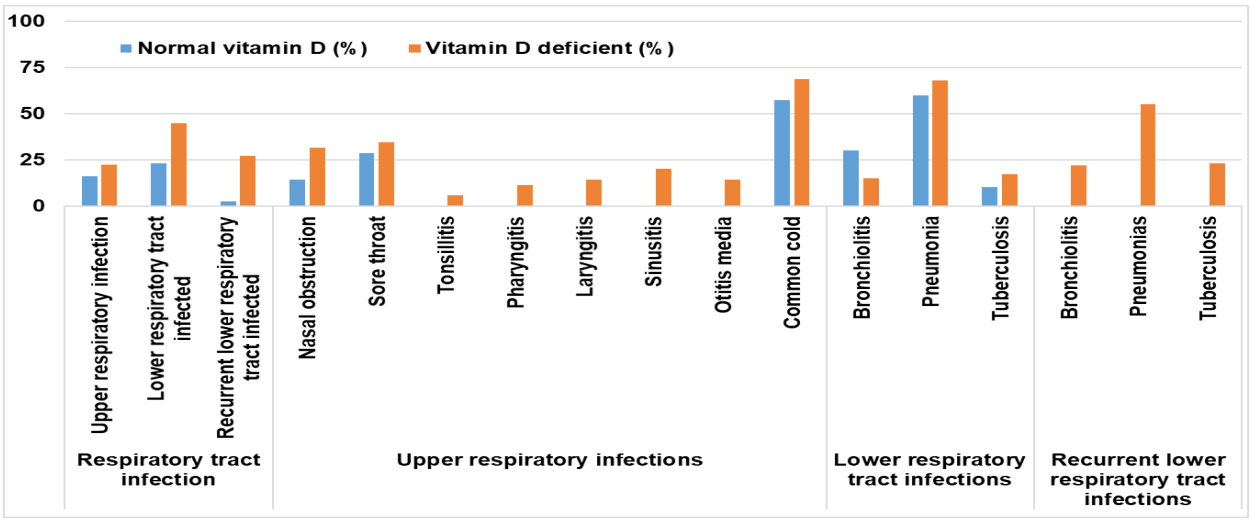

Figure No. 1: Respiratory tract infection in normal and vitamin D deficient children.

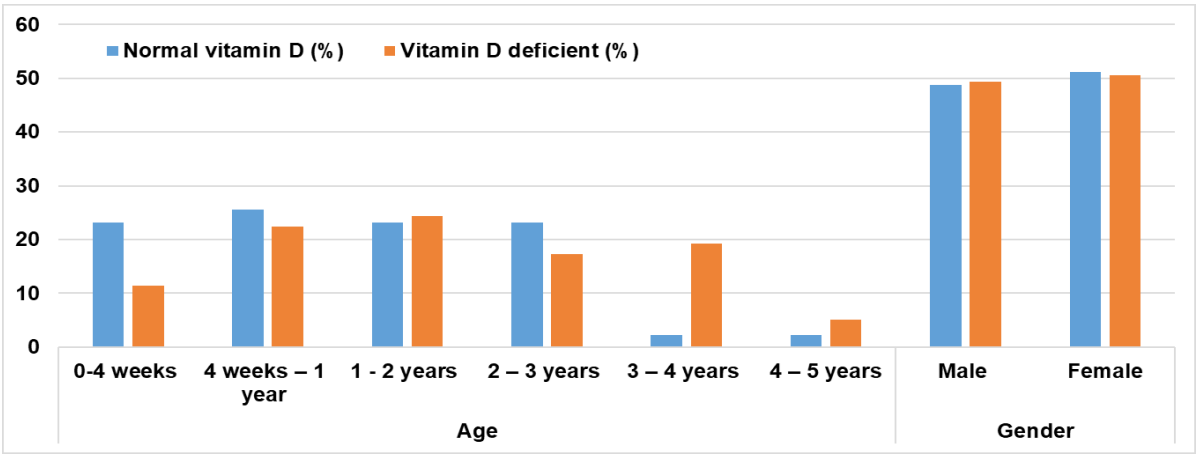

Figure No. 2: Age and gender wise distribution of children

DISCUSSION

The physiological functions needs sufficient amount of vitamin D via cutaneous synthesis initiated from the exposure of sunlight[11], whereas less amount is acquired from nutritional sources.[12] Number of social, cultural, and economic factors have been investigated that able to prevent dietary intake of vitamin D levels and adequate supply of sunlight that plays active role make the levels of 25-hydroxyvitamin D (25(OH)D) normal in the body.[13] Therefore, globally drastically increase incidence of hypovitaminosis D in number of resource-limited countries.[14] The deficiency of (25(OH)D) is one of the substantial factor in respiratory tract infection such as asthma in children of Mediterranean countries and in 9 North America. The author suggested its direct association with forced vital 10 capacities.[15] Around the globe, the great focus of attention is giving to prevent hypovitaminosis. Moreover, number of researchers are suggested to include vitamin D via dietary diversification, supplementation and fortification of foods.[16] They also considered adequate exposure of sunlight, and consumption of animal foods as sustainable strategy to maintain vitamin proportion to sustain the normal functions of the body easily.[14]

Besides, the study of Pham et al[17] suggested that 60 000 IU dose of vitamin D in monthly bolus insufficient to decline the overall susceptibility of acute respiratory infection, nonetheless it could produce slight reduction in the overall duration of symptoms to appear. They

suggested that the daily consumption of vitamin D supplementation is unlikely to produce significantly relevant impact in the prevention of acute respiratory infection.[17]

In the present study, the respiratory infections including upper, lower and recurrent lower respiratory tract infection were found associated with vitamin D deficiency. The most commonly found symptom in upper respiratory infection was common cold in vitamin D deficient children. Secondly, nasal obstruction and sore throat were found. While pharyngitis, tonsillitis, otitis media, sinusitis and laryngitis were found minimum prevalence but they were associated with vitamin deficiency. Beside upper respiratory tract symptoms, the high incidence of lower tract was pneumonia in deficient children, which was associated with vitamin D decrease level. Furthermore, tuberculosis and bronchiolitis were the next in the high prevalence and significantly associated with vitamin D deficiency. Moreover, in recurrent lower respiratory infection, bronchiolitis, tuberculosis and pneumonia and were identified. The significantly highest prevalence of pneumonia was found in lower respiratory tract infection, and this was associated with vitamin D level. Moreover, tuberculosis and bronchiolitis were shown moderate incidence but associated with vitamin D deficiency. Moreover, the findings shown insignificant infection rate with age. There was no association were found between vitamin D levels with gender and age of participants.

CONCLUSION

Vitamin D levels are essential for several metabolic activities. The decrease range of vitamin D is associated with the development of acute respiratory infection in upper and lower tract in the children of Peshawar.

Author's Contribution:

Concept & Design of Study:	Amin Ullah
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Data Analysis:	Hakim Zada, Abdul Qadir Khan, Sara Ziaullah
Revisiting Critically:	Amin Ullah, Rakshanda Kokab
Final Approval of version:	Amin Ullah

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

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Early Post-Operative Complication of Stapled Haemorrhoidectomy

Fida Ahmed Baloch[1], Shakeel Akbar[2], Mehreen Sattar[1], Bilal Elahi[1], Muhammad Yasir[1] and Afnan Khan[1]

ABSTRACT

Objective: To determine the frequency of early post-operative complications of stapled haemorrhoidectomy.
Study Design: Descriptive study
Place and Duration of Study: This study was conducted at the Department of General Surgery, Bolan Medical Complex Hospital Quetta 11th February 2019 to 11th August 2019.
Materials and Methods: One hundred and twenty six patients were observed. Stapled haemorrhoidectomy was performed by senior consultant's surgeons having a minimum of five year post-fellowship experience. In all patients, parenteral antibiotic dose was given at the time of induction of anesthesia. Acute urinary retention and constipation was noted in every patient according to the operational definitions.
Results: The mean age was 41±10.22 years and 40% patients were male and 60% patients were female. More over 23% patients had acute urinary retention while 10% patients had constipation.
Conclusion: The frequency of early post-operative complications i.e. acute urinary retention was 23% and constipation was 10% of stapled haemorrhoidectomy.

Key Words: Stapled, Hemorrhoidectomy, Degree hemorrhoids

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INTRODUCTION

Anal cushions are prominences of anal mucosa generated by loose connective tissue, smooth muscle, arterial and venous arteries. Haemorrhoids are one of the most prevalent anorectal diseases. When there is no prolapsed anal tissue, there is painless rectal bleeding during defecation.[1] Haemorrhoids affect around 5% of the general population, and one in three cases require medical attention.[2] Patients with haemorrhoids may require surgical therapy in 10 to 15 percent of cases. In order to achieve a complete cure, surgery is the only therapeutic option for symptomatic haemorrhoids of grades III and IV.[3] Surgeons perform open Milligan-Morgan and closed Ferguson techniques.

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Complications, such as urine retention, hemorrhagic, constipation, protracted wound healing and substantial postoperative pain due to the broad exterior lesions on sensitive anal skin, are common with these procedures.[4] Milligan-Morgan has served as a yardstick by which all other approaches are measured.[5] Low-Invasive surgery One of the most significant developments in the treatment of haemorrhoids for many years is the use of stapling. Sir Antonio Longo[6] first used this approach in 1997. Excessive rectal mucosa can be removed using the Longo technique or Stapled Haemorrhoidectomy procedure. As a day care surgery, there is less bleeding and pain, as well as a quicker return to work.[7]

Acute urine retention, constipation, and post-operative discomfort are the most common consequences following haemorrhoidectomy. The incidence of acute urine retention ranges from 9.0% to 19.0%, and the incidence of constipation ranges from 9.0% to 9.5%.[8,9]

Two years ago, we began routinely doing stapled haemorrhoidectomy. No published data from our hospital has compared our stapled haemorrhoidectomy with worldwide trials, therefore we don't know how it compares. Aiming to analyse early post-operative complications following stapled haemorrhoidectomy in Bolan Medical Complex Hospital Quetta, compared to published literature, is the rationale for this study. This study's findings will help to identify the most prevalent consequences of stapled haemorrhoidectomy following its completion.

After a stapled haemorrhoidectomy, it is important to identify the most common problems in order to work on preventing them in the future. Patients with haemorrhoids will be able to avoid these consequences by reducing their morbidity in this way.

MATERIALS AND METHODS

This descriptive study was conducted at outpatient department of Surgery, Bolan Medical Complex Hospital Quetta, during from 11-2-2019 to 11-08-2019. Total 126 patients of both genders presented with grade III and IV hemorrhoids were included in this study. Patient's ages were ranging between 35-55 years. Patients with previous history of anorectal surgery, concomitant anorectal disorders, and patients with fecal incontinence were excluded. An informed consent was taken from all patients before including their data in the study. Stapled haemorrhoidectomy was performed by senior consultant's surgeons having a minimum of five year post-fellowship experience. In all patients, parenteral antibiotic dose was given at the time of induction of anesthesia. Acute urinary retention and constipation was noted in every patient according to the operational definitions. Data regarding confounder variables e.g. age, gender, grade of haemorrhoids, co-morbid condition like history of diabetes mellitus, hypertension and duration of surgery was also be collected. The collected information was entered using SPSS-20.

RESULTS

There were 50 (40%) male patients and 76 (60%) female patients (Fig. 1). Seventy three (58%) patients were in age range 35-45 years, 53 (42%) patients were in age range 46-55 years. Mean age was 41±10.22 years. Eighty six (68%) patients had grade 3 haemorrhoids and 40 (32%) patients were had grade 4 haemorrhoids. Thirty five (28%) patients were diabetic and 47 (37%) patients were hypertensive. (Table 1) Mean duration of surgery was 30±10.22 minutes. Early postoperative complication was analyzed as 29 (23%) patients had acute urinary retention while 13 (10%) patients had constipation (Table 2). Stratification of Early post operative complication with grade of haemorrhoids showed no significant difference with p-value >0.05 (Table 3)

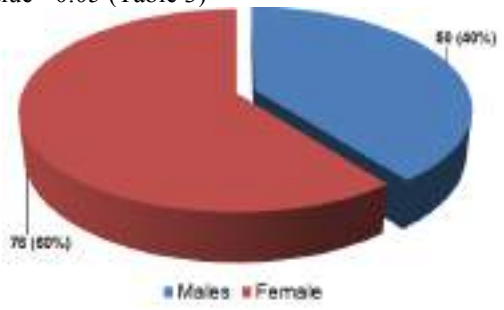

Figure No. 1: Gender-wise distribution

Table No.1: Baseline details of included patients

Variable	No.	%
Age (years		
35 – 45	73	58.0
46 – 55	53	42.0
Degree of Hemorrhoids		
III	86	68.0
IV	40	32.0
Co-morbidities		
Diabetes	35	28.0
Hypertension	47	37.0

Table No.2: Frequency of early postoperative complications (n=126)

Complication	No.	%
Acute Urinary Retention	29	23.0
Constipation	13	10.0
No complication	58	67.0

Table No.3: Stratification of early postoperative complication with respect to degree of hemorrhoids

Complication	Grade		P value
	3	4	
Acute urinary retention			
Yes	20	9	0.9252
No	66	31	
Constipation			
Yes	9	4	0.9363
No	77	36	

DISCUSSION

Haemorrhoids are a common anorectal disease that is defined as the symptomatic enlargement and/or distal displacement of anal cushions, which are prominences of the anal mucosa formed by loose connective tissue, smooth muscle, arterial and venous vessels. Haemorrhoids are one of the most common anorectal diseases that affect women. It is characterised by painless rectal bleeding during faeces, which may or may not be associated with prolapsing anal tissue. Haemorrhoids affect approximately 5% of the general population, with one-third of those who suffer from the condition requiring medical attention. The majority of people with haemorrhoids will eventually require surgical treatment for their haemorrhoids.[2,3] According to our findings, the mean age was 41±10.22 years. Patients were divided into two groups: 40% were male and 60% were female. The majority of patients had >23% experienced acute urine retention, with just 10% experiencing constipation.

