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Editorial

Save the Future of Young Population

Mohsin Masud Jan
Editor

In Pakistan there are only 250 trained psychiatrists for the entire population. Even children are being brought with mental health issues of various kinds, with some children having had reported that they have been suicidal for a long period. Suicide attempts among 12 year olds or younger have been reported as well.

40 percent of young people aged under 25 suffer mental health issues of various kinds ranging from depression to schizophrenia in Pakistan. Some studies also show that many medical students in Pakistan suffer depression and severe mental health issues, mainly as a result of stress and the pressures they faced.

We need to find out what is happening and why our children are facing such grave crises in their young lives, destroying their happiness at a time of life which should essentially be full of growth, learning, and joy. Several studies from around the world show that social media has played a large part in negatively affecting the mental health.

The American Academy of Paediatrics, for instance, recommends that social media use should be extremely limited among children, and managed by parents when it comes to children above the age of 12.

According to a new research, girls and young women are badly affected by the images of near-perfect people especially of young women posted all over the internet and aspire to look the same way. This is impossible given that many such images are photoshopped or have filters on them which present an image that is simply not attainable.

Parents are mainly responsible for determining what gadgets and websites their children have access to. Ideally, parents should be able to monitor children up till the age when they are mature enough to do so themselves. This could be 16 years for some, 18 for others, and far more for the rest. Even adults struggle with the problems created by the internet. Yet we see a growth in the use of the internet over telephones, tablets, and screens of all kinds. No one tries to stop it and few are aware of the problems that exist. Even in low-income households at least one tablet or smartphone is often available for use by the entire family.

Schools too need to be far more aware of the problems that are growing and taking a high toll on mental health. We have teenagers who have committed suicide because they did not find enough followers over the internet or because their pictures were not 'liked' by enough people. Specialists, who have discussed the problem before the US Congress, as the matter becomes a grave one around the world, have noted that the impact of social media apps such as Facebook, Instagram, and in particular Snapchat where the image disappears within a few minutes, is most harmful of all.

There is a need to do more to protect our young people and children. The rate of suicide, as we know, is extremely high in Pakistan as is the rate for attempted suicide. Many such deaths are covered up because of social and religious stigma. But realities have to be faced. We must understand that handing over our phone to a child and watching him/her look at its contents is not an act of entertaining the child. It is almost criminal, because it can damage the child's brain for life.

Psychologists and psychiatrists point out that how children and young adolescents interact with the internet is different from the manner in which adults do. Their brains respond in different ways to the images that flash across screens, and there is always the danger of unintended or intended access to inappropriate content. We, therefore, need a far more vigilant society, which keeps a tighter watch over the mental health of young people. When a 12- or 13-year-old child is suicidal, it implies that there is something wrong with his/her environment. There are also issues related to eating disorders, sometimes pushed forward by the internet and with sites which promote anorexic behaviour. There are a few websites that encourage children and young people to engage in dangerous activities. There needs to be a far greater degree of awareness, notably among parents from low-income groups, about what harm the internet can inflict.

Instagram images and videos is not just a harmless act but can also lead to dangers of all kinds. We need to go back to the time when children were more physically active and learned life lessons in various fashions, including direct contact with parents, other family members and peers. The two years of Covid-19 have further added to the problem. School classes on Zoom mean that there is no interaction with peers or teachers and children live in a virtual world to which they cannot always relate in a healthy or reasonable fashion. It is not their fault.

In our country, we need to pay even more attention to the mental health of young people, consider the suicides that have occurred, and watch out for the role of the internet. We can raise a generation of healthy persons rather than those who are in some way badly affected by the content they consume over internet sites meant to draw in vulnerable persons. All this require more and more attention of the parents towards to their growing children.

Original Article

APGAR Score and Neonatal Growth Parameters in Neonates of Mothers Passively Exposed to Cigarette

Wardah Anwar[1], Masooma Ahmad[2], Maria Ilyas[3], Ameena Nasir[4], Faiza Khan[5] and Huma Jawad[2]

ABSTRACT

Objective: To observe the relationship of low birth weight, head circumference, length and APGAR Score in different groups of different exposure to smoking with control group of non-exposed mothers.

Study Design: Cross-sectional comparative study

Place and Duration of Study: This study was conducted at the Physiology Department of Sheikh Zayed Postgraduate Medical Institute, and Gynecology & Obstetrics Department of Sheikh Zayed Hospital, Lahore for one year from October 2018 to August 2019.

Materials and Methods: This was a cross-sectional comparative study in which neonatal were measured and compared in 120 subjects divided in four groups i.e. non-exposure, 1-5 cigarette exposure, 6-10 cigarette exposures, more than 10 cigarettes per day.

