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CONTENTS

Extreme Misuse of Antibiotics During Covid-19 in Pakistan

Mohsin Masud Jan

Editor

Extreme misuse of antibiotics was observed in Pakistan in 2021 when bactericidal drugs worth Rs120 billion were consumed in the country, officials and experts said, claiming that over 70 per cent of the antibiotics consumed by patients were unnecessary.

According to the official data available that oral and injectable antibiotic medicines worth s119,745,122,879 were consumed in Pakistan in the year 2021 alone, which is around 10 per cent of the total expenditure on health in Pakistan. As per the Drug Regulatory Authority of Pakistan (DRAP), there are around 333 manufacturers of antibiotic medicines, both oral and injectable, in Pakistan, manufacturing different brands of 87 molecules (generic antibiotic medicines). These 333 drug manufacturers have 2013 antibiotic medicines registered with the DRAP, of which 1,604 are active products, which means that they are available in the local market.

"Last year (2021) was a unique year when an unprecedented increase in the consumption of antibiotics was observed all over the world, including Pakistan.

The expert claimed that due to abuse of antibiotics, most of the gram negative bacteria, which cause deadly infections, were not resistant to almost all the antibiotics available in the country, adding that new antibiotics which are effective against these drug-resistant bacteria are highly expensive and even not available in the country. "At the moment, we are faced with the problem of drug-resistant bacteria against whom we either have no or limited options available. This is because of extreme misuse of antibiotics in our society.

Claiming that the majority of people are consuming antibiotics unnecessarily in the country, an immediate end to over-the-counter availability of bactericidal drugs, ensuring presence of pharmacists at medical stores and in hospitals and rational prescription of antibiotic medicines by physicians in the country.

According to Pakistan's drug laws, only a qualified pharmacist is authorized to provide antibiotics to a person at a pharmacy, but, unfortunately, hardly one or two per cent pharmacies in the country have trained and qualified pharmacists available during their business timings. "Nowhere in the world, pharmacies and medical stores operate in the way they are doing in our country. We have uneducated and untrained people at pharmacies, who sell all kinds of medicines including antibiotics without even asking for a prescription. Similarly, our physicians are also misusing their authority and prescribing antibiotics without any justification, which is leading to antimicrobial resistance.

On the other hand, some of the pharmacists who tried to prevent the irrational use of medicines including antibiotics claimed that they were cursed and criticized when they tried to advise patients not to use antibiotics, steroids or other medicines not recommended for the treatment of their diseases.

Self-medication or advising against the use of antibiotics for the treatment of viral ailments, especially common cold and flu. We didn't sell medicines without a prescription and offer telemedicine consultation with a pulmonologist or infectious diseases experts in case of suspected or even confirmed cases of Covid-19 during the peak of the pandemic.

Medicines are not sold to patients without prescription and if there is a discrepancy in the prescription, it is referred to the pharmacist or the physician.

In our country, Common Quality Management System (CQMS) should develop in consultation with the provinces to prevent the misuse and abuse of antibiotics as well as other prescription medicines.

To set a minimum standard for pharmacies throughout the country should plan to develop Standard Operating Procedures (SOPs) for pharmacies all over the country and want to introduce good distribution, storage and disbursement practices of medicines to the end users. The presence of trained and qualified pharmacists at every pharmacy in the country will be ensured to prevent self-medication and abuse of prescription drugs.

The presence of trained and qualified pharmacists at medical stores and pharmacies, not only the issue of misuse of antibiotics and other prescription drugs can be prevented but the patients can also be guided properly by pharmacists regarding proper dosage and duration of medicines they should take.

Original Article

Association of Oral Hygiene Status and Dry Socket After Third Molar Surgery: A Prospective Cohort Study

Oral Hygiene Status and Dry Socket

Tariq Sardar[1], Umer Ullah[5], Umar Nasir[2], Gulrukh Sheikh[3], Bibi Maryam[4] and Zainab Shah[6]

ABSTRACT

Objective: This study evaluates the effect of oral hygiene status on frequency of dry socket after lower third molar surgery.

Study Design: Cohort study

Place and Duration of Study: This study was conducted at the Oral Surgery Department of Khyber College of Dentistry, from August 2017 to December 2020.

Materials and Methods: Total 270 patients were included in this study. Hygiene status of the oral cavity was evaluated using Oral Hygiene Index-Simplified (OHI-S). Data analysis was done using SPSS version 20. Simple and multiple logistic regression analyses were applied to measure the associations of independent variables and dry socket. A p-value of less than 0.05 was taken as significant.

Results: Total of 55 (20.4%) patients developed dry socket with 28 male patients and 29 belonging to age group 25 years or less. Association of dry socket with OHS (p=0.005) and duration of procedure (p=0.009) was statistically significant. Patients with poor OHS, fair OHS and duration of surgery more than 30 minutes were at higher odds of developing dry socket with adjusted odds ratio of 3.064 (95% C.I.:1.412, 6.647), 2.065 (95% C.I.:0.986, 4.329) and 2.097 (95% C.I.:1.133, 3.881) respectively. Association of age groups and gender with dry socket was statistically not significant.

Conclusion: Dry socket more commonly develops in patients with poor and fair oral hygiene after impacted MTM surgery, irrespective of gender and age.

Key Words: Impaction, Dry socket, Oral Hygiene Index-Simplified (OHI-S)

INTRODUCTION

Dry socket (DS), or alveolar osteitis, has been defined as "postoperative pain inside and around the extraction site, which increases in severity at any time between the first and third day after the extraction, accompanied by a partial or total disintegrated blood clot within the alveolar socket with or without halitosis.[1] It most commonly occurs after surgical extraction of impacted mandibular third molars (MTM).[2]

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Dry socket usually develops 1 to 3 days after extraction and characterized by moderate to severe pain that usually does not respond to analgesics. Other features of DS include local signs like open socket with food debris, tender inflamed gingiva, halitosis, exposed bone with severe tenderness.[1,3,4]

The precise pathogenesis of DS is not clear but increase in local fibrinolytic activity resulting in disintegration of the clot is suggested pathophysiology.[1] Fibrinolysis may occur as a result of direct tissue activators released due to trauma to the alveolar bone or release of indirect activators by bacteria.[5,6] The risk factors for DS include smoking, traumatic and difficult extraction, female gender, vasoconstrictors in local anesthesia, poor oral hygiene, excessive irrigation and curettage, pre-existing infection, oral contraceptives (OCP), diabetes and radiotherapy.[1,4,7-9]

Although many studies are conducted to identify the common risk factors that are associated with DS, the effect of oral hygiene status (OHS) on post-operative incidence of DS is little explored.[4,7,9] In this study we assessed the association of oral hygiene status with dry socket after surgical removal of impacted MTM. The results further clarified the role of OHS in the development of DS and may prompt the clinicians to

take preventive measures before embarking on the surgical extraction of impacted MTM when dealing with patients having poor oral hygiene.

MATERIALS AND METHODS

This prospective cohort study was conducted at Oral Surgery unit of Khyber College of Dentistry, Peshawar, from August 2017 to December 2020. Total 270 patients meeting the inclusion criteria were included in this study. All patients irrespective of age and gender, who had surgical extraction of moderately difficult impacted MTM with a Pederson score of 4 to 7 were selected consecutively in this study. The difficulty of surgery influences the incidence of DS so moderately difficult cases were selected to control its effect as confounding factor. All patients with systemic illness, immune-suppression, smokers, those on oral contraceptives, steroids and having undergone radiotherapy and chemotherapy were excluded from the study as these conditions are known risk factors for dry socket.

Ethical approval from the institution review board was taken. Detailed history and clinical examination was done after obtaining informed consent from all patients. Orthopantomogram (OPG) was done to evaluate MTM. A structured proforma was used to record the patients' demographics, OHS, duration of procedure (DoP) and presence or absence of dry socket. Duration of procedure was recorded from the start of the incision till the placement of last suture.

All the patients were evaluated for OHS using Oral Hygiene Index-Simplified (OHI-S) which is based on combined score of Debris Index-Simplified (DI-S) and the Calculus Index-Simplified (CI-S). The DI-S and CI-S were calculated independently and then added together to get the OHI-S. The results were interpreted as good, fair and poor based on OHI-S score of 0 to 1.2, 1.3 to 3.0 and 3.0-6.0 respectively.

Procedure

All the extractions were performed under local anesthesia, using a standardized method by a single operator who had completed post graduate training in maxillofacial surgery to control the operators' bias. After the procedure all patients were given post operative instruction in verbal and written form. All patients were advised Ibuprofen 400mg 8 hourly, orally for 5 days. Patients were advised to start warm saline gargles after 48 hours.

Patients were followed up on the phone to record the information daily and asked to return immediately in case there were any signs and symptoms of DS. Diagnosis of DS was based on increasing pain in and around extraction socket after 24 hours of extraction and empty socket with disintegrated or dislodged clot. All patients returned on 6th post-operative day for routine examinations and removal of stitches. The patients were examined and those who did not have any

signs and symptoms of dry socket were considered to have healed sockets.

The data was analyzed using Statistical Package for the Social Sciences (SPSS) version 20.0. Chi-square test was applied to assess the association between different variables and dry socket. Simple and multiple logistic regression analyses were used to find crude and adjusted Odds Ratio (with 95% confidence intervals) to measure the strength of relationships between independent variables (age groups, gender, OHS and DoP) and post-operative dry socket. Statistical significance level was kept at $p \leq 0.05$. Hosmer-Leme show test was used to make sure the model is a good fit to the data.

RESULTS

Out of the total 270 patients, 54.4% (n=147) were male. Majority of the patients in this study belonged to age group 25 years and below (n=156, 57.8%). Good OHS (n=111, 41.1%) was found in majority of the patients followed by fair and poor OHS. Extraction was completed within 30 minutes in majority of cases (169, 62.6%). Further details are given in table I.

Table No.I: Distribution of Age, Gender, Oral Hygiene Status and Duration (n=270)

Variables	N (%)
Gender	
Male	147 (54.4)
Female	123 (45.6)
Age Groups	
≤25	156 (57.8)
≥26	114 (42.2)
Oral Hygiene Status	
Good	111 (41.1)
Fair	98 (36.3)
Poor	61 (22.6)
Duration of procedure	
< 30 mins	169 (62.6)
>30 mins	101 (37.4)

Dry socket was diagnosed in 55 (20.4%) patients. Out of the total 147 male patients 28 (19%) returned with DS while 27 (22%) female patients developed DS. This difference was statistically not significant (P=0.555). Similarly, in this study DS developed in 29 (18.6%) patients belonging to 25 years and below age group while 26 (22.8%) patients were diagnosed with DS in 26 years and above age group. This association had no statistical significance (P=0.395). Dry socket was diagnosed in 21 (34.4%) patients out of the total 61 with poor OHS. The association of OHS and DS was statistically significant (p=0.005). Similarly, DS developed in 29 (28.7%) of total 101 patients whose DoP was more than 30 minutes. The association of DoP with dry socket had statistical significance (p=0.009). Details are presented in table 2.

Table No.2: Association of Age, Gender, Oral Hygiene Status and duration of procedure with Dry Socket (n=270)

Variables	Dry Socket		P value
	Yes n (%)	**No** n (%)	
Gender			0.555
Male	28 (19)	119 (81)	
Female	27 (22)	96 (78)	
Age Group			0.395
≤25	29 (18.6)	127 (81.4)	
≥26	26 (22.8)	88 (77.2)	
Oral Hygiene Status			0.005 *
Good	15 (13.5)	96 (86.5)	
Fair	19 (19.4)	79 (80.6)	
Poor	21 (34.4)	40 (65.6)	
Duration of procedure			0.009 *
< 30mins	26 (15.4)	143 (84.6)	
>30mins	29 (28.7)	72 (71.3)	

*p-value significant- <0.05

Table No.3: Regression Analysis for estimates of association between independent variables and Dry Socket

Variables	P Value*	Crude OR* (95% C.I.)	P value**	Adjusted OR** (95% C.I.)
Gender				
Male		R		
Female	.555	1.195 (0.661-2.163)	.470	1.254 (.678-.2.318)
Age Groups				
≤ 25		R		
≥26	.396	1.294 (0.714-2.346)	.510	1.231 (0.663-2.285)
Oral Hygiene Status				
Good		R		
Poor	0.002	3.360 (1.574-7.173)	.005	3.064 (1.412-6.647)
Fair	0.036	2.183 (1.054-4.520)	.055	2.065 (0.986-4.329)
Duration				
<30mins		R		
>30mins	0.009	2.215 (1.215-4.038)	0.018	2.097 (1.133-3.881)

*   Simple Logistic Regression
**   Multiple Logistic Regression
OR   Odds ratio
C.I.   Confidence Interval
R   Reference=1.0

Hosmer and Lemshow test suggested that the model is a good fit to the data as p>0.05 (p=.618).

Patient with poor OHS, fair OHS and those with DoP longer than 30 minutes are main determinants of post-operative DS in both simple and multiple logistic regression analyses. The odds of post-operative DS in patients with poor OHS was 3 times higher than those with good OHS with crude odd ratio of 3.36(C.I.:1.574, 7.173) and adjusted odds ratio of 3.064(C.I.:1.412, 6.647). Similarly, patients with fair OHS and DoP longer than 30 minutes were also at higher odds of developing post-operative DS in both simple and multiple logistic regression analyses. Details are given in table 3.

DISCUSSION

Dry socket is a well-established complication of wisdom tooth surgery that causes moderate to severe pain which is usually unresponsive to analgesics.[10,11] The incidence of DS after removal of moderately difficult impacted MTM in our study is 20.4%. Dry socket is significantly associated with OHS and DoP while its association with age groups and gender is statistically not significant. The overall incidence of 20.4% DS reported in this study is comparable to some other studies.[7,12] However this incidence is much higher than many other studies done worldwide.[12-14] This higher incidence of DS in our study can be due to the fact that we included moderately difficult extractions in our study. Some studies reported higher incidence of DS with increasing difficulty and longer duration.[8,12]

In this study we have found a significant relationship of OHS with DS. Similar results were reported by Akinbame and Godspower[15] who noted a significant relation of poor oral hygiene with DS in their study. Other studies also found bad oral health as a risk factor for development of DS.[11,12] Parthasarathi et al[16] in their study found that all cases of DS occurred in patients with poor oral hygiene while patients with good oral hygiene did not report any case of dry socket. Similarly, Peñarrocha et al[17] found that poor OHS was associated with greater post operative pain and required more analgesics as compared to patients with good OHS. Other studies have also reported poor oral hygiene and micro-organism as risk factors for higher incidence of DS.[1,8,9] However, Halabi et al[18] did not find any statistically significant relation between OHS and DS. The higher incidence of DS in patients with poor OHS in our study can be due to the higher number of oral micro-organism found in these patients that may activate fibrinolysis and thus, dry socket. Catellani[19] in his study on bacterial pyrogens postulated that they indirectly activate fibrinolysis. Another reason for higher incidence of DS in these patients may be lack of oral health awareness and motivation to follow the post operative instructions.

In this study the DoP is also significantly associated with DS. Some other studies also reported the association of increase DoP to post extraction DS.[8,10]

However Alwarikat[11] did not find any significant relation of DoP and DS. The higher incidence of DS with longer duration can be due to the increased trauma occurring in lengthy procedures, which results in increased inflammation of alveolar bone and release of direct tissue activators which may cause fibrinolysis and dry socket as proposed by Birn.[5]

In this study we have not found a significant association of age groups with DS. Similar results were reported by other authors who found no significant relation of DS to age.[7,9,10] However, Osunde et al[14] and Haraji and Rakhshan[20] found age as a significant factor and concluded that younger age lowers the risk of DS. Gbotolorun et al[21], on the other hand, found a higher incidence of DS in 25 years and below age group. Other authors have reported the 3rd decade as most common age group for DS.[8,13]

The study does not reveal any significant difference in the incidence of DS based on gender. Other studies around the world reported similar results.[4,8-10] This is in contrast to many other studies which found female gender as a risk factor for development of DS.[11,18,22] They attributed the higher incidence of DS in their studies to the use of OCP among female patients and the hormonal fluctuation in different phases of menstrual cycle during which the procedure is carried out. However, in our study we excluded female patients taking oral contraceptives. The limitation of this study is that we selected moderately difficult cases on the basis of Pederson score 4-7 to nullify the confounding effect of surgical difficulty, however, the difficulty within this score can vary greatly as there are other multiple factors influencing the surgical difficulty. Further studies with bigger sample sizes and more effective control of surgical difficulty and other confounding factors are needed to evaluate the association of OHS and DS.

CONCLUSION

This study reveals that patients with poor and fair OHS undergoing MTM surgeries are more likely to develop DS post operatively. Dry socket also developed more commonly after lengthy procedures. The incidence of DS is not affected by age and gender of the patients.

Recommendations: On the basis of this study we recommend that in patients with poor and fair OHS, optimal OHS should be attained before carrying out MTM surgery, wherever possible. Furthermore in patients with poor and fair OHS, and in those where DoP exceeds 30 minutes, strong consideration should be given to preventive measures such as pre-operative rinses and post-operative medicated dressing of the extraction socket.

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Original Article

Experience of Kangaroo Mother Care (KMC) at Children Hospital Chandka Medical College (SMBB Medical University Larkana

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ABSTRACT

Objective: To determine the effectiveness of kangaroo mother care in low birth weight infants at Larkana Children's Hospital.
Study Design: Descriptive, cross-sectional study
Place and Duration of Study: This study was conducted at the Kangaroo mother care unit, Children hospital CMC Larkana from 01.08.2021 to 25.02.2022.
Materials and Methods: Total of 490 newborns were included in the study, mostly of infants were registered in first week of life, participation of male 55% is more than female 45%. According to gestational age 56% infants were term and 40 percent were preterm, while 54% were below 1500g and 29% below 2000gms. All infants were on exclusive breast feeding.
Results: Average days required to start weight gain were 3.2 days Average weight gain per day were 33.4 grams per day. Average stay in KMC ward was 7.1 days.
Conclusion: KMC is a low-cost, safe strategy that has been demonstrated to reduce the length of stay in the hospital for preterm and/or low-birth-weight infants.
Key Words: Experience, KMC, Children, College, Larkana

INTRODUCTION

Kangaroo mother care is a type of preterm / low birth weight newborn care in which the infant is propped up against the parent's chest to allow for early skin-to-skin contact. Kangaroo mother care (KMC) is a compassionate, low-cost method of caring for premature or low-birth-weight infants that may be started as soon as feasible and finished quickly both in the hospital and at home once the baby is discharged.

Because of overpopulation and a lack of resources in his country's hospitals, researcher founded KMC in 1978 in Bogota, Columbia, as a simple and low-cost

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alternative to the conventional incubator treatment for low birth weight children. It has subsequently been proven that the KMC treatment does not raise the risk of preterm infant death from a physiological standpoint. In many low-income countries, including Pakistan, despite the benefits of KMC, it is still not a frequently used way of care for all LBW newborns.[1-3] The fundamental cause for this is a lack of understanding about how to execute existing cost-effective intervention programmes in low-resource settings.[4-6] Thermal care, exclusive breastfeeding support, and early detection and response to complications are the three main components of KMC. The benefits of KMC go beyond the hospitalization time; it also has a long-term good influence on weight growth by allowing for thermal management and healthy breast feeding.[7-9]

There are 2 types of KMC, continuous KMC, skin-to-skin contact practiced for 24 hours and intermittent KMC, and contact for shorter periods. The birth weight of a newborn is a sensitive indicator and key factor for neonatal death. Low birth weight (less than 2500 grames irrespective of gestational age) is a significant predictor of newborn mortality and morbidity. In respects of safety, thermal management, morbidity, mortality, as well as development, KMC is regarded equal to standard treatment. In extremely low birth

weight and preterm newborns, it appears to increase the humanization of baby care and facilitate mother-child bonding.[10-12] In Pakistan, the prevalence of LBW babies has been reported as 19-30% in various studies.[13] In Ghana when KMC was started, LBW rate ranged from 9.1% to 16%. KMC resulted in 66% reduction in serious neonatal morbidity and as a result, it was selected as one of the greatest solution of the problems with high infant death rates.[14-15] In low-income countries, like Pakistan where the neonatal mortality rate is very high (49/1000 live births), particularly in rural areas, where most of the births are unattended and neonatal intensive care is virtually unavailable.

Despite being thoroughly proved as a low-cost and efficient solution to the lack of thermal protection, which is still one of the biggest issues encountered by developing nations for newborn survival, kangaroo mother care is still inadequate.[16-20] On KMC, international literature is readily available, but local literature is scarce. As we belong to a genetically and geographically different population and a large number of the population belongs to poor socioeconomic status. So proper implementation of KMC requires a locally conducted study to practice in our community.

MATERIALS AND METHODS

Descriptive sectional study carried out at Kangaroo mother care unit, CMC Children hospital Larkana.

Kangaroo Mother Care: KMC involves skin-to-skin contact in a strictly vertical posture between the mother and the newborn. The baby will be placed between the mother's breasts and hidden behind her garments.

Low-birth-weight infants, regardless of gestational age, have a birth weight of less than 2500g (less than 2499g).

Neonates: A newborn baby aged 0 to 28 days is referred to as a neonate.

Efficacy: A patient's efficacy will be labeled as positive if they gain at least 15 grammes per kilogramme per day for three days after receiving kangaroo mother care.

Sample Size: In study, 345 sample size has been analyzed by taking WHO Sample size calculator, with the efficacy of KMC, is 66%[14], according to the following formula. But sample size were taken. However, the sample size was considered.490 infants in study.

SS= Z2 $\times$ (p) $\times$ (1-p)

SS = 345

Sampling Method: Consecutive sampling method (Non-probability)

Selection Criteria:

Inclusion Criteria:

● Age from 0 hours to 28 days.

● Newborns of both gender.

● Gestational age (30weeks to 36 weeks).

● All stable LBW newborn (1500 grams to 2499 grams).

Exclusion Criteria: Critically ill babies (Ischemic encephalopathy, CNS impairment, neonatal sepsis, UTI, or one of the twins) that are confirmed via detailed history & relevant investigations.

● Mothers/Caregivers of newborn LBW babies not willing to do KMC.

Data Collection Procedure: Cross sectional study conducted at Kangaroo mother care ward, CMC Children tertiary hospital, Larkana. In current study, total 490 consenting infants were selected regarding inclusion criteria, prior the starting of study, the ethical review approval was taken from ERC Committee of CMC SMBB Medical University Larkana. Data of all study participants was collected on a pre-designed study Proforma. The demographic data was collected including Postnatal age (In days), gestational age (in weeks,) gender and weight on admission. Exclusion criteria will be followed strictly to avoid confounding variables.

The position of Kangaroo mother care was conveyed to the participants in the research. In the Kangaroo mother care position, when they were naked and just wore a diaper and cap, mothers and babies were placed in a straight position between the mother's breasts and supported by a cloth bag or gown.

Weight was measured with an electronic weighing scale daily in the morning and final weight on the day of discharge was also be recorded and weight gain was taken as the effectiveness of kangaroo mother care.

Statistical Analysis: SPSS version 23 was used to enter and analyse all of the data. For categorical factors such child sex, domicile, and effectiveness, percentage and frequency were determined. For quantitative factors like age and weight, the mean and standard deviation were determined. Stratification was used to manage effect modifiers such as the child's age and gender. The ChiSquare test was used after stratification. The significance level was set at P<0.05.

RESULTS

Total of 490 newborns were included in the study. Most of infants were registered in first week of life 269(56.93%), and after the 1st week 211(43.07%), among them 45 percent were female and 55 percent were males (Table-1). In study, regarding gestational age, 56 percent infants were term, 40 percent were preterm and post term 00 percent (Table-1) whereas regarding the weight at the time of admission were categorized in four groups, 54 percent were below 1500g and 29 percent below 2000gms and below 2500 and 1000g weighted infants showed 00 % and 00% respectively. (Table-1). In study the frequency of infant feeding during the admission was observed that majority of infants on mother breast feeding 396(80.81%) and 94(19.19%) infants feeding was human donor milk plus mother milk. Average days required to start weight gain were 3.2 days, while

preterm age infants start gain weight minimum on 3rd day and average took 04 days, whereas term and post term infants were started gain weight on 2nd day minimum and 03 days were taken averagely.(Table-2)

Average weight gains per day were 33.4 grams per day, the majority averagely weight gain was observed among post term neonates 34.5 grams, while term and pre term showed and an 34grams and 32.5 grams respectively. In study, infants were stayed average 7.1 days at Kangaroo Mother Care ward, more stayed seemed in preterm infants. (Table-3).

Table No.1: Frequency of demographic and other variables N=490

Variable		NO	%
Age	<7 day	279	56.93%
	>7 day	211	43.07%
Sex	Male	269	54.89%
	Female	221	45.11%
Weight	<1000gm	11	02.25%
	<1500gm	217	44.28%
	<2000gm	203	41.42%
	<2500gm	59	12.05%
Gestational age	Preterm	196	40.00%
	Term	290	59.18%
	Post Term	04	00.82%

Table No.2: Average duration in days when weight gain started N=490

Gestational age	Minimum	Maximum	Average
Preterm (N=290)	03 Days	05 Days	04 Days
Term (N =196)	02 Days	04 Days	03 Days
Post Term (N=4)	02 Days	04 Days	03 Days

Table No.3: Average weight gain per day N (490)

Gestational age	Minimum	Maximum	Average
Preterm (N=290)	10 grams / day	35 grams per day	32.5grams per day
Term (N =196)	13grams per day	38 grams per day	34 grams per day
Post Term (N=4)	14 grams per day	43 grams per day	34.5grams per day

Table No.4: Duration in days stay in KMC Ward N (490)

Gestational age	Min.	Max.	Average
Preterm (N=290)	05 Days	11 Days	7.5 Days
Term (N =196)	05 Days	09 Days	6.5 Days
Post Term (N=4)	04 Days	08 Days	05 Days

DISCUSSION

Skin-to-skin contact between mother and baby, as well as frequent and exclusive or almost exclusive breast-feeding and early departure from the hospital, is referred to as kangaroo care. In study, weight increase of at least 15 grams per day for three consecutive days was our discharge criterion for LBW neonates, and commencement of weight gain in infants was noted on day three or four. In our investigation, we discovered an average weight increase of 33.4 grams per day, which was higher than the previous studies. Other research had found that KMC infants gained more weight every day on average. KMC groups gained an average of 24 grams, according to Indian study.[21]

Correspondingly, Rajasthan study found that mean weight increase in KMC neonates after the 07 days was 15.9 gm/day, whereas another study found that mean weight gain in KMC babies after the 07 days was 21.3 gm/day.[22,23] Exclusive breastfeeding is supported by KMC, which also helps to regulate body temperature and lowers baby morbidity.[25] According to another study, the average length of stay in the hospital was 15.5 days.[22]

KMC also discharged newborns 13.4 days after enrolment in Merida stud.[24] The average hospital stay in Delhi, according to studies, was 27.27% days.[23] In our current study, the average length of stay in the hospital was 7.1 days. With the support of human milk donors, all babies in our study were exclusively nursed by their mothers.

CONCLUSION

In our set up, we conclude that KMC is a helpful strategy of caring for LBW babies in terms of early weight growth. Other benefits of KMC include its low cost, promotion of exclusive breast feeding, increased mothers' confidence in handling young newborns, and the development of healthy mother-infant bonding. As a result, we propose it to the developing world, particularly Pakistan.

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Original Article

Diagnostic Utility of Immunohistochemical Expression of Calretinin in Hirschsprung's Disease

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ABSTRACT

Objective: To identify the ganglionic cells in colonic and rectal biopsies by Calretinin immunostain.

Study Design: Experimental and retrospective study

Place and Duration of Study: This study was conducted at the Life care Molecular & PCR Lab Services, Karachi from January 2019 to December 2021.

Materials and Methods: 100 large intestinal biopsy specimens of 50 patients were collected at Life Care Molecular Lab (between 2019-2021) for confirmation of Hirschsprung's disease and were evaluated with both routine H&E stain and immunohistochemistry using Calretinin.

Results: Children having age from 5 days to 8 years and Male: Female ratio 3:1. 32 cases out of 50 have Hirschprung disease and 16 cases without Hirschprung disease. Haematoxylin and Eosin stain showed false positive results in 25 out of 100 biopsies and 15 cases out of 50. Calretinin showed 100% accuracy in all 100 biopsies studied. Both specificity and accuracy of Calretinin was 92% while H&E showed only 83% and 92% respectively.

Conclusion: Diagnosis of Hirschsprung's disease on H&E alone may give false positive result resulting in wrong diagnosis and mismanagement. H&E combined with calretinin within aganglionic segment help to eliminate false positive findings during histological examination of specimens for this disease.

Key Words: Ganglionic Cells colonic, Rectal Biopsies, Calretinin immunostain.

INTRODUCTION

Hirschprung disease (HD) or congenital aganglionosis involves the hindgut and is caused by failure of migration, imbalanced proliferation and differentiation of tissue ganglionic crest cells due to which meissner's and myenteric plexuses shows absence of parasympathetic ganglion cells. On an average every 1 out of 5000 live birth showed Hirschsprung's disease with male predominance. Infants suffering from this disease are present initially with delay of meconium

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passage, abdominal distension and later on vomiting and constipation. Aganglionosis primarily starts from rectum, but later on more proximal areas get involved. On surgically resented specimens three zones are seen in most of the cases like aganglionic zone with constriction, and hypertrophied and dilated zone. A third transition zone, lies at the junction of aganglionic segment and the proximal normal bowel.[1,2,3]

Although the diagnostic criteria of this disease consists of clinical features and radiological findings but the definitive diagnosis and ultimately surgical resection depends entirely on histopathological examination of large intestinal biopsies for ganglion cells. However, reporting of absence of ganglion on routine hematoxylin-eosin is often misleading and difficult as it requires multiple serial sectioning and there is always a possibility of sampling tissue from the normal intestinal zone resulting in false positive results. Therefore, various Immunohistochemical staining techniques were established to eliminate these false positive results like acetylcholinesterase, PGP 9.5, S-100, synaptophysin and many more. Since these techniques are performed on frozen sections along with special handling which makes them difficult to perform.[4,5] Recently, calretinin as an immunohistochemical supplement tool with H&E is introduced for the diagnoses of HD. Calretinin is a 29 kD vit-D dependent calcium binding protein and is involved in the development and functioning of the central and peripheral nervous system through calcium

signaling pathway. Although, the negative expression of calretinin in the aganglionic segment of bowel was initially described by Barshack et al. in 2004, few studies have been done so far investigating the diagnostic utility of calretinin immunohistochemistry. Calretinin not only shows excellent cytoplasmic and nuclear staining of the ganglion or nerve cells but also stains intrinsic nerve fibers of normal bowel in a fibrillary pattern.[6,7]

MATERIALS AND METHODS

This study was conducted at the Life care Molecular & PCR Lab Services, Karachi from January 2019 to December 2021.

Sample size: An experimental and retrospective study, with 95% confidence level and 5% margin of error. 100 biopsies samples from 50 randomly selected patients with clinical features of Hirschsprung's Disease were collected. H&E and IHC is done on all selected biopsies respectively. 79 out of 100 biopsies showed all layers of intestinal wall i.e., mucosa, submucosa and muscle layer while 21 were partial thickness biopsies comprising of mucosa and submucosa only. (Table 1)

Methodology:
1. Written consent with complete history of all patients was recorded.
2. Radiological examinations and ultrasound reports of abdomen was recorded.
3. Gross as well as histopathological and morphological features of intestinal biopsies was done on slides prepared from paraffin embedded blocks for identification of ganglion cells.
4. At least four to five sections from paraffin block were taken for H&E stain and immunostaining for calretinin.

Inclusion criteria:

Non Hirschsprung's disease;
1. Presence of at least one ganglion cell on routine H&E in biopsy specimen.
2. Immunostaining by calretinin shows positive staining of nucleus and cytoplasm of ganglion cells along with fibrillary expression of nerve bundle in the mucosa and submucosa with upward extensions.

Hirschsprung's disease: Complete absence of ganglions as well as nerve fibers in the biopsy tissue identified by H&E and calretinin immunostain.

RESULTS

Age and sex wise distribution: 19 patients (37.22%) out of 50 were up to 0-1 month age. 16 patients (32.55%) were upto 1 year age and 15 (30.23%) patients were ranges from 1 to 10 years old. M:F ratio is 2.91:1 with 37 (74.42%) out of 50 patients were male and 13 (25.58%) were female.

Interpretation of IHC: Histopathological evaluation was done on all 100 biopsies with H&E and

Immunohistochemical staining by calretinin. Negative discrepancy was showed by positive control. 60 biopsies shows negative expression of calretinin indicating lack of ganglions in intestinal biopsy. (Table 3). H&E stain detected 32 cases while calretinin detects 40 cases as ganglion positive with a difference of 8 biopsies. Likewise H&E stain showed 68 cases while calretinin showed 60 cases as ganglion negative with or without hypertrophied nerve. H&E stain indicate 83% specificity, 88% positive predictive value and 92% accuracy. On the other hand IHC expression of calretinin comparatively give more specific results with 100% accuracy. (Table 4)

Table No.1: Site of Biopsies

Biopsy site	No of Bx (100)	%
Rectum	55	55%
Sigmoid colon	12	12%
Descending colon	8	8%
Transverse colon	8	8%
Ascending colon	5	5%
Transition zone	3	3%
Colostomy	8	8%
Ileum	1	1%
Total	100	100%

Table No.2: Classification of Cases (50)

Stain	HD	Isolated hypoganglionosis	Non HD
Calretinin	32	2	16
H&E	40	0	10

Table No.3: Discrepant result between H&E and calretinin (no of Bx 100)

	H&E stain	Calretinin
Ganglion positive	32	40
Ganglion negative with or without hypertrophied nerve	68	60

Table No.4: Predictive value & Sensitivity/ Specificity of IHC evaluation

Indicators	Definition	H&E Stain	Calretinin
No of Bx		100	100
Sensitivity	Tp/(Tp+FN)	60/(60+0):100 %	60/(60+0): 100%
Specificity	TN/(TN+FP)	40/(40+8):83 %	40/(40+0): 100%
Positive predictive value	TP/(TP+FP)	60/(60+8):88 %	60/(60+0): 100%
Negative predictive value	TN/ (TN+FN)	40/ (40+0): 100%	40/(40+0): 100%
Accuracy	(TP+TN)/TP +TN+FP=FN	(60+40)/60+ 40+8+0:92%	(60+40)/60+ 40+0+0: 100%
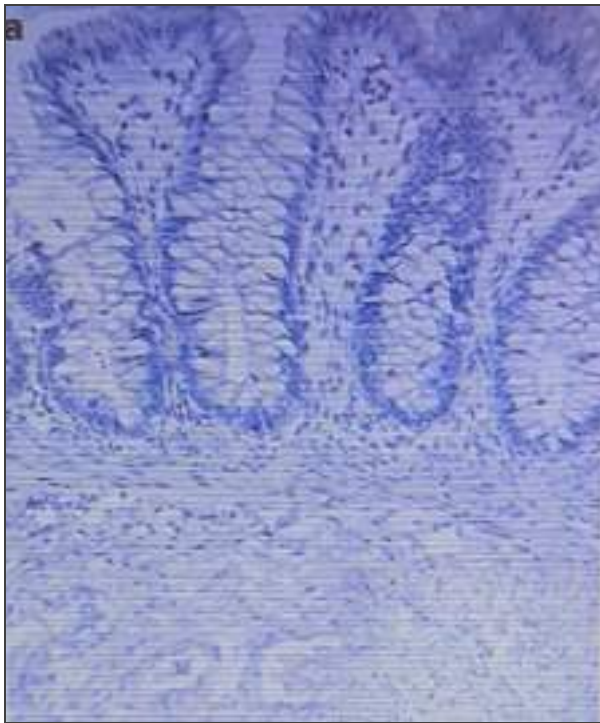
Figure No.1: Calretinin Negative (HD)
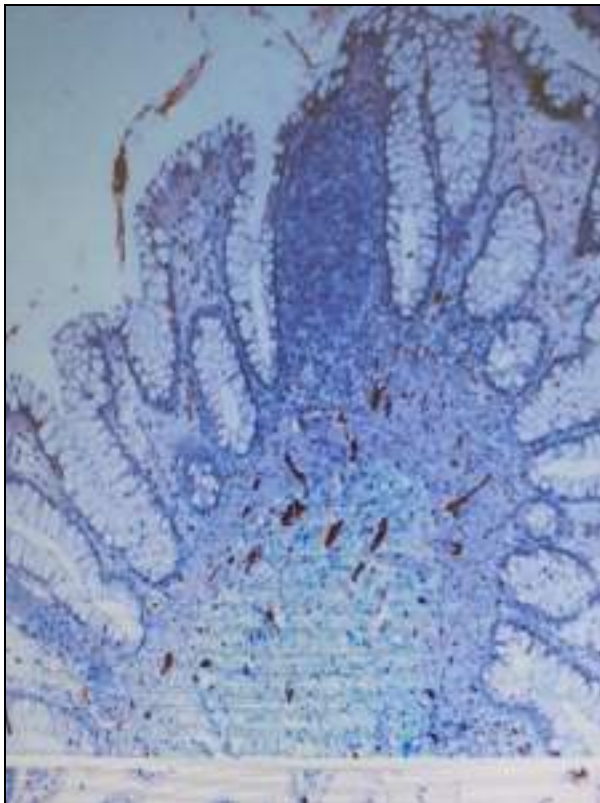
Figure No.2: Calretinin Positive (Non-HD)

DISCUSSION

Hirschprung disease is a birth disorder showing partial or complete absence of nerve cells in large intestine, so there is lack of peristaltic movements in child's intestine resulting in entrapment of stool in intestine. Studies on molecular levels have identified several genes responsible for agangliogenesis of the enteric nervous system.[8,9,10]

Figure No.3: Calretinin Negative (HD)

Hirschprung disease is a complex multifactorial disorder with no obvious and defined environmental factors. Genetic analysis have shown simultaneous involvement of several genes in concordance with the varying extension of aganglionic segment. Autosomal dominant and autosomal recessive patterns along with incomplete penetrance in HD variants have been found. Familial as well as sporadic cases are caused by those genes which are involved in signaling pathways. Thus, HD is proved to be a complex multigenic disorder and the role of different genes has been explained.[11,12]

Diagnosis of HD by conventional H&E is still a diagnostic technique for HD in many centers although it has many limitations particularly for those histopathologist which have less interaction with this disease. Several studies have been done so far regarding the combined utility of H&E and IHC for the diagnosis of HD compared with routine H&E. IHC has been proved very beneficial complementary tool to identify nerve and ganglion cells in intestinal tissues. Calretinin, is encoded by the CALB2 gene on human chromosome 8. In humans, calretinin is involved in calcium signaling pathways primarily in whole nervous system, therefore it has very efficient binding ability with ganglions and nerves fibers in enteric nervous system and showed positive fibrillary staining of this nervous fibers as a direct confirmation of presence of ganglionosis.[13,14]

Calretinin immunostain may be used along with H&E for the confirmed diagnosis of Hirschprung disease, since intensity of expression of this immune marker in the ganglions and nerve fibers reflects well with the extent and level of aganglionosis in intestinal tissue as compared to H&E in terms of false positive and false negative results. Further it has a much better sensitivity and specificity compared with H&E.