Another study conducted by Chalkoo et al[8] and Gura et al[9] found that post-operative pain, acute urinary retention, and constipation are the three most common complications of haemorrhoidectomy, with post-operative pain, acute urinary retention, and constipation

being the most common complications. It has been found that acute urine retention occurs in 9.0-19.0% of the population, while constipation occurs in 9.0-9.5% of the population. An further study carried out by Chik et al[10] found that 204 patients (100 men and 104 women; mean age, 49 years; age range, 20-82 years) had undergone haemorrhoidectomy throughout the study period. Stapled haemorrhoidectomy was conducted on 90 patients (44.1 percent), while closed haemorrhoidectomy was performed on the remaining 114 patients (55.9%). Seventy patients (34.3%) were operated on the same day they were admitted. One hundred and seventeen patients (57.4%) received surgery while under general anaesthesia, while 87 (42.6%) were operated on while under spinal anaesthesia Retention of urinary excretion was seen in 31 patients (seven patients with Stapled haemorrhoidectomy and 24 patients with CH, p=0.009). Logistic regression revealed that general anaesthesia (p=0.044; odds ratio [OR], 2.43; 95% confidence interval [CI], 1.02-5.97) and SH (p = 0.046; odds ratio [OR], 2.66; 95% CI, 1.02-7.00) were independent factors associated with a lower incidence of urinary retention than other variables. Another study, conducted by Oughriss et al[11], revealed that one hundred and five patients (95%), with a mean age of 51 years, had encountered difficulties after the procedure. Among the most common early consequences of stapled haemorrhoidectomy were bleeding (1.8%), severe anal pain (2.3%), urine retention (0.9%), and sepsis (0.1%). Chronic anal pain (1.6%), suture dehiscence (1.6 percent), anal stricture (1.6%), anal fissure (0.9%), external thrombosis (0.9%), fistulae and intramural abscesses (0.9%), anal incontinence (0.3%) and haemorrhoidal disease symptoms persistence or recurrence were the most common late complications (3.2%).

According to Bhuiyan et al[12], stapled haemorrhoidopexy is a safer option to open haemorrhoidectomy with less postoperative sequelae than open haemorrhoidectomy. Reactionary haemorrhage was discovered in 3.75% of patients, minor pain was discovered in 3.12% of patients, and residual prolapse was discovered in 1.25% of patients.

According to the findings of another study conducted by Panigrahi et al[13], stapled hemorrhoidectomy is both safe and effective when compared to open hemorrhoidectomy in terms of postoperative pain, hospital stay, and early return to work.

CONCLUSION

The frequency of early post-operative complications i.e. acute urinary retention was 23% and constipation was 10% of stapled haemorrhoidectomy in Bolan Medical Complex Hospital Quetta.

Author's Contribution:

Concept & Design of Study:	Fida Ahmed Baloch
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Data Analysis:	Bilal Elahi, Muhammad Yasir, Afnan Khan
Revisiting Critically:	Fida Ahmed Baloch, Shakeel Akbar
Final Approval of version:	Fida Ahmed Baloch

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

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Frequency of Hypothyroidism in Patients with Melasma in a Tertiary Care Hospital

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ABSTRACT

Objective: To determine the frequency of hypothyroidism in patients with melasma presenting at a tertiary care hospital.

Study Design: Cross-Sectional Study.

Place and Duration of Study: This study was conducted at the Department of Dermatology, PNS Shifa Hospital, Karachi from 12thSeptember 2020 to 11thMarch 2021.

Materials and Methods: After approval from the Hospital Ethical Review Committee, 145 patients reporting to Dermatology Department, PNS Shifa Hospital Karachi, clinically diagnosed as melasma and fulfilling the inclusion criteria, were enrolled. Informed consent was taken and all the patients were tested to see any thyroid hormone abnormality. A 2 ml venous blood sample was taken in a sterilized 5ml disposable syringe for each patient and sent to laboratory to check serum TSH and free T4.

Results: There were 40 (27.6%) males and 105 (72.4%) were females with mean age was 34.5±7.7 years. Hypothyroidism was found to be present in 31 (21.4%) patients. Out of these 31 hypothyroid patients, 22(71%) were young, females 19 (61%), obese 20 (65%), hypertensive 23 (74%), non-smokers 25 (81%), urban 18 (58%) and 25(81%) had no family history of melasma. Uncontrolled diabetes mellitus was seen in 60 (41.4%). Vitamin-D deficiency was found in 54 (37.2%) patients.

Conclusion: Hypothyroidism is seen in considerable number of patients presenting with melasma. These patients are usually young females, mainly from urban background with no family history and have tendency to be obese and hypertensive.

Key Words: Hypothyroidism, Melasma, MASI, Thyroid Function Tests, Diagnosis

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INTRODUCTION

Melasma is an acquired pigmentary disorder described as symmetrical blotchy or splotchy hyperpigmented macules and patches mainly localized in the sun-exposed body areas, namely chin, cheek, forehead, upper lip and rarely forearms.[1] Melasma is a common skin problem worldwide with a high burden among patients referred to dermatologists. Its prevalence varies from 8.8% in America to 40% in Asia being most common in India, Pakistan and Middle East. Pregnant ladies and those who use oral contraceptives (OCP) are particularly susceptible to develop melasma.

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The precise cause is unknown, however, a number of factors are implicated in the aetiopathogenesis of melasma. These include genetic influences, exposure to ultraviolet (UV) radiation, pregnancy, oestrogen-progesterone therapies, thyroid dysfunction, cosmetics and phototoxic and anti-seizure drugs.[2] The primary cells involved are the pigment producing melanocytes that originate from the neural crest and can be influenced by cells in close proximity (keratinocytes, fibroblasts).[1,3] Melasma primarily affects the visible parts of body most commonly face and causes remarkable emotional and social morbidity in both females and males.[2,4]

Melasma like hyperpigmentation occurs in a number of endocrine diseases, However, the occurrence of hyperpigmentation in thyroid dysfunctions is not often reported in the literature.[3] Hypothyroidism affects approximately 5% of the general population and 99% of affected patients suffer from primary hypothyroidism.[5] Hypothyroidism is generally under-reflected as many

patients remain undiagnosed.[6] Common causes of hypothyroidism include iodine deficiency and autoimmune thyroiditis. It is diagnosed biochemically with serum thyroid-stimulating hormone (TSH) concentrations above and thyroxine (T3 and T4) below the normal reference range.[5] Hypothyroidism is known to cause myriad of changes in the skin including thin, coarse and scaly skin (epidermal changes), myxedema, oedema of hands, feet and eyelids, pallor, carotenemia, (dermal changes), alopecia, dry and coarse hair, loss of lateral third of eyebrows, thin, brittle and dull nails (hair and nail changes), widespread xerosis especially on the extensor surfaces and hypohidrosis (sweat gland changes). Cold intolerance, purpura, dropping of upper eyelids and nerve entrapement syndromes are some other manifestations that can occur in hypothyroidism.[7]

A number of thyroid hormone responsive genes including the keratin genes and the "hairless" (hr) genes have been identified which may be responsible for cutaneous changes produced under influence of thyroid hormones.[7] In literature, thyroid disorders are also described in association with several pigmentary disorders like vitiligo and post inflammatory hypopigmentation or hyperpigmentation.[8] There have been few studies highlighting the association of hypothyroidism and melasma. Higher levels of TSH have been reported in patients of melasma and thyroid hormones are considered to play an imprtant role in melasma. The prevalence of hypothyroidism in melasma has variably been reported from 11% to 58% in these studies.[9]

The mechanism how thyroid hormones may affect melasma is not clear. Adrenocoticotropic hormone (ACTH) and Melanocyte stimulating hormone (MSH) probably activate melanocortin receptors in melanocytes, that induces melanogenesis. Increased sensitivity of melanocyte to MSH in patients of melasma can be suggested as one of the important factors in the pathogenesis of the disease. Moreover, interaction of melanocortin system with the hypothalamic-pituitary-thyroid axis is also established.[11] Higher circulating levels of pro-inflammatory cytokines seen in patients with thyroid disease also suggests that thyroid hormones induce production of inflammatory cytokines and epidermal-melanin unit in facial skin of melasma patients. Inflammatory stimuli cause pigmentation through melanogenesis. It can be postulated that melasma can be triggered by procedures that induce skin inflammation.[10.11]

Multiple treatment options are available for melasma like hydroquinone, Kligman s regimen, alpha and beta hydroxy acids, vitamin c, alpha arbutin, photoprotection, chemical and physical peeling and q-switch Nd-YAG laserbut there is no effective and long lasting treatment because most of the available therapies aim at controlling melanogenesis and are not directed at the actual cause of increased pigmentation.[12] As face is the most affected area in melasma and there is no permanent treatment, patients suffer considerable psycho-social distress.[4] If cause of the disease is established, it can be treated effectively by addressing the causative factors and patients can be saved from significant agony .Though thyroid hormones and thyroid autoimmunity is thought to play a role in the pathogenesis of melasma but the number of studies on this subject is few and the results are also conflicting.[9-11] This study was conducted to explore the possible association of hypothyroidism in patients with melasma and to generate local data by observing the magnitude of this association so that treatment can be rationalized on the basis of aetiology and patients managed in a better way.

MATERIALS AND METHODS

It was a cross sectional study carried out in dermatology department, PNS Shifa Hospital Karachi from 12th September 2020 to 11thMarch 2021 after approval from hospital ethical review committee (ERC/2020/Der/08). Patients were enrolled through non probability consecutive sampling technique. Sample size was calculated according to WHO calculator which came out to be 145 using prevalence (p) of hypothyroidism in melasma as 24.3%[9] and margin of error (d) 5%. Patients of either gender and in the age range of 20-60 years, having darkening of localized facial skin for ≥1 month duration and clinically diagnosed as melasma by a consultant dermatologist, were included in the study. The pregnant, lactating ladies and the patients already on thyroid hormone replacement therapy, OCP, tetracyclines, quinolones, lithium, interferon and amiodarone were not included. The patients with autoimmune connective tissue disorders, hepatic insufficiency, chronic renal failure and hematological malignancies were also excluded. Informed consent was taken after explaining the procedure, risks and benefits.

The data was collected on a pre-designed proforma that included age, gender, residence (urban or rural), family history of thyroid disease, educational status, duration of diseases, site and extent of melasma and presence or absence of any other possible effect modifiers like hypertension, smoking, uncontrolled diabetes mellitus and vitamin D deficiency. All the recruited patients were tested to see any thyroid hormone abnormality. A 2 ml venous blood sample was taken in a sterilized 5ml disposable syringe and sent to laboratory to check for thyroid hormone status. The hypothyroidism was labeled when serum TSH ≥10mU/L and serum free T4 <0.7ng/dl.The collected data was recorded and analysis was done by using SPSS-25. The stratification was done for age, gender, duration of diseases and post

stratification Chi-square test was applied at 95% confidence interval and the p-value ≤0.05 was considered as statistically significant.

RESULTS

There were 40 (27.6%) males and 105 (72.4%) were females. Mean age was 34.5±7.7 years with C.I (33.23-35.76), duration of disease was 16.3±4.2 months with C.I (15.6-16.98). 79 (54.5%) patients were resident of urban areas while 66 (45.5%) were resident of rural areas. Positive family history of thyroid disease was found to be in 34 (23.4%) patients. Educational status showed 14 (9.6%) illiterate, 26 (17.9%) primary education, 32 (22.1%) middle education, 14 (9.7%) secondary education while 59 (40.7%) had higher education.

Table No.1: Stratification of confounders with respect to hypothyroidism

Confounders	Hypothyroidism		P value
	Yes	No	
Age (years)			
20-40	22 (15.2%)	78 (53.8%)	0.786
>40	9 (6.2%)	36 (24.8%)	
Gender			
Male	12 (8.3%)	28 (19.3%)	0.118
Female	19 (13.1%)	86 (59.3%)	
Duration (months)			
1-12	17 (11.7%)	45 (31.0%)	0.125
>12	14 (9.7%)	69 (47.6%)	
Hypertension			
Hypertensive	23 (15.9%)	54 (37.2%)	0.008
Non-hypertensive	8 (5.5%)	60 (41.4%)	
Smoking status			
Smoker	6 (4.1%)	27 (18.6%)	0.610
Non-Smoker	25 (17.2%)	87 (60.0%)	
Obesity			
Obese	20 (13.8%)	60 (41.4%)	0.238
Non-Obese	11 (7.6%)	54 (37.2%)	
Uncontrolled DM			
Diabetic	15 (10.3%)	45 (31.0%)	0.327
Non-Diabetic	16 (11.0%)	69 (47.6%)	
Residential status			
Urban	18 (12.4%)	61 (42.1%)	0.625
Rural	13 (9.0%)	53 (36.6%)	
Vitamin D deficiency			
Yes	10 (6.9%)	44 (30.3%)	0.517
No	21 (14.5%)	70 (48.3%)	
Family history			
Positive	7 (4.8%)	25 (17.2%)	0.938
Negative	24 (16.6%)	89 (61.4%)	
Educational status			
Illiterate	3 (2.1%)	11 (7.6%)	0.9
Primary	6 (4.1%)	20 (13.8%)	
Middle	6 (4.1%)	26 (17.9%)	
Secondary	4 (2.8%)	10 (6.9%)	

Mean TSH was 4.72±2.05 with C.I (4.38-5.05) mU/L and free T4 was 1.09±0.23 with C.I (1.05-1.12) ng/dL Uncontrolled diabetes mellitus was documented in 60 (41.4%), Vitamin-D deficiency in 54 (37.2%) hypertension in 77 (53.1%). 80 (55.2%) patients were obese while 33 (22.8%) were smoker. Hypothyroidism was found to be in 31 (21.4%) patients. Stratification of age group, gender, duration of diseases, hypertension, smoking, obesity, un-controlled diabetes mellitus, residence (urban and rural), vitamin D deficiency, family history of thyroid disease and educational status was done with respect to hypothyroidism in order to asses significant difference as shown in Table 1.

