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Editorial

COVID-19 Vaccination

Mohsin Masud Jan

Editor

As the pandemic threatens Pakistan with the third phase, the government has so far received COVID-19 vaccine only from China.

It has not procured yet anything from the open market and is now awaiting more vaccines from the COVAX Facility, but it has not made any bilateral agreement with India in this regard. Recently Indian media reports referred to Pakistan receiving vaccines directly from India while some senior officials here had also mentioned this.

However, when the matter was taken up with the Foreign Office during the weekly media briefing, the spokesman made it clear that there was no bilateral procurement agreement with India.

"Regarding the procurement of Covid-19 vaccine, Pakistan has not entered into any bilateral procurement agreement for COVID-19 vaccine from India.

GAVI, the international vaccine alliance, has offered provision of vaccine doses to several countries, including Pakistan, under its COVAX Facility", he clarified. The procurement and supply mechanism of the vaccine doses are undertaken by GAVI and not the recipient countries. The spokesman said he did not have the exact details of the doses of the vaccine which were coming in and it was better for the Ministry of National Health Services, Regulations and Coordination to give the figures.

Covid cases are rising in the country, with positivity having gone up to 5.35 percent. All this is happening as the country enters the vaccination phase of the crippling pandemic that has taken so many lives across the world. Unfortunately, the general hesitation among people to use the vaccine – spurred no doubt by the near-ridiculous fake news doing the rounds on social media – and the level of confusion regarding the how, when, what of vaccination will be real hindrances to an effective vaccination drive. This will just lead to the risk of more cases appearing and fewer people being rendered immune to the disease. Doctors report ICUs are filling up again and they are struggling to cope with the problem.

What is urgently required is a mass awareness campaign regarding vaccination. The electronic media, the civil society, doctors' and nurses' associations – everyone – must be taken on board a well-thought-out campaign to introduce the vaccines, encourage compliance, and bust some disturbing myths and false rumours. What can be better than a common citizen seeing the country's top leaders – in politics or entertainment or other fields – roll up their sleeves and get their first shot of the vaccine. The power of celebrity or fame or influence must be used to ensure Pakistanis are vaccinated. Meanwhile, the government also needs to perhaps set out an FAQ sheet – because vaccine questions are many and till now we have not had luck with too many answers from the official end.

The reason all this is necessary is because there has been some lag in the country's vaccination process. But we wonder if this is enough and if anything can be achieved, until more focus is placed on making sure the vaccine reaches the maximum number of people.

The question we need to ask ourselves is how the government has handled the pandemic and what it has done to spare people the kind of suffering they seem to be going through. There needs to be a further investigation into the suicide rate in Pakistan. Generally, we do not talk about the problem at all. But especially in the context of Covid-19 pandemic, it does need to be discussed.

Like other countries around the world, Pakistan desperately needs vaccines. In Pakistan, we then have the additional problem of people who do not want to be vaccinated, and concern over the quality of the Chinese vaccine seems to be a factor in this. The government needs to work much harder to persuade people that vaccination is essential and also to follow the SOPs that seem to have been abandoned completely. People had already decided that the pandemic was over. Many of them had not believed in it in the first place.

This is a disaster. There is no point pretending that Covid-19 has spared Pakistan miraculously or that we do not need to take measures against it. The question of herd immunity has already been experimented with by countries such as Sweden, and also Brazil. It ended in failure. We need to stop the misery of people, we need to end the suicides, and to do so we need to bring the Covid-19 pandemic to an end by vaccinating all our population, regardless of their income bracket and regardless of their ability to access medical care or the vaccine itself.

Original Article

Prevalence of Malnourish Children among Malnourish Mothers in Tertiary Teaching Hospital Larkana, Pakistan

Malnourish Children among Malnourish Mothers

Nazia Faraz Shaikh[1], Delijan Mugheri[1], Shaista Laghari[1], Shankar Lal[1], Vijia Kumar Gemnani[2] and Saifullah Jamro[1]

ABSTRACT

Objective: To assess the prevalence of malnourished children among malnourish mothers in tertiary teaching hospital Larkana, Pakistan.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Pediatric Medicine department, Chandka Medical College / SMBBMU Larkana from 15.6.2018 to 31.6.2020.

Materials and Methods: After taken permission from the ethical review committee of CMC Children Hospital/ SMBBMU Larkana; patients who fulfilled the inclusion criteria were included in the study. Mid upper arm circumference (MUAC) of a child, as well as the mother, was measured, Child with MUAC <11.5cm and the Mother with MUAC <21 cm was labeled Malnourished. All the collected data were entered into the proforma attached at the end.

Results: Mean ± SD of the age of children and mothers were 16.20 ±7.96 with C.I (15.02- ---17.37) months and 27.57 ±4.83 with C.I (26.86----28.28) years respectively. 179 children 94 (52.5%) were male and 84 (47.5%) were female. Most of the women were found to be multigravida i.e. 154 (86%) and 25 (14%) had primigravida. The frequency of malnourished children among malnourished mothers was 150 (84%). 3

Conclusion: It is to be inferred that the frequency of maternal and child under-nutrition is high in both communities even though more seemed in rural areas. Efforts are needed to reduce the vicious cycle of undernutrition in children and mothers should focus on tending to hazard factors especially to each community. Males were more prone to contrasted with females.

Key Words: Malnourish Children, Malnourish Mothers, Larkana

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INTRODUCTION

Malnutrition (measured as poor anthropometric status) of under-five children is an important public health problem that is one of the major killers of children in developing countries. Worldly, about 35% of under-five deaths are related to malnutrition.[1]Child malnutrition can be expressed as a pathological condition resultant from inadequate nutrition, as well as under nutrition (protein-energy malnutrition) due to not enough intake of energy and other nutrients; Malnourished children are significantly more prone to die because of a typical childhood infection than the individuals who are enough nourished. In developing countries, of the almost 12 million children under 5 who die every year, basically from preventable causes, the deaths of more than 6 million, are either directly or indirectly attributable to malnutrition. Some 2.2 million children die from diarrheal dehydration as a consequence of persistent diarrhea that usually increases with malnutrition.[2] The World Health Organization during that MDG 4 has perceived that improved nutrition is vital in lessening the under-5-years mortality, particularly in the developing nations.[3] In Pakistan statistics, 800,000 children die every year and 35% of deaths happened due to malnutrition. The danger of death is nine times higher among malnutrition children as compared to balanced diet children.

In Pakistan, 40.2 percent of children under five are currently stunted according to the National Nutrition Survey (a prevalence considered 'critical' by WHO's thresholds). Besides, 17.7 percent of this age group are wasted (the highest level of wasting in the country's history) and 28.9 percent are underweight. [4]Globally, child malnutrition is the most critical problem, a wide

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range of deaths of children occurred due to malnutrition. The degree of malnutrition among children, outstandingly high in South Asia, like India, Bangladesh, and Nepal ranging from 45-48 percent, while in Pakistan and Sri Lanka 38% and 30% respectively.

Poverty, illiteracy, and lack of health services are the main underline cause of malnutrition. Anthropometric records showed the cumulative outcome of access to food, parental education, health, food practices as well as environmental health. Nutritional status is a sensitive indicator of preschool children, as they are more vulnerable to nutritional imbalances.[5] The employ of mid-upper arm circumference (MUAC) has improved quality to screen the acute malnutrition among children to enhance the reach and improve the quality of the Community-Based Management of Acute Malnutrition (CMAM) program.[6]World Health Organization (WHO) and UNICEF updated guidelines in 2009 that a MUAC cutoff of <11.5 cm as one of three screening standards for identifying and treatment of severe acute malnutrition in infants and children 6-60 months.[8] To a great extent because of the direction from WHO and UNICEF on a standardized cutoff, MUAC has become a widely utilized and effective diagnostic device for screening children and help to manage acute malnutrition.

Likewise, with children, the utilization of MUAC among younger and adults offers the benefits of being a simple and moderately economical measure that can be done in both community and facility-based situations.

MUAC measure requires minimum instruments and calculations as contrasted with weight and height estimations for figuring of the basal mass index (BMI) or other anthropometric estimations, for example, skinfold thickness.

Various investigations have indicated that MUAC relates well with BMI in an adult population.[6] According to the current study, it is demonstrated that there was no significant difference in the frequency of under nutrition sustenance as evaluated by BM1 and MUAC (50.5 VS 55.7%, p>0.05).

Around 23percent, 36percent and 3percent children were seemed to be stunted, underweight, and wasted.[7] It is also notified that the percent of malnourished infant was more in undernourished (CED) mothers.[7]

Rationale: In Pakistan, the frequency of malnutrition has not improved in the last two decades despite the increase in per capita food availability and increased intake of calories and protein. There is a need for immediate solution such as maternal, environmental and sociocultural factors also need to be improved. Poor maternal nutritional status can result in undernourished generation. Although data is available, but little work is done, we see the current magnitude of undernourished children among undernourished mothers.

Operational Definition:

Malnourished Child: Children with MUAC less than 11.5cm termed malnourished.

Maternal Malnutrition: Mothers had MUAC <21 then termed as malnourished

MATERIALS AND METHODS

Descriptive Cross-Sectional Study, was conducted at Department of Pediatric Medicine, CMC Children Hospital Larkana, during the period of 15-6-2018 to 31-6-2020.

A total of 179 patients who fulfilled the inclusion criteria was included in the study. Mid upper arm circumference (MUAC) of the child, as well as the mother, was measured, Child with MUAC <11.5cm and the Mother with MUAC <21 cm was labeled Malnourished. All the collected data were entered into the proforma.

Sample Size: The sample size was calculated by using the WHO Sample size calculator taking the prevalence of malnutrition 13.4%[7] with a confidence level of 95% and margin of error of 0.05 then the estimated sample size was n= 179

Sampling Technique: Non-probability consecutive sampling

Sample Selection

Inclusion Criteria

- Children of age 6 to 59 months
- Patients of both gender
- Mothers giving informed consent

Exclusion Criteria:

- Children having the congenital disease
- Cardiac disease Inborn error of metabolism
- Chronic Illness
- Celiac disease Tuberculosis Cystic fibrosis
- Miscellanies (Chronic kidney disease)
- CP child
- Major Family Problems (Divorce, Bereavement, etc)
- All these will be confirmed by detailed history and available records,

Data Collection Procedure: The study was conducted at CMC Children Hospital/ SMBBMU Larkana. All children who meet the inclusion criterion were enrolled into the study after taking written consent from Parents or Guardian and data was entered into study-specific Proforma, Mid upper arm circumference (MUAC) of the child as well as a mother had measured, the child with MUAC <11.5cm and Mother with MUAC <21 cm were labeled as Malnourished. Other data like age, gender, weight, and height/ length of the child were also recorded. All the measurement was done by the researcher herself under the supervision of a concerned supervisor.

Data Analysis Procedure: Data were analyzed applying SPSS version 21. Descriptive statistics were used to calculate mean and standard deviations for Quantitative Variables including the age of child and mother, the weight of the child, length/height of the child, MUAC of child and mother. Frequencies with percents were presented for qualitative variables like residence, educational, and socioeconomic status. Stratification was done further to control effect modifiers like age; gender, weight, and length of the child, MUAC of children and mothers, etc. Chi-square test was applied and $P \leq 0.05$ was taken as significant.

RESULTS

This study was planned to assess the prevalence of malnourished children among malnourished mothers. Total 179 patients were included in the study, after result analysis, 94 (52.5%) were male and 84 (47.5%) were female and the mean age of child's and mother showed 16.20 ±7.96 months and 27.57 ±4.83 years respectively, while the weight and height of child were 6.37 ±2.19 kgs and 63.25 ±8.61 cm respectively.

In the study, the demographic and other variables showed that the greater part of the patients have belonged to rural areas i.e. 169 (94%) and 10 (6%) belonged to urban. And also most of the women were found to be multigravida i.e. 154 (86%) while 25 (14%) seemed primigravida. (Table 01)

In the study, the educational status of most of the women was illiterate i.e. 153 (85%), secondary 16 (9%) and primary educated was 10 (6%), while the distribution of socioeconomic status family income of 132 (73.7%) families was between 10000---15000, 10 (5.6%) 16000----20000, 37 (20.7%) had family income between 21000---25000. (Table 01)

Table No.1: Demographic and Other Variables Regarding Children & Mothers

Children Data		Frequency	%
Gender	Male	94	47.5
	Female	85	52.5
Residence	Rural	169	94
	Urban	10	06
Malnourish child	Yes	150	86
	No	29	14
Mothers Data		Frequency	%
Parity	Multigravida	154	86
	Primigravida	25	14
Education status	Illiterate	153	85
	Secondary	16	09
	Primary	10	06
Socioeconomic status	10000-15000	132	73.7
	16000-20000	10	5.6
	21000-25000	37	20.7

The prevalence of malnourished children among malnourished mothers was 150 (84%). (Figure 01)

Middle upper arm circumstance (MUAC) measurement for child's and mother's malnutrition seemed 9.73 ±1.15 cm and 20.04 ±1.71 cm respectively.

In stratification of malnourished children concerning the age of child and mothers, the gender of children, weight, height, the number of children under five years of age, socioeconomic status educational and residential status were done. (Table: 02).

Table No.2: Stratification of Demographic and Other Variables

Children Data		Malnourish Child		P-Value
		Yes	No	
Age (month)	6-16	82	18	0.462
	>16	68	11	
Gender	Male	77	17	0.472
	Female	73	12	
Weight (Kgs)	3-6	58	15	0.190
	>6	92	14	
Height (cm)	45-65	95	15	0.240
	>65	55	14	
Children Muac (cm)	8-10	90	15	0.407
	>10	60	14	
Mothers data		Yes	No	P-value
Age (Years)	19-27	84	14	0.444
	>27	66	15	
Residence	Rural	140	29	0.152
	Urban	10	0	
Mother (MAUC)	18-22	144	23	0.001
	>22	6	6	
Parity	1-3	145	29	0.409
	>3	5	0	
Education Status	Illiterate	124	29	0.053
	Secondary	16	0	
	Primary	10	0	
Socioeconomic Status	10000-15000	103	29	0.002
	16000-20000	30	0	
	21000-25000	37	0	

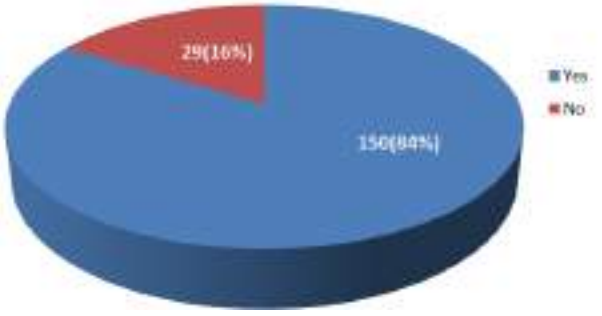

Figure No.1: Frequency of Malnutrition

DISCUSSION

Globally, according to Unicef, the prevalence of undernutrition in the particular community was found to be 16 percent underweight, 23 percent stunting and 7 percent wasting, according the 2016 survey undernutrition showed wasting 10.5percent, stunting 31.5 percent, and underweight 45percent.[9]

This demonstrates that the current investigation population is having a higher extent of stunting (chronic malnutrition) and underweight when contrasted with the public figures overall. In nutritional survey stated that interprovincial contrast was observed in the nutritional status of preschool children.[11] The study was done in two separate areas of the nation, at the north end and the south end has revealed that malnutrition was a medical issue of concern.[05,12] Southern Sri Lanka study revealed that 59% of the under-5 years old had some type of malnutrition. A greater part of them was wasted (42.7%). As per a similar report, the frequency of underweight and stunting among these children was 41.2 percent and 11.8 percent, respectively.[5] It has been accounted for in the war influenced Jaffna landmass the issue of malnutrition records to about 26 percent of the preschool children suffering from malnutritional problems. Along with 15.9 percent belonged to the poor socioeconomic group.[12]Therefore it is supported that the correlation of malnutrition with socio-economic conditions of the children. Amongst the socio-economic determinants of malnutrition of children, the education level of mothers proven to play a significant role. In different studies revealed that parental education was observed to be an important role in influencing the nutritional status of children. [13.14/15]

The current investigation likewise shows a significant association between parental education with the malnutrition health status of children, however not with the level of parents. In Bangladesh parent education, wealth status, drinking water facility, toilet facility, or even no of children to women showed a significant relation with the malnutrition of children.[10]

CONCLUSION

It is to be concluded that the prevalence of maternal and child under-nutrition is high in both communities although higher in rural communities. Efforts at reducing the vicious cycle of under-nutrition among mothers and children should concentrate on addressing risk factors specific to each community. Males were more commonly affected as compared to females. However, a larger prospective randomized study comparing the relationship between malnourished children and malnourished mothers will be needed. Further, more controlled prospective studies are necessary to compare the two treatment modalities to establish clinical protocols.

Author's Contribution:

Concept & Design of Study:	Nazia Faraz Shaikh
Drafting:	Delijan Mugheri, Shaista Laghari
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Revisiting Critically:	Nazia Faraz Shaikh, Delijan Mugheri
Final Approval of version:	Nazia Faraz Shaikh

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Original Article

Study to Determine the Indications and Frequency of Elective and Emergency Caesarean Section in A Tertiary Care Hospital

Elective and Emergency C- Section

Nargis Taj[1], Fouzia Jan[1], Ghazala Taj[1], Fouzia Anwar[1], Mohammad Hashim Mengal[2] and Safia Taj[1]

ABSTRACT

Objective: The objective of the analysis was to determine the frequency of elective and urgent cesarean sections as well as clinical indications.

Study Design: A Descriptive Cross-Sectional Study

Place and Duration of Study: This study was conducted at the Obstetrics and Gynecology Department unit III of Bolan Medical Complex Hospital Quetta for one-year duration from May 2019 to May 2020.

Materials and Methods: The study included consecutive females who gave birth throughout the study duration in the hospital. There were 750 patients in total who gave birth in the hospital. The basic demographics and mode of delivery of patients undergoing elective and emergency cesarean section were documented. The clinical signs of surgery were also documented.

Results: There were 750 births in the analyzed period. Of the 750, 190 were cesarean births, the rest were natural births. The frequency of cesarean sections was 25.33 per 100 deliveries. Of these, 81.05% (154) was an emergency cesarean section, 18.94% (36) was an elective cesarean section. Considering that the age of mothers of patients who have undergone cesarean section ranges from 18 to 45 years; 25% were under the age of 20, 60% were between 20 and 30 years of age, 13% were between 30 and 40 years of age and 2% were over 40 years of age. The most common pointers for C-section were failure to progress/ obstructive labour 18.80 % (n=29), foetal distress 20.1% (n=31), breech presentation 8.40% (n=13), previous caesarean section 15.0% (n=40), failed induction 6.50% (n=110), cephalo-pelvic disproportion 3.90 % (n=6) and pregnancy induced hypertension (PIH) 3.90% (n=6)

Conclusion: The cesarean section frequency was only somewhat advanced than endorsed by the WHO. Maximum of the cesarean sections were emergency cesarean sections.

Key Words: Cesarean Section, Frequency, Emergency, Elective, Indications.

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INTRODUCTION

The increase in the number of cesarean sections worldwide is the maximum discussed matters in maternity hospitals [1]. C. Section is a major operating method and, alike any surgery, it conveys a substantial jeopardy of mortality and morbidity [2-3]. Guideline for cesarean delivery should be developed and implemented and used only for clearly defined indications.

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Caesarean section is considered by many obstetricians to be a fairly simple, safe, effective, and psychologically well endured technique, far better than secondary interferences such as emergency or vacuum cesarean delivery, but there is the contradictory school of thought as well [4-5]. Therefore, a cesarean section is a matter of professional discussion[6]. There is also controversy about the rates of cesarean section. The comparative profits of lower or higher proportion of C-section are also controversial. Currently, C-section ratio is about 16–27% of all births in industrialized countries, and there is < 1: 10,000 maternal mortality [7].

The World health organization says that if the rate is higher than 10-15%, there are no further benefits of health related with a C-section [8-9]. The mother's request has an important role in caesarean section in established countries but in under developed countries; C-section rarely performed at her mother's request due to a lack of knowledge and comfort. Although the frequency of cesarean sections has increased in the preceding era, the main clinical signs are not changed, namely induction failure, fetal distress / previous cesarean section, and breech presentation [10-11].

It is difficult to estimate the number of cesarean sections as most births in Pakistan are done at home. Only complex cases or people with access to health centers benefit from this solution. For this reason, the frequency of emergency caesarean sections is much higher than in the case of elective C-section [12].

This analysis was held to govern the incidence of cesarean sections in our society and to analyze the indications. The study will also benefit to recognize factors that need to be discussed to reduce maternal mortality.

MATERIALS AND METHODS

This Descriptive Cross-Sectional Study held in the Obstetrics and Gynecology Department of Bolan Medical Hospital Quetta for one-year duration from May 2019 to May 2020.

The study included consecutive females who gave birth throughout the study duration in the hospital. There were 750 patients in total who gave birth in the hospital. The basic demographics and mode of delivery of patients undergoing elective and emergency cesarean section were documented. The clinical signs of surgery were also documented.

750 total patients received different treatment options. The analysis also comprised all of emergency C-sections that were specified during this time. The detailed proforma was supplemented with information about the mother's age, registered patient number, emergency or elective caesarean section in patients indicated for caesarean section. Elective caesarean section was classified as non-urgent and the decision was made before the onset of delivery. Emergency C-section is defined as a sudden maternal emergency or fetal distress, pre-eclampsia or arrested labor.

There are clinical indications for elective and urgent caesarean section. For more than one indicator, the three most important indicators are included for data analysis. The gestation period at the time of gravidity, presentation, obstetric and parity background was also recorded. Patients with more than one or less than five pregnancies were grouped as the multigravida and those with five or more pregnancies were grouped as the grand multigravida.

SPSS version 20.0 was applied for data analysis. The cesarean section proportion was determined as the number of cesarean deliveries per one-hundred deliveries. The fraction of emergency and elective cesarean sections was calculated. The cesarean section rates for each indication were calculated as the number of cesarean sections per 100 cesarean sections.

RESULTS

There were 750 births in the analyzed period. Of the 750, 190 were cesarean births, the rest were natural births. The frequency of cesarean sections was 25.33 per 100 deliveries. Of these, 81.05% (154) was an emergency cesarean section, 18.94% (36) was an elective cesarean section. Considering that the age of mothers of patients who have undergone cesarean section ranges from 18 to 45 years; 25% were under the age of 20, 60% were between 20 and 30 years of age, 13% were between 30 and 40 years of age and 2% were over 40 years of age.

The pregnancy and the duration of pregnancy during surgery were presented in Table-1.

Table No.1: Patients by gravidity and period of gestation

Gravidity	Emergency C-Section n=154 (%)	Elective C-Section n=36 (%)	Total n=190 (%)
Primigravida	56 (36.4%)	4 (11.1%)	60 (31.6%)
Multigravida	61 (39.6%)	17 (47.2%)	78 (41.1%)
Grand Multi Gravida	37 (24.0%)	15 (41.7%)	52 (27.4%)
Period of gestation			
34 or less Week	10 (6.5%)	4 (11.1%)	14 (7.4%)
35–38 Week	23 (14.9%)	7 (19.4%)	30 (15.8%)
39–42 Week	120 (77.9%)	24 (66.7%)	144 (75.8%)
More than 42 Week	1 (0.6%)	1 (2.8%)	2 (1.1%)

The clinical signs for elective C-section are presented in Table-2, and for emergency C-section in Table-3.

The most common pointers for C-sections were failure to progress/ obstructive labour 18.80 % (n=29), foetal distress 20.1% (n=31), breech presentation 8.40% (n=13), previous caesarean section 15.0% (n=40), failed induction 6.50% (n=110), cephalo-pelvic disproportion 3.90 % (n=6) and pregnancy induced hypertension (PIH) 3.90% (n=6).

Table No.2: Indications for elective caesarean section (n=36)

Indications for Elective Caesarean Section	**n**	**%**
Marked Oligohydromnios	5	13.90%
Previous Caesarean Section(s)	15	41.70%
Pregnancy Induced Hypertension	4	11.10%
Cephalo Pelvic Disproportion	5	13.90%
Twins with some complication	3	8.30%
Breech Presentation	3	8.30%
Maternal Wish (with bilateral tubal ligation)	1	2.80%
Bad Obstetrical History	3	8.30%
Miscellaneous	2	5.60%
Placenta Praevia	1	2.80%

Table No.3: Indications for emergency caesarean section (n=154)

Indications for Emergency Caesarean Section	n	%
Obstructed Labour/Failure to progress	29	18.80%
Foetal Distress	31	20.10%
Breech Presentation	13	8.40%
Previous Caesarean Section (s)	12	7.80%
Antepartum Haemorrhage	9	5.80%
Failed Induction	10	6.50%
Transverse lie	7	4.50%
Primary Dysfunctional Labour	8	5.20%
Miscellaneous	8	5.20%
Cephalo Pelvic Disproportion	6	3.90%
Twin and first Breech	3	1.90%
Cord Prolapse	3	1.90%
Pregnancy Induced Hypertension/eclampsia	6	3.90%

DISCUSSION

The frequency of cesarean sections in the analyzed period was 25.33%. This study found a higher rate than the WHO recommended Caesarean section should be 10-15%. However, Bolan Medical Complex Hospital, a tertiary care hospital, deals with more complex cases, as evidenced by more urgent caesarean sections. Therefore, in a region with hospitals, the actual caesarean section rate is much lesser [13]. This is partially because of deficiency of services and a deficiency of knowledge or care in the prenatal area. This contrasts with research in established regions and regions with improved health conditions. In June 2016, the WHO concluded that there is no experimental evidence for the recommended ratio of C-section as it is a controversial issue. Currently, world health organization recommends a caesarean section only when it is necessary [14].

Primigravida's are more at risk, so C-sections is more common amongst them. However, in our study, the rate of cesarean section was high in multigravida women (41.1%). This is probably because females in Pakistan get pregnant many times. This discovery agrees with the research around us [15]. The foremost indicator for cesarean section was fetal distress. Fetal distress is diagnosed by monitoring the load of the fetal heart and meconium. This is because of very innovative equipment's and technology available recently in some rural areas (e.g., Ultrasound). Fetal distress has constantly been the chief significant medical signs for cesarean section [16-17].

The 2nd maximum common indication in this study was obstructed labor (18.80%); In Pakistan, inadequate management of midwives is a common problem due to careless use of oxytocin drugs or unnecessary prostaglandin induction without prior evaluation [18].

A previous cesarean section is an important reason for a cesarean section; Therefore, after previous cesarean section, one should try vaginal delivery to control the increase in your cesarean section. Successful vaginal delivery afterward single C-section in a large population of multiparous women was not related with an augmented jeopardy of maternal complications compared to repeat caesarean section [19].

In this study, approximately 8.4% of cesarean operations were performed due to breech presentation. Breech presentation is related with increased mortality rate among mothers and disease, regardless of the course of delivery, due to fetal abnormalities and preterm delivery. However, if vaginal delivery is well chosen, vaginal delivery ensuring term delivery does not upsurge mortality and morbidity. The number of breech cesarean sections has now increased as most obstetricians find trying to deliver a child safer and easier. This led to an increase in the number of planned breech cesarean sections as revealed in our analysis. Cephalopelvic disparity was the 6th most communal reason; though, it was the 2nd most communal source of a planned cesarean section. The high percentage of cesarean sections diagnosed with prenatal cephalopelvic imbalance suggests a more aggressive approach leading to increased frequency of cesarean sections [20-21].

In this study, pregnancy-related hypertension was reported in 3.90% of cesarean sections. Good prenatal care can spot these problems sooner, and prompt treatment can help prevent complications. Pregnancy-induced hypertension increases the jeopardy of cesarean section and premature delivery [22].

Around 18.80% of cesarean deliveries were caused by failed progression of labor. It was lower than other surveys in Pakistan. The decision to perform a cesarean section seems to be a department strategy. The caesarean section safety invigorated obstetricians to prefer C-section. Antepartum hemorrhage (APH) was a significant signal for an emergency C-section (5.80%). A C-section is an imperative life-saving method in APH because it is mainly associated with the placenta praevia and carries a particular risk for both the baby and the mother if it is delayed [23-24].

In our analysis, all cesarean sections were accomplished with special medical indications. Females in Pakistan do not accept C-section as their primary method of delivery. Of the 190 cases where the mother requested a Caesarean section, only three were reported; However, other procedures such as bilateral tubal ligation were observed in these cases, and that was the cause of this case[25]. This condition is very diverse in advanced states, where females require elective C-section as the primary method of delivery.

There is presently no suggestion that elective caesarean section is beneficial than vaginal delivery. In fact, most of the evidence suggests that a cesarean section carries

a much greater risk than childbirth. Therefore, maternity care providers should continue to recommend vaginal delivery as the optimal method of delivery [26].

CONCLUSION

The cesarean section rate was only somewhat greater than the recommendation of WHO. Most of them are emergency caesarean section operations. The main reason for this is that tertiary hospitals often receive complex cases. Most cesarean sections in Pakistan are performed for a specific clinical indication.

Author's Contribution:

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Original Article

Pancytopenia in Balochistan Population

Zohra Samreen[1], Muhammad Idrees Achakzai[2], Iftakhar ul Haq Tareen[3], Bezan Baloch[4], Ashiq Hussain[5] and Muhammad Kamran Taj[6]

ABSTRACT

Objective: Pancytopenia is a common hematological parameter detected in Hospital. It is important to study pancytopenia for better management of patient.

Study Design: Cross Sectional study

Place and Duration of Study: This study was conducted at the Department of Medicine Bolan Medical Complex Hospital Quetta and this study was conducted from November, 2017 till February, 2019.

Materials and Methods: Patients presenting to medicine outpatient department of Bolan Medical Complex Hospital fulfilling the inclusion criteria were selected followed by their detailed history and physical examination. Informed consent was taken from all the patients.

Results: Pancytopenia represents a wide range of age groups and most pancytopenia is purely of bone marrow dysfunction origin. Overall, 65% male subjects were observed with pancytopenia as compared to 35% female patients. The results also showed that patients with age 21-40 were highly affected by pancytopenia (45%) followed by > 41 years (40%) and < 20 years (15%). Moreover, pancytopenia was more common in underweight patients (78%) followed by normal weight (18%), overweight (3%) and obese (1%). It was seen in study that illiterate patients presented more with pancytopenia (64%) than literate (36%). While in case of socioeconomic status pancytopenia was seen to be more frequent in upper middle class (55%) followed by lower middle class (30%) and lower class (15%).

Conclusion: A comprehensive clinical history and investigations give very useful information in the entire workup of patients with pancytopenia for understanding the disease processes, planning extra investigations, management, and ascertain the cause.

Key Words: Pancytopenia, Bone, Marrow, Balochistan

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INTRODUCTION

Pancytopenia is defined as a reduction in all three types of cellular components in peripheral blood and this involves anaemia, neutropenia, and thrombocytopenia.[1] It is an important clinico-hematological entity encountered in our day to day clinical practice.[2] There are varying trends in its clinical pattern, hematological change, treatment modalities and outcome.[3]

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Pancytopenia is a manifestation of many serious & life threatening diseases with an extensive differential diagnosis. It should be suspected on clinical grounds when a patient present with pallor, prolonged fever and a tendency to bleed. The etiology of pancytopenia varies in different populations depending on the differences in age patterns, nutritional status, climate and the prevalence of infections.[4]

It is not a disease entity but a triad of findings that may result from a number of disease processes - primarily or secondarily involving the bone marrow.[5] The bone marrow is the largest and most widely distributed organ in the body. It is the principal site for blood cell formation. The spectrum of disorders primarily and secondarily affecting the bone marrow may manifest with peripheral pancytopenia.[6] Pancytopenia cause is diagnosed by bone marrow aspiration and it is extremely helpful in the evaluation of pancytopenia.[7] Common etiologies of pancytopenia are malaria (29.44%) followed by tuberculosis (17.22%), leukemia (16.67%), aplastic anaemia (13.33%) and hepatitis (12.22%).[8]

The severity of pancytopenia and the underlying pathology determine the management and prognosis of the patients.[9] In Quetta (Balochistan), the causes of Pancytopenia are not well defined and pancytopenia

often creates a diagnostic dilemma for the treating physician. Rational of this study was to check the prevalence of pancytopenia, thus prompt therapy can be provided to patients after diagnosis. Thereby, this data will help in planning the diagnostic and therapeutic approach in patients with pancytopenia.

MATERIALS AND METHODS

Study Design: Cross sectional study
Setting: Department of Medicine Unit- I, Bolan Medical Complex Hospital Quetta
Sample Size: Total sample size calculated was 100 with confidence level of 95%, level of significance 5% and power of test 80%.
Sampling Technique:
Non probability consecutive sampling
Sample Selection
Inclusion criteria:

1. Sex: both males and females
2. Pancytopenia (as defined in operational definition)
3. Newly diagnosed pancytopenia i.e within a week time after clinical presentation.

Exclusion criteria:

1. Patient on cancer chemotherapy
2. Patient is taking other cytotoxic/anti metabolic drugs
3. Patient who is taking radiotherapy

They all were confounders as they suppress the bone marrow thus causing pancytopenia and if included in the study would have caused bias.
Age selection: All age group patients were included in study.
Educational Status in Study: A person able to write and read urdu were considered as literate. People unable to read and write urdu were considered as illiterate.
Body Mass Index (BMI): Patients with BMI of 16 to 18.5 were considered as underweight, 18.5 to 25 normal weight, 25 to 30 overweight and greater than 35 as obese.
Economical Status: Patients having monthly family income of less than 15000 pk were categorized as lower class, 15000to 30000 pk as lower middle class, greater than 30000 as upper middle class
Data Collection Procedure: Patients presenting to medicine outpatient department of Bolan Medical Complex Hospital fulfilling the inclusion criteria were selected followed by their detailed history and physical examination. Informed consent was taken from all the patients.
Data Analysis Procedure: The data was entered and analyzed on SPSS version 17 with 95% confidence level and 5% level of significance. Frequencies, percentages and Mean ± SD were calculated for gender, age, BMI, economical status, educational status. Effect modifier like age, gender, educational status and economic status were addressed through stratification and applying chi square test and P < than 0.05 was considered statistically significant.

RESULTS

In the present study 100 patients with pancytopenia were included. Among these 65 (65%) were males and 35 (35%) females as shown in Fig-1.

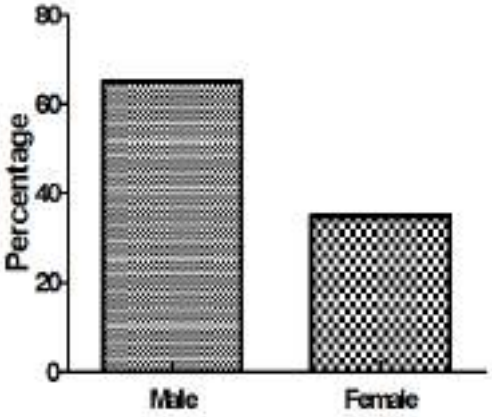

Figure No.1: Pancytopenia in relation to gender

The results showed that the most commonly affected age group of patients was 21-40 years (45%) followed by >41 years (40%) and <20 years (15%) as shown in Fig-2.

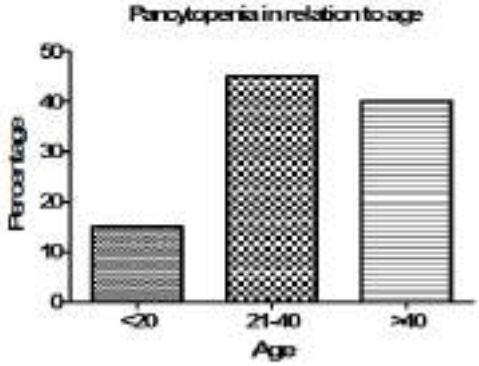

Figure No.2: Pancytopenia in relation to Age

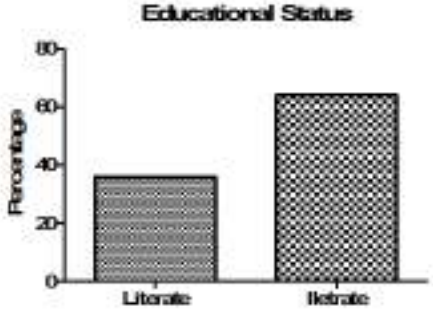

Figure No.3: Pancytopenia in relation to education status

In 100 patients it was seen that patients from a lower socioeconomic status presented more with

pancytopenia. Also, a significant difference was observed in the distribution of patients by education level with 64% patients were illiterate and 36% literate. This emphasizes the importance of literacy by showing that pancytopenia is more common in uneducated than educated persons as shown in Fig-3.

The chance of developing pancytopenia increases with decreasing body mass index (BMI), but there is strong evidence that at any given BMI the risk of pancytopenia is markedly high in low socioeconomic status. In our study it was seen that patients with low BMI presented more with pancytopenia, revealing pancytopenia in 78% of underweight, 18% of normal weight, 3% of overweight and 1% of obese patients as shown in Fig-4.

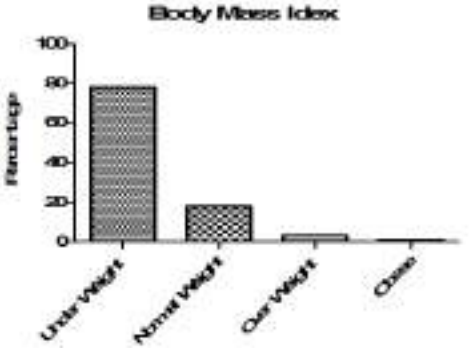

Figure No.4: Pancytopenia in relation to BMI

There is concern among public health professionals that the current economic downturn, initiated by the financial crisis could precipitate the incidence of pancytopenia. But in our study it was seen more in the upper middle class with 55 % of patients belonging to this class, 30% belonging to lower middle class and 15% belonging to lower class as shown in Fig-5.

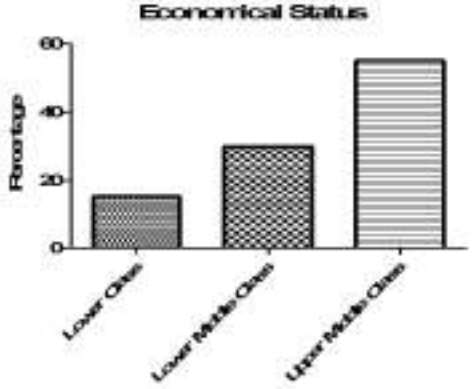

Figure No.5: Pancytopenia in relation to economical status

DISCUSSION

Pancytopenia is a clinical condition in which there is reduction in the number of the RBC, WBC and platelets[10]. As a large proportion of causes for pancytopenia are treatable and reversible, accurate diagnoses and timely intervention maybe lifesaving and will certainly have impact on the morbidity and mortality in these vulnerable patients [11]. Knowing the exact etiology is thus important for specific and timely treatment and for prognostication [12]. As the etiologies of pancytopenia are varied, so is the prognosis [13]. General physicians who are not hematologists are unlikely to be as well versed in the specific constellation of findings that characterize individual hematologic entities[14]. Stringent diagnostic criteria and a general conceptual framework for ascertaining the cause of pancytopenia is therefore very valuable and a demand of time. Overall, 65% male subjects were observed with pancytopenia as compared to 35% female patients. The same result was reported by Azaad et al[11] that incidence of pancytopenia is slightly higher in male populations[15-16]. The results also showed that patients with age 21-40 were highly affected by pancytopenia (45%) followed by > 41 years (40%) and < 20 years (15%) similar findings are reported by Tareen[8].

Moreover, pancytopenia was more common in underweight patients (78%) followed by normal weight (18%), overweight (3%) and obese (1%). It was seen in study that illiterate patients presented more with pancytopenia (64%) than literate (36%). While in case of socioeconomic status pancytopenia was seen to be more frequent in upper middle class (55%) followed by lower middle class (30%) and lower class (15%), similar finding was observed by Dadhy et al [7].

CONCLUSION

Pancytopenia is a common entity. However, it has received inadequate attention in the Indian subcontinent. A study of pancytopenia using easily available diagnostic techniques is therefore important. Age and sex distribution of patients with pancytopenia in this study was consistent with the findings in other studies. However, in view of a wide array of etiological factors, pancytopenia continues to be a challenge for hematologists.

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Final Approval of version:	Zohra Samreen and Muhammad Idrees Achakzai

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

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Original Article

Electrolytes Derangements with Hepatitis C

Correlation of Electrolytes Derangements with Hepatitis C induced Liver Cirrhosis Severity Indices

Muhammad Saleem Akhter[1], Muhammad Arif Mahmood[1], Hooria Bhatti[3], Muhammad Waqar Saleem[4], Ahsanullah M Mirbahar[2] and Junaid Riaz[1]

ABSTRACT

Objective: To find Correlation of Electrolytes Derangements with Hepatitis C induced Liver Cirrhosis Severity Indices.

Study Design: A cross-sectional study

Place and Duration of Study: This study was conducted at the Study was conducted at the department of medicine, Nishtar Medical University/Hospital, Multan, from April 2020 to Dec 2020.

Materials and Methods: We studied on 54 HCV infected cirrhotic patients confirmed by presence of Anti-HCV antibodies/ HCV RNA by PCR in their serum. MELD Score, Child-Pugh Score and Child-Pugh Class were calculated. Routine serum electrolytes were measured and electrolytes abnormalities were assessed for any significant relationship with MELD Score, Child-Pugh Score and Child-Pugh Class.

Results: Linear curve estimation analysis of Child Pugh score with sodium, potassium, calcium, phosphate and magnesium showed a statistically significant relationship ($p<0.05$) with Pearson correlation coefficient (r) 0.391, 0.125, 0.460, 0.370 and 0.087 respectively. Linear curve estimation analysis of MELD score with sodium, potassium, calcium, phosphate and magnesium showed a statistically significant relationship ($p<0.05$) with Pearson correlation coefficient (r) 0.430, 0.284, 0.129, 0.296, and 0.012 respectively. Chi Square test indicated a statistically significant association between sodium, potassium, calcium, phosphate and magnesium with Child Pugh class ($p<0.05$).

Conclusion: Our data suggest moderate to strong relationship between various electrolytes abnormalities with MELD Score, Child-Pugh Score and Child-Pugh Class in Hepatitis C induced liver Cirrhosis.

Key Words: Hepatitis C induced cirrhosis, Electrolytes Abnormalities, MELD Score, Child-Pugh Score, and Child-Pugh Class.

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INTRODUCTION

Chronic viral hepatitis C infection has more prevalence in developing countries with low to limited national per capita income [(1)]. Trickey et alreported in 2017 that, the infection of hepatitis C is more prevalent in Egyptianthan in Pakistani population [(2)].

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According to this survey, 9 million Pakistanis are infected with hepatitis C which are about 4.9% of country's population[2]. Most commonly we encounter hepatitis C virus which, in most cases, progresses to chronic hepatitis disease/cirrhosis[(3,4)].The progression can be slow or rapid, consistent or inconsistent depending upon the degree of active tissue inflammation and damage[5]. It usually progresses gradually over many years[6]. Hepatitis C virus does not cause cell death directly but provoke immune inflammatory response such as chronic injury to hepatocytes causes release of IL-2 and various other cytokines to stimulate Ito cells and fibroblasts to start synthesizing collagen type-I especially that result in progressive fibrosis, hepatocellular damage and cell death[7]. Cirrhosis and its associated complications are important cause of morbidity and mortality. Chronic liver disease starts with a non-specific symptoms labelled as compensated liver cirrhosis until the development of complications like ascites, jaundice and encephalopathy when it is called as decompensated liver cirrhosis. Different parameters are used for the grading of liver cirrhosis which are grouped as MELD

Score, Child-Pugh Score and Child-Pugh Class. Child-Pugh is simple and convenient prognostic measure to judge prognosis of liver cirrhosis. In Child-Pugh Class A& B, one year survival is about 70% and Child-Pugh Class C survival is poor. There is a connection between liver disease and Electrolyte imbalance and this imbalance has been observed in many studies[8]. Major electrolytes imbalance associated with cirrhosis is sodium concentration, and hyponatremia is commonly observed in30-48% cases of cirrhosisin different studies[9,10,11]. Chronic hyponatremia is labelled when sodium concentration is below 130 mEq/L and is present in about 22% of patients of cirrhosis[12]. These patients are usually asymptomatic when sodium concentration is above 120 mEq/L[9]. The hyponatremia is as a result of excessive water retention in comparison to sodium and other solutes. Resultant less amount of water excreted in urine as compared to water ingested leads to dilutional hyponatremia. Hyponatremic patients have less survival as compared to the patients who do not have hyponatremia[13]. According to different studies, hyponatremia is an important prognostic factor in cirrhotic patients and its weightage key factor in MELD score[14]. On other hand hypernatremia is also associated with higher mortality in cirrhotic, although it is uncommon. Increased renin release by kidney leads to secondary hyperaldosteronism and in cirrhotic patient's comparative solute free water retention causes dilutional hyponatremia. Hepatic dysfunction leads to potassium depletion to extent that potassium supplements and correction should be considered in the management. At any stage of liver disease, electrolyte imbalance can occur but cirrhosis is main culprit. Cirrhosis and hepatitis are the cause of serum and urinary electrolyte imbalance[15]. The aim of our study was to observe correlation of electrolytes derangements with hepatitis C induced liver cirrhosis severity indices.

MATERIALS AND METHODS

This study was carried out at department of medicine, Nishtar Medical University/Hospital, Multan. Before data collection we shared protocol of our study to all participants for the clarification of patient's concepts about our study, then Informed consent was obtained from those patients who were willing for participation in this research. This study was carried out from 28 April 2020 to 29 Dec 2020. Only infected with hepatitis C patients having chronic history were identified among the patients who were visiting medical ward and OPD of Nishtar hospital, Multan, and they were positive for HCV antibodies/detected positive HCV RNA by Polymerase Chain Reaction (PCR). Patient who had history of co-infection i.e; HBV/HCV and HCV/HIV and known patient of liver cancer were not included in the study. Total 54 patients were engaged over this period. Quantitative determination of the baseline viral load obtained by PCR and biomarkers (liver function tests (LFTs), albumin, bilirubin, prothrombin time and Complete Blood Count (CBC) were done. MELD Score, Child-Pugh Score and Child-Pugh Class were calculated. Routine serum electrolytes were measured and electrolytes abnormalities were assessed for any significant relationship with MELD Score, Child-Pugh Score and Child-Pugh Class.

RESULTS

We studied 54 patients, out of which 32(59.3%) were males and 22(40.7%) females. Twenty (37%) were government employee, 18(33.4%) laborer and 16 (29.6%) housewives by profession. Thirty (55.6%) were of Child-Pugh class B, 18(33.4%) were in class C. Patients with normal serum sodium were 36 (66.7%), hyponatremia 16 (29.6%) and hypernatremia 2 (3.7%). There was normal potassium in 36(66.7%), hypokalemia in 8 (14.8%), hyperkalemia in 10 (18.5%) subjects. Patients with normal serum calcium were 10(18.5%) and hypocalcemic were 44(81.5%). Subjects with normal serum phosphate levels were 42(77.8%) and hypophosphatemia were 12(22.2%). Patients with normal serum magnesium 44 (81.5%), hypomagnesemia 6 (11.1%) and hypermagnesemia were observed in 4 (7.4%). Electrolytes abnormalities distribution is given in table no.1.

Table No.1: Distribution of electrolytes abnormalities among study cases

Electrolytes	N/Percentage	p value*
Sodium 1. Normal 2. Hyponatremia 3. Hypernatremia	 36 (66.7%) 16 (29.6%) 2 (3.7%)	 0.020
Potassium 1. Normal potassium 2. Hypokalemia 3. Hyperkalemia	 36 (66.7%) 8 (14.8%) 10 (18.5%)	 0.012
Calcium 1. Normal calcium 2. Hypocalcemia 3. Hypercalcemia	 10 (18.5%) 44 (81.5%) NIL (0%)	 0.023
Phosphate 1. Normal phosphate 2. Hypophosphatemia 3. Hyperphosphatemia	 42 (77.8%) 12 (22.2%) NIL (0%)	 0.010
Magnesium 1. Normal magnesium 2. Hypomagnesemia 3. Hypermagnesemia	 44 (81.5%) 6 (11.1%) 4 (7.4%)	 0.040

*Chi Square Test results with Child Pugh Class and various electrolytes levels.

Table No.2: Descriptive statistics of our study population.

Variables	Mean	Std. Deviation
Age	41.33	11.11
Height	168.40	5.51
Weight	72.03	25.09
CHILD-Pough SCORE	9.29	1.21
MELD Score	15.52	3.03
Hb	9.51	1.43
T. Bilirubin	1.51	0.28
AST	58.59	56.02
ALT	82.44	49.55
ALP	160.08	93.25

Linear curve estimation analysis of Child Pugh score with sodium, potassium, calcium, phosphate and magnesium showed a statistically significant relationship ($p<0.05$) with Pearson correlation coefficient (r) 0.391, 0.125, 0.460, 0.370 and 0.087 respectively.

Linear curve estimation analysis of MELD score with sodium, potassium, calcium, phosphate and magnesium showed a statistically significant relationship ($p<0.05$) with Pearson correlation coefficient (r) 0.430, 0.284, 0.129, 0.296, and 0.012 respectively.

Table No.3: Pearson correlation coefficients (r) values of Child Pugh score and MELD Score with various electrolytes

Electrolytes	MELD Score (r) value	Child-Pugh Score (r) value
Sodium	0.430	0.391
Potassium	0.284	0.125
Calcium	0.129	0.460
Phosphate	0.296	0.370
Magnesium	0.012	0.087

*Chi Square test indicated a statistically significant association between sodium, potassium, calcium, phosphate and magnesium with Child Pugh class ($p<0.05$)

DISCUSSION

Chronic viral infection causes multiple waves of inflammation and tissue repair which involves deposition of extracellular matrix resulting in scarring or progressive fibrosis over time and ultimately liver cirrhosis occurs[6]. Most commonly we encounter hepatitis C virus which, in most cases, progresses to chronic hepatitis disease/cirrhosis. Chronic liver disease starts with a non-specific symptoms labelled as compensated liver cirrhosis until the development of complications like ascites, jaundice and encephalopathy when it is called as decompensated liver cirrhosis. Cirrhosis and its associated complications are important cause of morbidity and mortality. Different parameters are used for the grading of liver cirrhosis which are grouped as MELD Score, Child-Pugh Score and Child-Pugh Class. Child-Pugh is simple and convenient prognostic measure to judge prognosis of liver cirrhosis. In Child-Pugh Class A & B, one-year survival is about 70% and Child-Pugh Class C survival is poor [(16)]. Actually, liver failure, in most cases, develops gradually over the years. One of the feared complication of cirrhosis is electrolytes abnormalities. Kim et al. showed that 3.9% of the hyponatremic patients were likely to develop hepatorenal syndrome and its associated complications which are one of the most deadly outcomes associated with cirrhotic patients[9]. In cirrhotic patients there is dilutional type of hyponatremia. Fluid intake restriction half or less than output can correct false hyponatremia. Severity of hepatic disease also result in hypokalemia. Major electrolytes imbalance associated with cirrhosis is sodium concentration and hyponatremia is commonly observed in more than 57% of hospitalized cirrhotic patients[17]. Chronic hyponatremia is labelled when sodium concentration is below 130 mEq/L and is present in about 22% of patients of cirrhosis[12]. The hyponatremia is as a result of excessive water retention in comparison to sodium and other solutes. Resultant less amount of water excreted in urine as compared to water ingested leads to dilutional hyponatremia. Hyponatremic patients have less survival as compared to the patients who do not have hyponatremia. According to different studies, hyponatremia resulted due to reduced solute-free water clearance was a prognostic factor in hyponatremic patients in cirrhosis when sodium was incorporated into the MELD score[13].

In our study 29.6% patients were hyponatremic. Borroni et al[11] reported same result 29.8%, while higher level of hyponatremia which may be due to different demographic and large study population are reported by Angeli[10] et al and Kim et al[9] that is 49.4% and 47.9%. While near to our finding 35% of hyponatremia in cirrhotic patients was also reported in Bangladesh by Mamun et al[14] which is also closed to our study results.

Hypokalemia was observed in 14.8% cases in our study. Ahmed et al[18] reported similar results 14% and Alam et al[19] also reported 18% which is near to our study result. Diet, GIT loss and diuretic treatment can change potassium levels. Cirrhotic patients without edema or ascites may have total low body potassium level in presence of normal serum potassium. Potassium supplementation should be given orally or intravenously.

Our study showed that linear curve estimation analysis of Child Pugh score with sodium, potassium, calcium, phosphate and magnesium showed a statistically significant relationship ($p<0.05$) with Pearson correlation coefficient (r) 0.391, 0.125, 0.460, 0.370 and 0.087 respectively. Linear curve estimation analysis of MELD score with sodium, potassium, calcium, phosphate and magnesium showed a statistically significant relationship ($p<0.05$) with Pearson correlation coefficient (r) 0.430, 0.284, 0.129, 0.296, and 0.012 respectively. Chi Square test indicated a statistically significant association between sodium, potassium, calcium, phosphate and magnesium with

Child Pugh class ($p<0.05$). Hence hyponatremia and hypokalemia needs to be corrected immediately and electrolytes should be kept in check. This can improve prognosis. Our study also reported same results which were demonstrated by Borroni et al[11], Ahmed et al[18] and Alam et al [(19)] about frequency of hyponatremia and development of various complications due to cirrhosis and its associated electrolytes derangements. We also recommend control other confounding factors for various electrolytes. Hepatic dysfunction leads to potassium depletion to the extent that potassium supplements are necessary. At any stage of liver disease, electrolyte imbalance can occur but cirrhosis is main culprit. Our data suggested moderate to strong relationship between various electrolytes abnormalities with MELD Score, Child-Pugh Score and Child-Pugh Class in Hepatitis C induced liver Cirrhosis. So, we recommend that Hepatitis C patients should be treated as early as possible and meanwhile their electrolyte should be kept in check to avoid any associated complication like arrhythmias, hypotension, peripheral edema and CVS complications.

CONCLUSION

Our data suggest moderate to strong relationship between various electrolytes abnormalities with MELD Score, Child-Pugh Score and Child-Pugh Class in Hepatitis C induced liver Cirrhosis.

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Original Article

Comparison between Ultrasound-Guided Transversus Abdominis Plane Block with Ilioinguinal or Iliohypogastric Nerve Block for Post-Operative Analgesia in Patients of Inguinal Hernia Repair

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ABSTRACT

Objective: To compare ultrasound guided transversus abdominis plane block with Ilioinguinal or iliohypogastric nerve block in terms of post-operative analgesia.

Study Design: Prospective, randomized single-blind study

Place and Duration of Study: This study was conducted at the department of anesthesia and intensive care of DG khan & Nishtar Hospital, Multan from April 2017 to April 2018.

Materials and Methods: Hospital local research and ethical committee approved the study protocols consent was taken after complete information of study. Allocation of the patients into groups was done by using lottery method. Patients were divided into two groups I and II. Main variables of the study are postoperative analgesia requirement, dose of diclofenac sodium and VAS score. SPSS software was used for data analysis.

Results: Mean duration of rescue analgesic requirement and dose of tablet diclofenac required per minutes of Group I was 322.05±21.87 minutes and 207.05±9.77 mg, respectively. While, the mean duration of rescue analgesic requirement and dose of tablet diclofenac required per minutes of Group II was 413.04±12.13 minutes and 175.28±9.71 mg, respectively. The difference was statistically significant.

Conclusion: We concluded that Ilioinguinal (IIH) and Iliohypogastric (IHN) nerve block reduced the rescue analgesic requirement as compare to ultrasound guided TAP block. Duration of post-operative analgesia is longer in IIIH/IHN block.

Key Words: TAP Block, Ilioinguinal block, Iliohypogastric block, inguinal hernia repair, Analgesia

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INTRODUCTION

Inguinal hernia repair is a common surgical procedure that can cause moderate to severe pain in post operative time[1]. Pain is an unpleasant feeling which may results poor outcome and late recovery to the daily activities and affecting about 43% of patients.

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Main purpose of pain management in post operative period is to minimize the dose of medication to avoid the side effects[2]. Many pharmacological and non pharmacological techniques are available to reduce pain after hernia repair. This technique includes peripheral local anaesthetic, topical analgesics, epidural injections and some non pharmacological pain therapies[3].

Block of regional nerve provides a greater degree of post operative pain reduction and facilitates the ambulation and early discharge from hospital[4]. Among the regional blocks Ilioinguinaland iliohypogastric nerve blocks are commonly used regional blocks. For pain management after herniorrhaphy incidence of failure of regional blocks found to be 30% in experienced hands due to blind techniques[5]. Use of ultrasonography for administration of regional blocks reduces the adverse events and complications[6]. By reducing the pain outcomes can be improved to a significant level. Analgesia to the parietal peritoneum and deep muscles of the anterior abdominal wall can be provided with transversus abdominis plane block which

is a rapidly expanding and novel technique following lower abdominal surgeries[7,8]. Due to its efficacy and easiness transverse abdominal plane block becoming popular day by day. Accuracy and success rate of TAP block can be improved by using ultrasound during its administration[9]. Few previous studies demonstrate the effectiveness of TAP block for post operative pain relief following inguinal hernia repair but no study give the conclusive results that ultrasound guided TAP block are superior than blind procedures[10]. This study will fulfill local reference gap regarding this topic and available literature.