Results: Mean APGAR score and birth weight were significantly different in the study groups. Neonatal head circumference of group 1 was statistically significant as compared to group 4 while mean length of the neonates was not statistically significant.

Conclusion: Passive or second hand smoking have an effect on APGAR score and neonatal growth parameters.

Key Words: APGAR Score, Cigarette Smoking, Fetal length.

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INTRODUCTION

Second-hand smoking (SHS), also known as passive smoking, is the outcome of exposing a nonsmoker to tobacco smoke, often in a confined space.[1] Passive smoking has a detrimental impact on neonatal health, birth weight, and other factors. Passive smoking poses a significant risk for respiratory illnesses[2].

The development of the fetus during the intrauterine period affects the birth weight of the fetus in humans. Infant mortality and birth weight are hypothesized to be negatively associated[3].

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Obstetricians are worried about the development of the growing fetus since it is linked to various morbidities that may have long-term effects in addition to stillbirth. The second most significant factor to cause low birth weight in the human fetus is intrauterine growth restriction (IUGR). Normal birth weights should range between 2500 and 4200 grams when a baby is born at term.

Infants born to moms who smoke have a higher likelihood of low birth weight than those born to mothers who don't smoke. Second-hand smoke exposure (SHS), raises the risk for low birth weight[4,5] and is a significant contributing factor. There are an alarmingly high number of Low birth weight instances in Pakistan, estimated to be 12–25%[6].

Virginia Apgar, a physician and anesthesiologist, created the Apgar score, a technique for assessing a newborn's health at delivery. It is measured at one minute and then at five minutes after birth. It is evaluated against a scale from one to ten; out of which two scores for each clinical signs i.e. heart rate, muscle tone, reflex irritability, color and respiratory efforts. Low Apgar at five minutes is associated with increased incidence of mild to moderate adverse neurological outcomes[7].

The baby's length influences how tall he or she will be as an adult. This association is more evident in kids born between 39 and 41 gestational weeks than Preterm births[8].

One of the other parameter that is measured at birth is the Head Circumference (HC). Measurement of the HC lies in the fact that it can be used as a reference for monitoring growth of central nervous system, child health and conditions like microcephaly and megacephaly[9].

One of the risk factors that is modifiable to reduce the likelihood of adverse pregnancy outcomes is exposure to tobacco smoke during pregnancy. According to studies, smoking during pregnancy has a number of negative impacts on the mother's and the unborn child's health. Some of them include improper placental implantation, early rupture of the amniotic sac membrane, placental rupture, premature birth, stillbirth, low birth weight and sudden infant death syndrome[10,11].

MATERIALS AND METHODS

The cross-sectional comparative study was conducted in Physiology Department of Sheikh Zayed Postgraduate Medical Institute, in collaboration with Gynecology and Obstetrics Department of Sheikh Zayed Hospital, Lahore and Emergency Labor Room of Sir Ganga Ram Hospital, Lahore. Study was carried out after permissions from the respective head of departments.

Study Population: The population of my study included 120 neonate born to females between 20 to 35 years of age All females were full term i.e. 38+ week

Inclusion criteria:

The study comprised the following neonatal mothers:

- Normal pregnancy of 37 to 40 weeks with no family history of gynecological issues.
- 20 to 35 years of age.
- Single pregnancy.
- Women belonging to same socioeconomic class.
- Control group: pregnant female who weren't exposed to passive smoking
- Study group: pregnant female who were exposed to tobacco smoke by indoor smoking**.**

Exclusion criteria:

Following were excluded from the study,

- Diabetes
- Hypertension
- Respiratory, Cardiovascular disease
- Smoking mothers
- Drugs and alcohol addicts
- Pregnancy complications like anemia, poor weight gain, IUGR.

Sample Size: Using a 90% power of the test and a 95% confidence level, the size of the sample was computed. Its size was estimated to be 120. The sample was then split into four groups, each with 30 subjects.

Sample Technique: Convenient sampling/ non-probability sampling was done.

Data Collection: The total sample size was then divided up into four groups based on the rate of smoking exposure.

- Non-exposed i.e. control group (Group 1) n = 30
- SHS exposure of less than 05 cigarette per day (Group 2) n = 30
- SHS exposure of 05 to 10 cigarette per day (Group 3) n = 30
- SHS exposure of more than 10 cigarette per day (Group 4) n = 30

The Ethical Committee's approval was obtained before the study was carried out. In order for their newborns to participate in this research project, pregnant women who met the inclusion criteria were requested for written informed permission.