Our study showed very comparable results regarding age and sex with other studies like Yadav et al,[15] Anbardar et al,[16]

In our study calretinin showed 100% specificity, positive predictive value and accuracy compared with

H&E which showed specificity 83%, positive predictive value 88% and accuracy 92%. This is in concordance with other studies by Guinard et al,[17] Musa et al,[18] Fakhry et al,[19]

CONCLUSION

Although histopathological evaluation of Hirschsprung's disease by H&E is in routine practice in most of the centers but it has some limitations. The major drawback of H&E is that it requires multiple serial sectioning and repeated biopsies resulting in false positive and false negative results. By our study it is cleared that calretinin provides in time excellent interpretation and identification of ganglion cell in intestinal tissues compared with H&E without unnecessary serial sectioning. Therefore we recommend use of calretinin IHC along with H&E for diagnosis of HD.

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Comparison of 0.25% Bupivacaine with Tramadol Versus 0.125% Bupivacaine with Tramadol in Epidural B Analgesia for Labor Pain

Effect of 0.25% Bupivacaine VS 0.125% Bupivacaine with Tramadol for Labor Pain

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ABSTRACT

Objective: To compare the analgesic effects and effectiveness of 0.25% bupivacaine and % and 0.125% bupivacaine with tramadol in labor patients.

Study Design: A randomized comparative and double blind trial study

Place and Duration of Study: This study was conducted at the Anaesthesiology department, Divisional Headquarters teaching Hospital Mirpur from May 2020 to October 2020.

Materials and Methods: Patients who were undergoing for labor pain was given epidural analgesia and seventy females were divided into two groups (A and B). Patients of group A were given 0.25% bupivacaine with tramadol for epidural block. while patients of group B were given 0.125% bupivacaine with tramadol. Hemodynamic changes and pain score were recorded and then data was analyzed.

Results: Less pain was observed in group A then to group B. Blood pressure also dropped significantly in group A patients (6537%) (p-value <0.001) as compared to patients of group B (17.1%).

Conclusion: 0.25% bupivacaine showed better results and showed greater efficacy than 0.125% bupivacaine with tramadol in the treatment and prevention of painful delivery. This also prevents bradycardia and hypotension in epidurally induced labor.

Key Words: Analgesic effects, Bupivacaine, Tramadol, Caesarean section, Hypotension

INTRODUCTION

Labor is the most excruciating pain experience and even 30% of females find it even more painful then normally expected.[1] There are no general parameters to assess the intensity of the labor pain nonetheless it increased the tendency of cesarean section.[2] Increased pain intensity leads to different physiological and psychological changes including hyperventilation with higher oxygen demand, higher level of catecholamine which results in fetal hypoxia and uteroplacental hypoperfusion.[3]

Women pain experience vary from unbearable pain to moderate level on overall women' assessment of childbirth.[4,5]

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It negatively impact on women' psychological health and wellbeing.[6] Different pharmacological interventions have been proposed for painless labor out of which epidural labor analgesia is considered as golden method of pain-free labor with higher frequency of maternal satisfaction.[3] Bupivacaine is the commonest local anesthesia used during labor. For achieving better and reliable results, various adjuncts have been used in combination with local anesthesia.[3,7]

Many studies proposed tramadol as adjuncts with bupivacaine due to its anti-nociceptive effects. It also has local anesthetic properties that can be achieved by blocking nerve conduction either by inhibition of K-channels 8 or by interacting with calcium receptors. 9 Thus, tramadol in combination with bupivacaine can provide effective and efficient analgesic effect when given epidurally during labor.[10,11]

Present study was designed for the comparison of 0.25% bupivacaine and 0.125% bupivacaine with tramadol for evaluating pain level. Purpose of present study is to provide safer and better experience during epidurally induced labor that is safe both for neonates and mother.

Literature suggests that during elective c-sections an epidural with 0.75 percent ropivacaine with no opioid can be opted as an alternate of bupivacaine in 0.5%

having fentanyl. However, this has no benefit in providing rapid anesthetic effect and could result in denser and further extended motor block. Despite the frequent usage of spinal anesthetic 0.75 percent hyper-baric bupivacaine during cesarean most of the countries have only 1% available, therefore research has compared the two percentages for better optimization in patients with similar demographic histories as well as block onset and found that women who received 0.75% bupivacaine took longer time before complaining pain in post-operative care and lesser complications in comparison to 1% bupivacaine administered cases. Literature also supports the fact that isobaric as well as hyper-baric bupivacaine are highly effective during c-sections as a potent epidural. The post-operative time for analgesic activity is prolonged in intrathecal-morphine which further gets extended with the combination of bupivacaine.

MATERIALS AND METHODS

The present study was a comparative analytical study conducted at Div. HQs Teaching Hospital, Mirpur Azad Jammu & Kashmir within the duration of May 2020, to October 2021. This study was approved through the ethical committee before initialization. A total 70 pregnant women were enrolled as participant of the study after taking their written informed consent. The sample size was calculated through WHO based sample size calculator using 95% confidence interval and 5% margin of error keeping proportion 1 and 2 as 88% and 68%. The patients were further divided into two equal numbered groups each with 50 patients in it. Group A was administered 0.25% Bupivacaine with 5mg /ml tramadol while Group B was given 0.125% bupivacaine with 5mg/ml tramadol. The age of the patients was between 20 to 35 years with I and II ASA status and elected for cesarean. Those patients who were selected for epidural analgesia and were in labor were included in the study while patients having any systematic diseases were excluded from this study. Hartmann's-solution was administered as 15ml per kg weight in both groups' patients. Epidural block was delivered as per protocol with a standard positioning and three minutes wait for antisepsis. The procedure included identification of L4-5 and analgesic administration locally by 2-3ml xylocaine. Eighteen-gauge epidural needle was sued for injecting 0.25% and 0.125% bupivacaine post LOR procedure. Post supine positioning initial bolus dosage with 304cm cervical dilation was given in each group keeping a close monitoring of patient's vitals and pain score. The demographic information of each patient was entered in a well-structured questionnaire. Data was entered in SPSS version 25.0 and analyzed through chi square with a p value <0.05 as significant and also by mean and standard deviations.

RESULTS

The mean age of the patients was 31±4 years in group A while 27±4 years in group B. The mean weight of the group A women was 36±4 kg while of group B was 64±5 kilograms. The epidural in cesarean was indicated due to various scenarios including primigravida in 37.1 and 31.4% women while in 34.2 and 48.6% twin pregnancies and PIH 28.5 and 20% women. Table 1.

Table No.1: Comparison of demographic data of mothers in two groups

Variables	Group A (0.5% hyperbaric bupivacaine)	Group B (0.75% hyperbaric bupivacaine)
Age (years)(Mean ± SD)	31±4	27±4
(Weight (kg) (Mean ±SD)	63±4	64±5
Indication of C-Section n(%)		
Primigravida opted for Epidural	13 (37.1)	11 (31.4)
Twin pregnancy	12 (34.2)	17 (48.6)
PIH	10 (28.5)	7(20)

The baseline parameters as systolic and diastolic blood pressure, baseline HR had no significant variance within both groups with a p value >0.05. Table 2

Table No. 2: Comparison of hemodynamic parameters in two groups (Mean ± SD)

Parameter	Group A (n=35)	Group B (n=35)
Systolic	116±7	118±10
Diastolic	66±13	68±10
Mean	82±12	87±11
Baseline HR	102±12	96±15

P value >0.05

The blood loss was more evident in group A in comparison with the group B however patients had higher complains of nausea in group B than in group A. Table 3.

Table No.3: Comparison clinical parameters of mothers in two groups

Parameter	Group A (n=35)	Group B (n=35)
Group B (n=35)	945±60	960±75
Blood loss (ml)	180±60	150±60
Nausea(N)	2(5.7%)	5(14.2%)

The heart rate was observed at a similar rate within both groups as well as a significant decrease in blood pressure was noticed within both groups. In 17.1% cases where a significant decrease in blood pressure

was observed in group A, 10 mg ephedrine was administered where as in 65.7% of cases from group B received similar 10mg ephedrine due to hypotension. Fig 1.
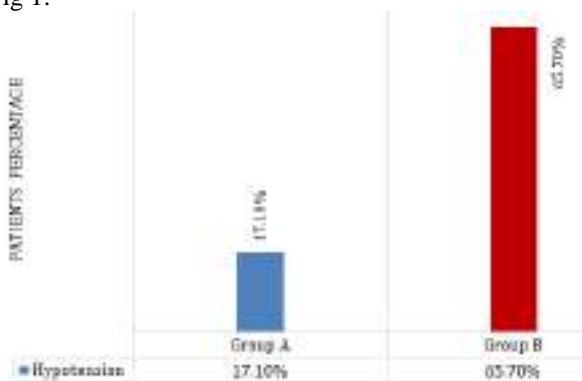
Figure No.1: Comparison of development of hypotension in the groups

DISCUSSION

In present study, 0.25% bupivacaine and 0.125% bupivacaine with tramadol was epidurally administered for better experience and painless delivery. Same dose of bupivacaine was administered in each participant regardless of their heights as studies proposed that, there is no effect of height on the amount of dose. Less incidence of adverse effects was observed with 0.125% bupivacaine. Significant positive effects were achieved with 0.25% bupivacaine in contrast to 0.125% bupivacaine.[12,13]

In present study, SBP significantly dropped after 0.25% bupivacaine administration in patients. Similar has been reported in somewhere else.[14,15] Heart rate was also not significantly dropped in any of the group. In current study, blood loss and nausea/vomiting was also noted in both the groups. Nausea was observed in 5.7% of the group A participants whereas 14.2% of group B participants. Results of other studies demonstrated upto 60% of vomiting/nausea rate after bupivacaine administration.[16,17]

Tramadol has been extensively used for epidurally induced labor that can be given through intramuscular[18,19] or intravenous routes 20. It gives satisfactory results without causing respiratory depressant effect and was safe both for fetus and mother. Incidence of maternal satisfaction was also analyzed. Excellent maternal satisfaction was observed through study participants. This study gives comparative analysis of dosage use for better labor outcomes and 0.25% bupivacaine with tramadol gave good results as compared to 0.125% bupivacaine.

CONCLUSION

Significant difference in pain scores and hemodynamic parameters between both the groups was observed. 0.25% bupivacaine with tramadol showed more effective results during analgesic labor in contrast to 0.125% bupivacaine in combination with tramadol.

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Original Article

Tap Block VS Port-Site Infiltration of Local Anasthesia in Laparoscopic Cholecystectomy; Our Experience in Qazi Hussain Ahmed Medical Complex, Nowshera

Kamran Hakeem Khan, Fazal Ghani, Muddasar Shahzad, Shahid Khan, Waseem Yar Khan and Zahid Khan

ABSTRACT

Objective: To compare the efficacy of ultrasound guided bilateral sub-costal transversus abdominis plane (TAP) block versus port infiltration of bupivacaine for treating post operative analgesia.

Study Design: cross sectional study

Place and Duration of Study: This study was conducted at the Qazi Hussain Ahmed Medical Complex Nowshera from February 2017 to November 2021.

Materials and Methods: All the patients undergoing elective laparoscopic cholecystectomy admitted to the surgical unit were included. Patients were divided into two groups, one group received ultrasound guided bilateral sub-costal TAP block (T) while other group had port site infiltration (I) with bupivacaine at the end of the surgery. Tramadol and diclofenac injectable were used as the postoperative analgesics if needed. Numerical Rating Scale (NRS) was used for pain assessment. NRS at 1 hr to 24 hr at different intervals after surgery, time to first analgesic request and total dose of analgesics in 24 h were recorded. Chi- square test and independent t-test were used for qualitative and quantitative variables respectively.

Results: A total of 500 patients were included and divided into two groups. Time needed to use first analgesic in Group I and Group T was 312 ± 45.03 and 613 ± 135.25 min and mean tramadol required was 125 ± 40.03 mg and 43 ± 16.09 mg, respectively ($P = 0.001$). Calculated mean NRS at different intervals between 1hr and 24 hr was significantly lower in Group T as compared to group I.

Conclusion: In the management of post Op pain, bilateral subcostal TAP block was found superior in controlling pain after laparoscopic cholecystectomy procedure.

Key Words: Tramadol, Laparoscopic Cholecystectomy, NRS, Transversus Abdominis Plane Block, Port Site Block

INTRODUCTION

Laparoscopic cholecystectomy is an efficient and safe procedure for symptomatic gall stones. This procedure has its own advantages like quick recovery, less pain resulting in early hospital discharge as compared to open procedure.[1,3] Although this procedure is minimally invasive, patients can still experience pain post-operatively in early hours.[4]

To control this pain, different methods are used. One of the procedures is subcostal transversus abdominis plane (TAP) block which provides sensory block of the thoracic nerves under ultrasound.[5] Another procedure is Port-site infiltration with local anesthetics.[6] This procedure has gained popularity recently for post op pain control. The transversus abdominis plane (TAP) block has shown to reduce perioperative opioid use in elective abdominal surgery.[6] It has also been found to be more efficient in providing analgesia below the umbilicus.[7] In one study it was used for postoperative analgesia following laparoscopic cholecystectomy, the port sites were moved to facilitate the regional distribution of the block.[7] However, literature on their comparison in Pakistani population is scarce.

MATERIALS AND METHODS

This cross sectional comparative clinical trial done in Qazi Hussain Ahmed Medical Complex form February 2017 to November 2021. The study included patients booked for non-emergency laparoscopic cholecystectomy and admitted in the surgical unit. Ethical approval was taken from the hospital ethical committee.

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This study included patients with age range of 18 to 70 years, who were scheduled for elective laparoscopic cholecystectomy. Patients were divided into two groups. Group 1 received ultrasound guided bilateral sub-costal TAP block (T) while other group had port site infiltration (I) post operatively. Per protocol informed consent was registered for each patient. Patients with allergy to local anesthetics, infection, dependency on opioid medication and patients receiving analgesic in 24 hr before surgery were excluded.

Patients were guided regarding NRS. During surgery paracetamol 1 g intravenous was given. For Post-operative analgesics were given with either port site infiltration or ultrasound guided bilateral subcostal TAP block. Ultrasound guided subcostal TAP block was done under guidance of experienced anesthesiologist using 0.25% bupivacaine.

Tramadol and diclofenac injectable were given as analgesia after procedure if needed by the patients. NRS for pain was assessed at intervals between 1 hr and 24 hr of surgery. Analgesics were given for NRS ≥4 or to comfort patient from pain. Time noted for the first analgesic request by the patient and NRS was noted at the same time if it was ≥4.

Statistical Package for the Social Sciences for Windows (SPSS Inc., Chicago) version 22 was used for data analysis. Qualitative data such as gender and adverse effects were compared with Chi-square test while quantitative data such as age, BMI, numeric rating scales, time to first analgesic request were compared using *t*-test. $P < 0.05$ was taken as statistically significant.

RESULTS

About 500 patients were involved in the study divided in two groups of 250 each. Time of request for analgesic in Group I and Group T was 312 ± 45.03 and 613 ± 135.25 min and mean tramadol required was 125 ± 40.03 mg and 43 ± 16.09 mg, respectively ($P = 0.001$). Mean NRS recorded between 1 hr and 24 hr at intervals was significantly lower in Group T as compared to I. Groups were comparable in demographic variables (Table 1).Mean age of patients in group T was 56+2.03 years while in group I was 54+3.01 years. Regarding use of analgesics, the mean dose of first analgesic (tramadol) was 125 ± 40.03 mg in Group I and 43 ± 16.09 mg in Group T (*P<0.05*). About 25 patients in in Group I were given another dose of analgesic diclofenac but only 5 patients required it in Group T. The time to requirement of analgesia was 312 ± 45.03 min in Group I and 613 ± 135.25 min in Group T (*P<0.05*). The mean NRS at first analgesic request was 7.16 ± 0.58 in Group I and 3.12 ± 0.59 in Group T (*P <0.05*). There was no significant difference in NRS for pain at 1 h between groups. The mean NRS at different intervals in Group I

and Group T are presented in Table 2. The results are consistent with lower NSR for Group T as compared to Group T excluding NSR at 1 Hr ($P < 0.05$).

Table No.1: Demographic variable of study populations (n=500)

Variable	Groups	Mean $\pm$ SD	P Value
Age	Group I	56+2.03 years	0.72
	Group T	54+3.01 years	
Weight	Group I	70.50±2.29	0.62
	Group T	72.84±3.06	
Height	Group I	162.85±5.48	0.49
	Group T	160.13±6.69	
BMI	Group I	23.09±3.20	0.23
	Group T	25.33±3.23	

Table No.2: Comparison of numerical rating scale in study population (n= 500)

NRS (Time)	Groups	Mean $\pm$ SD	P Value
NRS 1	Group I	0.00±0.00	-
	Group T	0.00±0.00	
NRS 2	Group I	0.20±0.46	0.004
	Group T	0.02±0.10	
NRS 3	Group I	3.05±0.76	0.001
	Group T	0.32±0.45	
NRS 6	Group I	2.10±1.00	0.002
	Group T	1.54±0.60	
NRS 12	Group I	3.48±0.72	0.001
	Group T	0.73±0.66	
NRS 24	Group I	2.55±0.39	0.001
	Group T	1.02±0.32	

DISCUSSION

Cholecystectomy is one of the most common surgical procedure done for various types of gall bladder conditions, mostly gall stones. Patients usually feel post-surgical pain which not only affects the physiology but also causes chronic pain.[8] For this very reason effective pain control with the help of local anesthetics is recommended. Different analgesic techniques are used but the most popular ones are "port site infiltration" and "TAP block".[9,11] In this study, we compared these two methods for pain control post operatively. The classic approach was through the lumbar triangle of petit.[12, 13] TAP block is a popular way but it causes some complications which resulted in introduction of ultrasound usage in regional anesthesia for clear demarcation of the anatomy and safety with effective infiltration of local anesthesia .[14,15]

In our study we used subcostal TAP block with ultrasound use for post operative pain control. 0.5% bupivacaine was used. A smaller concentration (0.25%) of bupivacaine was used in our study to avoid adverse effects.[16]

Our study had 500 subjects with 250 received port site infiltration (Group I) and 250 received USG guided bilateral sub costal TAP block (Group T). We observed not significant NRS after 1 hr of surgery in both groups, advocating equal efficacy of port site infiltration and TAP block but it was significantly lower for Group T as compared to Group I after 1 hr. The NRS at first analgesic request was more in Group I as compared to Group T. The same results were shown in two studies with mean pain scores at 1 h and 4 h less in TAP block as compared to port site infiltration after laparoscopic cholecystectomy.[9,17]

The duration of effect of analgesia was 312 ± 45.03 min in Group I and 613 ± 135.25 min in Group T. The slow absorption of the drug may be due to low vascularity of the site. "Mean tramadol requirement was higher in Group I than in Group T suggesting a good pain control with TAP as compare to infiltrative technique." This fact is also proved by other studies as well.[9,17] In one of the retrospective study, 51 patients underwent laparoscopic cholecystectomy, were analyzed for post operative pain scores and post operative fentanyl requirement influencing the cost for the post operative technique.[17] But no significant difference in pain scores was observed. However in this study ropivacaine was used without using ultrasound guidance, which may be the cause of such results. Similar contradictory results were found in another study, but in this study severity of the pain was not assessed.[18] This study also used 0.5% ropivacaine without ultrasound use for the block.

CONCLUSION

It is clear that USG guided TAP block is more effective as compared to conventional approach for post-operative analgesia post laparoscopic procedures, complimented by low pain scores and longer analgesic duration with reduced medication dose.

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Association of Age, Gender, and Duration of Illness with Hepatic Dysfunction in Patients with Malaria

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ABSTRACT

Objective: To determine the association between age, gender, and duration of illness with hepatic dysfunction in patients with malaria.

Study Design: Observational / cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Medicine in Baqai Medical University Fatima Hospital, Karachi from February to July 2021.

Materials and Methods: A non-probability consecutive sampling technique was used to collect data. A sample of 255 is taken by using Open Epi software with age of patient's ranges from 25-65 years with either gender. Patients with having fever >1040F for more than four days with chills and rigors and positive Malarial parasite tests were included. Patients with liver cirrhosis, and unexplained hepatomegaly were excluded. The blood samples were collected and sent to the pathology laboratory for biochemical analysis. Data were entered and analyzed in SPSS version 16.0. Mean and standard deviations were calculated for the quantitative variables (like age of the patient and duration of illness). Frequencies and percentages were calculated for the qualitative variables (gender, age groups, duration categories, and hepatic dysfunction).

Results: A total of 255 diagnosed patients of malarial infection with a mean age of 38.87 ± 9.94 years were included. There were 185 (72.5%) males and 70 (27.5%) females. Hepatic dysfunction was found in 85 (33.3%) patients with malaria. Only duration of illness showed significant association (p<0.03) with hepatic dysfunction, while the different age groups, gender did not showed significant association.

Conclusion: In our study results, only duration of illness showed significant association (p<0.03) with hepatic dysfunction.

Key Words: Hepatic dysfunction, malaria, age

INTRODUCTION

According to World Health Organization's (WHO) World Malaria (infectious disease caused by mosquito) Report 2020, there was an estimate of 229 million diagnosed cases of malaria and 409,000 malarial multi-systemic failure induced deaths reported worldwide in 2019 with an incidence of 57 per 1000 population at risk and a mortality rate of 10 per 100,000 population at risk.[1]

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According to Pakistan Annual Malaria Report 2019, there were 374,513 malaria cases reported during the year with 84% Plasmodium vivax (tertian fever) cases and 15% Plasmodium falciparum cases.[2]. Pertinent to malaria pathology is intravascular hemolysis. Moderate to severe hemolysis (breakdown of red blood cells or erythrocytes) renders a patient susceptible to systemic complications and may result in organ damage or multi organ failure – including kidneys (heamoglobinurea), liver (hepatomegaly, jaundice), spleen (splenomegaly), lungs, vessels, brain (convulsions or cerebrovascular accidents or CVA, altered level of consciousness), blood (hemolytic anemia or Hemoglobinb level <7.0 g/dL, thrombocytopenia or platelets <150,000 /μL) and gastrointestinal tract involvement (vomiting, loose motions).[3] Plasmodium falciparum has more commonly been associated with hepatic dysfunction leading to jaundice (increased bilirubin level above normal; >1 mg/dL) and raised liver enzymes (SGPT or ALT) secondary to intravascular hemolysis or breakdown of red blood cells (erythrocytes). The evidence regarding other mechanisms of liver injury in malaria is also evolving.[4]. These include granuloma formations, cholestasis, malarial pigmentation, and Kupffer cell

hyperplasia.[5] Hyperbilirubinemia is a pathological condition in which serum bilirubin concentration more than 3 mg/dL in plasma, and serum aminotransferase level also increased above thrice in blood or elevated aminotransferases (alanine aminotransferase ALT levels >39 U/L). This condition is considered as liver or hepatic involvement/ hepatopathy in malaria. It is further associated with complications such as shock, acute renal injury or Renal dysfunction in which creatinine i-e >1.5 mg/dL and Blood urea nitrogen i-e >40 mg/d levels, and cerebral malaria.[6] Plasmodium falciparum induced hepatocellular jaundice or malarial hepatitis causes severe illness with higher incidence of complications with poor outcome or poor prognosis. Plasmodium falciparum is associated with cyto-adherence of parasitized red blood cells or erythrocytes (RBCs) to the endothelium of vessels, and platelets induced agglutination. This was observed by Murthy et al. Malarial induced hepatocellular jaundice or hepatopathy in mild cases (flue like symptoms) presents with headache, fever with chills, fatigue or muscle pain and vomiting or abdominal discomfort and this presentation of patients resembles with viral infection or gastroenteritis or sepsis. It was observed in more severe cases, patients can present with jaundice (increased bilirubin level more than 3mg/dl or hyperbilirubenemia), altered level of consciousness (ALOC), and kidney injury. Fever, anemia, jaundice, hepatomegaly, and splenomegaly are core clinical findings in patients. Management is focused primarily on the malarial parasite (according to endemic sensitivity pattern) and hepatitis subsides as the organism clears from the system. These patients are more prone to other systemic complications or various organs failure – hypoglycemia, thrombocytopenia, and renal failure.[6,7.] Literature has reported variable frequencies of hepatic dysfunction in these patients ranging from 32%–37% in adults in one review article.[8]. In a landmark study by Murthy et al., 62% of patients with falciparum malaria had jaundice, and 21% malarial hepatitis.[9] This study aimed to determine the Association of age, gender, and duration of illness with hepatic dysfunction in patients with malaria.

MATERIALS AND METHODS

This study was done at Fatima hospital (medicine department) of baqai Medical University Karachi. It was observational cross-sectional study, from February to July (six months) was duration of study, and the sample size of study was calculated by using Open Epi software version 3.01 taking the margin of error as 5%, confidence level 95%, and estimated prevalence from the literature as 21%, which came out to be 255. [9] Written informed consent was taken from the admitted patients after having permission from the Ethics Committee of Baqai medical university, Karachi with reference no: BMU-EC/01-2021. A non-probability consecutive sampling technique was used to collect data from admitted patients of 25-65 years of age presenting with illness suggesting malaria i.e. having fever >104[0]F for more than four days with chills and rigors and positive Malarial parasite immuno-chromatographic test (MP-ICT). Patients with liver cirrhosis, portal hypertension, unexplained hepatomegaly, ascites , history of alcoholism, history of taking hepatotoxic drugs, history of positive viral markers for hepatitis (A, B, and C), blood film negative for malaria (even if having clinical features of malaria) were excluded. Patients having other causes of deranged liver function tests like dengue, sepsis, liver abscess, typhoid, and leptospirosis were also not taken into consideration. A brief history of the duration of illness was taken. The samples of blood were collected from admitted and enrolled patients with malaria of this study in a sterile manner for liver functions test (serum transaminase and bilirubin levels). The collected samples were sent to the pathology department and laboratory of Fatima hospital for biochemical analysis. The findings of variables were entered in a self-designed proforma and information saved. Patients were diagnosed with having hepatic dysfunction if there is a rise in serum alanine aminotransferase level (ALT) >100 IU and Jaundice or hyperbilirubinemia >3 mg/dL. Patients Age were categorized into groups like 25-35 years, 36-45 years, 46-55 years, and 56-65 years, while the duration of illness was grouped as 5-8 days, 9-12 days, and 13-16 days. The collected data was entered in computer and statistical analysis was done by using SPSS version 16.0® Mean and standard deviations were calculated for the age of the patient and duration of illness (quantitative variables). Frequencies and percentages were calculated for the gender, age in different groups, duration of disease into categories, and hepatic dysfunction (qualitative variables). Stratification according to age groups, gender, and duration of illness to see the effect of these on the outcome variable i.e. hepatic dysfunction. Post-stratification, the chi-square test was applied and a p-value of ≤0.05 was considered as statistically significant, and p-value of >0.05 was considered as statistically non-significant.

RESULTS

A total of 255 diagnosed patients of malarial infection with a mean age of 38.87 ± 9.94 years were included. The mean duration of illness was 7.22 ± 2.55 days. There were 185 (72.5%) males and 70 (27.5%) females as shown in table I. Hepatic dysfunction was found in 85 (33.3%) patients with malaria. When it was assessed according to the age groups, gender, and duration of illness, only the latter came out to be statistically significant (p<0.03). Stratification for gender showed that 57 (30%) of males and 28 (40%) of females developed hepatic dysfunction as shown in table 2.

Distribution according to different age groups and duration of illness is given in Figures 1 and 2.

Table No.I: Demographic profile of the participants.

Variables	Mean	±SD
Age (years)	38.87	±9.94
duration of illness (days)	7.22	± 2.55

Table No.2: Association of age, gender, and duration of illness with hepatic dysfunction in patients with malaria.

Varia-bles	Hepatic (liver) Dysfunction		Total	P-Value
	Yes (with)	No (without)		
Age (in years)				
25-35	39(36%)	69(64%)	108(100%)	
36-45	30(34%)	57(66%)	87(100%)	0.65
46-55	10(26%)	28(74%)	38 (100%)	
56-65	06(27%)	16(73%)	22 (100%)	
Gender				
Male	57(30%)	128(70%)	185(100%)	0.164
Female	28(40%)	42(60%)	70(100%)	
Duration of illness (in days)				
5-8	65(37%)	109(63%)	174(100%)	
9-12	17(30%)	39(70%)	56(100%)	
13-16	03(12%)	22(88%)	25(100%)	

p-value< 0.05-statistically significant
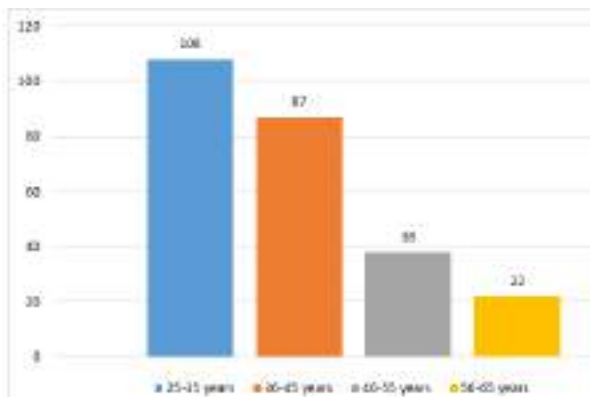
Figure No.1: Distribution according to age groups (n=255)
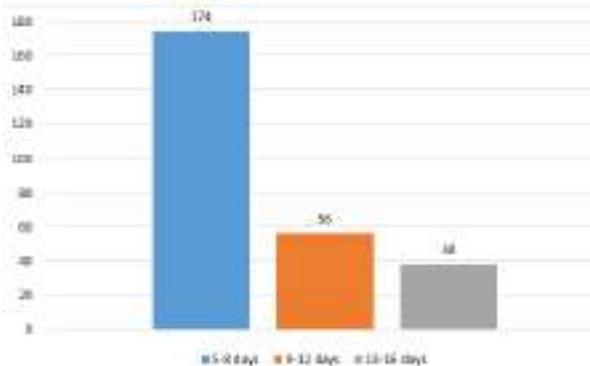
Figure No.2: Distribution according the duration of illness (n=255)

DISCUSSION

Malaria has remained a major public health though out the world and responsible for causing morbidity or mortality in malarial patients, especially in tropical sub-Saharan African and Eastern Mediterranean regions as reported by world health organization (WHO). Even with a substantial focus on preventive and curative programs, malaria still forms a significant chunk of the global infectious disease burden in terms of causing disability and deaths in malarial sufferers. [1] Along with the involvement of other systems, hepatic involvement and hepatic dysfunction are commonly observed in malarial sufferers with moderate to severe malaria with different complications like decreased serum sugar level or hypoglycemia, pH disorder like metabolic disorder, and multi-organ failure (MOF). The severity of malaria can be predicted by parasite species, duration of illness, and time of onset of antimalarial treatment.[10]. Literature pertinent to the incidence of hepatic dysfunction and jaundice in severe malaria is variable owing to the difference in geographic location, age, the status of malarial endemicity, and coexistence with other infections endemic to that region.[11,12] The results of this study indicated that almost one-third of patients (33%) with malarial infection was complicated with hepatic dysfunction. The youngest age group (25-35 years) suffered from hepatic dysfunction most frequently (36%). As far as gender was concerned, 40% of women suffered from hepatic dysfunction as compared to 30% of men. Patients with the shortest duration of illness (5-8 days) suffered from hepatic dysfunction most frequently (37%). Literature has shown extensive evidence of hepatic involvement with malaria falciparum.[13-14] Chawla et al. showed that 45% of patients with malaria had elevated serum bilirubin and 22% had elevated serum transaminases.[13] Anand et al. showed that as many as 33% of their malaria patients had elevated serum bilirubin. [15] Singh et al., in their work, showed 13% of malaria patients with serum transaminases more than thrice of the normal range.[15] Ahsan et al., in their work, showed that 46% developed jaundice and 57% had serum bilirubin severely raised (>10mg/dl).[16] There has been no significant difference in age of patients in terms of hepatic complications in malaria, however, literature has reported cases to be older than controls. As with our study, the gender differences were opposite with more females being diagnosed with malarial hepatopathy. Although the reasons remain unclear, most literature, especially from India, has reported a higher incidence of malarial induced hepatic dysfunction in males as compared to females.[17,18] According to our study results, the age of the patients and gender based comparison did not showed significant (p>0.05) association with hepatic dysfunction (yes or with and without or no Liver function test abnormalities) in patients with malaria.

Like our results, similar findings were observed in study, which is done by I.J. Reuling et al.[10] The pathophysiological basis for hepatic dysfunctioning in malarial patients is due to systemic inflammation (pro-inflammatory response and anti-inflammatory response) in liver hepatocytes, and ultimately injury occurs in liver cells. The oxidative stress is associated with inflammation, and develops liver injury. The inflammatory process and oxidative stress are causing malfunctioning of the host's mitochondria and hepatocyte apoptosis. It plays a vital or potential role in developing (pathogenesis) severe disease due to uncomplicated malaria in liver.[10] The Duration of illness (in days) of the admitted patients showed significant ($p < 0.05$) association with hepatic dysfunction (yes or with and without or no Liver function test abnormalities) in patients with malaria. Like our results, similar findings were observed in study.[19] Hepatic involvement in malaria is a common entity. It may even present in an earlier course of illness. Therefore, it becomes critical to evaluate patients of malaria for hepatic dysfunction even in the early course of illness. Early screening, timely investigations, and interventions are very crucial in ensuring a good disease outcome and for prevention or decrease in mortality rate and multi-organ failure (MOF).[5,19,20] This limitation of this study is single centered study and limited number of admitted patients. It is recommended that study should be multi-centered and number should be increased.

CONCLUSION

In our study results, only duration of illness showed significant association ($p < 0.03$) with hepatic dysfunction. Hepatic dysfunction in malaria is a common complication and as many as one-third of patients may present with it. In malaria-endemic areas, it is essential for managing physicians to consider hepatic complications even in the early course of illness.

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Original Article

Impact of Diabetes Mellitus Type-II on Patient's Quality of Life in Sindh, Pakistan

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ABSTRACT

Objective: To evaluate the impact of type II diabetes mellitus on patient's quality of life visiting tertiary care hospital in Hyderabad, Sindh, Pakistan.

Study Design: Descriptive Cross-sectional study.

Place and Duration of Study: This study was conducted at the Liaquat University Hospital, Hyderabad, from August 2019 to January 2020.

Materials and Methods: A sample size of 168 was obtained and participants were selected by using Non-probability convenient sampling technique and all Patients between the ages 25 years and 40 years, known cases of type2 diabetes mellitus, belongs to either sex, gave consent of participation, visited the outpatient department of diabetes/ medical clinics at Liaquat University Hospital during the study duration were included. Patient's information related to etiological factors of disease and its symptoms was collected using written questionnaire. Quality of life in type-II diabetics was evaluated through a World Health Organization D-39 Questionnaire. Data was analyzed using SPSS version. 23.

Results: Total 168 type -II diabetic patients were included in the study**.** Findings of the study were depicting the mean QoL score of type- II diabetics as 52.1. Score of various domains indicating the QoL in type-II diabetics was classified as 55% in physical, 47% in psychological, 55% in social and 50% in environmental domain of QoL. Overall domain wise scoring revealed an average QoL.

Conclusion: Type-II diabetes significantly affects the quality of life in physical domain along with psychological domain. QoL is badly affected in type-2 diabetic patients. Diabetes has an adverse influence on all the aspects of life in affected patient.