DISCUSSION

The precise aetiology of melasma has not been determined. However, multiple factors and associations have been implicated in its etiopathogenesis, including pregnancy, combined OCP, genetics factors, sun exposure, use of cosmetic products, certain drugs and thyroid dysfunction.[2,4] In our study we determined the frequency of hypothyroidism in melasma.

We found melasma more in females (>70%), as already established and may be attributed to peculiar hormonal environment (estrogens/oral contraceptive pills/ pregnancy) in females.[13] Although men share the same clinico-histologic characteristics as in women, hormonal factors do not seem to play major significant role in men.[13,14]

Mean age, duration of melasma and geographical distribution (urban vs rural) seen in our patients was in agreement with previous studies.[14,15]

We observed melasma in all subgroups based on education status but majority (>40%) belonged to higher than secondary education group. This suggests the possible role of stress and emotions related to higher education, stressful working environment and high intellect in this subgroup which may be responsible for increased concern and psychosocial stigmatization related to the disorder.

Thyroid disorders are usually described in association with certain skin disorders like vitiligo, Sjogren syndrome, pretibial myxedema. Melasma is a common skin problem worldwide with a high burden among patients referring to dermatologists but no consistent scientific evidence exists regarding its association with thyroid disorders.[16] Cakmak et al.[11] showed higher TSH levels among patients with melasma as compared to those without, while in another study Talaee et al.[18] reported similar levels among subjects with and without melasma. However by combining the results of multiple studies, an association between hypothyroidism and melasma especially among women has been suggested[16] which is in accordance with the results of our study.

In our study, we observed hypothyroidism in 31 (21.4%) patients with mean level of TSH 4.72±2.05 mlU/ which is similar to previously reported but we had quite a higher mean level of free T4.[11,17-19] While doing stratification of confounders with respect to hypothyroidism, we could see that majority of the melasma patients were young, obese, non-smokers females from urban background with no family history of hypothyroidism but statistically significant difference was noted in case of hypertension only. The difference in diabetes mellitus, residential status, vitamin D deficiency levels, and educational status were not statistically significant (Table1). Association of hypertension with hypothyroidism has also been reported earlier in the literature[20] and has to be further explored in larger studies.

We found hypothyroidism in patients of melasma in our study but we did not correlate the effect of thyroid hormone levels on severity of melasma. However, Rahman et al[21] did not observe any significant difference in thyroid hormone levels in patients with varying severity of melasma in their recent cross-sectional study on effect of free T4 and TSH on severity of melasma. Similar results were found when Syarif et al[22] studied the T3 and TSH in melasma severity in Padang, Indonesia.

There were certain other limitations in our study including small sample size, single centered study and regional variability. Moreover our study didn't clearly distinguish between primary or idiopathic and secondary melasma and because of cross sectional design, no risk factors and cause-effect relationship could be established. Therefore, further prospective large cohort studies are mandatory to evaluate trigger factors traditionally associated with melasma, as well as to verify the temporal association occurring between hypothyroidism and melasma.

CONCLUSION

Hypothyroidism is frequently seen in association with melasma and these patients are usually young females from urban background with no family history and have tendency to be obese and hypertensive. Timely diagnosis and appropriate management of hypothyroidism may prevent this disease and save the patients from significant psychosocial distress.

Author's Contribution:

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

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Hepatoprotective Effects of Apple Cider Vinegar on Gentamicin Induced Toxicity in Albino Rats

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Hepatoprotective Effects of Apple Cider Vinegar on Gentamicin Induced Toxicity

ABSTRACT

Objective: To assess the morphological effects of Apple cider vinegar on hepatotoxicity caused by gentamicin in male adult albino rats.

Study Design: Experimental study.

Place and Duration of Study: This study was conducted at the Department of Anatomy, Postgraduate Medical Institute (PGMI), Lahore, Pakistan for a period of 21 days starting on June 1st, 2019.

Materials and Methods: This experimental study comprised 30 male adult albino rats divided into three groups, A, B and C with 10 rats in each group. Group A was control and it received distilled water 4ml/kg/day via intra-peritoneal route for 21 days. Group B received only Gentamicin 100mg/kg/day from day 10th-21st intraperitoneally. Groups C received Apple cider vinegar 2ml/kg/day via oral gavage for first 10 days then along with Gentamicin 100mg/kg/day intraperitoneally for next 11 days upto day 21st. Rats were sacrificed on 22nd day. Histological parameters of liver i.e., size of hepatocyte, hepatocyte vacuolization and central vein congestion were studied. The results were analyzed by SPSS version 22.0.

Results: Hepatocyte size in group B was significantly higher when compared with group A and C (p value < 0.001). However, no significant difference was observed in the hepatocyte size between the group A and C. Hepatocyte vacuolization was absent in all rats of control group A but present in all rats of group B. While it was present in 3 rats (30%) of group C. No rat of group A showed congested central vein but all rats of group B showed congested central vein. Only 1 rat (10%) of group C showed congestion of central vein of liver.

Conclusion: From the foregoing results, it is clear that gentamicin can induce many histological changes in the liver causing severe toxicity that is reflected in the parameters i.e., size of hepatocyte, central vein congestion and hepatocyte vacuolization. It also demonstrates that apple cider vinegar protects against its hepatotoxicity on molecular level through its antioxidants pathways.

Key Words: Apple cider vinegar, gentamicin, hepatocyte vacuolization, micrometry.

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INTRODUCTION

Liver is the chief organ of drug metabolism. It consists of hexagonal hepatic lobules.[18] These lobules have a central vein and hepatocytes radiates from it in the form of cords, with associated thin-walled sinusoids that drain blood from the portal venule towards the central vein.[2] The fenestrations in endothelial cells of sinusoids allow the exchange of portal blood with the adjacent hepatocyte. The liver, mainly hepatocytes, is involved in metabolism of drugs, amino acids, lipids and glycolysis.[2]

Gentamicin is derived from Micromonospora purpurea and is prescribed to treat infective endocarditis, sepsis, meningitis, peritonitis, bacterial conjunctivitis and infections caused by gram-negative bacteria.[3] Despite the beneficial effects, it inhibits the non-enzymatic and enzymatic antioxidants in liver thereby elevating the levels of Reactive Oxygen Species (ROS). It results in enhanced oxidative stress and damage to lipids in membrane, cellular proteins and nucleic acids leading to liver injury.[8]

Apple cider vinegar contains beta-carotene and flavinoids which reduces oxidative stress, act as antioxidant phytochemical and decrease the level of Reactive oxygen species (ROS).[19] Vinegar also contains vitamins, mineral salt, amino acids, phenols

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and organic acid.[6] These compounds have a vast window of pharmacological functions, such as acting as an antioxidant, antidiabetic[17] and cholesterol lowering agents.[7]

MATERIALS AND METHODS

This study was conducted at the Department of Anatomy, Postgraduate Medical Institute (PGMI), Lahore, Pakistan for a period of 21 days starting on June 1st, 2019.

30 adult male albino rats were procured from animal house of PGMI. The healthy rats of 8-10 week of age with weight range of 180-220g were selected. They were properly acclimatized and kept in well ventilated and temperature maintained house at 24±2ºC, humidity 55 ± 5% and dark & light cycles, each cycle of 12 hours. Rat chow and water was given to the animals ad libitum.

Dissection and Tissue Sampling: At the end of experimental period, on 22nd day, 24 hours after the administration of last dose of the agent, each rat was anaesthetized. Skin was cut by giving a midline incision. Liver was identified in the right upper abdominal region and excised carefully. The other half was fixed using 10% NBF (Neutral Buffered Formalin).

Histological Techniques

Tissue Preservation: The liver of each animal was placed in neutral buffered formalin. Tissue was processed for up to 18 hours by using the automatic tissue processor (HISTOTOUCH III-USA). For embedding, liquid paraffin was then poured onto the tissue piece to make tissue block. By using microtome, sections of 3 μm thickness were obtained and stained with Hematoxylin and Eosin.

Histological Parameters

Quantitative:

1. Size of hepatocyte.

Qualitative:

1. Hepatocyte vacuolization.
2. Central vein congestion.

Histological Examination: For assessment and measurement of histological parameters, light microscope (Leica DM 1000) was used to examine the prepared tissue sections, using magnifications of 10X as well as 40X.

Micrometry (Size of hepatocyte): For measuring this parameter, an ocular micrometer was inserted into the eyepiece of Leica 1000 DM microscope and tissue sections were examined under 40X magnification. The ocular micrometer was calibrated with 40X objective lens as to precisely focus the engraved linear scale on its surface. After removing stage micrometer, ocular micrometer was used for measuring diameter of hepatocytes.[4] 3 hepatic sections from each of the 30 albino rats were observed. 5 or more hepatic lobules with central vein were identified in cross-sectional view (Fig.1); thus 450 in total of hepatic lobules with central veins were examined and the mean diameters of hepatocyte were noted down.

Qualitative Parameters

Central vein Congestion: Central vein of each hepatic lobule was assessed at magnification power 40X of objective lens using Leica microscope, DM 1000. 5 central veins in hepatic lobules in each section were examined and 3 sections from each animal were taken. Thus the central veins of 450 in total of hepatic lobules were recorded.[15] The mean was calculated in each rat using SPSS 22 in each group.

Hepatocyte Vacuolization: Following H&E staining, slides were meticulously observed at 10X for the presence of vacuolization of hepatocytes.[20]

Statistical Analysis: The analysis of gathered data was done by applying SPSS 22.0 (Statistical Package for Social Sciences). Mean ±S.D was given for quantitative variables like diameter of hepatocytes in liver. Kruskal Wallis test was used for the comparison of the hepatocyte size (μm²) among groups. The mean differences of qualitative variants, i-e central vein congestion and hepatocyte vacuolization parameters were determined by Fisher's exact test. *P*-value of ≤0.05 was considered as statistically significant.

RESULTS

Size of Hepatocyte (μm²): The mean hepatocyte size (μm²) in all groups was determined using micrometry. It was found that the hepatocyte size (μm²) in all groups were significantly different (p value < 0.001).

Table No.1: Experimental groups of animals, mode of intervention and dosage of drug

Groups	Intervention and Dosages	Number of Animals (N)	Method of Administration	Duration of Dosage	Day of Sacrifice
Group A	4ml/kg/day of distilled water	10	Intraperitoneally	21 days	22nd
Group B	Initially 4ml/kg/day distilled water for 10 days then gentamicin 100mg/kg/day for next 11 days up to day 21	10	Intraperitoneally	21 days	22nd

Group C	Apple cider vinegar 2ml/kg/day for 1st 10 days then both Apple cider vinegar 2ml/kg/day plus gentamicin 100mg/kg/day for next 11 days up to day 21	10	Gentamicin intraperitoneally and Apple cider vinegar Orally by gavage tube	21 days	22nd

Table No.2: Comparison of hepatocyte size (µm²) among groups

Variable	Group A Mean ± SD	Group B Mean ± SD	Group C Mean ± SD	P-value#
Hepatocyte size (µm²)	14.5 ± 0.80	22.8 ± 1.67	14.8 ± 0.65	< 0.001*
	14.2 (14.2 – 15.21)	23.3 (22.3 – 23.3)	15.0 (14.2 – 15.2) [a]	

#Kruskal Wallis test, Median (IQR) *p value ≤ 0.05 is regarded as significant statistically

Table No.3: Distribution of hepatocyte vacuolization among groups

Hepatocyte Vacuolization	Group A n (%)	Group B n (%)	Group C n (%)	p-value
Absent	10 (100.0%)	0 (0.0%)	7 (70.0%)	< 0.001*
Present	0 (0.0%)	10 (100.0%)	3 (30.0%)	

Fisher's exact test
*p value ≤ 0.05 is considered statistically significant

Table No.4: Distribution of central vein congestion among groups.

Central Vein Congestion	Group A n (%)	Group B n (%)	Group C n (%)	p-value
Absent	10 (100.0%)	0 (0.0%)	9 (90.0%)	< 0.001*
Present	0 (0.0%)	10 (100.0%)	1 (10.0%)	

Fisher's exact test
*p value ≤ 0.05 is considered statistically significant

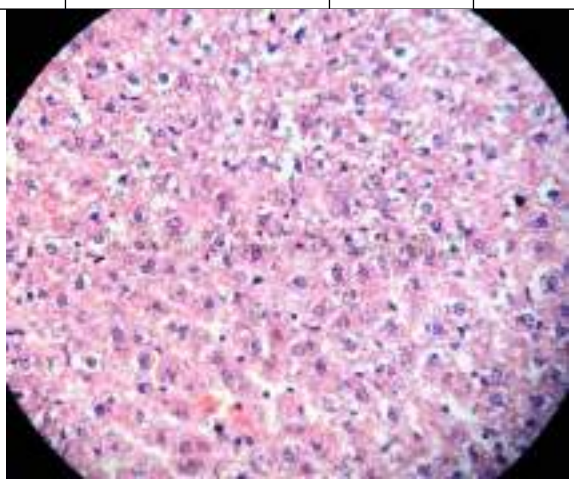

Figure No.1: Micrometery of the hepatocyte

Hepatocyte vacuolization: Hepatocyte vacuolization in all rats of control group A was absent. In group B, vacuolization in hepatocytes all rats were present while in group C, hepatocyte vacuolization was present in only 3 rats (30.0%).