In order to collect information, a questionnaire was developed. It was self-administered and answered by the subjects in the postnatal ward. Personal data which included name, age and weight at first visit was recorded from the antenatal cards. Height, education and employment status was also noted.

Height was determined using a stadiometer, and weight was determined in kilograms using a baby weighing equipment available in the labor and delivery department. Following information was obtained through questionnaire:

- Demographic data of mother (her age, education)
- Exposure of cigarettes smoked daily (on average)
- Medical history
- Baby examinations like measuring weight, height and head circumference.

A thorough history and examination were conducted, and the Performa was utilized to record the birth weight.

Statistical Analysis: Data was analyzed by using SPSS version 20.0. Data for length, weight, HC and APGAR for fetus was described by using Mean ± SD if normally distributed and Median with inter quartile range otherwise. One way ANOVA followed by Tukey's test were used to compare the groups. P-value ≤ 0.05 was regarded as statistically significant.

RESULTS

Neonatal Birth Weight: 3.31 ± 0.50 was Mean birth weight (kg) in group 1, 3.00 ± 0.28 in group-2, 2.92 ± 0.48 in group-3 and 2.66 ± 0.41 in group-4 (Table 1). Neonatal mean birth weight and their mothers' secondhand smoke exposure were inversely correlated.. Comparison of neonatal birth weight was made by using one way ANOVA which showed statistically significant difference between different study groups as p-value is less than 0.05. Post Hoc Tukey test showed that neonatal birth weight of group 1 was statistically significant as compared to other groups as p-value with

group 2, group3 and group 4 were 0.024, 0.003 and 0.000 respectively.

Table No.1: Showing comparison of neonatal weight (kg) among groups 1, 2, 3 and 4

		Mean	S.D	Min.	Max.	p-value
Weight (kg)	G-1(n=30)	3.31	0.50	2.30	4.40	0.001*
	G-2(n=30)	3.00	0.28	2.40	3.50	
	G-3(n=30)	2.92	0.48	2.00	4.00	
	G-4(n=30)	2.66	0.41	2.00	3.50	
	Total(n=120)	2.97	0.48	2.00	4.40	

* The mean difference is significant at the 0.05 level

Neonatal Head Circumference: Mean head circumference (cm) of neonates in was 34.63 ± 1.63, 34.00 ± 1.41, 33.87 ± 1.71 and 33.03 ± 1.03 in group respectively (Table 2). Mean head circumference of newborns likewise revealed a inverse relationship with mothers' SHS exposure. Comparison of neonatal head circumference was made by using one way ANOVA which showed statistically significant difference between different study groups as p-value is less than 0.05. Post Hoc Tukey test showed that value of neonatal head circumference of group 1 was statistically significant when compared to group 4 as p-value was less than 0.05.

Table No.2: Comparison of Mean neonatal head circumference (cm) in study groups

		Mean	S.D	Min.	Max.	p-value
HC (cm)	G-1(n=30)	34.63	1.630	31.00	39.00	0.001*
	G-2(n=30)	34.00	1.410	31.00	37.00	
	G-3(n=30)	33.87	1.710	31.00	38.00	
	G-4(n=30)	33.03	1.030	31.00	35.00	
	Total(n=120)	33.88	1.562	31.00	39.00	

* The mean difference is significant at the 0.05

Neonatal Length: Neonates in groups 1, 2, 3, and 4 had mean lengths of 49.30 1.70 cm, 48.77 1.47 cm, 49.40 2.12 cm, and 48.53 1.65 cm, respectively. It was observed that newborns belonging to various groups did not differ in length significantly.

Comparison of Apgar score: Mean Apgar score of neonate at 1 minute in group-1 was 6.43 ± 0.935, in group-2 was 6.40 ± 0.674, in group-3 was 6.27 ± 0.944 and in group-4 was 5.57 ± 0.897 (Table 3). It was seen that there was significant difference in Apgar score of neonates at 1st minute belonging to different groups as p-value was less than 0.05.

Table No.3: Comparison of Apgar score in all study groups

		Mean	S.D	Min.	Max.	p-value
APGAR score at 1 minute	G-1(n=30)	6.43	0.935	4.00	8.00	0.001*
	G-2(n=30)	6.40	0.674	5.00	7.00	
	G-3(n=30)	6.27	0.944	5.00	8.00	
	G-4(n=30)	5.57	0.897	5.00	8.00	
	Total(n=120)	6.17	0.928	4.00	8.00	

* The mean difference is significant at the 0.05 level

DISCUSSION

Passive smoking is one of the health risks that is prevalent worldwide and affects many individuals inadvertently. In our society, additional household members besides the smoking spouse expose pregnant women to cigarette smoke. Because we are combined families and usually sharing common sitting area. However, studies proved that SHS exposure is contributed mostly by the husband.