MATERIALS AND METHODS

Study was randomized controlled trial conducted in the department of anesthesia and intensive care of DG Khan & Nishtar Hospital, Multan, from April 2017 to April 2018. Hospital local research and ethical committee approved the study protocols consent was taken after complete information of study. Adult patients of more than 18 years of age both genders ASA status I and II and who were scheduled for inguinal hernia repair were included in the study. Patients with BMI more than 35 kg/m2, pregnant woman, alcohol abuser, history of taking painkillers, infection at the injection site, poor coagulation profile and who were refused to give consent were excluded from the study. Patients were informed and trained about visual analogue score. Tab Alprazolam 0.25mg and ranitidine 150mg given before 2 hours of surgery orally. Standard monitoring was attached like ECG, pulse oximetry and non invasive blood pressure. Propofol 2mg per kg atracurium 0.5mg per kg was given intravenously. After three of oxygen ventilation a mixture of Isoflurane and oxygen was given through inhalation rout, mixture of nitrous oxide and Isoflurane was used for maintenance of anesthesia. TAP block or Ilioinguinal nerve block was given in respective group. Allocation of the patients into groups was done by using lottery method. Patients were divided into two groups I and II. Patients in group I were administered TAP block 0.75% ropivacainein dose of 3mg per kg, similarly patients in group II were administered IIN or IHN block with 0.75% ropivacaine. During administration of TAP block ultrasound probe was placed at the costal margin or on the lateral abdominal wall. Surgeon was allowed to perform surgery after completion of block. Neuromuscular blockade was nullified with glycopyrrolate and Neostigmine. Patients were extubated when they are fully conscious and breathing spontaneous. Immediately after surgery standard analgesic agents was given to all patients. If VAS score was more than 4 Tramadol 2 mg per kg was given intravenously. In case of persistent score was more than 4 diclofenac 75mg was given intravenous. Oral diclofenac 75mg was given after 4 hours. To prevent the post operative nausea and vomiting injection ondansetron 4 mg was given intravenously. Data analysis was done by using SPSS version 24. Mean and standard deviation were calculated and presented for numerical data like VAS score, duration of first analgesic requirement, age of patient, weight, and height and hemodynamic parameters. Qualitative data was presented as numbers and percentages like gender incidence of nausea vomiting and patients satisfaction. Probability value ≤ 0.05.

RESULTS

Eighty patients were included in this study. The patients were divided into two Groups as n=40 in Group I and n=40 in Group II. The mean age, height, weight and BMI of Group I was 29.47±2.54 years, 167.85±2.91 cm, 68.22±2.43 kg and 25.69±2.21 kg/m^2, respectively. While, the mean age, height, weight and BMI of Group II was 30.42±2.38 years, 168.81±2.69 cm, 67.55±2.24 kg and 26.24±2.72 kg/m^2, respectively. The difference was statistically insignificant (Table. I).

Table No.1: Showed mean of age, height, weight and BMI in both groups

Variables	Group I n=40	Group II n=40	P-value
Age (years)	29.47±2.54	30.42±2.38	0.089
Height (cm)	167.85±2.91	168.81±2.69	0.133
Weight (kg)	68.22±2.43	67.55±2.24	0.201
BMI (kg/m^2)	25.69±2.21	26.24±2.72	0.322

Table No.2: Showed the mean VAS at rest of both groups

VAS at rest	Group I n=40	Group II n=40	P-value
0 minute	0.58±0.22	0.56±0.21	0.761
30 minutes	0.68±0.32	0.63±0.28	0.507
60 minutes	0.98±0.51	0.99±0.55	0.949
90 minutes	0.93±0.43	1.05±0.32	0.185
2 hours	1.74±0.35	0.79±0.29	0.000
4 hours	1.89±0.22	0.83±0.33	0.000
6 hours	2.20±0.64	1.31±0.36	0.000
8 hours	3.62±0.78	1.97±0.22	0.000
10 hours	3.69±0.74	2.67±0.34	0.000
19 hours	3.79±0.46	3.64±0.21	0.041
24 hours	3.81±0.31	3.17±0.33	0.000

Table No.3: Showed mean duration of rescue & dose of tablets

Characteristics	Group I n=40	Group II n=40	P-value
Duration of rescue analgesic requirement (minutes)	322.05±21.87	413.04±12.13	0.000
Dose of tablets diclofenac required per patient (mg)	207.05±9.77	175.28±9.71	0.000

The mean VAS at rest of Group I at 0 minute, 30 minutes, 60 minutes, 90 minutes, 2 hours, 4 hours, 6 hours, 8 hours, 10 hours, 19 hours and 24 hours was 0.58±0.22, 0.68±0.32, 0.98±0.51, 0.93±0.43, 1.74±0.35, 1.89±0.22, 2.20±0.64, 3.62±0.78, 3.69±0.74, 3.79±0.46 and 3.81±0.31, respectively. While, the mean VAS at rest of Group II at 0 minute, 30 minutes, 60 minutes, 90 minutes, 2 hours, 4 hours, 6 hours, 8 hours, 10 hours, 19 hours and 24 hours was 0.56±0.21, 0.63±0.28, 0.99±0.55, 1.05±0.32, 0.79±0.29, 0.83±0.33, 1.31±0.36, 1.97±0.22, 2.67±0.34, 3.64±0.21 and 3.17±0.33, respectively. The difference reached to statistically significant for 2 hours to 24 hours, as $p \leq 0.05$ (Table. 2). The mean duration of rescue analgesic requirement and dose of tablet diclofenac required per minutes of Group I was 322.05±21.87 minutes and 207.05±9.77 mg, respectively. While, the mean duration of rescue analgesic requirement and dose of tablet diclofenac required per minutes of Group II was 413.04±12.13 minutes and 175.28±9.71 mg, respectively. The difference was statistically significant (Table. 3).

DISCUSSION

A study was conducted by Peterson et al[11] on comparison of TAP block an Ilioinguinal block in terms of duration of analgesia after hernia repair and reported that there was not markable difference in morphine consumption within 24 hours of post operative period. Both Ilioinguinal block and TAP block have almost similar duration of analgesia and complication rate. Results of this study are comparable with our study conclusion.

Another study was conducted by Avelineet al[12]he included 273 patients in a study that were undergoing for inguinal hernia repair. He compared ultrasound guided TAP block and blind IHN block. He reported that morphine consumption after surgery was lower in TAP block group within 24 hours immediately after surgery TAP block was ultrasound guided in both studies and IHN block was blind in both groups.

Another study was conducted Kamal Ket al[13] and reported that ultrasound guided IHN block reduce the rescue analgesia requirement as compared to ultrasound guided TAP block. Duration of rescue analgesia was 319.8±115.2 minutes in TAP block and 408±116.4 minutes in IHN group p value was 0.005 which is a significant value. In TAP block rout 23.33% patients require tramadol in first 4 hours and in IHN group 6.67 % patients require Tramadol in first 4 hours. No patients require diclofenac intravenously in both groups.

Another study was conducted by Sujatha C et al[14] in 2017 on comparison of TAP block and Ilioinguinal block and iliohypogastric block and stated that ultrasound guided TAP block provides longer duration of analgesic effect as compare to Ilioinguinal and iliohypogastric block. But in complications view both techniques are safe (no complications observed in both groups). Results of this study are comparable with our results. Mean duration of analgesia was 5.900±1.881 hours in TAP block and 3.766 ± 1.754 hours in IIIH group.

In a study Yu et al[15] compared TAP block with infiltration of local anesthetic into the incision site and reported that infiltration technique is effective equally in short term analgesic effects but it is stated that TAP block provides longer duration of postoperative analgesia. Its long lasting effect prolongs to 24 hours after surgical management of any major problem. In our study we used local anesthetic in IIIH block and superiority of IIIH block was remained constant for long term analgesia. Results of this study were also comparable with our results.

Another study on this topic was conducted by Frassanito et al[16]and reported that patients in TAP block group have significantly lower VAS score after surgery immediately and in long term outcomes as compare to IIIH block. Not only in normal position but also at coughing and at the time of discharge from hospital VAS score was lower in TAP group and patients were satisfied in better terms. He concluded in his study and demonstrated that analgesia requirement is two times in IIIH group as compared TAP block group.

A similar study was conducted by Mohamed MH et al[17] in 2015 on this topic but he compared both groups' n pediatric patients and reported conclusion opposite to our conclusion. He observed that IIIH group is superior as compared to ultrasound guided TAP block group. Minimum incision no requirement of mesh in pediatric population but in adults' extensive dissection required. This conclusion is controversial. Another study by Willschke H et al[18] also reported similar results as reported by previous study. Both of these studies conducted on pediatric patients which concluded that ultrasound guided TAP block does not give better outcomes when compared in children.

Reid MF et al[19] and Anatol TI et al[20] also conducted studies on comparison of ultrasound guided TAP block and IIIH nerve block to compare in terms of analgesic effect and complications rate. Anatol TI et al[20] reported that both groups are equally effective no one have superiority over other but Reid MF et al[19] give contrast conclusion that IIIH group is superior in terms of analgesia duration.

CONCLUSION

Results of our study reveals that IIIH and IHN nerve block reduced the rescue analgesic requirement as compare to ultrasound guided TAP block. Duration of post-operative analgesia is longer in IIIH/IHN block.

Author's Contribution:

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Original Article

Prevention of Emergence Agitation with Dexmedetomidine in the Patients Undergoing Nasal Surgery Under Anesthesia with Desflurane

Syed Aushtar Abbas Naqvi[1], Mirza Shakeel Ahmad[1] and Zeeshan Khan[2]

ABSTRACT

Objective: To evaluate the effectiveness of Dexmedetomidine in the avoidance of emergence agitation occurring in the patients enduring nasal surgery under anesthesia with Desflurane.

Study Design: A randomized controlled trial study.

Place and Duration of Study: This study was conducted at the Department of Anesthesia and intensive care of DG khan/Sheikh Zaid Medical College & Hospital Rahimyar Khan, from May 2018 to August 2018.

Materials and Methods: Sixty patients were distributed into two equal groups, Dexmedetomidine was given to one while the other received normal saline as placebo. Primary outcomes included incidence of emergence agitation while hemodynamic stability, postoperative sedation, pain severity, analgesics and anti-emetics requirements, stay in PACU were included in secondary outcomes. The data was entered in SPSS v.23 and analyzed with independent t-test, Mann Whitney U-test and Chi-square test, as appropriate. P≤0.05 was considered statistically significant.

Results: Incidence of emergence agitation was 60% in group-N and 10% in group-D (p<0.001). Time to extubate, to attain BIS-90 and to get verbal reaction were prolonged in group-D (p<0.001). Stay time at PACU was considerablyextended in group-D (p=0.017). Ramsey sedation score was greater in Group-D than in group-N (p=0.016). The incidence of analgesics and anti-emetics use in PACU was 33.3% and 30% in group-N; and 10% and 6.7% in group-D, (p-value 0.028 and 0.020), respectively.

Conclusion: Dexmedetomidine is efficacious in reducing the occurrence of EA in the adult patients undergoing nasal surgery under general anesthesia with Desflurane but the degree of sedation is increased along with prolonged PACU stay.

Key Words: Emergence agitation, Dexmedetomidine, Desflurane, Nasal surgery

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INTRODUCTION

Anesthesia practice depends mainly on inhalational agents. The search for newer agents is still on the rise which aims at finding the agent which helps in rapid induction of anesthesia, is safe, pleasant smelling and free of adverse effects. Many newer agents including desflurane and sevoflurane have been discovered so far over the past one and half century but there are still some adverse effects associated with these agents which are holding them back from being the perfect anesthetic agents. Decreased awakening time and rapid eye opening, reaction to verbal command and time, place and person orientation are some of the important properties of desflurane[1]. Owing to these properties, emergence agitation occurs in the patients who are recovering from general anesthesia. Negative postoperative behavior and physical injury can also be associated with emergence agitation.

In spite of occurrence of emergence agitation for brief period of time, pharmacological intervention can be needed sometime to overcome this. Many agents including opioids, clonidine, ketamine and propofol have been used in the past for the prevention of emergence agitation. All of these agents are known to show increase in post anesthetic sedation, prolonged awakening time from anesthesia and some unwanted adverse effects including nausea and vomiting [2].

Dexmedetomidine is an agents which has selective action on alpha w adrenoceptors [3]. It is used commonly as adjuvant to ropivacaine in regional anesthesia a well as adjuvant in general anesthesia [4] to help reduce the

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consumption of opioids and inhalational anesthetics [5]. The block of nor adrenalin from alpha 2 adrenoceptors results in sedation and hypnosis [6]. Analgesia, sympatholysis and anxiolytics are very important functions of dexmedetomidine[7]. Stress responses of laryngoscopy are lessened when dexmedetomidine is injected intravenously[8]. Dexmedetomidine is used widely in children to reduce the occurrence of EA[9].

The studies to evaluate the efficacy of dexmedetomidine in reduction of EAin adult candidates are very few in number[10,11]. We directed our study to observe the effectiveness of dexmedetomidine in the reduction of EA and its effects on recovery in adult patients who underwent any type of nasal surgery under desflurane anesthesia.

MATERIALS AND METHODS

We conducted this randomized controlled trial in the Department of Anesthesia and intensive care of DG khan/Sheikh Zaid Medical College & Hospital Rahimyar Khan, from May 2018 to August 2018. Our study was accepted by the hospital review committee. The study conducted by Garg A. et al. [11] was taken as reference. The calculated sample size was 26 which was too small, therefore, we selected sixty (60) patients of American society of Anesthesiologist (ASA) physical status I or II and between 18-60 years of age, with non-probability consecutive sampling technique. All these patients were selected for the nasal procedures under anesthesia induced by desflurane on elective basis. All the patients who had systemic illness (such as cardiac, hepatic, endocrinal or neurological), substance induced disorder, psychiatric disorders or were taking medications such as alpha 2 agonists, beta blockers or tricyclic anti-depressants were excluded from our study. Thorough evaluation of all the patients was done one night before the surgery. Pulse oximeter non-invasive blood pressure monitor, ECG monitor and BIS electrodes were attached and baseline readings were taken. Two IV lines were secured. After pre oxygenation, midazolam 0.05mg/kg and fentanyl 2 µg/kg were given as slow intravenous infusion. Propofol 2-2.5 mg/kg was given intravenously for inducing anesthesia. Endotracheal intubation was facilitated by intravenous atracurium 0.5mg/kg body weight. We divided 60 patients into two equal groups: Group N was given desflurane in air and oxygen mixture (50:50) and normal saline placebo as bolus infusion for 10 minutes and as maintenance infusion after tracheal intubation; and group D was given desflurane in air and oxygen mixture (50:50) and a bolus of 1 µg/kg dexmedetomidine infusion for 10 minutes and 0.4 µg/kg maintenance dose as infusion following tracheal intubation. Drug was diluted keeping in view the body weight of the patients. Loading dose was given at 120 ml/h for 10 minutes and the maintenance dose 8 ml/h continued till the completion of surgery. The starting dial flow of desflurane was 6% in air and oxygen mixture (50:50) and it was titrated to sustain BIS 45-55 during the surgery. The tidal volume was maintained at 6-8L/kg and it was targeted at 35-40 mmHg end tidal CO_2 concentration. Analgesia and muscle relaxation was achieved by fentanyl and atracurium bromide. Blood pressure, BIS, O_2 saturation, end tidal desflurane concentration and CO_2 concentrations were noted every 10 minutes during the surgery. Desflurane and the drugs under study were stopped at the time of application of surgical dressing and the time (T_0) was recorded. Neostigmine and glycopyrrolate were given intravenously for antagonizing neuromuscular blockade. Tracheal extubation was performed when sufficient muscular power had returned. The time interval from T_0till the patient could tell his/her name was defined as emergence time. Level of agitation was evaluated by Ricker sedation-agitation scale (Table-I). The severity of pain was noted by Numeric rating scale (NRS) (0= no pain, 10= very severe pain). Verbal instructions and repeated verbal reminder of limit therapy was used in the patients with 5 or 6 emergence agitation score, respectively, whereas IV propofol at 1mg/kg dose was given to the patients with emergence agitation score of 7. NRS score was noted every 2 minutes for obtaining peak value. Time to extubate, to attain BIS-90, to get verbal response and stay time at PACU were documented. The degree of sedation was noted by Ramsey sedation scale [12]. Anti-emetics and analgesics requirement were also noted. Diclofenac sodium was given as rescue analgesic in PACU on the patient's demand.

Primary outcomes included the incidence of emergence agitation while hemodynamic stability, postoperative sedation, pain severity, analgesics and anti-emetics requirements, stay in PACU were included in secondary outcomes. The data was entered in SPSS v.23 and analyzed. The test applied were independent t test, Mann Whitney U test and Chi square test, as appropriate. $P \leq 0.05$ was considered statistically significant.

RESULTS

There was no noteworthy variance between the two groups in regard with age, weight, gander distribution and the types of the surgical procedures performed ($p>0.05$). The duration of surgery and anesthesia was 78.10±12.76 minutes and 108.01±10.93 minutes in group N; and 80.40±10.95 minutes and 112.37±12.30 minutes in group D, (p-value 0.457 and 0.152), respectively. Baseline heart rate was also not different in the groups ($p=0.757$). Mean arterial pressure was 88.90 ± 4.47 mmHg in group N and 86.03 ± 3.89 mmHg in group-D ($p=0.010$). Table-2

Time to extubation was 5.70 ± 0.94 min and 7.63 ± 1.10 min in group N and D, respectively ($p<0.001$).

Time for attaining BIS-90 and verbal response was 4.98 ± 0.65 min and 5.44 ± 0.81 min in group N; and 7.71 ± 0.93 min and 8.49 ± 0.94 min in group D, respectively (p<0.001). Occurrence of EA was 60% in group N and 10% in group D (p<0.001) and the difference was statistically noteworthy. Peak NRS score observed was 5.53 ± 1.43 and 5.27 ± 1.48 in groups N and D, respectively (p=0.482). Ramsey sedation score was higher in Group D than in group N (p=0.016). The incidence of analgesics and anti-emetics use in PACU was 33.3% and 30% in group N; and 10% and 6.7% in group D, (p-value 0.028 and 0.020), respectively. Stay in PACU was longer in group D i.e. 12.56 ± 4.94 min as compared to stay of group N i.e. 9.83 ± 3.55 min (p=0.017). Table-3.

Table No.1: Ricker sedation-agitation scale

Score	State	Behavior
7	Dangerous agitation	Climbing over bed railings, lashing side to side, demanding to remove lines, lashing at staff.
6	Very agitated	Restraints and recurrent verbal reminder of limits required.
5	Agitated	Physically agitated or anxious, calms to verbal directions.
4	Calm and cooperative	Follows commands, simply arousable and calm.
3	Sedated	Follows commands, difficult to awaken, awakes to verbal incentives.
2	Very sedated	Does not obey commands, awakes to physical stimuli.
1	Unarousable	Does not follow commands or communicate, slight or no response to harmful stimulus

Table No.2: Demographic and baseline data

Variable	Group N (n=30)	Group D (n=30)	P value
Age, years	29.83 ± 4.62	28.10 ± 5.58	0.195
Gender (male / female)	16 / 14	14 / 16	0.606
Weight, kg	58.73 ± 9.05	60.23 ± 7.57	0.489
Type of procedure, n (%)			0.793
FESS	5 (16.7)	8 (26.7)	
DCR	9 (30)	7 (23.3)	
Septoplasty	10 (33.3)	10 (33.3)	
Adenoidectomy	6 (20)	5 (16.7)	
Surgery duration, min	78.10 ± 12.76	80.40 ± 10.95	0.457
Anesthesia duration, min	108.01 ± 10.93	112.37 ± 12.30	0.152
Baseline heart rate, bpm	81.70 ± 4.53	81.30 ± 5.40	0.757
MAP, mmHg	88.90 ± 4.47	86.03 ± 3.89	0.010

Fess= functional endoscopic sinus surgery; DCR= dacrocystorhinostomy; MAP= mean arterial pressure; variables mentioned as mean ± S.D unless mentioned otherwise.

Table No.3: Outcome variables

Variable	Group N (n=30)	Group D (n=30)	P value
Time to extubation, min	5.70 ± 0.94	7.63 ± 1.10	<0.001
Time to achieve BIS-90, min	4.98 ± 0.65	7.71 ± 0.93	<0.001
Time to verbal response, min	5.44 ± 0.81	8.49 ± 0.94	<0.001
Emergence agitation, n (%)	18 (60)	3 (10)	<0.001
Peak NRS score	5.53 ± 1.43	5.27 ± 1.48	0.482
Ramsey sedation score, median (IQR)	3 (2 - 3.25)	3 (3 - 4)	0.016
Analgesics in PACU, n (%)	10 (33.3)	3 (10)	0.028
Anti-emetics in PACU, n (%)	9 (30)	2 (6.7)	0.020
Stay in PACU, min	9.83 ± 3.55	12.56 ± 4.94	0.017

DISCUSSION

It was observed in our study that the occurrence of EA was significantly reduced in the patients who were given intraoperative dexmedetomidine infusion. While keeping hemodynamic stability, dexmedetomidine is associated with delay in extubation and verbal response. Emergence agitation develops from quick recovery from anesthesia, especially with the short acting agents such as sevoflurane and desflurane. The state of purposeless restlessness, inconsolability and non-cooperation is defined as emergence agitation and it is associated with screaming, crying, thrashing and bafflement[13]. In spite of the occurrence of EA being more in pediatrics patients, 21.3% and 4.7% incidence has been observed in adult patients[14,15]. Variety of agitation scoring scales might be responsible for this much wide variation in the statedoccurrence of EA.

Increase in noradrenaline release from alpha-2 adrenoceptors in locus ceruleus of the preoptic rat brains had been demonstrated as causal for emergence agitation[16-17] but the association with inhalational anesthetics, pain, male gender, age and preoperative use of benzodiazepines had been proposed in other study[13]. Emergence agitation has been observed in 55.4% of the patients who underwent some sort of ENT surgery[14]. According to some studies, the occurrence of EA is higher in those who endured ENT surgery, especially nasal surgeries in which nasal packing was done, in both children as well as adults[14,15]. In our study,

occurrence of EA was 60% in the control group while 10% in the dexmedetomidine groups and these results were in agreement with some preceding studies[10,14]. Dexmedetomidine is also reported to significantly reduce the occurrence of EA in children and the researchers used a diverse dosing of dexmedetomidine and found it to be significantly superior to placebo in children[9]. In a study, 46% decrease in the occurrence of EA has been observed in grown-up patients with the intraoperative usage of dexmedetomidine at 0.4µg /kg dose without giving any bolus dose[10]. In the above mentioned study, time to extubate and verbal reaction was also prolonged with the use of dexmedetomidine, as observed in our study.

In this study, we witnessed no substantialalteration in heart rate but MAP was considerably lower in dexmedetomidine group, results similar those observed by Garg A et al[11]. But in contrast to our results, some studies observed significant decrease in intraoperative heart rate of the patients who were given dexmedetomidine[18-20]. In another study[11,21], MAP was witnessed to be considerably lower with the use of dexmedetomidine and their results were similar to those observed in our study. Significantly decreased heart rate and MAP were observed in another study with dexmedetomidine usage as compared to the use of placebo[22]. Dexmedetomidine has some anesthetic sparing effects which leads to decreased requirement of anesthetic agents which has been observed in some studies[23,24].

CONCLUSION

Dexmedetomidine is efficacious in reducing the frequency of EA in the adult patients enduring nasal surgery under GA with desflurane but the degree of sedation is increased along with prolonged PACU stay.

Author's Contribution:

Concept & Design of Study:	Syed Aushtar Abbas Naqvi
Drafting:	Mirza Shakeel Ahmad
Data Analysis:	Zeeshan Khan
Revisiting Critically:	Syed Aushtar Abbas Naqvi, Mirza Shakeel Ahmad
Final Approval of version:	Syed Aushtar Abbas Naqvi

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

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Original Article

Efficacy of Intense Pulsed Light Therapy in the Treatment of Facial Acne Vulgaris: Comparison of Two Different Fluence

Aliya Akhtar[1], Asma Bano[2], Nighat Fatima[3], Seemab Khan[4], M.Farooq Khan[2] and Saira Isa[1]

ABSTRACT

Objective: Objective of study is to compare efficacy of two fluencies normal and subnormal of IPL on facial acne vulgaris.

Study Design: Randomized controlled trial (RCT)

Place and Duration of Study: This study was conducted at the dermatology department of Nishtar Hospital Multan, from January 2020 to December 2020.

Materials and Methods: Study was conducted on 60 patients, normal fluence was used on right side of face and subnormal was used on left side of face. Number of lesions was used to calculate reduction in lesion. SPSS version 23 was used for data analysis.

Results: Excellent results were obtained in 15.0% of patients in right side and 10% in left side. The most common side effect noted in both left and right side was itching i.e. 76.7% and 68.3% respectively. (p=0.021).

Conclusion: IPL is safe and effective option for inflammatory acne vulgaris with minimal reversible side effects. Both fluencies subnormal and normal fluence are equally.

Key Words: intense pulsed light, Acne vulgaris, Skin, Lesion count.

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INTRODUCTION

Acne vulgaris is a common skin disease that usually affects young people and teenagers and can lead to low self-esteem and psychological distress[1]. In United States of America about fifty million people affected by acne vulgaris, among them 85% are teenagers. Acne can occur in all age groups but usual presentation is adulthood. Less than 20 blackheads or white heads labeled as mild acne and larger number of black or whiteheads considered under moderate acne[2].

In cases of severe acne blackheads present with nodules or cyst and pimples become painful. Combination of oil, hormone and bacteria cause acne vulgaris during puberty[3]. Most common causes are hormonal changes either in pregnancy or not, use of cosmetics, high sweating and humidity and polycystic ovary syndrome[4]. This chronic inflammatory disease altered the pilosebaceous unit under the skin and involved in increased production of sebum and abnormal shedding of follicular epithelium that is responsible for obstruction of pilosebaceous unit and comedo formation[5].

After sometime sebum in pilosebaceous unit pulls the Propionibacterium acnes and mediate the follicular inflammation. Available topical and oral anti-acne medications are less effective, more adverse and difficult to use[6]. Collectively antibiotic resistance, side effects of systemic and topical anti-acne medication and desire for advance technology based approaches are responsible for increasing interest of people in light based acne therapy[7].

Intense pulsed light also famous with name of photofacial is a mode improvement in texture and color of skin without any surgical treatment. It works by mode of undo of damage due to sun exposure or photoaging[8]. Most common places are chest, hands, neck and face. Intense pulsed light (IPL) therapy for treatment of acne vulgaris has three therapeutic roles photo-immunological, photochemical and photothermal[9]. IPL based on selective thermal damage of P. acnes, its synthesis and storage of porphyrins.

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These porphyrins become chemical active on exposure to visible light and converted into single oxygen atom and develop a bond with cell membrane to destroy structure of P. acnes[10]. In our study we used IPL monotherapy to compare two types fluence. One is subnormal and other is normal fluence.

MATERIALS AND METHODS

Study was conducted at dermatology department of Nishtar Hospital Multan from January 2020 to December 2020 in duration of one. Written informed consent was obtained from patients. Ethical approval was taken from hospital ethical board. Non probability consecutive sampling technique was used.

A total of 60 diagnosed patients of acne vulgaris were enrolled in study. Patients having tendency to form keloid and hypertrophic scar, history of seizures, photosensitivity, tanned skin, breastfeeding and used topical and systemic antibiotics were excluded from study. Patient's Fitzpatrick skin type, history of prior treatment, duration of the disease and medical history was noted. Patients were asked to remove make up and wash face before every sitting of treatment. Number of acne lesions was counted on both sides of face. Patients were treated with four sittings of IPL at 2 weeks interval and were followed up for 2 months every 2 weeks. Minimum wavelength used was 550 nm and maximum 1200 nm of IPL, pulse duration was 5 ms, interval 10 ms, fluence on left side was 20 J/cm ^{2} and on right side was 35 J/cm ^{2}. Intensity of fluence was reduces upto 20% on forehead and other bony appearances to overcome the complication of hyperpigmentation. Side effects were noted after each sitting of follow up. Reduction in lesion count was noted, 25% reduction counted as mild, 25-50% moderate, 50-75% good and 75-100% was considered as excellent.

SPSS version 23 was used for data analysis. Mean and SD was calculated for continuous data and frequency (percentages) were presented for categorical data. Test of significance (t test, chi square test) were applied to see association among variables. P values ≤ 0.05 was taken as significance.

RESULTS

Sixty patients were included in this study, n=35 (58.3%) males and n=25 (41.7%) females with mean age 25.30±3.54 years. Fitzpatrick skin Grade IV and Grade V was noted in n=33 (55.0%) and n=27 (45.0%), respectively. Acne lesions Grade II, III, and IV was observed in n=41 (68.3%), n=12 (20.0%) and n=7 (11.7%), respectively.

No significant difference was found in efficacy in two fluencies that was used on right and left sides on face in falling the frequency of acne lesion at first, second, third and fourth setting. (Table. I). No significant difference was found in efficacy in two fluencies that was used on right and left sides on face in falling the frequency of acne lesion at the end of follow-up. (Table. 2).

Table No.1: Mean distribution of lesion counts in one to fourth sittings on right and left sides of the face

Lesion counts	Right side	Left side	P-value
First Sitting	38.35±3.02	38.34±4.25	0.997
Second Sitting	33.75±3.46	34.49±3.44	0.410
Third Sitting	27.18±4.34	29.16±3.84	0.067
Fourth Sitting	24.82±4.82	26.39±3.97	0.174

Table No.2: Mean distribution of lesion counts in one to fourth follow-up

Lesion counts	Right side	Left side	P-value
First Follow-up	22.24±2.41	22.14±2.76	0.890
Second Follow-up	21.16±3.59	20.69±2.59	0.540
Third Follow-up	17.61±4.64	16.77±4.13	0.466
Fourth Follow-up	15.34±3.18	15.83±2.93	0.541

Table No.3: Distribution of lesion counts in one to fourth follow-up

Lesion counts	Right side	Left side	P-value
First Follow-up	n=33 (55.0%)	n=27 (45.0%)	0.938
Second Follow-up	n=32 (53.3%)	n=34 (56.7%)	0.651
Third Follow-up	n=33 (55.0%)	n=32 (53.3%)	0.077
Fourth Follow-up	n=41 (68.3%)	n=42 (70.0%)	0.856

Table No.4: Mean distribution of lesion counts at baseline and follow-up

Lesion counts	Right side	P-value	Left side	P-value
First sitting versus first follow-up	38.35±3.02 versus 22.24±2.41	0.000	38.34±4.25 versus 22.14±2.76	0.000
First sitting versus fourth follow-up	38.35±3.02 versus 15.34±3.18	0.000	38.34±4.25 versus 15.83±2.93	0.000
Fourth sitting versus fourth follow-up	24.82±4.82 versus 15.34±3.18	0.000	26.39±3.97 versus 15.83±2.93	0.000

Table No.5: Decreasing grade of lesion count

Grade	Right side	Left side	P-value
Mild (0-25)	n=4 (6.7%)	n=3 (5.0%)	0.748
Moderate (26-50)	n=17 (28.3%)	n=5 (8.3%)	0.000
Good (51-75)	n=30 (50.0%)	n=46 (76.7%)	0.000
Excellent (76-100)	n=9 (15.0%)	n=6 (10.0%)	0.041

Table No.6: Distribution of side effects of right and left sides

Side Effect	Right side	Left side	P-value
Erythema	n=3 (5.0%)	n=2 (3.3%)	0.854
Burning	n=5 (8.3%)	n=3 (5.0%)	0.642
Itching	n=46 (76.7%)	n=41 (68.3%)	0.021
Malia	n=6 (10.0%)	n=14 (23.3%)	0.000

The distribution of lesion counts at first, second, third and fourth follow-up shown in table-3. The mean lesion counts at baseline and at different levels of follow-up were shown in table. IV. The mean lesion counts at follow-up was less than the mean lesion counts at baseline. The differences were statistically significant. (Table. 4). Grade of reduction in lesion counts at right and left side was statistically significant. (Table. 5). The most common side effect noted in both left and right side was itching i.e. n=46 (76.7%) and n=41 (68.3%), respectively. (p=0.021). (Table. 6).

DISCUSSION

In spite of many advances treatment modalities of acne vulgaris, treatment of choice is still controversial. Many conventional treatment modalities are available but limited in use because of high cost, poor efficacy, recurrence, bacterial resistance and allergic reactions. There is obvious necessity of better treatment option, in this era of satisfaction IPL as monotherapy or in combination is a better option. Our study will made the use of IPL more beneficial by exploring its better type of fluence.

In our study at final follow up 57.9% reduction in acne lesion on left side and 63.49% on right side were observed. Kumaresan et al[11] conducted a study on comparison of single and burst mode of IPL and observed 49% reduction in acne lesion after final follow up of IPL monotherapy. Among both treatment option burst mode reduced acne severity 56% and single mode reduced 40%.

Use of high fluence in our study have more photochemical and photothermal effects but low fluence affiliated with photo-immunological effects. In a study by Paithankar et al12 used photothermal approach of IPL and found reduced inflammatory acne vulgaris upto 50%. Similarly, Elman et al13 conducted a study on 19 acne patients and efficacy of IPL was noted. More than 50% reduction in acne vulgaris lesion was found in 85% of patients.

In our study erythema, itching and burning like side effects were noted in a small proportion of patients. Kawana et al[14] acquitted a research on high and low frequencies of smooth pulse light and reported smooth pulse light with 1200 nm light more effective in treatment of acne vulgaris. No major side effects of IPL therapy were observed except transient erythema with or without stinging and burning.

Different theories were postulated on role and effectiveness of IPL to overcome the acne lesions, but its wavelength and duration is still under debate. Barikbinet al[15] carried out a study on comparison of different pulse duration and efficacy was assessed by counting the number of lesion after and before follow up. Longer duration of pulse light was reported more effective as compare to shorter duration.

Sami et al[16] carried a study on effectiveness of phototherapy and laser therapy in treatment of acne and reported that phototherapy is a growing modality for acne and can be used in place of antibiotic and other topical medicines. In this study IPL, pulsed dye laser PDL was compare and with use of IPL 41.7% reduction was observed and PDL reduced acne lesion upto 90%. Young et al[17] compared different wavelength of IPL and found all frequency useful in acne vulgaris.

Other than established benefits of IPL in acne vulgaris it is also associated with side effects like erythema, burning and stinging. In a study by Stanglet al[18] hyperpigmentation, dermatitis, infection, scaring and skin texture changes like side effects were observed. In another study Sadicket al[19] observed superficial cruting and transient hyperpigmentation like minor side effects. Bjerring et al[20] used special IPL with 950nm wavelength and observed common adverse effect purpura associated with burning sensation.

Limitations: we didn't use multiple parameters such as pulse duration, wavelength of higher and lower intensity, pulse duration and single and burst pulse mode in our study. Most of our patients belong to tribal or village areas, they didn't allow to include images of study results.

CONCLUSION

IPL is safe and effective option for inflammatory acne vulgaris with minimal reversible side effects. Both fluencies subnormal and normal fluence are equally.

Recommendations: Results of our suggested that IPL is effective and safe option for inflammatory acne vulgaris with few downtime and reversible adverse effects. Although the study was done using it as monotherapy, we suggest combination of IPL and systemic antibiotics for better and long-lasting outcomes

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Original Article

Frequency of Hypokalemia in Malnurished Children with Acute Diarrhea

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ABSTRACT

Objective: This study aimed to determine the frequency of hypokalemia in malnourished children with acute diarrhea.

Study Design: Cross sectional study.

Place and Duration of Study: This study was conducted at the pediatrics department of Ayub Teaching Hospital Abbottabad for six months from June 2017 to November 2017.

Materials and Methods: After approval from hospital ethical committee, sample size of 96 was calculated using WHO software for sample size determination in health studies by keeping confidence level of 95%, anticipated prevalence of hypokalemia in malnourished patients of 55% and absolute precision of 10%. Children of either gender aged six months to five years admitted in ward fulfilling the inclusion criteria of malnutrition with acute diarrhea were included in this study in a consecutive manner.

Results: Out of 96 patients, 44(45.8%) were male and 52(54.2%) were female. Mean age was 20.65±11.961 months. Hypokalemia was observed in 46 (47.9%) children whereas 50 (52.1%) children had no electrolytes imbalance. The frequency of hypokalemia was analyzed with respected to gender and age groups of the children and the p-values were 0.973 and 0.176 respectively.

Conclusion: In conclusion hypokalemia is a common electrolyte abnormality in children with malnutrition especially during acute diarrheal episodes. Therefore, the treating physician should be very vigilant for this common electrolyte abnormality and serial monitoring of serum potassium level and potassium supplementation should be done in children with malnutrition during acute diarrhea illnesses to avoid life threatening consequences of severe hypokalemia.

Key Words: Malnutrition, hypokalemia, Acute Diarrhea, frequency

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INTRODUCTION

Malnutrition is a major health problem throughout the world especially in developing countries. It interacts with diarrhea in a vicious cycle[1]. Electrolyte imbalance is a common problem in malnourished children [2]. The increase loss of electrolytes especially potassium and sodium in acute diarrhea increases the morbidity and mortality associated with malnutrition. Therefore, serum electrolytes should be keenly monitored in these patients [3].

Potassium plays a very important role in the stabilization and maintenance of electric potential in cardiac muscle cells. Their imbalance may have a detrimental effect on the normal electric activity of heart [4]. Therefore, it is highly essential to maintain normal level of potassium in malnourished children.

Malnutrition is the leading contributor to the global burden of diseases in children. It is responsible for more than half of all childhood deaths throughout the world[5]. In a survey conducted jointly by the Government of Pakistan and United Nations Children's Fund (UNICEF) showed that 41.5% of Pakistani children were underweight, 31% were stunted, 11.6% were wasted and 10% were anemic. In this survey, In Pakistan 44% of school going children were found to be malnourished[6]. Malnutrition also impairs children's physical and mental development and it results in poor academic performance[7]. In Pakistan the rate of childhood malnutrition is comparatively much higher than in other less developed countries in the world and its achievement in childhood nutrition and health is much slower as compared to other countries in this region [8].

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The association of malnutrition and diarrhea is an established fact [9]. Severe acute malnutrition account for about two million deaths annually with diarrhea being the most common cause[10]. Both the frequency and duration of diarrhea and the resulting mortality due to diarrhea are much higher in malnourished children as compared to well-nourished children. Acute malnutrition and diarrheal illnesses are also the major contributor to childhood morbidity[11]. Diarrhea is a common problem in our country and the prevalence of diarrhea in Pakistan is 51% reported by Syed M. Shah et al. in a study [12].

In children with acute malnutrition electrolyte imbalance is very common along with other complications. Acute diarrheal illnesses aggravate this electrolyte imbalance. Diarrheal episodes result in loss of sodium, potassium, bicarbonate and chloride ions form the body [13]. Among these electrolytes imbalances hypokalemia and hyponatremia can have a fatal outcome [14]. This loss of electrolytes especially severe hypokalemia has importance in immediate therapy to avoid life threatening situations. Malnourished children have poor ability to maintain normal electrolyte concentration and acute diarrhea exacerbates this problem. This results in overall decrease in electrolytes especially Sodium and Potassium. The concomitant electrolytes and water losses results in compensatory mechanism for water retention which may lead to edema in malnourished children [15].

Management of acute diarrheal illnesses and dehydration in children with severe malnutrition is often controversial. Diarrhea has been shown to have a poor outcome in these children in some studies while other studies have shown to have a little prognostic value upon successful management [16]. In patients with severe complicated acute malnutrition bacterial causes of diarrhea is more common and it is suggested to be caused due to the immunosuppressive effects of acute malnutrition and due to damage to the protective mucosal barrier in gastrointestinal tract [17].

Children with severe acute malnutrition are usually managed with antibiotic and oral rehydration fluids like well-nourished children without considering this electrolyte imbalance which can be highly dangerous and increases morbidity and mortality in these children. Therefore, it is highly recommended to detect and manage this electrolyte imbalance in malnourished children according to World Health Organization (WHO) protocols to reduce the associated life threatening consequences.

This current study was aimed to determine the frequency of hypokalemia in malnourished children with acute diarrhea so that this serious complication can be diagnosed and managed immediately to reduce the associated morbidity and mortality.

MATERIALS AND METHODS

This Descriptive cross sectional study was conducted in the pediatrics department, Ayub Teaching Hospital Abbottabad. Duration of study was six months from June 2017 to November 2017. After approval from hospital ethical committee, sample size of 96 was calculated using WHO software for sample size determination in health studies by keeping confidence level of 95%, anticipated prevalence of hypokalemia in malnourished patients of 55% and absolute precision of 10%. Children of either gender aged six months to five years admitted in ward fulfilling the inclusion criteria of malnutrition with acute diarrhea were included in this study in a consecutive manner. Hypokalemia was defined as potassium level less than 3.5mmol/L. children having weight for age less than 80% of the expected weight were considered malnourished. Acute diarrhea was defined as having more than three watery stools per day of less 14 days duration. Those patients fulfilling the above mentioned criteria were subjected to blood tests like serum potassium. The above mentioned information including name, age, gender, address, weight, and hypokalemia were recorded on a predesigned proforma. Data were analyzed using Statistical Package for Social Sciences (SPSS) version 16. Quantitative variables like age and potassium level were described in terms of means ± standard deviation (SD). Categorical data like gender and hypokalemia was described in the terms of frequency and percentages. All results were presented as tables and diagrams. Data was stratified by age and gender with respect to outcome variable i.e. hypokalemia. Post stratified chi square test at 5% level of significance by age and gender was used.

RESULTS

A total of 96 patients were included in this study. Of these, 44(45.8%) were male and 52(54.2%) were female. Children were divided in three age groups six to twelve months, 13-36 months, and 37-60 months. A total of 24 (25%) children were aged below 12 months, 66 (60.8%) were between 13-36 months, and 6 (6.2%) were between 37-60 months. Mean age was 20.65±11.96 months. Hypokalemia was observed in 46 (47.9%) children whereas 50 (52.1%) children had no electrolytes imbalance.

The frequency of hypokalemia was analyzed with respect to gender of the patients in which 47.7% (21/44) male patient had hypokalemia while, among female patients 48.1% (25/52) patients had hypokalemia. Frequency of hypokalemia was observed in 50% (12/24) of patients under 12 months of age, 43.9% (66/29) among patients in 13-36 months age group, and 83.3% (five out of six) of children with age between 37-60 months. Frequency of hypokalemia by sex and age group of patients is presented in Table 1.

Table No.1: Frequency of hypokalemia by sex and age group of patients

	Hypokalemia		P-value
	Yes	No	
Total	46	50	-
Sex of child			
Male	45.7% (21)	46% (23)	0.973
Female	54.3% (25)	54% (27)	
Age Groups			
6-12 months	26.1% (12)	24% (12)	0.176
13-36 months	63% (29)	74% (37)	
37-60 months	10.9% (5)	2% (1)	

DISCUSSION

Children with severe malnutrition are at increased risk to various infections and these infections either further compromised their nutritional status or causes malnutrition [18]. In developing countries about 165 million children are malnourished and malnutrition is the leading cause of childhood mortality throughout the world [19]. Diarrhea contribute significantly to childhood mortality and it causes more than 1.5 million deaths annually and predisposes children to malnutrition.

In our study the frequency of hypokalemia was 47.9%. Our finding was very similarly to study conducted by Yasmeen Memon in which the frequency of hypokalemia in malnourished children with diarrhea was 48% [20]. In his study 57 children were male and 43 were females and 12 children were with grade one malnutrition, 27 were in grade two malnutrition while 61 were in grade three malnutrition. While in our study 44(45.8%) were male and 52(54.2%) were female.

In another study from Pakistan conducted by Arif Zulqarnain and colleagues, the frequency of Hypokalemia in malnourished children with diarrhea was 61.1% and the electrolytes abnormalities were more common in children with grade three malnutrition[21].

Similar findings were observed in a study by Asma Bilal in Rawalpindi, Pakistan in which the frequency of hypokalemia in malnourished children with diarrhea was 55% while the frequency of hyponatremia was 32.5% and none of the patients have hypernatremia or hyperkalemia. In her study, of the 80 patients, 61.3% were boys and 38.7% were girls with a mean age of 1.9±1.4 years [22]. Rehana Majeed in a study reported the prevalence of hypokalemia in children with acute diarrhea was to be 37%, [23] while in an Indian study, the frequency of hypokalemia was 8.33% while that of hyponatremia was 13.33% and these were the most common electrolyte abnormalities in children with severe acute malnutrition [24].

In a Nigerian study the frequency of Hypokalemia was 23.4% in malnourished children presented with diarrhea and it was second to metabolic acidosis which the most common abnormality in these children. The frequency of hyponatremia was 13%, hypochloraemia 4.2% and hypernatremia was 3.1% [7]. Malnutrition has significant graded association with diarrhea and malnourished children has an increased incidence of diarrhea while similarly diarrhea leads to worsening of already compromised nutritional status. In malnourished children the duration of diarrhea also significantly prolonged as compared to normal weight children [25]. In a study conducted in Bangladesh founded a positive relationship between diarrhea and malnutrition as diarrhea leads to malnutrion while malnourished children have an increased incidence and duration of diarrheal illnesses [26].

CONCLUSION

In conclusion hypokalemia is a common electrolyte abnormality in children with acute malnutrition especially during acute diarrheal episode. Therefore, the treating physician should be very vigilant for this common electrolyte abnormality and serial monitoring of serum Potassium level and potassium supplementation should be done in children with malnutrition during acute diarrhea illnesses.

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Original Article

Frequency of Morphological Types of Ovarian Tumors in a Tertiary Care Hospital of Karachi

Alfarah Irfan[1], Mohammad Salman Zafar[2], Shah Jabeen[3], Nazia Qamar[2], Nadeem Nusrat[2] and Asadullah[4]

ABSTRACT

Objective: To determine the frequency of different morphological types of ovarian tumors in a tertiary care hospital of Karachi.

Study Design: A retrospective study of all cases of ovarian tumors

Place and Duration of Study: This study was conducted at the Department of Pathology, Jinnah Postgraduate Medical Centre Karachi over a period from July 2020 to December 2020.

Materials and Methods: Ethical approval was granted by ethical committee of organization. Laboratory request forms and histopathology reports of all histologically diagnosed ovarian tumors registered in last five years were retrieved from the record and were analyzed, excluding small biopsies. All cystectomy, oophorectomy, salpingo-oophorectomy and total abdominal hysterectomy (with bilateral or unilateral salpingo-oophorectomy) specimens were included. Patients with non-neo-plastic ovarian lesions and functional cysts were not included.

A total of 408 cases fulfilled the inclusion criteria. We reviewed all the histopathology slides and reports of the cases in the study, and analyzed for histopathological type, subtype, grade and age of the patients.

Results: In a total of 408 cases, 288 (70.6%) were surface epithelial tumors, 85 (20.8%) germ cell tumors and 28 (6.9%) were sex cord-stromal in origin. Among surface epithelial tumors, 190 (66%) were benign, 85(29.5%) were malignant and only 13 (4.5%) were found to be borderline. The commonest benign tumor was serous cystadenoma. The commonest malignant tumor was serous cystadenocarcinoma followed by mucinous cystadenocarcinoma.

Conclusion: We concluded that findings of our series correspond to majority of the published national and western data; however mucinous epithelial tumor and germ cell tumors turnout are more common in our population as compared to the western population. Moreover, ovarian cancers tend to involve relatively younger women in our region in contrast to West.

Key Words: Ovarian tumors, epithelial ovarian tumor, Germ cell ovarian tumors, Surface epithelial tumors, Ovarian cystadenoma

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INTRODUCTION

Gynecological cancers account for a huge burden of morbidity and mortality around the world; among which ovarian cancer is particularly deadly gynecological malignancy due to the fact that majority of them are associated with vague symptoms initially and therefore incurable when discovered at an advanced stage.

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According to American cancer society, an estimated 22,280 new cases and 15,500 deaths were expected to be caused by ovarian cancer in the U.S in 2012.[1] Moreover, it ranks second among the gynecological cancer following uterine cancer in U.K.[2]

In Pakistan, ovarian cancer ranked second among malignancies in adult females by Shaukat khanum collective cancer registry report (1994-2011).[3] However some of the studies has reported it as most common gynecological cancer as well.[4,5]

Although exact etiology of majority of ovarian cancers is not clear, but positive family history was found to have strongest association with ovarian epithelial malignancies in Pakistani women [6,7] suggesting genetic factors playing significant role in our patients.

It has been also observed that data available worldwide shows variability not only in incidence but in different morphological types of ovarian cancer as well.

Our pathology lab located in Jinnah postgraduate medical centre which is a tertiary care referral centre in Karachi, receives averaged 4800 specimens per year. The purpose of this study was to see frequency and

histological pattern of ovarian tumors in our setup and to compare our data with local and international studies.

MATERIALS AND METHODS

This study was a retrospective observational analysis of all consecutive cases with histopathologically proven ovarian tumors, reported from Department of pathology of BMSI, JPMC a tertiary care centre. Ethical approval was granted by ethical committee of organization. Laboratory request forms and histopathology reports of all histologically diagnosed ovarian tumors registered in last five years were retrieved from the record and were analyzed, excluding small biopsies. All cystectomy, oophorectomy, salpingo-oophorectomy and total abdominal hysterectomy (with bilateral or unilateral salpingo-oophorectomy) specimens were included. Patients with non-neo-plastic ovarian lesions and functional cysts were not included.

A total of 408 cases fulfilled the inclusion criteria. We reviewed all the histopathology slides and reports of the cases in the study, and analyzed for histopathological type, subtype, grade and age of the patients.

The data feeding and analysis was done on computer package SPSS (Statistical Packages of Social Sciences) version 16.0. Clinical characteristics was summarized in terms of frequencies and percentages for qualitative variables (age grouping, tumor grade and type of neoplastic lesions), mean ± S.D for age in years. In statistical analysis only p-value <0.05 was considered significant.

RESULTS

From the data of last five-year period, total of 408 cases of ovarian tumors were found to be received in our centre. World health organization classification of ovarian tumors was used for classification of tumors. As can be observed in TABLE 1, histopathological typing showed a markedly predominant frequency of surface epithelial tumors with 288 (70.6%) followed by germ cell tumors (20.8%) and then sex cord-stromal tumors (6.9%). The remaining 7 cases (1.7%) comprised of undifferentiated and metastatic tumors.

It has been seen (as shown in TABLE 2) that most of the epithelial tumors were benign (66%), 29.5% were malignant and only 4.5% were borderline. Among surface epithelial tumors, majority were serous (64%) followed by mucinous tumors (28.1%) as second most common type. 11 cases (3.8%) of endometroid carcinoma, 2 cases (0.7%) each of clear cell carcinoma and malignant mixed mullerian tumors, 1 (0.3%) of transitional cell carcinoma and 7 cases (2.4%) of poorly differentiated carcinomas were found.

Serous cystadenoma was found to be the commonest among benign surface epithelial tumor, while serous cystadenocarcinoma as commonest malignant tumor.

It has been also observed (as shown in table 3) that most of our patients with benign tumors belonged to the 3rd and 4th decade, while patients with malignant tumors to 5th decade. Patients with borderline tumors were mostly found in 4th decade of life.

Among germ cell tumors, majority (87.1%) were benign and all consist of mature cystic teratoma (including dermoid cysts), fewer (12.9%) were malignant comprises of dysgerminoma (7%), immature teratoma (4.7%) and yolk sac tumor (1.2%).

Among sex cord-stromal tumors, 53.6% were malignant and 46.4% were benign, in which granulosa cell tumor (50%) and fibroma-thecoma (46.4%) were the most frequently seen lesions respectively.

Table No.1: Distribution of Major Types of Ovarian Tumors According to Origin (n=408)

Types	No	%age	Confidence Interval CI
Ovarian epithelial tumors	288	70.6%	65.9-74.8
Germ cell tumors	85	20.8%	17.2-25.0
Sex-cord stromal tumors	28	6.9%	4.7-9.7
Others	7	1.7%	0.8-3.5

Table No.2: Different histologic types of ovarian neoplastic lesions

Histogenesis	Histopathology	Total	%tage
Surface epithelial tumors (n=288)	Serous		
	Total	184	64%
	Benign	131	45.5%
	Borderline	9	3.1%
	Malignant	44	15.3%
	Mucinous		
	Total	81	28.1%
	Benign	59	20.5%
	Borderline	4	1.4%
	Malignant	18	6.2%
	Endometroid	11	3.8%
	Clear cell	2	0.7%
	Mixed	2	0.7%
	Transitional	1	0.3%
	Poorly differentiated	7	2.4%
Germ cell tumors (n=85)	Teratoma		
	Total	78	91.7%
	Benign	74	87.1%
	Malignant	4	4.7%
	Dysgerminoma	6	7%
	Yolk sac tumor	1	1.2%
Sex cord-stromal tumors (n=28)	Benign	13	46.4%
	Fibroma-thecoma	13	46.4%
	Malignant	15	53.6%
	Granulosa cell tumor	14	50%
	Undifferentiated stromal tumor	1	3.6%
Other (7)		7	100%

Table No. 3: Distribution of ovarian epithelial neoplasms according to age (n=288)

n 288	Total no.	(11-20) (Yrs)	(21-30) (Yrs)	(31-40) (Yrs)	(41-50) (Yrs)	(51-60) (Yrs)	>61 (Yrs)	Mean age (Yrs)
Benign	190	16 (8.42%)	72 (37.89%)	44 (23.15%)	32 (16.84%)	22 (11.57%)	4 (2.1%)	36
Borderline	13	2 (15.38%)	3 (23.07%)	5 (38.46%)	0 (0%)	2 (15.38%)	1 (7.69%)	39
Malignant	85	0 (0%)	10 (11.76%)	18 (21.17%)	31 (36.47%)	18 (21.17%)	8 (9.41%)	47

DISCUSSION

In our study, attempt has been made to determine the frequency and distribution of ovarian tumors in a tertiary care hospital where a variety of malignancies are frequently seen.

According to the Karachi Cancer Registry, Karachi south and all urban population falls into a high risk region for ovarian cancer,[8] which accounts to second highest incidence in Asia after urban delhi.[9]

In our study, tumors of surface epithelial in origin were found to be the major type of ovarian tumors accounting for 70.58% of all cases. Our this finding is almost close to the observation made in most of national studies i.e. 63.5%, 70.9%, 68.4% respectively.[10-12] Our data also closely corresponds to the western figures in which frequency range of epithelial tumors is 65-70%[13] and to an Indian study reporting 67.9%.[14] The exact causes for this relatively high incidence of surface epithelial cancers in Pakistan are not clear; however Rashid et al mentioned in his study that substantial proportion of these cancers in Pakistani women is due to germ-line mutations in the BRCA1 and BRCA2 genes.[15]

In addition, we have found that among surface epithelial tumors, serous type being most common histological type, which is in accordance to majority of local and international figures. [10,14,16,17] It was also observed that most of local and south Asian [10,14,16] studies have mentioned mucinous subtype as second most common subtype similar to our results, which differs to western figures where endometroid ranked second behind serous tumors. [18,19] This could be due to the geographical variation of diseases.

In our series, most (65.97%) of epithelial tumors were benign in nature followed by malignant (29.51%). In a western literature by Kurman RJ, 57.5% of ovarian epithelial tumors were benign, 32.6% were malignant and 9.9% were reported as borderline, [17] which are in close proximity to our findings, but differed in part. Frequency of borderline tumors was found to be 4.51% in our series, which is lower as compared to western studies but approximately similar to a study done in Pakistan by Ahmed et al, [10] reporting 5.1%. The reason of low frequency in present study could be due to variation in environmental and genetic factors. Keeping in view a literature by Shih & Kurman, low grade serous carcinoma (but not high grade), mucinous, endometroid, clear cell and Brenner carcinomas are postulated to arise in a stepwise fashion from intermediate borderline tumors; [20] another possible reason could be the fact that our patients seek medical help late in the course of disease due to lack of awareness and low socioeconomic condition, which lead to progression of tumor from borderline to malignant grade.

We found that germ cell tumors and sex cord-stromal tumors comprised 20.83% and 6.83% respectively of all ovarian neoplasms. This was different from western figures where germ cell tumors and sex cord-stromal tumors comprised 3% and 5% respectively. [21,22] This is consistent with the high prevalence of germ cell and sex cord tumors in asian versus the western societies. Therefore, further research is required to more specifically determine the reasons for this disparity and to advance understanding of the disease in order to identify modifiable risk factors, develop effective early detection methods, and improve treatment.