Key Words: Psychological domain, Quality of Life, Type-II diabetes mellitus

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder affected over 422 million people worldwide. Regardless of the efforts of the World Health Organization (WHO) to impede this rise, the prognosis is not very promising that results in skyrocketing of DM related chronicity and complications.[1,2] In Pakistan, prevalence of diabetes is estimated to 6.9% or roughly 7 million populations. While, approximately, 3 million cases supposed undiagnosed that makes DM to be considered as the one of the top and major non communicable disease-causing mortality in the country.[3,4]

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Quality of life (QoL) is considered as an important construct as an individual think according to one's own cultural patterns and customs based on culture related value system, life targets, cultural opportunities and credentials.[5] As a chronic incapacitating illness, it may substantially affect the QoL causing impairment in all physical, social and psychological aspects of patient. Complexities related to Type II DM may result in higher burden of disease related disability that may further posed serious impact on the patient's QoL.[6,7] This QoL of a Type II diabetic may devastated by impairment in their dietary habits and nutritional deficiencies. Moreover, it also has an effect on psychological functioning of patients resulting in disturbing self-concept as well as thinking process. Furthermore, feelings of being a diabetic mentally upset a person resulting in social isolation and poor relations.[8] These malfunctioning are associated with further upsurge in the burden of diabetes linked complications and co-morbidities. This situation demands a need of need to modification of behaviors through a comprehensive management programmers to enhance QoL of diabetic patients.[9] These related effects could be combated by maintaining proper bodily functions, improved self-concept and

better relationships.[8,10] Moreover, to prove the negative consequences related to the QoL among type-II diabetics there is a need to emphasize on its outcomes by health care providers due to increasing rate of its complications. Keeping it in view, the present study was designed with an objective to evaluate the impact of type II diabetes mellitus on the quality of life in patients visiting tertiary care hospital in Liaquat university hospital, Hyderabad, Pakistan.

MATERIALS AND METHODS

A Cross-sectional study was conducted at department of medicine, Liaquat University Hospital, Hyderabad from August 2019 to January 2020. Patients between the ages 25 years and 40 years, diagnosed as having type II diabetes mellitus for over 6 months, belongs to either sex, gave consent of participation, visited the outpatient department of diabetes/ medical clinics at Liaquat University hospital during the study period were included. While patients below and above the age limit (<25 and >40 years), suffering from type 1 diabetes mellitus, pregnant women and those diagnosed for the first time in this visit during the study were excluded from the study. Non-probability convenient sampling technique was used for the selection of participants while sample size was calculated using the formula: N=4pq/L2. By keeping 5% margin of error and considering 15% of non-compliance[6], the total sample size of **168** was drawn. Patient's information related to etiological factors of disease and its symptoms was collected using written questionnaire. Quality of life in type-II diabetics was evaluated through a World Health Organization D-39 Questionnaire. It is a multi-dimensional scale comprised of total 39 questions for assessing the Health-related quality of life (HRQoL) of a type II diabetic patient.[11,12] The D-39 tool comprises of questions about the five different domains linked with diabetic patient's life: 1- Energy and mobility (15 items), Diabetes control (12 items), Anxiety and worry (4 items), Social burden (5 items) and Sexual functioning (3 items). Collected information was entered and analyzed using SPSS ver. 23.

RESULTS

Out of 168 type II diabetic patients, majority participants belonged to the age group 36-40 years followed by participant age group 25-30 years and 30-35 years. Gender wise distribution a male predominance was observed compared with their counterparts. Over half of the participant had a cigarette smoking history while over two third of them don't have any alcohol intake history. History of exercise was very limited among the participants as shown in table 1. The overall score related to QoL of type II diabetic patients was that majority 95(56.6%) reported the low quality of life followed by 55(32.7%) of patients with an average QoL while 18 (10.7%) of patients reported their QoL. There

was a statistically significant difference (p<0.05) in quality of type II diabetic patients. Table 2 is presenting the category based findings of QoL mean scores of type II diabetic patients with general perception of QoL. Higher scores of the five domains were associated with the perception of lower QoL and higher severity of disease.

Table No.1: Demographic details of study participants (n=168)

Demographic Variables	n	%
Age groups (Years)		
25-30	36	21.5
30-35	53	31.5
36-40	79	47.0
Gender		
Male	104	62.0
Female	64	38.0
History of cigarette smoking		
Present	96	57.0
Absent	72	43.0
History of alcohol intake		
Present	21	12.5
Absent	147	87.5
Regular Exercise		
Present	49	27.2
Absent	122	72.6
Family history of diabetes		
Present	50	29.8
Absent	118	70.2

Table No.2: Categories based findings of QoL scores of type 2 diabetic patients with general perception of quality of life (n=168)

Domain	QoL of Diabetic Patients		p-value
	Good	Low	
Diabetes Control	41.8±20.1	54.2±18.7	0.007*
Anxiety & Worry	52.7±23.8	70.2±21.1	0.001*
Social Burden	30.4±17.6	31.8±14.5	0.57
Energy & Mobility	46.8±19.8	60.7±28.5	0.008*
Sexual Functioning	42.8±24.7	64.5±28.3	0.031*

Table No.3: Domain wise type-2 diabetic patient's QoL scoring and perception of disease severity (n=168)

Domain	Perception of disease severity		p value
	High	Low	
Diabetes Control	58.8±18.4	33.1±18.3	0.003*
Anxiety & Worry	68.2±19.8	44.3±22.4	0.000*
Social Burden	28.2±17.8	24.2±11.7	0.001*
Energy & Mobility	61.7±17.4	40.8±29.3	0.001*
Sexual Functioning	50.9±21.3	47.2±29.3	0.352

There was a statistically significant (p<0.05) difference of domain of diabetes scale-39 with the perception of disease severity. Domain wise patient's QoL scoring is mentioned in Table 3. Among study participants gave poor results. In physical domain of QoL, the mean score was very low. There was a statistically significant difference (p<0.05) between the mean domain scoring among patients as shown in Table 3.

DISCUSSION

Type II DM poses a serious impact not only on the patient but also put burden on family as well as effecting the economy of the country. The disease may badly deteriorate the QoL of patients that demands a proper diagnosis and managements of disease for improving the QoL.[13]

Present study was designed with an objective to evaluate the impact of type II DM on the quality of life of patients. Majority (47.0%) participants belonged to the age group 36-40 years followed by participant age group 25-30 years and 30-35 years in this study while a male predominance (62%) was observed compared with their counterparts. Smoking is a big cause for the vascular complications. Research elaborates the concept of diabetic complication on the basis of cigarette smoking. As it is observed that cigarette smoking increases the risk for high blood pressure which interact further to raise the chances for diabetic complications like heart disease and stroke.[6] In this study over half (57.0%) of participants were smokers. Adriaanse et al in 2016 reported high involving (41.6%) of diabetics used to smoke cigarettes. Another important and significant factor for controlling the diabetes is active lifestyle, physical activity/exercise. Exercise had a close relation with diabetes control that improves the insulin levels of body.[14] It has been observed in the present study that only 27.4% type II diabetics do exercise and were physically active. A study conducted to assess the impact of type-II diabetes on QoL showed negative effects. Finding depicted strong relationships in physical and psychological domain as compared to social and environmental in type-II diabetics. Domains of QoL are indirectly related with diabetic complications. As complications increase, QoL decreases.[15-19] Results of study depict considerably low score in environmental domain of QoL which suggest the ill effects of environment on life quality of type II diabetics. Similar results were found in study of Garg et al.[20] Depicting mean score much lower in environment domain than other domains of QoL. In another study, Mahesh V. et al reported the lower scores in environmental domain than other QoL domains.[21] Domain wise QoL among study participants gave poor results, as in physical domain of QoL with a very low mean score with a statistically significant association (p< 0.05). A similar study conducted by Prajapati et al. that presented a domain wise result to show QoL. That study reported a good physical QoL (63%), good psychological QoL (69%), good social QoL (27%) and good environmental QoL (85%).[22] QoL further worsen as complications increase while poor quality of life in all domains showed strong negative effect of type II diabetes on QoL. Score for quality of life in our study was lower in physical domain than reported by others studies.[23,24] Whereas, the findings of present study were consistent with the findings reported by Majeed et al, Prasanth et al[6,25] This study was a single centered study conducted at the public sector hospital due to limited time and resources constrains, so there will be an issue related to generalizability of our findings.

CONCLUSION

The study concludes, that type - II DM significantly affects the QoL of diabetic patients and has an adverse influence on all aspects of patient's life quality. The physical, psychological and social domains of QoL of patients are also significantly affected by the type - II DM.

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

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Original Article

Incidence of Dry Socket in Islam Dental College, Sialkot

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ABSTRACT

Objective: To find the incidence of dry socket among tooth extraction cases operated in Islam Dental College Sialkot.

Study Design: Retrospective study

Place and Duration of Study: This study was conducted at the Oral and maxillofacial surgery department of Islam Dental College Sialkot from 1st January 2020 to 31st December 2021.

Materials and Methods: Patient records of extraction and follow up from last two years were assessed and incidence of dry socket was calculated. The various factors like gender, mode of extraction and post operative use of antibiotic was also assessed using statistical analysis.

Results: Out of 940 patients, 52 patients were diagnosed with dry socket and managed post-operatively. Surgical extraction had higher incidence (21.7%) than simple extraction (4.2%).

Conclusion: The incidence of dry socket after surgical extraction, female patients and smokers is relatively higher incidence of dry socket whereas the patients who took antibiotics post-operatively had less chances of developing this complication.

Key Words: Dry socket, surgical extraction, smoker patients.

INTRODUCTION

Dental extraction is one of the most common procedures performed in dental clinic worldwide[1].Dry Socket or Alveolar osteitis (AO) is one of the most common post extraction complication. It is also referred as necrotic socket, Alveolitis, Sicca Dolorosa or localized osteitis. It is characterized by severe pain in and around the extraction socket whose severity increases from 1st to 3rd day after extraction accompanied by total or partial loss of blood clot with food debris in the socket[2]. Clinically there may be mild swelling, redness of the gingival tissue, halitosis, bone exposure with severe tenderness on palpation. In case of dry socket, pain increases on the 3rd postoperative day and continue throughout the week. Though it is a self-limiting condition, but causes lot of problem for the patient[3].

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The incidence of dry socket mentioned in literature ranges from 0.5 to 5.6% after simple extraction and up to 30% following surgical extraction [4-6.] Associated risk factors are traumatic, difficult and prolonged extraction, pre and postoperative infection, smoking, oral contraceptives, bone disorders and underlying pathologies, irradiation, systemic illness such as diabetes mellitus, clotting problems, and failure to comply with post extraction instructions. However exact cause of dry socket is still not clear[7-9].

MATERIALS AND METHODS

The clinical record of the patients who had undergone extraction in our department, was evaluated from 1st January 2020 to 31st December 2021. The patient's age was from 16 and above. The patients were labeled as cases of dry socket that presented to our department in follow-up with complaint of pain that increased 2 to 3 days after tooth extraction, having exposed sockets and were managed with application of intra-alveolar dressing.

RESULTS

Total of 940 patients were included in the study, out of which 1012 extractions were performed on patients with age ranges from 18 to 85 years. Out of which 74 patients had undergone surgical extractions. The gender distribution was 58.3% (n=548) female whereas 41.7% (n=392) were male with ratio 1.3:1.

The antibiotics were prescribed in 48% (n=450) of the patient postoperatively. 13.5% (n=127) of the patients were smoker or smokeless tobacco user. The incidence of dry socket after simple extraction was4.2% (n=36). While in surgical extraction, 21.7% (n=16)cases of dry socket were reported. The collective incidence of dry socket in our center was 5.5%(n=52). Dry socket was reported 4.3%(n=17) in male patients whereas in females it was 6.3%(n=35).13.5%(n=127) patients were smoker with 8.7%(n=11) dry socket rate while 86.4%(n=813) nonsmokers' patients had comparatively less incidence of dry socket which was 5.0%(n=41).

Table No.1: Gender distribution and dry socket percentage

Gender	Patients	Dry socket
Male	41.71% (n= 392)	4.3% (n=17)
Female	58.3% (n= 548)	6.3% (n=35)
Total	N= 940	N=52

Table No.2: Relation of dry socket and smoking

Patients	Percentage	Dry Socket
Smokers	13.5% (n=127)	8.7%(N=11)
Non smoker	86.4% (n=813)	5.0% (N=41)
Total	N=940	N=52

Table No.3: Relation of dry socket and mode of extraction

Patients	N=940	Dry socket 5.5% n=52
Simple Extraction	92.2% (n=866)	4.2% (n=36)
Surgical Extraction	7.8% (n=74)	21.7% (n=16)

Table No.4: Relation of dry socket and antibiotics

Patients	N=940	Dry socket
Antibiotic Prescribed	47.9% (n=450)	4.8% (n=22)
Without Antibiotics	52.1% (n=490)	6.14% (n=30).

DISCUSSION

Tooth extraction is one of the most feared dental procedures performed, which is associated with pain and morbidity post-operatively[1, 2, 10]. Many patients are hesitant to undergo tooth extraction and delay it as it can bring lot of pain after the effects of anesthesia wear off. Dry Socket is a complication of tooth extraction in which patient experience growing pain after 3rd day of extraction[11, 12]. There are a lot of risk factors associated with the higher incidence of dry socket however exact cause is still unclear. In our study, the incidence of dry socket was higher in female (6.3%) as compared to male (4.3%) which can be related to the female hormonal status (estrogen) or use of oral contraceptive. In the study of Yumi, they concluded that the risk dry socket of women taking contraceptive can be two folds as compare to women not taking any

contraceptives[13,14,15]. One of the major risk factors of dry socket was the mode of extraction. In patients where tooth was surgically removed had 21.7% incidence of dry socket as compare to the patient where non-surgically removed. Our percentage is comparable with other studies where incidence of dry socket after surgical extraction ranges from 20 to 30%[12,16]. Surgical extraction causes more trauma to the tissues as compared to simple extraction so chances of clot dislodgment after surgical extraction is higher. Also, surgical technique and surgeon's skill play a role in this post-operative complication which needs to be evaluated in further studies. In literature, smoking is also associated with dry socket with the range of 3.4% to 12% and up to 40% after surgical extraction[17, 18]. In our study 13.5% patients were smoker, who had the incidence of dry socket of 8.7%, though all of the smokers were male patients. The sucking action of smoking a pipe or cigarettes creates a negative pressure which can dislodge the blood clot and leads to dry socket[19]. The patients who were prescribed with antibiotics post-operatively had the incidence of dry socket of 4.8% as compared to the group of patients where no antibiotics were prescribed. The less incidence of the dry socket in patient who took antibiotics could be due to the better control of certain bacteria in oral cavity responsible for clot lysis. In literature variety of antibiotics were used for prevention of dry socket with limited success[20-22].The status of patient's oral hygiene and incidence of dry socket is also associated in literature; however, this relationship could not be identified in our study due to lack of patient records relating to the oral hygiene[23,24].

CONCLUSION

The incidence of dry socket was seen higher after surgical extraction in female gender and smokers. Further studies with large sample scales are required to assess other possible relationships. This painful self-limiting condition could be treated with application of intra socket dressing.

Author's Contribution:

Concept & Design of Study:	Salman Ahmad
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Evaluation of Alloy Composition of A Brand of Stainless Steel K-Files

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ABSTRACT

Objective: The purpose of this experimental study was to determine the alloy composition of a brand of handheld stainless steel K files, acquired from different countries, in accordance with available standards.

Study Design: Comparative study.

Place and Duration of Study: This study was conducted at the Institute of Space & Technology (IST) Islamabad from November 2021 to March 2022.

Materials and Methods: 20 Mani stainless-steel K files of identical size (ISO#25), were acquired from Pakistan and were designated as Group A while 20 Mani K files were purchased from London, UK and designated as Group B. Alloy composition of both the sets of files was evaluated using energy dispersive X-ray spectroscopy. Data was statistically analyzed by independent sample T test and compared with American Iron and Steel Institute types 304 and 316.

Results: No significant difference was found between the two groups. Nickel and chromium contents of both the groups fell within AISI 304 but content of nickel in the alloy was found to be in the lower applicable range of the specified limit.

Conclusion: The results of this study indicate towards a general inclination of manufacturers towards using the lower applicable range of expensive alloying elements.

Key Words: Stainless steel endodontic K files, austenitic stainless steel, alloy composition, cost effectiveness, clinical efficiency.

INTRODUCTION

Stainless steel also known as INOX steel constitutes a group of corrosion and heat resistant alloys containing a minimum of 10.5% chromium[1]. Stainless steel has its usage dating back to more than a 100 years owing to its unique set of properties which makes it an ideal material for many applications[2]. Its resilience and high resistance to corrosion makes it an exemplary material for surgical tools and medical equipment. In dentistry, it has its applications in the manufacture of endodontic files for root canal cleaning and shaping, metal posts for root canal treated teeth, crowns and arch wires[2,3].

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The first endodontic file was designed by Edward Mynard in 1838 which he made by filing a watch spring. Stainless steel K-files, basically cutting instruments used for root canal debridement and shaping are the strongest of the handheld files, bypassing obstructions with far greater ease and are produced to give the operator a smooth tactile sensation within the canal during instrumentation[4]. The properties of endodontic files vary from one another depending upon their metallic composition. They also differ in terms of dentine cutting efficacy[5]. Consequently, their resistance to defect origination and breakage also varies[6]. Stainless steel files and reamers were established to be superior to carbon steel files in this regard[7]. Ni Ti files are three times more elastic than the stainless steel files but stainless steel files are more efficient cutting tools as compared to Ni Ti instruments[8]. However, their strength and resistance to corrosion is greatly affected by the composition of alloy used in fabrication of these files[5,9-11].

Most of the standard grades still employed today were discovered from 1913 to 1935, and then from 1970s onwards in Britain, Germany, America and France[1]. Stainless steel alloys can be divided into 5 basic categories depending on their crystalline structure. These are austenitic, ferritic, martensitic (named after the German metallurgist Adolf Martins), duplex and precipitation hardened alloys. Choosing the appropriate

stainless steel grades comprises considering four attributes in the following sequence of significance: corrosion resistance, mechanical properties, fabrication techniques and cost effectiveness[12]. Austenitic grades, known for their formability and high resistance to corrosion are the most widely utilized stainless steels, accounting for more than 70% of the total manufacture. The most commonly used austenitic stainless steel grades are 304 and 316. 304L and 316L are the low carbon versions of these alloys with a carbon content of less than 0.03%[2]. Type 304 is commonly known as 18/8 for its typical composition of nickel ranging from 8-10% and that of chromium from 18-20% by weight. Type 316 is also referred to as 18/10, with nickel content ranging from 10-14% and chromium ranging from 16-18% by weight[13].

Darbara, M., et al., concluded from their studies that AISI types 303 and 304 are the most commonly used austenitic grades for stainless steel files and reamers[13]. Previous studies have shown that alloy type has a an influence on the corrosion resistance of endodontic instruments as well as their strength and cutting efficiency[11,14]. Optimum amount of nickel, chromium as well as molybdenum in stainless steel gives the alloy its strength and high corrosion resistance. The addition of nickel, manganese and or molybdenum also helps in maintaining the austenitic structure of the alloy, improving its strength. Furthermore, nickel imparts ductility to the alloy[14].

For elemental investigation or chemical categorization of a sample, a methodical approach called Energy Dispersive X-ray spectroscopy (EDX) is employed. EDX has been used to determine the elemental composition of endodontic files in numerous studies[13,15]. It fundamentally works on the principle that each element has a distinctive atomic configuration permitting a distinctive set of crests on its electromagnetic emission spectrum. It is based on the interaction of a source of high energy particles (photons, electrons or a ray of x rays) and electrons within a specimen. To excite the emanation of specific x-rays from a sample, a high-energy ray of charged particle is directed onto the specimen being investigated. The incident ray stimulates an electron in an inner shell, releasing it while producing an electron hole in the shell. An electron from an external, higher-energy shell then occupies the empty space. The difference in energy between the higher and lower energy shells is emitted in the form of an x-ray photon. During chemo-mechanical preparation as well as during autoclaving, endodontic files are exposed to highly corrosive products including sodium hypochlorite which may debilitate the strength of the instruments as a result of pitting corrosion. These pits acting as stress raisers may cause sudden breakage of the instruments during the course of clinical use[11]. Hence, the role of material selection in maintaining the integrity of endodontic files, based on favorable chemical properties cannot be over emphasized. Pertaining to the dearth of information regarding the alloy composition of endodontic files, this study was aimed at evaluating and comparing the chemical composition of a brand of stainless K files (Mani Inc. Japan), acquired from Pakistan and United Kingdom in accordance with American Iron and Steel Institute (AISI) 304 and 316. Files of this particular brand were selected because of the availability of their non-standardized files in both local and international markets[12].

MATERIALS AND METHODS

Sample comprised of 40 stainless-steel K files (Mani, Inc. 8-3 Kiyohara Industrial Park Utsunomiya, Tochigi, Japan) of identical sizes, (ISO#25, 21mm). Out of the total, 20 K files, were obtained from Pakistan and named as Group A, while 20 K files brought from London, UK were named as Group B. The description about the files used for the testing purpose is given in Table 1.

Chemical composition of the files belonging to both the groups was determined using Energy Dispersive X-ray analysis. Emphasis was based on the nickel and chromium contents of the samples, since these two elements constitute the major portion of the alloying elements in austenitic stainless steels[13].

RESULTS

Nickel and chromium contents of the samples were statistically analyzed by independent sample T test and compared with AISI 304 and 316[13,16]. Nickel and chromium contents of the tested samples of Group A, as estimated with energy dispersive spectrometer analysis are given in Table 2, while those of Group B are given in Table 3.

Table No.1: Material used for testing

Sources (countries)	Type of files	No. of Files	Manufacturer	Lot Number	Grou PS Assigned
Pakistan (Rawalpindi/ Islamabad)	Stainless steel K files, 21mm #25	20	MANI, INC. 8-3Kiyohara industrial park. Utsunomiya, Tochigi, Japan.	R151412100	Group A
United Kingdom (London)	Stainless steel K files, 21mm #25	20	MANI, INC. 8-3Kiyohara industrial park. Utsunomiya, Tochigi. Japan	R110868200	Group B

The average means and standard deviations of nickel and chromium contents of the tested samples are given in Table 4. No significant difference between Groups A and B was found (p>0.05).

Table No.2: Nickel and Chromium contents by weight % of Group A files:

Sample Number	Chromium Content	Nickel Content
1.	19.57	8.27
2.	19.77	7.90
3.	19.03	7.52
4.	19.68	8.08
5.	19.03	5.97
6.	18.50	8.07
7.	19.50	8.11
8.	19.42	7.99
9.	17.88	7.24
10.	18.96	7.47
11.	18.38	7.41
12.	17.25	8.05
13.	17.29	6.87
14.	15.19	8.44
15.	18.44	8.47
16.	18.43	8.58
17.	18.88	8.63
18.	18.24	8.33
19.	19.20	8.61
20.	19.16	7.93

Table No.3: Nickel and Chromium contents by weight % of Group B files:

Sample Number	Chromium Content	Nickel Content
1.	18.73	7.69
2.	18.48	7.65
3.	17.43	8.36
4.	19.36	7.41
5.	19.44	8.31
6.	18.66	7.68
7.	18.32	7.45
8.	19.47	8.02
9.	18.18	7.88
10.	18.86	8.74
11.	19.51	8.54
12.	17.54	7.43
13.	17.93	7.56
14.	18.56	8.49
15.	18.83	7.80
16.	19.42	8.19
17.	19.31	7.33
18.	19.39	8.39
19.	17.33	8.46
20.	19.55	8.13

Nickel and chromium contents of the tested samples in both the groups fell within AISI 304. Nickel content however, was found to be in lower range of the specified limit. The absence of molybdenum in the chemical composition of the files showed that the files were not made from auestenitic type 316 stainless steel.

Table No.4: Means and standard deviations of Ni and Cr contents of Groups A & B:

Groups	N	Composition (%)	P Value
Nickel			
Group A	20	7.89 ± 0.66	0.66
Group B	20	7.97 ±0.44	0.66
Chromium			
Group A	20	18.59 ±1.07	0.67
Group B	20	18.71 ±0.73	0.67

DISCUSSION

The results of this study in terms of metallic composition of the files are consistent with a previous study[13]. Both the groups of files examined fell into one of the most commonly used austenitic type 304 stainless steel grades, which are easily recognized by the absence of molybdenum and percentage weight of nickel (8-10%) and chromium in their chemical composition (18-20%). It was however observed that nickel content of files in both the groups was in the lower range of the specified limit.

The price of stainless steel in general is markedly governed by the cost of alloying elements. The price of chromium which is the vital stainless steel element is not high, but incorporation of ingredients which enhance the corrosion resistance (mainly molybdenum) or which alter the manufacture properties (particularly nickel) add significantly to the overall cost[17]. These costs have a direct influence on the two most widely used grades: 304 (18%Cr, 8%Ni) and 316 (16%Cr, 10%Ni, and 2% Mo)[17]. Considering these facts, it was postulated that variations might exist in the chemical composition of stainless steel endodontic files, particularly the nickel contents.

Basically, stability between austenite former and ferrite former elements governs the microstructure of steel. Carbon, manganese, nitrogen and copper are all austenite former lower cost potential substitutes to nickel[18]. However, each element has a different function, and it is not likely to completely eliminate nickel and substitute it with either of these elements[19]. For example, manganese acts as an austenite former but is not as effectual as nickel, and Cr-Mn steels have greater strain hardening rates than do seemingly corresponding Cr-Ni steels. Similarly, carbon is a very effective austenite former, but has only partial solubility in austenite, so it is of limited significance in steel designed to be totally austenitic.

Similarly, limited solubility of nitrogen (<0.2%) does not have a very substantial influence on corrosion resistance of the alloy[18,20].

Mechanical integrity of an endodontic file depends to a great deal upon its chemical stability[14]. Lower amounts of nickel in an alloy may reduce its overall cost as well as its toxic potential, however, care must be taken to ensure a balance between the corrosion and strength properties[16]. Addition of nickel in stainless steel files improve their flexibility, so as to allow maneuvering of the curved / constricted canals relatively easier. Therefore, alteration in the alloy composition of nickel may compromise the clinical efficacy of a file, resulting in its sudden catastrophic failure at any point, during the course of clinical use[13].

In our study none of the low cost substitutes for nickel were found in composition of the endodontic files. Nevertheless, from lower range of nickel, it could be well postulated that to control and reduce cost of the instruments, manufacturers may be focused on reducing the cost of the raw material by employing the lowest applicable tolerance of expensive alloying elements. It should however be considered that the current study involved only one type of several files systems available on the market. Hence, to draw a more decisive inference on this matter, further research is required with several brands of files in multiple sizes.

CONCLUSION

No significant difference was found between locally and internationally acquired files and the alloy composition fell within AISI 304. Nickel content, however, was found to be in lower range of the specified limit in both the groups. Further investigation to evaluate the corrosion properties of these files is required for future research. Furthermore, studies on identifying the nickel contents in stainless steel endodontic files in general is required since the results of this study indicate towards a general inclination of manufacturers towards using lower amounts of nickel in the manufacture of stainless steel files. Evaluation of in-vivo performance of the files may add significantly to the data available on the importance of chemical composition in maintaining the integrity of stainless endodontic files.

Author's Contribution:

Concept & Design of Study:	Maryam Saeedullah
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Does Ultrasonically Measured Subcutaneous Abdominal Fat Relate with Grades of Non-Alcoholic Fatty Disease of Liver (NAFDL)?

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ABSTRACT

Objective: This study was designed to assess the relationship of SAFT and the presence of NAFDL along with its severity grade in T2DM and Obesity.
Study Design: Observational / cross section study
Place and Duration of Study: This study was conducted at the Department of Medicine, Rai Medical College Sargodha from January to December, 2021.
Materials and Methods: This study was carried out on the patients presenting in medical OPD, from 40 to 70 years of age, both genders. Obesity was assessed by the simplest and most practiced parameter of obesity as "Looking Obese" or having a "sacking or protuberant tummy". T2DM was confirmed on the basis of available blood sugar and HbA1c record. After applying inclusion (obesity and T2DM) and exclusion criteria, volunteering participants were asked to get an abdominal ultrasound (USG) examination for grading of Hepatic Parenchymal Echogenicity (HPE) in NAFDL and to measure Subcutaneous Abdominal Fat Thickness (SAFT) through the same acoustic window. Subcutaneous Abdominal Fat Thickness (SAFT) measured in mm during USG examination was divided into 4 grades, G1 (0 – 25), G2 (25.01 – 50), G3 (50.01 – 75) and G4 (75.01 – 100) for the convenience of evaluation.
Results: 420 females and 186 males were included in this study. Among the 420 females, 270 had G1 HPE, out of these 13% had G1 SAFT, 82% had G2 SAFT, 4% had G3 SAFT and none had G4 SAFT. There were 150 females exhibiting G2 HPE, out of these 92% had G1 SAFT, 4% had G2 SAFT, 4% had G3 SAFT and none had G4 SAFT. No female had G3 HPE. Out of 186 males, 102 males had G1 HPE, out of these 47% had G1 SAFT, 53% had G2 SAFT and none had G3 or G4 SAFT. There were 84 males exhibiting G2 HPE, out of these 29% had G1 SAFT, 71% had G2 SAFT and none had G3 or G4 HPE.
Conclusion: The relationship between upper quadrant and lower quadrant can be the subject of some future studies. The organizations can invite opinion for the recommendation of standard points of window.
Key Words: T2DM, NAFDL, Subcutaneous abdominal fat thickness, CLD.

INTRODUCTION

Obesity though known to exist from pre-historic times but recently the number of patients suffering from obesity has increased alarmly. Since 1980 the prevalence of being overweight and obese has risen 39% by 2015 as defined by Body Mass Index (BMI) in epidemiological studies.

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It is projected to rise to 57.8% by 2030 if present trends continue. In economically under developed societies higher prevalence is seen in middle-aged adults from wealthy and urban strata especially among females. On the contrary in high-income countries, there is not much a difference in gender or age groups but is disproportionately greater in disadvantaged groups. Psychosocial and personal cost of obesity are well known. Initially thought to be an evolutionary defense against unpredictable famines and times of shortage of food in different catastrophic events as subcutaneous fat depots, new data has produced abundant evidence of its health hazards highlighting the importance of the selective fat deposition around the viscera and its relationship with increased cardiovascular diseases (CVD). Recently focus has shifted to its deposition in the liver because of its

metabolic consequences and potential to cause cirrhosis. Paralleling this trend, over the past three decades the increasing incidence of T2DM and prediabetes are observed among children, adolescents and younger adults, it has more than doubled globally. The causes are embedded in a very complex group of genetic and epigenetics interacting within an equally complex societal framework that determines behavior and environmental influences. By 2010 estimates 285 million, 90% had T2DM. It is expected to rise to 439 million, 7.7%, by 2030, Asia being the epicenter, we are among the top 10.[1-3]

Grey scale USG is widely available and used parameter for estimation of both the SAFT and HPE change grades. USG of the liver is the reference for the detection of fatty liver. A multifactorial intervention approach on the risk factors can bring remission and prevent more severe complications.[4,5]

MATERIALS AND METHODS

This Observational / cross section study was carried out on patients presenting to Medical OPDs of RMCS, between the ages of 40-70 years, both genders, with obesity and T2DM from January, 2021 to December, 2021. Obesity was assessed by the simplest and most practiced parameter of obesity as "Looking Obese" or with "sacking or protuberant tummy" as the entry point into the study. T2DM was confirmed on the basis of available blood sugar and HbA1c record as per standard. (1)

After applying inclusion and exclusion criteria, volunteering participants were asked to get an abdominal USG examination by the participating Radiologists using standard 2-5MHz convex transducer and parameters for grading the HPE characteristic of NAFDL and SAFT through the same acoustic window as per standard.(6) SAFT measured in millimeters (mm) during USG examination was divided into 4 grades, G1 (0 – 25), G2 (25.01 – 50), G3 (50.01 – 75) and G4 (75.01 – 100) for the convenience of evaluation.

Inclusion Criteria:
40-70 years age, both sexes,

Obesity as defined.
T2DM as defined

Exclusion Criteria:
Seriously sick patient or terminally ill patient.
Untreated Chronic HBV and HCV disease
Established cirrhosis of liver
Regular alcohol use in last 3 Months
Any other metabolic cause of hepatomegaly or CLD
Pregnancy
Ascites of any etiology
Major end organ disease, liver, kidney, heart, lungs
Active steroid use in last 6 months
Hypothyroidism

Sample Size and Sampling Technique: A minimum sample size of 385 patients was calculated as minimum required to maintain a 5 % margin of error, a 95% confidence interval and a 75% response distribution, using a raosoft sample size calculator.

Statistical Analysis: Data analysis was done using Microsoft Excel version 2016 and Statistical Package for Social Sciences (SPSS) software version 25. Descriptive statistics (i.e. frequency distribution, percentages, mean and standard deviations) were the primary analytical methods used to relate NAFLD severity score with the subcutaneous abdominal fat pad thickness.

RESULTS

420 females and 186 males were included in this study. There were 270 females exhibiting G1 hepatic parenchymal changes (HPE), out of these 13% had G1 SAFT, 82% had G2 SAFT, 4% had G3 SAFT and none had G4 SAFT. There were 150 females exhibiting G2 HPE, out of these 92% had G1 SAFT, 4% had G2 SAFT, 4% had G3 SAFT and none had G4 SAFT. No female had G3 HPE. (table 1)

Out of 186 males, 102 males had G1 HPE, out of these 47% had G1 SAFT, 53% had G2 SAFT and none had G3 or G4 SAFT. There were 84 males exhibiting G2 HPE, out of these 29% had G1 SAFT, 71% had G2 SAFT and none had G3 or G4 HPE. (table 2).

Table No.1: Subcutaneous Abdominal Fat Thickness (SAFT), females. N 420

Liver Fat Grade		SAFT			
		Grade 1 (0 – 25)	Grade 2 (25.01 – 50)	Grade 3 (50.01 – 75)	Grade 4 (75.01 – 100)
Grade 1	270	13.33% (SD: +4.20, Mean: 20.57)	82.22% (SD: +5.96, Mean: 36.34)	4.44% (SD: +1.41, Mean: 51.99)	0 (SD: + 0.00, Mean: 0.00)
Grade 2	150	92.00% (SD: +7.22, Mean: 37.04)	4.00% (SD: +4.37, Mean: 55.87)	4.00% (SD: +6.13, Mean: 85.61)	0 (SD: + 0.00, Mean: 0.00)
Grade 3	0	0 (SD: + 0.00, Mean: 0.00)	0 (SD: + 0.00, Mean: 0.00)	0 (SD: + 0.00, Mean: 0.00)	0 (SD: + 0.00, Mean: 0.00)

Table No.2: Subcutaneous Abdominal Fat Thickness (SAFT), males. N186

Liver Fat Grade		SAFT			
		Grade 1 (0 – 25)	Grade 2 (25.01 – 50)	Grade 3 (50.01 – 75)	Grade 4 (75.01 – 100)
Grade 1	102	47.06% (SD: +4.01, Mean: 19.75)	52.94% (SD: +5.76, Mean: 30.93)	0 (SD: + 0.00, Mean: 0.00)	0 (SD: + 0.00, Mean: 0.00)
Grade 2	84	28.57% (SD: +1.82, Mean: 22.49)	71.43% (SD: +7.33, Mean: 32.76)	0 (SD: + 0.00, Mean: 0.00)	0 (SD: + 0.00, Mean: 0.00)
Grade 3	0	0 (SD: + 0.00, Mean: 0.00)	0 (SD: + 0.00, Mean: 0.00)	0 (SD: + 0.00, Mean: 0.00)	0 (SD: + 0.00, Mean: 0.00)

Same is graphically depicted as Graph 1.
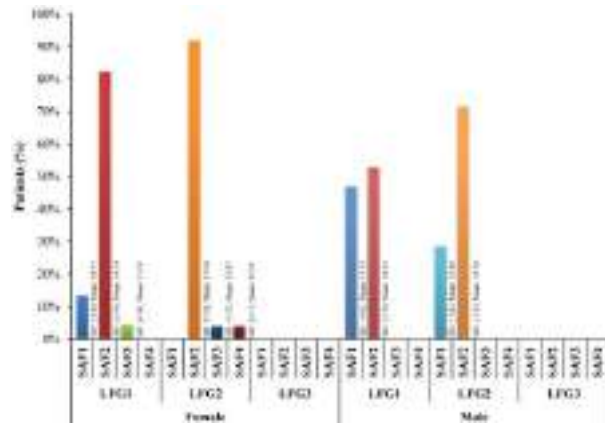
Graph No.1: Subcutaneous Abdominal Fat Thickness (SAFT), females and males

DISCUSSION

NAFDL is an umbrella term to cover spectrum from non-alcoholic fatty liver or steatosis (NAFL), a benign, non-progressive clinical entity to non-alcoholic steatohepatitis (NASH), fibrosis and CLD.[7,8] Diagnosis of NAFDL prevalence is based on hepatic steatosis diagnosed by histology or imaging modalities in nonalcoholic subjects (alcoholic liver disease occurs when daily alcohol consumption exceeds 20 g in women or 30 g in men) and appropriate exclusion of other liver diseases. The assessment of hepatic steatosis is typically based on observations of the liver echotexture, echo penetration, visibility of the diaphragm, and clarity of liver vessel structures.[9,10]

The pathophysiologic feature of NAFDL include abnormal glycemic and Lipemic axis, altered amino acid and hepatic Iron homeostasis with increased bile acid production in a complex dynamic multistage interaction between diet, genetics, environment and metabolism.[11] IR and elevated levels of circulating free fatty acids (FFAs) leads to excessive accumulation of triglycerides in liver cells.[12] The resulting lipotoxicity mediated by oxidative stress and exaggerated inflammatory response predispose to progressive hepatic injury.[13] IR links abundant but inefficiently processed glucose to lipids metabolism, NAFDL often exhibits both hyperinsulinemia and IR leading to TG accumulation and T2D, respectively. Amino acids simultaneously regulate both glucose and lipid metabolism. Bile acid plays its role through choline. Excess Iron accumulation in the liver fuels inflammation and oxidative stress. Oxidative stress in turn augments lipid accumulation by adding fatty acids and cholesterol, a vicious circle is activated, all contributing and influencing each other.[14]

The obesity must be prioritized for intervention due to high potential for prevention and reversal. Overweight or obese NAFDL patients are more likely to develop steatohepatitis and severe forms of liver disease. Obesity (excessive BMI and visceral obesity) is the most common and well documented risk factor for NAFLD. This bidirectional association between NAFDL and components of MetS has been strongly established. T2DM and NAFDL can develop almost simultaneously in patients with confounding effect on prevalence statistics of both conditions. Similarly the prevalence of NAFDL in individuals attending lipid clinics has been estimated to be 50%.[15]

Liver biopsy, though still is gold standard, has limitations due to small sample size subject to sampling errors, chances of bleeding and being an invasive procedure. Ultrasonography of the liver is the most widely used investigation in epidemiological studies due to its wide availability, cost-effectiveness, real time evaluation capability and reliability, however due to subjective nature of the test inter-observer agreement is relatively poor. CT assesses fatty liver on the degree of attenuation of parenchyma, steatosis appearing hypodense due to reduction in liver attenuation with sensitivity and specificity of 82% and 100% respectively of moderate-severe hepatic steatosis. However, both CT and USG have limited diagnostic accuracy for detecting mild steatosis. The Proton magnetic resonance spectroscopy (MRS) has emerged as most reliable non-invasively tool to quantify the fat

content in liver with sensitivity of (80-91%) and specificity of (80.2- 87%). [16]

CONCLUSION

In this study we couldn't find any relationship of SAFT with HPE grades in both sexes. This clearly implies that hepatic fat deposition is under multiple metabolic and hemostatic influences. Moreover we couldn't find any recommendation for any particular point of reference in the literature, we decided to take right upper quadrant, a standard point for the liver, for our study. In most cases of obesity the maximum subcutaneous fat deposition is below the umbilicus. The relationship between upper quadrant and lower quadrant can be the subject of some future studies. The organizations can invite opinion for the recommendation of standard points of window.