Secondhand smoke exposure during pregnancy affected 31% of Saudi women, who gave birth to babies with lower birth weights and shorter length [12]. A study by Sobh et al.[13] showed that newborns of mothers exposed to passive smoking had a statistically significant low weight at birth. Prince et al., also reported lower mean weight, length and head circumference in the newborns of SHS exposed group [14]. These results are in agreement to the results of our study. Anorexia is caused by either active or passive nicotine exposure of fetus during pregnancy. [15].

Present study revealed that head circumference was significantly different in different groups. There was inverse correlation between head circumference and cotinine level but this correlation was statistically insignificant. Soesanti et al. [16] also stated a lower increment in head circumference in SHS exposure (≥ 23 cigarettes) group. Our study does not find association of length of baby with SHS exposure and cotinine levels.

A recent study in Jordan [17] demonstrated lower first minute APGAR score in accordance with our results which showed statistically significant difference of APGAR score among groups. All these parameters are indicative of the effect of SHS on neonatal growth.

CONCLUSION

Passive or second hand smoking have an effect on APGAR score and neonatal growth parameters.

Recommendations: The general public should be made aware of the risks associated with SHS, and pregnant women in particular should be counseled to avoid both active and passive smoking.

Author's Contribution:

Concept & Design of Study:	Wardah Anwar
Drafting:	Masooma Ahmad, Maria Ilyas
Data Analysis:	Ameena Nasir, Faiza Khan, Huma Jawad
Revisiting Critically:	Wardah Anwar, Masooma Ahmad
Final Approval of version:	Wardah Anwar

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

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Original Article

Nephroprotective Effect of Metformin on Gentamicin Induced Renal Injuries in Rats

Sohail Ahmed[1], Ayesha Aftab[2], Syed Saif Ur Rehman[1], Abida Mateen[1], Muhammad Wajad Munir[1] and Yasir Mumtaz[1]

ABSTRACT

Objective: Metformin, an oral anti-diabetic agent has been studied in the past for its protective effects as an antioxidant. The study was conducted to compare the nephroprotective effects of two doses of metformin in aminoglycoside induced renal injuries in Sprague-Dawley rats.

Study Design: experimental study

Place and Duration of Study: This study was conducted at the Department of Pharmacology, ANMCH, Islamabad, Pakistan in collaboration with the animal house of National Institute of Health (NIH),Islamabad, Pakistan from July 2015 to December 2015.

Materials and Methods: 30 adult male Sprague-Dawley rats weighing 200 ± 50 g, kept under similar conditions for food and temperature, were randomly divided into three groups of Gentamicin treated control (C), Gentamicin & low dose Metformin treated 1 (M1) and Gentamicin & high dose Metformin treated 2 (M2). Renal failure was induced by injecting gentamicin (80mg/kg/day) intraperitoneally for eight days followed by oral metformin for 28 days. Sampling for serum creatinine, 24 hour urinary volume and 24 hour urinary proteins was done at day 0, 14 and 28.

Results: It was found that metformin administration in gentamicin induced renal failure results in significantly increased urinary output, reduced creatinine levels along with significantly decreased urinary proteins in M2 group as compared to M1 group. While in group C, all parameters of renal failure were increased.

Conclusion: Metformin in a dose of 150mg/kg prevents aminoglycoside-induced renal injuries in rats.

Key Words: Metformin, Gentamicin, Nephrotoxicity, Renal injuries, Nephroprotective effect

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INTRODUCTION

Kidneys play a vital role to maintain homeostasis. Renal injuries secondary to medications are not uncommon resulting in varying degree of damage from minor injury to complete renal failure. The extent of renal damage depends upon the dose and the duration of exposure to these drugs or substances[1, 2].

Gentamicin is an aminoglycoside derived from actinomycete Micromonospora .Therapeutically it is used for uncomplicated infections of lower urinary tract. It is often combined with β-lactam antibiotics for better penetration in the cells to treat hospital acquired pneumonias and multi drug resistant infections[3].

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In order to develop acute renal failure in animals for research purposes ,several animal models have been developed by administering higher doses of drugs such as glycerol (single dose10mg/kg IM) [4], gentamicin (80 mg/kg per day IP) for 7 days [5],non-steroidal anti-inflammatory drugs (NSAIDs) (single dose 3g/Kg PO) [6,7].