Majority of germ cell tumors in present study were found to be benign (87.05%), whereas malignant constituted 12.94%. Approximately similar findings were reported by Ahmed et al and Zaman et al with corresponding figures of (80.17% & 19.82%) and (81.08% & 18.91%) respectively. [10,12] Mature cystic teratoma comprises of 20% of all ovarian tumors in West.[15] Similar figure of 18.68% (74/397) have been found in our study also. Among malignant germ cell tumors, dysgerminoma seen to be the most frequent, which matches the observation of Ahmed et al who reported its frequency of 9.91%.[10]

Among group of sex cord-stromal tumors, fibroma-thecoma has made most (46.42%) of the benign turnout in our series; moreover, granulosa cell tumor being most common (50%) of all malignant ones. This is an agreement with Mondal et al[14] which denoted Fibroma-thecoma as commonest benign and granulosa cell tumors as commonest malignant tumors in their studies.

Similar to most of local, Asian and western studies, in our study serous cystadenoma was found to be the commonest i.e. 68.94% among benign and serous cystadenocarcinoma as commonest i.e. 51.76% among malignant epithelial tumors. Mucinous cystadenoma ranked second (30.89%) in benign epithelial neoplasms and mucinous cystadenocarcinoma (21.17%) ranked

second among epithelial tumors. No benign and borderline case of other histological types was observed in our study.

As we know, demographic factors play an important role in the process of carcinogenesis; therefore, keeping in view age is reported in majority of cancer incidence publications. Majority of our patients with benign ovarian epithelial tumors were in 3rd and 4th decade of life, while that of malignant were seen in 5th decade. In western literature, mean age of 63 yrs has been reported in patients with malignant ovarian tumors; [24] however we have found the mean age of 47 years similar to most of local studies. This feature of younger age at presentation in pakistani women with ovarian epithelial cancer is similar to Indian (48 yrs), Japanese (51 yrs), Irani (49 yrs) and African women (46 yrs).[14,25-27] Reasons for lower mean age of ovarian cancer could be difference in risk and genetic factors existing in societies of western and asian countries. Another possible reason given by Saeed & Akram was shorter life expectancy in population of developing countries as compared to the west.[28]

Peak incidence of borderline tumors is between age group of 31-40 yrs; moreover, the mean age for borderline epithelial ovarian tumors in our series is 39 yrs. This finding is compatible with Kennedy & Hart reporting a mean age of 38 yrs. [29] Moreover, we observed that majority (38.46%) of the patients with borderline tumors belongs to the age group of 31-40 yrs, followed by 23.07% of patients belonging to 21-30 yrs age group. This data is compatible with other asian study by Mondal reporting 54.28% and 21.42% of patients belonging to age group of 31-40 yrs and 21-30 yrs respectively.

However, a Sweden study reported the median age at diagnosis of borderline ovarian cancer was 55.2 years [30]. Another study reported that the median age at diagnosis of borderline ovarian cancer was 45 years in Caucasians [31]. This contrasts the age of patients with borderline tumors in our study, which is more than 10 years younger than other ethnicities. Taken together our data suggest that age at diagnosis of borderline ovarian cancer is also younger in our study population than Caucasians.

Due to the lack of widespread population based data, hospital based registries form the main source of data for epidemiological estimates in our country. Our study provides a comprehensive information regarding frequency of ovarian tumors and their pattern in population of Karachi. Although it was a simple analysis, but with hope that it could help in promoting larger studies and formulate better for ovarian cancer prevention and control strategies in our region.

CONCLUSION

According to our study, surface epithelial tumors are most common among ovarian tumors followed by germ cell tumors and then sex cord-stromal tumors. Serous cystadenoma is the commonest benign while serous cystadenocarcinoma is the commonest malignant tumor. Mucinous subtype of surface epithelial tumors and germ cell tumors appear to be more common in our population as compared to the west. Moreover, ovarian cancer found to involve relatively younger age group in our region in contrast to west.

Thus this research illuminates the epidemiology of diverse ovarian tumors with respect to age in our Karachi region, which will assist in spreading awareness in the public about the disease especially about the age groups in which ovarian tumors are common. It will also help contriving screening programs by providing the age groups which need to be targeted.

Author's Contribution:

Concept & Design of Study:	Alfarah Irfan
Drafting:	Mohammad Salman Zafar, Shah Jabeen
Data Analysis:	Nazia Qamar, Nadeem Nusrat, Asadullah
Revisiting Critically:	Alfarah Irfan, Mohammad Salman Zafar
Final Approval of version:	Alfarah Irfan

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

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Original Article

Role of Echo in Cardiac Risk Assessment

Role of Echocardiography in Cardiac Risk Assessment of Patients at Risk of Cardiac Disease before Non-Cardiac Surgical Intervention

Saeed Ahmed[1], Rashed Mahmood[1], Khurram Shahzad Khan[1] and Fareed Khan[2]

ABSTRACT

Objective: In our study we have tried to find the effectiveness and role of echocardiogram in cardiac risk assessment of patients who were at risk of cardiac disease before non-cardiac surgery.

Study Design: Prospective observational study

Place and Duration of Study: This study was conducted at the Kashmir Institute of Cardiology, Mirpur AJK, from Jan 2018 to Jan 2020.

Materials and Methods: Patients planned for non-cardiac surgery were referred to our department for cardiac evaluation, based on presence of 1 or more cardiac risk factors we performed their echocardiogram to diagnose and risk stratify their cardiac risk.

Results: 135 patients were observed in our setup.

Conclusion: In our study we used echocardiogram as a diagnostic test in patients who were planned for non-cardiac surgery. After risk assessment we did echocardiogram in such patients and found out that echocardiography does changes the decision about surgery in more than 40% of the patients due to presence of previously undiagnosed cardiac disease which includes wall motion abnormalities and valvar anomalies. So our recommendation is that echocardiography should be a routine test in patients who have more than 1 cardiac risk factors.

Key Words: Non cardiac surgery, echocardiography

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INTRODUCTION

Non cardiac surgeries are done all over world, Cardiovascular mortality and morbidity during such surgeries is a special concern in patients who either have risk of cardiac disease or have cardiac disease. Guidelines by AHA provide information for management of such patient due to this reason mortality rate from undiagnosed cardiac disease have fallen across all forms of surgeries[1].

Several risk factor models have been used till date, one such risk index is revised cardiac risk index (RCRI). These risk factors included type of surgery, history of coronary artery disease, previous stroke, diabetes, chronic kidney disease.

In our study we used same parameters to assess the outcome of non-cardiac surgery[2].

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Presence of coronary artery Disease, hypertension, heart failure, vulvular heart disease, congenital heart disease, arrhythmias poses a risk for development of cardiac complications during non-cardiac surgery[2,3]. Use of beta blockers in chronic hypertensive patients undergoing non cardiac surgery also has shown beneficial[4].

High risk of cardiac complications was seen in patients with severe or critical aortic stenosis[5]. Patient with Mechanical valves are at high risk during non-cardiac surgery, they need anticoagulation to be maintained during surgery to prevent the risk of thromboembolism[6,7,8]. In patients above 50 years SVT and A. fibrillation was very common and incidence of SVT and A. fibrillation was related to higher 30 days mortality after non cardiac surgery[8].

Type of surgery is also very important factor in determining the risk, High risk surgeries included aortic and other vascular surgeries, while intermediate risk surgeries included abdominal and intrathoracic surgeries, head and neck surgeries, orthopedic surgeries[9].

In our study we used brief history, Basic clinical examination, baseline blood labs including renal function tests along with echocardiogram to evaluate the cardiac disease. In our study we used echocardiogram in all patients as a basic test for pre anesthesia cardiac evaluation.

MATERIALS AND METHODS

This is an observational study and was performed in Kashmir institute of cardiology from Jan 2018 to Jan 2020 after approval from ethical committee. Inclusion criterion was ages 0 to 85 years, planned for non-cardiac surgery, referred from our medical department so that a close follow up and final outcome can be determined easily, unable to exercise due to obesity or joint problems. Exclusion criterion was ages more than 85 years, low GCS or unconscious patients, unstable angina, decompensated heart failure, severe valvular disease, conduction abnormalities.

After a verbal consent patient who were fit according to inclusion criterion, a brief history about Diabetes, high blood pressure, renal disease, previous coronary artery disease and about medicine was taken. Echocardiogram was done in patients who were unable to run or walk on treadmill, patients were given three risk scores 1: high risk, 2: moderate risk 3: low risk based on the presence of risk factors like diabetes, high blood pressure, age more than 50 years, previous coronary artery disease, de-arranged renal functions and echocardiogram findings. Each of these parameters was given a single score.

RESULTS

In our study we found that around 5% of patients had HTN, 3% had diabetes and 3% had previous coronary artery disease for which they were taking medicine.

Table No.1: Distribution by age

		Frequency	Valid Percent	Cumulative Percent
Valid	0-5 years	10	7.4	7.4
	5-20 years	4	3.0	10.4
	21-40 years	12	8.9	19.3
	41-60 years	60	44.4	63.7
	61-80 years	41	30.4	94.1
	more than 80 years	8	5.9	100.0
	Total	135	100.0	

In this study we had around 44% patient with age around 41-60 years and 30% patients with ages 61-80 years. So 75% of our patients had an age of 41-80 years. In our study 53% of patients were male and 46.7% of patients were females.

In our study 30.8% of patients were planned for cholecystectomy, 28% were planned for Laprotomy and 17.9% patients were planned for prostate surgery.

Incidental cardiac anomalies were found in many patients, around 6% of patients had mild mitral regurgitations and were asymptomatic, 2.2% patients had mild aortic regurgitation, 4.4% patients had asymptomatic mild tricuspid regurgitation on echocardiogram.

Table No.2: Distribution by gender

		Frequency	Valid Percent	Cumulative Percent
Valid	Male	72	53.3	53.3
	Female	63	46.7	100.0
	Total	135	100.0	

Table No.3: Type of surgery planned

		Frequency	Valid Percent	Cumulative Percent
Valid	cholecystectomy	12	30.8	30.8
	laprotomy	11	28.2	59.0
	head and neck surgery	1	2.6	61.5
	hysterectomy	2	5.1	66.7
	BPH surgery	7	17.9	84.6
	hip fracture surgery	2	5.1	89.7
	testicular surgery	2	5.1	94.9
	hernia repair	1	2.6	97.4
	hemorrhoids	1	2.6	100.0
	Total	39	100.0	
Missing	System	96		
Total		135		

Around 5.9% of patients in this study had reduced ejection fraction and out of these 3.7% patients had severely reduced ejection fraction on echocardiogram. Around 2.2% of the patients in this study had more than moderate diastolic heart failure which was asymptomatic.

Table No.4: LVEF

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	LVEF 55-75%	125	92.6	94.0	94.0
	LVEF 45-54	3	2.2	2.3	96.2
	LVEF 30-44%	3	2.2	2.3	98.5
	LVEF 15-30%	2	1.5	1.5	100.0
	Total	133	98.5	100.0	
Missing	System	2	1.5		
Total		135	100.0		

Based on these findings it is clear that around 5-10% of the patients had severe LV systolic or diastolic heart failure which was an incidental finding on echocardiogram. Based on these finding patients were labelled as at risk patients for non-cardiac surgery, most of these patients were deferred from their elective non-cardiac surgeries and were put on cardiac medicine and advised to follow up after 3-4 weeks for reassessment of their clinical condition.

Table No.5: Diastolic dysfunction

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0	1	.7	.8	.8
	grade 1 DD	125	92.6	96.9	97.7
	grade 2 DD	2	1.5	1.6	99.2
	grade 3 DD	1	.7	.8	100.0
	Total	129	95.6	100.0	
Missing	System	6	4.4		
Total		135	100.0		

DISCUSSION

In a study by Canty they used echocardiogram for diagnosis if cardiac disease in emergency non cardiac surgery cases, in their study echocardiogram lead to change in diagnosis and management in more than 60% of the patients [9].

Although echocardiogram is not class 1 recommended for pre anesthesia evaluation of routine patients [10]. But this modality is low risk, noninvasive and cost effective, it is used as first line test before non-cardiac surgery in many hospitals in korea. In these comparative studies in korea they found echocardiography as a very suitable test to predict to risk of cardiac complications in patients who were planned for non-cardiac surgery. [9,10.11,12]. We also had similar findings in our study all those patients who had normal echocardiogram underwent low to moderate risk non cardiac surgery with no complications. So based on these international data and our data we can safely conclude that echocardiogram being a safe and noninvasive modality should be used for cardiac risk assessment of patient undergoing non cardiac surgery.

CONCLUSION

In our study we used echocardiogram as a diagnostic test in patients who were planned for non-cardiac surgery. After risk assessment we did echocardiogram in such patients and found out that echocardiography does changes the decision about surgery in more than 40% of the patients due to presence of previously undiagnosed cardiac disease which includes wall motion abnormalities and valvar anomalies. So our recommendation is that echocardiography should be a routine test in patients who have more than 1 cardiac risk factors.

Author's Contribution:

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

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Original Article

Hypertension in Anxious Patient

Inadvertent Labelling of Hypertension in Anxious Patient Especially during Panic Attack

Mohammad Mohsin Rana[1], Muhammad Usman Ghani[2], Muazzam Fuaad[1], Muhammad Saleem Akhtar[1], Adnan Afzal[1] and Sara Jabbar[1]

ABSTRACT

Objective: This study was designed to document that temporary rise in BP is a very common phenomenon in anxiety patients and is especially true during panic attack. We assessed all of our proclaimed hypertensive patients on standard Manifest Anxiety Scale to document anxiety as the underlying cause. By doing this we could stop the unwarranted labelling and un-necessary antihypertensive medicine.

Study Design: Observational cross section study

Place and Duration of Study: This study was conducted at the Rai Medical College Sargodha and Private Consultancies of the participants from January, 2020 to December, 2020.

Materials and Methods: Patients presenting for the treatment of HTN, 30-70 years old, were asked to answer MAS questionnaire. The weekly averages of home BP during symptomatic and non-symptomatic phase were recorded for 4 weeks.

Results: Out of 2739 consenting patients, 1340 completed the study. On formal MAS scale, in the 30s age group 70% had high score, 24% had middle and 6% had low score. In 40s figures were 58%, 12% and 30% respectively. In 50s group respective figures were 92%, 6% and 2%. In 60s group respective figures were 45%, 32% and 23%. In the final analysis all patients in 30s turned out to be normotensive, in 40s group only 11% were proven to have hypertension, in 50s age group 32% turned out to be genuine hypertensive and in 60s age group 67% proved to be hypertensives.

Conclusion: Anxiety and panic attack are the most common medical conditions which cause a temporary rise in BP. Every hypertensive must be thoroughly evaluated for anxiety. Perimenopausal transition must be considered as a cause of sudden shoot-ups in BP. Even in genuine hypertensives stress management plays very important role.

Key Words:

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INTRODUCTION

Hypertension (HTN) is one of the commonest diseases with considerable morbidity and mortality in middle age. Anxiety and panic attack are the most common medical conditions which cause a temporary rise in Blood Pressure (BP). Worldwide prevalence of HTN is expected to rise to 1·56 billion by 2025 with an upward trend in senior years. In developed economies the incidence curve has flattened but with the adoption of modern westernized life style it is increasing in developing countries.

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Apparently more common in developed countries (37·3% vs. 22·9%), the absolute number of hypertensive persons is more in underdeveloped countries due to much larger population, stretching already strained health care systems. Cardiovascular disease (CVD) is responsible for 30% of all deaths. Inspite of all the hype about hypertension and awareness about its complication, undiagnosed HTN and undertreated HTN is expected to cause a staggering 12.8% of the total deaths and another 4.4% disability-adjusted life years globally by 2025. (1)

Any sense of foreboding, uneasiness and fear will elicit a defensive response. When it becomes disproportionately debilitating, it is a disease and is called anxiety. Among mood disorders, Anxiety disorder or more precisely Generalized Anxiety Disorder (GAD) is most prevalent globally.[2] WHO declared it the 2nd leading cause of global disease burden.[3] The average prevalence of anxiety reported in different Pakistani studies is about 33.62%, with a point prevalence of 45.5 % in women and 21.7% in men. In a Karachi, 420 volunteers were surveyed, 39.4% females and 23.3% males qualified for anxiety and/or depression. In other Pakistani surveys, figure ranging

from 7 to 50% are quoted from general public surveys while for the primary care centers it rises to 21% to 57%.[5]

HTN label has important lifelong implications on the patients in terms of lifestyle and medicine. Certain standard prerequisites must be met, unfortunately, it's not so. Actually, the symptoms of anxiety and panic attack bring the patient to the clinic and BP is found to be high. During follow-up even though BP is within the normal range, credit goes to antihypertensive medicine and patient is advised to continue the medicine unnecessarily.

MATERIALS AND METHODS

The study was approved by the "Ethical review committee and Internal review board" of Rai Medical College, Sargodha. We offered all the patients presenting to the respective OPDs of all the participating physicians for the treatment of HTN between the ages of 30-70 years to enter into this study. Participants with hypertension were defined as those who reported that they were told by a doctor to have high blood pressure, and/or those who were currently taking BP medicines. Hypertension was defined as per standard.[6]

After securing informed consent and basic biodata, all were required to answer a standard Manifest Anxiety Scale (MAS) questionnaire by the participating psychiatrist. Patients who qualified for the diagnosis of anxiety and/or panic attack according to the standard proforma were enrolled in the study. Their score on MAS questionnaire was recorded.

These patients were asked to record their BP and heart rate at least once daily while totally comfortable without any symptoms and at least once while experiencing any unpleasant symptoms. BP medicines were continued. All were followed at weekly interval for 4 weeks and weekly averages were entered into the proforma. The research team modified the anxiolytic or antihypertensive medicine on case to case basis.

Inclusion Criteria: Qualifying the criteria of anxiety and history of HTN

Exclusion Criteria: Secondary hypertension, pre-terminal or terminal illness, acutely or seriously sick person, coronary heart disease, major psychiatric disorder

Study Design: Observational cross section study.

Study Period: From 1st January, 2020 to 31st December, 2020.

Sample Size: Convenient sampling technique was used. The study sample size was estimated by using a single population proportion formula which calculated with following assumptions: level of significance (Alpha) at 5%, power of test at 90% (1- Beta) and test value of the population proportion at 33%[5]. Given these assumptions the required sample size was determined to be 169. Keeping in mind 10% margin of error, the final sample size was determined to be 186 by WHO Sample size calculator.

Statistical Analysis: Data analysis was done on Microsoft Excel version 2016 and Statistical Package for Social Sciences software version 25. Descriptive statistics (i.e. percentages, mean and standard deviations) were used as the primary analytical methods.

RESULTS

2739 patients consented to volunteer for this study. 849 patients did not qualified for the participation as they did not had clinically significant anxiety when interviewed by the psychiatrist. 556 patients were lost in the follow-up, they didn't either produced the home monitoring record or did not completed all 4 visits.

Table No.1: Demographic Data

Total number of patients	n =1340	n = 482 (36%) males	n = 858 (64%) females
socioeconomics	High income 27 (2%)	Middle income 241 (18%)	Low income 1072 (80%)
Education years	<5 years 750 (56%)	5-10 years, 442 (33%)	College education 148 (11%)

Table No.2: Detail of groups with scores

MAS Score		High score	Middle score	Low score
30-39	456 (34%) of participants	319 (70%) (Mean = 30.8,Std .Dev. = ±2.7)	110 (24%) (Mean = 12.2, Std .Dev. = ±2.3)	27 (6%) (Mean = 2.6, Std .Dev. = ±1.6)
40-49	163 (12%) of participants	95 (58%) (Mean = 31.1,Std .Dev. = ±1.1)	20 (12%) (Mean = 11.9, Std .Dev. = ±2.0)	48 (30%) (Mean = 2.4, Std .Dev. = ±1.8)
50-59	348 (26%) of participants	320 (92%) (Mean = 29.1, Std .Dev. = ±0.9)	21 (6%) (Mean = 11.3, Std .Dev. = ±1.1)	7 (2%) (Mean = 2.4, Std .Dev. = ±0.6)
60 plus	373 (28%) of participants	168 (45%) (Mean = 27.9, Std .Dev. = ±1.3)	119 (32%) (Mean = 11.2, Std .Dev. = ±0.8)	86 (23%) (Mean = 2.5, Std .Dev. = ±1.1)

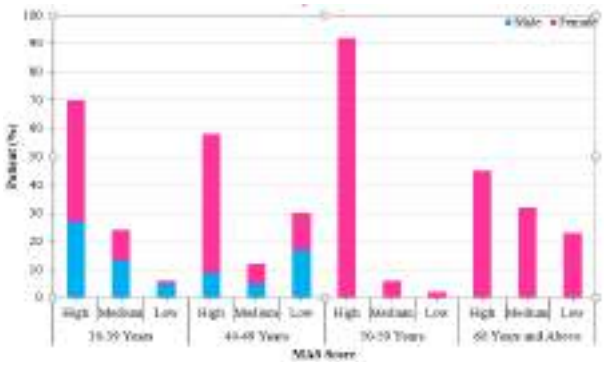

Figure No.1: Detail of gender with MAS Score

456 (34%) of the participant were in the 30s, 163 (12%) in 40s', 348 (26%) in 50s and 373 (28%) were in their 60s. On formal psychological interview as per proforma, in the 30s age group 319 (70%) participants had high score, 110 (24%) had middle and 27 (6%) had low score. In 40s figures were 95 (58%), 20 (12%) and 48 (30%) respectively. In 50s group respective figures were 320 (92%), 21 (6%) and 7 (2%). In 60s group respective figures were 168 (45%), 119 (32%) and 86 (23%) as summarized in Table 2 and graphically.

In the final analysis all patients in 30s turned out to be normotensive, their antihypertensive medicines were stopped and they were prescribed anxiolytics mainly on SOS basis. In 40s group only 18 (11%) were proven to have hypertension and were prescribed antihypertensive medicines. In this group, 95 (58%) scored high on MAS score, Serotonin Reuptake Inhibitors (SSRIs) and anxiolytics were prescribed for them. In 50s age group, 111 (32%) turned out to be genuine hypertensive, relevant medicine were continued or prescribed for them. As320 (92%) in this group scored high on MAS score, SSRIs and anxiolytics were prescribed. In 60s age group, 250 (67%) proved to be hypertensives and they were prescribed or asked to continue the medicine with dose and drug adjustment. 168 (45%) were prescribed SSRIs and anxiolytics on the basis of high MAS score. This is summarized in following Graph.

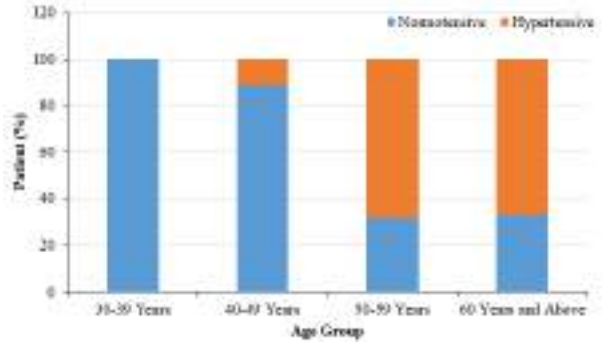

Figure No.2: Detail of Patients showing normotensive and hypertensive

DISCUSSION

In our study, out of 1340 patients, 64% were females, mainly from lower income and lower education group. We grouped them in age decades in each ascending order, 70%, 58%, 92% and 45% had high MAS score. This speaks loudly about the incidence of anxiety and its importance. The highest incidence in 50s can be explained on the basis of menopausal transition associated with high incidence of anxiety and depression.

With continuous public awareness campaigns by the medical community and media, checking Blood Pressure (BP) has become almost mandatory. Contrary to the popular view BP has no clinical symptoms of its own, symptoms are due to some other discomfort mostly anxiety and panic attack. False label of HTN is given during the symptomatic phase. During follow-up even though BP is within the normal range, credit goes to regular antihypertensive medicine. In our study, in 30s, all proclaimed hypertensive were proven wrong. Their BP remained in the normal range on anxiolytics only. Of our proclaimed hypertensives in forties, only 11% proved to be genuine cases. Even in 50s group, only 32% proved to be hypertensives. We had to prescribe anxiolytics to 92% of patients in this group.

Any severe pain, cocaine use, withdrawal of drugs of dependence or panic attack/ anxiety can cause a sharp rise in BP. Even hyperventilation typical of panic attack may precipitate a complex of symptoms mimicking pheochromocytoma. These facts are very well known for last thirty years.[7]

BP measurement even by trained clinicians and paramedics is often compromised due to well-known patient factors like diurnal variation, effect of physical activity, stimulant like caffeine, tobacco and alcohol intake. On the other hand, operator biases, poor technique in cuff application and low quality or wear and tear of apparatus, all contribute. [(8)] With widespread availability of the required gadgetry, Ambulatory or home BP monitoring has become a common practice but office reading are generally considered more reliable.[9]

One limitation of office BP recording is well known White Coat Effect (WCE) mediated through sympathetic. Mere presence of healthcare persons can cause a clinically significant elevation of >20 mmHg for SBP and >10 mmHg for DBP in a known hypertensive patient. It is mediated through sympathetic neuro-endocrine reflexes and leads to dose escalation or addition. This must be differentiated from White Coat Hypertension (WCH), encountered in 25-30% of office visits, usually in obese elderly women, where repeatedly only the office BP readings are above the reference range in a normotensive person while both ambulatory or home monitoring are within range. This intermediate stage has 2.5 time higher future chances of developing HTN. Masked Hypertension (MH) is the inverse of WCH where office BP readings are normal while ABPM and/or HBPM are high in persons not

taking any antihypertensive medications, it is associated with higher risk of target organ damage. [10]

Like many other multifactorial diseases, anxiety and hypertension have bidirectional cause and effect relationship. Sympathetic and renin angiotensin system activation is the link. It is associated with endothelial dysfunction, abnormal lipid metabolism, reduced renal blood flow, increased renal water and sodium retention, a sure recipe for HTN. The activation of hypothalamic-pituitary-adrenal axis is the second major response to any stress, steroid over-secretion further contributes to water and sodium retention. Anxious persons are much more likely to indulge in unhealthy lifestyle like dietary indiscretion, alcohol abuse, smoking, unwillingness for exercise and medicine. Knowing the diagnosis of HTN and feeling of some sinister disease looming around, these patients are much more likely to frequently visit emergency departments. [11, 12]

Just to quote the impact on health cost in USA, non-cardiac chest pain is the underlying cause for 50% of Emergency and 80% of Outpatient office visits. Repeated assessments fail to inspire any reassurances. [13]

The interface and gray areas between medical and psychiatric domains make it extremely challenging task especially in the background that very lucky ones have adequate interest, training or expertise in both fields. [14]

Targeting the possible mechanism shall be the rationale approach. One 2005 study published in American Journal of Hypertension documented that in acute hypertensive episode Diazepam was as effective as sublingual Captopril. [15]

We did not formally analyze but we had a strong impression that all these had far fewer spikes in BP and even dose was reduced in the majority. These figures argue strongly in favor of our hypothesis that every hypertensive must be thoroughly evaluated before starting the pharmacotherapy. Lifestyle modification must involve stress management and judicious anxiolytics. This is especially true in 30s and 40s. In 50s perimenopausal transition must be considered as a cause of sudden shoot-ups in BP. Even in genuine hypertensives stress management plays very important role.

CONCLUSION

Anxiety and panic attack are the most common medical conditions which cause a temporary rise in BP. Every hypertensive must be thoroughly evaluated for anxiety. Perimenopausal transition must be considered as a cause of sudden shoot-ups in BP. Even in genuine hypertensives stress management plays very important role.

Author's Contribution:

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

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Original Article

The Comparison of Physiology Learning in Undergraduate Medical and Dental Students

Learning of Physiology in Undergraduate in Integrated Curriculum

Sadaf Fatima[1], Syed Tousif Ahmed[2], Shazia Hashmat[2], Huma Salahuddin[2], Kevin Joseph Jerome Borges[3] and Syed Nudrat Nawaid Shah[3]

ABSTRACT

Objective: To study the difficulties and problems associated with learning of Physiology in undergraduate medical and dental students in integrated curriculum.

Study Design: Cross sectional study.

Place and Duration of Study: This study was conducted at the Ziauddin Medical College and Ziauddin Dental College, Ziauddin University, July 2017 to June 2018.

Materials and Methods: The study participants included 1st, 2nd, 3rd year medical students and 1st and 2nd year BDS students. There were 225 participants, 147 MBBS and 78 BDS students. A questionnaire was distributed to each medical and dental student. There were 23 items included in the questionnaire from why is Physiology hard for students to learn? The items were related to subject, teaching and learning of Physiology. The medical and dental students were asked to select a response for each item on like rt scale from 1 to 5.

Results: Regarding the Physiology learning responses, the comparison was done between MBBS and BDS students. A significant difference was found in factors including basic concepts (<0.001), use of scientific terms (0.01), covering large content in one lecture (0.01) and integration (0.002).

Conclusion: The medical and dental students identified the factors causing difficulties and problems in learning physiology and the reasons of these difficulties.

Key Words: Physiology, Teaching, Learning

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INTRODUCTION

To create 21st century physicians, the prime objective is to train future doctors and dentists who can effectively integrate the new sciences and technology into humane patient care[1]. Medical education must progress and develop because future doctors will come across patients in quite different health care circumstances from the present[2]. To meet the needs of medical education, numerous medical schools have started to design innovative medical curricula in their bachelor programs[2]. There is now increased emphasis on developing competencies and active learning strategies[3]. Curriculum integration of subjects is a significant strategy in medical education[4].

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Integration has essential importance in medical education because basic science learning placed in clinical context is considered more meaningful and relevant by students[5].

In the first two years of medical school, basic science knowledge forms a foundational framework for clinical skills[6]. An understanding of basic science concepts helps in learning the signs and symptoms of various diseases in the clinical years[7]. The retention of basic science concepts has a positive correlation with clinical knowledge[8]. In integrated curricula, basic science educators need to focus on their teaching content according to clinical relevance[9]. To more closely relate the basic and clinical sciences, early patient contact in the foundation years is provided simultaneously with basic science teaching[10]. For the competent medical practice, the understanding of applicability of basic science education in the establishment of diagnosis and treatment is critically important[11].

Physiology is one of the basic science subjects taught at undergraduate level in medical and dental professional education[12]. The importance of Physiology lies in its application in clinical practice[13]. In the recent innovative development of preclinical curricula, Physiology is facing changing trends in teaching. The employment of student centered learning methods has been found to be valuable in building of physiological concepts[14]. As Physiology learning is concerned with

understanding the dynamics and mechanisms of human body and it is required for good clinical practice, a questionnaire was designed to study the various aspects of Physiology learning. The objective of the study was to compare the difficulties and problems associated with learning of Physiology in undergraduate medical and dental students in integrated curriculum.

MATERIALS AND METHODS

The study design was cross sectional. The study was conducted at Ziauddin Medical and Ziauddin Dental College. The study participants included 147 MBBS students and 78 BDS students. The participants were selected by convenient sampling technique. The duration of the study was one year, from July 2017 to June 2018. The study was approved by Ethics review board of Ziauddin University. The participants were enrolled in the research study after getting the ethics approval. Informed consent was obtained from each participant.

To find out the difficulties and problems associated with Physiology learning, the questionnaire was distributed to 147 medical and 78 dental students. The questionnaire contained 23 items from why is Physiology hard for students to learn? The medical and dental students were asked to select a response for each item on likert scale from 1 to 5. The MBBS and BDS students provided their perspective about the difficulties and problems in learning physiology and the reasons of these difficulties. The questionnaires were collected and the data was analyzed.

The data were analyzed using SPSS version 20. The results of the quantitative data were expressed as mean ± SD. The comparison of qualitative data was expressed by Chi Square test. In all statistical analysis, only p-values ≤ 0.05 were considered significant.

RESULTS

There were 147 MBBS and 78 BDS students in the study. The mean age of students was 19.3± 1.4 years (male 34% & female 66%). The group comparison is shown in table I. Figure I showed Physiology learning response comparison of groups on the basis of individual items 1 to 12 in the questionnaire. Figure II showed score comparison of groups based on individual items 13 to 23.

Table I showed comparison of Physiology learning responses between MBBS and BDS students. It included items related to basic concepts, new researches in medical science, scientific terms, interaction between systems, well defined physiology syllabus, understanding physiology, commitment of time, case study, passing physiology by using short books, teaching by using concepts, correlating different topics, guiding students about learning resources, using graphs and flow charts, integration of physiology teaching, covering large content in lecture, responding to student questions and use of active learning methods. The frequency, percentage and chi square value for each item is mentioned in the table.

In figure 1, the x-axis showed the 12 individual items in Physiology learning response section and the y axis showed the individual score of each item.

In figure 2, the x-axis showed the 11 individual items in Physiology learning response section and the y axis showed the individual score of each item.

Table No.1: Comparison of Physiology learning response between MBBS and BDS students

Q.No.	n	Program	Frequency			Percentage			Chi Square
			A	B	C	A	B	C	
1	225	MBBS	95	22	30	57.6	88	85.7	<0.001
		BDS	70	3	5	42.4	12	14.3	
2	224	MBBS	125	13	8	63.5	76.5	80	0.336
		BDS	72	4	2	36.5	23.5	20	
3	225	MBBS	116	14	17	63.7	58.3	89.5	0.06
		BDS	66	10	2	36.3	41.7	10.5	
4	225	MBBS	109	27	11	65.3	62.8	73.3	0.761
		BDS	58	16	4	34.7	37.2	26.7	
5	225	MBBS	125	16	6	62.2	88.9	100	0.014
		BDS	76	2	0	37.8	11.1	0	
6	225	MBBS	122	19	6	64.6	70.4	66.7	0.835
		BDS	67	8	3	35.4	29.6	33.3	
7	225	MBBS	131	9	7	64.2	69.2	87.5	0.38
		BDS	73	4	1	35.8	30.8	12.5	
8	225	MBBS	132	10	5	63.8	83.3	83.3	0.247
		BDS	75	2	1	36.2	16.7	16.7	
9	225	MBBS	119	21	7	63.3	75	77.8	0.347
		BDS	69	7	2	36.7	25	22.2	
10	225	MBBS	100	28	19	62.5	65.1	86.4	0.08

		BDS	60	15	3	37.5	34.9	13.6	
11	225	MBBS	58	25	64	67.4	59.5	66	0.66
		BDS	28	17	33	32.6	40.5	34	
12	225	MBBS	130	12	5	64.8	63.2	83.3	0.632
		BDS	70	7	1	35.2	36.8	16.7	
13	225	MBBS	77	42	28	66.4	71.2	56	0.238
		BDS	39	17	22	33.6	28.8	44	
14	225	MBBS	71	35	41	70.3	67.3	56.9	0.18
		BDS	30	17	31	29.7	32.7	43.1	
15	225	MBBS	113	19	15	62.8	67.9	88.2	0.104
		BDS	67	9	2	37.2	32.1	11.8	
16	225	MBBS	116	19	12	64.8	90.5	48	0.01
		BDS	63	2	13	35.2	9.5	52	
17	225	MBBS	107	22	18	63.3	73.3	69.2	0.515
		BDS	52	8	8	36.7	26.7	30.8	
18	225	MBBS	93	25	29	72.1	67.6	49.2	0.009
		BDS	36	12	30	27.9	32.4	50.8	
19	225	MBBS	126	10	11	63.3	83.3	78.6	0.206
		BDS	73	2	3	36.7	16.7	21.4	
20	225	MBBS	126	16	4	62.4	88.9	100	0.059
		BDS	76	2	0	37.6	11.1	0	
21	225	MBBS	115	20	12	62.3	74.1	85.7	0.122
		BDS	69	7	2	37.7	25.9	14.3	
22	225	MBBS	117	20	9	64.6	60.6	90	0.31
		BDS	64	13	1	35.4	39.4	10	
23	225	MBBS	61	44	42	66.3	65.7	63.6	0.939
		BDS	31	23	24	33.7	34.3	36.4	

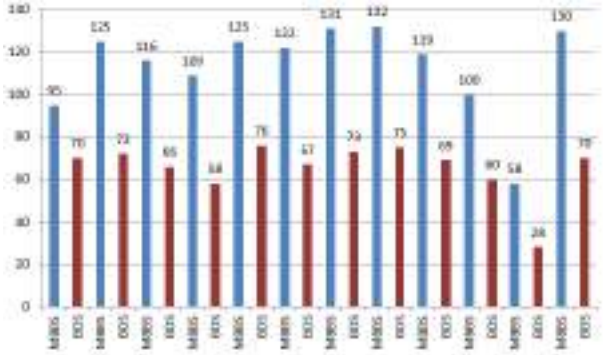

Figure No.1: The comparison of individual Physiology learning response items 1 to 12 between MBBS and BDS students

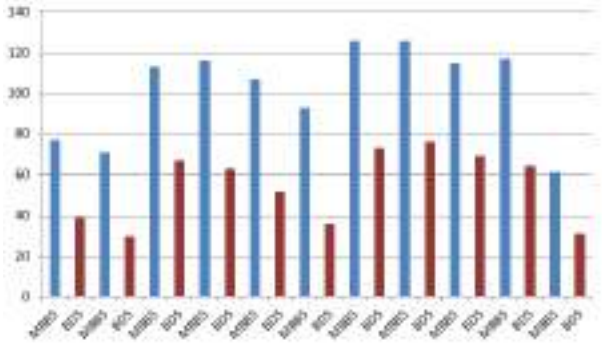

Figure No. 2: The comparison of individual Physiology learning response items 13 to 23 between MBBS and BDS students

DISCUSSION

In this study, difficulties and problems related to Physiology learning were revealed. As shown in Table I, there was a significant difference in Physiology learning response items 1, 5, 16 and 18 between MBBS and BDS students. Item 1 was related to knowledge of basic concepts of physics and chemistry. The finding related to item 1 in our study is consistent with Michael[15]'s study. In this study, it is mentioned that the ability to employ something learned in one context in the other context, is a difficult task, and this accounts for students' incapability to use their prerequisite knowledge (chemistry and physics) in learning physiology. In Michael's study the physiology faculty was asked to fill a questionnaire regarding difficulty in studying physiology. In a study done by Calthorpe et al[16] students were asked to identify the difficult topics according to the modules. Item 5 was regarding the ability to understand the scientific and medical terms. In our study, there was a marked difference in MBBS and BDS students regarding the understanding of scientific terms. Item 16 was related to teachers presenting large subject content in one lecture[17]. It is evident that active learning, student-centered strategies to teaching physiology work better than passive strategies[18]. Item 18 was regarding the integration of Physiology teaching with other skills. For preparing

students it is important for educators to use teaching strategies that makes the students involve in active learning, which increases their motivation, enhances their thinking, deepens learning and builds up collaboration in the classroom[19]. Although no single teaching method ensures a thorough understanding of a topic, various methods are being used in many institutes to reinforce lectures in teaching physiology, such as case-stimulated learning, problem-based learning and patient-centered learning[19]. In rest of the table items, there was no significant difference observed.

Physiology is a segment of core curriculum for all students studying in medicine and related professions[20]. It needs to be studied effectively so as to be placed in the context of disease when the students graduate and practice in the community[21]. The medical students rated the discipline of Physiology as one of the most difficult and toughest course[20]. Causal reasoning, use of graphs and sectionalize were remarkably important than any other aspect of teaching in making physiology hard to learn[15].

There is a remarkable difference between teaching and learning. In reality, there is excessive teaching and inadequate learning[22]. Teaching is not only passing the information to students but it is to make students understand the content that is taught. Physiology is a complex and continuously evolving subject, and teaching it, is not an easy task[23]. A substantial body of knowledge about cognitive processes and teaching and learning methods has gathered over the years[23]. Even with an active learning approach, physiology is hard to learn[22].

The duty of Physiology teachers is to help students learn the subject in an effective way. An urgent need of reforms is required to improve the teaching efficacy of human physiology in medical schools.

CONCLUSION

The medical and dental students identified the factors causing difficulties and problems in learning physiology and the reasons of these difficulties.

Author's Contribution:

Concept & Design of Study:	Sadaf Fatima
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Data Analysis:	Huma Salahuddin, Kevin Joseph Jerome Borges and Syed Nudrat Nawaid Shah
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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

Assessment of Diabetes Mellitus effect on Hearing, Mirpur AJK

Diabetes Mellitus effect on Hearing

Faisal Bashir[1], Arshid Mahmood[3], Tahmeena Sarfraz[4] and Asnad[2]

ABSTRACT

Objective: The objective of this study to evaluate Diabetes Mellitus effects on Hearing, Mirpur AJK.
Study Design: Cross-sectional study
Place and Duration of Study: This study was conducted at the department ENT Mohtarma Benazir Bhutto Shaheed Medical College Mirpur AJK and Department of Obstetrics and Gynaecology Mohi-ud-Din Medical College, Mirpur, AJK from January 2018 to August 2019.
Materials and Methods: Total 220 people (110 cases and 110 controls) were selected and analyzed in this study. All the subjects were divided into two groups: Group A (all patients with Diabetes) and Group B (persons without diabetes). A detailed history was taken about hearing loss, onset, duration of diabetes and associated symptoms Blood samples were collected for both groups centrifuged for thirty minutes and isolate serum which was biochemically analyzed. Blood glucose, lipid profile, urea and uric acid were estimated for both groups. Microlab 300 was used for estimation of biomolecules and Merk company kits were used. SPSS for Windows version 20 was employed for all statistical analyses.
Results: Cases type 2 Diabetic Mellitus 82.7% was found in Group A and remaining cases of group A was type 1 DM. The result showed that Sensori-neural hearing was significantly higher in group A as compare to Group B. In group A, 47.6 % was found Sensori-neural hearing and Group B 5.45%. Two sided hearing problem with SNHL (79.09%) was in found majority of the subjects. The result showed that hearing difficulty was found 72.5% two sided in diabetic patients. In pregnant women 23 % found Sensori- neural hearing with diabetic Mellitus.
Conclusion: Sensorineural hearing loss is high rate in diabetic mellitus patients as compare to non-diabetic control. There is more probability in the age of forty-five to sixty-two for men and women and the duration of diabetes Mellitus is more, there will more effects of hearing loss so diabetes Mellitus is one of risk factor.
Key Words: Sensorineural hearing loss, Diabetic mellitus, Pregnancy

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INTRODUCTION

Deficiency of insulin caused diabetes Mellitus which is clinical syndrome and considered as hyperglycemia. In type 2 diabetes mellitus, sensorineural hearing loss was 80% in study.[1] another observation showed 66% rate as prevalence.[2] among non-elderly people, diabetes and sensorineural hearing loss was 45%.[3] Diabetes related hearing loss is hypothetical it showed by pathophysiological description.

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Different autonomic functions and marginal sensation are affected by diabetic neuropathies.[2,4] Vasculature or the neural system of the inner ear was damaged and injured by diabetes with accompany pathological changes. Combination of angiopathic and neuropathic affects are produced by diabetes due to it pathogenicity. Sorbitol is produced from glucose. Sorbitol gathering is concerned in neuropathy by producing a reduction in my inositol quantity. Abnormal phosphoinositide metabolism is found due to diabetes and it is also caused reduce Na+/k+ ATPase activity.[2] Autopsied patients with diabetes showed vascular or neurological connection evidence (internal auditory artery sclerosis, basilar membrane thicker wall and also striavascularis wall, spiral ganglion atrophy and cochlear nerve demyelination).[5] In patients with diabetes showed outer hair cells loss.[6] 0.3% of deafness and 1% of diabetes association found. [7] Cochlear or an eight nerve lesion is used for sensorineural. Serum creatinine reflects hearing loss with improvement of disease. In the inner ear, micro-angiopathic disease found. Disabling hearing loss in adults was 16% prevalence rate found According to WHO and Nelson et al.[9] Estrogen and progesterone are increased in pregnant women significantly and these changes alter the electrolyte which ultimately increased extracellular

fluid volume.[10-12] The objective of this study to evaluate Diabetes Mellitus effects on Hearing, Mirpur AJK.

MATERIALS AND METHODS

This study was conducted in the department ENT and Biochemistry Department of Mohtarma Benazir Bhutto Shaheed Medical College Mirpur AJK and Sugery and Obstetrics and Gynaecology Department of Mohdud din Medical College, Mirpur, AJK from January 2018 to August 2019. Total 220 people (110 cases and 110 controls) were selected and analyzed in this study. All the subjects were divided into two groups: Group A (all patients with Diabetes) and Group B (persons without diabetes). A detailed history was taken about hearing loss, onset, duration of diabetes and associated symptoms Blood samples were collected for both groups centrifuged for thirty minutes and isolate serum which was biochemically analyzed. Blood glucose, lipid profile, urea and uric acid were estimated for both groups. Microlab 300 was used for estimation of biomolecules and Merk company kits were used. SPSS for Windows version 20 was employed for all statistical analyses.

RESULTS

Out of total 110 patients in each group. Cases type 2 Diabetic Mellitus 82.7% was found in Group A and remaining cases of group A was type 1 DM. The result showed that Sensori- neural hearing was significantly higher in group A as compare to Group B. In group A ,47.6 % was found Sensori- neural hearing and Group B 5.45%. Two sided hearing problem with SNHL (79.09%) was in found majority of the subjects. The result showed that hearing difficulty was found 72.5% two sided in diabetic patients. In pregnant women 23 % found Sensori- neural hearing with diabetic Mellitus.

Table No.1: Participant characteristics

	Diabetic Patients (n=110)	Non-Diabetic Control (n=110)
Age (years)	40.4 ± 10.2	40.7 ± 10.3
Male /Female (%)	55/55	55/55
Body weight (Kg)	69.8± 10.8	67.7± 11.2
BMI (kg/m2)	24.6± 2.6	24.4± 2.5

Table No.2: The Effects of Diabetes Mellitus on Hearing

Diabetic Patients (n=110)	Non-Diabetic Control (n=110)
Sensori- neural hearing	
91 (82.72%)	6 (5.45%)
Two sided hearing problem with SNHL	
87 (79.09%)	3 (2.7%)
Hearing Difficulty	
79 (71.81%)	1 (0.9%)

DISCUSSION

Jordao found association between hearing loss and diabetes mellitus in 1857.[13] Maia and de Campos also found diabetes mellitus and hearing loss found association at bibliographic review report.[14] In the current study Patients' sex to reduce its confusing role.[15] In the epidemiological study, hearing loss is effected by Cigarette smoking by Cruickshanks et al.[16] This study was conducted in the department ENT and Biochemistry Department of Mohtarma Benazir Bhutto Shaheed Medical College Mirpur AJK and Sugery and Obstetrics and Gynaecology Department of Mohdud din Medical College, Mirpur, AJK from January 2018 to August 2019. Total 220 people (110 cases and 110 controls) were selected and analyzed in this study. All the subjects were divided into two groups: Group A (all patients with Diabetes) and Group B (persons without diabetes). A detailed history was taken about hearing loss, onset, duration of diabetes and associated symptoms Blood samples were collected for both groups centrifuged for thirty minutes and isolate serum which was biochemically analyzed. Blood glucose, lipid profile, urea and uric acid were estimated for both groups. Microlab 300 was used for estimation of biomolecules and Merk company kits were used. SPSS for Windows version 20 was employed for all statistical analyses.

In the HTN there is association with hearing loss.[17] In the study of Helzner et al, they found that there is association of toxic drug and noise of occupation is closely linked with hearing loss[15] In the study of Kakarlapudi, Sawyer and Staecker , they find some relationship and association of Diabetes Mellitus and Sensorineural Hearing Loss in the United States.[18] Deficiency of insulin caused diabetes Mellitus which is clinical syndrome and considered as hyperglycemia. In type 2 diabetes mellitus, sensorineural hearing loss was 80% in study. Another observation showed 66% rate as prevalence. Among non-elderly people, diabetes and sensorineural hearing loss was 45%. Diabetes related hearing loss is hypothetical it showed by patho-physiological description. Different autonomic functions and marginal sensation are affected by diabetic neuropathies. Vasculature or the neural system of the inner ear was damaged and injured by diabetes with accompany pathological changes. Combination of angiopathic and neuropathic affects are produced by diabetes due to it pathogenicity. Sorbitol is produced from glucose. Sorbitol gathering is concerned in neuropathy by producing a reduction in myoinositol quantity. Abnormal phosphoinositide metabolism is found due to diabetes and it is also caused reduce Na+/k+ ATPase activity. Autopsied patients with diabetes showed vascular or neurological connection evidence (internal auditory artery sclerosis, basilar membrane thicker wall and also striavascularis wall,

spiral ganglion atrophy and cochlear nerve demyelination).In patients with diabetes showed outer hair cells loss. 0.3% of deafness and1% of diabetes association found. Cochlear or an eight nerve lesion is used for sensorineural. Serum creatinine reflects hearing loss with improvement of disease. In the inner ear, micro-angiopathic disease found. Disabling hearing loss in adults was 16% prevalence rate found According to WHO and Nelson et al. Estrogen and progesterone are increased in pregnant women significantly and these changes alter the electrolyte which ultimately increased extracellular fluid volume. In the diabetic middle-age men have high prevalence rate of hearing loss as compare to non-diabetic middle-aged men, reported by Sakutaet al[19]. Out of total 110 patients in each group. Cases type 2 Diabetic Mellitus 83% was found in Group A and remaining cases of group A was type 1 DM. The result showed that Sensori- neural hearing was significantly higher in group A as compare to Group B. In group A, 47.6 % was found Sensori- neural hearing and Group B 5.3%. Two sided hearing problem with SNHL (79%) was in found majority of the subjects. The result showed that hearing difficulty was found 72.5% two sided in diabetic patients. In pregnant women 23 % found Sensori- neural hearing with diabetic Mellitus. In the study of Dalton et al., they found high rate of hearing loss incidence in diabetic patients as compare to control but they did not found significant association.[20] The role of ageing and DM progression should be carefully monitored for hearing loss.[21] In the present study, we found that there closely association of Diabetes Mellitus and Sensorineural Hearing Loss but statically was not significant.

CONCLUSION

Sensorineural hearing loss is high rate in diabetic mellitus patients as compare to non-diabetic control. There is more probability in the age of forty five to sixty two for men and women and the duration of diabetes Mellitus is more, there will more effects of hearing loss so diabetes Mellitus is one of risk factor.

Author's Contribution:

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Final Approval of version:	Faisal Bashir

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

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Original Article

Analysis of Serum Ferritin Level in Patients of Decompensated Chronic Liver Disease

Shabir Ahmed Orakzai[1], Mohibullah Khan[1] and Salman Hakim[2]

ABSTRACT

Objective: To observe the different levels of ferritin among NAFDL and conducted to find a significant relationship between them.

Study Design: Observational study.

Place and Duration of Study: This study was conducted at the Pakistan Railway Hospital Rawalpindi within 1 year from Jan 2019 to Jan 2020.

Materials and Methods: We select 30 participants who undergone through NAFLD/NASH biopsy for the collection of their demographic, histological, laboratory data. All the patients were selected to form the Hepatology and gastroenterology department of Pakistan railway hospital Rawalpindi hospital.

Results: With the help of the Pearson formula, we found a significant relationship (0.011) between ferritin and the male gender. This value proves the statement that men had increased ferritin levels as compared to the female population.

Conclusion: Our studies conclude that in young people with 0 levels of obesity, ferritin serum is not only a single way to find disease severity.

Key Words: Serum ferritin, Histological analysis, Steotosis grade, fibrosis stage, liver biopsy, 0 Obesity

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INTRODUCTION

Globally chronic liver due to cirrhosis has a high mortality rate[1]. It has no specific signs or symptoms and only diagnosed incidentally during a medical examination. At the initial stage, cirrhosis is usually compensated. Cirrhosis at the compensated stage is harmless and can be treated with a high life expectancy[2]. But due to the asymptomatic at the initial stage, cirrhosis eventually reaches to decompensated form. Decomposition of compensated cirrhosis is defined as a situation in which ascites occurs very first time along with the oesophageal variceal bleeding, hepatic encephalopathy[3]. Some patients report an increase in bilirubin concentration during decomposition[3,4]. At the stage of decay, patients need rapid medical attention and frequent medical assistance. Mortality and morbidity rate risen to 80% reached its peak in a year after dissolution[5].

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Mostly the death rate of chronic liver disease is noted due to decompensated cirrhosis This disease causes acute, chronic liver failure, a condition in which critical hepatic decomposition caused the liver failure with cirrhosis[6]. Different studies explore the relationship between chronic liver disease and cirrhosis. They assume that chronic liver sometimes ends in the development of cirrhosis[6]. Decompensated cirrhosis is usually correlated with a viral infection, drug and alcohol consumption, ischemic hepatitis. These factors worsen the patient's situation and result in extrahepatic organ failure[7].

Due to the absence of laboratory test, imaging, liver biopsies, lack of standardized definition total number of cirrhosis cases are unknown[8]. Meanwhile, in 2017, in the whole world, 440,000 deaths were reported due to cirrhosis. The male population has more encounters with cirrhosis as compared to the female population (66.7% and 33.3%, respectively). Globally in 2017, death ration of cirrhosis increased from 1.9% to 2.4%. The high rates of death are reported in undeveloped countries due to their weak economy and inaccessible health care opportunities[9].

Some researchers demonstrate that nonalcoholic fatty liver disease (NAFLD) is a second major prevalent cause of cirrhosis. In the future, it will be the leading cause of cirrhosis and liver transplantation[10]. It arises due to the high obesity rate and increases the risk of cardiovascular disease, diabetes mellitus, and chronic kidney disease along with cirrhosis. The nonalcoholic fatty disease creates complications like hepatocellular

carcinoma that leads to death[11,12]. The pathogenesis of nonalcoholic fatty acid is still not defined yet.

In previous years, researchers notice ferritin serum for the best possible prediction for the NASH versus simple steatosis[13,14]. In one-third of the NAFLD patients, iron overload was originated as a significant issue[15]. Ferritin is an acute-phase reactant in NAFLD, but it is not a single predictor of disease. Many researchers define an association of serum ferritin with hepcidin level (a hormone that regulates the iron)[16]. Some other studies found a relationship of serum ferritin with hepatic iron in NAFLD patients[16]. Still, significant literature is missing to define a correlation between serum ferritin and NAFLD. This study aims to observe the different levels of ferritin among NAFDL and conducted to find a significant relationship between them.

MATERIALS AND METHODS

This study was conducted in Islamic international college Hepatology department in 1 year. We select 30 participants who undergone through NAFLD/NASH biopsy for the collection of their demographic, histological, laboratory data. All the patients were selected to form the Hepatology and gastroenterology department of Pakistan railway hospital Rawalpindi hospital. For better results, we asked senior hepatologists to confirm the severity of disease among patients chosen and recommend us for biopsy patients so that we further conduct a study for the evaluation of abnormal liver and biopsies. Senior radiologists conducted all the liver biopsies through ultrasonography. The results were also sent to the lab for further processing. During the investigation, if large fat vacuoles were found in liver parenchyma and had any impacts on the nuclei border of the cells, then it was counted in fatty liver disease. Affected hepatocytes, less than 33%, were considered as grade 1, whereas 33-60% affected hepatocytes were marked into category 2. For class 3, we prefer changed hepatocytes higher than 66%. This grading score was selected from the Brunt et al. study[17].

After the biopsy, serum ferritin was computed through an enzyme-linked immunosorbent assay (ELISA) test in which we further observed monoband and unstable angina. These readings were obtained within two weeks of biopsy. For analyzing serum iron and total iron-binding capacity, we used colorimetric. Both testings were administered at a parallel timeline. For a reasonable understanding of complete iron-binding, transferrin saturation was also noticed. All those victims who lack NAFLD in their chronic liver disease were avoided from the research. Patients have Hepatitis B or C, any rheumatologic disorders, using any iron supplements, access consumption of alcohol, or having any infectious disease were excluded from the research. Patients who are already using any medication for fatty liver disease at the time of studies, and patients using steroids, methotrexate, and tamoxifen and any other medicines that trigger the fatty liver disease among them were also excluded from the research. Only male participants were selected to check the validity of previous researches. All the young NAFLD patients were referred for the biopsy. All the patients underwent laboratory testing for measuring, hepatic, metabolic, and hematologic readings. A lipid test was also conducted on the selected population. For the formulating correlation in results, we measured blood pressure, body weight, and height of all patients.

All the data was measured through SPSS 23.0. One sample Kolmogorov test, t-test, and Pearson coefficient of Correlation were applied to the gathered information. For this study, p-value, 0.05, is supposed as significant[18].

RESULTS

A total of 30 biopsy proven NAFLD male patients were selected for the research. Recent studies show a high ratio of NAFLD, so we chose only male patients with a mean age of 37.9 years. After measuring the height and weight of patients, we get an average of 26.6 BMI in the study. Data was divided into four groups; mild, moderate, severe, and no steotoheptic for further laboratory testing. We observed 19 mild cases, four moderate, five non-steotoheptic. In contrast, only two severe cases were found.