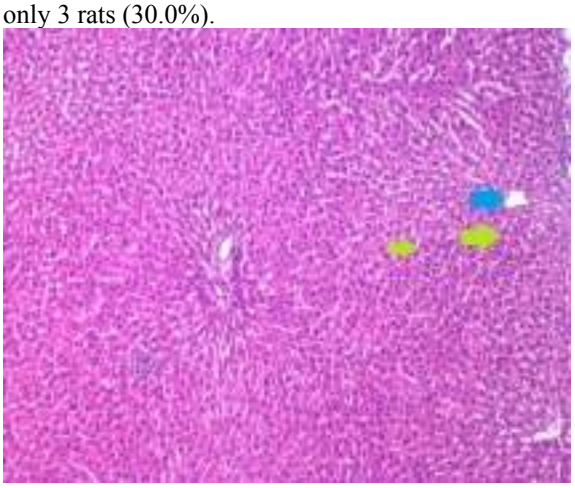

Figure No. 2: Photomicrograph of section of liver from Control group A showing central vein (blue arrow) and hepatocytes (green arrow) radiating from central vein. H&E stain 10X.

Figure. No.3: Photomicrograph of section of liver of gentamicin treated Group B showing vacuolization of hepatocytes (green arrow) and congested central vein (blue arrow). H&E stain 10X.

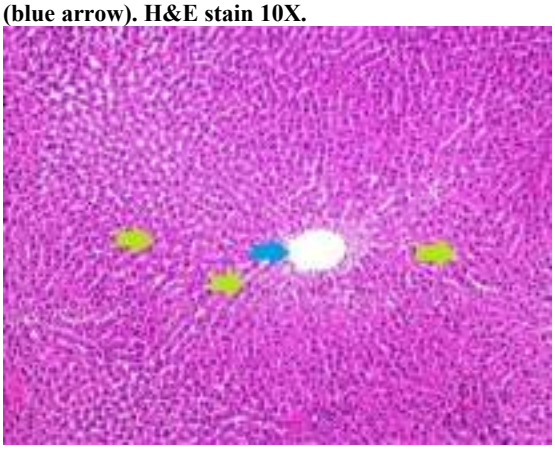

Figure No. 4: Photomicrograph of section of liver from Group C treated with gentamicin and apple cider vinegar showing hepatocytes (green arrow) and central vein (blue arrow). The liver architecture is preserved, no vacuolization is seen and central vein is lined by epithelium. H&E stain 10X.

Central vein congestion: Central vein congestion in all rats of control group A was absent. In group B, central vein congestion in all rats was present while in group C, central vein congestion was present in only 1 rat (10.0%). Tables 1-4 and Figures 1-7 be seen.

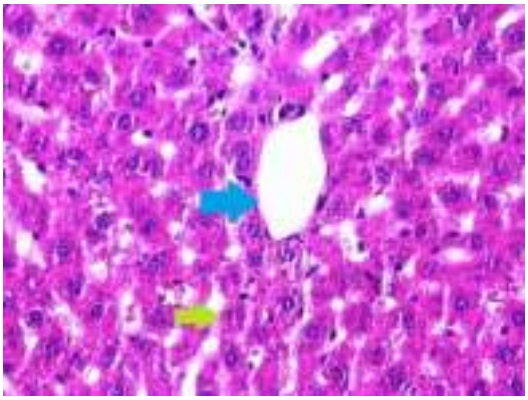

Figure No. 5: Photomicrograph of section of liver from Control Group A that shows central vein (blue arrow) and hepatocytes (green arrow). H&E stain 40X.

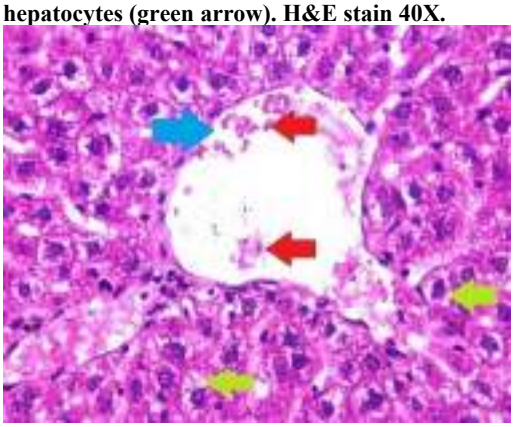

Figure No. 6: Photomicrograph of section of liver from Group B treated with gentamicin that shows congested central vein (blue arrow) and hepatocytes (green arrow). Epithelium of central vein (blue arrow) is disrupted and inflammatory and red blood cells (red arrow) are seen in dilated central vein. H&E stain 40X.

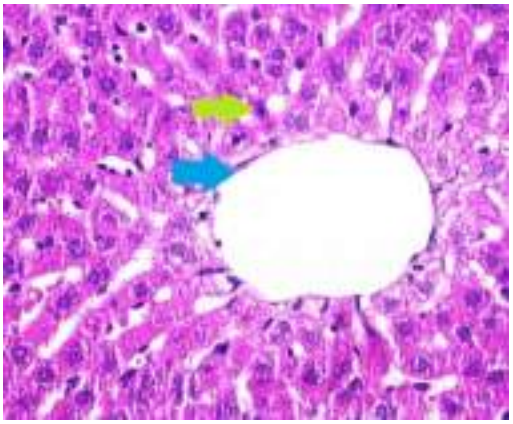

Figure No. 7: Photomicrograph of section of liver from Group C treated with gentamicin and apple cider vinegar showing central vein (blue arrow) and hepatocytes (green arrow). The liver architecture is preserved; central vein is lined by epithelium. H&E stain 40X.

DISCUSSION

Gentamicin enhances the oxidative stress in liver leading to generation of ROS (reactive oxygen species) that cause inflammation and cell necrosis.[14]

Apple cider vinegar (ACV) decreases serum lipid peroxidation and serum catalase activity while up regulates endogenous superoxide dismutase (SOD) activity in rats exposed to chronic restraint stress.[1]

A statistically significant increase in the mean hepatocyte diameter (µm) of gentamicin treated group B was observed as compared to group A. Control and group C showed no significant disparity. The increase in diameter of hepatocyte in group B is due to damage of cell organelles by Reactive oxygen species leading to accumulation of fatty vacuoles in hepatocytes. This is in agreement with the results of studies carried out by Hassan et al. (2018) and Nale et al. (2012).[10,12] The diameter of hepatocytes of group C is near to control

group A showing the protective effect of apple cider vinegar on liver hepatocytes by acting as an antioxidant and preserving the liver architecture. These findings were same as the data available by the previous studies by Omar et al. (2015) and Bouazza et al. (2016).[15,5]

Hepatocytes were observed for accumulation of fatty vacuoles in all groups. Hepatocyte vacuolization was not observed in any of the control group A rats. However, hepatocyte vacuolization was visible in all rats of group B and only 3 rats of group C. This is mainly due to generation of reactive oxygen species by gentamicin leading to damage of hepatocyte DNA and protein structure, thus damaging the organelles leading to accumulation of fatty vacuoles in hepatocyte.[12] These results are in accord to the study carried out by Hassan et al. (2018) which showed the presence of vacuoles in hepatocytes after treatment with 80mg/kg gentamicin for 15days.[10] While apple cider vinegar treated group C showed minimal vacuolization showing less hepatocyte damage. The main mechanism involved is through its antioxidant activity as well as its hypolipidemic effect.[9] Nazıroğlu et al. (2014) studied the role of apple cider vinegar in regulating the serum lipid profile in ovariectomized mice which were on high cholesterol diet and showed that apple cider vinegar normalizes the liver profile such as AST, ALT and lipid profile.[13]

Liver sections of all the rats in group A, B and C was observed for histopathologic changes in the central vein with respect to its epithelial lining and presence or absence of blood/inflammatory cells in its lumen. All observed sections of rats of control group A showed normal histology of central vein. There was damage to the epithelial lining of central vein as well as red blood cells and inflammatory were present in its lumen in all the observed sections of gentamicin treated rats of group B confirming for central vein congestion while only 1 rat of apple cider vinegar treated group C showed central vein congestion. The mechanism involved is formation of reactive oxygen species that cause damage to the endothelium of blood vessels and accumulation of blood cells as well as inflammatory cells.[11] While apple cider acts as an antioxidant to protect the endothelial lining of blood vessels.[15] These findings are similar to the studies carried out by Omer et al. (2016) and Jannat et al. (2018).[16,11]

CONCLUSION

From the foregoing results, it is clear that gentamicin can induce many histological changes in the liver causing severe toxicity that is reflected in the parameters i.e. size of hepatocyte, central vein congestion and hepatocyte vacuolization.

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

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Cervical Cancer Screening Using Pap Smear Test and Clinical Correlation

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ABSTRACT

Objective: To screen for cervical cancer with the help of pap smear test and to analyze its clinical correlation.
Study Design: Prospective study
Place and Duration of Study: This study was conducted at the Pak International Medical College, Peshawar from Jan 2019 to Jan 2020.
Materials and Methods: The study was carried out on 40 sexually active women for over 4 months. All females were of >25 years. Pap smear was taken in lithotomy position. The sample was drawn from ectocervix by using wooden Ayre spatula rotated to about 360 degrees. It was then taken to lab for results. The lesions were categorized into negative intraepithelial neoplasm as well as epithelial cell abnormalities (ECA) in which both squamous and glandular cells were present. Treatment was given in accordance with the disease stage. The data that was collected was transformed into variables on IBM SPSS statistics 26.
Results: In this study, 40 women were taken out of which 15 women revealed negative results while 25 showed signs of inflammation as well as infection. 20 women were asymptomatic, 7 revealed white vaginal discharge and 6 women were having irregular cycle. These were the most common symptoms. Others showed contact bleeding (n= 2), urinary incontinence (n=1) or excessive vaginal discharge (n= 4). The age of participants ranges from 26 to 65 years of age with mean age 37.07 years. Most of the women were falling in the age group of 30 to 50 years. Women having inflammation were starting from lower age group from 28 to 46 years.
Conclusion: Cervical cancer can be avoided if adequate screening methods are used. The most frequent procedure for earlier detection and confirmation of cervical cancer is testing through Pap-smear A Pap smear is a quick, non-invasive, low-cost procedure. In a gynecologic setting, it is simple to diagnose precancerous lesions in women.

Key Words: Pap smear screening, cervical cancer, malignancy

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INTRODUCTION

Cervical cancer begins in the cells of cervix, which is the part of uterus that connects to vagina. After breast cancer, it is the 2nd most common cancer found in women resulting in about 300,000 deaths around the world. Most of the cervical cancers develops in low or middle-income countries, which do not have proper screening as well as vaccination programs.

It still occurs in the developing countries due to unawareness or difficulties of implementing cytology-based screening tests. Existing research suggests that early detection as well as treatment of premalignant lesions could help in preventing cervical cancer from progressing to its advanced stages. Thus, efficient screening programs, particularly the systematic use of the Papanicolaou (Pap) smear testing for diagnosing premalignant alterations in the cervix, have helped to limit the prevalence of cervical cancer in developing countries.[1]

Cervical cancer screening service is significantly lower with in East African area, wherein age-standardized prevalence rate of cervical cancer is greatest because of insufficient testing systems. Routine pap screenings can help to minimize the risk of cervical cancer.[2]

The Pap smear is a safe, low-cost, and effective cervical cancer screening test. The Pap test has an overall sensitivity of about 70.80% in identifying a high grade squamous intraepithelial lesion (HSIL). A Pap test combined with an HPV DNA test improves the sensitivity for early identification of precancerous lesions.[3] It is necessary to expand cervical cancer screening awareness, provide education to women about cancer symptoms, as well as encourage them to attend the hospital to screen for cancer. Women, as well as all family members, must be counselled about the

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importance of cancer screening. Women who test positive for Pap smears require appropriate therapy as well as continuous follow-up. As a result, we must enhance our health services as well as health care systems to incorporate basic health care screening. The objective of this study was to use the Pap smear test to screen women for precancerous lesions as well as examine its clinical correlations.

MATERIALS AND METHODS

This study was carried out on 40 women for over 12 months. It was conducted in Pak international medical college Peshawar from Jan 2019 to Jan 2020.All women were sexually active and were more than 25 years of age. This research includes women without complaints as well as women with various complaints such as white vaginal discharge, increased vaginal secretion, irregular menstrual cycle, contact bleeding, as well as urinary incontinence. Signed consent for the study was acquired from all women. A sterilized bivalve speculum was introduced into vagina of women in the lithotomy position. To provide appropriate visibility of the cervix as well as vaginal wall, the posterior wall of vagina was pulled posteriorly while the anterior wall of vagina was pulled anteriorly. The ectocervix was sampled by turning a wooden Ayre spatula 360 degrees. The samples were sent to the labs for the results.

The method categories lesions as either positive for intraepithelial neoplasm or positive for epithelial cell abnormalities (ECA), which includes squamous as well as glandular cells. Therapy was given depending on the specific stage of the illness.

After providing detailed information regarding the purpose of the research, all patients provided verbal informed permission.

Statistical Analysis: The data that was collected was transformed into variables on IBM SPSS statistics 26. Data was analyzed and results were obtained in the form of frequency tables as well as pie chart.

RESULTS

In this research, 40 women were screened by using pap smear. About 75% (n=30) was taken adequately while 25% (n=10) had inadequate sample. About 37.5% (n= 15) were tested negative for malignancy while 62.5% (n=25) showed signs of inflammation as well as infection. 28% (n= 7) revealed mild inflammation while 44% (n= 11) were with severe inflammation.