Aminoglycosides' nephrotoxicity (including gentamicin & others) usually manifest as acute renal failure with some abnormalities on urinalysis[8].The glomerular filtration rate is reduced and proteins and hyaline and granular casts start appearing in the urine. Serum creatinine levels start rising. Inhibition of enzymes which further bring changes in the functions of mitochondria and ribosomes, leading to decrease formation of membrane derived prostaglandins, inositol phosphate and diacylglycerols is postulated mechanism of nephrotoxicity with gentamicin[9].

Metformin is usually used as a first line drug in type-2 diabetes mellitus. Metformin increases the insulin sensitivity and reduces glucose production by the liver as a result the circulating insulin levels are reduced[10]. Metformin reduces the oxidative stress and cell death by a mechanism which is dependent on a special type of pore opening in mitochondria. This pore is known as mitochondrial permeability transition pore

(PTP).Metformin also reduces the production of reactive oxygen species (ROS) in endothelial cells by inhibition of protein kinase C. Metformin inhibits hepatic glucose formation by increasing the small heterodimer partner (SHP) gene expression with the help of adenosine monophosphate-activated protein kinase (AMPK)-dependent pathway[11].The rationale of this study was to investigate protective effect of metformin as an antioxidant with two different doses i.e., 75 mg/kg and 150mg/kg, given by gavage tube to the rats in whom renal failure was induced by gentamicin.

MATERIALS AND METHODS

This experimental study was conducted at Department of Pharmacology, ANMCH, Islamabad, Pakistan in collaboration with animal house of National Institute of Health (NIH), Islamabad, Pakistan from July 2015 to December 2015. Healthy male Albino rats (Sprague-Dawley) weighing 200 ± 50 grams, were purchased from National Institute of Health Islamabad and kept at animal house of the same institute. Animals were kept in cages of 2x3 feet size at standard conditions. Animals (N=30) were divided into 03 groups of 10 rats in each group.

Control Group (Group C) was given gentamicin 80mg/kg[5] intraperitoneally from 0- 8 days along with distilled water (01 ml) by gavage from 0- 28 days as single morning dose.

Experimental Group I (Group M1) was given gentamicin 80mg/kg intraperitoneally from 0-8 days along with metformin (75mg/kg/day) dissolved in 01ml distilled water by gavage from 0-28 days as single morning dose.

Experimental Group II (Group M2) was given gentamicin 80mg/kg intraperitoneally from 0-8 days along with metformin (150mg/kg/day)[12] dissolved in 01ml distilled water by gavage from 0- 28 days as single morning dose.

Rats were placed in individual metabolic cages 24 hour prior to collection of urine. 24 hour urine samples were collected in glass flasks on day 0, 14 and 28 of the study .Urine volume was measured with the help of disposable syringes .24 hour urinary proteins and serum creatinine were measured using reagent kit. 1 ml of blood was taken by direct cardiac puncture on day 0, 14 and 28 after anesthetizing the animal with Chloroform. Data was analyzed by using SPSS (Version 19.0). Mean±SD values were calculated for each group. To calculate the descriptive statistics, one way ANOVA (Tukey's test) was applied. P-value ≤ 0.05 was considered as significant.

RESULTS

Mean ± SD values of serum creatinine of Sprague-Dawley rats at day 0, 14 and 28 of the experiment are shown in table 1.

Table No.1: Mean ± SD of values of Serum Creatinine (mg/dL) of Sprague-Dawley rats at day 0, 14 and 28 of experiment. (N=30)

Groups	Dose of drugs	Serum Creatinine (mg/dl)		
		Sampling Day 0	Sampling Day 14	Sampling Day 28
Control group (c)	Gentamicin (80mg/kg)	0.68 ± 0.20	1.82 ± 0.33	3.46 ± 1.35
Treated group 1 (m1)	Gentamicin (80mg/kg) + metformin (75mg/kg)	0.64 ± 0.15	1.72 ± 0.49	1.50 ± 0.41
Treated group 2 (m2)	Gentamicin (80mg/kg) + metformin (150mg/kg)	0.64 ± 0.08	1.78 ± 0.33	0.98 ± 0.19

Results of M2 group indicate that serum creatinine value was increased at 14th day as compared to 0 day value of this group but it was insignificantly lower than the 14th day value of the control group. Also when compared with the same day value of the M1 group, the difference again was statistically insignificant ($p>0.05$). The increasing trend was reversed at day 28 of the experiment where the value was found to be 0.98 ± 0.19 mg/dL showing a highly significant decrease ($p<0.005$) in comparison to the same day value of control group and reversing the serum creatinine levels very close to the normal values at day 0. When serum creatinine value of M2 group was compared with that of M1 group at day 28 of the experiment, they showed statistically significant difference ($p<0.05$) confirming that metformin in double dose (150 mg/Kg body weight) has more pronounced nephroprotective effect.