Table No.1: Demographic and histological analysis of Participants[18]

Characteristics	Severe Steotoheptic 2	Moderate Steotoheptic 4	Mild Steotoheptic 19	No Steotoheptic 5	All patients 30
Age mean	44.5 ± 17.6	32.75 ± 7.4	39.15 ± 12.7	34.8 ± 14.8	37.93 ± 12.5
Male sex (n%)	0	3 (75%)	13 (68.4%)	1 (20%)	17 (56.7%)
BMI mean (kg/m2)	29 ± 1.4	25 ± 1.8	26.8 ± 3.7	25.3± 8.3	26.45 ± 4.4
AST (IU/L)	112 ± 110	79.2 ± 34.7	49.8 ± 25.5	31.6± 20.7	54.8 ±37.7
ALT (IU/L)	151 ± 115.9	134.3 ± 92.2	71.1± 37.9	46.2± 29.3	85.7 ± 57.1
ALP (IU/L)	233.5 ± 89.8	204.5 ± 29.7	205.6± 75.8	338.4± 154.9	229.4 ± 98.7
Serum Ferritin (ng/mL)	241.6 ± 146.2	268.5 ± 61.8	212.1± 236	88.0 ± 106	200.8 ± 200.6
Fasting blood sugar (mg/dL)	225 ± 193	179 ± 153.3	95.3 ± 26.1	94.8 ± 13	115 ± 76.7

After a complete analysis, we found 43.3% patients at 0 stage, 10% cases at stage 1, 26.7% cases at stage 2. For stage 3 and 4 ratios were comparatively low (13.3% and 6.7% respectively).

Coming towards the steotoheptic analysis, we found 16.7% cases with no steotoheptic, 13.3% cases of moderate, and only 6.7% of severe steotoheptic. The ratio of mild cases was high (63.3%), where the disease was at its initial stage.

Among the selected population, in 36.3% ferritin level was above 200 ng/L. At the same time, 45% of ferritin saturation was found among the people. With the help of the Pearson formula, we found a significant relationship (0.011) between ferritin and the male gender. This value proves the statement that men had increased ferritin levels as compared to the female population.

Table No.2: Correlation among serum ferritin with histological examination[28]

Variables	Pearson correlation	p-value
Age	0.296	0.112
BMI	-0.032	0.869
AST	0.039	0.839
Cholesterol	-0.150	0.429
ALP	-0.351	0.057
Fasting plasma glucose	0.057	0.763
ALT	0.096	0.615
Triglycerides	-0.160	0.399
Transferrin saturation	0.312	0.093

DISCUSSION

We found no significant correlation between histopathological findings, especially stages, and with ferritin serum. An increase in the age of age had a severe impact on NAFLD. All the younger patients in our studies had mild and moderate, which was against our expectations. In the past, many studies were conducted to analyze the serum ferritin level among NAFLD[19,20]. In many studies, researchers demonstrate an association of high serum ferritin with severe histological disorders of the liver in NASH instead of iron overload[21]. A survey conducted by Kowdly observed an association of serum ferritin with a high risk of NAFLD. In their study, they found that the use of patients with metabolic syndrome had hight predatory liver fibrosis because of their higher serum level (>1.5 scales)[22].

A study conducted by Manousou explored an association of fibrosis with serum ferritin and BMI. They argued that increase BMI rate and change in ferritin levels cause adverse effects on fibrosis, which lobular inflammation among the NAFLD patients[23].

Meanwhile, retrospective study of Angulo did not find any significant relationship between ferritin with any liver fibrosis grade. They further argued that serum ferritin does do not affect the accuracy of non-invasive liver fibrosis. They also stated that the inclusion of serum ferritin could not explain the improvement in the accuracy rate. Thus they conclude serum ferritin had limited accuracy for the diagnosis and categorization of NAFLD patients[24].

A cohort study conducted in Japan depicts that other factors like age, sex, and metabolism of patients are the obstacles in the predictive test of liver fibrosis through serum ferritin. They further examine the association of independent serum ferritin with steatosis grade and fibrosis stage but unable to find its influence on predictive values of liver fibrosis[25].

In correspondence to these studies, we were also unable to find a significant association of serum ferritin with histological grades and stages. One of the reasons of insignificance among variables is the minimal population of our research. Only 30 participants were referred to as the biopsy and meet inclusion criteria at the time of examination. We had limited exposure with the elder age group due to their physician prohibition. We were unable to include them in studies. They might have increased risk of complications, so they were not suggested for biopsy and treated with comorbidities and using anti platelet medications at the time of research. Another reason for the insignificant relation could be the younger age of our participants with healthy BMI. Obesity is a factor that affects the iron profile. There is a possibility that a significant relationship will be found among young anemic NAFLD patients because anemia affects the iron profile.

CONCLUSION

Our studies conclude that in young people with 0 levels of obesity, ferritin serum is not only a single way to find disease severity. With a unique marker of ferritin, it's hard to find relevant information regarding the histology of NAFLD.

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Author's Contribution:

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Data Analysis:	Mohibullah Khan, Salman Hakim
Revisiting Critically:	Shabir Ahmed Orakzai, Mohibullah Khan
Final Approval of version:	Shabir Ahmed Orakzai

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

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Original Article

Protective Effect of L-Arginine on Diclofenac Mediated Renal Toxicity in Adult Albino Rats

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ABSTRACT

Objective: The objective of this study is to observe the protective effect of L-arginine in the Diclofenac sodium in experimental animal study.

Study Design: An experimental study

Place and Duration of Study: This study was conducted at the Institute of Bio Medical Sciences (IBMS) with the cooperation of Dow Diagnostic Research and Reference Laboratory (DDRRL) in Dow University of Health Sciences (DUHS), Ojha campus from December, 2013 to January 2014.

Materials and Methods: Forty adult albino rats weighing 200 ± 20 gms were used and divided into four groups. The rats in the control group A,(n=10) each were given intra-muscular injection, one cc of physiologic saline. The second group B,(n=10), was given Diclofenac sodium 2 mg/kg body weight, intra-muscular. The rats in the third group C,(n=10) were given Diclofenac sodium 2mg/kg by intra-muscular injection and L-arginine, 1mg/kg of body weight, by feeding tube. The fourth group D,(n=10) was given L-arginine, with the ratio of 1mg/kg of body weight, by feeding tube orally. Gross and histological changes were observed in the proximal convoluted tubules (PCT) of the kidney of albino rats, after completion of the two weeks treatment.

Results: The result of present study revealed that diclofenac sodium significant decrease in body weight in adult albino rats was after 2 weeks treatment with in a single daily dose of 2mg/kg intra muscular. There were changes in absolute kidney weight, cortical thickness of kidney and diameter of proximal convoluted tubules. Treatment with L-arginine in a daily dose of 1mg/kg body weight, partially prevented the Diclofenac sodium induced damage of proximal convoluted tubules. L-arginine alone in same daily dose had no adverse effect on kidney in young albino rats.

Conclusion: Diclofenac sodium, an NSAID induces nephrotoxicity and L-arginine when given simultaneously partially protects the kidneys from its harmful effects.

Key Words: Diclofenac sodium, L-arginine, proximal convoluted tubules

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INTRODUCTION

Diclofenac sodium, belongs to NSAIDs family, manifests its analgesic and anti-inflammatory activities by inhibiting cyclooxygenase pathway of prostaglandin synthesis.[1]

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As a consequence of its anti-inflammatory and analgesic activities, it has been recommended for pain management in various inflammatory disorders like ankylosing spondylitis, rheumatoid arthritis, degenerative joint disease etc.[2] It is available universally, so its side-effects are found frequently in the general population. Its unusual adverse effects are hypersensitivity, renal disease, gastrointestinal disorders, and cardiovascular disease.[3,4]

Diclofenac sodium decreases the formation of prostaglandin, by inhibiting an enzyme called cyclooxygenase in the cells. Prostaglandin ranges from 1.20 to 1.81 ng /ml in the plasma. Prostaglandin is produced and consumed by kidneys, which helps in renal physiology like glomerular filtration rate, control of renal blood stream, renin secretion, relocation of ion and water metabolism in the tubules.[5]It was postulated that prostaglandins, also participate in the self-regulation of renal blood supply, metabolism of renin and tubular exchange mechanisms.[6]

L-arginine an α-amino acid, it is levo-rotatory form of Arginine.[6] In humans, arginine commonly originates as

a semi essential or essential amino acid, relying on the growing phase and fitness of the person. Arginine is not synthesized by preterm infants, needs it from animal or plant sources.[7] L-arginine woks by producing Nitrous oxide (NO) is produced through L-arginine by nitrous oxide synthetase.[8] It is also postulated that arginases are group of enzymes made up of arginine, responsible for the healing of different tissues are made up of arginine.[8,9] However, in persistent renal illnesses, ureteral obstruction, diabetic nephropathy, high blood pressure and in aging process, valuable properties of L-arginine have been verified.[10]

The freedom to buy pharmaceutical drugs that have not been prescribed by registered health practitioners, is raising serious concerns in Pakistan. Unlike developed countries where the management of medicines is under effective regulations and over the counter medicines are well categorized. In Pakistan buying almost any type of medicine without prescription is easy.[11]

Self -medication is one of the causes of the renal injury. Diclofenac sodium is one of the commonest over- the-counter used drug. It is used commonly to manage pain and fever in pre and post-operative patients. Therefore, this study was conducted to assess the role of L-arginine in the renal tubular damage caused by the Diclofenac sodium in the albino rat.

MATERIALS AND METHODS

It was an experimental study. It was conducted after getting approval from Institutional Review Board (IRB). The experiment was accomplished in the Institute of Bio Medical Sciences (IBMS), with the cooperation of Dow Diagnostic Research and Reference Laboratory (DDRRL) in Dow University of Health Sciences (DUHS), Ojha Campus, Karachi in 2013. Non probability, purposive, sampling technique was used. Adult albino rats of both sexes, active and healthy, were included in the study. They were weighing 180-200 grams, and taking food and water normally. However, lethargic, inactive and constantly weight declining animals were considered unfit for the experiment. Sample size was forty albino rats of 180-200 grams of both sexes.

In the experimental room of animal house, animals were kept on well-adjusted food and water with 12 hours day and night cycle. Every animal was weighed at the start of experiment and before sacrifice. Animals were divided into four groups: A, B, C and D groups comprising of ten rats in each group.

Group –A (control): The animals of this group received normal saline 1 cc intra-muscular for 2 weeks.

Group-B (Diclofenac sodium treated group): Diclofenac sodium 2mg/kg body weight intramuscularly daily was given for 2 weeks.

Group-C (Diclofenac sodium + L-arginine treated group): Diclofenac sodium 2mg/kg body weight intra-muscular and L-arginine was given orally at a dose of 1mg/kg body weight, daily for 2 weeks.

Group-D (L-arginine treated group): L-arginine 1mg/kg body weight was given, daily for 2 weeks. (L-arginine was administered through feeding tube half an hour prior to the administration of Diclofenac sodium)

Each animal was anaesthetized in ether before sacrificing. A sharp scalpel was used for incision, starting from xiphoid process up to the pubic symphysis. A magnifying glass was used to recognized and examine the kidneys, for any noticeable variations in size, shape, color, outline and uniformity. The kidneys were isolated and "Sartorius balance" (Sartorius Precision Balance, Model No.MSE 1203S, Sartorius Lab Instruments, GmbH & Co.KG) was used to measure the absolute and relative weight of each kidney.

Tissue section was made by using a rotary microtome of "Bright instrument co. model OTF 5000 and UK" longitudinal sections of 5µm thick were cut, floated on a hot water bath of "Thermo- Fisher Scientific, USA" on a 370c, fixed on gelatinized glass slides. Histological sections of kidney tissue of approximately 10x10 mm in size from each group-A, B, C & D, were fixed in10% formalin and stained with heamatoxylin and eosin.

General morphology and architecture of the kidneys was observed and after screening, ten observations per animal were recorded. However, five observations for each of the parameters were recorded. Parameters noted in this study were, weight of animals (initial and after two weeks). However, microscopic variables were cortical thickness of kidney, in which 10X optical and 4X objective lens with the support of counting reticule were used to calculate the cortical thickness of kidney. The diameter of proximal convoluted tubules was calculated along their long and short axis, under 10X ophthalmic and 10X objective lens with the aid of counting reticule in randomly chosen five spots within the juxtamedullary regions in all animals.

Then micrometry is done by calibration of the ocular micro meter and the counting reticule and synchronized with stagemicro- meter. Right eye was used for ocular micro meter and left eye for reticule by using the3B Scientific Binocular course Microscope Model 300, Hamburg, Germany. Each and every observation and measurement was verified by the supervisor.

Statistical analysis: Statistical analysis was done by using SPSS version 16. To assess the significance between various groups studied, one-way analysis of variance (ANOVA) was applied. Multiple comparisons to a control are also referred to as many-to-one comparisons. The outcomes were stated as mean ± standard deviation and $p < 0.05$ was measured statistically significant at confidence interval of 95%.

RESULTS

During experimental period all the animals remained alive. The animals of group A (control), group-C (Diclofenac sodium and L-Arginine treated) and group D (L-Arginine treated) appeared healthy, reacted quickly to outer stimuli and increased weight steadily. However, the animals of group B (Diclofenac sodium treated) looked lethargic and revealed a weaker response to the outer stimuli gradually from 3rd to 14th day; their appetite and body weight was reduced.

Initial body weights of Albino rats were compared in the study. In group A(control) initial body weight was (204.20 ± 6.08 gm) compared to other group B (diclofenac treated, wt:199.90 ± 8.76 gm), group C (diclofenac and arginine, 193.50 ± 31.88 gm) and group D (L-arginine, 193.50 ± 31.88 gm) was insignificantly decreased (P-Value obtained at C.I of 95 % was 0.546).

However, after two weeks of administration of Diclofenac sodium and L-Arginine, final body weight of albino rats was reducing significantly (P- Value at C.I of 95 % obtained was < 0.001) where as insignificant decrease was observed when compared to group D (the P-Value at C.I of 95 % obtained was < 0.012) shown in Figure No.1.

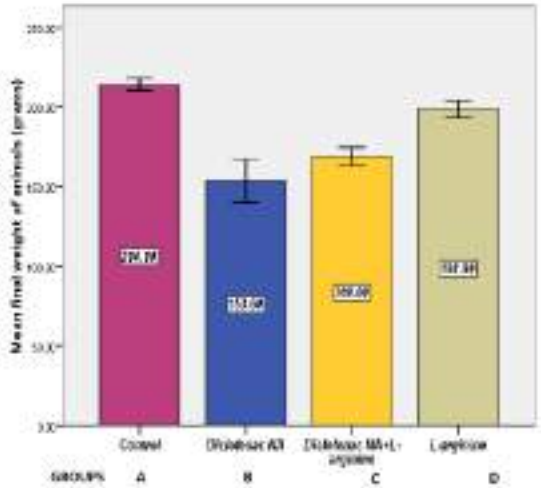

Figure No. 1: Mean final weight of animals (gram)

Table No. 1: Multiple comparison Dunnet test for cortical thickness (µm) among groups

Groups		Mean Difference	Std. Error	Sig.
Group (B) Diclofenac Na	Control Group (A)	8.000	6.109	0.426
Group (C) Diclofenac Na+ L-arginine	Control Group (A)	10.480	6.109	0.223
Group (D) L-arginine	Control Group (A)	7.740	6.109	0.452

In H & E stained sections, diameter of proximal convoluted tubules of kidneys was measured and compared between the control and the treated groupsshown in Figure No.: 2-5. Mean diameter of proximal tubule in group A was found to be 50.68 ± 11.86 µm. When compared with proximal tubule diameter in group B (113.52 ± 25.68 µm), a highly significant increase (P- Value at C.I of 95 % obtained was < 0.001) was observed. However, in histological sections ingroup C(67.94 ± 10.54 µm) diameter decreases insignificantly withP-Value at C.I of 95 % obtained was 0.051. Andgroup D (56.79 ± 9.40 µm) also reveal an insignificant decrease in diameter (P-Value at C.I of 95 % obtained was 0.722).

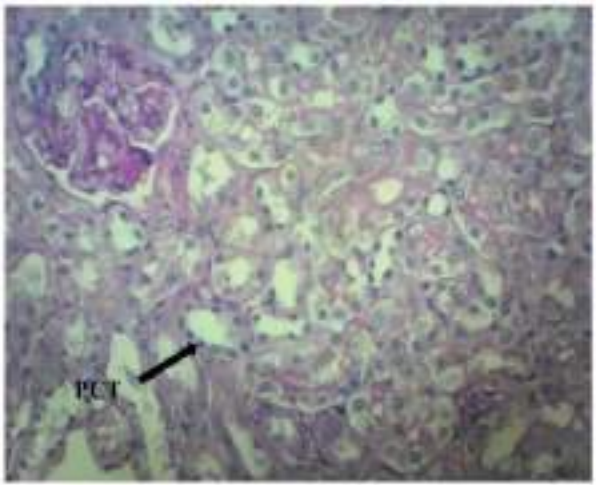

Figure No. 2: H&E stained, 5µm thick longitudinal section of kidney from group A (control) showing normal proximal convoluted tubule (PCT) 10x10 X

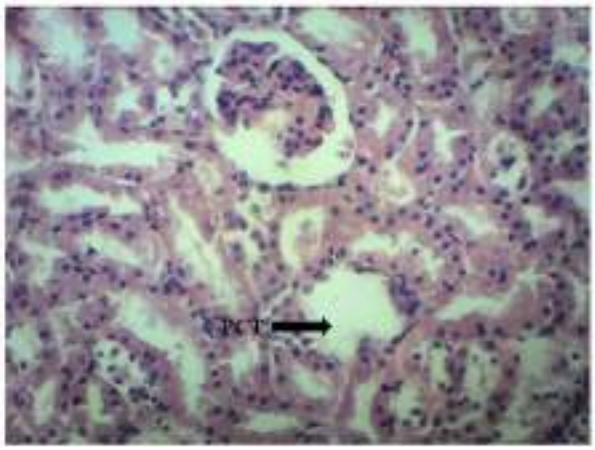

Figure No.3: H&E stained, 5µm thick longitudinal section of kidney from group B (Diclofenac sodium) showing dilated proximal convoluted tubule (PCT) 10x10 X

Microscopically, when assessment of cortical thickness of kidneys within the control group A (163.28 ± 16.84 µm) and the treated groups (group B: 171.28 ± 14.16µm, group C: 152.80 ±7.27 µm, groupD: 155.54

±14.45 µm) was compared. A significant reduction in the cortical thickness in kidneys was observed in all treated groups, except group B, in which cortical thickness was increased insignificantly shown in Table No.1.

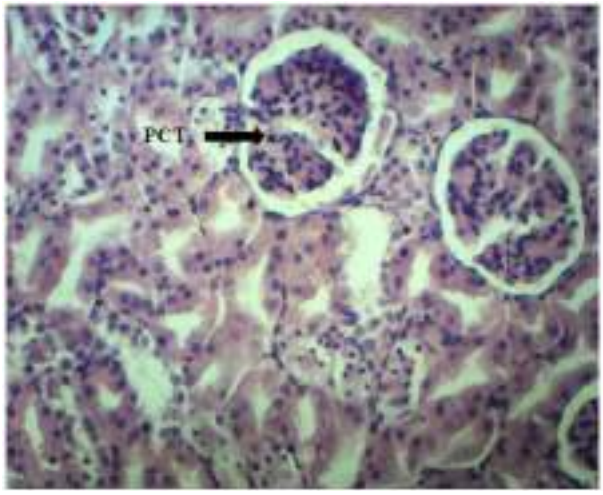

Figure No. 4: H&E stained, 5µm thick longitudinal section of kidney from group C (Diclofenac sodium + L arginine) showing near to normal proximal convoluted tubule (PCT) 10x10 X

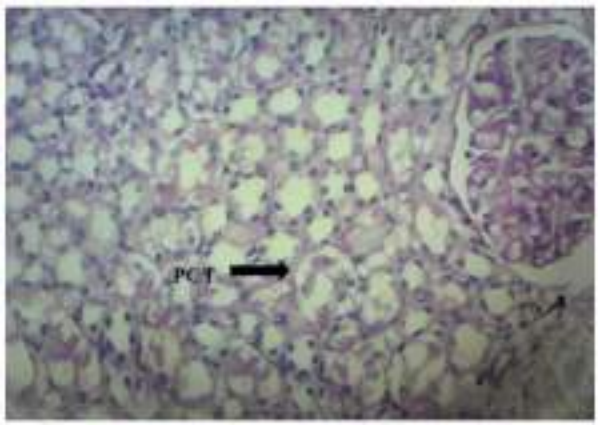

Figure No. 5: H&E stained, 5µm thick longitudinal section of kidney from group D (L-arginine) showing normal proximal convoluted tubule (PCT) 10x10 X

DISCUSSION

Non-steroidal anti-inflammatory drugs (NSAIDS) in prolong use causes nephrotoxicity, several researches have reported. Many attempts have been made to prevent the analgesic nephropathy with vitamins and anti-oxidants like ascorbic acid. However, a study reported that L-arginine produces a protective effect against drugs, radiations or nephrotoxicity induced by ischemia.[12]

In this study loss in body weight in albino rats was observed after treatment with diclofenac sodium. Reduction in the body weight was probably because of lack of hunger as one of the side effects of Diclofenac sodium on gastrointestinal tract. Our study observations are in agreement with Farag et al, who noted decrease in body weight in patients receiving Diclofenac sodiu.[13] However, insignicant decrease in body weight was seen in group D, which may be due to effects of L-arginine on proximal convoluted tubules, as it increases blood circulation causing vasodilatation. Our results are in agreement with Witting and Horwit, who also reported supportive effects of L-arginine on growth rate.[14]

Microscopically cortical thickness in group B was notably increased as compared to group A, which probably due to cell swelling, inflammation and dilatation of proximal convoluted tubules. This observation was in agreement with Lansa et al and Wua G et al.[15] However, significant reduction in cortical thickness was observed after treatment with L-arginine in groups C and group D, which may be attributed to protective effect of L-arginine that may have prevented the acute damage to kidney by ischemic release of free radicles. [16,17]

In this study microscopically, in renal cortex, diameter of proximal tubules was found tobe increased significantly in group B as compared to groups A, C and D, this might be due to cells destruction in proximal convoluted tubules and mild edema. Our findings are in complete agreement with Scott et al, who observed, after ingestion of NSAID there will be damage and shedding of renal tubular cells in urine.[18,19]

However, group C treated with L-arginine prior to administration of Diclofenac sodium there was no significant change in the diameter of proximal tubules when compared with control. These results may be explained on the basis of stabilization of the blood flow of proximal tubules due to beneficial effects of L-arginine. Our findings are in conformity with study conducted by Rhoden, who described that due to pre-treatment with L-arginine, lipid per oxidation of renal cells and renal dysfunction induced by renal ischemia in rats were significantly reduced.[20]

CONCLUSION

It is concluded that diclofenac sodium induces renal toxicity, however, L-arginine produces protective effect on Diclofenac sodium induced nephrotoxicity and these results could be reflected promising enough to permit further studies.

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Original Article

Platelet Rich Plasma in Tennis Elbow

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ABSTRACT

Objective: To study the platelet rich plasma in tennis elbow.
Study Design: Observational study
Place and Duration of Study: This study was conducted at the Idris teaching hospital Sialkot during Jan 2018 to Oct 2020.
Materials and Methods: 100 patients with tennis elbow and who visited our Idris teaching hospital Sialkot with conservative treatment were treated with PRP, and results were evaluated with raised platelet rich plasma. History, examination and X-ray of elbow was taken. Written informed consent was taken before taking History, examination and X-ray of elbow. The permission of Ethical Committee was considered before collecting the data and get publishing in Medical Journal. The data was analyzed for results by SPSS version 20.
Results: The incidence of Tennis elbow was maximum 17(32.69%) at age group 26-36 years and was minimum 3(5.76%) at age group 15-25 years. The incidence of Tennis elbow was 32 (61.53%) in male and 20(38.46%) in case of female. The incidence of Tennis elbow was maximum 26(50%) in middle class and was minimum 5(9.61%) in high gentry. The incidence Tennis elbow was 52(100%) in Platelet plasma rich injection given to patients having pain in elbow joint and was 00(00%) in plantar fasciitis.
Conclusion: In conclusion, local injection of obtained from the same individual Platelet rich plasma resulted to be a hopeful form of treatment for tennis elbow. It is both safe (avoiding surgical complications) and effective in relieving pain and improving function. It is a cost related method for the sick persons. The current available data support that repeated steroid injections are deleterious and may lead to serious consequences, and our study demonstrates a newer, safer, and better alternative for patients. However sustained efficacy of this promising and safer therapeutic option should be further evaluated in long-term follow-up studies that include a larger number of patients.
Key Words: Platelet, Plasma, Tennis Elbow.

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INTRODUCTION

Platelet-rich plasma (PRP) is an autologous mixture of platelets and growth factors produced by centrifugation of whole blood[1]. PRP may enhance soft tissue regeneration processes by releasing platelet-derived growth factors, cytokines, and other proteins capable of stimulating and modulating the inflammatory response[2–4]. Chen et al. in their in order to determine overall trends showed that Platelet Rich Plasma is a safe and beneficial way of helping tendon and ligament healing[1].

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In outside the body study have shown that human tenocyte growth increases when cultured in Platelet Rich Plasma showing that Platelet Rich Plasma start the promoting metabolic activity effect of growth factors increasing tendon matrix regrowth. An increased Transforming growth factor beta concentration has been coincided in many works with the clinical efficacy of Platelet Rich Plasma[5–7].

In disparity to the basic science data, the clinical effectiveness of Platelet Rich Plasma has been noted with incompatible result, including several methodical analysis and meta-analyses[8]. Platelet Rich Plasma has been used in many soft tissue pathologies such as pathology of tendon and ligament injuries. However, it remains unclear especially in chronic elbow conditions whether Platelet Rich Plasma should be suggested as a treatment method before doing a surgical treatment[1,8–10, 11]. The aim of this article is to provide a description knowledge review regarding the role of Platelet Rich Plasma in the most common elbow soft tissue pathologies.

MATERIALS AND METHODS

During Jan 2018 to Oct 2020, 100 patients with tennis elbow and who visited Idris teaching hospital Sialkot with conservative treatment were treated with platelet rich plasma (PRP) and results were evaluated with raised platelet rich plasma. History, examination and X-ray of elbow was taken. Written informed consent was taken before taking History, examination and X-ray of elbow. The permission of Ethical Committee was considered before collecting the data and get publishing in Medical Journal. The data was analyzed for results by SPSS version 20.

RESULTS

The incidence of Tennis elbow was maximum 17(32.69%) at age group 26-36 years and was minimum 3(5.76%) at age group 15-25 years as shown in table no 1.

Table No. 1: Age distribution in Tennis Elbow

Sr #	Age distribution	Patients	%age
1	15-25	3	5.76%
2	26-36	17	32.69%
3	37-47	14	26.92%
4	48-58	13	25%
5	59 on ward	5	9.61%
Total		52	100%

The incidence of Tennis elbow was 32 (61.53%) in male and 20(38.46%) in case of female (table 2).

Table No. 2: Gender distribution in Tennis Elbow

Sr #	Gender distribution	Patients	%age
1	Male	32	61.53%
2	Female	20	38.46%
Total		52	100%

The incidence of Tennis elbow was maximum 26(50%) in middle class and was minimum 5(9.61%) in high gentry as shown in table no 3.

Table No. 3: Socio Economic status distribution in Tennis Elbow

Sr #	**Socio Economic status**	**Patients**	**%age**
1	High gentry	5	9.61%
2	Middle class	26	50%
3	Lower class	21	40.38%
Total		52	100%

The incidence Tennis elbow was 52(100%) in Platelet plasma rich injection given to patients having pain in elbow joint and was 00(00%) in plantar fasciitis as shown in table no 4.

Table No. 4: Platelet rich plasma distribution in Tennis Elbow

Sr #	**Platelet rich plasma**	**Patients**	**%age**
1	Elbow joint	52	100%
2	plantar fasciitis	00	00%
Total		52	100%

DISCUSSION

The present work showed that local injection of Platelet rich plasma is an important form of therapy that provides significant treatment of pain and betterment in function in both tennis elbow and plantar fasciitis. However, it is possibly a method for sick persons than steroid use and surgery. The suggested method of action of autologous Platelet rich plasma is betterment of early neotendon properties and betterment of tissue healing by increasing cellular movement of a motile cell, growth and difference, removing of tissue waste, formation of new blood vessels and laying of non-cellular portion of a tissue.[12]

Relating to tennis elbow, our results are similar to those noted by Mishra and Pavelko[13,14,15] who showed a significant improvement of symptoms after eight wk in 60% of the sick persons treated with PRP. At the end of 6 month, patients treated with PRP noted 81% improvement in their VAS pain scores (P=0.0001). Our results also are in agreement with that observed by Peer booms *et al.*[10] who reported that 24 of the 49 patients (49%) in the corticosteroid group and 37 of the 51 patients (73%) in the PRP group were successful (P<0.001). [16,17,18]

In our study, we observed highly significant differences between VAS and DASH scores before and after injection (P<0.001); after 4 to 8 wk after injection, 75% patients had excellent VAS score improvement (>50% reduction) and around 62% had reduction of DASH score (>50%).[19-20]

In our study, significant results were observed when VAS and FHSQ were compared before and after injection (P<0.003); 82% patients had a decrease in VAS score (>50%) and around 60% had improvement in FHSQ score (>50%).

CONCLUSION

In conclusion, local injection of obtained from the same individual Platelet rich plasma resulted to be a hopeful form of treatment for tennis elbow. It is both safe (avoiding surgical complications) and effective in relieving pain and improving function. It is a cost related method for the sick persons. The current available data support that repeated steroid injections are deleterious and may lead to serious consequences, and our study demonstrates a newer, safer, and better alternative for patients. However sustained efficacy of this promising and safer therapeutic option should be further evaluated in long-term follow-up studies that include a larger number of patients.

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Original Article

Knowledge and Practice of Radiation Protection among Dental Surgeons Practicing in Lahore

Shahlisa Hameedi[1], Sana Chaudhry[2], Faryal Ali Syed[3], Nadia Muneer[4], Omair Anjum[5] and Muhammad Behzad Salahuddin[1]

ABSTRACT

Objective: The aim of this study is to evaluate the knowledge of radiation protection among dental surgeons practicing in Lahore, Assess the strategies adopted in department for radiation protection and recommend remedial measures to improve the existing conditions.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Dental practitioners practicing in Lahore from September 2019 to March 2020.

Materials and Methods: A pre-designed questionnaire, containing the demographic information, questions to judge the knowledge of radiation protection and different strategies adopted in their setups for radiation protection, was distributed among 217 practicing dental surgeons of Lahore. These questionnaires were then retrieved and the data was collected and analyzed.

Results: 55.3% of the respondents were male with mean age of 41.54 ± 4.2 years. Majority only had basic knowledge regarding the harmful effects of x-rays while being unaware of the radiosensitive organs of the body, ALARA principle or position distance rule. 11.1% were aware of annual recommended dose limit for occupationally exposed workers.46.1% used protective apparels with lead apron being most frequent. A significant number did not using any radiation monitoring device or use appropriate filtration and collimation.

Conclusion: Bulk of the dental surgeons exhibited unsatisfactory knowledge and adopted inadequate measures for radiation protection. The need of the hour is to organize periodic lectures and workshops to dispense latest teachings regarding the dangers of radiation and methods for the safety of workers as well as the patients.

Key Words: Dental Surgeons, Knowledge, Lahore, Practice, Radiation protection, x-rays

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INTRODUCTION

The accidental discovery of x-rays by German physicist Wilhelm Roentgen gave birth to radiology. However, x-rays are ionizing electromagnetic radiations and exposure can lead to an array of health hazards[1].

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Increased radiation exposure causes cell death, whereas limited exposure leads to damage or change in the DNA of irradiated cells[2]. These effects are categorized as either stochastic effects, which are not dose-related, such as cancer, or deterministic effects, such as necrosis or burns, which are only observed after relatively high-dose exposure[3].Children are even more susceptible to the effects of ionizing radiation, with the probability of developing carcinoma being the most in childhood and becoming less with progression of age[4].

Radiology holds fundamental importance in dentistry for diagnosis, planning and monitoring of treatment as well as follow up[5]. It plays innumerable roles from the basic diagnosis of caries, minute fractures to assisting in complicated processes like implant planning[6]. Dental surgeons employ radiographs more frequently than other medical specialties with the radiographic modalities varying from intraoral periapical radiograph to advanced techniques like cone beam computed tomography[7]. Increased use of cone beam computed tomography in orthodontics patients has been associated with the increased incidences of breast cancers in female patients, especially during age range of 10 to 30 years[8]. Various studies exhibit increased

incidence of thyroid and breast carcinomas in female dentists and more frequent development of melanomas in male dentists[9].

The main principle of radiation protection is to curtail radiation exposure to the least while permitting use of the radiation for specific advantageous purposes[10].In 1973, ALARA principle (as Low as Reasonably Achievable) was developed for optimization of radiographic doses with the aim of judicious use of radiation[11]. Partial/segmented dental panoramic views, that limit the x-ray beam only to the area of interest, can be used successfully to reduce radiation exposure[12].

This study was carried out to evaluate the knowledge and the steps taken for radiation protection among dental surgeons practicing in Lahore. By having a general insight to this data, we can further suggest remedial measures to improve upon the existing situation. This would also allow us to pinpoint specific areas which need to be focused in this regard.

MATERIALS AND METHODS

The study was conducted among dental surgeons privately practicing Lahore, from 15 September 2019 to 14 March 2020. 217 dental surgeons, both male and female, practicing in either private clinics or in academic institutions in Lahore, were included in the study. Dental surgeons without x-ray facility in their setups were excluded from the study. Sample size was calculated using openepi sample size calculator, taking usage of radiography in dental practice as 69%[13], confidence interval as 95%. 217 came out to be the sample size. Non-probability, purposive sampling was done. Approval of the institute's ethical committee for research was obtained before starting the research.

A structured questionnaire, consisting of multiple choice questions, was developed after research on the subject and discussion with experts. The first section consisted of basic information. The second section comprised of questions which dealt with the knowledge regarding radiation protection. The third section constituted of the various protocols adopted in the department for the purpose of radiation protection. The respondents were asked to select one option as the answer to the question.

The data collected was analyzed using SPSS version 21. Mean and standard deviation was calculated.

RESULTS

120 (55.3 %) of the respondents were male while 97(44.7 %) were females. The age range was from 25 years to 65 years while mean age was 41.54 ± 4.2 years.131 (60.4 %) had done B.D.S (graduation) while 86 (39.6 %) were holding a post-graduate qualification. 42.4 % had been practicing for 5 to 10 years, followed by those practicing for less than 5 years (35.5 %).63.1 % dental surgeons were practicing in private setups while 36.9 % were performing institutional duties. The demographic data is shown in table1.

Table No.1: Demographic data of the respondents

S.No	Demographic Data	Results
1.	**Gender**	
	Male	55.3%
	Female	44.7%
2.	**Age**	
	25 - 34 years	19.4%
	35 - 44 years	31.8%
	45 - 54 years	28.6%
	55 – 64 years	16.6%
	65 years and above	3.7%
3.	**Qualification**	
	Graduate (BDS)	60.4%
	Post-graduate qualification (MCPS/FCPS/Masters etc)	39.6%
4.	**Clinical Experience**	
	Less than 5 years	35.5%
	Between 5 – 10 years	42.4%
	More than 10 years	22.2%
5.	**Practicingat**	
	Academic institution	36.9%
	Private clinic	63.1%

Table No.2: Response regarding section-II of the questionnaire

S.No	Knowledge About Radiation Protection	Results
1.	**Are you aware of the harmful effects of x-rays on human health?**	
	Yes	93.1%
	No	6.9%
2.	**Do you know the most radiosensitive organs of human body?**	
	Yes	52.1%
	No	47.9%
3.	**Are you familiar with the ALARA principle?**	
	Yes	24.9%
	No	75.1%
4,	**Do you have an understanding of the Position Distance Rule?**	
	Yes	29.5%
	No	70.5%
5.	**Do you know the effect of filtration and collimation on radiation exposure?**	
	Yes	31.8%
	No	68.2%
6.	**Do you understand link between kVp and exposure time with radiation dose?**	
	Yes	26.3%
	No	73.7%
7.	**Are you aware of the annual permitted dose limit for occupationally exposed workers as recommended by the ICRP?**	
	Yes	11.1%
	No	88.9%
8.	**Have you ever attended any workshop / seminar regarding radiation protection?**	
	Yes	6.5%
	No	93.5%

Table No.3: Response Regarding Section-III of the Questionnaire

S.No.	Practice of Radiation Protection	Results
1.	**Are the following radiation protection apparel used in your department?**	
	A) Lead apron	
	Yes	46.1%
	No	53.9%
	B) Thyroid collar	
	Yes	24.9%
	No	75.1%
	C) Gonadal shield	
	Yes	35.0%
	No	65.0%
	D) Breast shield	
	Yes	25.3%
	No	74.7%
	E) Safety Glasses	
	Yes	30.4%
	No	69.6%
2.	**What mechanism is used for holding the film?**	
	Staff	63.1%
	Patients attendant	27.6%
	Film holder	9.3%
3.	**Do you stand behind a lead barrier when the x-ray is performed?**	
	Yes	44.7%
	No	55.3%
4,	**Are X-ray warning / caution signs displayed in the department?**	
	Yes	75.6%
	No	24.4%
5.	**What radiation monitoring devices are used in your department?**	
	Film badges	66.3%
	TLDs	0%
	OSLDs	0%
	Electronic personal dosimeters	0%
	None	33.7%
6.	**Is the Position Distance Rule strictly followed?**	
	Yes	28.6%
	No	71.4%
7.	**Can other people enter the room when x-ray is being performed?**	
	Yes	61.3%
	No	38.7%
8.	**Do you use appropriate collimation and filtration in your department?**	
	Yes	64.9%
	No	35.1%

93.1% had basic knowledge regarding the harmful effects of x-rays on human health however, only 52.1% were aware of the radiosensitive organs of the body. Only 24.9% understood the ALARA principle while 29.5% were familiar with the position distance rule. Only 11.1% were aware of the annual recommended dose limit for occupationally exposed workers. Bulk (93.5%) of the respondents had never attended a seminar, lecture or a workshop on radiation protection. Data regarding the answers to section II is shown in table 2.

Less than half of the respondents were wearing protective apparels in their departments while performing x-rays. In 63.1% of the departments, dental staff was holding the radiographic film while x-ray was performed. 33.7% were not using any radiation monitoring device. Radiation warning signs and cautions were not displayed in 24.4% of the departments. Answers to section III is in table 3.

DISCUSSION

Dental surgeons utilize x-rays more commonly as compared to any other medical branch[13]. Radiation exposure in dentistry has been linked with to increased incidence of tumors of the salivary and thyroid glands, meningiomas and increased frequency of low birth weight children in exposed pregnant females[14]. Radiation protection holds critical importance for health care professionals with the purpose of diminishing needless radiation exposure and reducing its hazards[15]. The three cardinal principles of radiation protection are justification (benefit of exposure should outweigh risks), optimization (exposure kept as low as possible) and dose limitation (total dose should be less than permissible dose for occupationally exposed workers)[16]. In our study, 55.3% participants were male, having age between 35 – 44 years.60.4% were graduates, 42.4% had clinical experience between 5 -10 years and 63.1% were working in private setups. Most of our respondents had only basic knowledge and lacked detailed awareness or critical insight on radiation protection. Similar results have been seen in other studies performed on this subject all over the world. A study concerning the knowledge of dental surgeons, x-ray technicians, dental undergraduate students and radiography students regarding radiation protection was conductedin Poland, Europe[17]. The study inferred that radiation awareness amongst all the four groups of respondents was unsatisfactory with the differences between them being not statistically significant.

In our study, only 29.5% of the dental surgeons were aware of the position distance rule while 70.5% were unfamiliar with it. Similarly, only 9.3% dentists, in our study, employed film holder to hold radiographic film while performing x-rays while in 63.1% cases, staff of the dental department was utilized to hold the film. A study carried out to evaluate the perception of radiation protection in dental surgeons in India, also yielded similar results [18]. Bulk of the dental surgeons included

in the study (54%) did not know the position distance rule while only 46% were familiar with it. Majority (59%) of the dentists did not utilize film-holding deviceswith only 41% employing film-holding devices.

Our study showed that the various steps taken for radiation protection in the departments were insufficient and needed improvement. Less than half of the respondents used protective apparels with lead apron being most frequent (46.1%). A study conducted to ascertain the radiographic safety practices of dentists, concluded that these practices were insufficient. Majority (60.4%) employed only lead protection for performing dental x-rays, even of pregnant females whereas a large proportion of respondents (39%) themselves placed the radiographic films insidethe mouth of the patient[19].

Hence, the results of our study agree with the different national and international studies performed for this purpose and reinforce them. The main limitation of our study is that it is a questionnaire based research and the answers may not accurately depict the exact knowledge and practice of the respondent in actual. Secondly, as the answers were fixed, there was lesser margin for the participants to provide answers that may correctly manifest their feelings on the subject. However, it appears from the results of our study that the situation in our setup locally is even more dismal and requires substantial improvements. Thiscalls for appropriate training of healthcare workers in the field of radiation protection to make sure that they possess sufficient knowledge and can implement consequential changes in their department. This information is crucial not only for all healthcare workers but is extremely critical for the patients visiting the hospitals as well as general public[20].

CONCLUSION

Bulk of the dental surgeons exhibited unsatisfactory knowledge regarding radiation protection while majority of the departments showed inadequate measures adopted for this purpose. The need of the hour is to organize periodic lectures and workshops to dispense latest teachings regarding the dangers of radiation and methods for the safety of workers as well as the patients.

Recommendations: On the basis of the research done for this study, following recommendations are made to improve the knowledge and practice of radiation protection.

1. Adoption of standard x-ray views to produce x-rays with acceptable quality and prevent repeat x-rays.
2. Daily maintenance of x-ray machine with periodic calibration to prevent leak radiation.
3. Usage of protective apparel to prevent exposure to radiosensitive organs.
4. Use of rare earth metal intensifying screen to reduce radiation exposure.
5. Use of appropriate collimation and filtration to limit the patient's exposure to low energy x-rays.
6. Employment of film holding devices when the x-ray is being performed.
7. Detailed chapter regarding radiation protection should be included in the curriculum, both at undergraduate and post-graduate levels.
8. Dental surgeons lacking proficiency in radiation protection should undergo dedicated lectures / seminars / workshops to enhance their knowledge of the field.
9. PNRA should hold periodic inspections in all institutions. Failure to meet safety standards should result in temporary cancellation of license till the situation is improved.
10. Creating awareness amongst the patients and the general public regarding the hazards of ionizing radiation and the basic radiation protection.

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Original Article

Pediatric Abdominal and Thoracic Trauma

Pattern of Pediatric Abdominal and Thoracic Trauma, Types of Organ Injury, Biochemical Parameters and Treatment Approaches

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ABSTRACT

Objective: To find out pattern of pediatric abdominal and thoracic trauma, types of organ injury and treatment approaches done at a tertiary care hospital of South Punjab, Pakistan.

Study Design: A descriptive observational study

Place and Duration of Study: This study was conducted at the Department of Pediatric Surgery, Bahawal Victoria Hospital, Quaid-e-Azam Medical College, Bahawalpur, from January 2017 to December 2019.

Materials and Methods: A total of 112 patients aged less than 15 years, having history of abdominal and/or chest trauma were enrolled. Demographic data along with mechanism, site, mode and nature of injury was gathered. Biochemical markers for acute abdominal trauma, serum alanine amino transferase (ALT), serum creatinine kinase (CK) and serum lipase were obtained. Definitive treatment in terms of conservative or surgical treatment was noted. All cases were handled using standard "Advance Trauma Life Support (ATLS)" protocols.

Results: Among of a total of 112 patients, mean age was noted to be 6.8+2.9 years. There were 68 (60.7%) boys and 44 (39.3%) girls. Road-traffic accidents were the commonest mode of trauma noted in 51 (45.5%) children, followed by fall 40 (35.7%), thermal injuries in 14 (12.5%) and assaults in 7 (6.3%). Abdomen was involved most frequently as seen in 54 (48.2%) children, thoracic trauma in 23 (20.5%) while combined thoraco-abdominal injuries were noted in 35 (31.2%). Among 82 (73%) patients, a very high serum ALT ≥ 100IU/L was found, similarly, 41(36%) patients were having raised serum CK (≥575U/L), and 26 (23%) were found with raised serum lipase (≥ 61U/L). There were 65 (58.0%) patients who were managed adopting conservative approach, minor interventions needing local anesthesia were done in 31 (27.7%), while major interventions were needed in remaining 16 (14.3%) cases. Mortality was reported in 3 cases.

Conclusion: Majority of the cases having thoraco-abdominal trauma were boys. Road-traffic accidents were the commonest mode of trauma followed by fall injuries and thermalinjuries. Abdomen was the most frequently involved anatomical site followed by combined thoraco-abdominal injuries. The most frequently raised biomarkers observed in acute abdominal injury were serum ALT, CK, and Lipase. Most of the patients were managed adopting conservative approach.

Key Words: Thoraco-abdominal trauma, road-traffic accidents, biochemical parameters conservative approach.

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INTRODUCTION

Pediatric trauma is known to be an important cause of death and disability especially in the developing countries.[1] Globally, around 5 million deaths are reported annually due to pediatric trauma.[2] Pediatric trauma is estimated to be the reason of more than 50% deaths in children between 1 to 14 years of age while after infections, it is also the 2nd most frequent cause of hospital emergency visits. [3] Regional data suggest that 15-20% of trauma deaths are reported in the pediatric age groups. [4]

Abdominal trauma is estimated to be the third leading cause of mortality among children. The reported incidence calculated blunt abdominal injury occurring in ~9/100000 children. [5] Blunt abdominal injuries seem to be more prevalent as compared to penetrating abdominal injuries whereas mechanisms behind these injuries differ in different pediatric age groups. [6] Paediatric thoracic injuries are estimated to account for 4-6% of hospital trauma cases while mortality rates are around 5% but when combined with abdominal injuries,

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the mortality rates starch around 25%.[7,8] Blunt as well as penetrating injuries among children can occur due to variety of reasons but most frequent cause is noted to be motor vehicle accidents. Most common sites of injuries are observed to be rib cage, lung parenchyma and other mediastinal structures. Frequently raised serum biomarkers in acute abdominal injury are serum ALT, CK and lipase [9].

It is vital to find out pattern and knowledge about paediatric abdominal and thoracic trauma to plan, implement and manage these types of trauma so that management can be done at initial levels to minimize the mortality and morbidity related to these injuries.[10,11] This study was planned to find out pattern of pediatric abdominal and thoracic trauma, types of organ injury and treatment approaches done at a tertiary care hospital of South Punjab, Pakistan.

MATERIALS AND METHODS

This descriptive observational study was done at Department of Paediatric Surgery, Bahawal Victoria Hospital, in collaboration with Pathology Department, Quaid-e-Azam Medical College, Bahawalpur, from January 2017 to December 2019. A total of 112 patients aged less than 15 years, having history of abdominal and chest trauma were enrolled. Patients having head, spine, facial, upper or lower limb trauma, poisoning or drowning were not included in this study. Children having any psychiatric illness were also not enrolled. Thoracic injury was labeled as injury between clavicles superiorly and the 12th rib inferiorly which resulted in clinically significant or suspected intra-thoracic injury.

A total of 112 patients fulfilling inclusion and exclusion criteria during the study period were analyzed and all the study information was noted on a predesigned proforma specifically made for this study. Demographic data along with mechanism, site, mode and nature of injury was gathered. Relevant laboratory investigations like blood complete examination, serum ALT, CK, Lipase were done. Definitive treatment in terms of conservative or surgical treatment was noted. X-ray skeletal survey, "focused assessment with sonography for trauma (FAST)" or "computed tomography (CT)" were done as per requirement. All cases were handled using standard "Advance Trauma Life Support (ATLS)" protocols.

RESULTS

Among of a total of 112 patients, mean age was noted to be 6.8+2.9 years ranging from 1 month to 14 years. There were 68 (60.7%) boys and 44 (39.3%) girls. Road-traffic accidents were the commonest mode of trauma noted in 51 (45.5%) children, followed by fall 40 (35.7%), thermal injuries (scalds, burns or electrical injuries) in 14 (12.5%) and assaults in 7 (6.3%) as shown in Figure 1. Thermal burns were referred to burn unit for further evaluation and management.

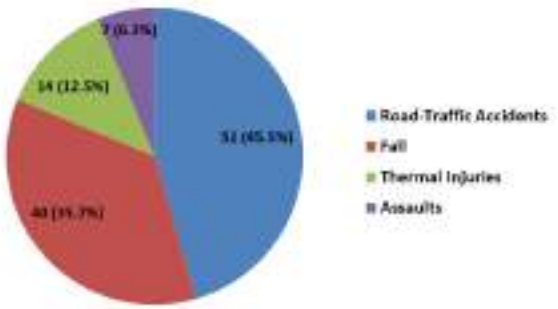

Figure 1: Mode of Trauma (n=112)

In terms of anatomical sites of thoraco-abdominal trauma, abdomen was involved most frequently as seen in 54 (48.2%) children while thoracic trauma was seen in 23 (20.5%). Combined thoraco-abdominal injuries were noted in 35 (31.2%).

Table No.1: Types of Injury in Isolated Thoracic Trauma (n=112)

Anatomical Sites of Trauma	Types of Injury / Organs Involved	Number (%)
Isolated Thoracic Trauma (n=23)	Lung Contusion	8 (34.8%)
	Pleural Laceration	6 (26.1%)
	Rib Fractures	5 (21.7%)
	Clavicle Fracture	3 (13.0%)
	Sternal Injury	1 (4.3%)
	Pericardial Hematoma	1 (4.3%)
Isolated Abdominal Trauma (n=54)	Liver	20 (38.9%)
	Spleen	11 (20.4%)
	Hollow Viscus	10 (18.5%)
	Kidney	6 (11.1%)
	Pancreas	4 (7.4%)
	Urinary Bladder	3 (5.6%)
Thoraco-Abdominal Trauma (n=35)	Chest and Liver	11 (31.4%)
	Chest and Spleen	10 (28.6%)
	Chest, Liver and Spleen	9 (25.7%)
	Chest, Spleen and Bowel Perforation	3 (8.9%)
	Chest, Diaphragm and Liver	1 (2.9%)
	Chest and Gastric Perforation	1 (2.9%)

Table 1 is showing details of anatomical sites of trauma along with types of injuries or organs involved. In patients having isolated thoracic trauma (n=23), lung contusions with hemo-pneumo-thorax was the commonest types of injuries noted in 8 (34.8%) patients, followed by pleural laceration 6 (26.1%) and rib fractures 5 (21.7%). In patients having isolated abdominal trauma (n=54), liver was the most frequently involved organ seen in 20 (38.9%) cases followed by spleen 11 (20.4%) and hollow viscus injuries 10 (18.5%). Among patients having thoraco-abdominal

trauma (n=35) as validated by X-ray skeletal survey, FAST and CT, combined chest and liver injuries were the most frequent seen 11 (31.4%) followed by chest and spleen involvement in 10 (28.6%), and chest, liver and spleen involvement in 9 (25.7%) cases.

In terms of management, 65 (58.0%) patients were managed adopting conservative approach (intravenous fluids, non-steroidal anti-inflammatory drugs and rest), minor interventions needing local anaesthesia were done in 31 (27.7%), while major interventions were needed in remaining 16 (14.3%) cases. Mortality was reported in 3 cases, out of which, 1 was due to grade-5 renal injury where nephrectomy was done while the 2 deaths were recorded in a children having thoraco-abdominal trauma involving multi-organ damage.

DISCUSSION

Trauma injuries account for nearly 12% of disease burden globally.[12] Researchers have pointed out towards estimating epidemiological aspects of trauma among pediatric age groups as most of these injuries are perceived to be preventable.[10,11] In the last few decades, incidence of paediatric thoraco-abdominal trauma has raised significantly all around the world.[3]

In the present study, majority of the cases (60.7%) were boys. Our results are aligned with the findings of Wabada S et al from Nigeria who evaluated 33 cases with abdominal trauma and found a male to female ratio of 3:1.[13] Kundal VK et al from India revealed 64.6% of their cases of thoraco-abdominal trauma to be male which is close to what we noted.[14] Being physically more involved in routine and outdoor activities could be major reasons for this male predominance in thoraco-abdominal trauma cases.

Road-traffic accidents were the commonest mode of trauma observed in 45.5% cases followed by fall (35.7%) injuries. Data from findings of Peclet MH et al[15] in 1990 revealed that 36% cases of thoracic trauma were due to pedestrian injury while recent studies show that road-traffic accidents to be most common cause of pediatric thoraco-abdominal injuries.[16] Study from Kundal et al found road-traffic accidents to be the most frequent mode of thoraco-abdominal trauma while some authors have noted fall injuries to be most prevalent in children but inclusion criteria involving children of younger age (less than 12 years) could be one reason for that.[14] Hyder et al analyzing children aged less than 5 years revealed that 36% of the cases were due to fall injuries.[17] Road-traffic injuries can occur as a passenger, driver, bicyclist or pedestrian. Generally, road-traffic accidents are more prone to induce blunt trauma while falls and outdoor recreational activities are more related with abdominal injuries.[18] Specific injury modes can help in early prediction about the presence of thoraco-abdominal injuries. Among paediatric age groups, distinctive anatomy having more labile physiologic reserve, less protective adipose and connective tissues as well as muscle mass.[19] We also know that bones of a child are not fully calcified which make them more flexible. Intra-abdominal organs are also more closely situated to each other that increase chances of multi-organ trauma. In this study, abdominal trauma was seen in 48.2% children, thoracic trauma in 20.5% while combined thoraco-abdominal injuries were noted in 31.2%. This is well aligned with the recently published regional data where authors found abdominal trauma to be the commonest anatomic site of trauma followed by combined thoraco-abdominal trauma.[14] Management of thoraco-abdominal trauma has seen significant shift from surgical to conservative management because of improvement in evaluation and grading of the trauma especially due to enhancement in USG and CT utilization.[20] Majority of the blunt injuries are managed conservatively but the decision to non-operative approach depends upon trauma surgeons depending upon hemodynamic status and CT findings assisted by standard ATLS guidelines.[14,20]

Our study had some limitations as well. We only included cases having chest and abdominal trauma presented at emergency department of our tertiary care health facility. We did not enrolled patients that had polytrauma like head-and-neck trauma. Patients having drowning or poisoning were not included while missing information about the exact mode of injury in some cases could possibly have influenced the true representation of thoraco-abdominal trauma in this study. We were also unable to document duration of hospital stay as, this was a single center study, more studies involving multiple centers and different sets of population will further add to what is known about the pattern, mode, types and outcomes of thoraco-abdominal trauma in children.

CONCLUSION

Majority of the cases having thoraco-abdominal trauma were boys. Road-traffic accidents were the commonest mode of trauma followed by fall injuries and thermal injuries. Abdomen was the most frequently involved anatomical site followed by combined thoraco-abdominal injuries. Most of the patients were managed adopting conservative approach.

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Original Article

Psychiatric Morbidity in Suicide

Pattern of Psychiatric Morbidity in Suicide Attempters

Jamil Junejo[1], Inayatullah Awan[2], Anoop Kumar[3], Jawed Akbar Dars[4], Bharat Kumar[5] and Zuhaib Ahmed[2]

ABSTRACT

Objective: To determine psychiatric morbidity among those who presented to the tertiary care hospital due to attempted suicide.

Study Design: An observational-cross sectional study

Place and Duration of Study: This study was conducted at the Sir Cowasjee Jahangir Institute of Psychiatry, Liaquat University hospital Hyderabad Pakistan from January 2011 to December 2011.

Materials and Methods: General Health Questionnaire -28 was used for Psychiatric screening; detailed medical antiquity and psychological state checkup were conducted by using the Diagnostic and Statistical Manual –IV Text Revised; the data was entered in excel sheet in SSP - 20 version; and Chi- Square test was applied.

Results: Prevalence of psychiatric disorders were reported: "mood disorders" (35%), "Anxiety disorders" (17.5%), "Schizophrenia" (5%), "Personality disorder" (4 %), "Substance use disorders" (15.5%), "Organic Mental Disorder" (2%), "Other Psychotic Disorders" (8%), and "Co-morbid Psychiatric Disorders" (13%).

Conclusion: The study concludes that psychiatric disorders were highly frequent among those who reported to hospital due to attempted suicide. It is suggested that the stigma about mental illness should be reduced and people should be encouraged to seek proper psychiatric consultation. Further, Undetected psychiatric illnesses may lead to untimely suicide attempt.

Key Words: Attempted suicide, Psychiatric Disorders and Stigma

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INTRODUCTION

Psychiatric disorders are very frequent and prevalent among the victims of suicide. Various studies reveal that almost 90% of patients who commits suicide have some psychiatric disorder [1,2].