Table No.1: Inflammation

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	negative	15	37.5	37.5	37.5
	mild	7	17.5	17.5	55.0
	Severe	11	27.5	27.5	82.5
	ASCUS	5	12.5	12.5	95.0
	LSIL	2	5.0	5.0	100.0
	Total	40	100.0	100.0	

Atypical squamous cells of unknown significance (ASCUS) as well as low grade squamous intraepithelial lesion (LSIL) were found in about 20% (n= 5) and 8% (n= 2) respectively.

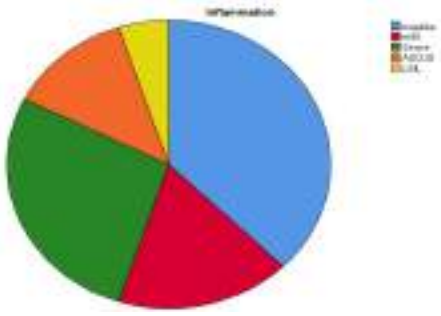

Figure No.1: Inflammation

The age of participants ranges from 26 to 65 years of age with mean age 37.07 years. Most of the women were falling in the age group of 30 to 50 years. Many women were multiparous about 67.5% (n= 27). About 10% (n= 4) were with post- menopause. Women having ASCUS were mostly falling in the age group of 41 to 60 years.

Table No. 2a: Menopause

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	pre	7	17.5	17.5	17.5
	post	4	10.0	10.0	27.5
	NO	29	72.5	72.5	100.0
	Total	40	100.0	100.0	

Table No. 2b: Parity

		Freq-uency	Percent	Valid Percent	Cumulative Percent
Valid	1-3	15	37.5	37.5	37.5
	more than 3	12	30.0	30.0	67.5
	None	13	32.5	32.5	100.0
	Total	40	100.0	100.0	

Table No.3: Symptoms

		Freq-uency	Percent	Valid Percent	Cumulative Percent
Valid	asymptomatic	20	50.0	50.0	50.0
	White vaginal discharge	7	17.5	17.5	67.5
	Irregular cycle	6	15.0	15.0	82.5
	Contact bleeding	2	5.0	5.0	87.5
	Urinary incontinence	1	2.5	2.5	90.0
	Excessive discharge	4	10.0	10.0	100.0
	Total	40	100.0	100.0	

Out of 5 ASCUS women, 2 were post-menopausal. 2 women were with LSIL with age 50 and 51 years. Women having inflammation were starting from lower

age group from 28 to 46 years. About 17.5% (n= 7) women were premenopausal while 10% (n= 4) were post-menopausal women. 30% (n= 12) women had more than three children while 37.5% (n= 15) had one to three children.

Out of 40 women, 20 women were asymptomatic, 7 revealed white vaginal discharge and 6 women were having irregular cycle. These were the most common symptoms. Others showed contact bleeding (n= 2), urinary incontinence (n=1) or excessive vaginal discharge (n= 4).

DISCUSSION

The Pap smear test, that is used for screening as well as identifying cervical cancer, is an efficient approach to minimize the onset of cervical cancer; nevertheless, community knowledge of the Pap smear test is relatively poor. As per the American Cancer Society (2012), a Pap smear testing is a regular cancer screening procedure which should be performed every three years, and a Pap smear combined with an HPV DNA test is suggested as a monitoring technique every five years.[4]

According to the United States Preventive Services Task Force (USPSTF), women of age 21 to 29 years are recommended to get tested for cervical cancer using cervical biopsy alone every three years. The USPSTF advises testing every three years by cervical cytology separately, every five years with human papillomavirus (hrHPV) testing, or every five years to screen hrHPV in conjunction with cytology for women of age 30 years to 65 years (co-testing).[5]

In this study, about 37.5% (n= 15) were tested negative for malignancy while 62.5% (n=25) showed signs of inflammation as well as infection. 28% (n= 7) revealed mild inflammation while 44% (n= 11) were with severe inflammation. Atypical squamous cells of unknown significance (ASCUS) as well as low grade squamous intraepithelial lesion (LSIL) were found in About 20% (n= 5) and 8% (n= 2) respectively. Out of 5 ASCUS women, 2 were post-menopausal. 2 women were with LSIL with age 50 and 51 years. Out of 40 women, 20 women were asymptomatic, 7 revealed white vaginal discharge and 6 women were having irregular cycle. These were the most common symptoms. Others showed contact bleeding (n= 2), urinary incontinence (n=1) or excessive vaginal discharge (n= 4).

According to research of Saudi Arabia, in a complete sample of 1171 ladies, 4.95 percent had squamous epithelial lesions.[6] According to research conducted in the United Arab Emirates, 1.8 percent of (ASCUS), 1.2 percent of (LSILs), and 0.3 percent of (HSILs) were discovered. According to a certain study, ladies with chronic inflammation must be treated correctly; else, the risk of cervical intraepithelial lesions rises. Following antibiotic therapy, a second Pap smear must be performed.[7]

According to several qualitative research, there are several hurdles to Pap smear screening enrollment, including a lack of information, incorrect ideas, concern of being detected with cervical cancer, stomach discomfort following Pap smear, as well as an unpleasant feeling during the procedure. On either hand, most quantitative research has identified Pap test humiliation and concern of cancer diagnosis as the primary obstacles in this respect.[8]

Furthermore, several elements were proposed as being the most essential motivators for Pap testing, such as physician, companion, or family suggestions, information regarding signs as well as procedures for early identification of the disease, recognizing the severity of cancer, and quick and affordable access to Pap test. According to the findings of several quantitative research, the recommendation of physicians and healthcare providers has been the primary promoter for Pap test taking.[9]

Each woman over Thirty years should get regular screening tests, even if she is post-menopausal. The Pap smear has long been considered the gold standard in cervical diagnostic tests. The efficiency for detecting cervical cancer is improved whenever the Pap test is coupled with an HPV DNA test. The society should be taught regarding Pap smear test, along with its purpose as well as the regularity with which it must be performed, through extensive educational as well as media campaigns. The majority of women who attend an outpatient department are unaware that cervical cancer screening is available.[10]

In this study, women having inflammation were starting from lower age group from 28 to 46 years. About 17.5% (n= 7) women were premenopausal while 10% (n= 4) were post-menopausal women. 30% (n= 12) women had more than three children while 37.5% (n= 15) had one to three children. The mostly common cytological abnormalities were found in age group 41 to 60 years.

According to a study Gupta. et al, the majority of abnormal cytology occurrences in their research (40.37 percent) were all in the 30 to 39 years age range, following 35.96 percent in the 20 to 29 years age range.

In this study, white vaginal discharge and irregular cycles were common symptoms. However, other symptoms include urinary incontinence, contact bleeding as well as excessive vaginal discharge.

Even though cytology based cervical cancer preventive strategies have lowered the prevalence of cervix cancer in many industrialized nations, the poor sensitivity of cytologic examination makes these programs complex and costly to sustain. As a result, it is probable that within coming years, we will start to shift away from cervical cytology-based screening programs and focus more on programs that tests for high-risk forms of human papillomavirus (HPV).[11]

CONCLUSION

Cervical cancers occur in the cells of cervix, through which a uterus is connected to the vagina. This cancer can leave impact on deeper tissues as well, thus increasing the chances of metastasis at different

regions. The most common cause of this disease is human papillomavirus (HPV) which can be avoided through proper vaccination.

The Pap smear is a safe, low-cost, and effective cervical cancer screening test. The Pap test has an overall sensitivity of about 70.80% in identifying a high grade squamous intraepithelial lesion (HSIL). A Pap test combined with an HPV DNA test improves the sensitivity for early identification of precancerous lesions.[12]

This study was carried out on 40 women for over 12 months. All women were sexually active and were more than 25 years of age. Most of the women were falling in the age group of 30 to 50 years. On pap smear screening, 15 women revealed negative results while 25 showed signs of inflammation as well as infection. 20 women were asymptomatic, 7 revealed white vaginal discharge and 6 women were having irregular cycle. These were the most common symptoms.

Cervical cancer can be avoided if adequate screening methods are used. The most frequent procedure for earlier detection and confirmation of cervical cancer is testing through Pap-smear. However, when manually pap-smear analysis is approached, error can present because of human error, as well as the procedure is laborious and quite lengthy. As a result, it is advantageous to build a computer-assisted detection tool to improve the accuracy and reliability of the pap smear testing.[13]

With time, it is being more evident that cytology offers no advantage over screening with HPV tests alone. As a result, in coming years, we will most likely utilised HPV screening solely to screen, and cervical cytology will be used to identify which HPV positive women need extra follow-up or colposcopy.[14]

Author's Contribution:

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

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Comparison of Extracorporeal Knot Tying Versus Metallic Endo-Clip in Laparoscopic Appendiceal Stump Closure in Patients with Uncomplicated, Acute Appendicitis

Saeed Mahmood[1], Muhammad Kareem Ullah[1], Shahzad Naveed Jawaid[2], Sobia Akbar[4], Ali Tariq[1], Mamoona Sarwar[3]

ABSTRACT

Objective: To explore the significant difference between metallic endo- clips and extracorporeal knot (Roeder's knot) majorly in terms of infection risks, hospital stay, operative time, and cost.

Study Design: A randomized control trial study

Place and Duration of Study: This study was conducted at the Department of Surgical Unit, Lahore General Hospital Lahore from 9th May 2020 to 9th May 2021.

Materials and Methods: After passing through inclusion and exclusion criteria, the patients were randomly categorized into two groups: Group A comprised of patients operated with metallic endo-clip technique and Group B was the extracorporeal knotting group. Following the surgeries in both groups, the data including demographics, hospital stay, surgery duration, overall cost, and postoperative complications were collected. SPSS 19 was used for statistical analysis and a P-value less than 0.05 for any variable was considered statistically significant.

Results: A total of 60 parties were categorized such that 32 (53.3%) were placed in group A and 28 (46.6%) in group B. The two groups didn't show a significant difference in terms of patients' age and their hospital stay ($p>0.05$). However, the mean surgical time for group A was shorter when group B (39 vs 41 mins, $p=0.03$). Moreover, extracorporeal knotting was economical (280 PKR) as compared to endo-clips (900 PKR). Among postoperative complications, the incidence rate of bleeding, postoperative ileus, intra-abdominal infection, and readmission rate was significantly higher in an endo-clip group.

Conclusion: Although, the use of endo-clips saves operative time but is costly as compared to extracorporeal knotting. The higher rate of complications reported in the former group is perceived as independent of the technique used. Therefore, both of the groups can be considered equally safe. However, given the simplicity of technique, we recommend the use of metallic endo-clips for beginners.

Key Words: Laparoscopic appendectomy, extracorporeal knotting, metallic endo-clips, appendix base closure, acute appendicitis.

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INTRODUCTION

Acute appendicitis is the most frequent reason behind intra-abdominal operative emergencies[1] and therefore appendectomy is found to be the most common operative procedure performed in 8all the surgical departments of the world[2]. The technique of laparoscopic appendectomy was first introduced 3 decades ago[3]. With the advancement in cutting-edge technology, it has evolved as an established operative procedure that offers minimum pain, early recovery, and quicker improvement in quality of life[4,5]. This technique is usually preferred in obese, females and those patients who couldn't be diagnosed accurately[6].

During appendectomy, the proper closure of the appendiceal stump is considered a critical step. In open

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appendectomy, the stump used to be buried in the caecum following the closure through purse-string suture to ameliorate the risk of intra-abdominal infection. Later on, it was found that this stump inversion doesn't significantly impact the outcomes but the technique remains to be performed by a large number of surgeons[6]. Laparoscopic appendectomy is also surrounded by similar concerns and was associated with a higher risk of postsurgical intra-abdominal infection when compared to the open technique[7]. Many techniques such as extra-corporeal knotting, endo-loops, metallic endo-clips, intra-corporeal knotting, hem-o-lock clip, and endo-staplers have been in use for the closure of the appendix base during laparoscopic appendectomy. This comparison between these techniques has been assessed in different prospective and retrospective studies[8-10]; however, no technique is unanimously recognized as the most effective therapeutic methodology.

Laparoscopic appendectomy along with other laparoscopic procedures have always been in debate due to their large influence on healthcare expenditures. The overall cost of these techniques is multiplied when novel and expensive base closure procedures are performed. Thus, the experienced surgeons usually option for intra or extra-corporeal knotting for base closure and perceive them as safer for treating inflamed and friable bases[11]. The novel techniques are, however, easy and quick to perform[12].

The metallic endo-clip technique was first introduced by Cristalli et al. in 1991 for the closure of the appendiceal stump[13]. The endo-clip is usually used to ligate cystic duct during laparoscopic Cholecystectomy and is a suitable alternative for appendix base closure[14].

So far, to the best of my knowledge, no sufficient studies have been conducted in Pakistan to compare the efficacy of all these procedures of base closure. This study aimed to explore the significant difference between metallic endo-clips and extracorporeal knot (Roeder's knot) majorly in terms of infection risks, hospital stay, operative time, and cost.

MATERIALS AND METHODS

A randomized controlled trial was conducted for the period of one year from 9th May 2020 to 9th May 2021 at the department of surgical unit in Lahore General Hospital Lahore. The patients diagnosed with acute appendicitis through clinical and laboratory evaluation and intended to undergo laparoscopic appendectomy were included in the study. Whereas, patients with the perforated appendix, diffuse or local peritonitis, inflammatory pelvic disease, and those who operated for any surgical procedure other than our study were excluded from the study. After seeking approval from Hospital Ethical Committee and informed consent from the participants, the patients were randomly classified into 2 groups: Group A: the metallic endo-clip, and Group B: extra-corporeal knotting. The data analyst was kept blinded for the procedural type. Following the selection criteria, 60 patients were included, out of which 32 were placed in Group A while 28 were in Group B.