Table No.2: Mean ± SD of values of 24 hour urinary volume (mL) of Sprague-Dawley rats at day 0, 14 and 28 of experiment. (N=30)

Groups	Dose of Drugs	24 Hour Urinary Volume (ml)		
		Sampling Day 0	Sampling Day 14	Sampling Day 28
Control group (c)	Gentamicin (80mg/kg)	3.43 ± 0.68	1.69 ± 0.24	1.10 ± 0.40
Treated group 1 (m1)	Gentamicin (80mg/kg)+ metformin (75mg/kg)	3.93 ± 0.61	2.57 ± 0.76*	2.01 ± 1.10
Treated group 2 (m2)	Gentamicin (80mg/kg)+ metformin (150mg/kg)	3.65 ± 0.84	2.24 ± 0.47	3.27 ± 0.61

Table-2 shows that in M2 group the urinary volume was decreased at day 14 as compared to day 0 value of this group but it was significantly higher than the 14th day value of control group. The value increased at day 28 to 3.27±0.61 mL showing a highly significant increase in urine output in comparison to the same day value of control group. The value at day 28 in M2 group was also close to day 0 values.

Table No.3: Mean ± SD of values of 24 hour proteins (mg/dL) of Sprague-Dawley rats at day 0, 14 and 28 of experiment. (N=30)

Groups	Dose of Drugs	24 Hour Urinary Proteins (mg/dl)		
		Sampling Day 0	Sampling Day 14	Sampling Day 28
Control group (c)	Gentamicin (80mg/kg)	11.84 ± 2.24	60.06 ± 15.48	68.50 ± 15.16
Treated group 1 (m1)	Gentamicin (80mg/kg)+ metformin (75mg/kg)	10.25 ± 1.74	35.23 ± 5.28**	30.60 ± 11.18
Treated group 2 (m2)	Gentamicin (80mg/kg)+ metformin (150mg/kg)	11.28 ± 2.40	19.79 ± 4.02**†	15.05 ± 3.33

Table-3 shows that at day 28 of the experiment, the 24 hour urinary proteins value was found to be 15.05±3.33 mg/dL showing a highly significant decrease ($p<0.005$) in comparison to the same day value of control group and reversing the 24 hour urinary proteins level very close to the normal values at day 0. When 24 hour urinary protein value of M2 group was compared with that of M1 group at day 28 of the experiment, they showed statistically significant difference ($p< 0.05$) confirming that metformin in a dose of 150mg/Kg body weight has more pronounced nephroprotective effect in gentamicin induced renal injuries.

DISCUSSION

Many clinically used drugs adversely effects renal system.[1,2] Nephrotoxicity with Gentamicin results in acute renal failure and manifests as abnormalities of urinalysis.[8] The powerful antioxidant effect of Metformin acts by diminishing oxidative stress and inhibit the aminoglycoside mediated acute renal failure by a mitochondrial dependent pathway .It can also prevent gentamicin induced renal injuries in rats[13].

In previous studies, efforts have been done to prevent renal damage by introducing Metform orally mixed in drinking water making it difficult to identify the exact dose of drug the animal has consumed as the gentamicin induced toxicity causes the rats to become inactive or anorexic[5]. So this experiment was designed to study the effects of two different doses of metformin i.e., 75 mg/kg and 150mg/kg, given by gavage tube to the rats in whom renal failure was induced by gentamicin.

Udupa and his colleague evaluated the effect of gentamicin in rats using urinary biomarkers and noticed significant change in serum BUN, creatinine level and urinary proteins which are also observed in our study. They used two doses of gentamicin 30 and 100mg/Kg/day where as we administered 80mg/Kg dose of gentamicin [14].

The rate of reduction in urinary volume with gentamicin toxicity in our study was similar to the findings of Morales et al .Their study proved that metformin prevent gentamicin induced renal toxicity by mitochondrial dependent pathway which restores its functions and also normalize oxidative stress[15] .In our study, urinary volume showed increasing trend in both metformin treated groups, especially in M2 group, at day 28 of experiment, 24 hour urinary volume of rats was close to the base line levels seen at day 0 .This proves the renoprotective effect of Metformin in our study which is also explained by Frid with his colleagues. They mentioned in their study that metformin increases the total antioxidant status (TAS) along with the normalization of lipid peroxidation and prevent the renal damage caused by oxidative stress[16]. The reduction in 24 hour urinary proteins, serum creatinine induced by gentamicin with the larger doses of metformin in our study is supported by literature.[17]. Metformin also reduces the production of reactive oxygen species (ROS) in endothelial cells by modulation of p38 mitogen–activated protein kinase expression which further contributes to its renoprotective effect.[18]

CONCLUSION

Based on the results of our study it was concluded that metformin at a dose of 150mg/kg produced a nephroprotective effect in gentamicin induced renal injuries in Sprague-Dawley rats.