Various psychiatric disorders such as depression, mania, pathological jealousy, schizophrenia, alcohol and substance abuse are linked with suicide [3].

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Compared to general population, the risk of suicide increases by twenty folds with depressive disorder, fifteen folds with bipolar disorder and twelve folds with dysthymic disorders [4]. Anxiety is present in 3 to 17% people with serious suicidal tendency; however, the prevalence will be higher as many studies did not report about anxiety disorder [5]. Panic disorder was reported in 20% of people who died of suicide [5]. Another psychiatric disorder that was associated with increase attempt of suicide was post-traumatic stress disorder (PTSD) [6]. Schizophrenia was presented in 6 and 19% of people who had attempted suicide or suicidal intent [7]. Substance abuse was present in 19% of people who died by committing suicide. Another study shows that with suicidal behavior range from 2.2 to 5.8 % [8]. Welter et al. reported 18-26% of those who died by committing suicide had alcohol in their blood at death time [9]. Various studies suggest that more than half of people who commits suicide have some sort of psychiatric illness [10, 11].

Psychiatric illness and suicide both are considered taboo in Pakistan. There is very limited data available related to prevalence of psychiatric illness in people who attempts suicide. In this study, we will determine the frequency of psychiatric illness in participants who have attempted suicide.

MATERIALS AND METHODS

This observational-cross sectional study was carried out in Sir Cowasjee Jahangir Institute of psychiatry,

Liaquat university hospital Hyderabad, from 1 January 2011 till 31 December 2011. Participants, who came to emergency department with attempted suicide, were recruited via consecutive convenient non-probability sampling technique. Informed consent was taken from attendant. For identifying psychiatric morbidity, subjects were interviewed, and General Health Questionnaire 28 was applied on them. Two hundred participants (200) who were identified with psychiatric illness through initial assessment were identified by exhaustive psychological story and mental health examination with the criterion of Diagnostic and Statistical Manual –IV Text Revised (DSM-IV).

Statistical software SPSS version 20 was used to analyze the data. Since the variables of study were categorical, they were represented as frequencies and percentages. Whereas, significant association in-between categorical variables were found Chi-square test. P- Value <0.05 was cogitated as statistically significant.

RESULTS

This study included a total 200 subjects, out of them males were 157 (78.5 %) and females were 43 (21.5%). Most prevalent psychiatric disorders found among those who presented with suicide attempt were "Mood Disorders" i.e. 70 subjects (35%) ensued by Anxiety disorders i.e. n= 35 (17.5%). Schizophrenia was diagnosed in 10 (5%) out of whom seven patients were males, and 3 patients were females. Personality Disorder was diagnosed in 8 (4 %) participants of the study. Other diagnoses included "Substance use disorders" 31 (15.5%), "Organic Mental Disorder" 4 (2%), "Other Psychotic Disorders" 16 (8%), and "Co-morbid Psychiatric Disorders" 26 (13%) (Table 1).

Table No.1: Psychiatric disorders among suicide attempter

S. No	Psychiatric Diagnosis	Males %	Females %	Total cases%	P value
1.	Mood disorders	52 (33.1)	18 (41.8)	70 (35)	0.287
2.	Substance use disorders	29 (18.4)	2 (4.6)	31 (15.5)	0.026
3.	Schizophrenia	7 (4.4)	3 (6.9)	10 (5)	0.502
4.	Personality disorders	5 (3.1)	3 (6.9)	8 (4)	0.260
5.	Organic mental disorders	3 (1.9)	1 (2.3)	4 (2)	0.863
6.	Other psychotic disorders	12 (7.6)	4 (9.3)	16 (8)	0.722
7.	Anxiety disorders	26 (16.5)	9 (20.9)	35 (17.5)	0.504
8.	Co-morbid psychiatric disorder	23 (14.6)	3 (6.9)	26 (13)	0.185

DISCUSSION

Various studies have found association between mental illness and attempted suicide. Leon AC et al. found that 90% of suicide victims had some sort of diagnosable psychiatric illness at the time of death [12]. Baxter D et al also reported similar result [13]. Result from meta-analysis reports geographical difference as well; as victims of suicide in south Asian populations have reported higher incidence compared to western population[14].

The most common reported mental disorder in our study was mood disorder (35%). Henriksson et al and Shibre T et al, also reported similar finding[15,16]. A local study from Pakistan founds 48% of participants with positive past history for suicide had depressive disorder[17]. Second most common disorder in our study was substance related disorder (15.5%). Kamath P et al reports that alcohol use was significantly associated with suicide attempt[18]. Pirkola SP et al also found an association with alcohol and suicidal behavior. Alcohol has an effect on mood, cognition and impulsivity; all of these factors can contribute to suicidal behavior[19]. Doger et al. also reported that addiction due to substance use could lead to suicidal behavior[20].

In our study, schizophrenia was found in 5% of subjects. Radomsky ED et al, while describing symptoms of schizophrenia, described that self-harm or suicide is common symptom in schizophrenia[21]. Haukka J et al. found that risk of suicide in patients with schizophrenia is clearly higher than that in the general population[22].

In our study, personality disorder was diagnosed in 4% subjects. Schneider B et al. in his study reported that axis II personality disorders have increased risk of attempting suicide[23]. Our finding was comparatively lower to other studies. Isomerta et al. found that 44% of participants in their study have some co-morbid personality disorder[24]. Cheng et al. reports 55-70% of participants who attempts suicide have some co-morbid personality disorder[25].

CONCLUSION

This study found that psychiatric disorders were highly frequent prevalent cause among those who were hospitalized due to the act of attempted suicide. Stigma is attached to psychiatric/mental illnesses in many societies including our society. Mostly people shun seeking psychiatric help/treatment due to that stigma.it is therefore essential to strive for reducing the stigma about mental illnesses which can help the individuals to seek psychiatric treatment whenever it is needed and hence reduce the risk of unfortunate deaths by committing suicide.

Author's Contribution:

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Original Article

Frequency of Depression in Patients with Schizophrenia

Depression in Schizophrenia

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ABSTRACT

Objective: Schizophrenia is a psychiatric disorder involving chronic or recurrent psychosis. It is commonly associated with impairments in social and occupational functioning. Schizophrenia also associated with different comorbidities including depression. This study is design to determine the prevalence of depression and its severity in schizophrenia in local population.

Study Design: Cross sectional study.

Place and Duration of Study: This study was conducted at the Sir Cowasji Jehangir Institute of Psychiatry Hyderabad from Jan 2018 to Dec 2018.

Materials and Methods: One hundred and twenty-six (126) patients with schizophrenia were included in this study. Depression was assessed on Hamilton depression rating scale (HDRS).

Results: Prevalence of depression in patients with schizophrenia was 39.68% (50/126). Regarding severity of depression, 15.87% (20/126) were mild and 23.81% (30/126) were moderate to severe. Prevalence of depression was high in self-employed and skilled labor as compare to professional and in those who run their business (p=0.0005). Prevalence of depression was also high in illiterate and low educated patients (p=0.003) as well as those patients whose household income was below 25,000 Pakistani rupees. (p=0.008)

Conclusion: In this study, depression is prevalent schizophrenic patients, particularly in patients with low education level along with poor socio-economic background. It should be recommended that complete assessment of each patient should be done and symptoms & severity of depression should be excluded in every patient. For this screen, strategies could be developed thereby for better quality of life early diagnosis and prompt treatment could be lead.

Key Words: Schizophrenia, Psychiatric disorder, Depression

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INTRODUCTION

Global burden of schizophrenia is variable and ranges between the prevalence of 0.3 to 0.7 percent [1]. Studies have shown that in patients of schizophrenia Quality of life (QOL) is increasingly important to the treatment outcome [2]. QOL among patients of Schizophrenia affected by unmet needs, Social support and medication side effects [3-5].

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Schizophrenia associated with different comorbidities including depression. Different studies have shown to have incidence of symptoms of depression in schizophrenic patients ranges between 20 to 80 percent [6,7] . In mid to late life patients non to minimal depression (Hamilton rating scale score 0-6) was found in 30% in males and 20% in females, mild depression (Hamilton rating scale score 7-16) was 63% and 60% in males and females respectively. Moderate to severe depression (Hamilton rating scale score ≥ 17) was 7% and 20% in males and females respectively [8]. In schizophrenia, depressive symptoms can be associated with decreased functioning, re-hospitalization and suicide [8-10]. Patients with schizophrenia and depressive symptoms have to face negative consequences, which affect their QOL[11]. There is significant relationship between depressive symptoms and QOL in younger patients with schizophrenia[12]. All patients with schizophrenia must be evaluated for the manifestation of depression symptoms [13]. In such a scenario, with early detection of depressive symptoms in patients of schizophrenia, re hospitalization can be prevented and by doing so

cost burden can be reduced this will help to improve the quality of life [8]. Decrease functioning and suicide also associated with depressive symptoms, early detection of depressive symptoms in patients of schizophrenia can leads to decrease suicide and increase functioning. In order to improve quality of life in schizophrenia, focused must be on negative symptoms and depressive symptoms [9,10,14].

As there is no local data available regarding prevalence of depression and its severity in schizophrenia in local population so the local burden is still unknown which is required for resource allocation and budgeting for psychiatric institutes. Furthermore, strategies could be developed to screen such patient's thereby early diagnosis and prompt treatment could lead to better quality of life.

MATERIALS AND METHODS

This cross-sectional study was carried out at psychiatry unit of Sir Cowasji Jehangir institute of Psychiatry from Jan 2018 to Dec 2018. Patients with documented evidence of diagnosis of schizophrenia, of either gender or aged between 18-60 years, were enrolled from outpatient departments via consecutive convenient non-probability sampling. Exclusion criteria included recent diagnosis of schizophrenia (less than 6 months). Patients taking drugs for other illnesses, patients with other neurological disease, mental retardation and significant physical morbidity were also excluded from study. With 95% CI, 7% bond on error and based on 20% prevalence of depressive symptoms in schizophrenia patients our sample size came out to be 126 schizophrenia patients[6].

After ethical review approval, Depression was assessed on Hamilton depression rating scale (HDRS). The questionnaire was filled by the researcher himself and scores of 0-7 was taken as normal. 8 – 13 as mild, scores of 14 – 18 as moderate and scores > 19 as severe depressions. These findings and demographics were entered in the self-structure proforma.

Data was analyzed through statistical analysis of social packages (SPSS) version 20. Continuous variables like age and duration of schizophrenia was expressed as Mean ± standard deviation. Whereas categorical variables like gender, marital status, education, occupation and monthly family income was presented as frequencies and percentages. Stratification was done on the basis of age, duration of disease, gender, educational status, marital status, occupation and monthly family income to control effect modifiers, Chi-Square test was applied and p value less than or equal to 0,05 was taken as significant.

RESULTS

In this study, mean age and duration of schizophrenia was 40 ± 10 years and 4 ± 1 years. Out of 126 cases, 72(57.14%) were male and 54(42.86%) were female. There were 20.63% patients were self-employed, 35.71% skill labor, 24.6% were professional and 19.05% were running business (Table 1).

Table No.1: Characteristics of Participants

Characteristics	Frequency (percentage)
Age group (in years)	
18-30	19 (15.0)
31-40	40 (31.7)
41-50	44 (34.9)
41-60	17 (13.4)
Gender	
Female	54 (42.86)
Male	72 (57.14)
Occupation	
Self-employed	26 (20.63)
Skilled Labor	45 (35.71)
Professional	31 (24.60)
Business	24 (19.05)
Educational Status	
Illiterate	6 (4.76)
Matric and below matric	33 (34.92)
Intermediate	47 (37.30)
Graduate	29 (23.02)
Marital Status	
Married	90 (71.43)
Never married	23 (18.25)
Widowed	10 (7.94)
Divorced	3 (2.38)
Household Income (in PKR)	
Less than 25,000	62 (49.21)
25,000 to 50,000	32 (25.40)
More than 50,000	32 (25.40)

Prevalence of depression (assessed by HADS score) in patients with schizophrenia was 39.68% (50/126). Regarding severity of depression, 15.87% (20/126) were mild and 23.81% (30/126) were moderate to severe (table 2).

Table No.2: Prevalence and Severity of Depression

HADS Depression	**Frequency (percentage)**
Depression	
Yes	50 (39.68)
No	76 (60.32)
Severity	
No Depression	76 (60.32)
Mild Depression	20 (15.87)
Moderate to Severe Depression	39 (23.81)

It was observed that prevalence of depression was high in self-employed and skilled labor as compare to professional and in those who run their business (p=0.0005). Prevalence of depression was also high in illiterate and low educated patients (p=0.003) as well as those patients whose household income was below 25,000 Rs. (p=0.008) (table 3).

Table No.3: Prevalence of Depression stratified according to variables

Variables	Depression		Total	P-Value
	Yes n=50	No n=76		
Age Groups				0.067
21to 30 Years	11(57.9%)	8(42.1%)	19	
31 to 40 Years	16(34.8%)	30(65.2%)	40	
41 to 50 Years	20(45.5%)	24(54.5%)	44	
51 to 60 Years	3(17.6%)	14(82.4%)	17	
Gender				0.83
Male	28(38.9%)	44(61.1%)	72	
Female	22(40.7%)	32(59.3%)	54	
Duration of Disease				0.51
≤ 3 Years	30(37.5%)	50(62.5%)	80	
>3 Years	20(43.5%)	26(56.5%)	46	
Occupation				0.0005
Self Employed	14(53.8%)	12(46.2%)	26	
Skilled Labor	30(66.7%)	15(33.3%)	45	
Professional	2(6.5%)	29(93.5%)	31	
Business	4(16.7%)	20(83.3%)	24	
Educational Status				0.003
Illiterate	3(50%)	3(50%)	6	
Matric and below matric	23(52.3%)	21(47.7%)	44	
Intermediate	21(44.7%)	26(55.3%)	47	
Graduate and Master	3(10.3%)	26(89.7%)	29	
Monthly household income (Rs.)				0.008
<25,000	32(51.6%)	30(48.4%)	62	
25,000 to 50,000	12(37.5%)	20(62.5%)	32	
>50,000	6(18.8%)	26(81.3%)	32	

Chi-Square applied for each stratified variables

Severity of depression was also not significant differences in these factors except monthly household income as shown in table 4.

Table No.4: Severity of Depression stratified according to variables

Variables	Depression		Total	P-Value
	Mild n=20	Moderate to severe n=30		
Age Groups				
21to 30 Years	5(45.5%)	6(54.5%)	11	
31 to 40 Years	6(37.5%)	10(62.5%)	16	0.73
41 to 50 Years	7(35%)	13(65%)	20	
51 to 60 Years	2(66.7%)	1(33.3%)	3	
Gender				
Male	10(35.7%)	18(64.3%)	28	0.48
Female	10(45.5%)	12(54.5%)	22	
Duration of Disease				0.55
≤ 3 Years	11(36.7%)	19(63.3%)	30	
>3 Years	9(45%)	11(55%)	20	
Occupation				0.056
Self Employed	2(14.3%)	12(85.7%)	14	
Skilled Labor	16(53.3%)	14(46.7%)	30	
Professional	0(0%)	2(100%)	2	
Business	2(50%)	2(50%)	4	
Educational Status				0.83
Illiterate	1(33.3%)	2(66.7%)	3	
Matric and below matric	8(34.8%)	15(65.2%)	23	
Intermediate	10(47.6%)	11(52.4%)	21	
Graduate and Master	1(33.3%)	2(66.7%)	3	
Monthly household income (Rs.)				0.007
<25,000	18(56.3%)	14(43.8%)	32	
25,000 to 50,000	1(8.3%)	11(91.7%)	12	
>50,000	1(16.7%)	5(83.3%)	6	

Chi-Square applied for each stratified variables

DISCUSSION

Although, depression in patients with schizophrenia is very common but remained mystery yet. The testified ratio of depression is 7% to 75%, with a modal rate of 25% in various studies [16,17]. Differences in cohort status, illness chronicity, and assessment methods all contribute to the variability of these estimates [18]. The significance of a concomitant disruption in mood amongst schizophrenic patients comprises enhanced menace of illness and death [18,19]. The rate of despair in schizophrenia is frequently correlated to depraved result, compromised working, intrusive distress, elevated degrees of deterioration or re-hospitalization, and even suicide, an event that ends the lives of an appraised 10% of patients with schizophrenia [18,20-24].

In this study the average age and duration of schizophrenia was 40.39±9.38 years and 3.64±0.96 years. Out of 126 cases, 72(57.14%) were male and 54(42.86%) were female. In Rocca et al study mean age was 36.13 ± 8.93 years; they were 32 females (41%) and 46 males (59%) [12].

In present study there were 20.63% patients were self-employed, 35.71% skill labor, 24.6% were professional and 19.05% were running business as reported. Most of the patients were intermediate and blow intermediate. Regarding monthly household

income of the patients, 49.21% income was below Rs. 25,000, 25.4% income was 25000 to 50,000 and 25.4% were earn more than 50,000. In Suttajit et al. study, the mean age of the 75 participants in this study was 46.0±13.6 years, and from them, 26 (34.7%) were male, 23 (30.7%) were married, 33 (44.0%) had no income [25]. In same study, half of participants had been diagnosed with schizophrenia for more than ten years, 38 (50.7%) were using typical antipsychotic drugs and 44 (58.7%) had at least one side effect [25].

Schizophrenia associated with different comorbidities including depression. In this study prevalence of depression (assessed by HADS score) in patients with schizophrenia was 39.68% (50/126). In this study observed that prevalence of depression was not significant among different age groups, gender and duration of disease. Depression is reportedly common among both the genders suffering from schizophrenia and was unrelated to family history, negative symptoms, any movement disorders or use of narcoleptics [26,27].

There is a variety of symptoms of depression among schizophrenia patients. In our study, we noted different depressive manifestations in schizophrenia group vs. the normal group such as sense of futility, feebleness (depressive mood) and psychomotor impedance. Though many further signs of depression were found in schizophrenia, they are not matching with conditions of major depressive disorder (MDD) [28].

Approximately 20% women suffering from schizophrenia scored ≥17 on Hamilton depression rating scale, which signifies moderate to severe depression. These symptoms were the major depressive symptoms, however when minor depressive symptoms which did not fulfil MDD criteria were included, it was observed that majority of the schizophrenic patients suffered from these symptoms, such that it can be considered as a whole subsyndrome [28]. In contrast, several studies have ruled out the significance of this subsyndrome stating that these occurred in part due to social dysfunction and debility, suicidal attempts and chances of advanced major depressive disorder [29].

CONCLUSION

It is concluded that prevalence of depression is more common in schizophrenic individuals, and severity of depressive symptoms in schizophrenic individuals is mostly moderate to severe. So all the patients having schizophrenia should go for detailed evaluation to exclude the symptoms of depression. To screen such patient's strategies could be developed thereby for better quality of life early diagnosis and prompt treatment could be lead.

Author's Contribution:

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Original Article

Effect of Low Sodium Dialysate on Regression of Left Ventricular Hypertrophy in Hemodialysis Patients

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ABSTRACT

Objective: To compare the effect of low sodium dialysate with the standard sodium dialysate in terms of regression of left ventricular hypertrophy in dialysis patients.

Study Design: Randomized controlled trial study

Place and Duration of Study: This study was conducted at the Nephrology Department, PIMS Islamabad. Duration of study from March, 2018 to August, 2018.

Materials and Methods: This study involved eighty-four Dialysis dependent patients (n=84) of either gender aged between 18-65 years with hypertension and LVEF>40%. They were randomly divided into two groups. Intervention group was switched to 136 mmol/L dialysate sodium (low sodium) while control group were kept on dialysate sodium concentration of 140 mmol/L (standard sodoum). Study outcomes were measured in terms of interdialyctic weight gain, blood pressure response and left ventricular mass index (LVMI) at six months.

Results: There were 71.4% (n=30/42) males and 28.6% (n=12/42) females in low sodium group and were 57.1% (n=24/42) males and 42.9% (n=18/42) females in standard sodium group. In low sodium group, mean age was 41.2 years ± 8.8 SD, mean height was 1.64 m ± 0.06 SD and mean weight was 73.4 Kg ± 10.4 SD. In standard sodium group, mean age was 44.7 years ± 9.5 SD, mean height was 1.68 m ± 0.06 SD and mean weight was 74.2 Kg ± 9.9 SD. In low sodium group, mean LVEF was 48.5 % ± 2.3 SD, mean interdialyctic weight gain was 2.58 Kg ± 0.43 SD, mean systolic BP was 155.2 mmHg ± 7.5 SD, mean diastolic BP was 99.5 mmHg ± 6.6 SD and mean LVMI was 123.6 g/m^2 ± 13.5 SD. In standard sodium group, mean LVEF was 49.1 % ± 2.6 SD, mean interdialyctic weight gain was 2.53 Kg ± 0.44 SD, mean systolic BP was 156.1 mmHg ± 7.9 SD, mean diastolic BP was 101.2 mmHg ± 6.6 SD and mean LVMI was 123.3 g/m^2 ± 14.6 SD. At six months, mean interdialyctic weight gain was 2.02 Kg ± 0.43 SD in the low sodium group compared with 2.53 ± 0.43 SD in standard sodium group, (P=0.001). Mean systolic blood pressure was 147.5 mmHg ± 7.9 SD in the low sodium group compared with 157.5 mmHg ± 8.2 SD in standard sodium group, (P=0.001). Low sodium tends to lower down the systolic pressure when compared to high sodium. Mean diastolic blood pressure was 99.5 mmHg ± 5.9 SD in the low sodium group compared with 101.2 mmHg ± 6.6 SD in standard sodium group, no significant difference was observed in diastolic blood pressure in both the groups at six months (P=0.06). Mean LVMI was 121.8 g/m^2 ± 13.5 SD in low sodium group while it was 131.8 g/m^2 ± 14.6 SD in standard sodium group (p=0.003).

Conclusion: Mean interdialyctic weight gain was significantly lesser and mean LVMI was significantly lower in low sodium group compared to standard sodium group. Low sodium tends to lower down the systolic pressure when compared with standard sodium group at six months.

Key Words: Dialysis, Dialysate, Sodium.

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INTRODUCTION

Dialysis is most commonly used modality of renal replacement therapy across the glob[1]. Unfortunately left ventricular hypertrophy (LVH) is considered as a main risk factor for sudden cardiac death in dialysis patients. Regression of LVH by any intervention can reduce cardiac mortality in these patients.[2] Regression of LVH can be achieved by removal of dialysis sodium along with better blood pressure control in these patients.[3]

The balance of sodium in dialysis patients mainly depends on intake of dietary salt and removal of sodium during dialysis. Volume overload is triggered by intake of salt.[4] Negative sodium gradient is when the dialysate sodium is lower than the patient's plasma sodium at the start of hemodialysis.[5] In chronic hemodialysis patients

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average intake of sodium intake is between 150-250 mmol/day. [6] Dialysis should therefore be optimized to remove excessive sodium, which accumulates during interdialysis period and by minimizing chronic fluid overload. [7,8] Thus, the major determinants of optimum diasyalate sodium removal are the volume of ultrafiltration during haemodialysis and the relationship between plasma levels of sodium and prescribed dialysate sodium concentration.[9]

Dialysis Outcomes and Practice Patterns Study (DOPPS) reported that about 57% of HD facilities adopt uniform Dialysate sodium prescriptions in more than ninety percent of patients. [10] Use of high Dialysate sodium may be beneficial for prevention of episodes of hypotension, but at the same time may result in to a positive sodium balance leading to an increase in BP and fluid overload. However, use of low dialysate sodium is associated with reduced thirst, BP and fluid overload but can sometime be detrimental, especially in patients who are prone to hypotension.

A panel of clinicians from fourteen large dialysis units in the USA have suggested that Dialysate sodium should not exceed 134–138 mmol/L. [11] However, researchers from DOPPS group quickly rejected this proposition and claimed that the standard range of 138–140 mmol/L should not be lowered before more evidence showing clear cut benefit is gathered.[12] With this background in mind, our aim was to perform a randomized controlled trial to analyse possible benefits of low versus standard Dialysate prescriptions in hypertensive patients on chronic hemodialysis.

MATERIALS AND METHODS

We enrolled a total of 84 patients of end stage renal disease on regular twice weekly dialysis for last 6 months with hypertension and Left ventricular Ejection fraction <40%. They were randomly divided into two groups (n=42 in each group) by coin method; an intervention (group A) and a control (group b) group. By echocardiography Left ventricular ejection fraction (LVEF), Mass of the left ventricle was measured and LVMI was calculated.

Intervention group was switched to 136 mmol/L dialysate sodium while control group dialysate sodium concentration was kept at 140 mmol/L. Interdialytic weight gain (IDWG) and BP was recorded in both groups at the time of study enrolment, at each dialysis during whole study period of 6 months. After 6 months echocardiography was repeated to see any change in LVMI along with improvement in IDWG and BP control in both groups.

RESULTS

There were 71.4% (n=30/42) males and 28.6% (n=12/42) females in low sodium group and were 57.1% (n=24/42) males and 42.9% (n=18/42) females in standard sodium group. In low sodium group, mean age was 41.2 years ± 8.8 SD, mean height was 1.64 m ± 0.06 SD and mean weight was 73.4 Kg ± 10.4 SD. In standard sodium group, mean age was 44.7 years ± 9.5 SD, mean height was 1.68 m ± 0.06 SD and mean weight was 74.2 Kg ± 9.9 SD.

In low sodium group, mean LVEF was 48.5 % ± 2.3 SD, mean interdialyctic weight gain was 2.58 Kg ± 0.43 SD, mean systolic BP was 155.2 mmHg ± 7.5 SD, mean diastolic BP was 99.5 mmHg ± 6.6 SD and mean LVMI was 123.6 g/m^2 ± 13.5 SD. In standard sodium group, mean LVEF was 49.1 % ± 2.6 SD, mean interdialyctic weight gain was 2.53 Kg ± 0.44 SD, mean systolic BP was 156.1 mmHg ± 7.9 SD, mean diastolic BP was 101.2 mmHg ± 6.6 SD and mean LVMI was 123.3 g/m^2 ± 14.6 SD (table 1).

At six months, mean interdialyctic weight gain was 2.02 Kg ± 0.43 SD in the low sodium group compared with 2.53 ± 0.43 SD in standard sodium group, (P=0.001, table 2). Mean interdialyctic weight gain was significantly lesser in low sodium group compared to standard sodium group.

Table No.1: Baseline patient characteristics in both groups

Variables	Groups	Mean	SD	P-value T-test
LVEF (%)	Low Sodium diasylate	48.5	2.3	0.377
	Standard sodiumdiasylate	49.1	2.6	
Interdialyctic Weight gain (kg)	Low Sodium diasylate	2.58	0.43	0.617
	Standard sodiumdiasylate	2.53	0.44	
Systolic bp (mmhg)	Low Sodium diasylate	155.2	7.5	0.622
	Standard sodiumdiasylate	156.1	7.9	
Diastolic bp (mmhg)	Low Sodium diasylate	99.5	5.9	0.227
	Standard sodiumdiasylate	101.2	6.6	
Lvmi (g/m^2)	Low Sodium diasylate	123.6	13.5	0.665
	Standard sodiumdiasylate	122.3	14.6	

Mean systolic BP was 147.5 mmHg ± 7.9 SD in the low sodium group compared with 157.5 mmHg ± 8.2 SD in standard sodium group, (P=0.001). Low sodium tends to lower down the systolic pressure when compared to

high sodium. Mean diastolic blood pressure was 99.5mmHg ± 5.9 SD in the low sodium group compared with 101.2 mmHg ± 6.6 SD in standard sodium group, No significant difference was observed in diastolic blood pressure in both the groups at six months (P=0.06) .

Mean LVMI was 121.8 g/m^2 ± 13.5 SD in low sodium group while it was 131.8 g/m^2± 14.6 SDin standard sodium group (p=0.003). Mean LVMI was significantly lower in low sodium group compared to standard sodium group at six months.

Table No.2: Outcomes in both groups at six months

Variables	Groups	Mean	Sd	P-value T-test
Interdialyctic Weight gain (kg)	Low Sodium diasylate	2.02	0.43	0.001
	Standard sodiumdiasylate	2.53	0.44	
Systolic bp (mmhg)	Low Sodium diasylate	147.5	7.9	0.001
	Standard sodiumdiasylate	157.5	8.2	
Diastolic bp (mmhg)	Low Sodium diasylate	97.5	5.9	0.06
	Standard sodiumdiasylate	100.2	6.6	
Lvmi (g/m^2)	Low Sodium diasylate	121.8	13.5	0.003
	Standard sodiumdiasylate	131.1	14.6	

DISCUSSION

Currently available clinical evidence supports a significant role of LVH in sudden cardiac death among dialysis patients. In one study, LVH was found to be associated with higher risk of mortality even after adjustment for age, known CAD, DM and BP.[13] It has been observed that in patients who or on dialysis with conventional technique, persistent elevation in BP and positive salt-water balance resulting in extra-cellular fluid overload significantly contribute to on-going LVH.[14-16]

It has been demonstrated that both BP and IDWG was increased when sodium was overloaded either by excessive dietary intake or by excessive diffusion via dialysate.[17] In addition, elevated sodium plasma levels may induce hypertension, which is independent of ECF volume. A number of observational studies as well as small uncontrolled clinical studies have shown that lower dialysate [Na+] associates with less thirst,[18-20] lower IDWG, lower ECF volume and lower BP, with only a minority of studies being completely negative.[21-27] A previous research by Solid trial team demonstrated that a decrease in dialysate [Na+] by 3 mM in 52 facility based patients was well tolerated and reduced systolic and diastolic BP by 4–5 and 2–3 mmHg, respectively.[28] The observation of improvement in intermediary outcomes such as BP suggest that lower dialysate [Na+] could be beneficial for improving LVH as well. There are at least two studies that examined the effect of lower dialysate sodium on structure and function of left ventricle.[29,30] One of the studies demonstrated a decrease in volumes of left ventricle associated with lower diasylate levels.[29] However, both the studies were not long enough to evaluate changes in mass of left ventricle.

Dunlop JL in a very recent systematic reviewed randomized controlled trials of low (< 138 mM) versus neutral (138 to 140 mM) or high (> 140 mM) dialysate [Na+] for maintenance HD patients. They demonstrated that low diasylate reduced the interdialytic weight gain compared to neutral or high dialysate [Na+]; probably reduced predialysis mean arterial BP; probably reduced post dialysis means arterial BP and could reduce consumption of antihypertensive medication. However, lower sodium diasylate was associated with increased events of hypotension when compared with neutral or high dialysate [Na+]. Whether lower sodium diasylate changed LV mass is uncertain due to low quality of evidence.[31]

Whether lower sodium diasylate influences the serum sodium levels is another concern for clinicians. Pre-dialysis serum [Na+] did change in several small prospective clinical trials after changes to dialysate [Na+], although often after a lag of several months. Several other studies have shown an association between low serum [Na+] and mortality in patients with kidney disease and authors suggested that an intervention that might potentially lower serum [Na+] needs stringent and careful scrutiny.[32-33]

CONCLUSION

In conclusion, this study shows that low sodium dialysate is an effective measure in decreasing left ventricular mass index and is especially recommended in patients with uncontrolled hypertension and excessive interdialytic weight gain.

Author's Contribution:

Concept & Design of Study:	Adnan Akhtar
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Revisiting Critically:	Adnan Akhtar, Shakeel Khan
Final Approval of version:	Adnan Akhtar

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

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Original Article

Radiological Examination of Elbow Joint: An Authentic Tool for Forensic Age Estimation

E-Rays of Elbow Joint for Forensic Age Estimation

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ABSTRACT

Objective: To determine the frequency of extent of fusion of epiphysis in the bones of elbow joint (lower ends of humerus and upper ends of radius and ulna).

Study Design: Descriptive observational study

Place and Duration of Study: This study was conducted at the Forensic Medicine and Radiology Departments, Govt. Khawaja Muhammad Safdar Medical College from October 2019 to September 2020.

Materials and Methods: Two hundred patients between aged 13-21 years were selected for this study. X-rays of elbow joint were taken in anteroposterior view to visualize the changes in epiphysis and diaphysis and extent of union. Subjects with fractured, malnourished and congenitally malformed elbow joint were excluded from the study after expert opinion from orthopedic surgeon.

Results: The complete fusion of epiphyses of the bones around elbow joints was observed at age of 19-21 years (Stage 4) in males and at age of 16-18 years (Stage 4) in females. Present study found that union of epiphyses of distal humerus and proximal radius and ulna appear in females earlier than in males.

Conclusion: 100% complete union of elbow joint bones, in male cases is at 19-21 year, and 100% complete union of bones of elbow joint in female cases is at the age of 16-18 years.

Key Words: Age assessment, Epiphyseal fusion, Elbow joints

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INTRODUCTION

Age assessment is a critical parameter which is used for the identification of individuals either live or dead, and for medico-legal purposes both in civil and criminal matters.[1] Estimation of age continues to be one of the most challenging aspect of skeleton analysis because of the complexity and individual variation of the aging process. Age of an individual can be assessed by using various methods such as physical examination, dentition, radiological examination, sutures of skull, graying of hair and arcussenils.[2]

Radiography is utilized extensively as investigational core in forensic and archaeological studies.[3] Undoubtedly, one of the accurate methods of estimation of age is radiological survey of ossification status of various bones.[4] Furthermore, it is considered to be a reliable guide in different methods of determination of age like appearance of epiphysis and its union with diaphysis .[5]

With increasing the cases of judicial litigation, both criminal and civil, a forensic expert has encounter with multiple issues of age estimation for which he/she has to be dependent mainly on study of different ossification centers activities. The union of epiphysis of different bones of a joint, is a reliable scientific and radiological parameter for accessing age of an individual, which is worldwide accepted by all courts of law.[6] Skeletal metamorphosis is the conversion of soft, membranous, non-ossified fetal bones into hard and ossified adult bones. The union of distal humerus, proximal radius and ulna occurs at elbow to make first joint of the body to unite.[8] Multiple ossification centers contribute in the development of a single bone. At different intrauterine ages, number of ossification centers in the bones of body are different for example at 11-12 weeks of IU life, the number of ossification centers is 806 and at birth it remains only 450, while an adult human skeleton only have 206 bones. The appearance of ossification centers and union of epiphysis with diaphysis is highly time framed, which is generally utilized towards determination of age.[6,9]

Therefore, this study's objective is to determine the frequency of extent of fusion of epiphyses in the bones of elbow joint in declared age group population. The

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variable of age can be determined accurately with the help of radiographs of elbow joint by visualizing the union of epiphysis and diaphysis between the age of 13 to 21 years.

In a society like Pakistan where forged documents are a problem too, assessment of age by forensic experts is needed. Moreover, we have a certain number of refugees and tribes who do not get them registered for age and their data is quite doubtful. Furthermore, there are many situations other than this like admission in educational institutes, retirement age, maturity, in case of marriages, adoption, guardianship, Govt. jobs, juvenile offenders, age limit for sports events at national and international levels, elections (voters and contestants) which all need age certification. Due to low literacy rate, unawareness, financial problems and shortage/ lack of time, many people do not get their children registered. There is a growing need of accurate method for age estimation in forensic medicine. However, this study is helpful to deal with such cases. The results of this study may help the forensic experts for administration of justice and for the purpose of law.

MATERIALS AND METHODS

This descriptive observational study selected 200 cases between the ages of 13-21 years presented to Radiology Department, Govt. Khawaja Muhammad Safdar Medical College Sialkot from 1st October 2019 to 30th September 2020 for X-ray of elbow joint. Convenience sampling technique was used. X-rays of elbow joint were taken in anteroposterior view to visualize the changes in epiphysis and diaphysis and extent of union. Subjects with fractured, malnourished and congenitally malformed elbow joint were excluded from the study after expert opinion from orthopedic surgeon. The study variables were epiphyseal center appearance and their fusion, age groups in both genders. Status of epiphysis union was divided into four stages. The data was entered and analyzed through SPSS-20.

RESULTS

This study observed 200 subjects including 121 males (60.5%) and 79 females (39.5%) having the age of 13 to 21 years (Fig. 1). Out of 121 male cases, lower ends of humerus fusion (LEHF) was seen in 78 males and in 74 female cases out of 79 subjects). On the other hand, an upper end of radius & ulna fusion (URUF) was observed in 78 male cases out of 121 subjects and URUF was observed in 71 females out of 79 females only (Table 1). Table-2 describes that complete extension of fusion was observed in n=78 cases (including n=10 at the Stage 3 and n=68 at the Stage 4). However, extension of Fusion was seen in 75 out of 79 female subjects at Stage 4. Furthermore, extension of Fusion was observed in n=10 male cases in the age group of 16-18 years and n=68 male subjects in the age group of 19-21 years whereas, it was observed in 75 female subjects in the age group of 13-15 years as presented in the Table-3.

Table-4 compared the reported age with the estimated age and this comparison found a significant difference between reported age and estimated age as 117 (male=73 and female=44) subjects reported their correct age. The difference between the reported age and estimated age is highly significant with the p-value <.001 out of 0.05. The results expressed the distribution of the subjects according to the reported age and actual age of the subjects. It was found that only n=63 subjects reported their age matching with their actual age and the remaining n=137 reported their age wrong as presented in Table-5.

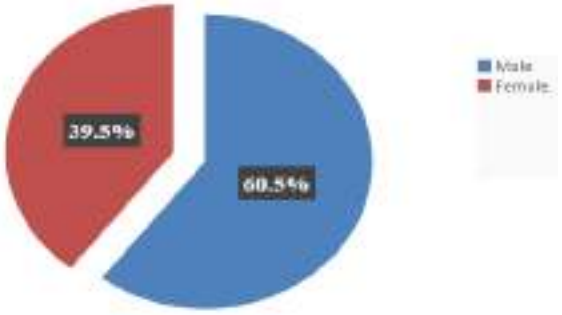

Figure-1: Distribution of gender

Table No.1: Gender-wise frequency of lower ends of humerus and upper ends of radius & ulna fusions

Variable	Gender					
	Male		Female		Total	
	n	%	n	%	n	%
Lower end of HF						
Observed	78	64.5	74	93.7	154	77.0
Not-observed	43	35.5	5	6.3	46	23.0
Upper end of RUF						
Observed	78	64.5	71	90	149	74.5
Not-observed	43	35.5	8	10	51	25.5

Table No.2: Gender-wise frequency of extension of fusion based on stages

Extension of fusion	Gender					
	Male (n=121)		Female (n=79)		Total (N=200)	
	Fused	Not Fused	Fused	Not Fused	n	%
Stage 1	0	41	0	0	41	21
Stage 2	0	2	0	0	2	1
Stage 3	10	0	0	4	14	7
Stage 4	68	0	75	0	143	71

Table No.3: Gender-wise frequency of extension of fusion based on age groups

Estimated age (group years)	Gender					
	Male (n=121)		Female (n=79)		Total (N=200)	
	Fused	Not Fused	Fused	Not Fused	n	%
13-15	0	41	0	4	45	22.5
16-18	10	2	75	0	87	43.5

19-21	68	0	0	0	68	34

Table No.4: Gender-wise comparison of reported age with estimated age

Reported age	Gender					
	Male (n=121)		Female (n=79)		Total	
	n	%	n	%	n	%
Did Match with estimated age	73	60	44	56	117	58.5
Did not match with estimated age	48	40	35	44	83	41.5

Chi-square=58.08, p-value < 0.001

Table No.5: Gender-wise status of reported age by matching with estimated age

Reported Age (years)	Matching status				
	Estimated age matched with reported		Estimated age did not match with reported		Total
	N	%	n	%	n
13	21	22	6	22	27
14	17	19	4	19	21
15	6	67	12	67	18
16	6	63	10	63	16
17	18	44	14	44	32
18	23	38	14	38	37
19	9	47	8	47	17
20	12	37	7	37	19
21	5	62	8	62	13
Total	117	58.5	83	41.5	200

Chi-square=48.24, p-value < 0.001

DISCUSSION

This study compared the reported and estimated age. This comparison found a difference between two as 117 (male=73 and female =44) subjects reported their correct age. The difference between both reported and estimated age is highly significant with the p-value <.001 out of .05. Similarly, Naik and Nagaraja[10] conducted a study with school children and college students with age group of 12 to 18 years. The age estimation in this was found to be equal to the actual age in 24 % of cases. The estimated age was found to be less than the actual age in 24% of cases by 4.5 months of age. Estimated age was found to be more than the actual age in 52% of cases by 8.5 months of age. So the average error in females was 6.5 months than the actual age. In males, the estimated age was found to be equal to the actual age in 40% of cases. The estimated age was found to be less than the actual age in 28% of cases by 7.5 months of age. The estimated age was found to be more than the actual age in 32% of cases by 5.5 months of age. It is interesting to note that both in the females and males belonging to this age group the range of error in the age estimation is 6.5 months.

This study identified that LEHF was seen in 78 subjects out of 121 male cases whereas in 74 subjects out of 79 female cases. Furthermore, 100% complete union of LEHF was seen in n=68 male cases in the age group of 19-21 years (stage 4). On the other hand, 100% complete union of LEHF was observed in n=74 female cases in the age group of 16-18 years (Stage 4). It was also found that union of LEHF was not observed in 41 male cases at the age group of 13-15 years (stage 1) and only4 female cases at the same age group and stage 3. It was found that complete union of LEHF appeared in female cases before the male subjects.

In a similar study, Nandanwar et al[11] found the age of fusion of composite epiphysis of lower end of humerus by 16-17 years in males and 14-15 years in females. Furthermore, age of union of composite epiphysis of lower end of humerus was almost similar for Europeans by Gray et al.[12] A quite old study conducted in Pakistani region by Ledger and Wasson, 1941[13] had also reported same age for girls with Nandanwar et al[11] but lower in case of boys.

This study found URUF in 78 male subjects out of 121 and in 71 female subjects out of 79 cases. Moreover, 100% complete union of URUF appeared in 68 male cases of the age group of 19-21 years (Stage 4). Whereas, 100% complete union of URUF was observed in 75 female cases of the age group of 16-18 years (Stage 4). It was also observed that union of URUF did not appear in 40 male cases at the age group of 13-15 years (Stage 1) in addition to 2 female cases at the same age group and stage. It was also found that complete union of URUF appeared in females before the male subjects.

In a similar study, Nandanwar et al[11] found that upper radial end fused with the shaft between 17 to 18 years in males and 14 to 15 years in females. This age, given by Gray et al[12] for Europeans matched with the present study and report by Ledger and Wasson[13] for Pakistanis which was also similar to that found in Nandanwar et al.[11] Nandanwar et al[11] also reviewed that union of upper end of radius and ulna appeared for Europeans is 16-17 years in males and 14-15 years in females.

Study describes that out of 121 male cases, extent of fusion of epiphyses in the bones of elbow joint was observed in 68 cases at Stage 4 for the age group of 19-21 years. Furthermore, the complete extension of fusion was observed in n=68 out of 121 male subjects of the age group of 19-21 years and Stage 4.

Similarly to my study, Nemade et al[5] performed a study among a total of 320 healthy subjects having ages of 13 to 23 years. Chronological age upto the day of examination was determined and A-P view of right elbow joint was taken in each case. This study determined that complete union of epiphyses in 100%

subjects was observed in male cases at the age of 16 to 17 years. Nandanwar et al[11] also found the union of epiphysis during the age of 17-18 years for boys.

Study found that extent of fusion of epiphyses in the bones of elbow joint was seen in 75 out of 79 female cases at Stage 3 for the age group of 16-18 years. Furthermore, the complete extension of fusion was found in 75 females out of 79 at the age group of 16-18 years (Stage 4).

Similarly, the study of Dixit and Bansal[14] found fusion of ossification centers in the upper ends of radius & ulna and lower end of humerus of females. This study discovered fusion of ossification centers found between 15 years to 15.5 years in 92% cases and between 15.5 years to 16 years in 96% cases but all the cases i.e. 100% showed fusion between 16 to 17 years. Jnanesh et al[15] reported that epiphyseal center for medial epicondyle fuses with shaft at the age of 14-15 years in females.

Memchoubi[16] described that all female participants showed their grade 3 elbow joint fusion at the age of 16 years, while Memon et al[17] concluded the grade 3 0ssification of elbow joint bones in female subjects at 14-15 years and same by Dere et al.[18]

Bokariya et al[19] reviewed that that in all studies females show earlier fusion than males. Nandanwar et al[11] also found the union of epiphysis during this very age of 14-15 years in girls.

Comparing all the studies, it was observed that fusion around elbow are by and large, similar to studies done by Nandanwar et al[11], Sangma et al[20], Memchoubi[16], Memon et al[17], Singh.[21] This similarity of age assessment by fusion of elbow joint can be attributed to this study.

The present study found difference in the ages of union of epiphyses for males and females. Similarly, the study of Nandanwar et al[11] also reported that epiphyseal union was found to be earlier in females than males.

CONCLUSION

Many participants (n=83) did not report their correct age. Due to this, a significant difference between reported age and estimated age of the subjects was determined with respect to their correct age. It was also identified that 100% complete fusion of elbow joint bones in males take place at the age of 19-21 years and in females it is at 16-18 years, means that fusion of elbow joint bones in females is earlier than in males. Assessment of age through epiphyseal fusion is an economical and reliable tool in Forensic Medicine.

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Original Article

Positive Predictive Value of Shear Wave Elastography in Predicting the Stage of Liver Fibrosis Taking Histopathology as Gold Standard

Rabia Asif, Amber Goraya and Abid Ali Qureshi

ABSTRACT

Objective: The objective of this study was to determine the positive predictive value of shear wave elastography (SWE) in predicting the stage 3 of liver fibrosis taking histopathology as gold standard.

Study Design: A cross-sectional study.

Place and Duration of Study: This study was conducted at the Research was conducted at Department of Diagnostic Radiology, Children Hospital Lahore, from April, 2019 to October, 2019.

Materials and Methods: This study involved 117 children of both genders aged between 1 to 15 years having chronic liver disease. Ultrasound abdomen was performed and stage 3 fibrosis was diagnosed on shear wave elastography (7.1-12.0 kPa). The diagnosis was later confirmed on histopathology of liver tissue. Diagnosis of histopathology was taken as gold standard and results of SWE on ultrasound were judged accordingly as true positive or false positive.

Results: The mean age of the children was 8.4±4.4 years while the mean weight was 32.1±14.9 Kg. There were 74 (63.2%) male and 43 (36.8%) female children. Histopathology confirmed diagnosis of Stage-3 liver fibrosis in 107 (91.5%) cases. Taking histopathological diagnosis of stage-3 liver fibrosis as gold standard, there were 107 (91.5%) true positive and 10 (8.5%) false positive cases. It yielded a positive predictive value of 91.5% for SWE on ultrasound in predicting stage 3 of liver fibrosis taking histopathology as gold standard. Similar positive predictive value was noted across various subgroups of children based on age (p-value=0.998), gender (p-value=0.824) and weight (p-value=0.969).

Conclusion: The positive predictive value of shear wave elastography on ultrasound was found to be 91.5% in predicting stage 3 hepatic fibrosis taking histopathology of liver tissue as gold standard.

Key Words: Hepatic Fibrosis, Ultrasound, Shear Wave Elastography, Positive Predictive Value

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INTRODUCTION

Liver fibrosis is considered to be a complex fibrogenic and inflammatory process resulting due to chronic liver injury and is known to represent initial steps in development of liver cirrhosis. Liver cirrhosis is an important health issue globally.[1,2]Known etiologies of liver cirrhosis vary geographically as alcoholism, chronic hepatitis C as well as nonalcoholic fatty lives disease (NAFLD) are the most frequent in developed western part of the world while chronic hepatitis B is the most common cause in Asia-Pacific Region.[3,4] Ultrasound-guided liver biopsy is considered to be the "gold standard" for diagnosing liver cirrhosis. However, ultrasonography (US), computed tomography, and magnetic resonance imaging (MRI) are being used to stage the fibrosis of the liver by non-incisive methods.[5] Guibal et al. in 2016 conducted a study on the patients suffering with liver diseases and found that the shear wave elastography (SWE) has positive predictive value (PPV) of 91.7% in predicting stage 3 fibrosis.[6]

There is no such local clinical study present on this topic to the best of our knowledge up to date. The SWE not only can lead to early detection of the fibrosis of the liver but also stages the fibrosis which corresponds with histopathology. As the PPV varies with the prevalence of disease there is a need to conduct this study in local population so that the PPV of SWE in determining the stage of fibrosis and progression of disease and this will ultimately help the clinicians to opt the management

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plane which reduces the progression of disease and to stop or delay reaching the cirrhosis and to reverse the fibrosis if the disease is treatable. The objective of this study was to determine the positive predictive value of shear wave elastography (SWE) in predicting the stage 3 of liver fibrosis taking histopathology as gold standard.

MATERIALS AND METHODS

This cross sectional study was done at Department of Diagnostic Radiology, Children Hospital Lahore, from 11/04/2019 to 10/10/2019. Approval from "Institutional Ethical Committee" was taken for this study. Informed consent was sought from parents or guardians of all study participants. A sample size of 117 cases was calculated by 95% confidence level and 5% margin of error while taking expected PPV of SWE as 91.7%.[6]

Inclusion criteria was patients of both sex groups with ages in the range of 1-15 years having stage-3 liver fibrosis on SWE. Patients with abnormal liver enzymes (ALT or AST >40IU) for more than 8 weeks as per clinical record undergoing SWE in the range of 7.1-12.0 kPa were labeled to have stage-3 fibrosis. All patients who had Hepatitis B or C on ELISA were excluded. Patients with congenital heart defects were also excluded. Patients who had abnormal peripheral smear as per clinical record were also not included. Patients with bleeding disorder (INR >1.5), ascites on ultrasound and histologically proven liver malignancy as per clinical record were also not included in this study.

After approval from ethical review committee of the hospital, 117 patients who presented in the radiology department, Children Hospital, Lahore fulfilling inclusion and exclusion criteria were enrolled. SWE was performed in the segment 5 of the liver. The right arm was placed in maximum abduction to enlarge the space between the ribs. During SWE acquisition, the patient was asked to stop breathing for 5 seconds. Real-time SWE 2D color map of the stiffness (in kPa) was frozen after a stabilization of at least 3 seconds. Under aseptic measures using 16-gauge needle, liver biopsy was taken and sent for the histopathology examination as per hospital protocol. Stage-3 fibrosis on histopathology was labeled as microscopic examination of liver showing bridging fibrosis along with architectural distortion.

All the data and information were noted into a specially made proforma. All the SWE were performed on the same machine by the same consultant of the radiology department and all the histopathologies were reported by the same consultant of the histopathology department to eliminate bias.

All the collected data was entered and analyzed through SPSS version 26.0. Numerical variables like age and body weight were presented by mean ±SD. Categorical variables like gender and histological diagnosis of stage 3 fibrosis were shown as frequency and percentage. Positive predictive value has been calculated by the following formula and is presented as frequency and percentage.

$$PPV = \frac{\text{True positive}}{\text{True positive + False positive}} \times 100$$

True Positive cases were patients having stage-3 liver fibrosis on SWE later found to be true on histopathology. False Positive cases were patients having stage-3 liver fibrosis on SWE later found to be false on histopathology. Data was stratified for age, gender and weight to address effect modifiers. Post-stratification, chi-square test was applied taking p-value≤0.05 as significant.

RESULTS

The age of the children ranged from 1 year to 15 years with a mean of 8.4±4.4 years. There were 74 (63.2%) male and 43 (36.8%) female children with a male to female ratio of 1.7:1. The weight of these children ranged from 8 Kg to 55 Kg with a mean of 32.1±14.9 Kg as shown in Table 1.

Table No.1: Demographic Characteristics of Cases

Characteristics		Number (%)
Age (years)	<5	35 (29.9%)
	5-10	36 (30.8%)
	>10	46 (39.3%)
Gender	Male	74 (63.2%)
	Female	43 (36.8%)
Weight (kg)	≤23	44 (37.6%)
	24-39	27 (23.1%)
	≥40	46 (39.3%)

Table No.2: Detail of PPV across various subgroups of children

Characteristics		Cases Outcome		PPV	P-value
		True Positive (n=107)	False Positive (n=10)		
Age (years)	<5	32 (91.4%)	3 (8.6%)	91.4%	0.998
	5-10	33 (91.7%)	3 (8.3%)	91.7%	
	>10	42 (91.3%)	4 (8.7%)	91.3%	
Gender	Male	68 (91.9%)	6 (8.1%)	91.9%	0.824
	Female	39 (90.7%)	4 (9.3%)	90.7%)	
Weight (kg)	≤23	40 (90.0%)	4 (9.1%)	90.9%	0.969
	24-39	25 (92.6%)	2 (7.4%)	92.6%)	
	≥40	42 (91.3%)	4 (8.7%)	91.3%	

Histopathology confirmed diagnosis of stage-3 liver fibrosis in 107 (91.5%) cases as shown in Table 2. Taking histopathological diagnosis of stage-3 liver fibrosis as gold standard, there were 107 (91.5%) true positive and 10 (8.5%) false positive cases. It yielded a positive predictive value of 91.5% for SWE on ultrasound in predicting stage 3 of liver fibrosis taking histopathology as gold standard.

Similar PPV was noted across various subgroups of children based on age (p-value=0.998), gender (p-value=0.824) and weight (p-value=0.969) as shown in Tables 2.

DISCUSSION

Recent studies have reported high positive predictive value of SWE in the non-invasive diagnosis of sage 3 fibrosis among such patients,[7-9] however, there was no such local published study which made us plan this work.

In the present study, the mean age of the children was 8.4±4.4 years. Parkash et al reported similar mean age of 8.5±2.7 years among children presenting with liver fibrosis.[10] A similar mean age of 6.9±1.8 years has been reported by Hashmi et al among such children presenting at Shifa International Hospital, Islamabad[11] while Tahir et al observed it to be 6.4±4.3 years at Fauji Foundation Hospital Rawalpindi.[12] A comparable mean age of 10.7±2.1 years was found by Dhole et al from India.[13]

We noted male to female ratio of 1.7:1. Similarly, male predominance has been reported in a number of local studies where Hashmi et al observed it to be 2.2:1 at Shifa International Hospital, Islamabad[11] and Anwar et al. reported it to be 2.1:1.[14] Dhole et al found male predominance from India in such children with male to female ratio of 1.5:1[13] while Rukunuzzaman et al observed it to be 1.4:1 in Bangladesh.[15]

We found that SWE had positive predictive value of 91.5% in predicting stage 3 of liver fibrosis taking histopathology as gold standard. Our results are in line with those of Ferraioli et al who reported similar PPV of 91.3% for shear wave elastography in Italy[16] and Guibal et al who reported it to be 91.7% in France.[6] Thiele et al reported it to be 90.0% in Denmark.[7] Comparable positive predictive value of 95.7% has been reported by Zeng et al in China.[8] Cassinotto et al observed much lower positive predictive value of 52.6% in a French study[9] while Jeong et al[17] and Zhuang et al[18] reported much higher PPV of 97.7% and 98.4% in South Korea and China respectively.

One of the limitations of this research was that we didnot consider the effect of this timely staging of liver fibrosis and anticipated management on the outcome of such children which would have further highlighted the role of SWE in the management planning of such cases.

CONCLUSION

The positive predictive value of shear wave elastography on ultrasound was found to be 91.5% in predicting stage 3 hepatic fibrosis taking histopathology of liver tissue as gold standard regardless of patient's age, gender and weight which along with its non-invasive and radiation free nature and widespread and bedside availability advocate its preferred use in future practice so that risk stratification and anticipated management may improve the outcome of such children.

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Original Article

Repair in Distal Hypospadias

Comparison of Outcome Complications between Snodgrass Technique and Mathieu's Repair in Distal Hypospadias Repair

Farasat Majid[1], Mohammad Siddique[1], Tabinda Yasmeen[3], Farhat-ul-Ain Tayyaba[4], Saleha Zafar[4] and Attiq-ur- Rahman[2]

ABSTRACT

Objective: To compare the outcome of complications between Snodgrass technique and Mathieu's repair in distal hypospadias repair.

Study Design: Randomized controlled Study.

Place and Duration of Study: This study was conducted at the Department of Pediatric Surgery, Bahawal Victoria Hospital, in collaboration with plastic surgery department and pathology department, Quaid-e-Azam Medical College Bahawalpur, from January 2019 to December 2020 over the period of 2 years.

Materials and Methods: Total 148 patients with sub-coronal and distal penile hypospadias having age 2-8 years were selected. Snodgrass technique was performed for Group A patients while Mathieu's repair was done for Group B patients. Post-operative complications were compared between the two groups.

Results: Mean age of the patients was 5.07 ± 1.73 years, mean age of patients of study group A was 4.96 ± 1.66 years and group B was 5.19 ± 1.78 years. In 6 (8.11%) patients of study group A and 21 (28.38%) patients of study group B, meatal stenosis was noted and difference of frequency of meatal stenosis between the both groups was statistically significant with p- value of 0.001. Total 5 (6.76%) patients of study group while 15 (20.27%) patients of study group B found with urethral stricture and the difference was statistically significant with p-value of 0.016. Urethrocutaneous fistula was found in 2 (2.70%) patients of study group A and in 9 (12.16%) patients of study group B. Difference of frequency of Urethrocutaneous fistula between the both groups was statistically significant with p-value of 0.028. Complete repair disruption was noted in 7 (9.46%) patients and 17 (22.97%) patients respectively in study group A and study group B and difference was statistically significant with p value 0.026.