Author's Contribution:

Concept & Design of Study:	Mohammad Mohsin Rana
Drafting:	Muhammad Saleem Akhtar, Burhan Rasheed
Data Analysis:	Muazzam Fuaad, Tahir Baig, Kamran Arzoo
Revisiting Critically:	Mohammad Mohsin Rana, Muhammad Saleem Akhtar
Final Approval of version:	Mohammad Mohsin Rana

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

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Role of Garlic (Allium Sativum) on Lead Induced Delayed Eruption of Incisors in Albino Wistar Rats

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ABSTRACT

Objective: This study planned to evaluate the therapeutic effect of Allium sativum on lead induced delayed eruption of incisors of albino Wistar rats.
Study Design:
Place and Duration of Study: This study was conducted at the Post Graduate Medical Institute, Lahore. Study duration was one year from March 2019 to March 2020.
Materials and Methods: 68 adult albino Wistar rats were divided randomly into four groups (n=17) i.e., control, lead acetate, lead acetate with garlic and garlic alone. Right mandibular incisors were marked 1mm above the level of gingival papillae. The incisors were cut above this mark. The readings were measured by digital Vernier caliper. Incisors length was measured at day 0, 3, 6, 12 and 15 and eruption was calculated. The data was analyzed using SPSS 22.
Results: Eruption of incisors in albino Wistar rats in control was 3.30±0.72mm, in lead 2.43±1.19mm, lead + garlic 3.25±0.71mm and garlic 3.13±.91mm. At day 15, difference between Lead and lead with garlic was statistically significant (p-value 0.049).
Conclusion: The results showed that excessive lead intoxication is also a causative factor of delayed tooth eruption. The use of Allium sativum in routine diet and medicinal formulation could be helpful in patients or residents of lead polluted areas.
Key Words: Garlic, Allium Sativum, Delayed Eruption, Incisors, Albino Wistar Rat.

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INTRODUCTION

The eruption of teeth is a biologic process that has been of considerable interest to humans since early times. Every tooth has a specific time to erupt in the oral cavity. But sometimes deviation is seen clinically in eruption time[1]. The cases of delayed eruption are commonly seen in practice and generally parents are more worried and concerned about it[2,3]. There are many factors affecting tooth eruption.

There are genetics, nutrition, preterm birth, socioeconomic factors, hormonal factors and systemic

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diseases like endocrine disorders, vitamin D-resistant rickets, long term chemotherapy, radiation damage, maxillofacial trauma and one of the most important factors is heavy metal intoxication[4].

Lead is one of the oldest and toxic heavy metals. It is common environmental and industrial pollutants that affect almost all biological systems [5]. Common sources of lead poisoning are car battery industries, manufacturing of ceramics, lead bearing paints, contaminated food, water and environment[6,7]. Lead can enter body mainly via eating, drinking or inhalation and transport to different tissues like kidney, liver, brain and bones[8]. Lead can pass through blood-brain barrier and placenta barrier[9].

Lead toxicity affects the dental and oral tissues. The presences of lead can interfere with development of enamel called amelogenesis[10]. Lead is found in saliva in children who have excessive lead exposure, which can affect their oral and physical health[11]. Mineralization is delayed during exposure to lead. This lack of mineralization is compensated by relatively longer duration of maturation, reflected in slow eruption[10]. Lead exposure to pregnant rats results in delayed teeth eruption and enamel development of their offspring's. Lead effect on delayed tooth eruption has been proved in hypo-functional incisors of Wistar rats[12].

Albino Wistar rats are monophyodont mammals. Incisors of albino Wistar rats are open-rooted, which means apical end of root never closes and grow throughout their life with average 1mm per day[13], that can be increased by trimming their incisal edges to make them hypo-functional.

There are many drugs or naturally occurring herbs which can be used as antidote against these heavy metal intoxications. Allium sativum has an important dietary and medicinal role. Garlic has anti-viral, anti-bacterial, antifungal, antioxidant, anti-atherosclerotic and anti-cancer properties[14]. It has been shown to reduce lead toxicity and tissue lead contents in lead exposed humans[15]. Rats suffering from lead toxicity were treated with garlic and vitamin c complex and it was found that they have curative and protective effect[15]. The therapeutic effects of Allium sativum extract on lead toxicity has been proved and published in literature[16, 17]. It contains many chelators which eliminate lead from the body[18] that decreases the accumulation of lead in bone and other tissues of the body due to its antioxidant and chelating ability[18]. However, there is no data available regarding its role in lead induced delayed eruption of teeth.

Keeping in mind the therapeutic and beneficial effects of Allium sativum in lead toxicity on different tissues of the body, this study was designed to investigate the therapeutic role of garlic on lead induced delayed eruption of incisors in albino Wistar rats.

MATERIALS AND METHODS

This study was conducted at Post Graduate Medical Institute, Lahore. Study duration was one year. Adult healthy male albino Wistar rats (n=68) were included in the study. They were equally divided into four groups (n=17).

Sampling Technique: Experimental animals were assigned numbers 1,2,3,4, till 68 using the random number generator and then randomly divided into four groups (n=17) and were assigned as group A, B, C and D. All the rats in each group were housed in an airy cage. Group A was control group, group B was lead group, group C was lead with garlic and group D was garlic group.

Selection of Experimental Animals: Adult healthy male albino Wistar rats were selected from Animal House at Post Graduate Medical Institute, Lahore. The animals were kept in experimental research laboratory at controlled room temperature (22-24°C) and humidity (45-65 %) under 12/12 hours natural light and dark cycle. All experimental animals were fed on rodent chow and distilled water ad libitum.

Preparation of Drug (1500 ppm leaded water): For the preparation of 1500 ppm leaded water, 30 g lead acetate, 8 ml 1N HCl (to ensure solubility) and 10 g glucose (for favorite taste) were dissolved in 20 liters of distilled water [19, 20].

Selection of Plant Material: Fresh bulb of Allium sativum were collected from the Botanical Garden of The Punjab University Lahore and the samples were verified by its Department of Botany.

Preparation of garlic juice: Fresh Allium sativum bulbs were collected, cloves were peeled, washed with distilled water and dried under shed. The clean bulbs were crushed with an electric grinder and the extract was decanted through muslin cloth[19.]. The fresh extract was made daily from 700-800g garlic.

Procedure: The experimental rats were housed in a climate-controlled environment in accordance with the international principles for the use of laboratory animals. Following acclimatization for one week, procedure was started. Animals were randomly assigned a group (n=17). Group A rats were given diet with rat chow and water. In Group-B, rats received leaded water (1500ppm). In Group-C, rats received leaded water and fresh garlic juice (1ml / 100g body weight) by gavages once a day [19] and group-D received just garlic juice.

All the rats were weighed on digital weighing machine and noted. The rats were anaesthetized with intraperitoneal ketamine injection (100 mg/kg body weight). Right mandibular incisors were marked 1.0 mm above the level of gingival papilla by rotary diamond bur TF-12 EF to make a reference point. Rest of the incisor above that reference mark was cut off by the diamond bur to make it hypo-function [12].

The readings were taken between upper boarder of gingival papillae and the marked reference point on right mandibular central incisors and were considered as day 0 [12].

After three days the distance was measured between the marked reference point and the upper margin of gingival papillae by digital Vernier caliper. This was considered second reading at day 3. The actual eruption was measured by subtracting the 1st reading from the 2nd reading on day 3. In the same way readings were taken on day 6, 9, 12 and 15 and eruption rate was calculated respectively.

Blood Lead Level: The blood samples of 0.5 ml were taken from cardiac puncture on day 0, 3, 6, 9, 12, 15. Blood Lead Count (BLC) was determined by atomic absorption spectroscopy with perkin-Elmer HGA (Heat Graphite atomizer)[21,12] in the department of environmental sciences, University of veterinary and animal sciences, Lahore.

RESULTS

In this study 68 rats were studied, among them 17 were studied as control group, 17 were studied as experimental group 1(leaded group) and 17 were studied as experimental group 2 (lead and garlic group) and 17 rats were studied in experimental group 3 (garlic group).

Figure No.1: Marking the reference point and cutting right mandibular

Figure No.2: Measuring between gingival papillae and reference point

Table No.1: Comparison of average difference in eruption (mm) among groups

	Control	Lead	Lead + Garlic	Garlic	p-value
Day 3	3.17±1.43	3.22±1.55	3.30±1.24	3.29±1.48	0.992
Day 6	2.94±1.45	3.01±1.52	2.85±1.27	3.03±1.24	0.981
Day 9	3.23±1.0	2.73±1.14	3.14±1.45	3.11±1.35	0.661
Day 12	3.15±1.33	2.57±1.55	3.03±1.12	3.24±1.06	0.436
Day 15	3.30±0.72	2.43±1.19	3.25±0.71	3.13±.91	0.022*

One way ANOVA, *P-value significant at 0.05

At day 15 as compared to day 12, there was statistically significant difference between mean eruptions of different groups (p-value 0.022).

Table No.2: Comparison of eruption (mm) between leaded and lead + garlic group

	Lead	Lead + Garlic	p-value
Day 3	3.22±1.55	3.30±1.24	0.998
Day 6	3.01±1.52	2.85±1.27	0.986
Day 9	2.73±1.14	3.14±1.45	0.773
Day 12	2.57±1.55	3.03±1.12	0.204
Day 15	2.43±1.19	3.25±0.71	0.049*

Post Hoc Tukey's test, *p-value significant at 0.05

No statistically significant difference was observed between lead and lead & garlic group at different time of study except at day 15 (p-value 0.049).

Figure No.3: Showing the refrence point mark level after 3 days
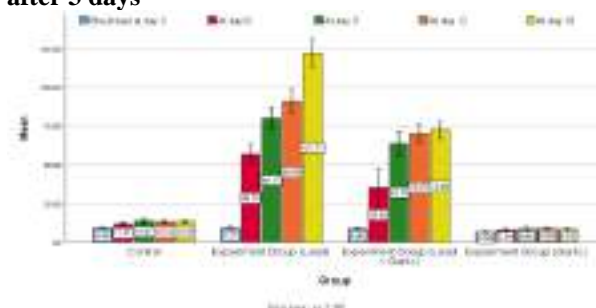
Figure No.4: Graphic comparison of BLC among different groups.

DISCUSSION

This study was conducted to determine the therapeutic effect of Allium sativum on the delayed eruption of incisors in albino Wistar rats due to lead toxicity. The role of Lead toxicity has been proved and documented in literature [12]. Multiple studied have been conducted to see the therapeutic effect of garlic on heavy metal toxicity in different tissues, but no study was available that explained the role of garlic on delayed eruption Gerlach et al. documented the role of lead toxicity on delayed tooth eruption in albino Wistar rats [12]. Methodology of both studies was different; however results of both studies proved delayed effect of lead toxicity on eruption (Table 1). The protective

management was incorporated in current study to avoid trauma to the pulp and gingiva, which has not been observed in the previous studies [12, 22].

Sadeghi et al. studied the therapeutic role of garlic to reduce lead toxicity in hippocampus of albino rats [23]. In both studies it was proved that garlic reduces the blood lead count (BLC), which showed the significant effect of Allium sativum in lead induced toxicity.

Bideskan et al. studied the effect of garlic in lead exposed pregnant rats [24]. In both studies Same dose of lead and garlic was used and comparable reduction in BLC was noticed by administration of garlic juice. Minor variation was seen that might be due to difference in weight of animals.

Saleh et al. conducted a study to see the protective effect of allium sativum on lead exposed pregnant rats. In lead group BLC was elevated but in lead with garlic group, it was reduced. The same beneficial effect was seen in the current study [25].

Mumtaz et al., documented the beneficial effects of garlic in lead induced toxicity in various organs of animal as well as human model. He reported that lead toxicity caused harmful effects in reproductive organs, kidney, CNS, liver, lungs, blood and bone. The garlic reversed these harmful effects by decreasing lead absorption in bones and soft tissues [15].

The associations between blood and lead were statistically significant. In the current study, the blood lead concentration was used as an important indicator of lead intoxication and its effect on tooth eruption. The figure-4 shows significant information regarding increased blood lead concentration in lead group but this intoxication was tremendously decreased in the lead with garlic group due to the neutralizing effect of garlic.

From this study, it has been found that garlic has therapeutic effect on lead induced detoxification and thus is effective in reducing delayed eruption of teeth. Excessive dose of garlic has its own adverse effects [26]. However, more studies are required to evaluate the detoxifying effect of garlic in lead induced delayed eruption of teeth.

CONCLUSION

Lead is an established environmental pollutant which effects tooth eruption and should be considered along with other local factors. However the use of garlic in routine diet should be suggested to such patients or residents of lead polluted localities so that toxic effects of lead could be neutralized. Community based human trials can be very much beneficial.

Author's Contribution:

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Developing Chick Embryo Under the Influence of Nicotine and Camellia Sinensis

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ABSTRACT

Objective: By research work to analyze the outcome of nicotine on the weight of developing embryo of chick and to estimate the safeguard effect in overcoming toxicity of nicotine by the leaves of green tea camellia sinensis.

Study Design: A randomized control study

Place and Duration of Study: This study was conducted at the Anatomy Department, HBS Medical and Dental College Islamabad, in association with Poultry Research Institute, Rawalpindi from June 2021 to November 2021.

Materials and Methods: Forty eggs of Fayoumi species fertilized in nature of chick embryo were selected at zero hour of incubation. The research work was formulated by creating four distributive groups, each consisting of ten eggs. The G1 group was labelled as control group 1 administered with dose of 0.1ml of 9% Normal saline. Experimental G2 Injected with 0.1ml of 8% Camellia sinensis. Experimental G3 Injected with 0.1ml of 0.0001% Nicotine solution. Experimental G4 Injected with 0.1ml of 0.0001% Nicotine solution and 0.1 ml of 8% Camellia sinensis. After 17 days of incubation embryo were collected for measurement. Data were entered in a database using SPSS (Statistical Package for Social Science) version 25. Data were presented as tables. Chi-square test, Anova and PosthocTukey test were used for analyzing data. P value < 0.05 was considered significant.

Results: The observations were made on the development of chick embryo by recording the weight of chick embryo and comparing with the control group and with each other. Data were entered and analysed using SPSS version 22. One-way analysis of variance (ANOVA) was used to compare weight of chick embryo among the different groups, p value of less than 0.05 was considered significant.

Conclusion: It was concluded that Nicotine oxidative stress responsible for decreasing the developmental growth of chick embryo. Whereas green tea suppresses the oxidative stress but cannot reverse the effect.

Key Words: Hatchery, Embryo, Nicotine, Weight.

INTRODUCTION

The skeletal system is composed of bones; they are further supported by ligaments, tendons, muscles and cartilages. It is responsible for maintaining the architecture, shape to the body. Exposure to environmental insults due to many reasons, can affect the developing skeleton.

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Nicotine a natural alkaloid and one of the constituent of cigarette responsible for increasing the chances of congenital malformations in humans. Nicotine is responsible for congenital defects abortions, premature delivery, and low on the size and weight in the study[2] Nicotine affects the fetus due to the stimulation of nicotinic cholinergic receptors.[3] Camellia sinensis considers as anantioxidant used in one of the type of tea known as green tea. Green tea used in different countries of Asia with different cultures. The different constituents of green tea had protective role against free radical production in body[4].

Habit of smoking during gestational period (pregnancy) and during reproductive age has high public health problem. According to the data, the ratio of smoking among pregnant women was 10–23%, even up to 59.3% in some parts.[5] According to the data driven studies, it showed that smoking at the time of gestation life responsible for congenital abnormalities causing several fetal problems. Tobacco component that is nicotine responsible for passing through the placental barrier by this reason amount of tobacco consumption appear more in the blood of fetus than in the mother's blood[6]. Another research work done with a conclusion

that tobacco smoke responsible for the condition of brochiolitis during infancy. [7] It is supported by the work of Talati A et al who mentioned oxidative effect of nicotine by effecting on the reproductive and developmental of embryo[8]. Nicotine intake causes decrease size of the skeleton and body mass index in developing family of rats[9]. In some of the other studies done it showed that the bone mass accumulation affected by the intake of nicotine[10]. In a research work done on neonatal rat pups responsible for growth retardation in neonatal rat pups[11]. It is supported by another work done by Chen B et al in which it showed nicotine consumption during pregnancy caused bony problems in developing rats family.[12]

Grean tea extracts consumption provide phyto-chemical, decreasing the process of oxidation. A substance used to counteract the deterioration by nicotine.[13]

The highest case showing universality of cigarette intake during reproductive age of female is increasing worldwide. Cigarette intake suppression campaign should be launched nationally and internationally and make the large places of the world smoke free zone as it is effecting more under twelve years old youngster and low socioeconomics group people.[14]

MATERIALS AND METHODS

The study work done in the Anatomy department, HBS Medical and Dental College Islamabad with a duration of six month after the Ethical review board approval. Forty Fayoumi fertilized eggs of chick included at zero hour of incubation. The research formulated by creating four distributive groups, each consisting of ten eggs. The control group was labelled as group one administered with dose of 0.1ml of 9% Normal saline. Experimental group two had ten number of eggs injected with 8% Camellia sinensis in same quantity as of above administered dose. Another group three had ten eggs injected with 0.1ml of 0.0001% Nicotine solution. Another group four had ten number of eggs injected with 0.1ml of 0.0001% Nicotine solution and 0.1 ml of 8% Camellia sinensis. Eggs of each group were injected with their respective solutions in same quantity with the help of insulin gauge needle under laminar flow fig 1.

The study was done on those eggs which at the age of zero hour of incubation. Those eggs with unknown time of laying, broken shell, abnormal shape, colour, texture or eggs stored in refrigerator were not considered for the research project. Total of forty eggs were placed in hatchery. Solutions used for the study were injected to the eggs of four groups (experimental) after two days that is forty eight hours of incubation. After incubating eggs for a period of 17 days, ten eggs from each group were selected for collection of 17th day old embryos. The embryos were collected by opening the blunt end by using the forceps. By removing yolk sac embryos

placed in the formalin filled jars for 48 hours. The embryos after taking out from jars kept on a piece of blotting paper. Precision digital balance with 0.001g readability were used for recording weight.[15]

RESULTS

The developing embryos of 17th days old were removed from fixative, placed on a piece of blotting paper. Each embryo weighed.[15] Mean weight of control group G1 and experimental group 2 were 8.539 ± 0.099g high in comparing of group 3and group 4 where they were 5.318±1.065g and 6.755±0.036g (Table 1). The p value in comparison of control group G1 with G2 was (1.000). The p value in comparison of control group G1 with G3 and G4 were significant that was (0.000). Experimental groups when compared with each other such as, G2 in comparison with G3 and G4 showed statistically significant result with p value (0.000). In contrast of group 3 and group 4 depicted statistically significant result with p value (0.011) (Table 1).The recorded weight of all the surviving embryo and their recorded weight showed in Table 2.

Table No.1: In contrast to weight (g) of developing chick embryo among different groups

Dependent Variable	Comparison Between Groups		p value
	(Group)	(Group)	
Weight of Embryo (g)	G1	G2	1.000
		G3	0.000
		G4	0.000
	G2	G1	1.000
		G3	0.000
		G4	0.000
	G3	G1	0.000
		G2	0.000
		G4	0.011
	G4	G1	0.000
		G2	0.000
		G3	0.011

p value $\leq$ 0.05 statistically significant

Figure No.1: Injection of different working solutions by insulin gauge needle into the incubated eggs.

Table No.2: Gross Study at 17th Day of Incubation

Control Group 1	Weight (g) Group 1	Exp Group 2	Weight (g) Group 2	Exp Group 3	Weight (g) Group 3	Exp Group 4	Weight (g) Group 4
1	8.55	1	8.53	1	6.75	1	6.75
2	8.54	2	8.54	2	5.99	2	6.95
3	8.50	3	8.54	3	6.75	3	6.66
4	8.50	4	8.55	4	5.99	4	6.75
5	8.44	5	8.45	**5**	1.11	5	6.66
6	8.52	6	8.55	-	-	6	6.76
7	8.55	7	8.53	-	-	**7**	6.76
8	8.47	8	8.55	-	-	**-**	-
9	8.55	9	8.55	-	-	-	-
10	8.55	**10**	8.55	-	-	-	-
Mean Weight	8.517	**Mean Weight**	8.54	**Mean Weight**	5.31	**Mean Weight**	6.75

DISCUSSION

The research work done by looking at how the nicotine effects the developing stages of embryo and preventive role of camellia sinensis (green tea) on it. The control group G1 was brought in comparison with other experimental groups and with each other. Nicotine exposure comes into the degree of environment hazard during the period of pregnancy, it can be first hand smoking or second hand smoking. Nicotine responsible to affect the offspring by influencing their epigenetic regulation. Nicotine is considered to be a reason for bringing against the normal functioning of multiorgan functional genes. Many studies showed that nicotine decreases the fetal adrenosteroid synthase expression and adrenal function system as well as osteogenic process got inhibition that is responsible for lowering the mass of the developing offspring due to nicotine exposure during gestational life come across as prenatal nicotine exposure.[15]

From the previous studies it was estimated that 400,000 developing stage of human embryo got exposure to harmful ingredients of tobacco smoke that is nicotine leading to the ultimate exposure in the way of carbonmonoxide. The tobacco extract intake causing developmental defect to the growing skeleton of fetus whose mother are in their gestational period.[1]

Other research work done to brought this evidence under consideration that epigenetic transformation played vital roles in the long-term developmental toxicity due to the exposure of environmental hazards.[16] As it is supported by another work which clearly concluded that long duration of exposure of nicotine responsible for bone developmental defects in neonates as well as uterine transformation.[17]

To support our research works, it has proven that green tea antioxidant quality can be effective as a therapy of different problems.[18] It was observed that resveratrol undo pathological injury of renal tissue by decreasing the fatty acid break down.[19] In other study done that revealed green tea, prior administration to nicotine, showed better reason of nephroprotection, shown by immense reduction in oxidative damage.[20]

Camellia sinensis that is green tea beverage taken in by large population of the world especially asian subcontinent. Green tea composition had polyphenols, which act as antioxidants. An antioxidant molecules are considered as a inhibitors for oxidative stressi.[12] Green tea has got catechins that will serve as a anticanacer agent in the area of tumor growth.[21] Green tea proved itself in a case of immune dysfunction as a immune modulators reason of any oncology treatment.[22]

CONCLUSION

It was concluded by the study that green tea (camellia sinensis) polyphenol molecules reduced the oxidative stress caused by nicotine but cannot reverse the toxicity completely.

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

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Original Article

Prevalence of Modic Changes in Cervical Spine and Their Association with Disc Herniation

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ABSTRACT

Objective: To evaluate the prevalence of Modic changes (MCs) in the cervical spine and their association with disc herniations (DH).

Study Design: A retrospective study

Place and Duration of Study: This study was conducted at the Department of Radiology, Ch. Pervaiz Elahi Institute of Cardiology Multan from 4th March 2021 to 4th March 2022.

Materials and Methods: A total of 250 patients elder than 50 years old were included in the study. The cervical MRI scans of these patients were analyzed for prevalence, location and category of MCs and DH. 100 scans among these scan images were assessed by an independent observer (medical intern) for interobserver reliable diagnosis and this observer evaluated the scans after 30 days again for intraobserver reliability.

Results: Only 215 participants were selected for final analysis among which Modic changes were found in 85 (39.5%). MCs type 1was less observed (3.5%) while type 2 was dominant (10.5%). DH were observed in 170 participants (79%). Both MCs and DH were mostly found at C5/6 and C6/7 discs. Modic changes and disc herniations were positively related (risk ratio=2.3). The intraobserver reliability was perfect (k= 0.78) and the interobserver reliability was upper-moderate (k=0.49).

Conclusion: Majority of patients showed Modic changes, mostly types two were seen in the cervical region, frequently in C5/6 and C6/7. MCs and DH were found in patients at the same level.

Key Words: Modic changes, disc herniation, bone marrow, bone marrow oedema, cervical spine

INTRODUCTION

Modic et al. first observed and categorized Modic changes in the dehydrated lumbar intervertebral disc in MR [1, 2]. According to him, Modic changes can be classified into three categories naming types 1, 2 and 3. He observed that 4% of patients had type 1 MCs and is associated with inflammation and bone marrow lesions[3]. Type 2 changes were most frequently found and represent increased fat mass index and a decreased inflow of blood in the infected bone marrow [4-6]. Type 3 MCs are the least common and reflect an increase in bone formation in the affected spine or subchondral sclerosis. Modic changes are associated with low back pain (LBP) and these lesions can be seen on magnetic resonance imaging scans[7].

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Most of the studies conducted related to Modic changes address the changes in the lumbar spine while one study, studied these changes in the neck region[8]. Due to limited literature on this subject, our study was conducted to study the prevalence, category and location of Modic changes in the cervical spine in a relatively large sample and compare the results with the already conducted study. We also assessed other processes during spine degeneration such as disc herniation and the association between disc herniation and Modic changes was evaluated as it had not been covered by the previous study. In addition, no study to date has reported the reliability scores in the identification of Modic changes in the cervical spine, this study aims to assess the prevalence and categorization of MCs in the cervical spine, the reliability scores and the association of marrow Modic changes and disc herniations.

MATERIALS AND METHODS

A retrospective study was conducted from 4th Mar 2021 to 4th Mar 2022 at the department of Radiology of Ch.Pervaiz Elahi Institute of Cardiology Multan.
A total of 250 patients elder than 50 years old were included in the study. The cervical MRI scans of these patients were used for analysis obtained from the radiology department. The patients who recently had

acute vertebral fractures, congenital bock vertebrae, hemodialysis spondyloarthropathy, spinal infections or tumours, surgical fusions, inflammatory spondyloarthropathy, acute traumatic Schmorl's nodes, and who had undergone radiotherapy were excluded from the study. All the patients provided their informed written consent to be a part of the study. The study was approved by the ethics committee of the hospital.

The consecutive MRI scans of 250 patients were selected for evaluation by one observer. A hundred scans were assessed by an independent second observer for an interobserver reliable diagnosis. These hundred patients were evaluated again by this observer after 30 days for intraobserver reliability. An expert radiologist and a medical intern, expert in understanding and evaluating the cervical MRI scans independently assessed the T1- and T2-weighted axial and sagittal scan images. Both the experts reported the scan characteristics by consensus and by following the standards in the literature. These standards were decided by both observers by initially assessing sample scan images.

Each patient was analyzed for age, sex, the existence of Modic changes, the dominant type of Modic changes and the segment level of MCs. Since type 3 is not common, only types 1 and 2 were evaluated. In addition, MCs are not common in the cervical region, only the motion segments C3/4, C4/5, C5/6, and C6/7 were assessed. While evaluating disc herniation, their type, appearance or non-appearance and segmental disc level were noted. Herniation was classified according to the interpretation by the radiologist. Disc herniation type 1 was regarded as bulging of the disc without compromising the spinal cord or nerve root, type 2 was reported as bulging of the outer annulus while compromising the spinal cord or nerve root. Axial and sagittal MRI scans were analyzed for figuring out the categorization and location of the disc herniation.

All the data were analyzed by using SPSS version 25. The presence of Modic changes and disc herniation was calculated based on the number of patients and the number of affected discs. Reliability scores were calculated by Cohen's Kappa statistics. A k value of 0.77-1.00 showed perfect reliability, while a value of 0.15 or less indicated poor reliability.

RESULTS

Only 215 were selected for final analysis as they were according to the inclusion criteria. The patients were elder than 50 years but not more than 85 years, the average age being 60.6 (SD± 8.72). A total of 850 motion segments were assessed, out of which 119 (14%) showed Modic changes and 30 (3.5%) were MCs type 1 and 90 (10.5%) were type 2. 30 (13.9%) patients had Modic changes in more than one segment. Modic changes were mostly observed in C6/7 and C5/6, 40 cases (33.6%) and 39 cases (32.8%) respectively.

Disc herniation was observed in 170 (79%) patients and 120 (55.8%) patients had herniation in more than one segment. Out of 850 motion segments, 112 (13.2%) had type 1 disc herniation and 238 (28%) had type 2 herniation. Herniations were frequent in C5/6 (35 type 1 and 75 type 2) and C6/7 (33 type 1 and 69 type 2). (Table I)

The association between Modic changes and disc herniation was shown through the risk ratio in Table II. As both existed at the same segment level, the risk ratio was 2.34(95%Cl: 1.86-2.95).

Seventy MRI scans were assessed by both observers (30 were excluded due to criteria) who could not see each other's results. The intraobserver reliability was almost perfect (k= 0.78) and the interobserver reliability was upper-moderate (k=0.49).

Table No.1: Prevalence of MCs and DHs in cervical spine

Abnormality	No of patients (n=215)	No of cervical motion segments (n=850)
Modic change		
Both types, n(%)	85 (39.5%)	119 (14%)
Type 1, n (%)	32 (14.4%)	30 (3.5%)
Type 2, n (%)	60 (28%)	90 (10.5%)
Patients with MC in more than one segment, n (%)	30 (13.9%)	-
Disc herniation		
Both types, n(%)	170 (79%)	350 (41.2%)
Type 1, n(%)	-	112 (13.2%)
Type 2, n(%)	-	238 (28%)
For patients with DH in more than one motion segment, n (%)	120 (55.8%)	-

Table No.2: Risk Ratios of Disc Herniation in Motion Segments with Modic Changes

Motion segment	Risk ratio	95% Cl
C3/4	2.55	1.58-4.99
C4/5	2.90	1.75-5.97
C5/6	1.49	0.98-2.25
C6/7	2.19	1.45-3.25
Pooled (C3/4-C6/7)	2.34	1.86-2.95

DISCUSSION

A high prevalence of Modic changes was observed in the cervical spine, especially in C5/6 and C6/7. These results were consistent with other studies based on cervical regions and this may be due to the same age group of patients i.e. elder than 50 years[8, 9]. The presence and absence of MCs did not relate to the gender or age of the patients. Due to the elderly population, MCs type 2 was more predominant than type 1. The previous study on this subject, however, showed different results in which type of MCs was more common and elderly people were most affected. This study had a large study size and patients with a less average age[8]. The disagreement between results may be due to the inclusion of a wider age group in the study[10].

The majority of the patients also showed disc herniations, both type 1 and 2 (79%). This is due to the high mean age of the patients and the patients included may have severe orthopaedic conditions. Disc herniations were frequently found in C5/6 and C6/7 motion segments. The other studies conducted for studying herniations in the spine have also reported the same results.

The risk ratio was calculated for comparing MCs and DH. The calculations showed that the patients with MCs were twice at risk of being affected by herniation at the same segment than patients with no modic changes. This can be seen in Table 2, although the 95% Cl score range is wide due to the small sample size. An association was found between MCs and disc herniation on the same segment. Jensen et al[11] reported the same results who observed an association between Modic changes and disc herniations in the spinal region. But the reason for this association in the same segment could not be known, which may be due to genetic disposition in study patients [12-14].

The reliability score of the present study was good and consistent with similar studies on the lumbar spine. This is quite encouraging as one observer was just a medical intern who received basic training on reading a scanned image and was reported about relevant literature. The radiologist can use the results of our study and quickly learn to characterize Modic changes and their effects.

Our study has some limitations. The inclusion of older patients affected the results such as a reduction in type 1 Modic changes. The patients included were mostly suffering from complex orthopedic conditions. Intensity inhomogeneity may also be observed in the MRI scans, altering the results which are crucial for assessing disc herniation.

CONCLUSION

Majority of patients showed Modic changes, mostly types two were seen in the cervical region, frequently in C5/6 and C6/7. MCs and DH were found in patients at the same level.

Author's Contribution:

Concept & Design of Study:	Hira Bushra
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Data Analysis:	Ayesha Zafar
Revisiting Critically:	Hira Bushra, Riffat Kamal
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Protective Effect of Henna (Lawsonia Inermis Linn.) at Different Doses in Acetaminophen Induced Hepatotoxicity in Albino Rats

Effect of Henna at Different Doses in Acetaminophen Induced Hepatotoxicity

Misbah Ishtiaq[1], Abeer Anjum[2], Irum Naz[1], Aneela Ahsan[1] and Uzma Azam[1]

ABSTRACT

Objective: To assess the protective effects of Henna (Lawsonia inermis Linn.) at two different doses on hepatotoxicity caused by acetaminophen in 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 12 days starting on June 1st, 2019.

Materials and Methods: The study comprised of 28 male adult albino rats that were divided into 4 groups A, B, C and D. Group A (control group) received 5ml/kg distilled water orally for 10 consecutive days followed by 5ml/kg normal saline intraperitoneally on day 10. Group B was given distilled water (5ml/kg) orally through gavage for 10 consecutive days followed by 750mg/kg acetaminophen dissolved in 5ml per Kg body weight normal saline intraperitoneally as single dose on day 10. Group C was given 100ml/kg Henna leaf extract dissolved in 5ml/kg distilled water given orally through gavage for 10 consecutive days followed by 750mg/kg acetaminophen dissolved in 5ml/kg normal saline intraperitoneally as single dose on day 10. Group D was given 400ml/kg Henna leaf extract dissolved in 5ml/kg distilled water orally through gavage for 10 consecutive days followed by 750ml/kg acetaminophen dissolved in 5ml/kg normal saline intraperitoneally as a single dose on day 10. All rats were sacrificed on day 12 i.e. 48 hours after administration of last dose. Livers were extracted out and sections were stained with Hematoxylin and Eosin stains. Morphological parameters such as diameter of central vein, blood vessels congestion and inflammatory cells infiltrate were studied. Biochemical parameters involved were serum ALT and AST. Results were analyzed by using SPSS version 22.0.

Results: In present study, Microscopic examination of hepatic lobules revealed abrupt increase in the diameter of central vein of Group B animals caused by acetaminophen. When this group is compared with group A (control group) while group C and D showed no significant change in diameter of central veins. Group B also showed blood vessels congestion with stagnant blood cells and disrupted endothelium causing hemorrhage within hepatic stroma. These findings were not observed in groups C & D. Signs of inflammation like infiltration of white blood cells were more appreciable in group B while this inflammation is less prominent in group C & D due to protecting effects of Henna leaf extract in these groups. Both ALT and AST were normal in control whereas raised in toxic group B. After treatment with protective agent at two different doses, ALT and AST were dropped in group C in which low dose of protective agent is used and become near to normal in group D in which high dose of protective agent was used showing hepatoprotective effects of lawsonia inermis Linn.