The patients from both groups were operated on by experienced, certified surgeons. Similarly, all the patients were anesthetized similarly and were administered the same antibiotics (I/V ceftriaxone) and skin preparation (10% povidone-iodine solution). 3 ports, in hypochondrium, on the right side of the abdomen, and the supera umbilical with camera port were used in all the patients. Before beginning the surgical process, the abdominal cavity was investigated to reconfirm appendicitis. The mesoappendix was then dissected to clear the base of the appendix. For group A, 3 metallic end clips (Titanium Clip Cartridge in two sizes and Ethicon LigaclipsR) were applied such that two were close to the base in the opposing direction while the third was 5mm away. The appendix was cut between the first two clips and was brought out through a hypochondrium port. On the other hand, for group B, vicryly2/0 was tied with the base of the appendix with 2 knots (Roeder's knot), at the distance of 5mm, and the appendix was amputated between these 2 knots. Following appendectomy in both groups, all the incisions were closed through 2/0 proline sutures and a proper dressing was given.

At the end of the surgical procedure, a similar antibiotic course-oral cefixime for one week- was prescribed to all the patients, and follow-up and stitch removal was done between the 8th to 12th postsurgical days.

A self-designed data sheet was used for the collection of data which consisted of demographics, 2 intra-operative variables-organ injury and bleeding- and 5 postsurgical consequences-post surgical ileuses, infection at the surgical site, intra-abdominal infection, readmission in hospital, and reoperation. All the manually collected was analyzed using SPSS (version 19). Continuous data were compared between two groups through student's T-test while the comparison of categorical data was through Chi-square test. A P-value for less than 0.05 for any variable was considered statistically significant.

RESULTS

The study was based on 60 patients, where 32 (53.3%) were placed in the metallic endo-clip group (group A) and 28 (46.6%) were operated using the extra-corporeal knotting technique (group B) for base closure. There was no statistical difference in the mean ages of the two groups (24 vs 22, p=0.89). However, the sex ratio of the two groups was statistically different (p=0.007). The metallic endo-clip technique cost higher than extracorporeal knotting. The mean surgical time of Group A patients was 39 ±7.5 against the time of 44.1 ± 8.6 in group B patients. Therefore, the procedural time

was significantly lower in the endo-clipping technique than the knotting (p=0.03). No major difference was found in terms of the hospital stay of the patients in both groups (p-0.2). (Table I).

Among intra-operative complications, 3 patients in group A developed bleeding against 1 in group B (p=0.04). The same patients later complained of abscesses and were readmitted. One of these patients in the endo-clipping group had to be re-operated to remove the abscess. The incidence of postoperative ileus (3 vs 1 patient, p= 0.04) and intra-abdominal infection (2 vs 0 patients, p=0.03) was significantly higher in an endo-clipping group than extra-corporeal knotting group (Table 2).

Table No.I: Baseline Variables of the Study (N=60)

Variables	Group A, n=32 (53.3%)	Group B, n=28 (46.6%)	p-Value
Age (mean, SD)	24 ± 7.2	22 ± 6.68	0.89
Gender (male/female)	8/20	23/9	0.007
Cost (PKR)	900	280	-
Surgical time (minutes)	39 ±7.5	44.1 ± 8.6	0.003
Hospital stay (hours)	28.2 ± 19.5	20.3± 13.2	0.2

SD: Standard deviation

Table No.2: Incidence of Intra-operative and Postoperative Complications in Two Groups (N=60)

Variables	Group A, n=32 (53.3%)	Group B, n=28 (46.6%)	P-value
Intra-operative complications (n, %)			
Bleeding	3 (9.3%)	1 (3.5%)	0.04
Organ Injury	1 (3.1%)	-	0.03
Post-operative complications (n, %)			
Postoperative ileus	3 (9.3%)	1 (3.5%)	0.04
Infection at the surgical site	3 (3.1%)	2 (7%)	0.07
Intra-abdominal infection	2 (6%)	0 (0)	0.03
Readmission	2 (6%)	1 (3.5%)	1
Reoperation	1 (3%)	0 (0)	0.45

DISCUSSION

Laparoscopic techniques have been widely used in diverse surgeries and appendectomy is one of them. Laparoscopic appendectomy has dominance open appendectomy in many aspects such as lesser pain, better imaging of the peritoneal cavity, and quicker recovery. However, factors such as longer surgical timing, costly instruments, and demand for technical expertise raise concerns about laparoscopic techniques[15].

The technique adopted for closure of appendix stump plays a critical role in post-operative complications in both surgical methods for appendectomy. This has led to the introduction of various techniques and each of them has been found to have its pros and cons. This study has been designed to compare the most commonly used techniques for appendix base closure-metallic endo-clip and extra-corporeal knotting- in 3 major aspects, cost, operative time, and postoperative complications. Among both groups, a total of 4 patients developed unusual bleeding due to adhesions and cutting of mesoappendix while one of these cases also demonstrated cecal wall injury with serosal tear during dissection of adhered appendix away from the cecal wall. This serosal tear was repaired laproscopycally with suture vicryl 2/0. Following the removal of the drain, some of these patients revisited the hospital on the 8th day with the complaint of high fever and a CT scan revealed intra-abdominal collection. 1 of these patients had to be re-operated as the abscess was not resolving with an oral antibiotic course. Postoperative ileus and surgical site infections were also reported post-operatively but the incidence rate was significantly higher in end clipping group patients.

Two cases in the metallic endoclip group reported pre-operative intra-abdominal abscess. These patients were put on an antibiotic course and were managed conservatively. Since the leucocyte count remained in a range and the appendix base looked healthy, patients were operated on the 3rd day of hospital admission. However, postoperative ileus and collection of pus in the right iliac fossa were observed in a follow-up period of these patients. However, the complication was resolved by administering antibiotics, and reoperation was not required.

It was observed that the incidence of infection in both groups wasn't directly associated with the technique used but may be associated with pre-operative inflammation in the surgical area or dense adhesions. The complications reported in our study are comparable to the existing relevant literature. Our study reported ileus in 9.3% of cases in endo-clipping and 3.5% of patients in the knotting group. Whereas, Gonenc et al. [(14)] reported incidence in endo-clipping (1.6%) than knotting group (4.3%). However, in studies conducted by Arcovedo et al.[16] and Di Saverio et al.[(11)], no complication of ileus was reported by using the knotting technique. The high incidence rate in our study can be attributed to the comparatively smaller sample size. The rate in our study, however, remained

significantly high in the endo clipping group. Similarly, a higher occurrence rate of surgical site infection is reported in our study when compared with previous studies[12,17,18]. It could again be due to the limited sample size or might be possibly due to improper sterilization or postsurgical wound care. However, no significant difference was noted in the incidence of wound infections between the two groups. Moreover, since all the surgeries were performed by expert surgeons, thus it removed the risk of performance bias in the study variables.

Our study was majorly limited in terms of smaller sample size and failure to conduct the double-blinded study as the data collectors were informed of the study groups and blinded investigators couldn't be arranged due to lack of funding. Usually, the sample size is based on study variables, for instance, risk of infection in our case, with the power of at least 80%, but these conditions would have extended our study period. Although, the smaller sample size of our study lowered the power, the sample size is still comparable to related studies conducted in different countries[11,19]. Lastly, the study had a shorter follow-up period; therefore, it couldn't observe other possible complications such as clip slip or migration which has also been observed rarely[20].

CONCLUSION

Extra-corporeal and metallic endo-clip are two effective techniques for appendix base closure in laparoscopic appendectomy. Although usage of metallic endo-clip caused a shorter surgical time, it was found to be expensive and associated with more complications. However, it is anticipated that the higher rate of complications was not related to the technique but with confounding factors such as pre-operative conditions. Given the simplicity of the technique, we recommend using metallic endo-clips for base closure, but in poor economic setups, extra-corporeal knotting is suggested.

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Antibiotic Resistance Profile of Helicobacter Pylori Isolates from Dyspeptic Patients of Civil Hospital, Khairpur

Shehzad Tariq[1], Farukh Imtiaz[1], Tabish Akbar[3], Bakhtiar Ahmed[4], Sarmad Saeed[2] and Bakhat Ali Ansari[5]

ABSTRACT

Objective: To examine the frequency of H. pylori in patients with dyspepsia and also to test the antibiotic susceptibility profile of isolates.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Department of Microbiology, Shah Abdul Latif University, Khairpur for one year from 01-Jan-2019 to 31-12-2019.

Materials and Methods: Biopsy specimen from 100 patients with dyspepsia from both sexes was collected from civil hospital, Khairpur. After culturing the samples in Microbiology Institute, Shah Abdul Latif University, Khairpur, the identification of the samples was carried out (gram staining, catalase, oxidase and urease). The susceptibility profile to ten common antibiotics was tested by Disk diffusion method.

Results: From total 100 subjects, 100 biopsy samples from were collected. Mean age of the patients in years were 40±15.4. Out of 100 biopsies, 30 were positive for H. pylori. From these positive samples, majority of 56.7% were isolated from males and 43.3% from females. Out of 30 isolates, 11.7% isolates were sensitive and 88.3% showed intermediate resistance. From 30 isolates, 4.7% isolates were sensitive to amoxicillin, 2.46% to metronidazole, 18.94% isolates to amikacin, 1.07% to novobiocin, 21.57% to ciprofloxacin, 31.88% isolates to levofloxacin, 31.88% to lincomycin and 22.90% isolates were sensitive to clarithromycin.

Conclusion: The results showed that clarithromycin, levofloxacin, ciprofloxacin and moxifloxacin were sensitive while Amikacin and clavulanic acid/ amoxicillin showed intermediate resistance and novobiocin, amoxil and metronidazole, were resistant to H. pylori.

Key Words: H. pylori, Gram negative bacterium, Antibiotic susceptibility test, Dyspepsia.

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INTRODUCTION

H. pylori belong to Helicobacteraceae family and is a Gram negative bacterium [1]. Globally, it is one of the most prevalent bacterial infections with 4.4 billion people infected with H. pylori.

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Global H. pylori infection prevalence is 44.3%. Prevalence rate (50.8%) is higher in developing countries and Africa (70.1%) when compared with other regions. Prevalence rate differ widely in different regions, the rate is high in developing countries[2]. It show well-established association with socio-economic status and sanitation[3]. H. pylori is foremost source of gastro-intestinal illnesses and most significant risk factors for gastric cancer as well as mucosa-associated lymphoid tissue (MALT) lymphoma[4]. For elimination of H. pylori, PPI and antibiotics are first-line treatment. Successful eradication of H. pylori primarily depends on the selection of suitable antibiotics. But universally, the anti-microbial susceptibility testing for H. pylori is nearly absent. It is suggested to select an effective empirical eradication therapy is built on region and antibiotic resistance patterns specific to that population[5].

Unfortunately, over last decade, rate of eradication by above-mentioned treatment has declined to less than 90% mostly because of rapid antibiotic resistance, specifically against clarithromycin and metronidazole[6]. H. pylori antibiotic resistance differs considerably in different countries and among regions of same country[7]. So, surveillance of antibiotic resistance at local level is essential.

Antimicrobial resistance of H. pylori is a severe problem leading to eradication failure. For selection of a proper treatment regimen, knowledge of antimicrobial susceptibility is significant. Before the selection of an optimal treatment regimen, it is essential to have information regarding the frequency of resistance to a specific antimicrobial agent. The reports show that resistance rate vary from 10 to 90% for metronidazole, 5-59% for tetracycline, 0-45% for clarithromycin and 0-33% for amoxicillin[8]. Worldwide increase in resistance of H. pylori to metronidazole, clarithromycin and amoxicillin is reported[9]. The increase has serious implications as, not only for patient compliance, but also for determining the results of antibiotic treatment[10]. Antibiotic resistance might fluctuate over the years and not stable. It fluctuate in different regions [11]. Knowledge of the patterns of drug resistance is key to formulate the strategies to minimize the development of resistance and to help clinicians to improve treatment guidelines[12]. The objective of current study was to assess the H. pylori resistance rate to the different antibiotics used in local setting.

MATERIALS AND METHODS

This cross sectional study was conducted at department of microbiology, Shah Abdul Latif University, Khairpur. Duration of study was one year from 01-Jan-2019 to 31-12-2019 and non probability consecutive sampling technique was used for collection of samples. Sample size was calculated by openepi.com at 10% margin of error, 95% confidence level and taking H. pylori prevalence in functional dyspepsia as 64.4%.

Patients of either gender, with age range of 15 to 60 years who were admitted with signs and symptoms of dyspepsia included in this study.

Patients age les than15 years and greater than 60 years, females who were pregnant and lactating, patients using PPI, receiving H. pylori treatment and patients not suitable for gastroscopy were excluded from study.

Ethical approval of the study was taken from hospital ethical committee. After giving details of study, informed consent (written) was obtained from patients. To collect samples of patients, endoscopy was done in gastroenterology department in patients with gastritis (acute or chronic) and peptic ulcer problem. Stuarts transport medium was used to transport biopsy samples to histopathology lab. In case of identification of H. pylori infection by gram staining method report was considered positive. Disk diffusion method was used to test anti-microbial sensitivity. Commercially available antimicrobial discs were purchased. Bacterial isolates were cultured overnight in Muller Hinton agar (MHT). To see number of bacteria, turbidity was matched with 0.5 McFarland assay. Lawn of bacterial isolates was spread on MHT plates and inoculation disks were dispensed on plates after 15 minutes of. Plates were incubated at 37°C, plates for 24 hours. Test was performed in triplicate with both controls (positive & negative). Zone of inhibition was measured after 24 hours of incubation. Antibiotic were labeled as resistant when inhibition zone was less than 9 mm, intermediate diameter when zone range from 10-35 mm and sensitive at diameter of greater than 36 mm. (Figure 1 & 2).