Conclusion: Our study has revealed that TIP urethroplasty has an edge on Mathieu's urethroplasty, so we recommend the TIPurethroplasty in all primary and distal cases of hypospadias. TIP repair is associated with excellent cosmetics and few manageable complications. It offers a safe and reliable modality for primary repair of distal penile hypospadias. Cosmetic appearance of the external urethralmeatus is highly satisfactory with tubularized incised plate urethroplasty.

Key Words: Hypospadias, Snodgrass, Mathieu's repair, and urethro-cutaneous fistula

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INTRODUCTION

Hypospadias is an abnormality of anterior urethral and penile development in which the urethral opening is ectopically located on the ventrum of the penis proximal to the tip of the glans penis, which, in this condition, is splayed open.[1] It is one of the common congenital anomalies occurring in approximately 1 of 200- 300 live male births.[2] Hypospadias are classified as Distal or Anterior, middle and proximal or posterior which constitute 71%, 16% and 13% respectively.[4] In urology, surgical management of hypospadias are most controversial.[4] For urethral reconstruction, about 200 methods have been reported and they continues as modification of modifications.[5] The surgical goal in patients with hypospadias is to construct a straight penis with meatus as close to normal site as possible to allow a forward directed stream and normal coitus.[6] The common hypospadias repair techniques are Glanuloplasty, Snodgrass, Meatal Advancement and glanuloplasty (MAGPl), Mathieu, Mustarde and Thiersh-Duplay. Of these techniques, widely practice

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techniques are Snodgrass technique and Mathieu's technique.[7]

In different studies, post-operative complications of hypospadias repair like formation of urethro-cutaneous Fistula reported in 5-24% patients followed by meatal stenosis in 1.1-22.7% patients, stricture formation 0-10% patients and repair dehiscence in 1.3-6% patients.[1,5,8]

As Snodgrass and mathieu's repair are the commonly used technique for distal hypospadias repair in the worldwide but there is still a question mark on the superiority of anyone of these and more research should be required on this topic in terms of complication rate in randomized controlled trials. So, we will conduct this study between Snodgrass (tubularized incised plate urethroplasty) and Mathieu's repair to evaluate the better technique in distal hypospadias repair in terms of complication rate. Then based on these results, the better technique among these could be routinely implicated in our general practice for these particular patients in order to reduce the morbidity of our population.

MATERIALS AND METHODS

This randomized controlled trial was conducted at Department of Pediatric Surgery, Plastic surgery department, Bahawal Victoria Hospital, and Pathology department QAMC, Bahawalpur from January 2019 to December 2020 over the period of 2 years. Total 148 patients with sub coronal and distal penile hypospadias having age 2-8 years were selected.

Patients with middle and proximal hypospadias, patients with Glanular and Coronal hypospadias, patients with H/O failed repair, patients having hypospadias with chordee, patients with diseases which affect healing process i.e. Diabetes Mellitus (assessed on history) and patients' guardians not willing to be included in the study were excluded from the study.

An approval was taken from institutional review committee before conducting the study. Written consent was taken from each patient's parents.

All the selected patients were randomly divided into two equal groups i.e. group A and group B. Blood samples of 5ml was taken in EDTA tube from each patient to perform complete endocrinal profile including FSH, LH and Testosterone. The samples were performed in Pathology Department QAMC, on fully automated hormone analyzer Access-2(Beckmann coulters).

Snodgrass technique was performed for Group A patients while Mathieu's repair was done for Group B patients.

Patients were frequently visited post-operatively and followed fortnightly for presence of any complication (repair disruption, urethrocutaneous fistula, meatal stenosis and urethra stricture). The final outcome was noted at the end of the 3 months postoperatively. Samples for hormonal profile were also taken postoperatively.

All the findings along with demographic profile of the patients were noted on pre-designed proforma.

The collected information was analyzed by computer software SPSS version 20.0. Mean and standard deviation was calculated for age. Frequency and percentage was calculated for site of hypospadias, urethrocutaneous fistula, repair disruption, meatal stenosis and urethral stricture. Both groups were compared for presence of any difference among the urethra-cutaneous fistula, repair disruption, meatal stenosis and urethra stricture (present/absent). Chi Square test was used to compare the frequency of complications and p-value ≤ 0.05 was considered as significant. Effect modifiers like age and site of hypospadias was controlled through stratification and post-stratification chi square test was applied to see their effect on outcome. P-value ≤ 0.05 was considered as significant.

RESULTS

Mean age of the patients was 5.07 ± 1.73 years, mean age of patients of study group A was 4.96 ± 1.66 years and group B was 5.19 ± 1.78 years. Table 1 showing comparison of complications between the two study groups. In 6 (8.11%) patients of study group A and 21 (28.38%) patients of study group B, meatal stenosis was noted and difference of frequency of meatal stenosis between the both groups was statistically significant with p value 0.001. Total 5 (6.76%) patients of study group A while 15 (20.27%) patients of study group B found with urethral stricture and the difference was statistically significant with p value 0.016. Urethrocutaneous fistula was found in 2 (2.70%) patients of study group A and in 9 (12.16%) patients of study group B. Difference of frequency of Urethrocutaneous fistula between the both groups was statistically significant with p value 0.028. Complete repair disruption was noted in 7 (9.46%) patients and 17 (22.97%) patients respectively in study group A and study group B and difference was statistically significant with p value 0.026. Patients were divided into two age groups i.e. age group 2-4 years and age group 5-8 years. Among patients of age group 2-4 years, there is no patient of meatal stenosis in study group A while meatal stenosis was seen in 9 (32.14%) patients of study group B. Difference of meatal stenosis among study group A and B was statistically significant with p value 0.000. Urethral stricture was seen in 2 (2.70%) patients and 5 (17.86%) patients of study group A and B but difference was not statistically significant with p value 0.13. Urethrocutaneous fistula was observed in 1 (2.94%) patients of study group A while in 3 (10.71%) patients of study group B. But difference was insignificant with p value 0.21. Complete repair disruption was noted in 4 (11.76%)

patients and 8 (28.57%) patients respectively in study group A and B. Difference was statistically insignificant with p value 0.096. (Table 2)

In age group 5-8 years, meatal stenosis was seen in 6 (15%) patients and 12 (26.09%) patients respectively in study group A and B. Difference of meatal stenosis between both groups was statistically insignificant with p value 0.207. Urethral stricture was noted in 3 (7.5%) patients of study group A and in 10 (21.74%) patients of study group B. Difference was statistically insignificant with p value 0.066. Urethrocutaneous fistula was found in 1 (2.5%) patient and in 6 (13.04%) patients of study group A and B. Difference of frequency of urethra-cutaneous fistula between both groups was statistically insignificant with p value 0.075. Complete repair disruption was seen in 3 (7.5%) patients and 9 (19.57%) patients of study group A and B, but difference was statistically insignificant with p value 0.107. (Table 3)

Out of 48 patients of study group A and 47 patients of study group B, meatal stenosis was noted in 5(10.42%) patients and 13 (27.66%) patients of group A and B respectively. Difference was statistically significant with p value 0.032. Urethral stricture was noted in 4 (8.33%) patients of study group A and 11 (23.40%) patients of study group B. Difference of frequency of urethral stricture between both groups was statistically significant with p value 0.04. Urethrocutaneous fistula was observed in 2 (4.17%) patients and 4 (8.51%) patients but the difference was statistically insignificant with p value 0.38. Complete repair disruption found in 3 (6.25%) patients of study group A while in 13 (27.66%) patients of study group B. Difference was statistically significant with p value 0.005. (Table 4)

Table No.1: Comparison of complications between the two groups

Group	Complications		Total	P. Value
	Yes (%)	No (%)		
Meatal stenosis				
A	6 (8.11)	68 (91.89)	74	0.001
B	21 (28.38)	53 (71.62)	74	
Urethral stricture				
A	5 (6.76)	69 (93.24	74	0.016
B	15 (20.27)	59 (79.73)	74	
Urethrocutaneous fistula				
A	2 (2.70)	72 (97.30)	74	0.028
B	9 (12.16)	65 (87.84)	74	
Complete repair disruption				
A	7 (9.46)	67 (90.54)	74	0.026
B	17 (22.97)	57 (77.03)	74	

Total 26 patients of study group A and 27 patients of study group B found with distal penile site of hypospadias. Meatal stenosis was found in 1 (3.85%) patients of study group A while in 8 (29.63%) patients of study group B. Difference of frequency of meatal stenosis between both groups was statistically significant with p value 0.012. Urethral stricture was observed in 1 (3.85%) patients and 4 (14.81%) patients of study group A and B respectively. But the difference was not statistically significant with p value 0.17. Levels of LH and FSH done were significantly raised, but testosterone levels were low pre-operatively.

Table No. 2: Comparison of complications between the two groups for age group 2-4 years

Group	Complications		Total	P. Value
	Yes (%)	No (%)		
Meatal stenosis				
A	0 (0)	34 (100)	34 (45.95)	0.000
B	9 (32.14)	19 (67.86)	28 (37.84)	
Urethral stricture				
A	2 (2.70)	32 (94.12)	34 (45.94)	0.13
B	5 (17.86)	23 (82.14)	28 (37.84)	
Urethrocutaneous fistula				
A	1 (2.94)	33 (97.06)	34 (45.95)	0.21
B	3 (10.71)	25 (89.29)	28 (37.84)	
Complete repair disruption				
A	4 (11.76)	30 (88.24)	34 (45.94)	0.096
B	8 (28.57)	20 (71.43)	28 (37.84)	

Table No.3: Comparison of complications between the two groups for age group 5-8 years

Group	Complications		Total	P. Value
	Yes (%)	No (%)		
Meatal stenosis				
A	6 (15)	34 (85)	40 (54.05)	0.207
B	12 (26.09)	34 (73.91)	46 (62.16)	
Urethral stricture				
A	3 (7.5)	37 (92.5)	40 (54.05)	0.066
B	10 (21.74)	36 (78.26)	46 (62.16)	
Urethrocutaneous fistula				
A	1 (2.5)	39 (97.5)	40 (54.05)	0.075
B	6 (13.04)	40 (86.96)	46 (62.16)	
Complete repair disruption				
A	3 (7.5)	37 (92.5)	40 (54.05)	0.107
B	9 (19.57)	37 (80.43)	46 (62.16)	

Table No.4: Comparison of outcome between groups at the end of three months for sub-coronal site of hypospadias

Group	Complications		Total	P. Value
	Yes (%)	No (%)		
Meatal stenosis				
A	5 (10.42)	43 (89.58)	48 (64.86)	0.032
B	13 (27.66)	34 (72.34)	47 (63.51)	
Urethral stricture				
A	4 (8.33)	44 (91.67)	48 (64.86)	0.04
B	11 (23.40)	36 (76.60)	47 (63.51)	
Urethrocutaneous fistula				
A	2 (4.17)	46 (95.83)	48 (64.86)	0.38
B	4 (8.51)	43 (91.49)	47 (63.51)	
Complete repair disruption				
A	3 (6.25)	45 (93.75)	48 (64.86)	0.005
B	13 (27.66)	34 (72.34)	47 (63.51)	

Table No.5: Comparison of outcome between groups at the end of three months for distal penile site of hypospadias

Group	Complications		Total	P. Value
	Yes (%)	No (%)		
Meatal stenosis				
A	1 (3.85)	25 (96.15)	26 (35.14)	0.012
B	8 (29.63)	19 (70.37)	27 (36.49)	
Urethral stricture				
A	1 (3.85)	25 (96.15)	26 (35.14)	0.17
B	4 (14.81)	23 (85.19)	27 (36.49)	
Urethrocutaneous fistula				
A	0 (0)	26 (100)	26 (35.14)	0.021
B	5 (18.52)	22 (81.48)	27 (36.49)	
Complete repair disruption				
A	4 (15.38)	22 (84.62)	26 (35.14)	0.95
B	4 (14.81)	23 (85.19)	27 (36.49)	

DISCUSSION

The purpose of present study was to compare the complications between Snodgrass technique and Mathieu's repair in distal hypospadias repair. The mean age (5.07±1.73 years) of the patients in our study was more as compared to the age reported by other authors.[9-10] This may be due to lack of awareness and education on the part of parents and delayed referral from rural health care centers. In our study there were 64.2% cases were sub-coronal site of hypospadias and 35.8% were distal penile hypospadias. The position of meatus in our study was consistent with that reported by, Bath et al., and Sugarman et al.[11-12]

In our study, over all post-operative complication rate was found significantly low in the group A, where Snodgrass technique was performed. As evident in our series, the urethrocutaneous fistula and meatal stenosis rate was more in Mathieu's group as compared to that of Snodgrass group. One explanation for this is the need for two suture lines in case of only flap technique on either side which might be jeopardizing the vascular supply of the flap. In a study by Hakim et al, Mathieu technique results with and without urethral stenting were compared in 336 cases of anterior hypospadias. No significant difference was seen in fistula formation (2.63% vs. 2.7%) and total surgical complications rate (2.63% vs. 3.6%) between these two groups.[13] In the study by Imamoglu et al, 56 patients were operated on using Snodgrass technique and 54 patients were operated on using Mathieu technique .They concluded that if the urethral plate is intact, Snodgrass technique will be preferable and if not, Mathieu technique will be much better.[14] In the study by Oswald J et al, total 60 patients were operated, 30 by Snodgrass technique and 30 by Mathieu technique and results were compared regarding fistula formation, appearance, and duration of surgery in patients with anterior hypospadias. They concluded that Snodgrass technique is accompanied by better results and more natural meatal appearance.[15] In yet another study[16] both the procedures were combined to avoid the risk of devascularisation of the neo-urethral flap**.**

CONCLUSION

Our study has revealed that TIP urethroplasty has an edge on Mathieu's urethroplasty, so we recommend the TIPurethroplasty in all primary and distal cases of hypospadias. TIP repair is associated with excellent cosmetics and few manageable complications. It offers a safe and reliable modality for primary repair of distal penile hypospadias. Cosmetic appearance of the external urethralmeatus is highly satisfactory with tubularized incised plate urethroplasty.

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Original Article

Efficacy of Copper Sulphate to Prevent Ophthalmic and Dermatological Human Infections

Naseer Ahmad Raja[1], Aneela Khawaja[2], Durdana Zafar[3], Uzma Nazim[1], Rubina Tallay Qasim[4] and Muhammad Arshad Rana[5]

ABSTRACT

Objective: Copper is an essential trace element for human body. To date unfavorable effects of copper sulphate are related to environmental or occupational matters. No information has been documented regarding its use for healing or preventive purposes. This study determines the efficacy of copper sulphate in preventing ophthalmic and dermatological infections in humans in village of Punjab, Pakistan.

Study Design: Descriptive observational study

Place and Duration of Study: This study was conducted at the Community Medicine,Rahbar Medical & Dental College, Lahore from January, 2010 to December, 2020.

Materials and Methods: Total 400 study participants of different age groups (5-60 years), living in same environmental conditions, were divided into 2 equal groups as cases (n=200) and control (n=200). Gender distribution was equal in all age groups of both cases and control. Verbal consent was taken from all the adult subjects (18-60 years) and from parents of children (5-17 years). The participants of case group took Crystals of copper sulphate orally, in dose of 1 µgper Kg of body weight (¼ of millets size) after meal once weekly, usually with glass (250 ml) of milk. Control subjects did not take any medicine.

Results: Among 200 case participants, only 1.5% acquired ophthalmic and dermatologic infection. None of the children among case group developed any ophthalmic or skin disease. Among control group, 57% of the adult subjects expressed eye and skin infections (p-value .0016), while 16% children and 15% children developed eye and skin infection respectively.

Conclusion: The use of copper sulphate for therapeutic purposes has been reported for the first time. Local authorities must take regulatory measures regarding public awareness in terms of beneficial effects of copper sulphate.

Key Words: copper sulphate, beneficial effects, dermatologic, ophthalmic, infection

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INTRODUCTION

Copper is an essential micronutrient element, that maintains the health status of an individual adequately. The medicinal use of copper sulphate ranges from treatment as antibiotics, as prophylactic for skeletal muscle disorders, anemias, hypotrophy, and in diagnostic radiology for neoplastic disorders.[1,2] Although microelements are consumed in very less amount but several physiological roles like enzymes and /or hormone production, growth regulation, developmental and functional progress of immune and reproductive systems are regulated by essential trace elements.[3]

Consumption of copper by human civilizations dates back to 5000 BC. With the advancement of science and technology, now we know that copper maintains the epithelial and connective tissues within the body, and tensile strengthening of the skin and circulatory system. Some vital key roles i.e., production of different pigments and hormones cannot occur without copper. Therapeutic application of copper containing combinations shows vast biological activity as antibiotic, antifungal, anti-inflammatory, antimalarial as well as anticancer[4, 5].

Among different groups of people oral use of copper sulphate is a traditional and hereditary norm. These groups correlate a number of beneficial effects of

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copper sulphate on human body as treatment and prevention of different diseases, i.e., improved vision and prevention of eye infections, treatment of skin diseases, better quality life, prevention of neurological disorders as its deficiency or low concentration in early life can result in underdevelopment of central nervous system.[6,7]

Previous studies have documented use of copper sulphate as an emetic to achieve intoxication after exposure to poisonous substances [8] A Bordeaux mixture named as invented in the Bordeaux region of France, contains copper sulphate is used as fungicide in farming. Although, it was introduced as preventive remedy, but prolonged use became poisonous to human subjects and weather pollutant [9].

The aim of this descriptive observational study is to assess the efficacy of copper sulphate in preventing ophthalmic and dermatological infections in humans.

MATERIALS AND METHODS

This study was conducted at the Community Medicine, Rahbar Medical & Dental College, Lahore from January, 2010 to December, 2020. Total 400 study participants enrolled on voluntary basis, were divided into 2 equal groups as cases (n=200) and control (n=200). Verbal consent was taken from all the subjects above 18 years of age, and from parents of children (age 5-17 years); after explaining the good and bad/ dangerous effects of copper sulphate on human body, including use of over dose and empty stomach. Children less than 5 years of age, pregnant women and adults not giving verbal consent and not willing to participate in the study were excluded. Demographic variables like age in years, height in inches, weight in kilogram and body mass index (BMI) of all the case and control subjects was noted. Gender distribution was equal in cases and controls. The participants of case group took crystals of copper sulphate orally, in dose of 1 µgper Kg of body weight (¼ of millets size) after meal. This dose was taken once weekly, usually with glass (250 ml) of milk. Some persons complaint of vomiting after ½ to 2 hours because of gastric irritation. A metallic taste was felt in the mouth for about one day. Some individuals took it in capsule and some preferred in jaggery, to avoid the bitter/metallic taste of copper sulphate in mouth. None of the case subjects took copper sulphate on empty stomach. Control group did not take any medicine. All the study individuals were living in the same environmental conditions and for cooking, drinking and washing purposes consuming same irrigation system.

Statistical analysis: The data was analyzed using SPSS version 20. Continuous variables were summarized as mean and standard deviation (±SD) while categorical variables were expressed as frequency and percentages. Statistically, P-value ≤ 0.05 was considered significant

RESULTS

Gender distribution was same in both case (n=200) and control group (n=200). Age wise distribution among both case and control group is shown in figure 1 (p-value=.50). None of the children in case group acquired either ophthalmic or dermatological infection. On the other hand, 32 children (16%)and 25 adults (12.5%) got eye infections; 30 children (15%) and 27 adults (13.5%) developed skin infections from control group as shown in Table 2 (p-value significant, .0016).

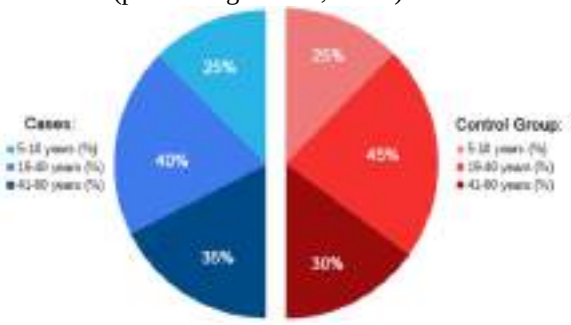

Figure No.1: Frequency distribution of different age groups in cases and controls (n=400)

Table No.1: Demographic Details of Study Population (n=400)

Demographic Variables	Mean ± SD (Cases)	Mean ± SD (Control)
Age (years)	32.35 ± 15.07	31.3 ± 14.49
Height (inches)	64.3 ± 3.81	64.3 ± 3.81
Weight (kilogram)	62.94 ± 15.25	62.28 ± 14.85
Body mass index (BMI)	23.6 ±8.6	23.3 ±8.45

Table No.2: Comparison of Ophthalmic and dermatological infections in study population (n=400)

Variables	Cases (n=200)		Control (n=200)	
	Males	Females	Males	Females
Ophthalmic Infections	None	01	35 (17.5)	22 (11)
Dermatological infections	02	None	33 (16.5)	24 (12)
Total (%)	02 (01)	01 (0.5)	68 (34)	46 (23)
	3 (1.5)		114 (57)	
Chi-sq p-value	0.338 .56		9.87 .0016*	

(*p-value → highly significant)

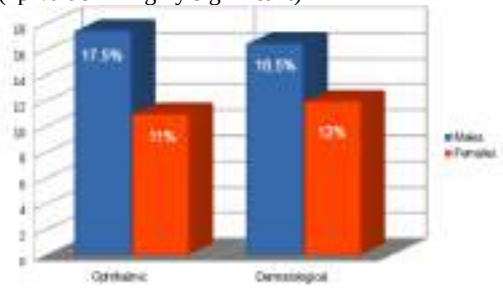

Figure No.2: Frequency percentage of ophthalmic and dermatological infections in control group (n=200).

DISCUSSION

Copper metabolism is directly or indirectly involved in some of the neurological disorders (acerulo-plasminemia, Alzheimer disease, amyotrophic lateral sclerosis, Huntington disease, Menkes disease, occipital horn syndrome, Parkinson disease, prion disease, and Wilson disease). Inadequate levels or low concentration of copper can lead to incomplete development of central nervous system can be prevented by suitable levels of copper sulphate. Minimal mood changes had been documented by our study participants using copper sulphate regularly. This positive effect is comparable with the antidepressant effect of copper sulphate use documented by Słupski. [7]

The beneficial effects of copper on spinal cord ischemia -reperfusion injury have been observed in animal models. [10] Medicinal effect of copper sulphate along with hot spring water on eczematous skin condition has been documented by Ribet et al. [11]

Currently, various applications of copper are of vital importance in day-to-day life. With the advancement of technology, metallic copper surfaces have greatly reduced the percentage of nosocomial pathogens in health care centers [12, 13]. This date back, when copper was used for sterilizations of drinking water, disinfections of swimming pools, eye ailments, burns, skin ulcers, chest wounds, headache and other neurological symptoms since 2000 B.C. Researchers have documented possible health effects of copper tubing, home wells and in childhood hepatic disorders. [14,15]

CONCLUSION

The efficacy and real benefits of copper sulphate on human subjects need further elaboration. Data supporting favorable use of copper sulphate as a trace element is lacking. To the best of our knowledge not a single case of copper over dosage and or poisoning was seen in our study subjects.

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Original Article

Comparison of the Prophylactic Effect of Dexamethasone, Ondansetron with the Combination of Dexamethasone on Decreasing Nausea and Vomiting in Children

Sheharyar Ashraf, Jawad Hameed, Abid Haleem Khattak and Sajjad Orakzai

ABSTRACT

Objective: The study aims to predict the efficacy of dexamethasone alone and dexamethasone plus ondansetron in a pediatric population age range from 3 to 10 years old. This research is specifically designed for measuring the outcomes of PONV incidents among the pediatric population and confirm the success ratio of these two anti-emetogenic drugs.

Study Design: Double-blinded randomized controlled trial study.

Place and Duration of Study: This study was conducted at the Anesthesia and Critical Care Department Lady Reading Hospital-MTI Peshawar from January to December 2019.

132 patients in total, were selected for the study. Patients on physical status stage I and II described by the American Society of Anesthesia (ASA) were selected for this research. We administer a 30mg dose of dipyrone NSAID as a placebo. Initially, 0.1 mg dose of ondansetron associated with dexamethasone was used later on dose was increased up to 4 mg whereas 0.15 mg dexamethasone was used alone.

Results: Postoperative vomiting was observed in 16 total cases, out of which the majority belonged to placebo and dexamethasone alone group (14.3% and 14% respectively). Little (6.8%) cases of postoperative vomiting were found among the ondansetron group. We did not find any significant statistical differences in our study. All the p values were greater than 0.05.

Conclusion: There is a need for routine administration of anti-emetogenic drugs among the high emetogenic risk surgeries in order to avoid PONV. Whereas in low emetogenic risk surgeries regular administration of prophylactic treatment is not much necessary.

Key Words: Postoperative Nausea and vomiting, Placebo study, Dexamethasone, Ondansetron plus dexamethasone.

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INTRODUCTION

After surgery, complications like nausea and vomiting occurs immediately which causes adverse effects on the patient's health.[1-5] This condition causes discomfort among patients and needs proper treatment[6-7]. It may also result into the maximization of the hospital stay of patients[8]. This lengthened hospital stay leads to excessive hospital stay cost which might be a financial burden on many patients[9].

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The literature revealed that the risk of postoperative nausea and vomiting is comparatively high (8.9% to 42%) among the pediatric population as compared to adults[10-11]. Not every child expresses his discomfort of nausea which results in unreported cases and is considered as a major obstacle in measuring the actual incidence of nausea among the pediatric population[11]. PONV causes dehydration, esophageal rupture, bleeding, and increased morbidity among patients[13].

Many treatments are introduced in the market to sort out this issue. The majority of the children had less tolerance of nausea and vomiting which needs proper management for this age group[14]. Children are sensitive and not all kind of medicine suits them. There is a limitation of drugs for children and physicians prefer different drugs with limited side effects which helps to control complications of nausea and vomiting among the child age group[14]. Still, there is no specific drug found yet for this age group. Most commonly physicians used serotonin 5-HT3 receptor antagonists (ondansetron) and the dexamethasone but still, it is not considered as an ideal treatment for the pediatric group[15-17].

In this study we try to predict the efficacy of dexamethasone alone and dexamethasone plus ondansetron in a pediatric population age range from 3 to 10 years old. This research is specifically designed for measuring the outcomes of PONV incidents among the pediatric population and confirm the success ratio of these two anti-emetogenic drugs.

MATERIALS AND METHODS

This double-blind randomized Placebo-controlled trial was conducted in Lady Reading Hospital Peshawar, from January to December 2019. A total of 129, children from the age group 3 to 10 years were admitted to the surgical department during studies. All the patients were divided into three major categories; dexamethasone, ondansetron in combination with dexamethasone, and placebo for the prophylactic treatment of POV. Patients were selected only after they fulfill inclusion criteria and their parents signed written consent. The sample size was extracted from two previous studies in which they report 8.9%[10] vomiting incidence in the group receiving dexamethasone plus ondansetron whereas in the placebo group they report 42% vomiting incidence[11-12]. With the help of this population proportion, the stat calc function formula was used to calculate sample size with a 5% margin of error on a 90% confidence interval. After the calculation of sample size, 120 patients were allocated equally into three groups (40 in each). Predicting a loss of about 10%, 12 more patients were included and then 132 patients were randomly assigned into three subdivisions with an equal number of participants (44 each). A random allocation software program was used for the randomized allocation of participants. Patients on physical status stage I and II described by the American Society of Anesthesia (ASA) were selected for this research. All the children who already use anti-emetogenic drugs, having a history of vomiting within 24 hours of the pre-surgical process, and having any kind of previous allergic history of dexamethasone and ondansetron were excluded from this research.

We collected all the information regarding patient age, sex, gender, anesthesia stage, surgery type, postoperative pain, the occurrence of vomiting, and vomiting following discharge from hospital as a major variable of this research.

For this research, vomiting is described as a condition in which one episode of forceful expulsion of the stomach content occurs from the mouth in between admission in PACU and 24 hours of hospital discharge. Those patients who fulfilled inclusion criteria were shifted to the anesthesia preparation room. In the operation room, a regular checkup was conducted including cardioscopy, capnography, monitoring through oximeter, and we measured blood pressure of patients. After these observations, anesthesia was administered by inhalation of sevoflurane and nitrous oxide with the help of a facemask. Patients were strictly prohibited from taking any food and drink before the surgical process. 20 ml /kg Ringer's lactate solution was immediately administered to the patient and maintained throughout the procedure. Bupivacaine 0.25% was used as general anesthesia. We administer a 30mg dose of dipyrone NSAID as a placebo. Initially, 0.1 mg dose of ondansetron associated with dexamethasone was used later on dose was increased up to 4 mg. Whereas 0.15 mg dexamethasone was used alone.

The dose was injected through syringes which were prepared by another anesthesiologist who prepared two syringes containing 5ml and 10ml dose respectively in order to conduct a double-blind study. Physicians who evaluated the patient's condition were also blind about the medication. Frequency of vomiting and pain was observed during the study. In the case of medical emergency 0.15 mg metoclopramide was used as a rescue drug. When the child retains consciousness, pain was observed and for those cases who had no complaint of pain were allowed to take oral ingestion of clear fluids. We formed discharged policy on the following criteria; those who retain their consciousness with drowsiness, mild pain, and low vomiting frequency, and who easily tolerate oral ingestion. A telephone call was conducted after the 24 hours of discharge in order to investigate the frequency of vomiting and pain[18].

For the statistical analysis, we used SPSS version 23.0 to apply a t-test for the independent group. All the data were analyzed by using the Chi square test $\chi 2$. A Chi square test was applied to calculate the original ratio with our expected outcomes. To analyze the frequency of vomiting and pain we used Chi square and Fisher's formula. $P < 0.05$ was set as significant and two-tail tests were applied for all variables.

RESULTS

During the study time, a period total of 219 children underwent from surgery. From these participants, only 134 patients fulfilled the inclusion criteria. From these selected participants, patients of two children did not agree to give written consent which was excluded from the research. In each group 44 participants were allocated, unfortunately, two from the placebo group and one from the dexamethasone group refuse to participate in the study anymore. Homogeneous baseline characteristics were taken for the studies to create harmony in our results. The majority of the patients were male and belong to ASA I stage. We observed that 5 participants had a family history of PONV and two of them had vomiting before surgery. The inguinal hernia was the most frequently performed surgical process during the study interval.

A total of 16 cases of postoperative vomiting was observed and the majority of them belong to the

placebo and dexamethasone alone group (14.3% and 14% respectively). Little (6.8%) cases of postoperative vomiting were found among the ondansetron group. We did not find any significant statistical differences in our study. All the p values were greater than 0.05.

Table No.1: Demographic characteristics of selected participants[18]

Variables	Group			P-value
	Dexame-thasone n= 43	Placebo n= 42	Ondan-setron+ dexame-thasone n= 44	
Gender				0.92
Male	33 (76.7)	31(73.8)	34 (77.3)	
Female	10 (23.3)	11(26.1)	10 (22.7)	
Weight	20.6 (8.8)	19.8(6.9)	19.5(6.0)	0.76
Age	4.6 (2.5)	5 (2.4)	4.7 (2.4)	0.79

Table No.2: Baseline characteristics, information regarding type of surgery and postoperative observations.[18]

Variables				P-value
	Dexame-thasone n= 43	Placebo n= 42	Ondanse-tron+ dexame-thasone n= 44	
ASA				0.65
I	41(95.3)	42(100)	43 (97.7)	
II	2 (4.7)	0 (0.0)	1 (2.3)	
Surgery type				0.1802
Orchidopexy	2 (4.7)	3 (7.1)	1 (2.3)	
Phimosis surgery (circumcision	10 (23.3	8 (19.0)	16 (36.4)	
Double surgical procedure	4 (9.3)	4 (9.5)	2 (4.5)	
Umbilical hernia	6 (14.0	10 (23.8)	14 (31.8)	
Inguinal hernia	21 (48.8)	17 (40.5)	11 (25.0)	
Vomiting (n/%)	6.0 (14.0) 2.0 (4.7)	7.0 (16.7)	3.0 (6.8) 0 (0.00)	0.47
Pain	4.0 (9.3)	8.0 (19.0)	5.0 (11.4)	0.37
Vomiting following discharge from hospital	2.0 (4.7)	3.0 (7.1)	0 (0.00)	0.16

DISCUSSION

Post-operative nausea and vomiting are complications which cause discomfort in patients. The majority of the children had less tolerance of nausea and vomiting which needs proper management for this age group. Children are sensitive and not all kind of medicine suits them. There is a limitation of drugs for children and physicians prefer different drugs with limited side effects which helps to control complications of nausea and vomiting among the child age group[14]. Still, there is no specific drug found yet for this age group[15]. For this study, we use prophylactic ondansetron plus dexamethasone, dexamethasone alone. Our results revealed that Dexamethasone alone had no significant results to control the Nausea in the high-risk pediatric population. On the other hand, combination of these two drugs with droperidol enhance the postoperative adverse events. The majority of the patients suffer from drowsiness after the administration of drugs[19].

In past, a very limited amount of studies had been conducted to access the benefits of anti-emetogenic drugs for children. A prospective study evaluates the efficacy of anti-emetogenic drugs on adult patients and revealed that these drugs decrease the postoperative Nausea and Vomiting incident ratio from 28% to 22%[20]. On the other hand, we observed that Ondansetron plus Dexamethasone reduce the incidence of POV among high-risk children. Recent studies show that almost 30-70% of children are at high risk of POV in the absence of anti-emetogenic drugs[21]. Our results are in accordance with the previous study of Gunter and colleagues in which they found greater efficacy in the group using Ondansetron plus Dexamethasone as compared to the group who used three anti-emetogenic drugs (Ondansetron, dexamethasone, and droperidol) at the same time[22].

Our study demonstrates that the risk of POV is found in 12% of children without any significant difference between groups. In 5 patients vomiting reported after the hospital discharge. During the study, we did not find any difference in POV at the time of surgery, duration of anesthesia, in the post-anesthesia care unit, and in-hospital stay. In a previous study of Kovac and Schofield, the ratio of PONV among ranges from 8.9%-42%[10-12]. This ratio depicts that the risk of PONV is twice higher than the adults[11,23]. Difficulty in estimating true incidents of nausea induce a high variation of incidence. After the introduction of ondansetron different researches were conducted to justify its efficacy as a prophylactic treatment of PONV in the pediatric population[14,24,25]. Researchers claim that Ondansetron is the best treatment for preventing Nausea and vomiting complications among children especially when combined with dexamethasone[26]. In our study the risk of POV was very low still we did not find any significant statistical significance of ondansetron. These contradictory results might occur due to the difference in a surgical procedure. There is a chance that this treatment will be effective in case of

surgeries like adenoidectomy, tonsillectomy, strabismus with high emetogenic potential[27].

In tonsillectomies, a high risk of POV occurs due to the serotoninergic receptors (5-HT3)[28]. Many studies observed that PONV increases hospital stay and enhance the risk of re-admission among pediatric population[28-29]. This risk can be avoided with regular administration of anti-emetogenic drugs. Some other researchers revealed that due to the absence of nausea reports by children the incidence of nausea and vomiting is highly underestimated in the pediatric population[30]. In our study, we found a low ratio of POV, and the incidence of POVN did not increase hospital stay. POV incidence was not frequent, so the any significant association with the adverse event and other risk factors like a family history of POV was not found.

CONCLUSION

We conclude that there is a need for the routine administration of anti-emetogenic drugs among the high emetogenic risk surgeries in order to avoid PONV. Whereas in low emetogenic risk surgeries regular administration of prophylactic treatment is not much necessary. We recommend that more studies will be conducted on this age group to find an association between adverse events and the history of patients in order to establish an efficient method of management.

Author's Contribution:

Concept & Design of Study:	Sheharyar Ashraf
Drafting:	Jawad Hameed, Abid Haleem Khattak
Data Analysis:	Sajjad Orakzai
Revisiting Critically:	Sheharyar Ashraf, Jawad Hameed
Final Approval of version:	Sheharyar Ashraf

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

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Original Article

Assessment of Oligohydramnios in Pregnant Women: Outcome of Hydration Therapy

Oligohydramnios in Pregnant Women

Sadia Rashid[1], Samia Perwaiz Khan[2], Safia Izhar[3], Shazia Kadri[3], Saira Ghafoor[1] and Nazish Ali[4]

ABSTRACT

Objective: The study was designed to determine the role of ultrasound as a tool in assessing of low amniotic fluid index (AFI) or Oligohydramnios and perinatal outcomes. Determination of improvement in low AFI on Hydration therapy.

Study Design: Case-Control study

Place and Duration of Study: This study was conducted at the tertiary care hospitals from May 2019 to May 2020. Data was collected from Obstetrics & Gynecology and Sonology departments (Jinnah Medical and Dental College Hospital JMDCH and Medicare Cardiac & General Hospital) for period of one year. Four hundred pregnant women were included in the study.

Materials and Methods: Total two hundred pregnant women with oligohydramnios were included as cases and equal normal pregnant women as controls were included in study with no other medical issue. All those with any associate medical issue were excluded from this study. Amniotic fluid volume was measured by amniotic fluid index (AFI) or single deepest pocket (SDP)in pregnant women. Amniotic fluid index 5 cm was considered to be oligohydramnios and cause of number of complications such as preterm labour, low Apgar score , birth weight, infections and even cause fetal demise were recorded.

Results: Out of total, 200 pregnant women had the ultrasound finding of oligohydramnio. AFI less than 5 cm were oligohydramnios and between 5.1 to 7cms were borderline. Delivery before 37 weeks in 134 (69%) oligohydramnios cases and 30(15%) were normal controls. Birth weight less than 2.5 kg in 44 (22%) cases and 34 (17%) controls. Low APGAR scores calculated in cases both at 1 minute was 178(89%), at 5 min 22(11%) . NICU admission were done for 22(11%) neonates as compared to 14(7%) neonates o from normal pregnancies. Hydration therapy improved the amniotic fluid index (AFI) and outcome of pregnancies.

Conclusion: Oligohydramnios increases the risk of early delivery with low birth weight, APGAR score and increase risk of NICU admissions. Hydration therapy improved the amniotic fluid index (AFI)

Key Words: Amniotic fluid index, Oligohydramnios**,** Ultrasound, Hydration therapy. Amniotic fluid volume, Single deep pocket.

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INTRODUCTION

Amniotic fluid is not only necessary for the protection and movement of fetus but also most important for overall well being of fetus and normal delivery. The measurement of amniotic fluid index is most important in obstetrics evaluation for the perinatal outcomes and delivery.

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The key factors regulating the amniotic fluid volume (AFV) during the subsequent half of the pregnancy are foetal pulmonary excretion and development of fetal urine, fetal swallowing and intramembrane movement between fetal blood and placenta. The calculation of the amniotic fluid may take place ultrasoundwise using amniotic fluid index(AFI), amniotic fluid volume 2 by 2 scales, single deep baggage (SDP), amniotic fluid index and maximum vertical bag.[1] Normohydroamnios (range 7-20 cm), oligohydramnios (less than 5 cm), and polyhy adroamnios may be measured amniotic fluid index (25 cm and above). Low amniotic fluid volume may be idiopathic or idiopathic through underproduction. Underproduction can be the result of missing kidneys or failure, obstruction of the urinary tract, impaired placental activity, or maternal dehydration. Loss mostly due to membrane breakup. The work for this irregular sign of life in prenatal tests includes maternal history, ruptured membranes assessment, renal system evaluation and foetal bladder

evaluation, as well as the assessment of placental and foetal growth functions [1-5].

The outcome of pregnancy with low Amniotic Fluid Index (AFI) /Oligohydramnios. Amniotic fluid index (AFI) is an estimate of amniotic fluid volume in pregnant uterus. Normal values of amniotic fluid index varies with gestational age. Amniotic fluid index range between 5-25 cm is considered normal, medial amniotic fluid index level is 9-14 cm from week 20 to 35. Amniotic fluid index 5 cm or less is considered oligohydramnios. Amniotic fluid index (AFI) is 7 cm for second and third trimester pregnancies, and amniotic fluid index of 5cm or less is diagnosed as oligohydramnios. AFI 25 cm or greater is considered to be polyhydramnios[1-] . Amniotic fluid has important functions during pregnancy and at the time of delivery. It forms a hydrostatic wedge pressure which facilitates dilatation of the cervix, prevents obstruction, maintains placental circulation during uterine contractions, antibacterial properties that protect against the risk of infections. Abnormalities associated with amniotic fluid like meconium staining, congenital malformations, growth restriction and fetal hypoxia. Thus, the ultrasound measurement of amniotic fluid volume is an important part of antenatal fetal investigations. It is also an important indicator of fetal well-being during pregnancy and delivery. Sufficient amount of amniotic fluid is most essential for normal pregnancy and delivery outcome[2,5] . Oligohydramnios (AFI< 5) was associated with more number of preterm deliveries, fetal distress and more NICU (neonatal intensive care unit) admissions. More studies are needed for defining threshold levels for measuring AFI.[2]

In a study[2], the measurement of AFV (amniotic fluid volume) was done by ultrasound, and then actual AFV was directly measured during the cesarean delivery to compare the subjective method (SM), amniotic fluid index (AFI), single deepest pocket (SDP), and 2-diameter pocket . Another study [5] including 235 pregnant women with normal AFI ≥10 and borderline AFI≤5 was done to evaluate risk of premature delivery and low Apgar scores.

The abnormalities associated with low amniotic fluid include growth restriction, preterm delivery, fetal hypoxia and demise .Thus it is essential to assess AFI during antenatal follow-ups. It is also an important indicator of fetal well-being during pregnancy and delivery. Study [5] has shown significance poor outcome of borderline oligohydramnios. The purpose of this study was to find out pregnancy outcome with low AFI /Oligohydramnios.. Amniotic fluid index between 7-25 cm is considered normal, medial amniotic fluid index level is 14 cm from week 20 to 35. Amniotic fluid index less than 5 cm are oligohydramnios and between 5.1 to 7 is considered to be borderline pregnancies with oligohydramnios and this may result in a of number of complications such as preterm labour, low Apgar score, birth weight, infections and may even cause fetal demise.

The study was designed to determine the role of ultrasound as a tool in assessing of low amniotic fluid index (AFI) or oligohydramnios and perinatal outcome. Effects of hydration therapy on low AFI.

MATERIALS AND METHODS

This study was conducted at Jinnah Medical and Dental College Hospital (JMDCH) and Medicare Cardiac & General Hospital from May 2019 to May 2020. Total two hundred pregnant women with oligohydramnios were included as cases and equal normal pregnant women as controls were included in study with no other medical issues and intact membranes. All those with any associate medical issue were excluded from this study. Transabdominal Ultrasound was done on Xario-100 machine. Measurement of AFI in four quadrants of abdomen and pelvis and single deep pocket methods for the calculation of amniotic fluid volume. AFI was calculated by four quadrant 2x2 (5-25 cms)and single deep pocket measurement SDP(2-8cms) . In this study pregnant woman with oligohydramnios was divided in two groups as AFI ≤ 5cm and AFI≤ 5.1 to 7cm was taken as a borderline.

Total two hundred cases and equal control pregnant women were included in study with no other medical issue. All those with any associate medical issue were excluded from this study (ruptured membranes, hypertension, diabetes, preeclampsia, birth defects etc). Abdominal and pelvic ultrasound examination was done in patient in supine position. After the exposure, the abdomen gel was applied and abdomen was divided into four quadrants. By using umbilicus as the reference point in each quadrant, the measurement in the deepest pool of amniotic fluid avoiding the fetal parts calculated. Sum up of four measurements of all four quadrants done to calculate AFI.the anteroposterior diameters of the largest empty fluid pocket (no umbilical cord or fetal parts) in each quadrant are added together. The normal AFI range between 7 to 25 cm. In addition, Single deep pocket method was also performed by measurement of the largest vertical pocket of amniotic fluid, free from fetal parts or umbilical cord. Each individual pocket of fluid was 2 to 8 cm in normal pregnancies.

All the participants filled consent form and ethical approval was taking from the ERC, Jinnah Medical and Dental College. Data were collected from the Obstetrics and Gynecology and Sonology departments. In this study oligohydramnios cases were divided into two groups as low AFI ≥ 5 and borderline AFI≥ 5.1 - 7cm. Hydration therapy was recommended in cases of oligohydroamnious by Obstetrician and measurement of AFI were repeated.

The pregnancies with low AFI were divided into two groups with one group less than 5 cm and one group 5-7 cm as only pregnant women with 7 cm AFI fulfill the requirement for being eligible for Cesarean-section. The ultrasound examinations were on pregnant women in third trimester of pregnancy with no known obstetric on medical complication with only reported low amniotic fluid index in previous ultrasounds.

The results were statistically analyzed and students't-test compared the four quadrants values of amniotic fluid were summarized to get AFI. Students t-test was applied to compare characteristic p-value 0.05 was considered significant. Categorical variables were given as percentages. The data was collected using SPSS 20.0 and comparisons was done between oligohydramnios (cases) and normohydroamnious (controls) perinatal outcome by applying students t- test. Women having 20-35 weeks single pregnancy were included in the study. All those with twin or multiple pregnancies or any other fetal defects were excluded from the study. Study was approved by Ethical Review Committee.

RESULTS

In a study done on four hundred pregnant women visiting the obstetrics and gynecology department and Sonology department JMCH and Medicare cardiac and general hospital. Out of total of 400 pregnant women the ultrasound finding of pregnant women with oligohydramnios were two hundred over a period of one year. Age range was between 18 - 40 years. AFI was (less than 5cm) booked oligohydramnios cases 138(69%) and in normal control 182 (91%). Un - booked oligohydramnios cases were 62 (31%) and normal controls were 18(9%). Primigravida with oligohydramnios were 158 (79%) and controls were 168 (84%) whereas multipara cases were 42 (21%) and 32 (16%). Gestational age at delivery below 37 weeks in cases 134 (69%) and controls 30(15%). Gestational age above 37 weeks in cases was 66(33%) and a control was 170 (85%) and p-value was highly significant (table-1).

Table No.1: Characteristics of pregnanices with oligohydroamnious & controls.

Maternal characteristics		**Oligohydramnios** (AFI less than 5 cm)	**Control** (AFI 5-25 cm)	**p-value**
Age (18-40yrs) Amniotic fluid index		200 pregnancies Amniotic fluid index (AFI)	200 normal pregnancies Amniotic fluid index (AFI)	-
Booking status	Booked patients	138 (69%)	182 (91%)	0.001
	Un booked Patients	62 (31%)	18 (9%)	0.065
Parity	Primary	158(79%)	168(84%)	0.246
	Multipara	42(21%)	32(16%)	0.589
Gestation age at delivery	Before 37wks	134(69%)	30(15%)	0.001
	After 37wks	66(33%)	170(85%)	0.001

Table No.2: Perinatal outcome of pregnancy with oligohydroamnious.

Outcomes	**Oligohydramnios (n=200)**	**Control (n=200)**	**P-value**
Birth Weight ≤ 2.5kg ≥2.5kg	44 (22%) 156(78%)	34(17%) 174(87%)	0.002 0.51
APGAR score at 1 min (normal range 7-10)	178(89%) (Range 0-6)	16(8%) (Range of 7-10)	0.05
APGAR score at 5 min (normal range 9-10)	22(11%) (Range of 0-5)	14(7%) (Range of 9-10)	0.05
NICU admission	22(11%)	14(7%)	0.05

Table No.3: AFI* before and after hydration therapy in oligohydroamnious cases.

AFI*	**Oligohydramnios (n=100)**	**Control (n=100)**
Before treatment	4.1 (4-5 cm)	14 (7-20cm)
After Hydration therapy	7.1 (7- 9cm)	14 (7 -20cm)
Improvement in AFI	3.0 (+ 3-5)	0.02 (+0.00-0.02)

***AFI-** Amniotic Fluid Index.

Outcome of pregnancy was determined by birth weight less than 2.5 kg in 44 (22%) cases and 34 (17%) controls. Birth weight 2.5kg was found in 156(78%) case and 174(87%) control. Low APGAR score at 1 min (range of 5-7) 178(89%) and 186(93%) controls (range 7-10). APGAR score at 5 min in 22(11%) cases (range of 5-6) and 14(7%) controls (range was 7-10). NICU admission was required for 22(11%) cases and 14(7%) controls (table -2). Before hydration therapy the oligohydramnios and after hydration therapy shown improvement in amniotic fluid index above 7 (+3-5cm) (table-3).

DISCUSSION

Amniotic fluid index was found to be an essential biomarker in determining the mode of delivery and perinatal outcome of pregnancy, was by assessed by measurement of AFI 2x2 and single deep pocket methods in the study. Studies [2-7] has shown that in assessment of amniotic fluid volume by AFI and single deep pocket was the methodology most commonly used and have positive correlation. Sonographic estimation of amniotic fluid can be done by AFI measurement or single deep pocket (SDP). Amniotic fluid index was helpful in determining the delivery method and the outcome of pregnancy (the birth weight, Apgar score, NICU admission etc). In this study it has shown the outcome of two hundred pregnancies with oligohydramnios has shown 134(69%) deliveries before 37 week of gestation as compare to 30(15%). In addition, the delivery after 37 weeks was in 44 (22%) pregnancies with oligohydramnios as compared to 170(85%) with normal volume of AFI. .Study shown to be Oligohydramnios is a condition of abnormally low amniotic fluid volume that has been associated with poor pregnancy outcomes[7-8]. In study it seen that oligohydramnios (AFI< 5) was associated with more number of preterm deliveries, fetal distress and higher NICU admissions. [7]

This study shown high frequency of oligohydramnios in pregnant women in population of Karachi is a one of common problem in low socioeconomic populations and developing countries[8-11]. The prevalence of this disorder and its findings have not been well described in low-middle-income countries with a restricted use of ultrasound for pregnancy diagnosis. Low income antenatal treatment was conducted to determine the prevalence and adverse maternal, foetal and neonatal effects of oligohydramnios[11].

In the study we used AFI measured in four quadrants and single deepest pool . Multiple studies and trials[12-16], have shown that no single sonographic method (AFI, SDP) has emerged superior to the others. Randomized trials in difficult pregnancies showed no difference to delivery, NICU intake, umbilical artery pH or APGAR score relative to the use of SDP (single deep pocket) against amniotic fluid index (AFI). The only significant result has been that AFI has found more pregnancies than deep pockets as oligohydramnios (SDP) [17-18].

Our study has shown increase in preterm deliveries, low Apgar scores (1 minute and 5 minutes), more frequent ICU admission of neonate in pregnancies with oligohydroamnious . Management depends on the gestational age when diagnosed in pregnancy with oligohydramnios. If after 37 weeks of gestational age and membranes rupture is removed, labour induction will be an option. A retrospective cohort study found that 206 pregnancies of oligohydramnios had labour induction outcomes as compared with 206 spontaneous work with normal AFV, thereby raising the likelihood of operational delivery (forceps, vacuum and caesarean)[19].

The pregnant women on diagnosis of oligohydramnios were provided oral / intravenous hydration therapy which improved AFI to above 7 thus increased overall outcome of pregnancies and reduced risk of preterm cesarian sections or stillbirths. Studies done on providing hydration therapy in pregnancies with oligohydramnios in third trimester and this management reduced the risk of adverse outcomes due to reduced amniotic fluid volume Study[20] done with isolated oligohydramnios and itsmanagement of the pregnant women by oral hydration. Studies[21-22] done reporting improvement in outcome by hydration. Studies[23-24] have shown intravenous hydration increased amniotic fluid index and overall outcome of pregnancies without causing any complications. A questionnaire based study was conducted on management of isolated oligohydroamnious (without maternal or fetal abnormality) , participants were from Korean Society of maternal and fetal medicine. Although 47.2% reported that oral and intravenous hydration have found to be useful in management of isolated oligohydroamnious but further studies were recommended[25] Similarly this study reported improvement in AFI after oral or intravenous hydration therapy.

CONCLUSION

Amniotic fluid index (AFI) was found to be most important biomarker for the diagnosis of oligohydroamnious. As normal amniotic fluid volume is required for perinatal well being and outcome of pregnancy including term delivery, intrauterine growth and prevention of post-delivery NICU admission of neonate. This study has shown that oligohydramnios is high frequency in developing countries like Pakistan and it is essential to do follow-ups by ultrasound measurement of AFI in order to have safe and healthy outcome of pregnancy and reducing the risk of adverse outcomes. Study also supports management by hydration therapy, especially beneficial in borderline.

Author's Contribution:

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Original Article

Frequency of Silent Gallstones in Acute Pancreatitis

Allah Nawaz[1], Ahmad Hassan Khan[1], Raza Farrukh[2], Khalid Mahmood[1], Nazim Hayat[4] and Amir Nazir[3]

ABSTRACT

Objective: The aim of this study is to determine the frequency of silent gallstones in acute pancreatitis.
Study Design: Observational/ cross-sectional study
Place and Duration of Study: This study was conducted at the Department of Surgery, District Headquarter Teaching Hospital Sargodha from January 2019 to July 2020.
Materials and Methods: One hundred and sixty two patients were included in this study. Patients were aged between 18-80 years. Patients who developed acute pancreatitis were presented in this study. Patients detailed demographics age, sex and BMI were recorded after taking written consent. Frequency of silent gallstones was measured. Complete data was analyzed by SPSS 24.0 version.
Results: Out 162 patients 65 (40.12%) were males and 97 (59.88%) were females. Mean age of the patients were 40.5±7.22 years with mean BMI 28.9±3.45 kg/m^2. Frequency of silent gallstones was 45 (27.8%) and rest 117 (72.22%) were acute biliary pancreatitis with previous history of biliary colic. In 117 patients of acute biliary pancreatitis frequency of females was greater.
Conclusion: In this review, we concluded that the incidence of silent gallstones is more likely to have acute biliary pancreas.

Key Words: Silent gallstones, Pancreatitis, Biliary tract

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INTRODUCTION

The majority of adults in Europe and the USA are affected by the occurrence of silent stones in the general population1. However, only a small proportion of these patients experience symptoms or complications[1]. In effect, most gallstones are referred to as clinically "silent," typically injuries which are often discovered during the abdominal investigation.[2] Some of those with gallstones experience painful bile colic symptoms that can lead in the event to conditions such as pancreatitis or acute cholecystitis.[3] But the incidence is very low, only in 2% to 3%.[4]

Acute pancreatitis, an inflammatory disease of the pancreas, in about 80 per cent of patients is usually mild and self-resolved without lasting effects.

It involves a complex cascade of events, from acinar cell damage to pancreatic cells, leading to pancreas leakage and premature activation. It initiates auto digestion; the breakup of enzymes triggers edema and bleeding tissues and cells.[5] The bile or the pancreatic duct may be migrated and blocked by gallstones. Due to the obstruction of the ducts, pressure in the pipe is increased and therefore, the digestive enzymes are not triggered in a controlled manner which increases the risk of pancreatitis[6,7].

Gallstone pancreatitis (GSP) is a moderate, complicated disease in 80% of cases and death risk is 1–3%[8]. The gallstones of faeces have been found at 90% of gallstone pancreatitis, suggesting that stones are randomly distributed through the duodenum. Many stones with a diameter of less than 5 mm and cystic conduct with a large lumen (5 mm or more) are included[9].

The gallstone size is closely linked to acute biliary pancreatitis development risk. The risk of developing pancreatitis is 4 times greater in patients with Gallstones smaller than 5 mm diameter compared with patients with larger Gallstones.[10] Accurate diagnosis of Acute Biliary Pancreatitis is critical as stone removal reduces possibility of recurrence. Photos are the gold standard for biliary lithalsas diagnosis. In uncomplicated cases, but with acute biliary pancreas, ultrasound sensitivity is greater than 95 per cent, whereas gallstone detection is less than 80 per cent, since the distension of ileus and bowel is less than sensitive.[11] The serum lipase sensitivity for the diagnosis of acute pancreatitis is marginally more sensitive than that of serum amylase. Serum lipase

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levels occur earlier and remain longer as well. Thus patients should undergo a serum lipase test for confirmation in order to make a tentative diagnosis of the acute pancreas. To make the diagnosis it is important to raise serum lipase 3-fold from the upper normal limit.[12] This research has been undertaken to retrospectively assess the possible association of silent, small gallstones with bile pancreatitis.

MATERIALS AND METHODS

This cross-sectional/observational study was conducted at department of Surgery, District Headquarter Teaching Hospital Sargodha. The study was conducted for duration of Eighteen months from January 2019to July 2020 and comprised of 162 patients. After taking informed written consent, detailed demographics including age, sex and body mass index were recorded. Patients were aged between 18-80 years. Patients who developed acute pancreatitis were presented in this study. Acute pancreatitis diagnosis was based on typical signs and symptoms, seral and lipase levels, ultrasound findings and abdominal CT scans. Frequency of silent gallstones was measured in terms of frequency and percentage. Complete data was analyzed by SPSS 24.0 version.