Conclusion: Taking in account the above mentioned observations and results, it gives a strong support that Henna Leaf (lawsonia inermis Linn.) has significant prophylactic effects on the microarchitecture of the liver that would be destroyed by the toxic effect of acetaminophen.

Key Words: Henna leaf, acetaminophen, hepatotoxicity, micrometry

INTRODUCTION

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Acetaminophen, also called paracetamol is a commonly used analgesic and antipyretic drug.[1] It suppresses prostaglandin synthesis by acting on cycloxygenase pathway COX 2 by acting centrally.[2] It is safe when administered in therapeutic doses but overdose causes toxicity primarily in the liver. It causes mitochondrial dysfunction and centrilobular necrosis.[3] Acetaminophen produce potentially toxic effect on liver and kidneys by the formation of highly active metabolite, N-acetyl-p-benzoquinon imine (NAPQI).[4] Lawsonia inermis commonly called Henna, Mehndi is a perennial plant belongs to Family Lytheraceae. It is cultivated for

cosmetic and pharmaceutical purposes.[5] It has analgesic, antipyretic, antioxidant, antiarthretic, antiulcer, antifungal and anticancer effects.[6] It is also cited that Lawsonia inermis (Henna) has protective role in acetaminophen induced hepatotoxicity in rats [7] but its dose dependent prophylactic effects against APAP induced hepatotoxicity has not been studied yet. Keeping this in view, an experimental study was designed to observe the prophylactic effect of Lawsonia inermis leaf extract at two different doses on acetaminophen induced hepatotoxicity in adult albino rats.

MATERIALS AND METHODS

This study was conducted at the Department of Anatomy, Postgraduate Medical Institute (PGMI), Lahore, Pakistan for a period of 12 days starting on June 1st, 2019. 28 adult male albino rats that were healthy,8-10 week of age,180-220g in weight 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 12th day, 48 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.

Parameters

1. **Biochemical parameters:**
   a) serum ALT
   b) serum AST
2. **Histological parameters:**
   a) Quantitative:
   i. Diameter of central vein (μm)
   b) Qualitative:
   i. Blood vessels congestion.
   ii. Inflammatory cells infiltrates.

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. Diameter of central veins were measured with ocular micrometer. 3 hepatic sections from rat were observed. 5 hepatic lobules with central vein were identified in

cross-sectional view; the cross-sectional maximum diameters of central vein were measured twice at angles perpendicular to each other i.e. horizontal & vertical diameters; the mean diameter was calculated (Fig. 1); thus 450 in total of hepatic lobules with central veins were examined and the mean diameters of central veins were noted down.

Sinusoids of each hepatic lobule was assessed for congestion and presence of inflammatory cells. 5 sinusoids in hepatic lobules in each section were examined and 3 sections from each animal were taken. Thus, the sinusoids of 450 hepatic lobules were recorded.

Statistical Analysis: All experimental data was compiled in Microsoft Word® and Excel(R) sheet. For analysis of experimental results, SPSS 22.0 (Statistical Package for Social Sciences) was used. Mean ± S.D was given for quantitative variables like diameter of central vein. Chi square was applied to observe the mean differences for qualitative variables i-e. blood vessels congestion and inflammatory cell infiltrate. For multiple comparisons, post hoc Tukey test was used. P-value of ≤0.05 was considered as statistically significant.

RESULTS

Diameter of Central Vein (μm): The mean diameter of central vein (μm) in all groups was determined. It was found that the diameter of central vein in all groups were significantly different (p value < 0.001) (Table 2). For multiple comparisons, post hoc Tukey test was used which indicated that diameter of central vein in group B was significantly higher when compared with group A, C and D. However, no significant difference was observed in the diameter of central vein between group A and D.

Blood Vessels Congestion: In all rats of group A, there was a normal looking endothelial lined blood vessels (central vein and sinusoids) with no congestion. In group B, blood vessels were dilated with disrupted endothelial lining and retained RBC's in lumen in all rats. In group C, blood vessel congestion was present in 5 (71.4%) rats whereas in group D, blood vessel congestion was observed in only 2 (28.6%) rats. (Table 3).

Inflammatory Cells Infiltrate: Fisher's exact test showed that there was an association between inflammatory cells infiltrate and groups. In group A, inflammatory cells infiltrate was absent in 5 (71.4%) rats while mild inflammation was observed in 2 (28.6%) rats. In group B, foci of inflammatory cells containing mainly lymphocytes were observed in all rats. In group C, mild inflammation was observed in 5 (71.4%) rats and moderate inflammation was observed in 2 (28.6%) rats whereas in group D, inflammation was absent in 5 (71.4%) rats while mild inflammation was observed in 2 (28.6%) rats. (Table 4)

Table No.1: Showing detail of animal groups and duration of therapy.

Group	Animals (N)	Intervention and Dosage	Duration of Dose	Day of Sacrifice
A	7 Control	Distilled water 5ml/kg via oral gavage	10 consecutive days	Day 12
		Normal saline 5ml/kg intraperitoneally	As a single dose on day 10	
B	7 Experimental	Distilled water 5ml/kg via oral gavage	10 consecutive days	Day 12
		Acetaminophen 750mg/kg dissolved in normal saline 5ml/kg intraperitoneally	As a single dose on day 10	
C	7 Experimental	Henna leaf extract 100mg/kg dissolved in distilled water 5ml/kg via oral gavage	10 consecutive days	Day 12
		Acetaminophen 750mg/kg dissolved in normal saline 5ml/kg intraperitoneally	As a single dose on day 10	
D	7 Experimental	Henna leaf extract 400mg/kg dissolved in distilled water 5ml/kg via oral gavage.	10 consecutive days	Day 12
		Acetaminophen 750mg/kg dissolved in normal saline 5ml/kg intraperitoneally	As a single dose on day 10	

Table No.2: Comparison of diameter of central vein (μm) among groups.

Variable	Group A Mean ± SD	Group B Mean ± SD	Group C Mean ± SD	Group D Mean ± SD	p-value
Diameter of central vein (μm) D*10	61.3 ± 8.2	150.3 ± 12.6	98.7 ± 6.8	59.6 ± 12.5	< 0.001*

One way ANOVA.   *p value ≤ 0.05 is regarded as significant statistically

Table No.3: Distribution of blood vessel congestion among groups

Blood Vessel Congestion	Group A n (%)	Group B n (%)	Group C n (%)	Group D n (%)	p-value
Absent	7 (100.0%)	0 (0.0%)	2 (28.6%)	5 (71.4%)	< 0.001*
Present	0 (0.0%)	7 (100.0%)	5 (71.4%)	2 (28.6%)	

Fisher's exact test   *p value ≤ 0.05 is considered statistically significant

Table No.4: Distribution of inflammatory cells infiltrate among groups.

Inflammatory Cells Infiltrate	Group A n (%)	Group B n (%)	Group C n (%)	Group D n (%)	p-value
Absent	5 (71.4%)	0 (0.0%)	0 (0.0%)	5 (71.4%)	< 0.001*
Mild	2 (28.6%)	1 (14.3%)	5 (71.4%)	2 (28.6%)	
Moderate	0 (0.0%)	3 (42.9%)	2 (28.6%)	0 (0.0%)	
Severe	0 (0.0%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	

*p value ≤ 0.05 is considered statistically significant`
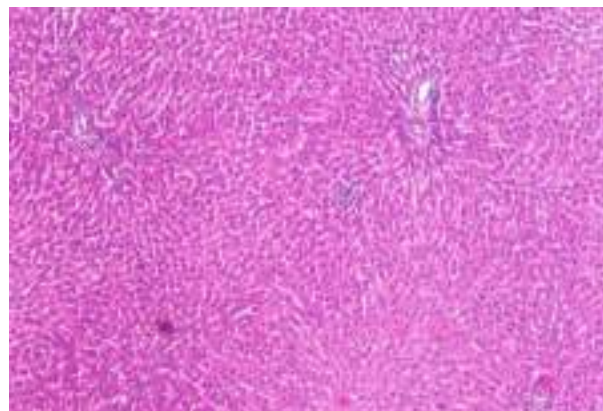
Figure No. 1: Group A showing Normal Liver Architecture
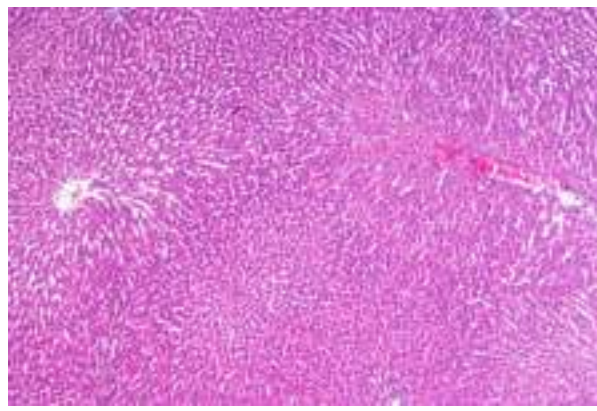
Fig No. 2: Group B showing Liver section with Congested blood vessels, wide caliber central veins full of inflammatory infiltrates
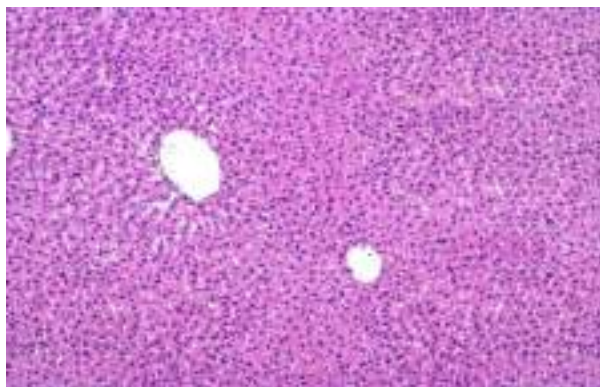
Figure No. 3: Group C showing mild congested blood vessels and moderate inflammatory cells infiltrate
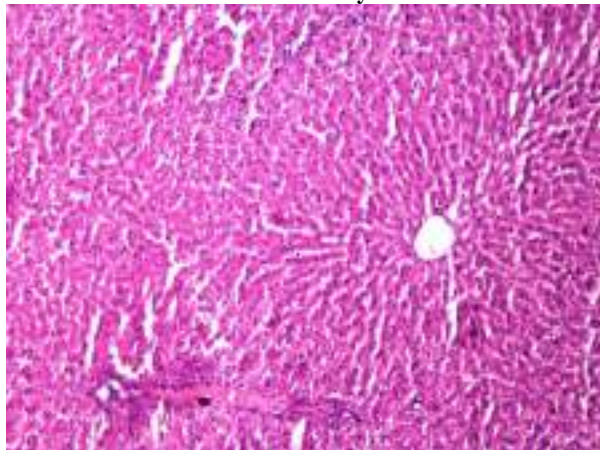
Figure No. 4: Group D showing normal caliber of central veins, normal endothelium lining of vessel and sparse presence of inflammatory cells.

Serum ALT (U/L): One way ANOVA test was used for the comparison of the serum ALT levels among groups. It was found that the mean serum ALT levels in all groups were significantly different (p value < 0.001) (Fig 5).
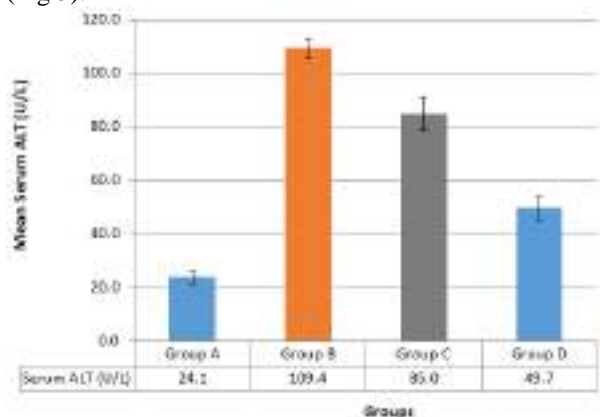
Figure No. 5: Bar chart displaying comparison of serum ALT levels among groups.

Serum AST (U/L): The mean serum AST level in all groups was determined. One way ANOVA test was used for the comparison of the serum AST levels among groups. (Fig 6).
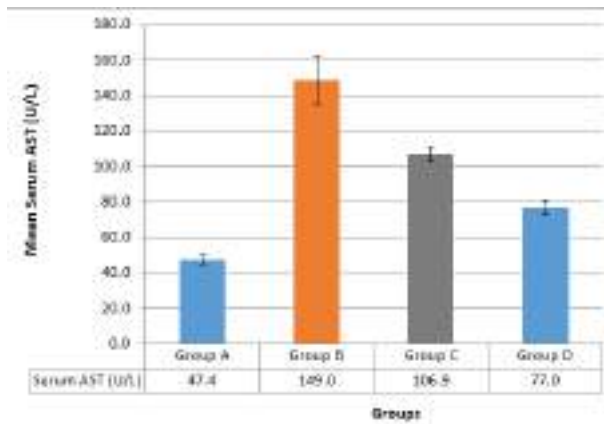
Figure No. 6: Bar chart displaying comparison of serum AST levels among groups.

DISCUSSION

Acetaminophen commonly called paracetamol is one of the most common analgesic drugs used worldwide. When dose exceeds from therapeutic level, it produces hepatotoxic effects due to excessive NAPQI (N-acetylp-benzoquinoneimine) formation.[3]

As an antioxidant, Lawsonia inermis might had reduced oxidative stress by inhibiting lipid peroxidation, quenching free radicals thus depicting protective effects on liver microvasculature.[8]

In present study, Microscopic examination of hepatic lobules revealed abrupt increase in the diameter of central vein of Group B animals caused by acetaminophen. When this group is compared with group A (control group) and group C and D (Protective groups). It shows that there is no significant increase or decrease in diameter of central veins in group A, C and D. These changes in microarchitecture correlate with previous study done on APAP or henna by Mudassir Sohail & Muzaffar, 2018.[9]

On H&E staining, signs of inflammation like infiltration of white blood cells (mainly lymphocytes) could be more appreciable in group B while this inflammation is less appreciable in group C & D due to protecting effects of Henna leaf extract in these groups. These also correlate with similar results shown in study done by Hsouna et al., 2013 in which fruit extract of lawsonia inermis was studied at dose of 250mg/kg.[10]

Blood vessels congestion with stagnant blood cells and disrupted endothelium causing hemorrhage within hepatic stroma in acetaminophen treated group B may be due to prevention of prostaglandin synthesis which could have regulated blood flow. These findings were not observed in groups C & D and correlate with studies done by Sabiba et al., 2013 who observed congestion of hepatic blood vessels following administration of acetaminphen 900mg/kg i.p.[11] Protective effects of lawsonia inermis supported by results given by Hsouna et al, 2013.[10]

Biochemical parameters used in this study were ALT and AST. Both ALT and AST are the enzymes that catalyzes the important reactions that are involved in the transfer of α-amino groups from aspartate and alanine to α-keto group of ketoglutamic acid to generate oxaloacetic and pyruvic acids respectively which are important contributers to citric acid cycle. Alanine aminotransferase is mostly present in cytoplasm of hepatocytes while AST attain both cytoplasmic and mitochondrial position. If hepatic injury occurs, it results in the release of both ALT and AST in serum causing increased level of both enzymes.[3] Both ALT and AST were normal in control whereas raised in toxic group B. After treatment with protective agent at two different doses, ALT and AST were dropped in group C in which low dose of protective agent is used and become near to normal in group D in which high dose of protective agent was used showing hepatoprotective effects of lawsonia inermis.

CONCLUSION

Taking in account the above mentioned observations and results, it gives a strong evidence that lawsonia inermis has significant prophylactic effects on the microarchitecture of the liver that would be destroyed by the toxic effect of acetaminophen. However, more long term studies can be made to further explore the genetic effects of this drug therapy on liver.

Author's Contribution:

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Data Analysis:	Aneela Ahsan, Uzma Azam
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Final Approval of version:	Misbah Ishtiaq

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

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Original Article

Comparison of Efficacy of Intralesional 5-Fluorouracil Plus Triamcinolone Versus Triamcinolone Alone in the Treatment of Keloids

Seemab Khan, Muhammad Usman and Tooba Malik

ABSTRACT

Objective: To compare the efficacy of triamcinolone acetonide (TAC) alone versus triamcinolone plus 5-fluorouracil (5-FU) in patients with keloids in terms of the proportion of patients who improved significantly.

Study Design: A Randomized controlled study

Place and Duration of Study: This study was conducted at the Department of Dermatology/Plastic Surgery, Bakhtawar Amin Teaching Hospital Multan from 18th March 2019 to 18th March 2020.

Materials and Methods: We enrolled 160 patients at the Bakhtawar Amin Teaching Hospital and randomly assigned them to receive Intralesional triamcinolone (group 1) or a combination of TAC and 5-fluorouracil (5-FU) for one year (group 2).

Results: The average age at the time of the survey was 30.748.47 years. There were no statistically significant variations between the two groups in terms of age and gender distribution in this study. Males made up 40% of the group, while women made up the rest (a 25 % male to female ratio). Only 16% of the TAC patients responded to treatment, but 75% of the 5-FU + TAC patients responded. There was a statistically significant difference between the two groups, and this was confirmed by a p value of 0.05.

Conclusion: The efficacy in terms of frequency of patients with good to outstanding improvement in keloids was significantly greater in triamcinolone + 5-FU group as compared to the triamcinolone alone group.

Key Words: Intralesional triamcinolone, Keloids, Hypertrophic scars, Triamcinolone acetate, 5- Fluorouracil

INTRODUCTION

A keloid is an abnormal response of the skin to injury, inflammation, surgery, or burns. It is more common for people who are prone to keloids to develop them. These growths of dermal collagen can cause patients to have both physical and psychological challenges. They could cause long-lasting discomfort and irritation. According to the Centers for Disease Control and Prevention (CDC), 4.5 to 16 % of people with darker skin have been diagnosed with the condition. Between the ages of 10 and 25, keloid scars are most common in Asian and African cultures.

There are a variety of treatment options, including Intralesional injections of corticosteroids.

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With a success rate ranging from 58% to 93%, excision and triamcinolone have been the gold standard in cancer treatment for decades now. Failures of previous therapy must be acknowledged. In addition, up to 37% of people have had unfavorable outcomes, including as hypopigmentation, atrophy, and telangiectasia's, among others.[1]

5-fluorouracil, mitomycin C, and bleomycin, which target scar tissue fibroblasts, have been demonstrated to be an effective treatment for scar tissue. The combination of 5-FU and triamcinolone may be more successful than intralesional steroids alone in treating wounds, according to clinical trials. Synonym for 5-FU, this pyrimidine analogue is helpful against skin wounds' excessive collagen formation by rapidly reproducing fibroblasts. Triamcinolone and 5-FU, which can be taken in combination with corticosteroids, were first shown to increase efficacy and reduce injection discomfort by Fitzpatrick's research team.

Sadeghina's recent research has shown that 5-FU tattooing is more effective than intralesional triamcinolone (TAC) injections in the treatment of keloids. The combination of 5-FU and triamcinolone has been proven to be more successful than intralesional steroid therapy alone in the treatment of keloids, according to studies. Over the course of their analysis, the scientists uncovered 102 keloids. In

combination with steroid medication and excision, 5-FU patients had an average lesion reduction of 92% compared to 73% in patients who didn't receive 5-FU. 'For individuals who got 5-FU/steroid without surgical excision, statistically significant differences were found between the two groups (p 0.05).[2]

40 patients were randomly randomized to receive intralesional triamcinolone acetonide (TAC) or 5-fluorouracil as part of a combination therapy in a separate study by Darougheh and colleagues (5-FU)[3]. Groups 1 and 2 had response rates ranging from excellent (40%) to passable (15%), although there was no statistically significant difference between the two groups (p = 0.08). Triamcinolone alone will be compared against triamcinolone mixed with 5-FU due to anecdotal data showing inconsistent outcomes (in the Davison study, there was a substantial difference, while in the Darougheh study, the difference was not statistically significant).

MATERIALS AND METHODS

The study was conducted from 18th March 2019 to 18th March 2020 at Bakhtawar Amin Teaching Hospital Multan. The Hospital Ethic Committee granted permission for the collection of this data. Each patient was asked to sign a written informed consent after a thorough conversation. Dermatology patients were also seen at other places. If any tests were done, their results are included in this section as well as the patient's medical history and physical exam findings Clinical evidence was used to arrive at the diagnosis. Through the use of a lottery system, patients were divided into two groups, one for Group A and one for Group B.[4]

The length of the lesion was measured in millimeters and a ruler was used to take a snapshot of the lesion along the length of the lesion. Using Vernier calipers, the maximum horizontal thickness of the material was determined. Group A participants received intralesional corticosteroid injections. At a dosage of 40 mg/ml, triamcinolone was injected. A 30 gauge needle connected to a 1 ml insulin syringe was used to inject the corticosteroid directly into the keloid. Treatment volumes ranged from 0.01 to 0.05 milliliters per centimeter of lesion. Although the volume varied from patient to patient, it was customary to inject 0.01 milliliters per centimeter of skin. Group B, on the other hand, received a corticosteroid injection and 5-FU Intralesional injection. In this solution, a 75% 5-FU solution is mixed with a 25% Triamcinolone solution at a concentration of 40 mg/ml. Each centimeter of the lesion was injected with a 0.1 ml solution.[5]

For eight weeks, patients received weekly injections. Using a ruler and a previous photograph as a guide, we measured the lesions' size and thickness in millimeters once more at the end of week 12, exactly as we had done before to beginning therapy.[6]

Data Analysis: In SPSS for Social Sciences version 11, the acquired data was transformed into variables, and the results were examined. Visual representations of numerical data, such as age, mean, and standard deviation, were available. Gender and effectiveness are two examples of categorical variables that were expressed using frequency and percentages. The %age of patients who saw a significant improvement in their condition was compared between two groups, with some surprising results.

RESULTS

Eighty individuals were referred to the TAC group and the remaining eighty were referred to the TAC plus 5-FU group. 18 to 55-year-olds had an average age of 30.74 + 8.47 years. The mean and median ages were determined to be 30,5 and 23, respectively. Patients in the TAC and 5FU plus TAC groups had a mean age of 31.779.14 years, while those in the 5FU plus TAC group had a mean age of 29.776.66 years. The p-value for this difference, which was 0.124, indicated a non-significant difference. There were 40 men and 120 women in the study. TAC's membership included 17 men and 19 women (63.33 %). Thirteen males (43.33 %) and eleven women (36.67 %) were enrolled in the hypertonic saline trial. The difference is not statistically significant, as indicated by the p value of 0.598.[7]

At baseline, the diameters of tumors ranged from 10 to 109 millimeters. There were 64.723.27mm keloids on average. The median and mean diameters of keloid were 66.5 and 67 millimeters, respectively. Compared to patients in the 5-FU plus TAC group, those in the TAC group had keloids measuring 67.5821.78 mm on average at baseline (S0). This difference was not statistically significant, as indicated by the p-value.

In our study, the size of the keloids at 12 weeks ranged from 0 mm to 88 mm. It measured 34.58mm x 23.82mm in size. The diameter of the most prevalent keloids was 36 mm, while the tiniest keloids had a diameter of 0 mm. At the conclusion of the 12-week study, patients in the TAC group had keloids (S12) ranging in size from 0 to 88 mm on average, while those in the 5-FU + TAC group had keloids (S12) ranging in size from 0 to 65 mm on average. The 12-week results demonstrated statistical significance. This instance revealed a statistical difference of p 0.01. After 12 weeks of treatment, the prevalence of keloids dropped from 100 % to 100.33%. The size of keloids decreased by between 52.27 and 52.98 %. The median and average sizes of the keloids decreased by 47% and 100%, respectively. The 12-week decrease in keloids in the TAC and 5-FU groups was 34.2621.8% and 70.2725.7%, respectively. Statistical significance was established if the p-value was less than one.[8]

Effectiveness was defined as a 50 % or better reduction in symptoms and a good-to-excellent improvement. There were 13 TAC responders, compared to 60 in the

5-FU plus TAC group, which had a response rate of 75%. This difference was statistically significant, with a p-value of 0.01, according to the results (Table 4). Combining 5-FU with TAC proved to be much superior to TAC alone, according to the results of the study. There were five full remissions in the TAC group and 31 in the 5-FU + TAC group, a difference of 63.3%.[9]

The vast majority of patients (n=80; 50%) were under the age of 30. In the TAC group, just 22.6 % of patients responded; in the 5 FU plus TAC group, 85.6 % of patients responded (p = 0.000). At 30 years of age, 5 FU was found to be more effective than TAC alone. The TAC group had a success rate of 14.3%, but the 5 FU and TAC group had a success rate of 63.3% (p=0.000). When compared to 5 FU alone, TAC was completely ineffective in the 31-year-old age group.

TAC was well tolerated by 6/23 (26 %) of the 40 male patients, whereas 13/17 (76.5 %) of the patients in the 5

FU plus TAC group were successful in their therapy. TAC by itself was not as effective in men as 5 FU was. It was shown that the TAC and 5 FU plus TAC groups had response rates of 6/57 (10.5 %) and 47/63 (74 %) in this trial of 120 female patients. The combination of 5 FU with TAC was substantially more effective in females than TAC alone.[10]

79 people, or 50 %, had keloids on the trunk and head. TAC alone was ineffective in treating keloids on the trunk and head (p=0.000). 5 FU + TAC was more effective than TAC alone. TAC group patients responded to treatment at a rate of just 19%, compared to a rate of 77% in the 5 FU + TAC group (p=0.000)[11]. Half of the patients had keloids, which could be seen on their limbs. There were six patients in the TAC group, and 27 in the 5-FU and 5-FU + TAC group; the p-value was 0.0001. In treating limb keloids, 5 FU with TAC performed better than TAC, according to this study.[12]

Table No.1: Comparison of baseline keloids size between the two groups

	Group	N	Mean	Std. Deviation	Std. Error Mean	P value♣
Baseline Size	TAC group	80	67.5875	21.78531	2.43567	0.119*
	5 FU plus TAC group	80	61.8500	24.47375	2.73625	

Table No.2: Efficacy in different age groups among in TAC and 5-FU plus TAC groups

Age group		Efficacy			P value♣
		Yes	No	Total	
≤ 30 years	TAC group	7	31	38	0.000
	5 FU plus TAC group	36	6	42	
	Total	43	37	80	
≥ 31 years	TAC group	6	36	42	0.00
	5 FU plus TAC group	24	14	38	
	Total	30	50	80	

Table No. 3: Efficacy in different sites among TAC and 5-FU plus TAC groups

Site of keloid		Efficacy			P value♣
		Yes	No	Total	
Trunk and head	TAC group	7	29	36	
	5 FU plus TAC group	33	10	43	0.000
Limbs	TAC group	6	38	44	
	5 FU plus TAC group	27	10	37	0.000

Table No.4: Efficacy in different duration groups among TAC and 5-FU plus TAC groups

Duration of keloid		Efficacy			P value♣
		Yes	No	Total	
< 6 months	TAC group	5	38	43	
	5 FU plus TAC group	20	8	28	0.000
> 6 months	TAC group	8	29	37	
	5 FU plus TAC group	40	12	52	0.000

Within six months of the procedure, 68 (42.5 %) of the patients had keloids that had disappeared. Treatment with TAC was successful in 5 of 43 patients (11.6%), compared to 20 of 28 (71.4%) patients treated with 5 FU plus TAC (p=0.000). TAC was less effective than 5 FU in the treatment of keloids lasting less than six months, according to the results of this study. 95 patients (57.5%) had keloids that had persisted for more than six months in their treatment. In the TAC group, 21.6 % of patients reacted, whereas in the 5 FU plus TAC group, 77 % of patients responded, p-value = 0.000.'s. Keloids can be successfully treated with TAC and 5 FU for a longer period of time than with TAC alone, according to this study[9].

DISCUSSION

Keloids and hypertrophic scars occur as a result of aberrant skin repair following an injury[2]. Patients frequently seek medical therapy as a result of the considerable functional and emotional consequences of the diseases. Injections of corticosteroids are frequently used to treat keloids and hypertrophic scars. My research purpose was to determine whether intralesional TAC+5-FU is more effective in treating keloids than TAC alone, in order to offer a more informed therapeutic recommendation.[13] TAC and 5-FU intralesional injections were evaluated for their efficacy in reducing initial scar size in keloid patients. I conducted a randomized controlled experiment for 1 year at the Bahawalpur Amin Teaching Hospital. 168 participants were randomly assigned to receive intralesional triamcinolone acetonide injections or intralesional corticosteroid injections plus 5-FU.[14] Lesions were measured in millimeters (mm) along the same dimensions as before therapy at the completion of week 12. The fraction of keloids that shrank by more than half was used to measure efficacy, suggesting a good-to-excellent response. There were 40 men and 120 women, with a mean age of 30.74 years and an average standard deviation of 8.47 years.[15] Between the two groups, there was no statistically significant difference in the distribution of age or gender. This suggests that the age and gender distributions of the two groups were comparable. Demographic factors have no influence on the efficacy variation. Thirteen (13.3%) patients in the TAC group responded to treatment, whereas sixty (75%) patients in the 5-FU plus TAC group did. A statistically significant difference was detected, with a p-value of 0.0.000. As a result, the triamcinolone + 5-FU group demonstrated significantly greater efficacy than the triamcinolone alone group in terms of patients who improved significantly.[16]

CONCLUSION

The efficacy in terms of frequency of patients with good to outstanding improvement in keloids was significantly greater in triamcinolone + 5-FU group as compared to the triamcinolone alone group.

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

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Original Article

Comparison of the Frequency of Short Labour Duration With or Without Exercise

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ABSTRACT

Objective: To compare the frequency of short labour duration with or without exercise started from second trimester of pregnancy till delivery.

Study Design: Randomized control trial study

Place and Duration of Study: This study was conducted at the Department of Obstetrics &Gynecology, Services Hospital Lahore from 24-01-2021 to 24-12-2021.

Materials and Methods: 400 patients were included in the study. Patients were divided into two groups. One group is with exercise and other is without exercise. Then females were followed up. 12 patients were lost to follow up, leaving 388 patients in the study. Outcome was noted. The collected data was entered and analysed on SPSS version 21.

Results: The mean age of exercise group patients was 30.79 ± 6.32years and in no exercise group was 30.26 ± 6.27years. 113 patients had less than primary education and 125 patients belonged to low socioeconomic group. The efficacy for short labour duration was achieved in 231(59.5%) patients, out of which 139 were from exercise group and 92 were from no exercise group i.e. p-value=0.001.

Conclusion: Exercise started during second trimester of pregnancy and continued till delivery can help in shortening the duration of labour.

Key Words: Duration of labor, Exercise, Women, Pregnancy, Second trimester

INTRODUCTION

Pregnancy has traditionally been associated with discomfort. Pregnant women remain constantly apprehensive about birth and the attendant discomforts. This apprehension leads to reduced physical activity in antenatal period.[1] Evidence suggests that women should remain physically active throughout pregnancy.[2] Physical activity during pregnancy elevates mood-enhancing hormones in the brain and reduces pregnancy related blues.[3] Prenatal physical exercise has been increasingly suggested across the world in recent years as a vital requirement for healthy pregnancy and uneventful delivery.[4]

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Antenatal exercise leads to maintained maternal health status, less backache and less maternal weight gain during antenatal period. It also impacts labor duration, type of delivery, and severity of pain during labour, leading to a change in attitude of pregnant women towards labour and new born outcome.[5] Women who exercise throughout labour and delivery experience fewer problems than those who do not.[6]

Skeletal muscles movement during exercise improves cardiorespiratory fitness. It helps to maintain body weight, reduces maternal obesity, improves general health status and results in overall maternal wellbeing. Mothers should be motivated to continue physical activity in pregnancy. Controversy regarding association of maternal exercise with miscarriage, restricted fetal growth or preterm labour continues to prevail among some obstetric care providers.[7-9] Proponents of this belief refer to studies where the fetal heart rate rises by 10–30 beats per minute after maternal physical activiy.[10]

The pelvic floor muscles along with abdominal muscles are involved in the labour process .The pelvic floor muscles hang like a sling and support bladder, uterus, and other pelvic organs.These are strengthened by Kegel's exercises. Abdominal muscles along with leg muscles on the other hand are strengthened by stretching activities. It assists to prevent cramping and sprains.

Rationale of this study is to compare the frequency of labour duration in mothers who exercised during second trimester and continued it till delivery with those who did not exercise in the same time period. In our society, routine, exercise is not encouraged during pregnancy. Moreover, no local evidence is available in favour of exercise during pregnancy. However Literature shows that exercise during pregnancy can help in reducing the duration of labour. But not much work has been done in this regard. This study will help to improve local practices and will help mothers to reduce the duration of labour and complications of prolonged labour.

MATERIALS AND METHODS

This Randomized Controlled Trial study was conducted at Department of Obstetrics and Gynecology, Services Hospital Lahore for one year from 24-01-2021 to 24-12-2021.

Sample Size: 400 patients were included in the study. Patients were divided into two groups. One group is with exercise and other is without exercise. Then females were followed up. 12 patients were lost to follow up, leaving 388 patients in the study.194 cases in both groups. This sample size is calculated with 80% power of test, 5% level of significance and taking expected percentage of short duration of labour i.e. 65% with exercise and 51% without exercise.

Sampling technique: Non-probability consecutive sampling.

Selection criteria: Pregnant females of 20-40years of age with parity of 1 with previous SVD (spontaneous vertex delivery) with or without episiotomy were included in the study. They presented for antenatal check-up with singleton pregnancy at gestational age of 24-32 weeks. While females with multiple pregnancy, history of uterine surgery, or medical disorders were excluded. Also females with intrauterine fetal death, with antepartum hemorrhage or with abnormal placental implantation (previa, accrete, increta) were also excluded from the study.

Data collection procedure: 400 patients who fulfilled the inclusion criteria were included in the study. These patients initially reported in OPD of Department of Obstetrics & Gynecology, Services hospital Lahore. Informed consent was taken. Demographic information (name, age, parity, gestational age, BMI) was recorded on predesigned performa. Women were randomised into two groups by lottery method. In group A, females were advised to exercise while in group B, females were not given specific advise to exercise. Group A women were advised strengthening and stretching exercises for 2 sessions per week till delivery. These involved abdominal, pelvic, and back muscles. Duration of exercise was increased from 30 minutes in the early sessions to 60 minutes in later sessions.12 patients were lost to follow up, leaving 388 patients in

the study. 194 cases in both groups. Both groups were followed-up till delivery. If duration of labour was less than 12 hours, then efficacy was labeled. All this information was recorded through proforma (attached).

Data analysis: Data entry and analysis was performed by using IBM-SPSS 21.0. Mean and standard deviation was calculated for continuous (quantitative) variables. Both groups were compared for efficacy for short labour duration by using chi-square test with p-value≤0.05 taken as significant. Data is presented in tables.

RESULTS

Table No.1: Demographic Profile of Women

	Study Groups		
	Exercise	No exercise	
n	194	194	
Age (years)	30.79 ± 6.32	30.26 ± 6.27	
Gestational Age (weeks)	27.99 ± 2.43	27.47 ± 2.61	
BMI (Kg/m^2)	23.72 ± 3.37	24.33 ± 3.23	
Education of female			Total
Less than primary education	56	57	113
Below matric	63	67	130
Matric & above	75	70	145
Socioeconomic status			
Low	60	65	125
Middle	79	55	134
High	55	74	129

The mean age of patients in exercise group (Group A) was 22.79±6.32years and in group with no exercise (Group B) was 22.26±6.27years.The mean gestational age at delivery of the patients in exercise group was 37.99±2.43 weeks and in no exercise group was 37.47±2.61 weeks. The mean BMI of patients in exercise group was 23.72±3.37kg/m^{2}while in no exercise group was 24.33±3.23kg/m^2. Statistically insignificant difference was found between groups for gestational age at delivery and BMI of women i.e. p-value=0.077 and p-value=0.069. In this study 113 patients had less than primary education. Out of theses 113 patients, 56 performed exercise (Group A) and 57 did not do exercise (Group B).The patients with education below matric were 130. Out of theses 130

patients, 63 performed exercise (Group A) and 67 did not do exercise (Group B). Similarly, the patients with education of matric & above were 145. From these 145 patients 75 performed exercise (Group A) while 70 did not do exercise (Group B). In our study, 125 patients had low socioeconomic status , from which 60 were from exercise group and 65 were from no exercise group, 134 patients had middle socioeconomic status. From which 79 were from exercise group and 55 were from no exercise group and 129 patients had high socioeconomic status, from which 55 were from exercise group and 74 were from no exercise group. Table 1

The mean duration of labour for patients of exercise group was 9.97±3.68 hours and for patients of no exercise group was 13.25±4.52hours. Statistically significant difference was found between groups for duration of labour i.e. p-value=0.000. Table 2

Efficacy was reached in total of 231 cases. Out of these 231 cases, 139 were from exercise group and 92 were from no exercise group. Efficacy could not be reached in 157 cases from which 55 were from exercise group and 102 were from no exercise group. Statistically significant difference was found between the two groups in terms of efficacy (p-value=0.000). Table 3.