Data was analyzed by SPSS version 25. For quantitative data like age mean and SD was calculated. While for qualitative data, frequency percentages were calculated. Chi-square test was applied to see association between study variables. p-value ≤ 0.05 was taken as significant statistically.

RESULTS

100 samples were collected from 100 subjects from which 35% were females and 65% were males (figure 3). Mean age of the patients in years were 40±15.4 years. Majority of patients with H. pylori positive were from age group between 40-60 years, from which 56.7% of them were H. pylori positive; while 30% of patients were from age between 20-40 years of age and only 13.3% were from age below 20 years of age.

Figure No. 1: Inhibitions zone for amoxicillin

Fig 2: Inhibition zone of metronidazole

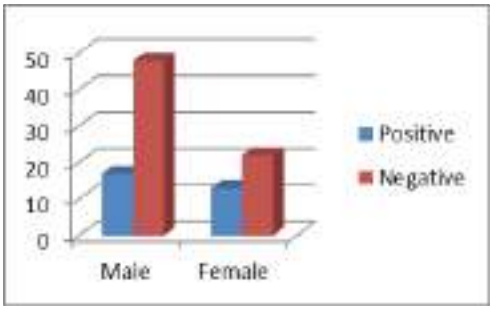

Figure No.3: Gender-wise distribution of Patients - H. pylori prevalence according to gender

Biopsies of 30 subjects were positive for H. pylori out of 17 (56.7) were males and 13 (43.3) females. So, positivity rate was more in males compared to females.

This study shows that a range of multidrug resistant H. pylori isolates were presented in untreated patients posing risk for nearby population. From 30 isolates, 11.7% isolates were sensitive and 88.3% showed intermediate resistance. From 30 isolates, 4.7% isolates were sensitive to amoxicillin, 2.46% to metronidazole, 18.94% isolates to amikacin, 1.07% to novobiocin, 21.57% to ciprofloxacin., 31.88% isolates to levofloxacin, 31.88% to lincomycin and 22.90% isolates were sensitive to clarithromycin.

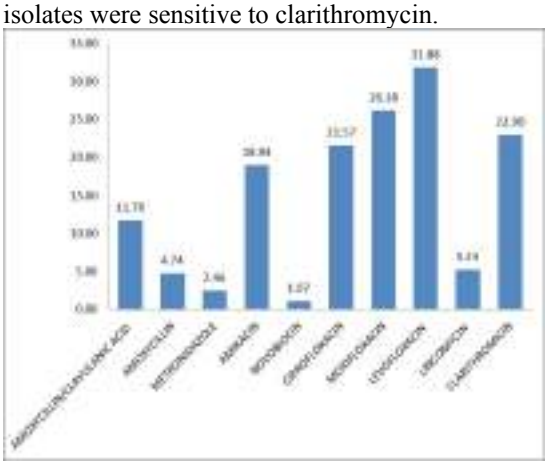

Figure No.4: Antibiotics susceptibility of H. pylori isolates

DISCUSSION

Helicobacter pylori belongs to Helicobacteraceae family and is a Gram negative bacterium. H. pylori is etiological agent of peptic and gastritis ulcer. For gastrointestinal pathologies is antibiotics are the principle treatment. Globally, resistance of antibiotics is a public health problem comprising of diverse bacteria. In 2017, H. pylori is categorized as a pathogen of high priority by WHO because of increased number of clarithromycin resistance[13]. For establishing the finest treatments with maximum efficacy and minimum adverse effects, knowledge of actual antibiotic resistance in each patient is necessary.

This is the first study to the best of our knowledge that reports the antibiotic susceptibility profile in dyspeptic patients in Interior Sindh. From total 100 subjects, 100 biopsy samples from were collected. From 100 biopsies, 30 were positive for H. pylori. From 30 positive samples, 56.7% were isolated from males and 43.3% from females. Our results are comparable to the study conducted by Faisal Rasheed et al which showed prevalence of H. pylori as 32.7%[10]. Our results are noticeably lesser as compared to old studies. A study by Mujataba et reported the prevalence of H. pylori as 41.6%.[14] Results by Tahir et al displayed the frequency of H. pylori as 56.4% from a study carried out at in Mansehra's King Abdullah Teaching Hospital [15].A study from Nilore, Islamabad conducted by Qureshi et al in dyspeptic patients displayed very high prevalence of 66.5% of H. pylori infection[16].Another study from at Liaquat National Hospital, Karachi by Tooba et al et reported 64.4% prevalence of H. pylori infection[17].

Current study investigated the anti-microbial sensitivity of isolates from dyspeptic patients. Antibiotic susceptibility of H. pylori isolates was tested for 10 antibiotics. Sensitivity to amoxicillin was 4.7%, 2.46% to metronidazole, 18.94% isolates to amikacin, 1.07% to novobiocin, 21.57% to ciprofloxacin, 31.88% isolates to levofloxacin, 31.88% to lincomycin and 22.90% isolates were sensitive to clarithromycin. Similar findings are stated in other studies carried out in different countries as well as in Pakistan. A meta-analysis showed antibiotics resistance to Clarithromycin (37%), Levofloxacin (19%), Amoxicillin (37%)[18]. In last 10 years, the increase in resistance to clarithromycin from 2.2 to 7.5% is of substantial health importance, because resistance to clarithromycin has decreased the effectiveness of standard therapy bases on clarithromycin up-to 70%. But Amikacin and clavulanic acid/ amoxicillin showed intermediary resistance. Whereas novobiocin, amoxil, metronidazole showed resistant to H. pylori. In Asian pacific region, amplified macrolides consumption might be responsible for clarithromycin resistance from 7% before 2000 to 21% in 2011–15. Resistance to metronidazole resistance is greater in developing countries as compared to developed countries. In developing countries, practice of economical antibiotic for other infections added to this difference [18].

The range antibiotics use among diverse groups of community is related to the geo-graphical differences in the antimicrobial resistance of H. pylori. There is undiscriminating usage of antibiotics for treatment of various infections for treatment of various infections in Pakistan, particularly that of amoxicillin, erythromycin, metronidazole, tetracycline and clarithromycin. Additionally, free access of medicines due to unobstructed sale of antibiotics encourages the self-prescription. This is contributing cause of the augmented anti-microbial resistance in H. pylori isolates to amoxicillin clarithromycin, tetracycline and metronidazole.

Current study displays that H. pylori from untreated patients are multidrug resistant. This poses a severe risk to neighboring population. Easier access to antibiotics lacking proper prescription and use for respirational and skin infections may explain these findings.

CONCLUSION

The results showed that clarithromycin, levofloxacin, ciprofloxacin and moxifloxacin were sensitive while Amikacin and clavulanic acid/ amoxicillin showed intermediate resistance and novobiocin, amoxil and metronidazole, were resistant to H. pylori. This study shows that H. pylori from untreated patients grasp a variety of multi-drug resistance which carries serious risk to nearby population.

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To Compare the Efficacy of Bolus Dose of Propofol versus Control in Patients Undergoing Elective Cesarean Section under Spinal Anesthesia

Iftikhar Shah[1], Arshi Naz[2], Mirza Shahzad Baig[2], Sidra Javed[3], Vijai Kumar[2] and Samita S. Khan[2]

ABSTRACT

Objective: The compare the efficacy of bolus dose of Propofol versus control in patients undergoing elective cesarean section under spinal anesthesia.

Study Design: Randomized controlled trial study

Place and Duration of Study: This study was conducted at the Department of Anesthesia, Dow University of Health Sciences and Civil Hospital, Karachi from 1st January 2018 to 30th June 2018.

Materials and Methods: All women aged 18-38 years presented with full-term, para 0-5, weight between 50–75 kg, ASA class I & II underwent elective cesarean section under spinal anesthesia were included. Participants were randomly allocated equally to the control group (Group C) or Propofol groups (Group P) using a lottery method. Efficacy was labeled as positive if there was no vomiting intraoperatively.

Results: Mean age of the women was 32.89 ±4.03 years. The mean weight, height, and BMI of the women were 60.07±5.12kg, 1.54±0.06m, and 26.98±5.15kg/m^2 respectively. Efficacy was found 42 (93.3%) significantly higher among women with propofol as compared to placebo 30 (66.7%) (p=0.002).

Conclusion: The efficacy of bolus dose of propofol was found higher among control in patients undergoing elective cesarean section under spinal anesthesia.

Key Words: Efficacy, Propofol, Elective caesarean section, Spinal anaesthesia

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INTRODUCTION

Spinal anaesthesia has established itself as the primary anaesthetic option for caesarean section[1] because it is both safe and quick[2]. Despite the fact that this procedure is generally regarded safe, it is associated with a few distinct but severe side effects, the most notable of which is post-operative nausea and vomiting (PONV)[2-3]. While caesarean delivery is common, it can occur in as many as 50 percent to 80 percent of women who give birth if no prophylactic antiemetic is taken during the pregnancy.

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The use of prophylactic antiemetics in patients undergoing caesarean delivery is therefore recommended[4-5].

There are several medications available to treat post-operative nausea and vomiting (PONV), such as 5-HT3 antagonists (ondansetron and granisetron), dopamine antagonists, and antihistamines, that are utilised in the United States.

On the other hand, the disadvantages of each of these treatments include the high cost of 5-HT3 antagonists, the possibility of extrapyramidal symptoms from dopamine receptor antagonists, excessive sedation from antihistamine drugs, and tachycardia from antihistamine medications[6,7].

When propofol was administered at a subhypnotic dose (1.0 mg/kg/hr) during spinal anaesthesia for caesarean section, the results showed that it was effective in reducing gastrointestinal symptoms[8]. Propofol was administered at a subhypnotic dose (1.0 mg/kg/hr) in several studies, with the findings demonstrating that it was effective in decreasing gastrointestinal symptoms during caesarean section. When administered with propofol, the reported incidence of vomiting was 3.3 percent and 23.3 percent, respectively[9], while the reported incidence in the control group was 23.3 percent and 3.3 percent.

A plasma concentration of 1000 ng/mL propofol administered during caesarean section, as compared to placebo, significantly reduced the incidence of post-delivery nausea, but had no influence on the incidence of retching or vomiting episodes occurring during the procedure, according to Niu et al[10].

A clinical trial conducted by Rosillo-Meneses et al to compare the efficacy of propofol versus ondansetron in the prevention of postoperative nausea and vomiting in nasal surgery revealed that there is no statistically significant difference between the two drugs in terms of protection, leading to the conclusion that administering propofol or ondansetron for postoperative antiemetic prophylaxis is equally effective[11].

In addition, despite an extensive search, no local studies on propofol administered intraoperatively for the prevention of vomiting in patients undergoing elective caesarean section under spinal anaesthesia have been located. If the efficacy of propofol is revealed to be greater than expected as a consequence of this experiment, it is hoped that it will be used in the future to avoid vomiting in patients undergoing elective caesarean section under spinal anaesthesia in the future.

MATERIALS AND METHODS

This randomized controlled trial was conducted at the Department of Anesthesia, Dow University of Health Sciences and Civil Hospital, Karachi from 1st January 2018 to 30th June 2018. The participants in this study were 90 full-term pregnant women ranging in age from 18 to 38 years, with an ASA class I or II and who underwent elective caesarean delivery under spinal anaesthetic. Ineligible patients included those who had any obstetric complication such as eclampsia or gestational diabetes that was evident from their history and medical records, patients who had evidence of foetal compromise, patients who had acute gastroenteritis, gastroenteritis with hepatitis, or patients who had received any antiemetic within 24 hours of the study's start. Patients who had received any antiemetic within 24 hours of the study's start were also excluded. After explaining the potential risks and advantages of the research medicine, patients were asked to sign an informed written permission form. Through the use of a lottery system, participants were assigned evenly to either the control group (Group C) or the propofol group (Group P).

Propofol 2ml (20 mg) bolus was administered to patients in group P, and normal saline 2ml bolus was administered to those in group C. Immediate intravenous administration of propofol was initiated following acclamation of the umbilical chord A supervisor was there to oversee the entire operation, which was completed entirely by the researcher. In the event of two or more episodes of emesis during surgery, an antiemetic (metoclopramide 10 mg) was given. If there was no vomiting throughout the operation, the efficacy was considered to be good (from the administration of the drug to the last stitch). An annexure contains a proforma on which this information, as well as age, parity, length of operation, and BMI, was entered. SPSS-21 was used to conduct the statistical tests. The chi-square test was used to evaluate the efficacy of the two groups. The significance level was set at 0.05.

RESULTS

The majority of the women in both the propofol and placebo groups were over 30 years old, with 39 (86.7%) and 37 (82.2 %) respectively. Many cases in both the propofol and placebo groups had a BMI of less than 30 kg/m2.

Table No.1: Baseline Details of all the included patients

Variable	Propofol group (n=45)	Placebo group (n=45)
Age (years)		
<30	6 (13.3%)	8 (17.8%)
>30	39 (86.7%)	37 (82.2%)
Body mass index (kg/m^2)		
≤30	28 (62.20%)	24 (53.30%)
>30	17 (37.80%)	21 (46.70%)
Duration of surgery (minutes)		
<40	19 (42.20%)	17 (37.80%)

>40	26 (57.80%)	28 (62.20%)
Parity		
Nulliparous	3 (6.70%)	11 (24.40%)
Primiparous	13 (28.90%)	22 (48.90%)
Multiparous	29 (64.40%)	12 (26.70%)
ASA Score		
I	18 (40%)	29 (64.40%)
II	27 (60%)	16 (35.60%)

Table No.2: Comparison of efficacy with respect to group (n=100)

Group	Efficacy		P value
	Yes	No	
Propofol	42 (93.3%)	3 (6.7%)	0.002
Placebo	30 (66.7%)	15 (33.3%)	

The average surgery time was 42.2±4.9 minutes. Maximum number of the patients in both the propofol and placebo groups were awake for more than 40 minutes. Man ycases in the propofol group were multiparous 29 (64.4%), while higher number of the women in the placebo group were primiparous 22 (48.9%). The majority of the cases in the propofol group (60%) were given ASA level I, whereas the in the placebo group (64%) were given ASA status II (Table 1).