RESULTS

Out 162 patients 65 (40.12%) were males and 97 (59.88%) were females. Mean age of the patients were 40.5±7.22 years with mean BMI 28.9±3.45 kg/m^2. (table 1)

Table No.1: Detailed demographics of enrolled cases

Variables	Frequency	%age
Gender		
Male	65	40.12
Female	97	59.88
Mean age	40.5±7.22	
Mean BMI	28.9±3.45	

Frequency of silent gallstones was 45 (27.8%) and rest 117 (72.22%) were acute biliary pancreatitis with previous history of biliary colic. Mostly patients 122 (75.1%) were from the age group greater than 30 years. (table 2)

Table No.2: Frequency of silent gallstones

Variables	Frequency	%age
Silent gallstones	45	27.8
Acute pancreatitis	117	72.22
Distribution with age (years)		
<30	40	24.9
>30	122	75.1

We concluded from the results, frequency of acute biliary pancreatitis was higher in females and in elder adults.

DISCUSSION

Prevalence of gallstones is about 15% of the general population.[13] Age, sex and obesity are the main risk factors. Childbearing, alcohol abstinence and certain drugs are among the least risk factors.[14] Silent gallstones were observed for the abdominal pain in 27.8% of the participants who suffered from acute pancreatitis. In our study mostly patients 122 (75.15) were greater than 30 years of age. In some global estimates gallstones and alcohol account for around 70% to 80% of the cases, constitute the most frequent aetiology of acute pancreatitis.[6]

Gallstones in our sample were observed more often in women than in men or in the age group. In addition to a German report on the aetiology of pancreatitis, acute pancreatitis has been shown to be closely linked to older age and female predominance.[15] Out 162 patients 65 (40.12%) were males and 97 (59.88%) were females. Mean age of the patients were 40.5±7.22 years with mean BMI 28.9±3.45 kg/m^2. These results were comparable to the previous studies conducted by Amna Shahab et al.[16] Diehl et al presented 50% of acute pancreatitis patients contained 20 stones or more of a dimension less than 5mm[17]. We also found similar results in our research. Since abdominal ultrasound is readily available, silent gallstones are diagnosed with increased frequency. The treatment remains controversial, however. For patients with a high risk of complications, gallbladder, diabetic or immune-suppressive treatment, prophylactic cholecystektomy is recommended.

AsGS is important because postoperative immune suppression is required in patients undergoing transplantation. The masking of signs and symptoms due to immunosuppression can cause a rising level of morbidity and mortality. Some of the immunosuppressive medicines, like cyclosporine and tagrolimus, are prolithogenic. The purpose of prophylaxis is to remove a potential septic flag, as the mortals of emergency cholecystectomy in patients with immunosuppression have been documented to be higher. Around 10 percent of infection-related cases of acute pancreatitis have occurred. These infectious agents include bacterial agents such as mycoplasm, legionella, leptospira, viruses like the cytomegalovirus, human immunodefi virus, herpes simplex virus and varicellazotervirus.. Pancreatitis can also be rarely caused by fungi (aspergillus) and parasites (toxoplasmosis, ascaris, cryptosporidium).[19] Patients with several small gallions have a higher risk of acute biliary pancreattitis. For asymptomatic patients with microlithiasis, cholecystectomy may be advised but not urgently needed.. ERCP with biliary sphincterotomy may be the preferred method of treatment for patients who are weak surgical candidates.

CONCLUSION

In this study, we concluded that the incidence of silent gallstones is more likely to have acute biliary pancreas.

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Original Article

Comparison of Efficacy of Oral and Vaginal Tablet Misoprostol for Medical Management of Missed Miscarriage

Rubina Amjad[1], Kausar Parveen[2], Saima Umer[5], Nargis Taj[2], Zohra Samreen[3] and Ashiq Hussain[4]

ABSTRACT

Objective: To compare the efficacy of tablet Misoprostol orally and vaginally for medical management of missed miscarriage.

Study Design: Double blind randomized clinical trial study.

Place and Duration of Study: This study was conducted at the Gynecology and Obstetrics department (Tertiary care hospital Bolan Medical College / Hospital, Quetta for 6 months since 2nd June 2019 to 2nd Dec 2019.

Materials and Methods: Total of 180 patients with clinically diagnosed of missed miscarriage and confirmed by ultrasound were included in this study. Patients were divided into two groups. The group A received tablet Misoprostol orally while group B received tablet Misoprostol vaginally.

Results: Out of 180 patients with clinically diagnosed of missed miscarriage were used. Age wise distribution shows that women of most cases were effective with Misoprostol between 21-30 years followed by 31-40 years and <=20 years in both groups.General characteristics such as mean age, gravity, parity and gestational age were not important between groups.Rate of successfully complete miscarriage was significantly high in vaginal Misoprostol patients (Group B) as compare to oral Misoprostol patients (Group A)[78.9% vs. 54.4%; p=0.001]. Stratification analysis was also performed to control effect of age and parity. Rate of successfully complete miscarriage was significantly high in vaginal Misoprostol patients (Group B) as compare to oral Misoprostol patients (Group A) for the age 21 to 30 years of age cases while below and equal to 20 as well as above 30, it was not observed significant.For primiparous and multiparous groups, successfully complete miscarriage was significant between groups while nulliparous it was not significant

Conclusion: It is concluded that Misoprostol is an effective and safe agent so it may be used for second trimester termination of pregnancy.

Key Words: Miscarriage, Misoprostol, Oral, Vaginal, Tablet.

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INTRODUCTION

Clinical miscarriage accounts for approximately 12% of pregnancies [1]. Dilatation and curettage, which is usually done in an operating room, has been the preferred procedure for missed miscarriage for the last 50 years, thus greatly raising the costs [2].

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Worldwide abortions over the mid-trimester constitute only 10%-15% of all induced abortions, but they are responsible due to its higher success rate due to its particular myometrial sensitivity, Misoprostol has substituted all other methods for pregnancy termination, as well as being inexpensive, stable at room temperature, can be kept for a long time, and easily accessible[3].

However, compared to similar studies from China and India that used 600ug of sublingual and vaginal Misoprostol and reported an overall success rate of 87.5 percent and 86 percent, respectively, it is much less than that reported [4].

A second trimester pregnancy termination study of oral verses of vaginal Misoprostol shows that the success rate at 24 hours in the vaginal group 70 percent corresponds to oral group 50 percent in addition, no significant difference in the success rate at 48 hours oral 65 percent and 70 percent [5]. There are few retrospective studies that show that there is no increased risk of uterine rupture[6].

Given the reported better efficacy and comparatively easy absorption of misoprostol for medical management of missed miscarriage, this study aims to analyze the effect of this treatment specially in the perspective of a population belonging to a relatively less developed areas of this country. This study will help our understanding regarding some important aspects in terms of efficacy and less complication of misoprostol treatment for missed miscarriage in such a population and will open the avenues for further research in this area.

MATERIALS AND METHODS

All patients who presented with sign and symptoms of missed miscarriage diagnosed by consultant having experience of 10 years and senior registrar having experience of 5 years and also confirmed by ultrasound was admitted in Gynecology and Obstetrics department (Tertiary care hospital BMCH) through OPD and giving the informed consent and fulfilling the inclusion and exclusion criteria was included in this study.

Complete data of patients regarding age, gravidity, parity, last menstrual period, gestational age, ultrasound finding (conformation of missed miscarriage) was taken. These findings were observed by a single person of level of consultant or senior registrar so as to avoid any intra observational bias in the misdiagnosis of missed miscarriage. Patients were divided into two groups. The group A received tablet Misoprostol orally while group B received tablet Misoprostol vaginally. The researcher was blind by giving tablet Misoprostol to each group.

The dose of Misoprostol 400micrograms (2 tablets) was given at the start. The effect of the tablet was seen four hourly and if the product of conception are expelled within 16 hours by 4 doses given by either route, then drug was labeled as efficacious with that particular route of administration. Clinical outcome in the form of complete expulsion of product of conception successful or unsuccessful and complications was compared in two groups and was filled on proforma by researcher herself.

Statistical analysis: The data collected was analyzed using computer packages SPSS version 17.0. The quantitative data like age, gravidity, parity, gestational age was analyzed by calculating mean and standard deviation (SD). The study result like complete miscarriage (successful/ unsuccessful) was compared among group A and group B to look the efficacy of oral and vaginal tablet Misoprostol for medical management of missed miscarriage, frequency and percentages was analyzed in both groups by chi square test. The level of significance was less than and equal to 0.05. Stratification was done to controlled effect modifies like age and parity. Post stratification chi-square test was done.

RESULTS

A total of 180 patients with clinically diagnosed of missed miscarriage and confirmed by ultrasound were included in this study. Patients were randomly allocated into two groups; group A were treated with tablet Misoprostol orally while group B were treated with tablet Misoprostol vaginally.Age wise distribution shows that women of most cases were effective with Misoprostol between 21-30 years followed by 31-40 years and <=20 years in both groups as shown in Figure-1.

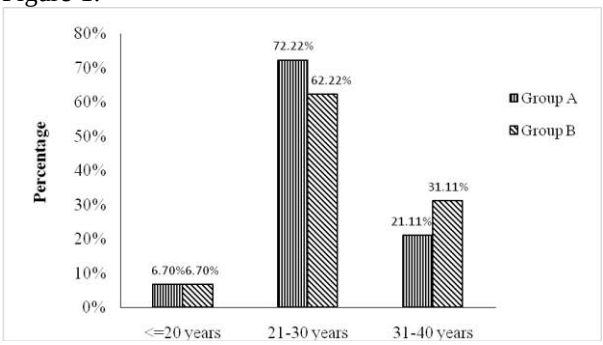

Figure No.1: Age wise distribution of the patients with respect to Groups (n=180)

General characteristics such as mean age, gravity, parity and gestational age were not important between groups as shown in Table-1.

Table No.1: Comparison of general characteristics of the between groups

Variables	**Group A** (Oral) **n=90**	**Group B** (Vaginal) **n=90**	**P-Value**
Age (Years)	27.40±4.54	28.08±5.33	0.36
Gravida	2.41±0.51	2.47±0.58	0.41
Parity	1.20±0.71	1.29±0.72	0.40
Gestational Age (Weeks)	20.46±2.78	19.87±2.96	0.17

*Data are presented as mean and standard deviation Independent sample t test.

Table No. 2: Compare the efficacy of oral with vaginal tablet Misoprostol for medical management of missed Miscarriage

Complete Miscarriage	**Group A** (Oral) **n=90**	**Group B** (Vaginal) **n=90**	**Total**
Successful (Efficacy-Yes)	49(54.4%)	71(78.9%)	120(66.7%)
Unsuccessful (Efficacy-NO)	41(45.6%)	19(21.1%)	60(33.3%)

Comparison of the efficacy of oral with vaginal tablet Misoprostol for medical management of missed miscarriage is presented in Table-2. Rate of

successfully complete miscarriage was significantly high in vaginal Misoprostol patients (Group B) as compare to oral Misoprostol patients (Group A) as shown in Table-2.

Efficacy was measured in terms of complete expulsion (successful) of dead fetus after 4 doses given over 16 hour's period without complications. Stratification analysis was also performed to control effect of age and parity. Rate of successfully complete miscarriage was significantly high in vaginal Misoprostol patients (Group B) as compare to oral Misoprostol patients (Group A) for the age 21 to 30 years of age cases while below and equal to 20 as well as above 30, it was not observed significant as shown in Table-3.

Table No. 3:Compare the efficacy of oral with vaginal tablet Misoprostol for medical management of missed miscarriage with respect to age groups

Age Groups (Years)	Complete Miscarriage	Group A (Oral) n=90	Group B (Vaginal) n=90	P-Value
≤ 20 Years	Successful Unsuccessful Total	3(50%) 3(50%) 6	5(83.3%) 1(16.7%) 6	0.22
21 to 30 Years	Successful Unsuccessful Total	34(52.3%) 31(47.7%) 65	48(85.7%) 8(14.3%) 56	0.0005
31 to 40 Years	Successful Unsuccessful Total	12(63.2%) 7(36.8%) 19	18(64.3%) 10(35.7%) 28	0.93

For primiparous and multiparous groups, successfully complete miscarriage was significant between groups while multiparous it was not significant as shown in Table-4.

Table No.4:Compare the efficacy of oral with vaginal tablet Misoprostol for medical management of missed Miscarriage by parity

Parity	Complete miscarriage	Group A (Oral) n=90	Group B (Vaginal) n=90	P-Value
Nulli-parous	Successful Unsuccessful **Total**	9(75%) 3(25%) **12**	4(50%) 4(50%) **8**	0.25
Primi-parous	Successful Unsuccessful Total	24(47.1%) 27(52.9%) 51	41(77.4%) 12(22.6%) 53	0.001
Multi-parous	Successful Unsuccessful Total	16(59.3%) 11(40.7%) 27	26(89.7%) 3(10.3%) 29	0.009

*Data are presented as n(%). Chi-Square test applied for each age categories

DISCUSSION

In our part of the world, Termination of Pregnancy (TOP) is performed only if there is a significant risk of a fetus with severe congenital abnormalities, intrauterine fetal death or in the presence of medical conditions that pose a real threat to the health or life of the mother. Other prostaglandins, such as prostaglandin E2 and prostaglandin F2 alpha (PGF2 alpha), were mostly used for second trimester terminations prior to the availability of Misoprostol (a synthetic analogue of prostaglandin E1). These agents are effective but costly, require refrigeration and need higher doses, which in a high percentage of patients are associated with side effects such as nausea, vomiting, diarrhea and fever.[7]Since 1993, abortifacient properties of Misoprostol have been documented in medical literature for second trimester termination.[8] Misoprostol is an economical agent, can be kept at room temperature, sustainable for years, and has few systemic effects[9].Misoprostol is an economic and efficient abortifacient drug for second trimester pregnancy termination in these days of financial constraints with shorter induction to abortion interval with few side effects.[10] Due to scary economic resources and high temperatures, this agent is particularly important for a country like ours. In these days of financial constraints, Misoprostol is an economical and effective abortifacient drug for second trimester pregnancy termination with shorter induction to abortion interval with few side effects.[10] This agent is especially relevant for a country like ours because of scare economic resources and high temperature.[11]

Age wise distribution shows that women's of most cases were effective with Misoprostol between 21-30 years followed by 31-40 years and <=20 years in both groups.General characteristics such as mean age, gravity, parity and gestational age were not important between groups. In Shah et al[12] study there was no significant difference with respect to age, parity, gestational age and uterine size between the two groups.

In this study rate of successfully complete miscarriage was significantly high in vaginal Misoprostol (Group B) as compare to oral Misoprostol (Group A) [78.9% vs. 54.4%; p=0.001]. In a study regarding oral verses vaginal Misoprostol in second trimester pregnancy termination shows that the success rate at 24 hours at vaginal group 70% corresponds with oral group 50% in addition, no significant difference in the success rate at 48 hours oral 65% and 70%.[5.] Few observational studies have shown that there is no increased risk of uterine rupture in women who experience Misoprostol second trimester pregnancy termination.[6]Second trimester pregnancy termination that is complicated by fetal demise is usually more predictable with a shorter induction-expulsion interval than that conducted when the fetus is alive, an observation revealed this could be due to the increased sensitivity of the uterus to prostaglandins and the release of tissue factors following fetal demise.[13]Bebbington et al[14], Dickinson[15] and Ho et al[16] revealed a shorter induction-expulsion interval for vaginal route of the drug as compared to oral route for Misoprostol it. Ho et al [16] used

mifepristone as a pre-induction agent and none of pregnancy in their study were terminated because of fetal demise or fetal anomalies, whereas in the present study pregnancies were terminated mainly because of fetal demise and structural anomalies.Surgical evacuation was required in about 37% of cases in oral group versus 33% in vaginal group in Mahjabeen et al[17] study, while Iqbal quoted the need of surgical evacuation in 21.4% in oral protocol versus 13.8% in vaginal protocol.[18] The difference in the results could be due to higher dosage schedule as compared to this study, which also resulted in decreased failure rate in their study.A study which compared the efficacy of sublingual and vaginal Misoprostol in second trimester termination of pregnancy has reported a higher success rate (85%) for vaginal Misoprostol compared to sublingual Misoprostol (64%) at 24 hours but there was no significant difference in the abortion rate at 48 hours.[19]A study from UK which compared sublingual and vaginal Misoprostol for medical abortion also reported unpleasant taste in 63.9% of women in the sublingual group as compared to 37.5% of women in the vaginal group ($p = 0.02$).[20] In addition, two other studies comparing sublingual and vaginal Misoprostol have reported a significantly increased frequency of unpleasant taste in women taking sublingual misoprostol.[21] It is suggested that this side effect may be overcome by making the misoprostol tablet sugar coated. Other side effects like nausea and shivering were also seen slightly more frequently in the sublingual group. This increased frequency of side effects may be explained by the higher bioavailability of sublingual misoprostol.[22]

Gilbert and Reid[23] also reported no significant difference in side effects between both groups of oral and vaginal misoprostol.[23]However, Bebbington et al[15] reported increased febrile morbidity in patients who received misoprostol by vaginal route. This may be due to high dose of the drug (400 µg) in their study. Dickinson et al[16] also noticed more side effects with higher dosage of vaginal misoprostol, while Kamalet al[24] reported no significant difference between side effects of misoprostol while comparing vaginal with orovaginal route.The main limitation was single center study, smaller sample size and involvement of different gastroenterologists. So additional studies with larger sample sizes are necessary.

CONCLUSION

Misoprostol is an effective and safe agent so it may be used for second trimester termination of pregnancy. Vaginal route of administration appear to more effective as compared to oral route so vaginal route can be a convenient option as it will be preferable for patients as well as health care providers.

Author's Contribution:

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

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Original Article

Demographic Trends of Substance Abuse, Treatment

The Elephant in the Room: Demographic Trends of Substance Abuse, Treatment, Admissions in South Punjab, Pakistan

Yusra Hanif Khan[1], Muhammad Asif[1], Nouman Amjad[3], Qurrat-ul-Ain Fatima[2], Mehwish Liaqat[2] and Hani Saeed[2]

ABSTRACT

Objective: To determine pattern of demographic trends of substance abuse treatment admission in southern Punjab.
Study Design: Cross-sectional study
Place and Duration of Study: This study was conducted at the Multan Medical & Dental College, Multan, from October 2020 to December 2020.
Materials and Methods: After taking informed written consent from the participants and approval from the institutions, a self-formulated questionnaire was filled by health care professionals [physician or staff nurses] while interviewing the participants. This questionnaire included various parts related to the demographic details as well as potential risk factors. Participants were ensured confidentiality and ethical approval from relevant institution was taken. Data was entered and analyzed via SPSS version 23.0.
Results: We recruited 163 patients with substance abuse, 98.2 % (n=160) were male and 1.8 % (n=3) were females having 29.57 ± 7.33 years mean age, ranging from 18 – 60 years and 58.3% (n=95) had ages less than 30 years. Substance used for addiction was Heroine in 15.3 % (n=25), cannabis 10.4 % (n=17), Opioids 8.0 % (n=13), alcohol in 8.6 % (n=14) and 57.7% (n=94) used combination of these substances and mean frequency of daily use was 3.83 ± 1.25 (range; 1 – 6 daily). Route of administration was 3.1 % (n=5) inhalation, ingestion in 12.3 % (n=20), injection in 3.7 % (n=6), sniffing in 8.0 % (n=13) and 73.0% (n=119) had multiple routes. Mean age at 1st time was 20.13 ± 4.94 years (14 years to 32 years maximum). Peer pressure was the main cause in 76.7 % (n=125), relationship issues in 1.8 5 (n=3), family conflicts in 12.3 % (n=20), health issues in 7.4 % (n=12) and stress in 1.8 % (n=3). Dependence among family members was 31.3 % (n=51) and in friends was 80.4 % (n=131). Current admission was done by patient itself by will in 57.7 % (n=94), family by will 17.2 % (n=28) and 25.2 % (n=41) were admitted by family against the will.
Conclusion: The results of our study indicate that addiction is more common in young male adults living in poverty in joint family system having basic education. Peer pressure and dependence of close friends on drug addiction were the main causes of addiction. Heroin, Cannabis and Alcohol consumption were noted to be main substances used for addiction.
Key Words: Drug abuse, Socio-demographic, Distribution, Cannabis.

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INTRODUCTION

Substance abuse or drug dependence in general is a mammoth dilemma and a growing concern across cultures and all ages. The short-term and long-term repercussions of drug dependence create a ripple effect affecting both the individual and the society at large. It is indeed alarming and unfortunate that the recent trends show a significantly increasing frequency of drug dependency all over the world. The DSM-V defines substance use disorders as patterns of symptoms resulting from use of substances that one continues to take despite the occurrence and knowledge of harmful effects[1].

Illicit drugs are drugs for which non-medical use has been banned by international drug control treaties for half a century because they are believed to present intolerable risks of addiction to users. International

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control has since been extended from plant-based drugs—heroin, cocaine, and cannabis—to synthetic drugs, such as amphetamines and methylene dioxymetam fetamine (MDMA), and pharmaceutical drugs such as buprenorphine, methadone and benzodiazepines[2].

Globally, Over 700 000 excess deaths occurred in dependent illicit drug users in 2010 compared with only 44 000 deaths which were coded as the cause of death[3]. Drug dependence and substance use disorders adds on to the economic burden on the country and results in a significant loss of potential youth and adults who may have contributed positively towards the society. In a US-based study, Relative to non-abusers, abusers had significantly higher annual health care resource utilization, leading to $14,810 in per-patient incremental annual health care cost[4]. There is also a noticeably higher risk of mental illnesses and transmissible blood-born infectious disease in such patients[5]. Pakistan is currently the 6th most populous country in the world (population: 197 million) and holds a very important strategic position in the south-Asian region. It is one of the three countries, including Iran and Afghanistan, which form the infamous 'Golden crescent' and is the principal global site for opium distribution and production. The rates of drug use and addiction have increased at an alarming rate in the last few years. A collaborative study done by the Government of Pakistan's Ministry of Interior and Narcotics Control reports that nearly 6.7 million people had used any controlled substance including misuse of prescribed drugs. Cannabis was the most commonly used drug with a prevalence of 3.6 per cent among individuals with age ranged from 15 to 64 years. About 860,000 individuals are regular heroin users and 320,000 are opium users that are about 0.8 and 0.3 per cent of the population respectively[6].

Considering the burden of substance abuse and drug dependence, the research and literature available is present but not adequate[7]. While there are some studies done on the drug users admitted in the treatment centers or present in the community[8-12]. It is largely confined to major cities and urban centers[7]. South Punjab which is often ignored and rarely reported has its own fair share of drug dwellers and is collapsing under the burden of this engulfing epidemic aggravated by poverty, limited resources and lack of knowledge. The Indian side of Punjab also complains of suffering from being the transit hub of epicenter of drug trafficking and the Pakistani side of Punjab shares the same narrative[7].

Southern Punjab is one of the most diverse yet poverty-stricken and underdeveloped areas within Pakistan. It also merges with the tribal areas bordering Baluchistan where drug trafficking is prevalent and law enforcement agencies have little authority. This study aims to collect initial data and demographic landscape of those currently admitted for drug detoxification in treatment and rehabilitation centers in Multan, the largest city in southern Punjab. The aim is to throw light on the current situation of drug users in south Punjab and to generate interest and encourage capacity development initiatives by government as well as private shareholders in the future.

MATERIALS AND METHODS

This cross-sectional study was conducted in Multan Medical & Dental College, Multan & five major drug and rehabilitation centers in Multan [including two tertiary care hospitals with inpatient psychiatric facility] using non – probability convenient sampling technique from October 2020 to December 2020. Currently admitted cases for the purpose of drug detoxification/rehabilitation and fulfilling the DSM-V criteria of substance use disorder [as assessed by a consultant psychiatrist] of either sex aged more than 18 years having history of substance abuse for more than 6 months were included in the study. Those with prior mental illness and not giving consent of participation were excluded from our study. A total of 163 patients with substance abuse were taken, sample size was calculated using p = 12 % Cannabis substance abuse as reported by Prajapati et al[13], d = 5 % and 95 % CI, we used single proportion formula of Epi – info of CDC for sample size calculation.

After taking informed written consent from the participants and approval from the institutions, a self-formulated questionnaire was filled by health care professionals [physician or staff nurses] while interviewing the participants. This questionnaire included various parts related to the demographic details as well as potential risk factors. Participants were ensured confidentiality and ethical approval from relevant institution was taken. Data was entered and analyzed via SPSS version 23.0. Age and duration of addiction was presented in the form of mean and SD. Socio-demographic variables like gender, residential status, socioeconomic status, literacy and occupation was presented in the form of tables and figures. Where relevant, Pearson chi-square test was applied on categorical variables and p-value of < or equal to 0.05 was considered statistically significant.

RESULTS

We recruited 163 patients with substance abuse, 98.2 % (n=160) were male and 1.8 % (n=3) were females. The mean age range was 29.57 ± 7.33 58.3% (n=95) had ages less than 30 years.

Of these 163 substance abusers, 38.7 % (n=63) were from rural areas and 61.3 % (n=100) were from urban areas. Majority belonged to low income class i.e. 62.0% (n=101) while 30.1 % (n=49) were middle income and 8.0 % (n=13) belonged to high-income socioeconomic status. Of these 163 study cases, 15.3 % (n=25) were illiterate, 34.4% (n=56) had elementary level education,

15.3 % (n=25) had secondary level education, 17.2 % (n=28) had higher secondary education and 17.8 % (n=29) had done their graduation or above. Most of the study participants were unmarried i.e. 52.8% (n=86) while 42.9 % (n=70) were married and 4.3 % (n=7) were divorced.

In terms of religion, Muslims were 96.9% (n=158). It was observed that joint family system was present in 93.3 % (n=152).

Un-employment was noted in 24.5 % (n=40), unskilled workers were 35.6% (n=58), skilled workers were 26.4% (n=43) and 13.5 % (n=22) were professionals. Substance used for addiction was Heroine in 15.3 % (n=25), cannabis 10.4 % (n=17), Opioids 8.0 % (n=13), alcohol in 8.6 % (n=14) and 57.7% (n=94) used combination of these substances and mean frequency of daily use was 3.83 ± 1.25 (range; 1 – 6 daily). Route of administration was 3.1 % (n=5) inhalation, ingestion in 12.3 % (n=20), injection in 3.7 % (n=6), sniffing in 8.0 % (n=13) and 73.0% (n=119) had multiple routes. Mean age at 1st time was 20.13 ± 4.94 years (14 years to 32 years maximum).

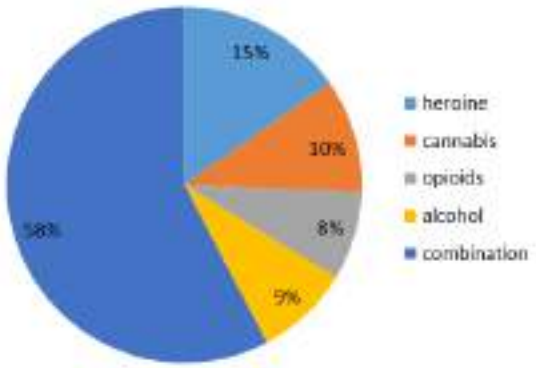

Figure No.1: Frequency of substance abused

Peer pressure was the main cause in 76.7 % (n=125), relationship issues in 1.8 5 (n=3), family conflicts in 12.3 % (n=20), health issues in 7.4 % (n=12) and stress in 1.8 % (n=3). Dependence among family members was 31.3 % (n=51) and in friends was 80.4 % (n=131). Current admission was done by patient's own self by will in 57.7 % (n=94) of cases, by family but with patient's will 17.2 % (n=28) and 25.2 % (n=41) were admitted by family against the will of patients**.**

DISCUSSION

Substance abuse is an important social health issue worldwide which is prevalent in all parts of the world and across all cultures, hence it is regarded as a global phenomenon[14]. Alcohol abuse and tobacco consumption are endemic almost in every society while abuse of other psychoactive agents is also growing concern in different societies like Pakistan.

We recruited 163 patients with substance abuse, 98.2 % (n=160) were male and 1.8 % (n=3) were females. Available data reveal high burden of drug abuse among males. A study conducted by Lamptey et al [15] from Nigeria has also reported 90 % male drug abusers, similar to our results. A Study conducted in India by Prajapati et al [13] 98 % male drug abusers. Javed et al [16] reported 100 % male drug abusers, similar to our results. While the figures show male predominance in inpatient units, we cannot assume the same in community without any evidence.

Mean age was 29.57 ± 7.33 years mean age, ranging from 18 – 60 years and 58.3% (n=95) had ages less than 30 years. Demirci et al [17] also reported drug abuse being more prevalent among youth. Another study by Randhawa et al [18] reported 27.25 years mean age. This strongly indicates that in order to tackle this issue, we need to focus our attention on the youth and initiate drug awareness campaigns and screening clinics for the school and college population of urban and rural Pakistan.

Of these 163 substance abusers, 38.7 % (n=63) were from rural areas and 61.3 % (n=100) were from urban areas. Majority were from lower income group indicating multiple socio-economic factors at play which lead to drus dependence. Rather et al [19] from India reported 58 % poverty in drug abusers. Of these 163 study cases, 15.3 % (n=25) were illiterate, 34.4% (n=56) had elementary level education, 15.3 % (n=25) had secondary level education, 17.2 % (n=28) had higher secondary education and 17.8 % (n=29) had done their graduation or above. A study conducted by Lamptey et al [15] from Nigeria has also reported 18.4 % had tertiary level of education, 34.5 % had secondary level of education and 12.6 % had basic level of education, showing similar trends of literacy among drug abusers. A Study conducted in India by Prajapati et al [13] reported 28 % drug abusers were graduate, also indicating high burden of drug abuse among qualified young adults. Rather et al [19] from India reported 53.5 % drug abusers had high school education.

Un-employment was noted in 24.5 % (n=40), unskilled workers were 35.6% (n=58), skilled workers were 26.4 % (n=43) and 13.5 % (n=22) were professionals. A study conducted by Lamptey et al [15] from Nigeria has also reported similar results. A Study conducted in India by Prajapati et al [13] reported 47 % drug abuse in skilled workers.

Substance used for addiction was Heroine in 15.3 % (n=25), cannabis 10.4 % (n=17), Opioids 8.0 % (n=13), alcohol in 8.6 % (n=14) and 57.7% (n=94) used combination of these substances and mean frequency of daily use was 3.83 ± 1.25 (range; 1 – 6 daily). Route of administration was 3.1 % (n=5) inhalation, ingestion in 12.3 % (n=20), injection in 3.7 % (n=6), sniffing in 8.0 % (n=13) and 73.0% (n=119) had multiple routes. Another study form India by Randhawa et al [18] reported similar results.

Mean age at 1st time was 20.13 ± 4.94 years (14 years to 32 years maximum). Demirici et al [17] also reported 13 years mean age at the start of addiction. Peer pressure was the main cause in 76.7 % (n=125), relationship issues in 1.8 5 (n=3), family conflicts in 12.3 % (n=20), health issues in 7.4 % (n=12) and stress in 1.8 % (n=3).

The authors strongly feel that these two factors mentioned above are very crucial. The young age of onset as well as peer pressure being the most frequent factor leading to drug use again emphasizes the fact that government policies need to be targeted and customized for youth. There is a dire need for estimating the extent of the problem and realizing that it is severely impacting the productivity of young people in Pakistan.

Dependence among family members was 31.3 % (n=51) and in friends was 80.4 % (n=131). A Study conducted in India [13] reported 62 % dependence in friends.

Our study helps in throwing light at the concerning issue of rampant drug use in the South Punjab region and builds a case to conduct more research in this area. It also serves as a reminder for the non-governmental organizations as well as government policy makers to address this issue with all seriousness and sincerity.

CONCLUSION

The results of our study indicates that in South Punjab, addiction appears to be more common in young male adults living in poverty in joint family system having basic education. Peer pressure and dependence of close friends on drug addiction were the main causes of addiction. Heroin, Cannabis and Alcohol consumption were noted to be main substances used for addiction.

Further robust research is needed to ascertain the extent of the problem and to embark on the journey towards its eradication.

Author's Contribution:

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Original Article

Comparison of Frequency of Menorrhagia after Immediate Versus Delayed Intrauterine Contraception Device (IUCD) Insertion

Shakila Yasmin, Salma Jabeen, Sidra Younus and Shazia Saeed

ABSTRACT

Objective: To compare the frequency of menorrhagia after immediate versus delayed intrauterine contraception device insertion.

Study Design: Randomized controlled trial.

Place and Duration of Study: This study was conducted at the Department of Obstetrics & Gynaecology, QAMC Bahawalpur from 14th February 2019 to 13th August 2019.

Materials and Methods: A total of 110women willing for intrauterine contraceptive device insertion of age 18-40 years were included. Women having sepsis, PROM, uterine anomalies & fibroid uterus were excluded. Group A included the women in which intrauterine contraceptive device was inserted within 24 hours of delivery and Group B included the women in which intrauterine contraceptive device was inserted after 6 weeks of delivery. All the above patients were tracked for 3 months by the researchers themselves for presence or absence of menorrhagia.

Results: The mean age was found to be 28.67 ± 5.72 years in group A and29.02 ± 5.63 years in group B. The mean parity in both groups were 3. Menorrhagia in group A (immediate IUCD) was seen in 04 (7.27%) and in group B (delayed IUCD) was seen in 24 (25.45%) females with p-value of 0.010.

Conclusion: This study concluded that there is less frequency of menorrhagia after immediate IUCD compared to delayed intrauterine contraception device insertion.

Key Words: Intrauterine Devices, Post-Placental, Menorrhagia, Contraception

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INTRODUCTION

Intrauterine devices are the most cost effective long-acting reversible contraceptives (LARC).[1]Globally, 14.3% of women of reproductive age use intrauterine contraception, more than 80% of them live in Asia, with almost 64% of them reside inChina.[2]

The efficacy of copper IUCDs, especially the TCu 380A when used over long period of time, has shown equivocal results in comparison with tubal sterilization, with additional benefit that it can be removed anytime, & is a reversible method.[3] The main drawback of IUCD contraception is dysmenorrhea and heavy menstrual bleeding which may end up in its early removal & sometimes it is expelled spontaneously.

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There are various factors that may affect the outcome of IUCD use and many researchers have studied on them.[4,5] Reported failure rate of IUCD is 0.8/100 women at one year and at the end of 10 year use, failure rate is 1.9/100 women which is almost similar to female sterilization.[6] FDA has approved that if copper IUC is left in place for 10 years, its efficacy does not lost. According to medical eligibility criteria WHO, post-placental insertion of Cu T is recommended in both lactating & non lactating moms.[7] Post placental insertion & birth by caesarean section are linked with lesser expulsion rates in comparison of delayed insertion & vaginal births. It was observed that risk of complications like perforation and infection linked with insertion of IUD are not increased if it is placed in post-partum period [7]

IUCD may be inserted in postpartum period, post abortal or in interval period.[8] IUD insertion within 48 hours after childbirth is labeled as Post-partum IUD insertion. While if it is inserted within 10 minutes of placental expulsion is referred as post placental IUD insertion. In 1970 first time concept of post-partum IUD insertion was floated.[9] PPIUCD has the advantage of convenience, saves time of additional visit, &associated with less complaints of initial dysmenorrhea, & menorrhagia without increase in risk

of uterine perforation.[11]Over the period of time, improvements in expulsion rates have been reported lesser more recently.[12,13]In a study, the incidence of menorrhagia after immediate IUCD insertion was found to be 5.2% and after delayed IUCD insertion was 21.2%.[12] In another study, it was found to be 4.0% in both groups.[13]

As the menorrhagia is the most common complaint after intrauterine contraceptive device insertion and previous studies described above have shown controversial results regarding the better time of IUCD insertion, so the purpose of this research work was to compare the incidence of menorrhagia after immediate postpartum versus delayed intrauterine contraception device insertion in local population. As the ethnic factors have great impact on the tolerability and efficacy of contraception devices, so our study will provide the local stats in this regard. Then depending upon these findings, the appropriate timing with less incidence of menorrhagia can be opted in our routine practice guidelines and our population can be motivated and encouraged for using contraception to improve maternal & family health.

MATERIALS AND METHODS

It is a Randomized Controlled trial, conducted at Department of Obstetrics & Gynaecology QAMC, from 14th February 2019 to 13th August 2019.

After approval from the ethical review committee, 110 women willing for intrauterine contraceptive device insertion after child birth in OBGY department of QAMC, Bahawalpur were selected. They were of age 18-40 years, &parity ranging from 2-6. Women having sepsis, PROM, uterine anomalies, fibroid uterus,& who did not returned back were excluded. After explaining the merits and demerits of study and taking informed written consent, all selected cases were divided randomly in 2 equal groups (A & B). Group A included the women in which intrauterine contraceptive device was inserted within 24 hours of delivery and Group B included the women in which intrauterine contraceptive device was inserted after 6 weeks of delivery. Following IUD insertion, patients were asked to visit within 4 weeks. At this first follow-up visit, any complaints were asked & on examination the IUD strings are confirmed.

Follow-up for 3 months were done for all patients by the researcher themselves for presence or absence of menorrhagia (>80ml menstrual blood loss/month). Menorrhagia was assessed after 3 months of insertion by using Pictorial Blood Assessment Chart (PBAC) and was taken as positive if both of these present i.e. blood loss lasting longer than 7 days and PBAC score >50.All this data was entered on a specially designed proforma

Statistical Analysis: SPSS version 22.0 was used to enter & analyze all the data. Age, and BMI were presented as mean and standard deviation. Parity, mode of delivery, hypertension, diabetes mellitus, & menorrhagia (present/absent) were presented as frequency and percentage. Chi square was used to compare the menorrhagia of both groups and p-value ≤ 0.05 was considered as significant.

Effect modifiers like age, BMI, parity, mode of delivery hypertension &diabetes mellitus were controlled through stratification and chi square was then applied to see their effect on menorrhagia (post-stratification). P-value ≤ 0.05 was considered as significant.

RESULTS

Age range in this study was from 18 to 40 years with mean age of 28.89 ± 5.68years.The mean age of women in group A was 28.67 ± 5.72 years and in group B was 29.02 ± 5.63 years. Majority of the patients 70 (63.64%) were between 18 to 30 years of age as shown in Table I.

Table No. 1: Comparison of patients with regard to Group

	Group A		Group B		Total	
Age(yrs)	No. of patients	%	No. of patients	%	No. of patients	%
18-30	33	60	37	67.27	70	63.64
31-40	22	40	18	32.73	40	36.36
Mean+SD	28.67+5.72		29.02+5.63		28.89+5.68	
Parity						
2-3	33	60	37	67.27	70	63.64
4-6	22	40	18	32.73	40	36.356
Mean +SD	3.02+1.11		3.16+ 0.96		3.11+1.05	
BMI						
< 27	21	38.18	18	67.27	39	35.45
> 27	34	61.82	37	32.73	71	64.55
Mean +SD	28.44 ± 2.46		27.85 ± 2.25		28.14 ± 2.33	
Mode of delivery						
Vaginal	29	52.73	19	34.55	48	43.64
Cesarean	26	47.27	36	65.45	61	56.36
Past history						
Hypertension	16	19.09	20	36.36	36	32.73
Diabetes	10	18.18	13	23.64	23	20.91

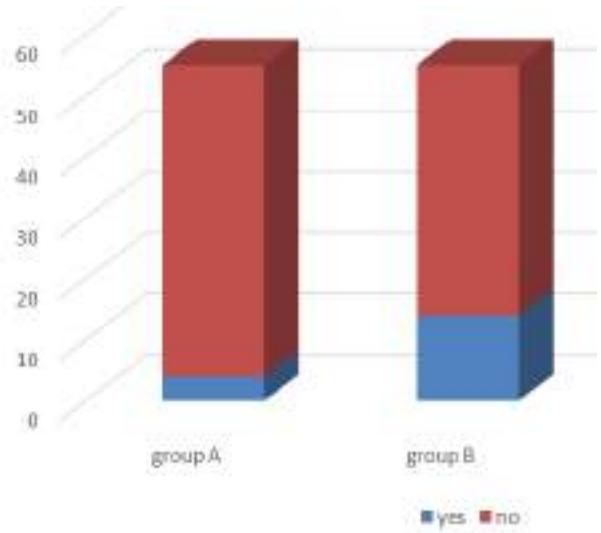

Figure No.1: Bar graph showing frequency of menorrhagia after immediate versus delayed intrauterine contraception device insertion (n=110).

Table No.2: Detail of Menorrhagia with regard to Group A and B.

	Group A menorrhagia		Group B menorrhagia	
	Yes	No	Yes	No
Age(yrs)				
2-3	1	32	11	26
4-6	3	19	3	15
BMI				
< 27	1	20	6	12
> 27	3	31	8	29
Mode of delivery				
vaginal	1	28	6	13
Cesarean	3	23	8	28
Hypertension				
yes	1	15	2	18
no	3	36	12	23
diabetes				
Yes	1	9	4	9
No	3	42	10	32

The Table 1 showing the mean parity in group A was 3.02 ± 1.11 and in group B was 3.16 ± 0.96, & the mean BMI in group A was 28.44 ± 2.46 kg/m^2 and in group B was 27.85 ± 2.25 kg/m^2. Distribution of patients according to mode of delivery, hypertension and diabetes mellitus in both groups is also shown in Table 1.

Menorrhagia in group A (immediate IUCD) was seen in 04 (7.27%) and in group B (delayed IUCD) was seen in 24 (25.45%) females with p-value of 0.010 as shown in figure/graph 2.

Stratification of menorrhagia with respect to age, parity, BMI, mode of delivery, hypertension and diabetes mellitus in both groups is shown in Table 2.

DISCUSSION

The intrauterine device (IUD), is a type of long acting reversible contraception (LARC), considered one of most safe & effective birth spacing methods. As this is a patient-independent method, so it is related with low rate of unplanned pregnancies which increases its efficacy.[13] Recent literature supports its safety in terms of low rates of, perforation, infection and expulsion that make it an appropriate contraceptive choice for all women of reproductive age.

Short inter-pregnancy interval (<than 2years) has been related with increased maternal &infant morbidity and mortality when it is correlated to long inter pregnancy intervals.[14,15] To achieve this recommended pregnancy spacing, postpartum IUD insertion is an ideal choice.As counseling services by health care providers are easily available in the immediate postpartum period so women are more determined& motivated for birth spacing.[16] Insertion of the IUD can be done at any time from 48 hr after delivery of the placenta, till 4-6 week postpartum.[17,18.]Although the expulsion rate is high with immediate placement but its role to prevent unplanned pregnancies may predominates the risk of expulsion.[17, 18,]

It can be associated with menorrhagia, dysmenorrhea & spontaneous expulsion. We carried out this research to compare the frequency of menorrhagia after immediate versus delayed intrauterine contraception device insertion.

The results of my study & a study conducted by Jain N &colleagues, supported that immediate insertion is associated with less chances of menorrhagia[11].My study showed that menorrhagia in group A (immediate IUCD) was 04 (7.27%) and in group B (delayed IUCD) was 24 (25.45%) that found to be significant. While Jain N &colleagues, concluded that incidence of menorrhagia after immediate IUCD insertion was found to be 5.2% and after delayed IUCD insertion was 21.2%.InterestinglySrivastava S & his colleagues found equal no of percentage (4%) of menorrhagia in both groups.[12] Indian researchers also strengthened the results of our study, they found incidence of irregular vaginal bleeding was 23.5% in PPIUCD group and 88.5% in interval IUCD group.[1]Shukla et al found occurrence of menorrhagia (27.2%) as a frequent complaint, when CuT 200 was inserted in postpartum women.[15] Many other researchers also noted same correlation of menorrhagia & dysmenorrhea (6% to 8%) with use of CuT-380 that ultimately ended up in its removal.[19,20] The different rates of bleeding problems are probably associated with different types of IUCD.

Celen S et al (2004)[21] reported cumulative rates of bleeding equalant to 11.4% and 8.2% respectively. Another study highlighted that post-partum insertion is more superior than interval Cu-T insertion with few expulsions and low rate of complications.[22]Immediate

insertion group was linked with less occurence of heavy menstrual bleeding because there was different duration of lactationalamenorrhoea in the postpartum period. To overcome this bias of lactational amenorrhoea, long duration of observation is needed. Ei-Shafei et al noted, that in women whom CuT380A was inserted within 10 min after placenta delivery, 9% of them develop menorrhagia when followed for 1 year.[23]Eroglu et al mentioned that in post placental group, menorrhagia was observed in 2/84 clients, in comparison to interval/ delayed insertion group where 8/130 complained of menorrhagia. All patients were followed for 1 year. These findings matched with our study results.[24]

The study showed that maternal age is an important factor in contraceptive acceptance. A study by Usha Ram et al have shown that the unmet need for birth spacing is alarmingly high . He highlighted the higher number (56%) of IUCD users belong to the age group of 21-25 years' followed by the 32% in women of 26-30 years' group [25] Our study showed that majority of the acceptors also belonged to 20 – 30 years of age showing the need to catch them young for proper spacing and limiting of births. In a study published by a teaching institution in Nigeria showed that model age group of participants was 25-29 years (32.5%) among 852 IUCD acceptors.[26]

A study pointed out that PPIUCD was more popular method among multiparas (73.3%) as compared to primis (26.7%).[27] According to Rivero-Fuentes et al women's selection for any contraceptive method is influenced by their knowledge about post-delivery return of fertility and resumption of sexual activity (40% in <3 months and 90% by one year) hence focus should be on young primiparas who are reluctant to return for interval contraception.[28.]

The satisfaction rate of PPIUCD found in one study was 93%, irrespective of complaints of complications like expulsion, menorrhagia, &infection.[29] Now world has realized thatpostpartum family planning can be a game changer for prevention of unplanned pregnancies (within the first year after childbirth) & to prolong the inter-pregnancy interval.[30]

CONCLUSION

This study concluded that there is less frequency of menorrhagia after immediate IUCD compared to delayed intrauterine contraception device insertion. So, we recommend that immediate IUCD insertion after delivery should be used as a best time for insertion in order to decrease the complications as well as morbidity of these women.

Author's Contribution:

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

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Original Article

Correlation of Surgical Incision Length with Corneal Endothelial Cell Count

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ABSTRACT

Objective: To study the Correlation of Surgical incision length with corneal endothelial cell count.
Study Design: Prospective study
Place and Duration of Study: This study was conducted at the Imran Idris Teaching Hospital Sialkot and Sahara Medical College Narowal during Feb 2019 to May 2020.
Materials and Methods: One hundred persons with ageing process leading to cataracts were requested to take part in the study. It was a study in which the study material was collected once. All those samples were operated for cataract with new technique. To perform the operation the incision was given at the edge of cornea. This incision given followed the 360^0. With the help of specular microscope width of different layers of cornea were measured at the center as well as 3mm away from the center. Then with new technique phaco chop procedure, the eye surgeon removed the cataract through a very little hole incision. The thickness of various layers of the cornea was measured 2 times after operation at 1 weak and 3 months later.
Results: However, three months post operation, the mean of central endothelial cell count with superior incisions and mean central endothelial cell count with temporal incisions were bit elevated. For the Superior to temporal incisions results of endothelial cell count was bit lower than the other two groups. Overall, one month post operative, mean central endothelial cell count was ten point eight percent and mean endothelial cell count in the sector of the incisions was fourteen percent.
Conclusion: A superior to temporal modern cataract surgery incision may have less endothelial cell count as compared to other incisions. The amount of central endothelial cell count may be less marked in sick persons with longer axial lengths and with methods utilizing less DIALECT.

Key Words: Endothelial Cell Loss; Incision; Phacoemulsification

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INTRODUCTION

Since the main phacoemulsification methodology per framed by Kelman[1] in nineteen hundred sixty seven, corneal. Endothelial cell misfortune stays a genuine straightforwardness and somewhat visual sharpness. In this manner, endeavors to ensure the corneal endothelium and to limit their harm can assume a significant function in improving personal satisfaction in sick person with cataracts.[3,4] The site through which this technique is performed can effects the loss of corneal endothelial cell count drastically.[5] The results of pervious study According to past findings, utilizing a burrow cut of sclera, there is no big difference between incidence and transient cuts chosen dependent on before operation of cataract.[2] However, so as to limit after operation astigmatism, the area access of corneoscleral may change;[2] and again, the expert must perform superior to temporal cuts. In the recent findings we suggested about the measure of ECL after clear cornea modern operation of cataract utilizing not rivaled, transient, or superior to temporal cuts. What's more, we assessed. In modern operation of cataract, the measure of ECL decides final after operation corneal patient's refraction. Just eyes in which the lines of longitude on a globe. perpendicular meridian of the cornea was 200 inward of the 0°, 180°, or 90° tomahawks or inside 10° of the 45° (for the left eye) or one hundred thirty five degree (for the correct eye), For each eye, three estimations were done and the normal worth was calculated determined; in any event hundred cells were assessed in every estimation. ECD estimation was rehashed multi week, multi month and three months after operation. So as to quantify ECL we utilized the accompanying recipe.

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MATERIALS AND METHODS

This study was conducted at the Imran Idris Teaching Hospital Sialkot and Sahara Medical College Narowal

during Feb 2019 to May 2020. One hundred persons with ageing process leading to cataracts were requested to take part in the study. It was a study in which the study material was collected once. All those samples were operated for cataract with new technique. To perform the operation the incision was given at the edge of cornea. This incision given followed the 360^0. With the help of specular microscope width of different layers of cornea were measured at the center as well as 3mm away from the center. Then with new technique phaco chop procedure, the eye surgeon removed the cataract through a very little hole incision. The thickness of various layers of the cornea was measured 2 times after operation at 1 weak and 3 months later.

Inclusion criteria: Age range, forty to sixty years sharp corneal circle at zero degree, one eighty degree or ninety degree ± twenty degree, and forty five degree or one thirty five degree ± ten degree NS three+ to four+ old age cataract non complicated modern cataract surgery

Exclusion criteria: Diabetic patient KR>48 D or <40 D AL>28 mm or <23 mm ECD<1500 cell/mm2 preoperatively Complicated cataract surgery History of intraocular surgery or ocular trauma Pseudoexfoliation or corneal endothelial dystrophy

RESULTS

One hundred patients (100 eyes) including 45 men (45%) and 55 women (55%) with mean age of 53.0±4.5 (range, 42 to 60) years were allocated to three groups according to the incision site: temporal (24 eyes, 24%), superior (34 eyes, 34%) and superotemporal (34 eyes, 34%). Baseline patient data are presented in table 1.

Table No. 1: Baseline patient data

Factor	Mean± SD	Minimum	Maximum
Age (years)	52.96 ± 4.53	41.99	59.99
Axial length (mm)	23.98 ± 0.68	22.96	25.96
Operation time (min)	6.97 ± 0.86	5	
EFT (sec)	6.32 ± 1.66	3	10
Central ECD (cells/mm2)	2540.8 ± 194.00	2003.99	2896
ECD (temporal)	2542.7 ± 247.96	2144	3237
ECD (superior)	2743.9 ± 205.99	2243	3252
ECD (Superotemporal)	2750.2 ± 230.97	2320	3342

EFT, effective phaco time; ECD, endothelial cell density; SD, standard deviation; Min, minimum; Max, maximum

Table No. 2: Mean ECD (cells/mm2) in the central cornea and the meridian of the incision

Incision group	Central cornea				Meridian of the incision			
	Pre op	1 week Later	1 month later	3 months later	Pre op	1 week later	1 month later	3 months later
Temporal	2573.4±221.8	2360.2±215.96	2296.1±206.8	2304.3±204.7	742.5±247.96	2430.8±250.98	357.99±240.96	2337.9±260.98
Superior	2498.7±180.2	2298.1±170.6	2256.3±180.1	2264.8±185.96	2749.4±230.98	2438.9±216.75	2369.9±220.98	2356.96±227.98
Supratemporal	2497.7±180.8	2330.3±186.6	2256.1±200.96	2266.5±199.96	2745.9±205.96	2428.9±296.95	2364.9±301.99	2350.96±300.96
P-value*s	0.643	0.715	0.701	0.72	0.95	0.92	0.95	0.945

Pre op, preoperatively; SD, standard deviation; ECD, endothelial cell density *ANOVA

Table No. 3: Mean ECL (%) in the central cornea and sector of incision in different incision groups

Incision group	Central cornea			Sector of incision		
	1 week Later	1 month later	3 months later	1 week later	1 month later	3 months later
Temporal	7.99±2.22	10.75±2.30	9.96±2.59	11.40±2.41	14.00±3.11	14.84±4.42
Superior	8.40±2.29	10.96±2.42	10.59±2.90	10.98±5.90	13.98±6.34	14.40±6.40
Supratemporal	7.76±2.00	9.98±2.76	10.30±2.82	11.20±1.90	13.82±2.59	14.20±3.10
P-value	0.378	0.847	0.920	0.91	0.96	0.91

Table No. 4: Correlation between study parameters and mean ECL 3 months postoperatively

Parameter	Corneal center		Meridian of incision	
	Pearson co-eff	P-value	Pearson co-eff	P-value
Age	-0.079	0.447	0.016	0.870
Axial length	-0.410	<0.001	0.115	0.270
EFT	0.535	<0.001	-0.015	0.875
Operation Time	0.159	0.042	-0.140	0.179

ECL, endothelial cell loss; EFT, effective phaco time; Pearson coeff, Pearson coefficient

DISCUSSION

Lately, different methods have been utilized in waterfall medical procedure. The pattern in present day waterfall medical procedure is to limit results, for example, careful injury, corneal consume and loss of lines internal body cavities and the lumens of vessels and to decrease the size of the entry zone to limit after operation astigmatism.[6,7] Modern cataract surgery is a protected and forceful master plan and thinks to the best quality level for cataract medical procedure. By and by it is still linked with injury.[6] One of the difficulties of trauma is decrease in corneal early childhood development. In this examination, we assessed the impact of various point of entry locales on corneal early childhood development after operation, and looked at early childhood development in different cut areas and furthermore the focal cornea. As per our outcomes, mean focal early childhood development, many week, many month, and three months after operation were eight point twelve percent, ten point eighty five percent, and ten point forty four percent individually, and was practically identical with different cuts.

Three months after medical procedure, mean sectoral early childhood development was equivalent between the examination bunches at fourteen point nine percent for international cuts, fourteen point five percent for unequalled entry points, and fourteen point four percent for superior to temporal cuts. Previous examinations have detailed various measures of early childhood development (four point three percent, eight point two percent[8,9] eleven point eight percent, three and eighteen point three percent[10], which might be because of different factors, for example, individual careful method, cut type and area, and cataract thickness. The measure of early childhood development in our sick person was higher than that of previous results. The justification might be that the totally of our sick person had atomic sclerosis of three+ to four+ requiring more significant EFT and henceforth larger early childhood development.[5,11] We find out the activity through a three point two mm cut on the unmistakable cornea which was depend upon to limit ECL.[12] Similar to the examination by Walkow et al2, we chose the entry point site as indicated by before operation an instrument for measuring the curvature of the cornea. They utilized an matchless scleral burrow for cataract removing and their outcomes showed ECL of eight point five percent at a year after operation. This figure was eleven point nine percent in the short in its duration quarters of a circle and eleven point four percent in the matchless quadrant.[14-19]

CONCLUSION

A superior to temporal modern cataract surgery incision may have less endothelial cell count as compared to other incisions. The amount of central endothelial cell count may be less marked in sick persons with longer axial lengths and with methods utilizing less DIALECT.

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Original Article

Effect of Peri-Operative Dexmedetomidine on Incidence of Delirium in Elderly Patients After Cardiac Surgery

Syed Imran-ul-Hassan, Zehra Hasnain, Kanwal Awan, Maryam Liaquat, Maria Ikram and Javairia Saleem

ABSTRACT

Objective: The aim of this study was to compare the frequency of delirium in patients of elective cardiac surgery treated peri operatively with dexmedetomidine with those treated with midazolam.

Study Design: Randomized controlled trial study.

Place and Duration of Study: This study was conducted at the Department of cardiac surgery, Punjab Institute of Cardiology, Lahore, Pakistan from July, 2020 till December, 2020.

Materials and Methods: Dexmedetomidine was given to half of the patients included in the study and other drug was taken as a controlled drug, Midazolam.The objective of this study was to compare the frequency of delirium in patients of elective cardiac surgery treated with peri operatively with dexmedetomidine with those treated with midazolam prei-operatively. Delirium was assessed using the scale - MMSE Scoring scale. Mini-Mental State Examination (MMSE) Score is of total 30 score. Patients were asked some questions in the form of an interview and 1 mark was given for each correct answer. Any patient with a score of less than 24 was labeled as having a cognitive impairment or delirium.

Results: The comparison of frequency of deliriumin patients of cardiac surgery treated with perioperative dexmedetomidine vs midazolam was done, 8.57% (n=2) in Dexmedetomidine group and 22.86%(n=8) in midazolam group were found with delirium, p value was 0.04.