Table No.2: Comparison of duration of labour

		Study Groups	
		Exercise	No exercise
Duration of labour	n	194	194
	Mean	9.97	13.25
	SD	3.68	4.52

Ind. t test= 7.831, p-value=0.000*

Table No.3: Comparison of efficacy

		Study Groups		Total
		Exercise	No exercise	
Efficacy	Yes	139 (71.6%)	92 (47.4%)	231 (59.5%)
	No	55 (28.4%)	102 (52.6%)	157 (40.5%)
Total		194 (100%)	194 (100%)	388 (%)

Chi value=23.633, p-value=0.000*

DISCUSSION

It is commonly known that maternal activity during pregnancy provides several health benefits for mothers, ranging from enhanced fitness, reduction of unnecessary weight gain to reduced incidence of maternal medical disorders, and enhanced post-partum recovery. The American College of Obstetricians and Gynecologists recommends encouraging the low risk pregnant women to exercise for at least 30 minutes.[11]Our study shows that the efficacy for the shorter duration of labour was achieved in 231(59.5%) patients. 71.6% (139) of these patients who attained efficacy performed exercise during pregnancy while 47.4% (92) did not perform exercise during pregnancy. The result shows statistically significant difference in terms of efficacy attained for shorter duration of labour between the two groups, with the group performing exercise showing better results (p-value=0.001). Very less data is available on this topic and results of those available studies are comparable with our study. In our study, exercise group showed better outcome than no exercise group.

Szymanski et al.in a cohort study, studied the effects of vigorous activity on the umbilical artery blood flow, fetal heart rate, and biophysical profiles before and after exercise. They found that both women and fetuses withstood 30 minutes of vigorous exercise well, in both active and sedentary pregnant women. Thus showing the beneficial effects of exercise during pregnancy.[12] May et al., in a study found that exerciser moms and their babies spent less time in the hospital than non-exercisers [6].Overall, the shorter labor, less preterm labor, fewer problems, and a shorter stay in the hospital all add up to lower health-care expenses.This study's findings are consistent with our findings, indicating that exercise during pregnancy can help shorten labor duration, enhance vaginal birth, and less cesarean sections, all of which minimize hospital stay after birth.The link between exercise during pregnancy and pregnancy outcomes is poorly known.[2] However, a research found that short labour length (less than 12 hours) was effective in 65 percent of exercising pregnant women, whereas in the control group, the shorter duration of labor was only accomplished in 51 percent of instances.[13]

Similar results were reported by Clapp et al. According to this study exercise during pregnancy may result in reduced labor and delivery times for all women.[14] Parity affects the duration of labor. Multiparas had shorter labor than nulliparas, according to Pomerance et al.[15] To overcome this compounding factor only those women with parity of one were inducted in our study. Although data from randomized controlled trials is scarce, observational studies have suggested that women who exercise throughout pregnancy have reduced risks of gestational diabetes mellitus,[9,16-18] cesarean births and surgical vaginal procedures.[19-21] These women also have better postpartum recovery.[21]

Exercise during pregnancy also helps to maintain maternal weight. Meta-analysis of gestational weight gain interventions suggests that physical activity is a

successful strategy in restricting excessive maternal gestational weight gain.[22]

The other school of thought suggests insignificant tendency among exerciser mothers for earlier commencement of labour and delivery at term, shorter labour, and reduced incidence of problems during delivery (like cesarean delivery, using forceps or induction of labor, vaginal tears, and fatigue) as reported by Clapp and Sternfeld et al.[23,24] However in these trials, infants born to women who exercised had better Apgar ratings, and their moms recovered faster after giving birth. Clapp also discovered that women who stay active during their pregnancies are more likely to return to their pre-pregnancy physical state earlier after childbirth.[23]

Exercising during pregnancy does not cause premature labor, contrary to common perception. Rather women who exercised throughout labour and delivery experienced fewer problems than those who did not. More significantly, no signs of fetal distress were detected during the labour and delivery procedure. Measures of fetal distress, such as Apgar scores, indicated no difference or benefits in response to exercise exposure. In comparison to non-exercising moms and their children, exercising women along with their children spent less time in the hospital. Overall, the findings of possible shorter labour, less preterm labour, fewer problems, and a shorter stay in the hospital all add up to lower health-care expenses. In this area, more study is required.[25]

CONCLUSION

According to this study patients who exercised during second and third trimester of pregnancy and remained active till delivery showed significantly shorter duration of labour than to those without exercise. Efficacy for shorter duration of labour was achieved in 71.6% patients with exercise during pregnancy.

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Data Analysis:	Wajid Ali, Tabeer Malik
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

The Expression of Soluble C-Type Lectin-Like Receptor-2 (sCLEC-2) in Metabolic Syndrome

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ABSTRACT

Objective: To find out the levels of "soluble C-type lectin-like receptors-2 (sCLEC-2)" in subjects of metabolic syndrome.

Study Design: Cross-Sectional Study

Place and Duration of Study: This study was conducted at the Ziauddin University and Hospital, Karachi from 30th April 2021 to 1st January 2022.

Materials and Methods: The study comprised 45 patients fulfilling the criteria of metabolic syndrome (MetS) based on AHA, which includes the following risk factors: diabetes mellitus, hypertension, central obesity or dyslipidemia. A group of 10 healthy individuals was also recruited as a healthy group. The study was approved by the ethics review committee (ERC) reference code: 3440321TKBC. Demographic and anthropometric data were gathered following informed consent. A physical examination was performed. Venous blood (5 ml) was drawn by using an aseptic technique. Serum was obtained and sCLEC2 levels were assessed by ELISA kit (Bioassay Technology Laboratory BT LAB Cat. No. E7510Hu). The mean, standard deviation (SD), median, and interquartile range (IQR) were used to report numerical data, along with the r and p values. P-value < 0.05 was considered as statistically significant.

Results: The mean of sCLEC-2 levels among 45 MetS individuals was 371.8 pg/ml $\pm$ 320 pg/ml whereas the median was calculated to be 237 pg/ml IQR of 358.6 pg/ml. In healthy subjects, the mean sCLEC-2 level was 90.6 pg/ml ($\pm$37.09 pg/ml) and the median was 98.6 pg/ml (IQR 45 pg/ml). The serum sCLEC-2 levels were significantly high in metabolic syndrome than the healthy individual (*p* value 0.0001).

Conclusion: The increased soluble CLEC-2 expression in metabolic syndrome patients as compared to healthy individuals might be linked to platelet activation and development of atherosclerosis in metabolic syndrome.

Key Words: Metabolic Syndrome (MetS), "soluble C-type lectin-like receptor 2 (sCLEC-2)", Diabetes Mellitus, Hypertension, Dyslipidemia, BMI

INTRODUCTION

Metabolic syndrome (MetS) is a set of risk factors that include hyperglycemia, obesity, dyslipidemia, and hypertension (Gui et al., 2017)[1]. Metabolic syndrome (MetS) has a strong correlation with coronary artery disease (CAD) which is caused by atherosclerotic plaque buildup (Mahalle et al., 2014)[2]. A proportion of 20 to 25% of the adult population is affected by MetS, globally(do Vale Moreira et al., 2020)[3]. South Asians are more likely to develop MetS due to their high body fat percentage, abdominal obesity, and insulin resistance than the general population (Enas et al., 2007)[4]. According to one study, the prevalence of MetS in the Pakistani population has increased from 35% to 64% over last decades. (Hai et al., 2019)[5]

Platelets play a significant role in the advancement of atherothrombosis by inducing hyper-reactivity or activation, which is a major component in the development of CAD in MetS patients. This result is due to the intricate interaction between obesity and MetS features: insulin resistance, inflammation, and oxidative stress are all factors that contribute to endothelial dysfunction (Santilli et al., 2012)[6]. Platelet activation is characterised by shape changes, microparticle shedding, and overexpression of receptors which are now being studied with different atherothrombotic diseases.(Rubenstein and Yin, 2011)[7]

C-type lectin-like receptor 2 (CLEC-2) is one of the platelet membrane activation proteins, it is a type of pattern recognition receptor (PRRs) (Gitz et al., 2014)[8]. Pattern recognition receptors have been reported in the platelet membrane activation and one of them is CLEC which functions via a tyrosine kinase-dependent pathway. It causes effective activation of platelets via

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the tyrosine kinase-dependent pathway, which strongly relates to platelet activation.(Martyanov et al., 2020)[9]. Studies showed the significant relationship of sCLEC-2 to thrombus stabilization and its mechanism of shedding during platelet activation. This makes it an ideal marker for detecting atherosclerosis prior to the event. (Lombard et al., 2018)[10] Several studies have linked platelet activation membrane receptors to various thrombotic diseases. However, there is a dearth of studies evaluating soluble CLEC-2 in metS, which is considered a transitional stage between being healthy and developing a morbid event such as a myocardial infarction or stroke.(Poddar and Banerjee, 2020)[11] (Fryar et al., 2012)[12] Therefore, we aimed to find out the levels of sCLEC-2 levels in a group of metabolic syndrome patients**.**

MATERIALS AND METHODS

Total of 45 individuals were recruited in the current study via consecutive sampling techniques from Ziauddin medical hospital, Karachi, Pakistan. The ethics review committee (ERC) at Ziauddin University (reference code: 3440321TKBC), approved the study protocols, based on the Declaration of Helsinki. All of the subjects had at least three risk factors out of four to be diagnosed with metabolic syndrome. For the purpose of determining the mean CLEC-2 levels in healthy subject, 10 healthy individuals were also recruited after taken informed consent.

The inclusion of subjects were based on diagnostic criteria for metabolic syndrome, which include having at least three of the following conditions: waist circumference of greater than 120 cm (or more than 88 cm for women) (B) Fasting blood sugar less than 100 mg/dL or on antidiabetic medications (C) HDL-C less than 50 mg/dL in females or 40 mg/dL in men (D) Triglycerides less than 150 mg/dL or on antidyslipidemic therapies (E) SBP less than 130 mmHg or DBP less than 85 mmHg or on antihypertensive medication (Benjamin et al., 2019)[13]. Whereas, patients having septicemia, autoimmune disease, malignancy, pregnancy and any cardiovascular diseases other than coronary artery disease were excluded from the study on the basis of medical records.

Sample Preparation and ELISA: Using aseptic approach, 5ml of blood was drawn from a venepuncture. 2.5ml blood was discharged into an EDTA tube for CBC, which was thoroughly mixed by inverting the tubes 8 to 10 times to avoid coagulation. For ELISA, another 2.5ml of blood was collected in a gel tube and centrifuged at 3000 rpm for 15 minutes at room temperature. Supernatants were carefully collected and divided into 250 mL aliquots in Eppendorf tubes. All of the samples were kept at -20°C. Each tube was used once only test to avoid freezing-thawing cycles. The serum level of sCLEC-2 was determined according to the manufacturer's protocol using a commercial enzyme-linked immunosorbent assay (ELISA) kit (Bioassay Technology Laboratory BT LAB Cat.No. E7510Hu).

Statistical analysis: Statistical analysis was carried on SPSS version 20. The normality of data was assessed by Shapiro-wilk test. Continuous variables were presented as the median and interquartile range. Categorical data expressed in frequency and percentages. The comparison between the two groups was assessed by Mann Whitney test and spearman correlation was performed. (P-value less the 0.05 consider significant)

RESULTS

The study subjects were predominantly males 24 (53.3%) than females 21(46.7%) with median age of 54 (IQR 24.7) years. Whereas, majority of study subjects had smoking and positive family history of coronary artery disease. All the study subjects had hypertension followed by diabetes and hyperlipidemia, indicating that these comorbidities are prominent in metabolic syndrome as depicted in Table 1.

Patients of MetS have higher values of Body mass index (BMI) (27.9 IQR 5), Systolic B.P (140 IQR 20 mmHg), Waist circumference (40 IQR 7.5 inches), Fasting blood sugar (120 IQR 66 mg/dl), Random blood sugar (231 IQR 104 mg/dl), HbA1c (8.3 IQR 5), Urea (38.5 IQR 36.5 mg/dl), Creatinine (1.2 IQR .79 mg/dl) and lipid profile [Total Cholesterol 160 IQR 60, Triacylglycerol (TAG) 145 IQR 84.5, HDL 40 IQR 11.2, LDL 120 IQR 98] then the normal ranges. All these factors showed no significant correlation with the sCLEC-2 concentration except for HbA1c which showed p value 0.05 with correlation coefficient r 0.297.

Table No.1: The sCLEC-2 levels in relation to demographic and clinical characteristics of participants

Variable	Metabolic syndrome Frequency n (percentage %)	CLEC-2 levels	P=value
Gender: Male Female	24 (53.3%) 21(46.7%)	M= 257.7(I.R 502) F= 213.6 (I.R 181)	0.275
Family History: Yes No	28 (62.2%) 17(37.8%)	Yes= 231.3 (I.R 114.6) No= 329.1 (I.R 384.1)	0.271
Smoking: Yes No	28(62.2%) 17(37.8%)	Yes= 257 (I.R 408.6) No= 206 (I.R 68)	0.440
Hyperlipidemia: Yes No	36 (80%) 9(20%)	236.7(I.R 352) 233.4 (I.R 151.7)	0.650
Diabetes Mellitus: Yes No	43(95.6%) 2 (4.4%)	Yes= 242 (I.R 311.3) No= 143.2 (I.R 90)	0.098

Figure No.1: Serum levels of sCLEC-2 in Metabolic syndrome and healthy subjects

The expression of sCLEC-2 was assessed in the serum of 45 patients with metabolic syndrome and 10 healthy people. The median was 233 pg/ml (IQR 275.5 pg/ml) and the mean was 371.8 pg/ml (±320 pg/ml) in patient of MetS. Whereas the sCLEC-2 levels in healthy individuals was observed as mean 90.6 pg/ml (±37.09 pg/ml) and the median was 98.6 pg/ml (IQR 45 pg/ml). As shown in figure 1, the difference between the MetS and healthy groups is statistically significant with p value 0.0001 at 95% CI. (Fig 1)

DISCUSSION

The syndrome refers to a group of metabolic abnormalities such as dyslipidemia, hypertension, and insulin resistance (IR), which are all linked to central fat deposition and contribute as a risk of coronary artery disease (CAD). The primary mechanism involved in CAD development is atherosclerosis. Membrane activating receptors are considered to be potential tool for assessing under lying atherosclerosis and CLEC-2 is one of them (Watson et al., 2010)[14]. Studies verified that CLEC-2 and its ligand have significant role in initiation and progression of atherosclerotic plaque but its clinical importance in sub-clinical coronary artery disease is still not fully established specially in patients of metabolic syndrome(Fox et al., 2020)[15], which has highest chances of developing atherosclerotic plaque. In current study, it was observed that the s-CLEC-2 levels were seen to be higher in MetS when compare to healthy group, with highly statistically significant (*p*=0.001) difference between them. Similar to our study, Kazama et al. measured sCLEC-2 levels in 25 diabetes patients and compared them to 10 healthy people. They found that DM patients had greater levels than healthy people, however the differences were not significant in their investigation. The rationale to explain our observation is the assumption that MetS is a collection of several disorders, as opposed to DM, which is a single disease entity. It might be due to the recruitment of diabetic patient based on their HbA1c (>8.0%) rather than diabetic patient with complications that mainly involve vascular disorders. (Kazama et al., 2015)[16]

Platelets expressed CLEC-2, when they are exposed to inflammatory conditions (Meng et al., 2021)[17]. The Inoue et al., explained the expression of CLEC-2 ligand (S100A13), on vascular smooth muscle at the site of atherosclerotic lesions, especially, during the conditions of oxidative stress.(Inoue et al., 2015)[18] This supports the finding of current study, as MetS is a well-known oxidative condition. Following the process of platelet activation, CLEC-2 shed in to the blood in soluble form in proportional to the atherothrombotic activity and this can be detected by ELISA. Inoue et al. stated that sCLEC-2 have higher prognostic, therapeutic and diagnostic benefits in clinical setting compare to other platelet membrane activation receptor like GPVI in patients of stable angina, acute coronary syndrome and healthy individual.(Inoue et al., 2019)[19]. Literature suggested, CLEC-2 have role beyond homeostasis as during the development of deep vein thrombosis (Suzuki-Inoue et al., 2018)[20].

Clec-2 levels, on the other hand, were shown to be significantly higher in patients with coronary artery disease (CAD) and ischemic heart disease (IHD) as compared to healthy individuals, which were similar to MetS levels in the current investigation. (Zhang et al., 2019, Wu et al., 2019)[21,22]. This stresses the predictive usefulness of increased clec-2 levels, since levels were comparable to MetS but also in other advanced illnesses such as CAD and IHD, implying that these levels might be useful early biomarker for identifying high-risk CAD proband. (Fei et al., 2020)[23]

In conclusion, considering the existing data sCLEC-2 levels might be an indicator for corresponding platelet activation which most probably be related to the underlying atherothrombotic process, therefore, more studies should be design or conducted for analyzing the sCLEC-2 levels in Pakistani population and its relation with different parameters of atherosclerosis.

CONCLUSION

The increased soluble CLEC-2 expression in metabolic syndrome patients as compared to healthy individuals might be linked to platelet activation and development of atherosclerosis in metabolic syndrome.

Author's Contribution:

Concept & Design of Study:	Syeda Tehreem Kanwal, Zil-e-Rubab
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Frequency of Different Cheiloscopic Patterns Among Young Pakistani Population

Hira Munir[1], Hira Anjum[2] and Hafiza Naima Anwar[3]

ABSTRACT

Objective: To determine the frequency of different lip patterns among the young Pakistani population.

Study Design: Descriptive, cross-sectional study.

Place and Duration of Study: This study was conducted at the Department of Forensic Medicine & Toxicology, QAMC/ Bahawal Victoria Hospital, Bahawalpur from 01.07.2021 to 31.12.2021.

Materials and Methods: A total 203 of medical students 18-30 years of age of either gender were selected. Subjects with previous lip surgery, lip trauma and any lip deformity were excluded. In this research, non-glossy and dark coloured lipstick was utilized to obtain the lip prints of the subjects. The lipstick was smeared in a uniform pattern on the cleaned lip using a swap. The smear settled for a minute, and then lip print was collected using tape, and applied to the lip from right to left. For all samples, the cellophane tape was removed in one swing and stuck to an A4 paper. Collected lip prints were studied and analysed through standard scientific procedures to obtain results.

Results: Mean age was 24.17 ± 2.87 years. Out of these 203 subjects, 110 (54.19%) were males and 93 (45.81%) were females with a male to female ratio of 1.2:1. In this study, the most common lip patterns found were Type I (26.11%) and Type II (20.69%), followed by Type I' (18.72%), Type III (18.23%), Type IV (10.34%) and Type V (5.91%). Conclusion: This study concluded that cheiloscopy might provide valuable information in the identification of an Individual.

Conclusion: The study concluded that in the young Pakistani population lip patterns found were Type I (26.11%) and Type II (20.69%), followed by Type I' (18.72%), Type III (18.23%), Type IV (10.34%) and Type V (5.91%). So, it is concluded that cheiloscopy and its study in varying avenues might provide valuable information with regard to the identification of an Individual.

Key Words: Cheiloscopy, Identification, Gender

INTRODUCTION

Every human being is born with certain peculiar features which differentiate him from every other human being ever born. These features make the basis for identification. Identification of an alive or dead individual human is based on the fundamental theory that every individual is unique.

A person can be identified subjectively by external features such as facial features, shape and colour of iris, height, weight, the colour of hair or any particular

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birthmark. Photographs of individuals and morphological data has traditionally been kept in records sespecially in criminal records where a mug shot of a person is taken where his height and facial features are recorded but all these features are not reproducible and cannot yield authentic results in most cases. So, more precise methods are required for forensic identification. Various unique features have been identified in human beings which have been traditionally used to document the identity of individuals. Fingerprints are the most common method used for identification and this is because every person has different fingerprints. Advancement in biological research has identified even more accurate and authentic methods of identification. In the late twentieth century, research led to DNA mapping of humans and it has been established that this is the most accurate method as the uniqueness of human beings is based on differences at the genetic level. All other unique features develop from genetic peculiarities in the genome. DNA can also be obtained from the dead and even decomposed dead bodies for the purpose of identification. The technique used to identify individuals by DNA is known as DNA fingerprinting. DNA fingerprinting not only requires expensive

technology but also highly trained personnel. A developing country like Pakistan doesn't have the resources to apply such sophisticated and advanced techniques routinely. Various other unique features which may be utilized for identification has been recently described but many of these methods like frontal air sinus pattern and skull suture pattern need complex technology like x ray, CT scan and expensive equipment. An identification method which is to be used routinely should not only be accurate but also be simple, less expensive and readily available. Identification of the individuals is becoming more important not only in legal medicine but also in crime scene investigation and Genetic Research[1]. The fingerprint-based identification system was introduced in India in 1858 by Sir William Herschel for the first time. This method is the most widely used method. But it has certain limitations as well. In civil cases, with advancing age fingerprints diminish and failure to match fingerprints leads to legal disputes. Moreover, skin conditions like leprosy and amputation of the limb may lead to the inability of matching fingerprints. In criminal cases, criminals are well aware of methods to avoid leaving their fingerprints on the crime scene. Therefore, in this technological age, the identity of an individual can be determined by a combination of different methods. The identification process, based on the combination of different methodologies, makes the identification process of individuals relatively flawless[2]. Due to the high cost and availability of the required technology, modern molecular biological techniques are not always a source identification process. Therefore, in such circumstances, a reliable technique like lip prints can be utilized[3]. The wrinkle pattern on the lips is a similar feature to the figure prints of the individual. Various elevations and grooves form a distinctive pattern on the lip's external surface, named "lip prints", which are unique and do not change during the entire life of the human. Lip prints are not affected by age making them a better choice. In addition to this, there is no chance of losing this identification method due to any amputation. As it is a less common method, criminals can unintentionally leave his lip prints in the crime scene. Lip prints can be easily collected at the crime scene from various objects like cups, clothing, glasses, cigarettes etc[4,5]. Fischer was the first who described the lip prints in 1902. However, its use for the identification of individuals was first recommended in France by Locard and Synder also endorsed it [6 7 8].

Dr. Santos in 1966[9 10 11] classified the wrinkles on lips as "simple and compound". The simple was then further categorized as a "straight line, an angled line, a curved line and a sine-shaped one". Similarly, the compound was further subdivided into "bifurcated, trifurcated, and anomalous groups". Santos also classified the lip based on thickness[12] as "a thin, medium, thick, and mixed type". The author also reported multiple types of commissures like "horizontal, flat, and elevated"[13]. According to the shape and groves, followings are the six types of lip prints as shown in Figure 1.

According to the study [8], Type III (20%) and Type IV (20%) are the most common lip patterns in males compared to females who have lip prints of Type I and Type I′ (25% each). The Forensic Sciences Laboratory in Bangalore has classified the microstructural, wrinkles and grooves, and macro-structural, size and shape, patterns of lips[14]. Similarly in Korea, forensic investigators are using biometric systems including the lip prints in personnel identifications [15]. Many authors think that a smear from a lip print contains DNA evidence to identify a suspect[16]. In 1998, Ehara and Marumo reported in a study that "lipstick smears are frequently encountered in forensic science laboratories as one of the most important forms of transfer evidence. Lipstick smears on suspects' clothing can indirectly prove a link between the suspect and a female victim and smears left on cigarette butts, glasses or cups can prove a link between a suspect and a crime scene." In another research focused to obtain DNA from porous surfaces described the lips prints DNA attempts as "The developing of latent lip prints on porous surfaces is more recent than that for fingerprints. The first research showed that traditional reagents used for fingerprints are not successful. It has recently been determined that lysochromes (Sudan Black) are quite effective in developing recent latent lip prints, as well as older ones, on porous surfaces. Once the print has been detected, a trace is available from which to procure cell remains that can supply enough DNA to be analysed by the polymerase chain reaction technique. The results of this study indicate that latent prints on paper and developed with Sudan Black can be used as a potential DNA source for forensic identification"[17]. Very few studies have been conducted international and no local study is available on this with a large sample size, so the main aim of my study was to determine the frequency of different lip patterns between males and females in the local population. The results of my study will provide information regarding sex determination by lip prints and also provide stats regarding different lip patterns in both sexes. This information will help to identify the gender information at the crime scene.

MATERIALS AND METHODS

Study Design: Descriptive, cross-sectional study.
Setting: Department of Forensic Medicine, QAMC/Bahawal Victoria Hospital, Bahawalpur.
Sample Size: The calculated sample size is 203, with 95% confidence level, 3% absolute precision and taking type V pattern in females as 5%.[8]
Sampling Technique: Multistage sampling, a stratified random sampling technique was used to divide samples of 203 into different groups. The target population for

this study was students in the 1st, 2nd, 3rd, 4th and final years of QAMC. Proportional allocation was made 55 for was classified according to its total strength as follows; First year = 339/1664 x 203 = 41. Second-year = 333/1664 x 203 = 41. Third year = 331/1664 x 203 = 40. Fourth year = 326/1664 x 203 = 40. Final year = 335/1664 x 203 = 41. After making strata, a simple random sampling technique was applied to collect the desired number of students.

Inclusion Criteria:
a. Medical students of age 18-30 years.
b. Both genders.

Exclusion Criteria:
a. Subjects with previous lip surgery, lip trauma and any lip deformity (assessed on history).
b. Subjects not willing to be included in the study.

Data Collection Procedure: A total of 203 subjects fulfilling the inclusion criteria were selected after approval from the ethical review committee of BVH. Informed written consent was taken from each subject. Nonglossy and dark coloured lipstick were utilized to obtain the lip prints of the subjects. The lipstick was smeared in a uniform pattern on the cleaned lip using a swap. The smear was allowed to settle for a minute, after which lip print was collected using a transparent tape applied to the lips in a direction from right to left. For all samples, the tape was removed in one go and saved on A4 paper. Samples of the lip prints were collected by the researchers themselves Patterns of lip prints were noted as a pre-operational definition. All the findings were recorded on proforma.

Data Analysis Procedure: All the information was entered into SPSS 22.0 and was analysed through its statistical package. Quantitative variables like age were presented as mean and standard deviations while qualitative variables like gender, area of residence (Punjab/Sindh/KPK/Balochistan/Kashmir) and different lip patterns (I/ I'/II/III/IV/V) were presented as frequency and percentage. Effect modifiers like age, gender and area of residence (Punjab/Sindh/ KPK/ Balochistan/Kashmir) were controlled through stratification. Post-stratification chi-square test was applied to see their effect on different lip patterns and p-value.

RESULTS

Table No.1: Distribution of subjects according to lip pattern (n=203)

Lip pattern	No. of subjects	%age
I	53	26.11
I'	38	18.72
II	42	20.69
III	37	18.23
IV	21	10.34
V	12	5.91

The age range in this study was from 18 to 30 years with a mean age of 24.17 ± 2.87 years. The majority of the subjects 133 (65.52%) were between 18 to 25 years of age. Out of these 203 subjects, 110 (54.19%) were males and 93 (45.81%) were females with a male to female ratio of 1.2:1.
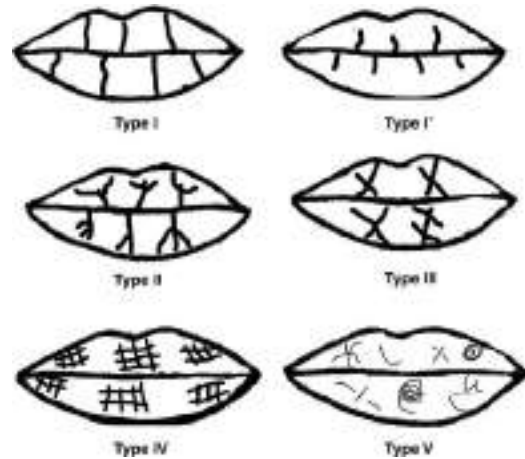
Figure No.1: Suzuki and Tsuchihashi classification of lip prints

Table No.2: Stratification of different lip patterns with respect to gender

Different lip patterns		Male n=110	Female n=93	p-value
I	Yes	34	19	**0.090**
	No	76	74	
I'	Yes	17	21	**0.195**
	No	93	72	
II	Yes	30	12	**0.012**
	No	80	81	
III	Yes	16	21	**0.140**
	No	94	72	
IV	Yes	09	12	**0.271**
	No	101	81	
V	Yes	04	08	**0.135**
	No	106	85	

Table No.3: Stratification of different lip patterns with respect to the area of residence

Different lip Patterns		Punjab n=126	Sindh n=16	KPK n=23	Balu-chistan N=11	Kashmir N=27	p-value
I	Yes	39	05	03	01	05	0.182
	No	87	11	20	10	22	
I'	Yes	22	03	07	02	04	0.648
	No	104	13	16	09	23	
II	Yes	26	04	06	01	05	0.034
	No	100	12	17	10	22	
III	Yes	21	00	05	01	10	0.027
	No	105	16	18	10	17	
IV	Yes	10	01	02	05	03	0.003
	No	116	15	21	06	04	
V	Yes	08	03	00	01	00	0.087
	No	118	13	23	10	27	

In this study, the most common lip patterns found were Type I (26.11%) and Type II (20.69%), followed by Type I' (18.72%), Type III (18.23%), Type IV (10.34%) and Type V (5.91%).

Stratification of different lip patterns with respect to gender is shown in Table 2.

Table 3 has shown the stratification of different lip patterns with respect to the area of residence.

DISCUSSION

Lip prints can be used for identification as every individual has unique lip prints and they do not change throughout life. Identification through lip prints does not require any expensive equipment and not even highly specialized technical staff. A lip print at the crime scene can offer a clue to answer various questions like the crime type, the number of criminals involved, sexes of suspects, habits, the pathological changes of lips and occupational traits. Suzuki and Tsuchihashi reported cases where lip prints were useful in the identification of criminals. Literature review shows that lip prints are as good as fingerprints in the identification process when there are no other sources of identification are available[19].

Research studies regarding the use of lip prints as evidence of racial discrimination are inadequate. In study [20][21], Type II and III were the most predominant pattern among Indian and African males whereas Type I was the most predominant pattern among both Indian and African females. The results of the study are in line with our results presented in Table I. Similarly, Manypady, in a comparative study of lip prints of Indian and Chinese individuals results that Type II patterns are more common among Indians[22]. Results reported by the Nagpal et al. also showed that Type III as most common lip pattern in Malaysian males whereas Type I and Type I' are predominant in Malaysian females. Our study also noted Type I as the most frequent pattern in both sexes. The stratification of results of different lip patterns on basis of gender, ethnicity, age and area of residence can be further done on larger scale to collect data which can be used in crime scene investigations.

CONCLUSION

The study concluded that in the young Pakistani population lip patterns found were Type I (26.11%) and Type II (20.69%), followed by Type I' (18.72%), Type III (18.23%), Type IV (10.34%) and Type V (5.91%). So, it is concluded that cheiloscopy and its study in varying avenues might provide valuable information with regard to the identification of an Individual.

Author's Contribution:
Concept & Design of Study: Hira Munir, Hira Anjum
Drafting: Hafiza Naima Anwar
Data Analysis: Hafiza Naima Anwar
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Frequency of Grief Among Women Presenting with Perinatal Loss in Previous Pregnancy and Now Coming For Antenatal Check in First Trimester

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ABSTRACT

Objective: To find the frequency of grief among pregnant women in first trimester who experienced perinatal loss in previous pregnancy.

Study Design: Descriptive Cross sectional Study.

Place and Duration of Study: This study was conducted at the Department of Obstetrics & Gynecology, Services Hospital Lahore from November 2020 to October 2021.

Materials and Methods: 18-40 years of age pregnant women with gestational age < 12 weeks with history of perinatal loss in previous pregnancy were included in the study group. Pregnant women with any diagnosed psychological illness or those not willing to participate were excluded from the study. Females were questioned whether they were feeling guilt or anger for their loss or if they felt nothing about the perinatal loss. HADS score(Hospital Anxiety and Depression Score) was noted. All the collected data was entered and analysed on SPSS version 21.

Results: In our study the mean age was 29.29 ± 6.57 years, the pregnancy loss was noted in 94 (47%) patients and neonatal death was noted in 106 (53%) patients. The grief was found in 147 (73.5 %) patients.

Conclusion: Frequency of grief among women having perinatal loss in previous pregnancy was 53.2% when they presented for antenatal check up in first trimester in new pregnancy.

Key Words: Grief, Pregnancy loss, Neonatal death, Trimester

INTRODUCTION

Perinatal loss is the loss of fetus during pregnancy. Loss may occur early in pregnancy in the form of miscarriage, ectopic pregnancy or later on in the form of intrauterine fetal demise or intrapartum death. Perinatal loss causes grief but may also cause anxiety and apprehension in regards to the future pregnancy[1]. Pregnancy is the time of intense emotional experience by the parents. Parents specially mother hopes and dreams about the baby.

Any adverse outcome may become the root cause of prolonged distress. Support from the caregivers is great source to overcome their grief.[2]

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Psychological impact of perinatal loss menifests in many ways. Early embark on another pregnancy, maternal anxiety, emotional vulnerability, fear of again going through the same experience of loss are among the few manifestations of emotional distress felt by the woman. This may lead to preterm birth and low birth weight in the subsequent pregnancies.[3]

A U.K longitudinal study reported that emotional stress of adverse perinatal outcome may influence the next pregnancy and it may even persists afterwards causing disputed maternal attachment and long term emotional and social morbidity.[4]

Perinatal mortality or perinatal death, refers to the death of a fetus or neonate and is the basis to calculate the perinatal mortality rate.[5] 6.3 million perinatal deaths are reported in a year, globally. Majority of these occur in developing countries. While 27% alone are among the least developed countries.[6]

Grief after the perinatal loss is troublesome in the sense that our society expects only a healthy live baby. Such an outcome is celebrated whereas in case of adverse outcome woman and her partner are left alone to mourn and are usually not extended enough support by the society.[7] Women are not given the chance to see, hold or kiss the baby. This may complicate the grieving process for the couple.[8] Clinically grief can be

quantified with Hospital Anxiety and Depression Scale (HADS) scoring. It is a fourteen-item scoring system to measure anxiety and depression. Both anxiety and depression have seven sub-scales. A score from zero to three is given for each sub-scale. We have used this scoring system in our study.[9]

The rationale of this study is to find the frequency of grief among women presenting during first trimester of pregnancy with history of perinatal loss in previous pregnancy. Literature shows that more than 50% females feel grief or undergo stress after perinatal loss.[1] In antenatal clinics, a number of women report with history of perinatal loss. The emotional and psychological aspects related to grief pertaining to previous perinatal loss are usually not given attention by the caregivers. But proper evidence is missing. This study will help to guide the caregivers extend social and emotional support to the mothers to overcome the grief and reduce the anxiety for the outcome of current pregnancy.

MATERIALS AND METHODS

This descriptive cross sectional study was conducted from Nov 2020 to Oct 2021 in the Obstetrics & Gynecology Department, Services Hospital Lahore. Informed written consent was obtained from patients. Sample size of 200 cases were calculated with 95% confidence level, 7% margin of error and taking expected percentage of grief i.e. 53.2% in females presenting with perinatal loss. Pregnant women of 18-40 years of age presenting with gestational age < 12 weeks with history of perinatal loss in previous pregnancy were included in the study group. Pregnant women with any diagnosed psychological illness or those not willing to participate were excluded from the study.

Demographic details (name, age, education, parity, socioeconomic status) were also obtained. Women were interviewed whether they were feeling guilt or anger for their loss or if they felt nothing about the perinatal loss. Their responses were recorded on predesigned performa. Recorded responses were evaluated and HADS score was calculated with the help of psychiatrist. Urdu version was used for better understanding of the patients. If HADS score of > 9 was obtained, then grief was labelled. Data was entered in SPSS 21. Quantitative data such as age was presented as mean and standard deviation. Categorical data like gender, type of perinatal loss and grief, educational status and economic status were presented as frequency and percentage. Data was stratified for age, parity, socioeconomic status, education, type of perinatal loss and inter-pregnancy interval. Post-stratification, chi-square test was applied to compare frequency of grief in stratified groups with p-value ≤ 0.05 was taken as significant. Parity was presented as frequency.

PROFORMA
Frequency of grief among women presenting with perinatal loss during first trimester
Case No: **Reg. No.:**
Date:
Name:
Age:
Parity:

Education of female:
Illiterate □ Matric □ Graduation □
Socioeconomic status:
Low (<10,000Rs/month). □
Middle (11-50,000Rs/month) □
High. (>50,000Rs/month) □
Type of perinatal loss:
Pregnancy loss □ Neonatal death □

Inter-pregnancy interval: ——— years
HADS score:

Grief: Yes □ No □

RESULTS

In our study, total 200 patients were enrolled. The mean ages was 29.29 ± 6.57 years with minimum and maximum ages of 18 & 40 years respectively. In this study 54 (27%) patients were with zero parity, 63 (31.50%) patients were with parity one, 46 (23%) patients were with parity two and 37 (18.50%) patients were with parity three. 69 (34.5%) patients were from low socioeconomic status, 61 (30.5%) patients were from middle socioeconomic status (SES) while 70 (35%) patients were from high socioeconomic status. The illiterate patients were 67(33.5%), patients with matric education were 57 (28.5%) and the patients with graduate education were 76(38%). Table no. 1

The study results showed that total patients with age ≤ 30 years were 109 and grief response was noted in 59 out of these 109 cases, similarly the patients with age > 30 years were 91and grief response was noted in 49 out of these 91 cases .There was no statistically significant difference between the grief response with age i.e. p-value = 0.968. Table no.4

Patients with primary parity were 117 and grief response was noted in 60 cases, while the patients with multi-parity were 83 and grief response was noted in 48 cases. No statistically significant difference was found between the two groups (p-value = 0.360). Similar results with no statistically significant difference were obtained for the grief response with parity, SES and educational status of women. i.e. p-value of 0.360 , 0.767 and 0.344 as shown in Table no.4

Early pregnancy loss was noted in 94 (47%) patients and neonatal death was noted in 106 (53%) patients. Grief was noted in 147 out of 200 (73.5 %) patients (HADS score > 9) and stable emotional condition

(HADS score ≤ 9) was noted in 53 out of 200 (26.5 %) patients. Table no.2.