Efficacy was found 42 (93.3%) significantly higher among women with propofol as compared to placebo 30 (66.7%) (p=0.002) (Table 2).

DISCUSSION

To overcome post-operative nausea and vomiting (PONV) many treatments has been tried, such as 5-HT3 antagonists (ondansetron and granisetron), dopamine receptor antagonists and antihistamine drugs. However, each has some drawbacks, i.e. cost effectiveness, sedation etc.

Some authors have used an infusion of propofol with a sub hypnotic dose (1.0 mg/kg/hr) and found that it was effective in the prevention of emetic symptoms during spinal anesthesia for cesarean section.[8] Incidence of vomiting with propofol has been reported as 3.3% and respectively while for the control group as 23.3%respectively.[9] In our study efficacy was found 42 (93.3%) significantly higher among women with propofol as compared to placebo 30 (66.7%).

In one study it has been associated with more maternal hypotension, possibly increased risk of maternal awareness, and worse Apgar scores in the neonate when compared with thiopentone. Other studies however have shown no difference. No studies have shown the superiority of propofol. Ketamine has a place in the management of the hypovolaemic obstetric patient requiring cesarean section and experience and confidence with this drug is likely to be far greater in many under-resourced areas than in the UK. A major advantage of propofol is the expected rapid emergence from anesthesia.[12-15] The antiemetic actions of propofol have been demonstrated in previous investigations[16-17] with either a bolus dose or a continuous infusion. Furthermore, only a small number of clinical trials have proven that infusion of propofol at a modest dose (1.0 mg/kg/h) is useful in the prevention of nausea and vomiting during and after caesarean section[18].

Numazaki et al[19] came to the conclusion that a subhypnotic dose of propofol 1.0 mg/kg/h reduces the incidence of post-delivery nausea and vomiting in parturients undergoing caesarean delivery without excessive sedation, and that it is a more effective antiemetic than traditional antiemetics (droperidol and metoclopramide) for reducing the severity of nausea and vomiting[20]. There are no definitive explanations for how propofol prevents intraoperative and post-delivery emesis; however, according to Smith et al[21], there is a possibility that propofol has direct antiemetic properties, and that reduced levels of serotonin in the area postrema are associated with these antiemetic properties, as determined by Cechetto et al[22]. Thirteen percent of the propofol group vomited, according to Gan et al[23], indicating that propofol has direct depressive effects on the chemoreceptor trigger zone, the vagal nuclei, and other brain regions associated with nausea and vomiting.

CONCLUSION

In patients undergoing elective caesarean delivery under spinal anaesthesia, the efficacy of a bolus dosage of propofol was found to be higher than in the control group.

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A Qualitative Study of Reproductive Health Education Among the Medical Students of Karachi

Reproductive Health Education Among Medical Students

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ABSTRACT

Objective: This study was to explore the need for reproductive health education among medical students as the students are ignorant regarding the education of reproductive health before their marriages.
Study Design: Qualitative exploratory study
Place and Duration of Study: This study was conducted at the Sir Syed Medical College for Girls, and Al-Tibri Medical College and Hospital. Karachi, from March to July 2020.
Materials and Methods: This study was conducted among the medical students from two different Institute. The studied sample consisted of students of all the medical years. We conducted a total of 14 focus groups and 12 in-depth interviews. Hence, a purposive sampling technique was used to collect the data. The content analysis method was used to analyze the data. According to the perceptions of participants, various themes were identified, such as (1) lack of reproductive health knowledge, (2) barriers to avail reproductive health services, (3) consequences of an individual and (4) social-cultural consequences.
Results: Twenty-six medical students, both married and unmarried, were included belonging to the age group of 18–25 years were interviewed. A lack of knowledge regarding sexual reproductive health was seen among the medical students of Karachi. Girls and women in our country hardly learn from their parents and teachers regarding reproductive health.
Conclusion: The need for reproductive health education was being prioritized by most of the participants, not because of the diseases associated with reproductive health but also because of other issues individuals face.
Key Words: Reproductive health education, Medical students, Qualitative study

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INTRODUCTION

According to the World health organization (WHO), reproductive health education is defined as "a state of physical, emotional, mental and social well-being; it is not merely the absence of disease, dysfunction or infirmity in all matters relating to the reproductive system and to its functions and processes. If reproductive health to be attained and maintained, the rights of reproductive health of all persons must be respected, protected and fulfilled." (WHO, 2006a)

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The main idea of reproductive health education is to spread the information and motivate people to enhance their reproductive health by implementing different types of informative activities[1]. Through this effective reproductive health education, one can prevent diseases and help live a healthy lifestyle[2]. With time, the need for reproductive health education has been rising, and it is also considered a fundamental human right by most international organizations[3]. Hence, where the community emphasizes its need, the community has to go through its challenges due to the orthodox mindset of the society and cultural barriers, specifically in South Asia and its neighbouring countries[4]. In Pakistan, reproductive health is considered a social taboo because of cultural traditions and norms. The people of Asia think providing information regarding reproductive health at an early age may lead to various problems such as it can ruin the innocence of children at an early age[5]. Most South Asian countries do not have a proper platform for reproductive health education, along with a

lack of knowledge regarding main reproductive functions, contraception, and other associated diseases[6]. One of the qualitative studies was conducted in Iran in which girls were unaware of the changes that take place during puberty, and they found their experience very unpleasant[7]. Another qualitative study was conducted among girls college of Saudi Arab which also revealed that they had no idea of menarche. They also showed their negative perception of the process of puberty[8]. Hence in Pakistan, various studies have proved that students have poor knowledge regarding reproductive health. For this purpose, a qualitative study was conducted among the medical students of Karachi to explore the need for reproductive health education among medical students.

MATERIALS AND METHODS

A qualitative exploratory design was conducted from March-July 2020, among 50 medical students through purposive sampling technique from different institutes. Out of which 25 were FGD's and 25 were IDI's. Only those students who were interested were included and those who were not willing to participate were excluded from the study. A digital voice recorder was used to record the interviews of the participant between 45–60 minutes. The data was organized, coded and then categorized so that the themes could be extracted. All Ethical issues have been well-thought-out.

RESULTS

Lack of reproductive health knowledge: Our study revealed that lack of reproductive health knowledge is mainly due to lack of formal education in communities, and homes. The participants were shy to share their problems with their parents as well. In this regard, one of the participants stated that

"Health system of Pakistan is still far behind in terms of reproductive health education. No one in our society is considering this issue as an important element of our lives" (IDI, Final year Medical student).

"Most Asian families specifically in Pakistan are ashamed of talking about reproductive health issues with their children; if children ask something out of curiosity, parents pretend they have no idea what their children are talking about or at times they change the topic immediately and start asking them other things unrelated to it, because they believe that children should remain stay away from such type of education and awareness as it would create problems for them and become hard for the parents to control them" (FGD, all years of Medical students)

Another finding of our study revealed that one of the reasons for the lack of reproductive health information among most of the participants was the lack of knowledge provided by the teachers. They emphasized that reproductive health education should be part of the curriculum in schools like in western countries. As one of the participants stated that;

"Almost all schools have specialized faculty and qualified teachers; but, topics related to reproductive health education were not included in the syllabus and also staff and faculty does not have adequate knowledge " (FGD, Final year, Medical students)

Table No.1: The main five themes and their sub-themes were identified in this study

Themes	Sub-themes
Lack of reproductive health knowledge	Lack of proper education, availability of reliable sources, lack of education from elders and teachers
Barriers to avail reproductive health services	lack of policies, lack of social and cultural support, pricey consultation, lack of qualified workforces, lack of insurance policies for consultation
Challenges of Individual in the society	increase in the divorce rate, helpless feeling, negative impact in the relationship
Socio-cultural consequences	The idea of modern and traditional world, lack of religious knowledge, obsession to media

Barriers to avail reproductive health services: The results of this study revealed that the participants were concerned regarding the barriers faced by the people during the provision of reproductive health services. The main reason was the lack of priority of policy-making, lack of social support due to which there were no services available. One of the participants stated that:

"Many of the problems faced by the society was related to lack of support system " (IDI, Third year, Medical students).

Another important finding of the study revealed that the culture inhibits society from developing a proper channel for reproductive health services. The participants mentioned that the social stigma of these services has made their availability impossible for the community. One of the participants stated that:

"Many people in our society feel shy and avoid talking about reproductive health problems and they don't realize this was a natural process of the human body" (FGD, Final year, Medical students).

Another important finding revealed by the participants was the high cost of such consultation services. As one of the participants stated that,

"The consultation fees taken by the doctor was too high that they think doctors would not tell them something different, it was better to google instead of going to the doctors"(IDI, all years of Medical students).

Another important finding of the study revealed a lack of insurance coverage for consultations, and inadequate workforce as a result of which reproductive health was neglected. One of the participants stated that:

"For just few minutes consultation, had to pay so much money from our pocket and the government has not provided us with any insurance cards"(FGD, Final year, Medical students).

Challenges of individuals in a society: Most medical students believed that divorce rate is increasing day by day. One of its leading causes was insufficient knowledge regarding reproductive health. One of the participants stated that:

"Reproductive health problems were one of the indirect causes of divorce as the couple felt uncomfortable to talk about their reproductive health in front of everyone because of the shame or at times they neglect such issues. However, it is undoubtedly hidden cause of divorce and leaves a negative impact in the relationship"(IDI, First year, Medical students).

"If a relationship between the couple was not healthy, the couple would lose interest towards each other and couple felt so helpless at such moments which would lead to emotional divorce" (FGD, Second year, Medical student).

Socio-cultural consequences: One of the findings of our study revealed that most of the participants believed that Pakistan is entering into modern world by forming big gap in terms of conventional practice and modernity. This modern culture has a significant influence on our personalities this was all due to weak religious beliefs. One of the participants stated that:

"Most of the people were confused between the modern and old culture. Now a day's people believe that everything should be open without any shame but when it comes to reproductive health, its always neglected" (FGD, Third year, Medical student)

Another participant mentioned that now a day's addiction of cell phones was harmful as its provide the information in the wrong manner. One of the participants stated that:

"They send private and vulgar photos to each other via applications such as face book and whatsapp". (FGD, First year, Medical student)

Another important finding of the study is the frequent availability of satellite channel as they show such modern things on TV which should not be allowed for kids to watch at home. As one of the participants stated that:

"The effect of satellite channels on our youth could not be ignored at any cost ; however, there are still some families in our cities who do not have satellite receivers, but still their kids go to school and could easily get harmful information. Hence this is the worst invention of this era for the new generation" (FGD, Final year, Medical students)

DISCUSSION

This was the first type of qualitative study conducted among the medical students of Karachi to emphasize the importance of reproductive health education among the masses. Hence, the data analyzed resulted in four main themes: lack of reproductive health knowledge, Barriers to avail reproductive health services, and challenges of Individual and socio-cultural consequences. The participants believe that one of the reasons for socio-cultural norms faced by the Pakistani community in recent times was the difference between modern and old traditional mindsets. The transition of our society was due to western culture and ideas, which had a deep impact on the cultural and behavioural models, leading to various approaches to cater reproductive health problems[9]. Some participants believe that there was a big threat to reproductive health because of weak religious beliefs. Hence the results of our study were similar to another study.[10] He also mentioned that deviation from reproductive health behaviour was due to a lack of religious beliefs. Another finding observed in our study was a decline in reproductive health education, as a result of which there was an increased incidence of reproductive health diseases, and it causes a negative impact on one's personality and relationship of a couple[11]. Another frightening factor was addiction which threatens reproductive health[12]. The findings of our study were similar to a study conducted by Gray et al.[13] They also revealed that youth was exposed to false reproductive health information through TV channels. Worldwide different strategic planning has been done to prevent the youth from these newly emerging harms of technology, but, unfortunately, no particular plan has been developed in Pakistan. In our study, participants discussed that insufficient knowledge regarding reproductive health was also mentioned as one of the factors[14-17]. Hence, lack of formal education from parents, schools and teachers were the main causes of insufficient knowledge regarding reproductive health[8]. Unfortunately, in our society and many other cultures, parents do not feel comfortable discussing reproductive health issues with their children; due to which parents are not considered as an effective source of information, and they provide no support to their children regarding these issues, as a result of which children engage themselves into unreliable resources which creates misconceptions in their minds[18] which were not healthy for their character building[19]. In the east, there was certain mindset regarding reproductive health which inhibits the youth to obtain information[20]. Most of the participants in this study discussed the barriers which they faced during reproductive health education. Our findings were similar to another study conducted by Roudsari et al[21]; in this study, they revealed that there was a large gap when it comes to providing reproductive health services. In Pakistan, the biggest dilemma was that there was no formal education for reproductive health services for youth. According to another study conducted by Mitton et al[22], reproductive health program also needs social support. Therefore, it is the duty of the policy-makers to

implement reproductive health education as an integral part of the education system.

CONCLUSION

Although there were many barriers but that does not mean that reproductive health education would be impossible. The results of our study suggested that the integration of reproductive health education into the pre-marital educational program could help in the promotion by creating awareness regarding reproductive health.

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