Conclusion: Delirium is a stressful complication observed in the post-operative period. With the use of dexmedetomidine along with the induction of general anesthesia, the chances of post-operative delirium can be reduced. This trial should be done on a larger scale documenting the effects of DEX on all the parameters monitored during the general anesthesia.

Key Words: Peri-Operative Dexmedetomidine, Incidence of Delirium, Elderly Patients, Cardiac Surgery

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INTRODUCTION

Apart from the other complications of surgery done under general anesthesia, some of the complications are related to the drugs used by the anesthetist for the induction and maintenance of anesthesia. Among these complications, post-operative delirium (POD) is an acute disorder of the central nervous system with disturbed conscious level and change in the cognition and perception.

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It is a common compliant of elderly patients in the initial days of post-operative period, mostly patients of cardiac and thoracic surgeries. The exact pattern of changes in the CNS leading to the cognitive impairment and post operative delirium (POD) is still not clear.[1]

The incidence of POD in the old age patients ranges from 10% to 50% varying mostly with age. It negatively affects the overall quality of life (QOL) after the surgery along with long-term outcomes, mortality, cognitive disorders, stay inside the hospital.[1,2]

Prevention of POD in elderly patients is now considered as a part of successful surgical outcome. Among various other drugs used in the prevention of POD, dexmedetomidine is now recommended because of its neuro-protective effect, still trials are under way to reach a decision and results of previous studies on various anti-psychotics and sedatives show inconsistent results.[3,4]

Dexmedetomidine, an alpha-2selective adrenergic agonist, with its opioid-sparing property, decrease in the anesthetic dose required and neuroprotective effects, is now commonly used by consultant anesthetists in cardiac and thoracic surgeries.[5] It is also

a used as a sedative drug the high risk units. Many studies have shown its significant role in the prevention of POD after cardiac as well and non-cardiac surgeries.[6] Even than some studies have concluded with opposite results, like Deiner et al[7] showed that dexmedetomidine had no significant advantage in the reduction of incidence of POD.

To date very limited local studies are available comparing the role of dexmedetomidine versus placebo or propofol or midazolam in the prevention of POD. As there is inconsistent results of trials done previously and controversy regarding the effect of dexmedetomidine on the incidence of POD, controlled trials should be done in our local population determining the frequency of POD after treatment with dexmedetomidine and comparing this frequency with other sedatives commonly used like midazolam.

MATERIALS AND METHODS

This study was conducted in the department of cardiac surgery and anesthesia, Punjab Institute of cardiology. In this randomized controlled trial patients of elective cardiac surgery were enrolled and divided into two groups. One of the sedative drugs used before the start of surgery was dexmedetomidine which was given to half of the patients included in the study. Other drug was taken as a controlled drug often used pre-operatively, Midazolam.

The objective of this study was to compare the frequency of delirium in patients of elective cardiac surgery treated with perioperatively with dexmedetomidine with those treated with midazolam prei-operatively.

Data collection for this study was done from July, 2020 till December, 2020 in the Punjab Institute of Cardiology. The study was approved by the clinical research ethics Committee of the Punjab Institute of Cardiology (PIC).

Each of the patients included, was explained about the procedure of the data collection and detail and purpose of the medicines used and a written informed consent was taken individually. Adult and elderly patients of age 55 to 75 years old scheduled for elective cardiac surgery, like coronary artery bypass graft surgery CABG, valve surgery, or combined surgery with cardiopulmonary bypass were enrolled into the study.

Patients with ASA class I and II were included and those of ASA class III and IV were not included in the study. All those patients with history of kind of psychiatric illness, those with difficulty in communicating with the primary investigator before the surgery and those already diagnosed with cognitive disorder (on history taking) were not included in the data collection process for this study. Any patient admitted for cardiac surgery but had preoperative sick sinus syndrome, significant fall in heart rate (heart rate less than 50); or with 2nd-degree or more severe atrioventricular heart block without pacemaker or those who had any signs of liver or kidney failure were also removed from the study. Those patients who couldn't communicate due to visual, hearing, language difficulty and those who had history of head trauma were also excluded from the study.

Sampling was done through non probability consecutive sampling technique. Sample size 70 was calculated using the WHO sample size calculator with expected percentage of patients developing Delirium in dex group of 6.52%[10] and in the midazolam group of 21.74%[10] taking the power of the test of 80% and level of significance of 5%. 35 patients were randomly assigned to group 1 and 35 were randomly divided into group 2.

In order to remove bias, neither the patients were aware of the type of drug they were given nor were the person administering the drug was aware of the drug. One of the drugs was labeled as A (DEX) and other was labeled as B (MID).

Along with the other drugs to induce general anesthesia, patients in the group 1 were given dexmedetomidine infusion in the theater with a dose of 0.7 μg/kg/h and was later continued into the high dependency unit at a dose of 0.4 μg/kg/h.

Delirium was assessed using the scale - MMSE Scoring scale. Mini-Mental State Examination (MMSE) Score is of total 30 score. Patients were asked some questions in the form of an interview and 1 mark was given for each correct answer. Any patient with a score of less than 24 was labeled as having a cognitive impairment or delirium.

Electrocardiogram – ECG, blood pressure, heart rate were monitored during the whole procedure. Patients in the second group were given IV injection of Midazolam (0.05 μg/(kg.h) in the theater and then intravenous injection 0.02-0.08 μg/(kg.h) to maintain the anesthesia. After the procedure analgesic drugs were given and all types of narcotic drugs were stopped.

Cognitive impairment post-operatively was accessed using the Mini-Mental State Evaluation (MMSE) scoring. MMSE was accessed in the pre-operative room and later just after the surgery at 6 hours, 24 hours, 48 hours and 72 hours in the post operative period.

Data was enter in excel and SPSS data analyzing software (SPSS-23.0) and analyzed to calculate frequency and percentages of categorical data and mean with standard deviation for continuous data. The frequency of delirium in the post op period was documented and compared with the two groups using chi square test. Data was stratified for age and gender, post-stratified chi square test was applied to see the effect of these variables on the outcome variable. $P<0.05$ was taken significant.

RESULTS

In this randomized controlled study, patients of old age group admitted for elective cardiac surgeries were enrolled to determine the effect of dexmedetomidine on the incidence of POD. Half of patients in our study were given dexmedetomidine and half of the patients were given midazolam. Patients were randomly assigned in one of the two groups in order to prevent bias. A total of 70 cases (35 in each group) fulfilling the selection criteria were enrolled to compare the frequency of deliriumin patients of cardiac surgery treated with perioperative dexmedetomidine vs Placebo (midazolam).

In our study, majority of the cases i.e. 74.29%(n=26) in Dexmedetomidine group and 68.57%(n=24) in midazolam group were between 55-65 years of age whereas 25.71%(n=9) in Dexmedetomidine group and 31.43%(n=11) in midazolam group were between 66-75 years of age, mean age was 59.64±12.47 years. (Table 1). Gender distribution shows 54.29% (n=19) in Dexmedetomidine group and 57.14%(n=20) were male cases and 45.71%(n=16) in Dexmedetomidine and 42.86%(n=15) in placebo group were females. After 24 hours, Mean MMSE scores in Dexmedetomidine group was 27.84±6.87 and in midazolam group it was calculated as 23.67±11.43. (Table 2). The comparison of frequency of deliriumin patients of cardiac surgery treated with perioperative dexmedetomidine vs midazolam was done and illustrated in Table No. 3, where 8.57%(n=2) in Dexmedetomidine group and 22.86%(n=8) in midazolam group were found with delirium, p value was 0.04.

Table No. 1: Age Distribution (n=70)

Age(in years)	Dexmedetomidine group (n=35)		Midazolam group (n=35)	
	No. of patients	%	No. of patients	%
55-65	26	74.29	24	68.57
66-75	9	25.71	11	31.43
Total	35	100	35	100

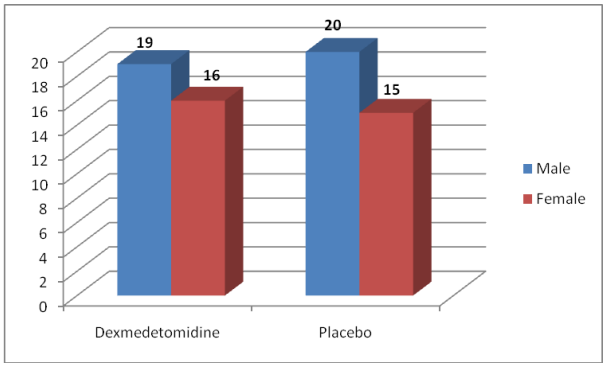

Figure No. 1: showing the Gender Distribution of patients included in our study

Table No. 2: Mean Mmse Scores (n=70)

MMSE Scores	Dexmedetomidine group (n=35)		Midazolam group (n=35)	
	Mean	SD	Mean	SD
	27.84	6.87	23.67	11.43

Table No. 3: Comparison of frequency of deliriumin patients of cardiac surgery treated with perioperative dexmedetomidine vs midazolam. (n=70)

Delirium	Dexmedetomidine group (n=35)		Midazolam group (n=35)	
	No. of patients	%	No. of patients	%
Yes	2	8.57	8	22.86
No	32	91.43	27	77.14
Total	35	100	35	100

P value=0.04

DISCUSSION

Postoperative delirium (POD) is one of the major complications seen in post-operative period among the old age patients of cardiac surgery. The incidence of POD varies among various populations and age groups, with reported peak incidence of upto 50% in old age group patients of cardiac surgery.As it is a very stressful condition for the patients and their families with disorientation and sudden loss of cognition, leading to prolonged hospital stay and rise in the cost of treatment, its prevention is necessary for the treating surgeon and anesthetist.[8]

Dexmedetomidine is a potent sedative, used previously in the post-op period as sedative following prolonged surgeries including cardiac and thoracic surgeries. Studies have proven that its use peri-operatively in the theatre showed significant reduction in the dose of anesthetic drug and morphine-sparing effect.[9]

In our study, patients of old age group admitted for elective cardiac surgeries were enrolled to determine the effect of dexmedetomidine on the incidence of POD. Half of patients in our study were given dexmedetomidine and half of the patients were given midazolam. Patients were randomly assigned in one of the two groups in order to prevent bias. The comparison of frequency of deliriumin patients of cardiac surgery treated with perioperative dexmedetomidine vs midazolam was done; 8.57%(n=2) in Dexmedetomidine group and 22.86%(n=8) in midazolam group were found to have delirium, p value was 0.04.

A randomized controlled trial similar to our trial was done by Yu D, et al. They recorded the incidence of delirium in the post-operative period after administration of DEX in the theatre. They reported that the time of recovery from general anesthesia, extubation time and awakening time, time of onset of POD, and total duration of POD, all these parameters

were shorter and better in the group treated with DEX as compared to midazolam. POD was seen in only 6.52% patients in the treatment group and its incidence was around 26% in the midazolam group (P<0.05). Patients were evaluated using the Mini-Mental State Evaluation (MMSE) scores to diagnose POD.[10] This was close to the results seen in our study.

In a similar study, Su X, et al collected data for 2 years and included around seven hundred patients, half of these were given dexmedetomidineand half were given some placebo. The percentage of patients who had POD was significantly less in the first group as compared to the placebo group. (9%vs 23%). They also studied the possible complications that can develop with the use of dexmedetomidine. Data showed that percentage of patients with hypertension and tachycardia during the surgery was also less in the trial group compared to placebo (10% vs 18% and 7% vs 14% patients, respectively), p value was also significant. Percentage of patients with hypotension and bradycardia was not significantly different between the two groups.[11] In our study, incidence of POD was almost similar to this reported, but we didn't collected the data related to heart rate changes and blood pressure changes.

Another recent study showed that POD was seen in around 40% patients treated with propofol as compared to 26%patients treated with dexmedetomidine. Along with the incidence of POD, patients who were given dexmedetomidine showed a delay in the onset and total duration of POD as compared to control group patients. Data analysis should that the stay in the ICU and overall hospital stay was not significantly different between the two group.[12]

Likhvantsev VV, et al also reported a significant difference in the incidence of POD after dexmedetomidine treatment as compared to placebo (7.1% vs 18.8%; $p < 0.05$). Data regarding duration of stay in the high risk unit and total stay in the hospital was also reduced with the use of dexmedetomidine. Mean stay in the ICU was 18 hoursin the dexmedetomidine group and 22 hours in the control group; $p < 0.05$; similarly, mean stay in the hospital was 17 days vs 19 days in dex vs control group, $p< 0.05$. They concluded that Dex if given during and after the general anesthesia for heart surgery showed a significant reduction in the rate of postoperative delirium and intensive care unit and hospital lengths of stay.[13] In our study, we didn't collected data regarding the hospital stay and stay in the ICU, but the incidence of POD was similar.

Different other trials have been done to comparing Dex with other drugs. Djaiani G, et al[14] reported the incidence of POD in Dex vs propofol of 17.5% and 31.5%, respectively, and proved that Dex can delay the onset and total duration of POD. Few studies also compared the incidence of atrial fibrillation during and after cardiac surgery with the use of Dex vs placebo. The incidence of AF was reduced but was not statistically significant (30% vs 34%).

Some studies have reported an increase in the episodes of bradycardia with the administration of Dex.[15,16] Serious adverse effects were seen in around 5% patients with the use of Dex during cardiac surgery, including bradycardia and fall in BP, pulmonary embolism, and deep venous thrombosis.[17]

Dexmedetomidine can be very effective in preventing the postoperative cognitive dysfunction and POD, especially in the old age group of cardiac surgery. It can improve the postoperative awaking time, decrease the chances of delirium, delay the onset and total duration of POD, thus decreasing the overall stay in the ICU and in the hospital, decaying cost of treatment.

CONCLUSION

Delirium is a stressful complication observed in the post-operative period. With the use of dexmedetomidine along with the induction of general anesthesia, the chances of post-operative delirium can be reduced. This trial should be done on a larger scale documenting the effects of DEX on all the parameters monitored during the general anesthesia.

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Original Article

Dexmedetomidine for Heart Arrhythmia Prevention in Coronary Artery Bypass Surgery Patients

Sana Siddiq[1], Syed Imran-ul-Hassan[2], Zehra Hasnain[2], Kanwal Awan[2], Maria Ikram[2] and Javairia Saleem[2]

ABSTRACT

Objective: The aim of this study was to compare the incidence of various types of cardiac arrhythmias between the two groups of CABG cardiac surgery treated peri operatively with dexmedetomidine with those treated with placebo in the department of cardiac surgery, Punjab Institute of Cardiology, Lahore, Pakistan.

Study Design: Randomized controlled trial study.

Place and Duration of Study: This study was conducted at the Department of Cardiac Surgery and Anesthesia, Punjab Institute of Cardiology, Lahore from January 2020 to June 2020.

Materials and Methods: Patients of elective cardiac surgery were enrolled and divided into two groups. As per the inclusion criteria step in the research proposal all the patients undergoing off-pump CABG surgery of ASA class II and III, with age of 35 to 75 years having ejection fraction (EF) of >35% were enrolled. Patients in the trial group or DEX group was given 0.5 mcg/kg/h of dexmedetomidine during the induction process and later on an infusion was started at a dose of 0.5 mcg/kg/h till the completion of the surgery even till the shifting of the patient in the High risk units.The frequency of atrial fibrillation and other types of arrhythmias was documented and compared with the two groups using chi square test. Data was stratified for age and gender, post-stratified chi square test was applied to see the effect of these variables on the outcome variable. $P<0.05$ was taken significant.

Results: A total of 60 cases (30 in each group) fulfilling the selection criteria were enrolled to compare the incidence of various types of cardiac arrhythmias between the two groups of CABG cardiac surgery treated peri-operatively with dexmedetomidine with those treated with placebo. Patients treated with DEX had an overall lower incidence of various types of arrhythmias. Most common arrhythmia was ventricular tachycardia and premature ventricular contractions.

Conclusion: With the use of dexmedetomidine as a sedative and adjuvant of general anesthesia drugs, the incidence of various tachyarrhythmia is decreased during cardiac surgery and in the post-operative period; but the decrease in the incidence was not statistically significant for all types of arrhythmias.

Key Words: DEX, dexmedetomidine, tachyarrhythmia,atrial fibrillation, Anesthesia, Cardiac surgery

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INTRODUCTION

In the past few years, the outcomes of cardiac surgeries have improved a lot due to significant advancements in the field of diagnostics, anesthesia and postoperative ICU care.[1] Still complications can occur varying from case to case depending upon the expertise of the surgeons and co-morbidities in the patients.

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Among various lethal morbidities and sometimes complications of cardiac surgery is the incidence of heart arrhythmias. Its incidence varies from 15 to 50%, and mostly commonly seen after the coronary artery bypass grafting surgery (CABG).[2]

Changes in the levels of epinephrine and nor-epinephrine while operating on the heart after surgical stimulation lead to significant Hemodynamic disruption and other changes in the body. This hemodynamic disruption leads to disturbance in the myocardial oxygen supply and demand ending up into ischemia with rise in the morbidity.[3] With the development of arrhythmias during or after the surgery can lead to significant rise in hospital stay and cost of the treatment.[4,5]

Many drug trials have been done to prevent heart arrhythmias and the hemodynamic disturbances during the heart surgeries, but still no specific treatment strategy have been recommended for routine use. One of these drugs is dexmedetomidine. It is short-acting

alpha-2 stimulator which can decrease the norepinephrine level in the body. With the fall in the level of nor-epi chances of development of tachycardia, hypertension, delirium are reduced. Even with the peri-operative treatment with DEX, need of analgesic is reduced.[6,7]

Prevoius studies have shown that dexmedetomidine treatment can prevent cardiac arrhythmias but the effect was statistically significant in most of the studies.[8,9,10] A meta-analysis concluded that DEXcan effectively decrease the incidence of atrial fibrillation at the cost of hypotension.[1]

Till today limited local studies are available comparing the effect of DEX with any other drug or placebo on the incidence of various heart arrhythmias. As there is inconsistent results of trials done previously and controversy regarding the effect of dexmedetomidine, controlled trials should be done in our local tertiary care hospitals.

MATERIALS AND METHODS

This study was conducted in the department of cardiac surgery and anesthesia, Punjab Institute of cardiology from January 2020 to June 2020. In this randomized controlled trial patients of elective cardiac surgery were enrolled and divided into two groups. As per the inclusion criteria step in the research proposal all the patients undergoing off-pump CABG surgery of ASA class II and III, with age of 35 to 75 years having ejection fraction (EF) of >35% were enrolled for the randomized controlled trial.

Any patient previously diagnosed with any kind of cardiac arrhythmias or any type of heart block, or those with any previous heart surgery or history of any valvular cardiac disease were not enrolled in the study. All patients diagnosed to have a large sized left atrium or enlarged heart size (cardiomegaly) was also excluded.

Non-probability consecutive sampling was done in this randomized controlled trial. The patients were either allocated in the DEX group or the control group. Allocation process was random and the anesthetist administering the drug was unaware of the allocated group of the patient and which trial drug will be given to a particular patient.

Induction process involved the administration of standard dosage of midazolam, atracurium and propofol. Patients in the trial group or DEX group was given 0.5 mcg/kg/h of dexmedetomidine during the induction process and later on an infusion was started at a dose of 0.5 mcg/kg/h till the completion of the surgery even till the shifting of the patient in the High risk units.

All the patients in the control group were administered with equal amount of infusion of normal saline as placebo. All the patients were monitored as per the protocols of the anesthesia and cardiac surgery. Regular medication was used for the maintenance of anesthesia were continued as protocol.

In order to control the blood pressure which may fall with the administration of dexmedetomidine, mean arterial pressure- MAP was monitored if a fall of >30% is observed during the surgery, fluid therapy was done and later dexmedetomidine infusion was reduced to 50%, along with the inotropic support. With the revival of MAP to its baseline level, dex infusion was also slowly increased to its previous rate. Similarly, if any patient developed raised blood pressure (change in the MAP of > 30%), an infusion of nitroglycerin was started.

Variables recorded include gender, age, ventricular ejection fraction, platelets, hemoglobin and INR as part of the checklist to meet the inclusion and exclusion criteria. All patients were given general anesthesia with standard protocols. All patients had off-pump CABG surgery by consultant cardiovascular surgeon.

The objective of this study was to compare the incidence of various types of cardiac arrhythmias between the two groups of CABG cardiac surgery treated peri operatively with dexmedetomidine with those treated with placebo in the department of cardiac surgery, Punjab Institute of Cardiology, Lahore, Pakistan.

Data collection for this study was done from Aug, 2020 till Jan, 2021 in the Punjab Institute of Cardiology. The study was approved by the clinical research ethics Committee of the Punjab Institute of Cardiology (PIC).

All the patients enrolled were explained about the procedure of data collection and purpose of the medicines used. A written informed consent was taken individually from each patient in the presence of their family members to use the data collected for the purpose of research.

Sampling was done through non probability consecutive sampling technique. Sample size 60 was calculated using the WHO sample size calculator with expected percentage of patients developing atrial fibrillation in dex group of 7.8% and in the controlled group of 26.3% taking the power of the test of 80% and level of significance of 5%. 30 patients were randomly assigned to group 1 and 30 into group 2.

In order to remove bias, neither the patients were aware of the type of drug they were given nor were the person administering the drug was aware of the drug. One of the drugs was labeled as A (DEX) and other was labeled as B (placebo).

At baseline i.e. just before the induction of anesthesia, MAP and heart rate – HR was noted. Readings were taken again after laryngoscopy, then after sternotomy, later while handling distal and proximal grafts. MAP and HR were again documented at the closure of the sternum and lastly in the ICU.

Epinephrine was used in case of significant fall in the MAP and atroprine was given for significantfall in the

HR. Continuous monitoring of the heart was done with ECG to pick any arrhythmias. These include premature atrial contraction – PAC, premature ventricular contractions – PVC, ventricular fibrillation - VF, atrial fibrillation - AF, ventricular tachycardia– VT were recorded from the start of induction to ICU admission.
Data was enter in excel and SPSS data analyzing software (SPSS-23.0) and analyzed to calculate frequency and percentages of categorical data and mean with standard deviation for continuous data. The frequency of atrial fibrillation and other types of arrhythmias was documented and compared with the two groups using chi square test. Data was stratified for age and gender, post-stratified chi square test was applied to see the effect of these variables on the outcome variable. $P<0.05$ was taken significant.

RESULTS

In this randomized controlled trial conducted in the department of cardiac surgery, Punjab Institute of cardiology, a total of 60 cases (30 in each group) fulfilling the selection criteria were enrolled to compare the incidence of various types of cardiac arrhythmias between the two groups of CABG cardiac surgery treated peri-operatively with dexmedetomidine with those treated with placebo in the department of cardiac surgery. Table no. 1 shows the distribution of the age of the patients included in our study. Table no. 2 shows the distribution of gender among the patients enrolled.

Table No. 1: Age Distribution (n=60)

Age(in years)	Dexmedetomidine group (n=30)		Control group (n=30)	
	No. of patients	%	No. of patients	%
35-50	11	36.67	14	46.67
51-75	19	63.33	16	53.33
Total	30	100	30	100

Table No. 2: Gender Distribution (n=60)

Gender	Dexmedetomidine group (n=30)		Control group (n=30)	
	No. of patients	%	No. of patients	%
Male	16	53.33	18	60
Female	14	46.67	12	40
Total	30	100	30	100

Table No. 3: Comparison of various types of cardiac arrhythmias in both groups (n=60)

Variables	DEX group(n=30)		Control group(n=30)		P value
	No. of patients	%	No. of patients	%	
PAC	5	16.67	17	56.67	0.001
VF	2	6.67	3	10	0.64
AF	3	10	8	26.67	0.09
VT	6	20	24	80	<0.00001
PVC	7	23.33	24	80	0.00001

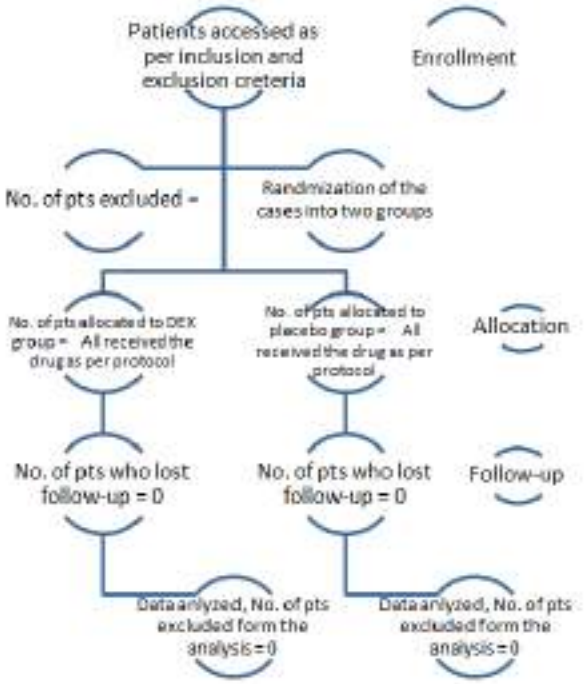

Figure No.1; CONSORT diagram showing the flow of participants through each stage of a randomized trial

Table no. 3 shows the frequency of various types of cardiac arrhythmias that was recorded during the monitoring of heart rhythm during CABG and after surgery in the stay in the ICU. Patients treated with DEX had an overall lower incidence of various types of arrhythmias. Most common arrhythmia was ventricular tachycardia and premature ventricular contractions.

DISCUSSION

Dexmedetomidine is a potent sedative drug and a short acting alpha-2 agonist. Some controlled trial have shown that its peri-operative administration can significantly reduce the chances of development cardiac arrhythmias, delirium, post-op anxiety and hypertension, along with its morphine-sparing effect.11
Many international studies have compared the incidence of atrial fibrillation during and after cardiac surgery with the use of DEXagainst some other drugs or placebo. Some of these studies showed a statistically significant reduction while most of them were non-significant. Some studies reported a significant association bradycardia among the patients administered with Dex.[12,13] Apart from bradycardia some other serious side effects were reported in around 5% of the patients treated with Dex during cardiac surgery. These include fall in BP, pulmonary embolism, and deep venous thrombosis.[14,15]
As DEX can lead to anti-anxiety and sedation without disturbing the respiration of the patients, it can be used in patients undergoing heart surgery. In this study, dexmedetomidine was administered and monitoring of

all the parameters was done throughout the CABG to detect any type of heart arrhythmias. The frequency of various types of heart arrhythmias was compared between the two groups: one treated with DEX and other treated with placebo. DEX treatment followed by continuous follow-up was done to see the role of DEX in the prevention of cardiac arrhythmias including pre-mature atrial contractions, pre-mature ventricular contractions, ventricular tachycardias, atrial fibrillation and other changes in the cardiac rhythm.[16]

Soltani G, et al reported that with the use of dexmedetomidine during cardiac surgery can decrease the incidence of atrial fibrillation in around 90% cases. Patients in DEX group also had a lower mean MAP and HR as compared to that in the control group at points during the surgery and during the stay in the ICU. Data analysis showed the incidence of various cardiac arrhythmias in DEX and placebo group as: PAC (55% vs. 15.7%), PVC (81% vs. 21%), AF (26% vs. 8%), VT (21% vs. 2.6%) $p<0.05$.16 Liu et al. also reported in a similar study that dexmedetomidine decreased the incidence of AF by 18%.[4]

Some studies have shown opposite results. In a larger study, patients of cardiac surgery were monitored for various adverse effects. Among the total patients enrolled in the study, 23.8% developed AF. Around 400 patients were treated with DEX and 400 patients were given a placebo drug. Data analysis showed that AF developed in 30% of the patients in the DEX group and 34% in placebo group. Of the total number of patients included in each group, 5% in the DEX group while 2% of the placebo group, had serious side events. They concluded that clinicians and anesthetists should not reply on the DEX should not be infused to reduce atrial fibrillation or delirium in patients having cardiac surgery.[17] Similarly, Zhu Z, et alanalyzed data from 9 studies with total around 1300 patients. Data analysis showed that DEX group was not significantly linked to decrease in the AF development as compared to the control group.[18]

Yared JP, et al concluded that incidence of AF was 41% in the patients treated with placebo and 30% in the DEX group. It was seen after data analysis of inflammatory markers produced during and after the surgery, that DEX reduced the release of these inflammatory markers.[19]

Turan A, et al reported after collecting data of 765 cardiac surgery patients treated with DEX as a sedative in the post-op period. Patients in the DEX group showed small percentage of atrial arrhythmias.[20]

In another study, cardiac surgeries were performed and DEX was administered in the immediate postoperative period. Data was compared with that of the control group showed that, group of patients who received DEX had much less incidence of tachyarrhythmias (29% versus 38%;$P<0.05$).[21]

As there is controversy in the data regarding the role of dexmedetomidine as compared to other drugs or placebo in altering the incidence of various cardiac arrhythmias, further trials should be done. However many other studies have shown significant decrease in the incidence of heart arrhythmias, specially the incidence of atrial fibrillation.

CONCLUSION

With the use of dexmedetomidine as a sedative and adjuvant of general anesthesia drugs, the incidence of various tachyarrhythmia is decreased during cardiac surgery and in the post-operative period; but the decrease in the incidence was not statistically significant for all types of arrhythmias.

Author's Contribution:

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

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Original Article

Gestational Diabetes and the Preterm Births in Obese Women in Low Socioeconomic Group

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ABSTRACT

Objective: To determine Gestational Diabetes and the Preterm births in obese women in low socioeconomic group.
Study Design: Prospective case control study.
Place and Duration of Study: This study was conducted in Obstetrics and Gynecology Department Unit III at Abbasi Shaheed hospital from January 2018 to December 2018.
Materials and Methods: Total 182 patients were included in study. The inclusion criteria involved women of reproductive age group i-e; 16- 45years, pregnant obese and non-obese females visiting outpatient department and also admitting in inpatient department due to complications, belonging to lower socioeconomic class. Pregnant females with comorbid like previously diagnosed diabetes mellitus, hypertension, end stage renal disease, bleeding disorders were not included in study.
Results: Out of 182 patients enrolled in the study the mean age of the patients was 32.7± 3.76 yrs. Most of the patients belong to age group 31-35yrs, n=84(46.2%). There were 91 women in both obese and non-obese groups. The average BMI of patients was 33.04mg/kg body weight. Out of 91 obese women, mostly women were in the range of mild obesity i.e.; n=64(35.2%) while 27(14.8%) were with moderate obesity. There was total n= 138 preterm births seen among women enrolled. The mean preterm births took place at 34weeks ±3.1 weeks. The preterm births when compared between obese and non-obese, increased number of preterm births were found with statistical correlation found. (p value-0.000). The mean of random blood sugars of patients was 279.4mg/dl± 37.02 mg/dl.
Conclusion: The obese women with gestational diabetes are at increased risk of preterm births. The increased incidence was seen among women of low socioeconomic class with non-adherence towards treatment due to unawareness, financial issues and casual attitude towards gestational diabetes.
Key Words: Preterm births, gestational diabetes

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INTRODUCTION

Worldwide, incidence of overweight and Obesity incidence is increasing among women of reproductive age[1-5.] Around 38.4% women in reproductive age are overweight and 63.39% obese in Pakistan. In US, the incidence among obese 11-40% and in overweight 12-38% among pregnant women[1]. According to American Medical association, obesity and overweight are preventable causes of mortality.

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Preterm births itself is one the most common cause of neonatal morbidity and mortality and also later in life childhood morbidity [1].

In Pakistan, studies have shown 20.4% incidence of gestational diabetes in women had pre-pregnancy obesity[6]. Various studies had also shown that there is increased risk of preterm births, cesarean sections, macrosomic babies also large for gestational age babies in overweight as well as obese women[4-8]. A large population based study by Su et al in 2019 has shown increased risk of preterm births and other pregnancy related complications in women with pre-pregnancy weight [4]. Another study by Anwar et al has shown incidence of 22.7%-31.8% preterm births in women with gestational diabetes[11].

Lower socioeconomic population in Pakistan constitutes around 17.2% [9]. The social norms, dietary habits, unawareness towards outcomes of gestational diabetes and preterm births, no adherence to treatments, lack of knowledge, fear of antidiabetic medications affecting births are the common observations among pregnant women [10].

The aim of the study was to determine the frequency of preterm births in patients with gestational diabetes in

obese and non-obese lower socioeconomic class visiting hospital in order to know the impact of morbidity due to it and its influence on society reduce the increasing maternal and neonatal health burden of society.

MATERIALS AND METHODS

This was a prospective case-control study conducted in Abbasi Shaheed hospital for a period of one year from January 2018 to December 2018 in Obstetrics and Gynecology Unit III from patients meeting inclusion criteria. The Ethical consent was taken from Ethical review committee of the hospital. The inclusion criteria involved women of reproductive age group i-e; 16-45years, pregnant obese and non-obese females visiting outpatient department and also admitting in inpatient department due to complications. Patients belonging to lower socioeconomic class was included in study with salary income below 15k. Pregnant females with comorbid like previously diagnosed diabetes mellitus, hypertension, end stage renal disease, bleeding disorders, overweight pregnant women were not included in study. The sampling technique used was probability consecutive type with sample size of 182 patients keeping prevalence of 22.7% and margin of error of 9%[11]. Gestational diabetes was labelled by oral glucose tolerance test with fasting glucose 105 mg/dl, after1 hour 190 mg/dl, after 2 hours 165 mg/dl and after 3 hours 145 mg/dl. Preterm birth was defined as birth of child below 37weeks of gestation. According to WHO classification, preterm births were divided into extreme preterm births <28weeks, very preterm 28-32weeks, moderate to late preterm 32- 37weeks.Informed consent was taken from the patient and two groups were made by lottery method. Group 1 was patients who were obese labelled after checking body mass index greater than 30kg/m2. While group 2 included all normal weight patients. Detailed history regarding preconception weight and height, previous illnesses for exclusion or previous history of gestational diabetes was recorded in data. Patients were followed throughout pregnancy for pregnancy related complications i-e; preterm births.

The statistical analysis was performed by using SPSS.20. Mean +/- SD were calculated from age of patient, and duration of gestational diabetes mellitus and gestational hypertension. Stratification was done regarding to preterm births with obesity and normal weight patients. Chi square test was applied keeping p value <0.05 to be significant.

RESULTS

Out of 182 patients enrolled in the study the mean age of the patients was 32.7± 3.76yrs. Most of the patients belong to age group 31-35yrs, n=84(46.2%), while the rest 25-30yrs, n= 50(27.5%)and 36-40yrs, n=48(26.4%) (table 1). There were 91 women in both obese and non-obese groups. Most of the women were of age group 31-35yrs n=84, with frequency higher in both obese and non-obese women, but this was statistically not significant with no correlation was found. (p value-0.157). (table 2). The average BMI of patients was 33.04mg/kg body weight. Out of 91 obese women, mostly women werein the range ofmild obesity i.e.; n=64(35.2%)while 27(14.8%) were with moderate obesity (table 1).There was total n= 138 preterm births seen among women enrolled (figure 1). The mean preterm births took place at 34weeks ±3.1 weeks.The preterm births when compared between obese and non-obese, increased number of preterm births were found with statistical correlation found. (p value-0.000). Mostly there were very preterm births then moderate to late preterm. Extreme preterm births were more frequently observed among women with higher sugar levels and non-compliance to medications. Patents who were diagnosed with gestational diabetes were followed with advise for strict glycemic control but most of the women did not take medicines properly due to lack of availability due to financial constraints in almost all the patients n=120 while some took strict control of blood sugars. The mean of random blood sugars of patients was 279.4mg/dl± 37.02 mg/dl. The complications occurred in patients who were not vigilant in their glycemic control and therefore presented with preterm births. Around 95 patients underwent cesarean sections with n=55 patients from group 1 obese patients and remaining n=40 from group 2 i-e; non obese.

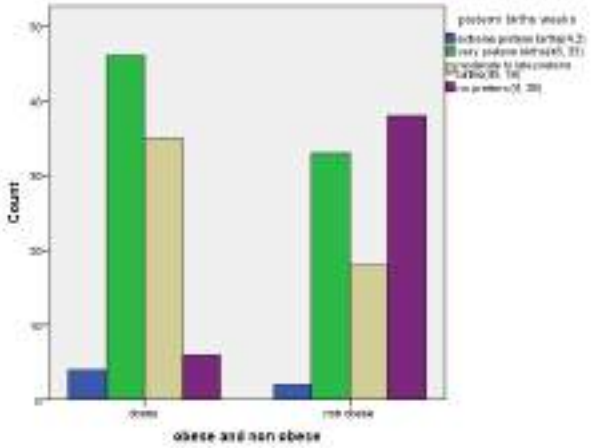
No maternal or neonatal mortality was noted with no patient presented with any emergency condition with very high blood sugars.

Table No.1: Demographic factors

Demographic factors	Mean ±SD
Age in years	32.7± 3.76
Gestational diabetes (Blood sugars)	279.41±37.02
Preterm births in weeks	34.12±3.158
Obese women Mild obesity Moderate obesity	91(50%) 64 (35.2%) 27(14.8%)

Table No.2: Variables

Variables	Obese N=91	Non obese N=91	P value
Age in years			
25-30yrs	25	25	0.770
31-35yrs	44	40	
36-40yrs	22	26	
Gestational random blood sugars range			
200-250mg/dl	12	35	0.000
251-300mg/dl	48	36	
301- 350mg/dl	31	20	



P value 0.000

Figure No.1: Preterm birth with Obese vs non-obese

DISCUSSION

Preterm births are the common cause of morbidity and mortality especially among neonates. In Pakistan, preterm birth 4.9%-11.2% according to estimates of study in 2014 [13- 16]. While the gestational diabetes was reported to be 20.4% in obese antenatal women as concluded by study by Syed in 2014[6]. Our study has shown the incidence of 31.8% preterm births with an observation increasingly found in lower socioeconomic group. The women belonging to socioeconomic group were either had financial constraints, noncompliance of medications, unawareness of complications associated with gestational diabetes and their outcomes.

Obesity is the problem encountered worldwide[17-20]. Around 28.4%-34% women belonging to reproductive age group are suffering from obesity in US, according to 2010 estimates[14]. In our study, the mean age of the patients in obese and non-obese group was nearly same. However, the women in obesity group has age mostly in the range of 31-35yrs. The Center of Disease Control has identified morbid obesity i.e. 7.8% in this reproductive age group of population [14]. In our study the women, mild obesity 35.2%, moderate obesity 14.8%.The patients who were obese has higher incidence of preterm births compared to non-obese patients i-e; 20.8%:10.9%.

Mostly patients in reproductive age group also had raised random blood sugars diagnosed during pregnancy and on follow up too when treatment was advised, women did not show compliance to medicines and resulted in raised blood sugars and therefore leading to preterm births. These preterm births were higher in obese women compared to women who are not obese. This increased rate of preterm births seen in our study is most likely to two major risk factors i.e. obesity and gestational diabetes with non-adherence to treatment mostly due to financial constraints in lower socioeconomic class and other cause was non awareness regarding complications.

Among reproductive age group mostly women have problem of obesity and during pregnancy it leads to some health problems affecting both mother and child. There are different effects of obesity in pregnancy like during early gestation spontaneous abortions, congenital abnormalities, due to risk of insulin resistance, in late gestation fetal abnormalities, increased risk of cesarean sections, postoperative wound infections with delayed healing, thromboembolism, postpartum depression and other related illnesses[6, 11, 12]. However, in our study as patients had mostly mild to moderate obesity and were not strikingly very high; therefore, no other complication besides lower segment cesarean sections were slightly more in obese compared to non-obese but this result was no statistically significant.

In our study patients with preterm births did not had any previous illness, nulliparous women, belonging to lower socioeconomic class. The preterm births in our study among obese compared to non-obese women were n= 86 vs 53, with increased ratio seen among obese gestational diabetic's women compared to non-obese women. The results of our study therefore are consistent with Hanif et al has concluded in his study that preterm births early or late can be reduced by reduction in modifiable factors[12]. While Syed et al[6] has found 15.2% obesity in antenatal women enrolled in study, with gestational diabetes found in 20.4% cases, increased lower segment cesarean sections in 30.4% cases, pre-eclampsia 4.8%, pregnancy induced hypertension in 17.2% of women.

CONCLUSION

The obese women with gestational diabetes are at increased risk of preterm births. The increased incidence was seen among women of low socioeconomic class with non-adherence towards treatment due to unawareness, financial issues and casual attitude towards gestational diabetes.

Author's Contribution:

Concept & Design of Study:	Aisha Khatoon
Drafting:	Shabnam Nadeem
Data Analysis:	Muhammad Saad Usmani, Alvia Saad
Revisiting Critically:	Aisha Khatoon, Shabnam Nadeem
Final Approval of version:	Aisha Khatoon

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

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Original Article

Proximal Convoluted Tubular Cells of Kidney In Impaired Kidney

Histomorphological Effect of Celecoxib on Nuclear Diameter of Proximal Convoluted Tubular Cells of Kidney with Ameliorative Effect of Lycopene in Albino Rats; An Experimental Study

Sadia Sundus[1], Sarwath Fatimee[5], Nadira Hameed[1], Jamil Ahmed Siddiqui[2], Imran Bakar[3] and Shah Jabeen[4]

ABSTRACT

Objective: Toevaluate the nuclear diameter of proximal convoluted tubular cells in celecoxib impaired kidney with amelioration by lycopene.

Study design: Experimental study.

Place and Duration of study: This study was conducted in Animal House of BMSI, JPMC, Karachi from May 2015 to June 2015.

Materials and Methods: In this study we took 90-120 days old, forty healthy adult male Albino rats of 200-220gm weight. Rats were divided into 4 groups, control group was nominated as Group A, rats of Group B were given Celecoxib 50 mg/kg orally, rats of Group C were given Celecoxib 50 mg/kg with lycopene50 mg/kg and Group D were givenonly lycopene 50 mg/kg orally for 30 days. After the completion of experimental study, rats were dissected and renal tissue sections were stained with hematoxylin and eosin.

Results: The nuclei of renal cells became pyknotic and the cells showed apoptotic changes in rats of Group B. Hematoxylin and eosin stained sections showed apoptosis, hemorrhage, necrosis and vacuolation in Group B of albino rats, however renal structure were improved in Group Crats which were given celecoxib with lycopene.

The proximal convoluted tubules of kidney became dilated due to apoptotic changes in renal cells and pyknosis of their nuclei. Renal interstitium showed inflammation, edemaand congestion.

Conclusion: This experimental study accomplishes that lycopene improved the pyknotic changes of Group B.

Key Words: Apoptosis, reactive oxygen species (ROS), acute kidney injury (AKI), prostaglandins (PGs), interstitial nephritis (AIN), and glomerular filtration rate (GFR).

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INTRODUCTION

Celecoxib is4-[5-(4-methylphenyl)–3-(trifluoromethyl)-1H-pyrazol-1-yl] benzenesul- fonamide,is asubclass of NSAIDs,used for pain, fever, redness and edema. [1,2]It selectively inhibits COX-2 enzyme activity because COX-2 enzyme stimulates NADPH oxidase activity,[3] which causes oxidative stress, resulting in excessive production of ROS that leads to tissue injury and metabolic disturbance.[4] COX-2-selective inhibitors were associated with less Gastrointestinal symptoms but increased risks of cardiovascular events via vasoconstriction and platelet aggregation and 2.7 times increase risk of acute Kidney Injury by sodium retention estimated glomerular filtration rate (GFR) alteration, hyperkalemia and raise the blood pressure.[5,6,7]vascular injury and multiple organ failure in sepsis. [8]

NSAIDs reduces renal blood flow which results in tubular obstruction through crystal deposition, which causes acute kidney injury (AKI) and interstitial nephritis (AIN). [9] Raised levels of cyclooxygenase derived oxylipins causes cystic kidney diseases.[10] There is strong association between acute kidney injury (AKI) and usage of NSAIDs. [11]NSAIDs inhibits prostaglandins (PGs) and enzyme cyclooxygenase (COX) production, which converts arachidonic acid into PGs, thromboxanes, and prostacyclins.COX-2 is

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always activated when there is any injury occur in the body and release of inflammatory mediators, leading to the stimulation of PGs synthesis.[12]

Celecoxib decreases the synthesis of different inflammatory "prostanoids" byCOX-2 enzyme inhibition[13] because COX-2 enzyme is mainly activated due to inflammation and cell transformation processes[14] and produces prostaglandin E2 (PGE2), which boosts the resistance to apoptosis, probability for invasion, angiogenesis, cell-proliferation and metastasis.[15] It treats different clinical conditions like musculoskeletal disorders, pain, dysmenorrhea and colorectal polyps. Gastrointestinal and bleeding risks are lower with celecoxib, so it is also used for the treatment of OsteoArthritis but it did not improve endothelial.[16] Celecoxib radiosensitize cancer cells leads to suppression of cancer cell proliferation, which shows its strong chemopreventiveaction[17,18]Itinduces apoptosis in tumor cells due to activation of the anti-apoptotic kinase, which promotes apoptosis in cells.[15] Celecoxib is primarily metabolized in the liver and excreted in urine and feces. [12]

Lycopene (LPN) is a member of red-colored carotenoid, found in tomato,[19] red fruits like watermelon, Momordica cochinchinensis, Spreng fruit, papayas, pink grapefruit, vegetables.It possesses a strong antioxidant activity caused by free radicals in human tissues, thusinhibit cellular damage due to reactive oxygen species.[20,21,22,23] It is a lipid-soluble antioxidant, inversely associated with lipid peroxidation and reduced oxidative stress and inflammation. It has several biological activities like aging prevention, anti-cancerous, and anti-inflammation. [24,25]Lycopene played a vital role in the activation of Nuclear factor erythroid 2-related factor 2 (Nrf2) which causes regulation of cellular oxidative stress response.[26]

The intake of tomatoes and its products are associated with raised blood levels of lycopene. It gives protection to cellular damage caused by (ROS) and against oxidation of lipids, proteins, and DNA, so it have substantial roles in preserving tissue and cellular integrity. [27,28]

Meanwhile, No experimental study bring in observation up till now regarding morphometric and histo-pathological changes occur due to Celecoxib along with ameliorative effect of lycopene, therefore this opportunity has been availed to commence this research. As we know that Celecoxib hasadverse effects on kidney and altered its morphology as well as functions while lycopeneis a bioflavonoid and have highest oxygen-quenching capacity. This is the reason we plannedthe study to seelycopene protective effect on celecoxib persuaded renal tissue.

MATERIALS AND METHODS

It is a four weeks study, which was conducted in the Animal House of BMSI, JPMC, Karachi. 90-120 days old, forty healthy adult Albino rats of 200-220gm weight were brought from the Charles River Breeding Laboratories, Brooklyn, Massachusetts, USA. We observe their well-being and nutritional behaviors one week before the commencement of experimental study. According to the study plan dosage of Celecoxib and lycopene were given to animals.

We divided the animals into four groups.

- Group 1: as standard group.
- Group 2: were given Celecoxib 50 mg/kg orally.
- Group 3: were given Celecoxib 50 mg/kg + lycopene 50 mg/kg orally.
- Group 4: were given lycopene 50 mg/kg orally.

Prior the commencement of experimental study every animal was weighed and retained in animal house cages before drug administration. To note behavioral changes and general conditions all the animals were kept under observation. They were weighed and sacrificed at the end of study.

The animals was sedated under ether and then fixed on a dissecting board. A sagittal incision were given from manubrumsterni to pelvic bone by scalpel. Another incision were given at right angle to the previous incision to get appropriate exposure of thoracic and abdominal cavity. Kidneys were recognized and exposed. They were inspected for noticeable change in pigmentation, contour, and substance. They were detached and absolute weight was recorded with sartorious balance. Both kidneys were excised into longitudinal halves for separate fixative after cleaning with normal saline. For H & E staining one half was retained in 10% formalin and the other section for PAS staining in alcoholic formalin for a day. It was treated in ascending grades of alcohol (70% – 100%) for dehydration and cleared in xylene. Paraffin wax was used for infiltration and embedding and with the help of rotatory microtome, 4 to 5 microns thick longitudinal sections were taken and they were fixed on albumenized glass slides.

By SPSS version 20.0 data was evaluated. One sample t-test is used for the significance of tissue slides at 40x.P-value < 0.05 was anticipate as statistically significant.

RESULTS

Group1: Group 1rats were alive and healthy and their dietary habits as well as response to external stimulus was usual during the study. The mean value of nuclear diameter of Group 1 proximal tubular cells was 6.2±0.84µm (Figure-1a) (Table-A).

Group 2: Group 2 animals were looking lethargic and their food consumption was reduced as well as their response to stimuli was sluggish. The mean value of nuclear diameter of Group 2tubularcells was 4.2±0.83µm. A remarkable decrease in Group 2($P<0.05$) in the mean value of nuclear diameter of

tubular cells was observed as compare to Group 1(Figure-2a& 3a) (Table-A).

Group 3: Group 3 animals seemed relatively healthy and active. Their response to stimuli was improved as compared to Group 2 animals as well as food intake was normal. The mean value of nuclear diameter of Group-3 proximal tubular cells were 6.0±0.70µm. Group 3 showed a remarkable raise (P<0.05) in nuclear diameter of proximal tubular cells in comparison with Group 2 and an unremarkable shrinkage (P>0.05) in nuclear diameter of proximal tubular cells ofGroup3was observed as equated to Group 1(Figure-4a) (Table-1).

Group 4: The Group 4 animals were taken to determine that rather lycopene can produce any changes in the architecture of renal tissue of rat. The outcomes of Group 4 was same as Group 1.

Table No.1: Mean values of nuclear diameter of proximalconvoluted tubular cells of kidney (µm) in different groups of albino rats

Groups	Treatment given	Mean value of nuclear diameter of proximal tubules
1 (n=10)	ND	6.2±0.84
2 (n=10)	Celecoxib	4.2±0.83
3 (n=10)	Celecoxib +Lycopene	6.0±0.70

*Mean±SEM

Analysis of data in the mean nuclear diameter of proximal convoluted tubular cells in various Albino Rats groups.

Data comparison	P-value
2 vs.1	P<0.05**
3 vs. 1	P>0.05*
3 vs. 2	P<0.05**

Key:

Non-significant*
Significant**
Moderately significant***
Highly significant****

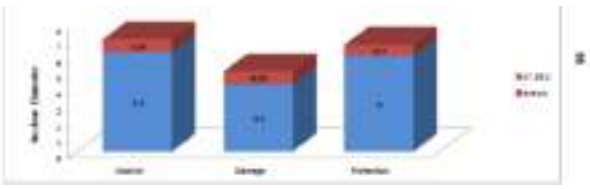

Figure No.1: Mean values of nuclear diameter of proximal convoluted tubular cells of kidney (um) in different groups of albino rates

Group 1animals on microscopic examination exhibited usual renal architecture. Proximal convoluted tubular epithelial cells was shown with regular brush border and centrally located spherical nucleus. (Fig-1a)

Microscopic examination of Group 2animals showed apoptosis and dilatation of renal tubules with pyknotic nuclei, infiltration ofproximal convoluted tubular cells. (Fig-2a). Microscopic examination of Group 3animals revealed restoration of renal architecture, slight dilatation of renal tubules with regular brush border, centrally located spherical nucleus. (Fig-3a)

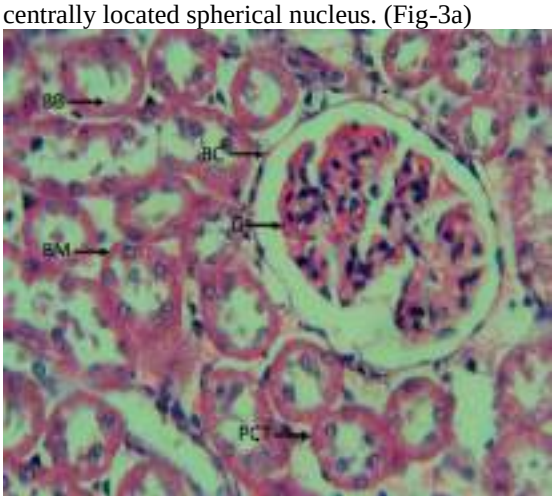

Figure No.1a: Photomicrograph showing normal cytoarchitecture of kidney normal glomerulus, proximal and distal renal tubules in control group-1 at 40x

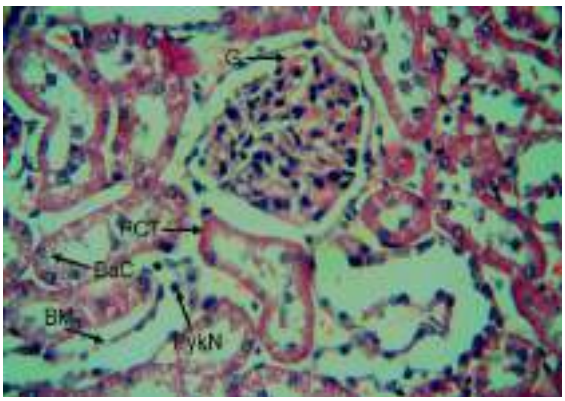

Figure No.2a: H& E stained, 4 µm thick section of celecoxib treated rat kidney (Group-2) shows proximal convoluted tubules, congested and hemorrhagic slightly shrunken glomerulus and ballooning of cells (BaC) with pyknotic nuclei (PykN). (Photomicrograph x 400).

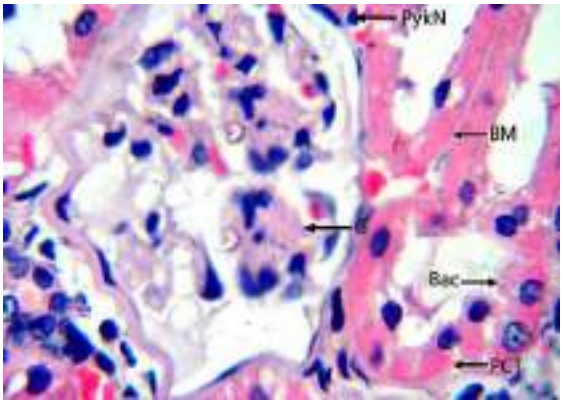

Figure No.3a: H& E stained, 4 µm thick section of celecoxib treated rat kidney (Group-2) showing proximal convoluted tubule (PCT), slightly shrunken glomeruli (G)and ballooning of cells (BaC) with pyknotic nuclei (PykN). (Photomicrograph x 1000)

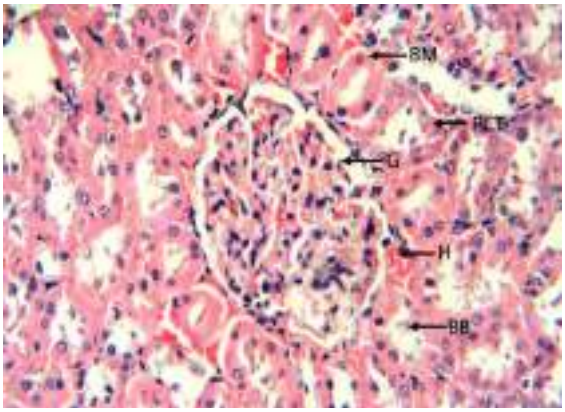

Figure No.4a: Photomicrograph showing preserved cytoarchitecture of kidney glomeruli has less vacuolation, brush border of proximal is restored and not as much of hemorrhage in group-3 (lycopene treated) at 40x

DISCUSSION

Celecoxib is one of the subclasses of ANSAIDs, used for pain, dysmennorhoea, inflammation, redness, edema and fever.[1] Histological examination exhibits apoptosis, pyknosis, infiltration of mononuclear cells and tubular dilatation.[2]

Lycopene is a member of carotenoid family.[19] It possesses antioxidant activity and inhibits cellular damage because of reactive oxygen species (ROS). Red colored fruits such as tomato, pink grape fruit and vegetables contains lycopene.[20]It contributes in multiple biological activities such as aging prevention, anticancerous and anti-inflammatory agent.[21,22]

Group B animals were sluggish and reduced their body weight because of cytotoxicity and cell mediated immune injury which leads to apoptosis and pyknosis.[15]Pyknotic nuclei, degenerative and apoptotic changes were observed in proximal convoluted tubular cells as described by. [2]

Group C animals were healthy just like Group A and slight body weight is reduced as compared to Group B because it inhibits production of reactive oxygen species, thus reduces apoptosis and cellular damage.[24,25] Group C showed reversal of the renal parenchyma degenerated changes induced by celecoxib. Lycopene plays a substantial role in maintaining tissue and cellular integrity as described by.[27,28] who described that lycopene gives protection to cells against oxidative damage.

CONCLUSION

This experimental study determined that Group B had significant decrease in body weight due to apoptosis with pyknotic nuclei, oxidative cellular damage and tubular dilatation however Group C exhibited increase in body weight, reversal of pyknosis and apoptosis. So this is our suggestion that don't use celecoxib frequently and if needed always used it with lycopene to decrease its adverse effects.

Author's Contribution:

Concept & Design of Study:	Sadia Sundus
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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