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

Incidence of Diastolic Dysfunction in Poorly Controlled Type 2 Diabetes Mellitus without Hypertension and Coronary Artery Disease

Syed Saif Ur Rehman[1], Safdar Hussain[1], Abida Mateen[1], Ghulam Mujtaba Nasir[3] and Ayesha Basharat[2]

ABSTRACT

Objective: The purpose of this study was to study the incidence of left ventricular diastolic dysfunction in type 2 diabetes mellitus patients without hypertension and coronary artery disease and its relation to duration of diabetes mellitus.

Study Design: Descriptive case series study

Place and Duration of Study: This study was conducted at the Department of Medicine of Al- Nafees Medical College & Hospital, Islamabad from April, 2019 to September, 2019.

Materials and Methods: Patients with diabetes mellitus between age of 40 -70 years with poor glycemic control having HbA1c >9% and without history of hypertension, coronary artery disease, heart failure, or valvular heart disease were recruited. The study was conducted after the approval from hospital ethical committee. All the patients were educated and an informed written consent was taken. Exercise tolerance test and Resting ECG were done on every subject to exclude ischemia and echocardiography was performed to assess left ventricular.

Results: A total of 60 poorly controlled diabetic type 2 patients meeting inclusion and exclusion criteria of this study were registered. Of these 60 study cases, 26(43.33%) were male and 34(56.66%) were female. Diastolic Dysfunction was found to be present in 37(61.66%) while it was found to be absent in 23(38.33%) of poorly controlled diabetic (type 2) patients without coronary artery disease as well as hypertension.

Conclusion: Diastolic Dysfunction is very common, over 60%, in poorly controlled type 2 diabetic patients and this finding correlates with HbA1c levels and duration of diabetes mellitus and does not correlate with age and gender.

Key Words: Diabetic Cardiomyopathy (DCM), Coronary Artery Disease (CAD), Left ventricle diastolic dysfunction (LVDF), Hypertension (HTN), Diabetes Mellitus (Type 2)

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INTRODUCTION

There are almost 537 million adults (20-79 years) are living with diabetes according to The International Diabetes Federation (IDF).[1] The leading universal health crisis of twenty-first century is T2DM, and there is rapid increase in its prevalence and incidence especially in adults. [2]

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The major cardiovascular disease related with T2DM are coronary artery disease, ischemic heart disease, heart failure , stroke, and peripheral artery disease, and these complications lead to death in at least 50% of patients with T2DM.[2] Diabetic cardiomyopathy refers to cardiac dysfunction in diabetic people who do not have ischemic heart disease, valvular heart disease, or hypertension.[3]

Autonomic nervous system dysfunction, microangiopathy, and abnormal cellular calcium transport are all factors that cause diabetic cardiomyopathy. The stiffening of the ventricular wall is caused by structural changes in intracellular proteins in the myocardium and the buildup of collagens. Thirty percent to fifty percent of all heart failure hospitalizations are due to diastolic dysfunction.[4]

Heart failure rate in the old age have risen dramatically in recent years. It is believed that diabetes is a significant independent risk factor for the onset of diastolic dysfunction. Diastolic dysfunction of the left ventricle may be the earliest sign of diabetic cardiomyopathy, highlighting the need for regular

monitoring of blood sugar levels in people with diabetes. There is evidence linking poorly managed diabetes to diastolic dysfunction.[5] Clinical and pathological studies have demonstrated that even in the absence of large-vessel atherosclerosis, abnormalities of left ventricular function, cardiomegaly and failure can occur. This may be related to microangiopathy of the coronary circulation. Up to half of individuals with diabetes mellitus in the community develop heart failure due to diastolic dysfunction despite LV adequate ejection fraction (EF), as demonstrated by several epidemiological surveys.[6]

In the Framingham Heart Study, diabetes mellitus was considered an independent risk factor for heart failure. [7] Left ventricular diastolic dysfunction (LVDD) is considered the first manifestation of cardiac remodeling in diabetic patients by many researchers. The only 1% increase in HbA1c level is related with 8% increased risk of HF, independently of other cardiovascular risks. Moreover, quality of life and the therapeutic effect of hypoglycaemic agents is also worsen by heart failure. There should be early detection and management of myocardial dysfunction in the diabetic patients before the development of overt heart failure.[8]

In this study, we investigated the incidence LV diastolic dysfunction in poorly controlled type 2 diabetes mellitus patients without hypertension and coronary artery disease.