With factor analysis of the pregnancy loss it is seen in our study that among 94 patients with early pregnancy loss grief response (HADS score >9) was noted in 48 out of 94 (51%) cases while HADS score ≤ 9 was noted in 46 out of 94 (48.9%) patients. However from the 106 patients who experienced neonatal death in any previous pregnancy 99 out of 106 (93.39 %) cases had HADS score > 9 showing grief and only 7 out of 106 (6.6 %) patients had HADS score ≤ 9 depicting stable emotional state. Table 3.

Table No.1: Demographics of patients

Age		Frequency (%)
	Mean+ SD	29.29+ 6.57
Parity	No Parity	54 (27%)
	One	63 (31.50%)
	Two	46 (23%)
	Three	37 (18.50%)
Education Level	Illiterate	67 (33.5%)
	Matric	57 (28.5%)
	Graduate	76 (38%)
Socioeconomic Status	Low	69 (34.5%)
	Middle	61 (30.5%)
	High	70 (35%)

When the grief response of women with early pregnancy loss (48 out of 94) was compared with grief response of women with neonatal death (99 out of 106)

Statistically significant difference was found (P-value < 0.05) . Table 4.

Patients with ≤ 12 months inter-pregnancy loss interval were 112 from which grief response was noted in 59 cases, similarly the patients with inter-pregnancy interval >12 months were 88 from which grief response was noted in 49 cases. Statistically insignificant difference was found between the grief response with inter-pregnancy interval i.e. p-value = 0.672 .Table no.4

Table No.2: Frequency Distribution of Perinatal Loss & Grief

		Frequency (%)
Perinatal Loss	Pregnancy Loss	94(47%)
	Neonatal Death	106(53%)
Grief	Yes	147(73.5%)
	No	53(26.5%)

Table No.3: Factor Analysis of grief experienced with type of pregnancy loss

	Early Pregnancy Loss	Neonatal Loss	Total
Grief Experienced	48 (51% of 94)	99 (93.3% of 106)	147 (73.5 % of 200)
Grief Not Experienced	46 (51% of 94)	7 (6.6 % of 106	53 (26.5 % of 200)
Total	94	106	200

Table No.4:Comparison Grief response with demographics

Comparison Grief response with age, parity, education, SES, Perinatal Loss and Inter-pregnancy interval				
		Grief Experienced (HADS > 9)	Grief not experienced (HADS ≤ 9)	P value
Age (Years)	≤ 30	59 (29.5%)	50 (25%)	
	> 30	49 (24.5%)	42 (21%)	0.968
Parity	Primary	60 (30%)	57 ((28.5%)	
	Multiple	48 (24%)	35 (17.5%)	0.360
Education	Illiterate	34 (17%)	33 (16.5%)	
	Matric	28 (14%)	29 (14.5%)	0.344
	Graduate	46 (23%)	30 (15%)	
Socioeconomic Status	Low	37 (18.5%)	32(16%)	
	Middle	31 (15.5%)	30 (15%)	0.767
	High	40 (20%)	30 (15%)	
Perinatal Loss Type	Pregnancy Loss	48 (24%)	46 (23%)	< 0.05
	Neonatal Death	99(49.5%)	7 (35%)	
Inter-pregnancy interval	≤12 months	59 (29.5%)	53 (26.5%)	0.672
	> 12 months	49 (24.5%)	39 (19.5%)	

DISCUSSION

Pregnancy is a state of hope and aspiration for the future child. Losing a pregnancy or a neonate is usually a very traumatic event for both the woman and her partner. This trauma results into emotional stress and psychological upset. Different studies suggest that abrupt separation of the baby from the mother, can lead to feeling of uncertainity, sadness and low morale of the parents specially the mother.[10]

Grief is an exclusively internal process which follows a set pattern. Emotional response to the loss may result in deviant behaviour such as change in daily routine activities, social withdrawal symptoms, depressive thinking, and denial of the event. Such behavioural patterns may continue for variable time periods.[1,11]

In our study the grief condition (HADS score > 9) was noted in 147 (73.5 %) patients. In one study, it was observed that about 53.2% females had grief of their perinatal loss (n=62).[16] Another study showed that 6.25% (n=16) had grief (felt guilty) for her perinatal loss.[12] A study by Gisele Ferreira Paris et al. resulted that the presence of grief was higher among Brazilians (35% prevalence) in comparison to the Canadians (12% prevalence).[13]

A study by Anette Kersting et al, reported that grief scores were initially relatively high but declined over the first year. However the 2-year follow-up of the grief process showed that 41 % of cases showed a normal decline of grief scores, the remaining 59% showed different patterns of arrest or delayed resolution of grief. In our study for the group with inter pregnancy interval of more than 12 months, grief was found to be present in 55 % of the patients while resolution of the grief after 12 months was noted in 45 % of patients.[14]

With factor analysis of the pregnancy loss it is seen in our study that among mothers who had neonatal loss 93.3% experienced grief while among mothers who had early pregnancy loss 51% experienced grief .One more study by Marianne H. Hutti et al, demonstrated that mothers in the neonatal death group experienced more intense grief when compared with mothers in the miscarriage or stillbirth groups.[15]

Social support therefore is of utmost importance for the psychological wellbeing of mothers because grief after the pregnancy loss may persist upto and through the duration of next pregnancy. Social support helps mothers to overcome the grief, reduces anxiety, depression and prepare herself to become the new baby.[16]

CONCLUSION

According to our study the frequency of grief among women presenting with perinatal loss in previous pregnancy and now coming for antenatal check in first trimester was 73.5 %.

Author's Contribution:

Concept & Design of Study:	Sadia Aman
Drafting:	Bushra Haq, Saira Riaz
Data Analysis:	Ammara Gill, Wajid Ali, Tabeer Malik
Revisiting Critically:	Sadia Aman, Bushra Haq
Final Approval of version:	Sadia Aman

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

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Original Article

Frequency of GERD with Risk Regurgitation & Aspiration during Anesthesia in Different Age & Weight Groups with Their Histological Findings on Biopsy

Syed Sohail Abbas Naqvi[1], Abdullah Khilji[2], Munir Ahmad Channa[3], Abdul Hayee Phulpoto[4], Maqsood Ahmed Siddiqui[5] and Syeda Abiya Amber Naqvi[1]

ABSTRACT

Objective: To determine the frequency of GERD with risk of regurgitation and aspiration during anesthesia in different age and weight groups with their histological findings on biopsy.

Study Design: Comparative / observational study

Place and Duration of Study: This study was conducted at the Department of Pathology, Civil Hospital, Khairpur Pakistan from 1st May 2021 to 30th November 2021.

Materials and Methods: One hundred and sixty patients of both genders were enrolled. Age of the patients was between 15-75 years. All the patients had gastro-esophageal reflux disease (GERD) were included. Patients were equally categorized into two groups. Group I had 80 patients with ages 15-40 years and above than 40 years of age were presented in group II. All the patients were underwent endoscopic biopsy under sedation/anesthesia. Findings among both groups were assessed in terms of risk of regurgitation and aspiration under anesthesia and histological findings were compared.

Results: The mean age in group I was 34.23±6.13 years and in group II mean age were 60.54±3.36 years. We found majority of the patients were males 55 (68.6%) and 51 (63.6%) among both groups. We found that severity of symptoms were higher in group I as compared to group II with p value <0.005. Esophagitis severity, barret esophagus and esophagus cancer were more prevalent in group II as per biopsy findings with p value <0.003. Frequency of hiatus hernia in group II was 32 (40%) higher as compared to group I 15 (18.6%) with p value < 0.004.

Conclusion: Rare and severity of symptoms were high in the group of patients presented with young age had GERD as compared to elder group but as per endoscopic biopsy under anesthesia findings severity of esophagitis, cancer, hiatus hernia, regurgitation and aspiration was more prevalent in the patients with ages >40 years had GERD as compared to young age patients with GERD.

Key Words: Gastro-esophageal reflux disease (GERD), Biopsy, Anesthesia, Clinical outcome, Symptoms

INTRODUCTION

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Since Barrett oesophagus (BE) is the known precursor lesion to esophageal adenocarcinoma in white males over the age of 50 with long-term and severe symptoms of gastro-esophageal reflux disease (GERD), many epidemiologic studies in the late 1990s recommended screening for BE among these men.[1-5] In spite of the fact that 95 percent of esophageal cancer patients do not have endoscopic screening or are not diagnosed with BE, most present with advanced illness and little hope of recovery.[6] Despite these suggestions, though.[7] Even yet, doctors have been unable to identify persons at risk of developing GERD and stratify them for early detection or prevention because of the screening criteria.[8-10]

Recent studies show that screening is no longer beneficial, even for the most at-risk individuals, and that it should instead be "individualised to the patient." Due to the lack of a link between the intensity of GERD symptoms and the likelihood of developing cancer,

patients who don't show any symptoms or show symptoms that are trivial or unusual are often overlooked for endoscopic screening, resulting in a silent disease progression. If symptoms are reduced or eliminated, patients may be overlooked for screening because they believe their disease has been well treated by PPIs. Drugs that block the proton pump.[8-10]

Gastro-esophageal reflux disease symptoms are more common in those over the age of 65 than in anyone else. Barrett's esophagus, cancer of the oesophagus, and recurrent aspiration pneumonias can all be diagnosed with a thorough examination of the oesophagus.[11] Endoscopic or histological damage to the oesophagus causes reflux esophagitis. Esophagitis is a complicated condition caused by an imbalance between the systems that defend against reflux and those that promote it. It is crucial that the esophageal mucosa's heightened acid sensitivity and the LES pressure diminish. Back pain, burning or discomfort in the epigastrium that spreads into the oesophagus are the most common symptoms of reflux disease. After a meal, relaxing or slouching forward might increase heartburn. GERD can also cause symptoms such as difficulty swallowing, chest pain, a globus sensation, belching, and coughing. Angina pectoris is frequently accompanied by chest pain that spreads to the left arm, chin, or neck.

Alternately, Barrett's esophagus is a stage of stomach cancer in which aberrant cells proliferate in the metaplastic columnar epithelium.[12] Barrett's oesophagus can only be diagnosed with an endoscopy and a tissue sample. intestinal metaplasia can be diagnosed by analysing biopsy samples collected from the distal esophageal mucosa, which has an aberrant appearance. Barrett's oesophagus is found in 10–15% of patients who undergo endoscopy. It's important to the progression of adenocarcinoma. Annual adenocarcinoma incidence in patients with BE was around 1 percent. Dysphagia and weight loss are typical in patients in their seventh or eighth decade.[13]

Due to the extraesophageal implications of GERD in the elderly, gingivitis, sinusitis, otitis media, tooth erosions, and respiratory disorders such aspiration pneumonia and chronic cough are common. Modern GERD diagnostic testing is utilized on those who are younger and exhibit symptoms of the condition. BE and esophageal cancer are more likely to occur in patients over the age of 50, hence an aggressive treatment plan is recommended rather than a conservative one.[14,15] An endoscopy should be conducted in order to get a diagnosis.

There is still a danger of stomach regurgitation and aspiration under general anaesthesia. On a postal survey of New Zealand anaesthetists, it was found that 71% of respondents had at least one career objective, with some saying they had up to ten.[16] Reduced incidence of this consequence has been made possible by recent advances in our knowledge of stomach motility

pathophysiology and variables that regulate normal function. The fasting requirements are also being adjusted so that patients can get fluids closer to the time when anaesthesia is being administered without restriction.[17]

MATERIALS AND METHODS

This comparative/observational study was conducted at the Department of Pathology, Civil Hospital, Khairpur for the duration of six months from May 2021 to November 2021 and 160 patients were enrolled. Patients were included after taking informed written consent for detailed demographics such as age, gender, BMI and cause of GERD. Pregnant patients, history of esophagus surgery and those patients did not provide any written consent were excluded. Age of the patients was between 15-75 years. Every single one of the patients was diagnosed with GERD. In equal numbers, the patients were divided into two distinct groups. The 80 patients in groups I and II, ranging in age from 15 to 40, were compared to the 40 patients in groups II. It was thought that symptoms such as dysphagia, odynophagia, and burping were not typical of acid reflux. All patients had been receiving proton pump inhibitors for at least a month (PPIs). However, none of them had progressed. Upper endoscopy was performed on these individuals under sedation and anesthesia because of persistent symptoms despite PPI medication, the need to identify the underlying cause of their GERD, and their advanced age. Equipment from Fujinon was used for endoscopic operations. The current endoscopic staging for esophagitis is based on the Los Angeles system. It is characterised by the replacement of the stratified squamous epithelium that normally lines the distal oesophagus with metaplastic columnar epithelium. Biopsy samples of the salmon-colored mucosa are used to make a BE diagnosis when gastric and intestinal metaplasia are found there. It was decided to compare the groups based on their demographics and clinical information.

The data was entered and analyzed through SPSS-25. Statistical significance was defined as a p-value of 0.05 or less. Pearson's Chi-square test and Fisher's exact test were used to assess the effects of sex and endoscopic or clinical reflux esophagitis severity on statistical comparisons.

RESULTS

The mean age in group I was 34.23±6.13 years and in group II mean age were 60.54±3.36 years. Mean BMI in group I was 24.12±3.32 kg/m^2 and in group II mean BMI was 32.01±3.14 kg/m^2. We found majority of the patients were males 55 (68.6%) and 51 (63.6%) among both groups. Fried food, fast food, fatty meats and poor sleep were the main causes of GERD among both groups (Table 1).

We found that severity of symptoms burning, regurgitation, dysphagia/odynophagia, dry cough and burping were higher in group I as compared to group II with p value <0.005 (Table 2). Esophagitis severity, barret esophagus and esophagus cancer were more prevalent in group II as per biopsy findings with p value <0.003 (Table 3). Frequency of hiatus hernia in group II was 32 (40%) higher as compared to group I 15 (18.6%) with p value <0.004 (Table 4)

Table 1: Characteristics details of enrolled causes

Variables	Group I	Group II
Mean age (years)	34.23±6.13	60.54±3.36
Mean BMI (kg/m²)	24.12±3.32	32.01±3.14
Gender		
Male	55 (68.6%)	51 (63.6%)
Female	25 (31.4%)	29 (36.4%)
Cause of GERD		
Fried food	30 (37.5%)	31 (38.6%)
Fast Food	28 (35%)	22 (27.5%)
Fatty meats	17 (21.3%)	25 (31.3%)
Poor Sleep	15 (18.8%)	2 (2.5%)

Table 2: Comparison of severity symptoms of symptoms burning, regurgitation, dysphagia/ odynophagia, dry cough and burping

Symptoms	Group I	Group II
Burning		
Yes	42 (52.5%)	20 (25%)
No	38 (47.5%)	60 (75%)
Regurgitation/Aspiration		
Yes	35 (43.8%)	31 (38.8%)
No	45 (56.2%)	49 (61.2%)
Dysphagia/Odynophagia		
Yes	38 (47.5%)	19 (23.8%)
No	42 (52.5%)	61 (76.2%)
Dry cough		
Yes	28 (35%)	17 (21.3%)
No	52 (65%)	63 (78.7%)
Burping		
Yes	48 (60%)	24 (30%)
No	32 (40%)	56 (70%)

Table No.3: Association of diseases among endoscopic biopsies

Diseases	Group I	Group II
Esophagitis severity		
Yes	24 (30%)	55 (68.8%)
No	56 (70%)	25 (31.2%)
Barret esophagus		
Yes	7 (8.8%)	11(13.8%)
No	73(91.2%)	69 (86.2%)
Esophagus cancer		
Yes	1 (1.3%)	4 (5%)
No	79 (98.7%)	76 (95%)

Table No.4: Comparison of HH among both groups

Hiatus Hernia	Group I	Group II
Yes	15 (18.6%)	32 (40%)
No	65 (81.4%)	48 (60%)

DISCUSSION

When GERD affects the elderly, it may lead to more life-threatening problems. Older people are also less likely to have symptoms of GERD, such as heartburn, regurgitation, and other clinical characteristics.[17] While retrosternal burning is more common in older individuals, dysphagia and excessive food regurgitation are more common in younger people. Even in stage C–D esophagitis, retrosternal discomfort and burning may not be noticed owing to alterations in the patient's perceptual threshold. This may be the most prevalent benign cause of swallowing difficulties in older people. Patients over the age of 60 should also be evaluated for the presence of comorbid disorders, such as neurological diseases (such as Parkinson's disease) or drug side effects (such as calcium antagonist usage). Reflux is a frequent medical condition. While community reflux prevalence ranges from 1% to 25%, it has been found that among men and women over the age of 65, reflux affects 10.9% and 5.3% of the population, respectively.[18] Degenerative alterations in smooth muscles, decreased pressure in the esophageal-sphincter, and reduced peristalsis are all signs of ageing. This leads to an increase in the esophageal reflux of stomach contents. An esophageal mucosal injury and symptoms might vary widely in this illness. When it comes to gastroesophageal reflux disease (GERD), heartburn and acid regurgitation are the most prevalent symptoms, and antacid medication is generally enough to alleviate them. Although heartburn is more common in older people, the incidence of severe heartburn declines, presumably owing to decreased pain sensitivity and atrophic gastritis.

Only one in 350 000 people in NAP4 died from aspiration-related anaesthetic complications, which is lower than the prior estimates of between one in 50,000 and 200,000 people. Airway-related deaths are most frequently caused by aspiration.[19]

In the present study, the mean age in group I was 34.23±6.13 years and in group II mean age were 60.54±3.36 years. Mean BMI in group I was 24.12±3.32 kg/m² and in group II mean BMI was 32.01±3.14 kg/m². Above mentioned findings of our study was comparable to the studies conducted in past.[20,21] We found that severity of symptoms burning, regurgitation, dysphagia/odynophagia, dry cough and burping were higher in group I as compared to group II with p value <0.005. Esophageal and extraesophageal symptoms were greater in young patients in a research by Sidhwa et al[22] which is comparable to our investigation. The LES tonus may be damaged in elderly people with GERD who also have a

concomitant illness. Anxiety medicine, antidepressants, and anticholinergics may potentially cause reflux in patients with concomitant conditions, such as nitrates.[23] Comorbid illnesses were shown to be more prevalent among the elderly. However, esophagitis is more common in elderly people, and this may be due to this disorder. Our theory is supported by research indicating that lung and heart problems and the medications used to treat these conditions may cause gastroesophageal reflux disease.[21] Despite the fact that polypharmacy, a typical practise among the elderly, has been linked to GERD, the study's retrospective design prevented researchers from getting access to the drugs used by study participants.

We found that dysphagia and/or odynophagia were more prevalent in the younger group than in the elderly in our research. Smoking and drinking, fast food diets, and irregular lifestyles (eating late, going to bed soon after supper) among the young patient population may be to blame for this problem.[24] Esophagitis severity, barret esophagus and esophagus cancer were more prevalent in group II as per biopsy findings with p value <0.003.[25,26] Frequency of hiatus hernia in group II was 32 (40%) higher as compared to group I 15 (18.6%) with p value <0.004. Although the frequency of hiatus hernias has been shown to increase with age, no sex effect has been established; different studies show male predominance, female preference, or no difference.[20] During our research, we found that hernia and sex were not statistically different (p = 0.50). One important distinction could be found between the young and the elderly. Only 5% of young patients and 13.8 percent of elderly patients (p = 0.002) had hiatus hernias larger than 2 centimetres in size. As a result of our research, we found that older and younger patients with GERD had distinct differences. While their symptoms may be less severe than those of younger people, the endoscopic results are more worrisome in older patients with GERD.

CONCLUSION

Rare and severity of symptoms were high in the group of patients presented with young age had GERD as compared to elder group but as per endoscopic biopsy under anesthesia findings severity of esophagitis, cancer and hiatus hernia was more prevalent in the patients with ages > 40 years had GERD as compared to young age patients with GERD.

Author's Contribution:

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Efficacy of Negative Pressure Wound Therapy on Thoracic Wounds After Esophagectomy

Javed Mirdad Tarar[1], Kashif Nadeem[1] and Amjad Ali[2]

ABSTRACT

Objective: To evaluate the efficacy and effectiveness of NPWT in healing thoracic infections after esophagectomy in comparison with traditional open wound therapy.

Study Design: A retrospective study

Place and Duration of Study: This study was conducted at the Bakhtawar Amin Medical & Dental College & Hospital Multan from 10th July 2021 to Jan 10th 2022.

Materials and Methods: A total of 100 patients with oesophagal cancer were included in the study who underwent esophagectomy. Only 30 patients were selected for final analysis, among which 20 patients were treated with NPWT and 10 patients were administered open wound therapy. The NPWT device was operated by inserting a drainage tube in the wound. None of the patients reported any complaints about the procedure. The remaining 10 patients were administered traditional wound dressing. After the growth of granulation tissue and the infection was minimized, patients were discharged. The dressing change was done in the outpatient department.

Results: The rate of infection in our study was 30%. No patients showed any adverse reaction to the NPWT. All the patients treated with NPTW showed complete and successful wound healing. Patients experienced anastomotic leak and pneumonia as postoperative complications. The body temperature after the procedure and hospital stay did not differ significantly between both groups. However, the healing time of patients treated with NPTW was shorter I.e 12 days as compared to the other group i.e. 19 days.

Conclusion: Facilitated NPTW is a safe, inexpensive and effective method for the treatment of thoracic wounds in comparison with open wound therapy.

Key Words: Negative pressure wound therapy, open wound therapy, esophagectomy, and thoracic wounds.

INTRODUCTION

Oesophagal cancer is one of the most prevalent and dangerous cancer in the world with significant morbidity and mortality cases. Esophagectomy is frequently used to treat this cancer, however, this procedure also poses the risk of postoperative morbidity mostly due to infection[1, 2]. This type of infection occurs as a result of an anastomotic leak and is a serious complication, at the same time surgical site infection also poses a great clinical risk. The prevalence of surgical site infection is increasing at an accelerated rate, causing discomfort and financial burden on the patient due to related risk of morbidity and mortality[3].

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Although Thoracoscopic esophagectomy is a less invasive and comparatively safe procedure leading to less frequent infection, oesophagal cancer is mostly treated with open surgery[4]. It is observed that the choice of method of treatment can prevent surgical site infections. Negative-pressure wound therapy (NPWT) is an effective technique to heal surgical wounds by applying negative pressure. It has been used in various studies and has yielded positive results[5, 6].

Negative pressure wound therapy contributes to wound healing by preventing infectious agents and removing interstitial fluid, decreasing oedema and promoting oxygen perfusion, formation of new blood vessels and formation of granulation tissue. NPWT is used frequently in both adults and neonates in various types of wounds. In addition to its use in other procedures, thoracic wounds are also healed by this technique as it treats infections and maintains chest wall integrity [7, 8]. Besides all the evidence, the working of NPWT in incision infection is still vivid. This study aims to evaluate the efficacy and effectiveness of NPWT in healing thoracic infections after esophagectomy in comparison with traditional open wound therapy.

MATERIALS AND METHODS

A retrospective study was conducted in the surgical thoracic department of Bakhtawar Amin Medical & Dental College & Hospital Multan from 10th July 2021 to 10th Jan 2022. A total of 100 patients with oesophagal cancer were included in the study who underwent esophagectomy. Only 30 patients were selected for final analysis, among which 20 patients were treated with NPTW and 10 patients were administered open wound therapy. An in-depth history of patients was noted including age, sex, smoking status, history of alcoholism, BMI, comorbid conditions, complications after surgery, hospital stay, intraoperative data, pathological history and duration of wound healing.   All the patients provided their informed consent to become a part of the study. The ethical committee also approved the study design of the research.

30 patients were treated with NPWT after the operation. The NPWT device was operated by inserting a drainage tube in the wound. These tubes extended out with the transparent dressing surrounding the infection site. Negative pressure was maintained by connecting the drainage tube to a negative pressure suction ball. Both the suction ball and the tube were fixed at one position. After the infection was treated, the dressing was removed, revealing a healed wound. None of the patients reported any complaints about the procedure. The remaining 10 patients were administered traditional wound dressing. After the growth of granulation tissue and the infection was minimized, patients were discharged. The dressing change was done in the outpatient department. All the patients were prescribed prophylactic antibiotics postoperatively. The antibiotic use was continued until no infection was found by culturing and testing.

All the data were analyzed by SPSS version 20. Standard deviation was used to present parametric data and the results were compared by performing a t-test. Mann-Whitney test was used to analyze nonparametric data. Fisher's test was used to compare both groups. A p-value <0.05 was regarded as statistically significant.

RESULTS

The rate of infection in our study was 30%. All the tumors were squamous cell carcinomas and were confined to thoracic portion of oesophagus. Standard oesophagectomy procedures including lvor Lewis and Mckeown techniques were used via posterior mediastinal approach. The patients' characteristics and intraoperative data is illustrated in Table I and II respectively. Patients of both groups did not differ significantly with respect to clinical features.

All the infections were treated during the hospital stay or outpatient department visits. No patients showed any adverse reaction to the NPWT. All the patients treated with NPTW showed complete and successful wound healing.

Table No. I: Demographic data of both groups

Variable	NPWT group (n=20)	Open wound therapy group (n=10)	p
Age	62.2±6.0	62.1±5.0	0.745
Sex			0.349
Male	15 (75%)	9 (90%)	
Female	5 (25%)	1 (10%)	
History of alcoholism	1 (5%)	-	0.335
Smoking	13 (65%)	5 (50%)	0.365
High blood pressure	12 (60%)	4 (40%)	0.174
Diabetes	3 (15%)	1 (10%)	0.919
Body mass index	21.9±2.1	21±2.9	0.743
Tumour location 0.199			
Upper thoracic	2 (10%)	1 (10%)	
Middle thoracic	12 (60%)	5 (50%)	
Lower thoracic	4 (20%)	4 (40%)	
Pathological stage 0.172			
I	1 (5%)	1 (10%)	
II	12 (60%)	6 (60%)	
III	6 (30%)	2 (20%)	
IV	1 (5%)	-	

Table No.2: Intraoperative data of both groups

Variable	NPTW group	Open wound therapy group	p
Surgical procedure 0.655			
Ivor-Lewis esophagectomy	15	7	
McKeown esophagectomy	5	3	
Anastomotic site			
Above aortic arches	12	8	
Below aortic arches	8	2	
Operative time (minutes)	220± 50.9	217.1±55	0.672
Intraoperative blood loss (mL)	425.6±214.2	395.4± 233	0.630

As shown in Table 3, patients experienced anastomotic leak and pneumonia as postoperative complications. The body temperature after the procedure and hospital stay did not differ significantly between both groups. However, the healing time of patients treated with NPTW was shorter i.e. 12 days as compared to the other group i.e. 19 days.

2 patients from the NPTW group and 1 from the wound therapy wound showed Enterococcus faecalis in the wound fluid and were prescribed macrolides antibiotics. The treatment cost of wound therapy was twice that of the NPTW procedure.

Table No.3: Postoperative details of surgery patients

Variables	NPTW group	Open wound therapy group	p
Anastomotic leak	3 (15%)	2 (20%)	0.717
Pneumonia	13 (65%)	6 (60%)	0.825
Postoperative maximum temperature (℃)	37.1±0.75	37.1±0.70	0.895
Postoperative maximum WBC (×109 /L)	12±3.0	14.5±5.5	0.124
Postoperative stay (days) 0.088			
Median	23	18	
Range	13-200	13-100	
Wound healing time (days) 0.003			
Median	12	19	
Range	6-35	8-32	

DISCUSSION

The rate of infection in our study was 30%. The average rate of infection after open surgery is 1.89-18.92%[9]. The difference in the rate of infection can be explained by the small sample size. Traditionally, open wound therapy is used to treat the wounds after the operation, however, this procedure is lengthy, costly, painful and requires daily dressing changes. On the other hand, we suggested a far safer and more convenient method to treat surgical site infections.

Negative pressure wound therapy was developed in 1993 by Fleischmann[10]. Firstly, it was used to treat patients with open fractures which lead to successful results. Now, this therapy is used for healing different wounds including postoperative wounds [11-13]. This procedure involves applying negative pressure on the wound bed to facilitate the formation of granulation tissue by preventing the lacuna formation and increasing blood circulation[14]. The transparent dressing keeps the wound covered and also allows observing it without changing the dressing repeatedly.

This not only lessens the patients' discomfort and doctors' labour.

The working of NPTW in wound healing is not clear. It can be due to the fact that it keeps the wound covered and maintains a stressed and hypoxic environment which leads to the activation of mechanoreceptor and hypoxia-mediated signalling pathways[15, 16]. This in turn results in angiogenesis, formation of granulation tissue and reconstruction of extracellular matrix, contributing to the healing process.[17]

A lot of complications including postoperative infections have been reported after thoracic surgery. NPTW has proved to be effective in curing these infections. However, surgical site infections pose less risk than thoracic infections so they are not paid much attention, although their rate is increasing and they also pose the risk of morbidity and mortality. Currently, open wound therapy is used for these infections until none is left. But it requires daily dressing changes which slow the healing process. This NPTW should be preferred instead to treat infection way more quickly as evident from our results[18, 19].

The results of our study are in agreement with Sharp[20] who administered PICO and traditional vacuum-assisted closure devices to adult patients. The method led to issues like difficulties in the use of the device, patient transportation, pain, lack of staff training and site and size difficulties. Therefore, the author used NPWT which showed much better results. Not only did the wounds heal but the pain score was lower and the patients were comfortable with this device. The hospital time was also less than in the use of the traditional unit.

The traditional device is hard to use and the medical staff is not trained for it, although it is more effective than traditional wound therapy. An expert can only operate such as device and its maintenance is also a difficult task. On the other, the use of facilitated NPTW as in our study eliminates all such issues and makes the patients and practitioners comfortable.

CONCLUSION

Facilitated NPTW is a safe, inexpensive and effective method for the treatment of thoracic wounds in comparison with open wound therapy.

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Original Article

Prevalence of Anxiety and Depression in Cardiac Patients Undergoing Coronary Bypass Surgery

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ABSTRACT

Objective: To evaluate the prevalence of psychiatric comorbidity pre and post-surgery in CAD patients undergoing coronary artery bypass grafting.
Study Design: A prospective study
Place and Duration of Study: This study was conducted at the Department of Cardiology, Ch.Pervaiz Elahi Institute of Cardiology Multan for 1 year from 8th April 2019 to 8th April 2020.
Materials and Methods: A total of 60 patients with coronary artery disease were included in the study that was undergoing coronary artery bypass grafting. All the patients awaiting CABG or undergoing CABG were tested for depression and anxiety by Beck's Depression Inventory and Beck's Anxiety Inventory. The patients were admitted to the hospital two days before the surgery and tests were performed after 1 day before the surgery and 3rd day after the surgery with the in-hospital patients. These tests were repeated 1 week and 1 month after the surgery with out-hospital patients.
Results: The average depression and anxiety scores before surgery were 7.21±4.33 and 10.12±6.53 respectively. These scores increase on the 3rd day after surgery, 11.24±5.22 and 17.09±8.92 respectively. However, the scores after 1 week and 1 month did not differ significantly. Similarly, patients showed more depression and anxiety symptoms post-surgery. No significant difference was found in the relation of depression and anxiety scores with the age and gender of subjects.
Conclusion: Depression and anxiety in CAD patients undergoing CABG are not related to heart disease, therefore early management and mental support can improve these conditions and lifestyles after surgery.
Key Words: Depression, Anxiety, Coronary artery disease, Coronary artery bypass grafting

INTRODUCTION

The morbidity and mortality rate of coronary heart disease (CHD) is increasing every year globally. Disease clustering is also very frequent in patients diagnosed with CAD. These diseases include diabetes, high blood pressure and dyslipidemia etc. In addition to these diseases, mental illness including depression and anxiety are also correlated with coronary heart disease, however, the rate of patients justifying this correlation is insignificance. Literature reports that about 20-40% of CAD patients suffer from depression[1], similarly, 20-30% of CAD patients have been diagnosed with anxiety[2, 3]. Similar co-morbidity has been seen in other heart diseases excluding coronary artery disease.

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The prevalence of anxiety and depression is increasing in coronary conditions such as chronic heart failure[4, 5]. The most common treatment prescribed for CAD is coronary artery bypass grafting. Most of these patients suffer from angina and complain of polypharmacy due to consuming antianginal medications such as antidiabetics, antiplatelets and antihypertensives. Besides these problems, patients also experience fear and stress before the surgery. These factors contribute to psychiatric comorbidity in these CAD patients. Patients who suffer from anxiety and depression before the surgery have also shown worse results after the surgery[6]. If these mental illnesses are not treated timely, the patient may not be successful in completing cardiac rehabilitation after the surgery. Therefore, it is important to examine the CAD patients undergoing surgery for psychiatric comorbidities. With the increase in CAD every year, the number of CAB surgeries is also increasing at an accelerated rate. But the data regarding psychiatric comorbidity is still scarce. This study aims to evaluate the prevalence of psychiatric comorbidity pre and post-surgery in CAD patients undergoing coronary artery bypass grafting. We also assess the signs and symptoms of comorbid conditions with respect to age and gender.

MATERIALS AND METHODS

A prospective study was conducted in the cardiology department of Ch.Pervaiz Elahi Institute of Cardiology Multan from 8th April 2019 to 8th April 2020. A total of 60 patients with coronary artery disease were included in the study that was undergoing coronary artery bypass grafting. Only those patients were included who had no history of psychiatric medication and chronic psychological conditions. All the additional medical history of the patients was also noted for including them in the study. The patients who had hemodynamic instability were excluded from the study. All patients provided their informed consent to become a part of the study.

All the patients awaiting CABG or undergoing CABG were tested for depression and anxiety by Beck's Depression Inventory and Beck's Anxiety Inventory. The tests were performed in a quiet room where the doctor asked questions to the patient. The data was collected by the answers of the patients.

The patients were admitted to the hospital two days before the surgery and tests were performed after 1 day before the surgery and 3rd day after the surgery with the in-hospital patients. These tests were repeated 1 week and 1 month after the surgery with out-hospital patients. The ethical committee approved the study design.

All the data were analyzed by using SPSS version 15. Friedman's test was performed to assess the quantitative data of dependent variables and independent variables were analyzed by t-test and Wilcoxon Rank Sum test. The association between quantitative quantities was found by Spearman's correlation. A statistical value of less than 0.05 was considered significant.

RESULTS

The average age of the patients in the study was 60 ± 10.2 years. 50 patients were men and 10 were women. The depression and anxiety scores before surgery and after surgery are shown in Table I. The average depression and anxiety scores before surgery were 7.21 ± 4.33 and 10.12 ± 6.53 respectively. These scores increase on the 3rd day after surgery, 11.24 ± 5.22 and 17.09 ± 8.92 respectively. However, the scores after 1 week and 1 month did not differ significantly. The average depression score after 1 week and 1 month was 10.11 ± 5.85 and 11.65 ± 8.01 respectively. The average anxiety score after 1 week and 1 month was 16.16 ± 8.55 and 15.42 ± 10.18 respectively (Table I). Similarly, patients showed more depression and anxiety symptoms post-surgery (Table 2). The correlation between age and gender with BDI and BAI test scores is shown in Table 3 and Table 4 respectively.

Table No.1: Data collected from Beck's Depression Inventory and Beck's Anxiety Inventory

		Mean standard deviation	Range	Median
Beck's Depression Inventory	Preoperative period	7.21±4.33	0-20	7
	3rd day after surgery	11.24±5.22	1-32	12
	1 week after surgery	10.11±5.85	1-33	10
	1 month after surgery	11.65±8.01	1-37	9
	P= <0.001			
Beck's Anxiety Inventory	Preoperative period	10.12±6.53	0-32	8
	3rd day after surgery	17.09±8.92	2-52	16
	1 week after surgery	16.16±8.55	2-47	14
	1 month after surgery	15.42±10.18	1-44	13
	P=<0.001			

Table No.2: Symptoms of psychiatric comorbidity pre and post-surgery

	Preoperative period		3rd day after the operation		1 week after the operation		1 month after the operation	
	n	%	n	%	n	%	n	%
BDI scores (Depression score)								
Less than 10 symptoms, normal	38	63.3	21	35	24	40	30	50
10-16 symptoms, mild	19	31.7	24	40	18	30	15	25
17-29 symptoms, moderate	3	5	14	23.3	17	28.3	14	23.3
30-60 symptoms, severe	-		1	1.7	1	1.7	1	1.7
BAI scores (Anxiety score)								
<8 symptoms, normal	20	33.3	3	5	8	13.3	11	18.3
8-14 symptoms, mild	27	45	23	38.3	22	36.7	28	46.7
16-25 symptoms, moderate	10	16.7	22	36.7	19	31.7	6	10
26-60 symptoms, severe	3	5	12	20	11	18.3	15	25

Table No.3: Correlation of age with depression and anxiety scores

		Age	
		Rho	**p**
Beck's Depression Inventory	Preoperative period	0.115	0.295
	3rd day after surgery	0.179	0.129
	1 week after surgery	0.145	0.222
	1 month after surgery	0.144	0.205
Beck's Anxiety Inventory	Preoperative period	0.999	0.399
	3rd day after surgery	0.089	0.445
	1 week after surgery	0.098	0.378
	1 month after surgery	0.029	0.549

Table No.4: Correlation of gender with depression and anxiety scores

		Male		Female		p
		Mean standard deviation	**Median**	**Mean standard deviation**	**Median**	
Beck's Depression Inventory	Preoperative period	8.43±5.47	7.9	5.50±3.76	4	0.298
	3rd day after surgery	11.55±5.01	12	10.64±6.33	10	0.629
	1 week after surgery	10.21±5.52	10	10.30±7.11	10	0.858
	1 month after surgery	11.92±7.81	9	11.36±8.81	8	0.909
Beck's Anxiety Inventory	Preoperative period	10.44±6.30	8	9.00±4.88	8	0.968
	3rd day after surgery	17.72±7.84	16.5	16.00±10.54	13	0.332
	1 week after surgery	16.88±8.38	16	15.12±9.85	14	0.439
	1 month after surgery	16.77±10.0	14	14.02±10.34	11	0.284

DISCUSSION

This study aimed to evaluate the prevalence of psychiatric comorbidity pre and post-surgery in CAD patients undergoing coronary artery bypass grafting. We also assess the signs and unipolar symptoms of comorbid conditions with respect to age and gender. A study reported that the prevalence of depression was found in 15-20% of the patients undergoing coronary artery bypass grafting[7]. These findings are consistent with the results of our study.

Literature reports that almost 30-40% of the CABG patients suffer from depression[8]. This rate increases after the surgery and patients develop new symptoms of depression.

McKhann et al.[9] conducted a study on 124 patients undergoing CABG. On follow up after 30 days and 12 months, 13% and 9% of patients were diagnosed with clinical depression, however, symptoms were not so severe pre-surgery. In our study too, the depression score was higher after the surgery and patients showed more depressive symptoms post-surgery. But research shows that the increased depression is not related to CAD[10].

Similar outcomes were observed when anxiety was assessed in these patients. Patients had high anxiety score before surgery, which is explained by the fear and

stress of the operation. Losing a vital organ is a justified reason for the change in behaviour and severe emotional reaction. The uncertainty of outcomes of the surgery is even more strong than the pain from the disease[10].

Research has shown that patients show more depressive and anxious symptoms before surgery as that time on the waiting list is quite distressing[11]. A study indicated that supports these findings noted the postoperative results for a period of 7 days[12]. In our study, the depression and anxiety scores were high after surgery because the preoperative period I.e 2 days was shorter than the mean postoperative period I.e 5 days. A study showed that more than 19 thousand CABG patients had an average hospital stay of 12 days[13]. Whereas in our study, the patient stayed in a hospital for 7-15 days. Researchers recommend depression and anxiety screening after coronary artery bypass grafting to ensure successful rehabilitation post-surgery[14]. We examined the patients till 1 month after surgery. Studies show that managing the psychological conditions can decrease hospital stay, drug use and risk of morbidity after surgery and patients can deal in a more healthy way later[15, 16]. Kazukauskiene et al.[17] reported that depressive symptoms and other mental illnesses are related to exercise in rehabilitation after CABG surgery. We did not manage the depression before the surgery,

however, its early management affect the hospital stay, use of medication and morbidity in a positive way.

Literature provides evidence that depressive symptoms in CABG surgery are associated with atherosclerotic progression. Wellenius et al.[18] show results that support this finding where patients with a history of CABG patients had high depression scores as atherosclerosis progressed in saphenous vein grafts. Similarly, depression is also related to cardiac mortality according to Frasure-Smith et al[19] which decreased with early management.

There is also evidence that other psychological conditions also predict surgical outcomes. Optimism showed decreased readmission rate after coronary artery bypass grafting[20], and pessimism predicted psychological conditions like depression and anxiety and ineffective postoperative coping mechanisms[21]. Everson et al[22] reported that severe hopelessness predicted incident heart attack and mild hopelessness was related to incident cancer. Our study did not diagnose psychological conditions nor provided psychological therapy. Also, as we included patients who did not have any history of psychological illness or drugs, the increased depression and anxiety were not related to the heart disease.

CONCLUSION

Depression and anxiety in CAD patients undergoing CABG are not related to heart disease, therefore early management and mental support can improve these conditions and lifestyles after surgery.

Author's Contribution:

Concept & Design of Study:	Naeem Amjad, Nauman Mazhar
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Evaluation of Features for Ground Glass Opacities in Lung Cancer Patients Positive with Covid-19

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ABSTRACT

Objective: To evaluate radiological features of Covid-19 and early lung cancer through High-resolution computed tomography (HRCT) and demonstrate the disparity between them.

Study Design: A retrospective study

Place and Duration of Study: This study was conducted at the Covid-19 ward, Oncology, Radiology Ward of Nishtar Medical University & Hospital Multan from 12th Nov 2019 to 12th Nov 2020.

Materials and Methods: A total of 100 Covid-19 patients and 300 patients with pulmonary ground-glass opacities undergoing lung surgery (control group) were included in the study. After propensity score-matched analysis, patients were divided into two groups with 80 matched pairs each. The clinical, pathological, epidemiological, and radiological characteristics (evaluated through HRCT) of both groups were compared.

Results: It was observed that Covid-19 patients presented more definite symptoms, were mostly younger men, and had higher BMI (body-mass index). After the radiological analysis of the matched patients, it was revealed that single lesion patients constituted 17% of Covid-19 cases and 89% of lung cancer cases. Patients in both groups mostly presented peripheral lesions. Covid-19 lesions had more lobes, segments and had various types with patchy forms. On the other hand, lung cancer tended to have only one type and had an oval form.

Conclusion: Both Covid-19 and lung cancer showed ground-glass opacities with similar but independent characteristics. These characteristics combined with pathogen detection, short-term CT examination, and laboratory tests will aid in improved diagnosis.

Key Words: Covid-19, lung cancer, radiology, propensity score analysis, ground-glass opacity

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused COVID in 2019, and WHO declared it a global health emergency on January 30, 2020[1]. The virus infected 8,525,000 people and caused 456,000 deaths till June 20, 2020. Pathogenesis of this infection usually has three stages. During the early stage, the virus binds to angiotensin-converting enzyme 2 (ACE-2) infecting nasal cells leading to low inflammatory response. Afterward, the virus reaches the respiratory airways and clinical manifestations appear by this time.

Lastly, the virus infects alveolar cell type II of the lungs by entering gas exchange units. Almost 20% of infected individuals reach this stage and have pulmonary

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infiltrates, serious disease including acute respiratory distress syndrome (ARDS) and frank lung injury develops in some cases[2]. Rapidly transmitting virus calls for the establishment of consensus guidelines for preventing transmission and facilitating diagnosis[3].

At present gold standard for its diagnosis is virus gene sequencing and Real-time polymerase chain reaction (RT-PCR), but these procedures are time-consuming resulting in an extended diagnostic cycle[4]. Different stages of COVI-19 are remarkably demonstrated by chest high resolution computed tomography (HRCT)[5]. Consolidative pulmonary opacities or patchy ground-glass opacities (GGOs) are mostly observed on CT scans. Consolidation and enlargement of GGOs imply an increase in pneumonia[5,6]. Along with having a central role in the evolution of the extent of pulmonary involvement in the disease, thoracic Ct significantly detects false-negative COVID-19 patients having nucleic acid tests because diagnostic CT findings are observed in these patients[7].

Currently, early stages of lung cancer have been effectively screened using low-dose CT (LDCT). Potentially malignant lesions are indicated by GGOs on this CT[8]. It may be difficult to distinguish early lung cancer from COVID -19 because of the similarity of CT finding in both, particularly in nucleic acid positive and asymptomatic patients. According to some reports,

patients with both COVID-19 and early lung cancer did not show symptoms of pneumonia. Few were surgically treated but had serious pneumonia, life-threatening and even death[9]. Therefore, it is important to differentiate between two diseases, both of which are indicated by GGOs. In this study, we will evaluate radiological features of Covid-19 and early lung cancer through High-resolution computed tomography (HRCT) and demonstrate the disparity between them.

MATERIALS AND METHODS

A retrospective was conducted from 12th Nov 2019 to 12th Nov 2020 in the Covid-19 ward, Oncology, radiology ward of Nishtar Medical University & Hospital Multan for 1 year. A total of 100 Covid-19 patients and 300 patients with pulmonary ground-glass opacities undergoing lung surgery (control group) were included in the study. People with neurological disorders, chronic illness, and having cancer of other areas were excluded. Medical records of the patients were used to obtain demographic data, symptoms, history, CT findings, and laboratory tests. Patients were also interviewed to obtain data not present in the record. Common chest protocol was followed for CT examinations: the patient was laid in a supine position, arms were raised and the patient was asked to hold breath. Following characteristics were analyzed in each patient: lung lesion type, lesion distribution, lesion form, number of affected lobes, frequency of lobe affected, number of segments affected, frequency of segment affected, and other findings like air bronchogram, tree-in-bud, centrilobular nodules, bronchial dilation, reticular pattern, cystic change, subpleural linear opacity, pleural retraction, pleural effusion, lymphadenopathy, and vessel convergence sign. CT scans were evaluated by trained radiologists. The study was conducted after approval ref# 11-108 dated 23-09-2019 from the ethical board.

Propensity score-matched (PSM) analysis was performed between both groups for minimizing bias resulting from non-randomized data collection. A multivariable logistic regression model with covariates was used for calculating propensity scores for each patient. This model showed significant baseline differences including age, gender, body mass index (BMI), tumor history, digestive disease, and cardio-cerebrovascular disease. Wilcoxon rank-sum test was used for comparing continuous variables between both groups. These were represented as median (interquartile range (IQR)). Categorical variables were compared using Fisher's exact test or Pearson's Chi-squared test. R software was used for statistical analysis. P value<0.05 was statistically significant.

RESULTS

A total of 300 patients with early lung cancer and 100 patients with COVID-19 were included in the study.

Subjects in the COVID-19 group were younger and had higher BMI as compared to those with lung cancer. Commodities like digestive disease, tumor history, and cardiovascular disease were much lower in patients with COVID-19. The clinical and demographic data before and after PSM are shown in Table 1. After propensity score-matched analysis, patients were divided into two groups with 80 matched pairs each. Before PSM, the majority of COVID-19 patients had an exposure history, some traveled to pandemic areas and some had close contact with infected patients. Pneumonia symptoms, including fever, cough, snot, dyspnea, sputum, muscle soreness, diarrhea, and chest distress, were more prevalent in COVID-19 patients as compared to those with lung cancer. According to laboratory tests at the time of admission, patients with COVID-19 had lower white blood cell count and lymphocyte count and higher aspartate aminotransferase than the patients with lung cancer. D-dimer, alanine aminotransferase, and Neutrophil count did not significantly vary between both the groups. The difference in laboratory findings, the incidence of symptoms, and exposure history were consistent after PSM. Nevertheless, the incidence of muscle soreness and dyspnea were no longer much difference in the two groups. D-dimer and neutrophil count reached a significant difference.

According to the results of the CT scan, 10 patients with COVID-19 had negative radiological findings. 1000 lung lesions were observed in 100 COVID -19 patients. 400 lesions were observed in 300 lung cancer patients. Peripheral lesions were predominantly present in both groups (760/1000 in COVID-19, 296/400 in lung cancer). The proportion of consolidation, mixed GGO, and pure GGO were 15%, 59%, and 28% respectively in COVID-19 patients, while in lung cancer patients these proportions were 6%, 48%, and 47%.

CT findings between both groups were quantitatively compared (Table 2). The form, type, number, specific features, and distribution of lesions before and after PSM were comparable. Among the matched groups a single lesion was present in 14/80 COVID-19 patients and 71/80 patients with lung cancer. More lobes and segments were involved in COVID-19 patients as compared to lung cancer patients. More than one type of lung lesion was found in the majority of COVID-19 patients (54/80, 67%) while patients with lung cancer either had mixed GGO (32/80, 40%) or pure GGO (40/80, 50%). COVID-19 patients had patchy lesions while those with lung cancer had oval lesions. Pleural effusion and lymphadenopathy were observed in 6/80 (8%) and 3/80 (4%) patients respectively. Cystic change and air bronchogram were present in both groups. COVID-19 patients had more frequent air bronchogram while cystic changes were rare. Moreover, reticular pattern, bronchial dilation,

subpleural linear opacity, tree-in-bud, and centrilobular nodules were observed in COVID-19 patients, while none of these were observed in lung cancer patients. On the other hand, lung cancer patients had vessel convergence signs, pleural retraction, and lobulated signs while COVID-19 patients did not show any of these.

Table No.1: Comparison of variables before and after PSM

Variables	Before PSM			After PSM		
	COVID-19 n=100	Lung Cancer n=300	P value	COVID-19 n=80	Lung Cancer n=80	P value
Sex (%)			<.0001			1.00
Male	55 (55%)	105 (35%)		38 (48%)	38 (47%)	
Female	45(45%)	195 (65%)		42 (52%)	42 (53%)	
Age (years), median	47(37-56)	59 (50-67)	<.0001	51(42-58)	53(42-61)	.77
BMI kg/m2, median	25(22-27)	24(22-26)	.014	24(22-26)	24(23-27)	.71
History of exposure (%)			<.0001			<.0001
Contact with infected person	31 (31%)	0 (0%)		24 (30%)	0 (0%)	
History of travel to the epidemic area	54 (54%)	0(0%)		46 (57%)	0 (0%)	
Comorbidity (%)						
Cardiovascular disease	18 (18%)	84 (28%)	.027	17 (21%)	18 (22%)	.88
Digestive disease	5 (5%)	36 (12%)	.034	6 (7%)	5 (6%)	1.00
Endocrine disease	6 (6%)	27 (9%)	.35	6 (7%)	3 (4%)	.41
Neuropathy	0 (0%)	6 (2%)	.19	0 (0%)	2 (2%)	.50
Respiratory disease	2 (2%)	12 (4 %)	.34	2 (2%)	3 (3%)	.68
Tumor history	1 (1%)	21 (7%)	.0087	2 (2%)		1.00
Symptoms (%)						
Fever	78(78%)	3 (1%)	<.0001	67 (82%)	0 (0%)	<.0001
Cough	59(59%)	15 (5%)	<.0001	46 (58%)	6 (7%)	<.0001
Sputum	32 (32%)	6 (2%)	<.0001	23 (29%)	1 (2%)	<.0001
Dyspnea	2 (2%)	0(0%)	.026	2 (2%)	0(0%)	.50
Snot	4(4%)	0(0%)	.00062	3 (4%)	0 (0%)	.060
Chest distress	10(10%)	3 (1%)	<.0001	9(11%)	1 (2%)	.020
Diarrhea	8 (8%)	0(0%)	<.0001	5 (6%)	0 (0%)	.014
Laboratory findings, median						
White blood cell	4.7 (3.7-6.1)	5.2 (4.4-6.1)	.00027	4.6(3.4-5.8)	5.5 (4.6-6.5)	.0001
Neutrophil	2.65 (2.0-4.0)	2.82 (2.31-3.61)	.16	2.70 (1.90-4.00)	3.08 (2.50-3.70)	.032
Lymphocyte	1.30 (.99-1.66)	1.71 (1.40-2.1)	<.0001	1.20 (.91-1.60)	1.75 (1.51-2.11)	<.0001
Alanine aminotransferase	20.1(14.1-34.0)	20.0 (15.0-27.0)	.11	18.6 (13.4-33)	20.0(15.0-30.0)	.85
Aspartate aminotransferase	24.0 (20.0-35.5)	21 (18.0-26.0)	<.0001	24 (20-34.5)	21.0 (17.0-25.0)	<.0001
D-dimer	.26 (.19-.53)	.25 (.19-.38)	.29	.28 (.20-.64)	.22 (.17-.33)	.017
Viral nucleic acid detection	100 (100%)	NA	NA	80 (100%)	NA	NA

Table No.2: Comparison of variables before and after PSM

Variables	Before PSM			After PSM		
	COVID-19 n=100	Lung cancer n=300	P value	COVID-19 n=80	Lung cancer n=80	P value
Single lesion	17 (17%)	261 (87%)	<.0001			<.0001
No. of involved lobe, median	5 (2-7)	1 (1-1)	<.0001	14 (17%)		<.0001
No. of segments	7 (2-13)	1 (1-1)	<.0001			<.0001

involved, median						
Type of lesion						
Pure GGO	4 (4%)	141 (47%)	<.0001	1 (1%)	40 (50%)	<.0001
Mixed GGO	17 (17%)	126 (42%)	<.0001	17 (21%)	32 (40%)	.0013
Consolidation	3 (3%)	12 (4%)	.95	3 (4%)	2 (2%)	.45
Pure and mixed GGO	34(34%)	18 (6%)	<.0001	26 (32%)	4 (5%)	<.0001
Pure GGO and consolidation	1 (1%)	3 (1%)	1.00	1 (1%)	1 (1%)	1.00
Mixed GGO and consolidation	16 (16%)	3 (1%)	<.0001	10 (12%)	2 (2%)	.0044
Pure and mixed consolidation	20 (20%)	0 (0%)	<.0001	19 (24%)	0 (0%)	<.0001
Form of lesion						
Oval	4 (4%)	189 (63%)	<.0001	4 (5%)	53 (66%)	<.0001
Patchy	49 (49%)	90 (30%)	<.0001	43 (54%)	24 (30%)	.00026
Oval and patchy	36 (36%)	21 (7%)	<.0001	27 (34%)	3 (4%)	<.0001
No lesion	11 (11%)	0 (0%)	<.0001	6 (7%)	0 (0%)	.0033
Distribution of lesion						
Unilateral lung	17 (17%)	285 (95%)	<.0001	75 (94%)	78 (97%)	<.0001
Bilateral lung	72 (72%)	15 (5%)	<.0001	59 (74%)	2 (3%)	<.0001
No lesion	7 (7%)	0 (0%)	<.0001	6 (7%)	0 (0%)	.0033
Lymphadenopathy	4 (4%)	0(0%)	.0011	3 (4%)	0 (0%)	.060
Pleural effusion	7 (7%)	0(0%)	<.0001	6 (8%)	1 (1%)	.014

DISCUSSION

Thousands of people have been affected by the COVID-19 pandemic worldwide. The major challenge is ensuring the specificity and sensitivity of diagnosis. CT scan, in addition to the nucleic acid test, is a practical diagnostic method for COVID-19. Additionally, despite the negative nucleic acid test COVID-19 still could be present[10,11]. It is very important to differentiate the early stages of lung cancer from COVID-19 at present time. GGO appearing CT scans show attenuation and damage to alveoli. Imaging results were matched with the pathological findings like proteinaceous exudes and alveolar edema, where multinucleated giant cells, vascular congestion, and inspissated secretion were seen in the airspaces. Additionally, alveolar activity was decreased due to the proliferation of interstitial fibroblasts and pneumocytes[9]. GGO is predominantly found in the radiographic image of both early lung cancer and COVID-19. Both could demonstrate patchy or oval, unilateral or bilateral GGO in form of multiple or single lesions, due to which it is challenging to discriminate between both. This similarity can confuse the surgeons and lead to inappropriate surgical intervention. Despite these difficulties, differentiating characteristics are found. This study shows that patchy bilateral GGOs are predominantly present in COVID-19, while oval unilateral GGOs are present in lung cancer. Distribution and shape are consistence with the past studies[12]. COVID-19 can be distinguished by reticular pattern, bronchial dilation, subpleural linear opacity, tree-in-bud, and centrilobular nodules. On the other hand, lung cancer is featured by vessel convergence, cystic change, pleural retraction, and lobulated signs. During the initial stage of COVID-19, classical GGO and occasional consolidation are observed. After five days lesions lesion increase in size with disease progression, and additional features like crazy paving pattern, reverse halo sign and fibrous stripe begin to appear, increase in GGO is related to progressing malignancies.[13]

Though, these are subtle differences but are of high value to distinguish these diseases. However, diagnosis of COVID-19 requires thorough assessment along with epidemiological investigation, laboratory tests, and clinical symptoms. Patients with shortness of breath, fever, myalgia, and cough should be focused[14]. Travel history to epidemic areas and contact with those infected with COVID-19 are also considered during diagnosis. Above all, the nucleic acid test remains the gold standard for definite diagnosis[15]. It is important and clinically significant to analyze the distinction between CT findings of early lung cancer and COVID-19. GGO in CT scan can help in the diagnosis of asymptomatic COVID-19 patients and those with negative nucleic acid pneumonia, and thus can limit transmission and decrease the rate of missed diagnosis. Patients with lung cancer should be extensively evaluated to exclude COVID-19 before surgery. The possibility of misdiagnosis of COVID-19 as lung cancer and vice versa should be reduced. Rash decision expose patient to COVID-19 and surgical trauma. Upon reaching a definitive diagnosis treatment of COVID-19 should be prioritized.

CONCLUSION

The distinctive features of GGOs in patients with early-stage lung cancer and COVID-19, along with laboratory tests, patient history, and pathogen detection will aid in differential diagnosis and lower the rate of miss diagnosis**.**

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Patterns of CT-Scan Findings Among Head Injury Patients Presenting to the Emergency Department in a Tertiary Care Hospital

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ABSTRACT

Objective: To analyze the pattern of CT-scan findings among head injury patients presenting to the emergency department in a tertiary care hospital.

Study Design: Retrospective, observational study

Place and Duration of Study: This study was conducted at the Department of Radiology / Neurosurgery, Liaquat National Hospital, June-December, 2021.

Materials and Methods: Patients' medical record files were reviewed to retries socio-demographic profiles and CT-scan findings. Data was entered in SPSS version 25 for statistical analysis.

Results: 423 records were reviewed. Median age was 40 (IQR= 26 – 55) years. Majority were males (n=326, 77.1%). Top most cause of head injury was road traffic accident (n=246, 58.2%) followed by fault (n=105, 24.8%), assault (n=29, 6.9%), others (n=12, 2.8%) and unknown mechanism (n=31, 7.3%). Injury of others included all those accidental fall of objects on head. Nearly half of the patient depicted normal findings of CT scan (n=190, 44.9%). The most frequent fractured site was parietal (n=78, 18.4%), temporal (n=73, 17.3%), frontal (n=60, 14.2%), occipital (n=13, 13.1%), maxillary (n=27, 6.4%), sphenoid (n=24, 5.7%), ethmoid (n=19, 4.5%), zygomatic (n=13, 3.1%) and mandible (n=6, 1.4%). Contusions, subarachnoid hemorrhage and subdural hemorrhage was present in 36.2% (n=153), 30.3% (n=128) and 10.4% (n=44) cases respectively. Few cases presented with blood in sinuses (n=65, 15.4%), extradural hemorrhage (n=62, 14.7%), intraparenchymal hemorrhage (n=31, 7.3%), intracranial mass (n=3, 0.7%), intraventricular bleed (n=30, 7.1%).

Conclusion: The current study analyzed that RTA was the leading cause of head injury and patterns of CT-scan findings was significantly different among all mechanism of injuries with a significantly higher proportion of abnormal CT-scan findings among RTA patients.

Key Words: Traumatic brain injury, emergency department, CT-scan findings, subarachnoid hemorrhage, extradural hemorrhage, subdural hemorrhage

INTRODUCTION

Traumatic brain injury (TBI) as a consequence of head trauma is a usual presentation in emergency rooms, accounting for more than one million yearly visits[1]. According to the Centers for Disease Control and Prevention (CDC), a TBI results from a bump, blow, jolt to the head, or a penetrating injury that upsets normal brain functioning. Traumatic injuries may be categorized as closed (non-penetrating) or open (penetrating)[2,3]. TBI is a leading cause of death and everlasting disability among the age group 29-45 years[4].

TBI is frequently referred to as the silent epidemic and a rising public health concern and is considered the highest contributor to death and disability worldwide among all trauma-related injuries[5]. Globally, nearly 55.5 million were estimated to have sustained a head injury (HI)[6]. Global data shows that low- and middle-income countries (LMICs suffer from the major burden of this problem, the underlying key source being road traffic accidents (RTA)[4,7]. LMIC encounter at least 3 times higher HI proportion than occurred in high-income countries[8].

Available literature shows highly variable findings regarding the epidemiology of TBI which may be due

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to different definitions, inclusion and exclusion criteria, study approaches, and reporting styles[9]. Efforts for uncovering epidemiological facts about TBI are still required as the global trauma burden is continuously rising as a threat to public health[10]. Therefore, we planned a current study to investigate patterns, causes, and CT-scan findings among head injury patients presenting to the emergency department in a tertiary care hospital in Karachi, Pakistan.

MATERIALS AND METHODS

This retrospective study reviewed the records of head injury patients present in the emergency room in Liaquat National Hospital from June-December 2021. The study protocol was approved by the Ethics Committee of the hospital (IRB# 0777-2022 LNH-ERC). Records of the patients, who were brought dead, were not reviewed. Patients' medical record files were reviewed to retrieve their age, gender, and mechanism of injury. CT-scan findings were also recorded and all the gathered was documented in a pre-designed proforma.

Data was entered in SPSS version 25 for statistical analysis. Frequencies and percentages were computed for categorical variables. Numerical variable age was presented as median with interquartile range (IQR) after assessing the assumption normality with the Shapiro-Wilk test. CT scan findings were compared in patients with a different mechanism of injury and the incidence of neurological defects was compared with fractures using Chi-square or Fisher exact test. P-value less than or equal was defined as statistically significant.

RESULTS

A total of 423 records were reviewed. The median age of patients was 40 (IQR= 26 – 55) years. More than half of the injured were males (n=326, 77.1%). Topmost cause of head injury was road traffic accident (n=246, 58.2%) followed by fall (n=105, 24.8%), assault (n=29, 6.9%), others (n=12, 2.8%) and unknown mechanism (n=31, 7.3%). Injury to others included all those accidental falls of objects on the head. Nearly half of the patients depicted normal findings of CT scans (n=190, 44.9%). Table 1 shows the comparison of CT findings among patients with different mechanisms of injury. Frequency of abnormal CT scan findings, SAH, SDH, fracture of cranial vault and skull base, parietal, temporal and zygomatic, EDH, contusions, and blood in sinuses were significantly different among different mechanisms of injury.

Table No.1: Comparison of CT scan findings among patients with a different mechanism of injury

CT scan findings	Mechanism of injury					p-value
	RTA n(%)	Fall n(%)	Assault n(%)	Other n(%)	Unknown n(%)	
Abnormal CT scan findings	143(58.1)	46(43.8)	23(79.3)	4(33.3)	17(54.8)	**0.003
SAH	84(34.1)	23(21.9)	11(37.9)	2(16.7)	8(25.8)	0.117
SDH	28(11.4)	10(9.5)	3(10.3)	1(8.3)	2(6.5)	†0.965
Intraparenchymal bleed	13(5.3)	13(12.4)	4(13.8)	1(8.3)	0(0)	*†0.029
Cranial vault fracture	41(16.7)	8(7.6)	7(24.1)	2(16.7)	6(19.4)	**†0.008
Skull base fracture	17(6.9)	2(1.9)	2(6.9)	0(0)	4(12.9)	
Both vault and skull base fracture	41(16.7)	10(9.5)	6(20.7)	0(0)	2(6.5)	
Frontal	38(15.4)	7(6.7)	6(20.7)	2(16.7)	7(22.6)	*†0.045
Parietal	55(22.4)	8(7.6)	9(31)	1(8.3)	5(16.1)	**0.005
Occipital	7(2.8)	3(2.9)	2(6.9)	0(0)	1(3.2)	†0.673
Temporal	51(20.7)	7(6.7)	11(37.9)	0(0)	4(12.9)	**<0.001
Zygomatic	21(8.5)	2(1.9)	3(10.3)	0(0)	1(3.2)	†0.950
Nasal	10(4.1)	1(1)	2(6.9)	0(0)	0(0)	†0.275
Ethmoid	12(4.9)	2(1.9)	2(6.9)	0(0)	3(9.7)	†0.265
Maxillary	21(8.5)	3(2.9)	2(6.9)	0(0)	1(3.2)	†0.296
Sphenoid	18(7.3)	1(1)	3(10.3)	0(0)	2(6.5)	†0.054
Mandible	4(1.6)	0(0)	2(6.9)	0(0)	0(0)	†0.132
EDH	39(15.9)	11(10.5)	5(17.2)	1(8.3)	6(19.4)	†0.574
Intracranial mass	2(0.8)	1(1)	0(0)	0(0)	0(0)	†1.000
Contusions	99(40.2)	24(22.9)	17(58.6)	2(16.7)	11(35.5)	**†0.001
Blood in sinuses	47(19.1)	6(5.7)	4(13.8)	1(8.3)	7(22.6)	*†0.010
Intraventricular bleed	17(6.9)	8(7.6)	2(6.9)	1(8.3)	2(6.5)	†0.984

EDH: Extradural hemorrhage, RTA: Road traffic accident, SAH: Subarachnoid hemorrhage, SDH: Subdural hemorrhage, †: Monte-carlo Fisher-exact test was reported, *Significant at p<0.05, **Significant at p<0.01

Table No.2: Association of CT scan findings with fractures.

CT findings	Fractures				p-value
	Cranial vault n(%)	Skull base n(%)	Both vault and skull base n(%)	Absent n(%)	
SAH	42(65.6)	9(36)	39(66.1)	38(13.9)	**<0.001
SDH	12(18.8)	0(0)	11(18.6)	21(7.7)	**<0.001
EDH	29(45.3)	5(20)	20(33.9)	8(2.9)	**<0.001
Intracranial mass	0(0)	0(0)	1(1.7)	2(0.7)	0.534
Contusions	49(76.6)	12(48)	48(81.4)	44(16.1)	**<0.001
Blood in sinuses	9(14.1)	12(48)	37(62.7)	7(2.6)	**<0.001
Intraventricular bleed	9(14.1)	1(4)	5(8.5)	15(5.5)	†0.105
Intraparenchymal bleed	4(6.3)	2(8)	5(8.5)	20(7.3)	†0.938

EDH: Extradural hemorrhage, SAH: Subarachnoid hemorrhage, SDH: Subdural hemorrhage, †: Fisher-exact test was reported, *Significant at p<0.05, **Significant at p<0.01
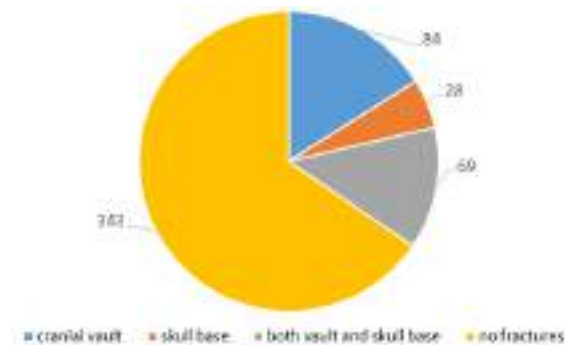

Figure No.1: Frequency of fractures among study participants

Figure 1 shows the frequency of fractures among patients with abnormal CT findings. The most frequent fractured site was parietal (n=78, 18.4%), temporal (n=73, 17.3%), frontal (n=60, 14.2%), occipital (n=13, 13.1%), maxillary (n=27, 6.4%), sphenoid (n=24, 5.7%), ethmoid (n=19, 4.5%), zygomatic (n=13, 3.1%) and mandible (n=6, 1.4%). Contusions, subarachnoid hemorrhage and subdural hemorrhage was present in 36.2% (n=153), 30.3% (n=128) and 10.4% (n=44) cases respectively.

Few cases presented with blood in sinuses (n=65, 15.4%), extradural hemorrhage (n=62, 14.7%), intraparenchymal hemorrhage (n=31, 7.3%), intracranial mass (n=3, 0.7%), intraventricular bleed (n=30, 7.1%).

Table 2 shows the association of CT scan findings with fractures. SAH (p<0.001), SDH (p<0.001), EDH (p<0.001), contusions (p<0.001), blood in sinuses (p<0.001) were significantly associated with fractures site.

DISCUSSION

Worldwide mobilization and urbanization trend is giving a high incidence of trauma as one of the leading public health concerns. Among all other traumatic injuries, TBI remains considered a top cause of death and permanent disability in young people, particularly in the developing world[11]. The rising burden of HI requires knowing patterns and causes of injuries for devising and modifying the management strategies to appropriately manage ER rooms and treat the victims.

In the present study, the median age of patients presenting with HI is forty years. In literature, it is reported that most of the trauma victims are of youth to middle age group with an age range of 21-40 years when the period of productive activity is at its peak[12]. Another Pakistani study analyzing HI patterns reported that nearly half (48%) of the HI patients included in the study were in the age range of 20-49 years[13]. An Indian study demonstrating clinical profile and autopsy findings in fatal head injuries reported that the median age injured was 43 years[14]. Similar studies from Saudia Arabia and Uganda also reported that victims were the youth age group with a mean age of 27.01 ± 13.9 years and 29.34 ± 14.13 years respectively[11,15].

In the present study, the majority of the victims were males, which is consistently reported finding in across the globe the hat male gender is more exposed to the accidental injuries than women and the reason is obvious that men are more frequently engaged in outdoor activities than females due to which they are highly exposed to traumatic injuries[12-14].

In low and middle-income countries, road traffic crashes are the leading causes of TBI in young people while falls are the leading causes in the elderly[1]. It must be noted that RTAs contribute 2.12% to the total global mortality[15]. The same phenomenon is depicted in our study that the most frequent cause of injury was RTA followed by fall and assault and blast injuries whereas the cause was unknown in some of the injuries. Another report from Pakistan also reported the same pattern of cause; RTAs followed by falls and assaults[7]. Studies from Saudi Arabia, India, and China also reported RTAs as the leading cause of HI[8-10].

According to the CDC guidelines, CT is indicated with the loss of consciousness or posttraumatic amnesia only if one or more of the following is present: headache,

vomiting, age > 60 years old, drug or alcohol intoxication, deficits in short-term memory, physical evidence of trauma above the clavicle, posttraumatic seizure, GCS score < 15, focal neurologic deficit, or coagulopathy[16]. In our study, nearly half of the patients (44.9%) had normal CT scan findings. A similar study conducted in Bangladesh reported that 47.03% patients of with head injury were found to have traumatic brain injury[17]. A Nigerian study assessing the patterns of CT findings in head trauma reported a lower proportion of normal findings of CT ((35.81%)[18]. Clinical and radiological findings could vary among the studies due to differences in the severity of the cases.

In our study, the most frequently occurred abnormality on CT scan was contusion followed by (36.2%) followed by subarachnoid hemorrhage (30.3%), blood sinuses (15.4%), extradural hemorrhage (14.7%), subdural hemorrhage (10.4%), intraparenchymal hemorrhage (n=31, 7.3%), intraventricular bleed (n=30, 7.1%) and intracranial mass (n=3, 0.7%). Another Pakistani study reported frequent head injury patterns as extradural hemorrhage (27.5%) followed by subdural hemorrhage (22.3%), contusions (21.8%), diffuse axonal injury (13.2%), skull fracture (7.3%), subarachnoid hemorrhage (4.2%) and intracerebral hemorrhage (19). Onwuchekwa and Alazigha reported that intra-axial hemorrhage in nearly half of the patients (42.26%) whereas extra-axial hemorrhage was found in nearly a quarter of the patients (23.55%)[18]. Alnaami et al reported that EDH (22.9%), SDH (18.1%), SAH (20.4%), contusions (19.3%), IVH (11.9%) and fractures (7.4%) were seen on CT scan findings[15]. MS Islam reported that SDH (35%), EDH (27%), concussions (15%), cerebral contusion (14%), diffuse axonal injury (6%), and SAH (3%) were causes of traumatic brain injury among patients presenting with head trauma[17].

In the present study, the frequency of fractures among patients with abnormal CT findings was 64% whereas 27.5% had a fracture of the cranial vault only, 10.7% of patients had skull base fractures only and 25.3% had a fracture of both cranial vault and skull base. Onwuchekwa found an incidence of 28.06% of skull fractures among patients with abnormal CT findings and the parietal bone was the most involved in fractures which is a comparable finding to our study (18). In the present study, the frequency of SAH, EDH, and contusions was significantly higher among patients with cranial vault fracture only whereas SDH frequency was significantly lower among patients with fractures than patients not having fractures. Moreover, the frequency of blood in sinuses was significantly higher in patients with skull base fractures only. In contrast to our study, skull base fracture was found to be associated with paranasal sinus collection and cerebrospinal fluid leakage in previously available literature[18,20].

The present study suffers from some limitations including a retrospective review of a single-center study. The study was not focused to assess the impact of CT findings on the survival of the patient. Furthermore, we only disclose adults' data, which could underestimate the overall burden of head injuries presented in a hospital. Therefore, a multi-center study may be conducted in the future to overcome these limitations.

CONCLUSION

The current study analyzed that RTA was the leading cause of head injury and patterns of CT-scan findings was significantly different among all mechanism of injuries with a significantly higher proportion of abnormal CT-scan findings among RTA patients.

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