MATERIALS AND METHODS

The descriptive case series study was conducted at outpatient department, Al-Nafees Medical College & Hospital, Islamabad from 1st April 2019 – 30th September 2019 after approval from hospital ethical committee. The sample size was calculated (n=60) with confidence interval 95%, estimated true proportion 50% by Epitools software.

Patients with evidence of diastolic dysfunction according to criteria of American society of echocardiography and European association of cardiovascular imaging were selected through echocardiography by mitral E/A ratio, average E/e/ ratio and LV relaxation [10] after fulfilling the inclusion criteria as poorly controlled Type 2 diabetic patients without hypertension and coronary artery disease while excluding patients having valvular heart disease, congestive heart failure, hypertension, connective tissue disease, known coronary artery disease, myocardial infarction (recent or previous), renal and thyroid disease.

Complete history, full clinical examination and relevant laboratory and imaging tests done on every patient. The history highlights complications, ischemic heart disease, and duration of diabetes mellitus, drug history, heart failure and hypertension. The HbA1c level is used to diagnose diabetes mellitus.

After collecting the data, it was entered in a specially designed performa. Data was analyzed by the Statistical Package for Social Sciences (SPSS) version 23. Age, gender, the length of diabetes, hemoglobin A1c, and the Ejection fraction on Doppler echocardiography with intact diastolic function and with diastolic dysfunction are the factors. Information presented as Mean±SD. The differences between participant groups evaluated using analysis of variance. Chi square test was used to compare the dysfunction of the left ventricle during diastole. A 0.05 p-value is regarded as significant. The degree of relationship between two variables is assessed using Pearson's correlation analysis.

RESULTS

A total of 60 type 2 diabetes individuals who matched the study's inclusion and exclusion criteria were registered. 26 (43.4%) men and 34 (56.7%) women made up 60 study cases (Table-1). The study's sample's average age was 55. (minimum age was 40 years while maximum was 70 years). The majority of instances, according to the study's findings, were between the ages of 45 and 65. Diastolic dysfunction was found in 37 (61.7%) of the studied cases whereas it wasn't in 23 (38.4%) as shown in Figure 1. The results of diastolic dysfunction with mitral E/A ratio and average E/e/ ratio with LV relaxation are shown in Table 2 and 3. The patients were also asked how long they had diabetes, on average in years (the lowest was 5 years and the highest was >15 years) as shown in Table 4.

Table No.1: Frequency of Gender wise distribution in patients with poorly controlled Type 2 Diabetes Mellitus. (n=60)

MALE/FEMALE				
Gender	Frequency	Percent	Valid Percent	Cumulative Percent
Male	26	43.3	43.3	43.3
Female	34	56.7	56.7	100.0
Total	60	100.0	100.0	

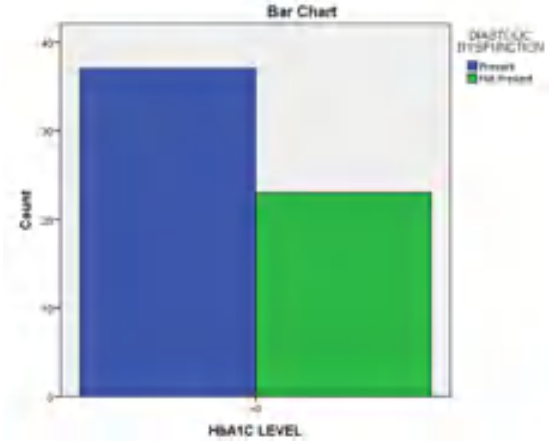

Figure No.1: Diastolic Dysfunction Frequency in poorly controlled Type 2 Diabetes Mellitus with HbA1C level (n=60)

Table No.2: Diastolic Dysfunction by Mitral E/A Ratio with HbA1C level in poorly controlled Type 2 Diabetic patients with Diastolic Dysfunction. (n=60)

Count		Mitral e/a ratio		Total
		0.8	0.8-2	
Diastolic dysfunction	Present	0	37	37
	Not present	23	0	23
Total		23	37	60

Table No.3: Diastolic Dysfunction by Average E/e/ Ratio with HbA1C level in poorly controlled Type 2 Diabetic patients with Diastolic Dysfunction. (n=60)

Count		Average e/e/ ratio with Lv relaxation		Total
		<10 with impaired lv relaxation	>10 with impaired lv relaxation	
Diastolic dysfunction	Present	3	34	37
	Not present	0	23	23
Total		3	57	60

Table No.4: Frequency of Diastolic Dysfunction in poorly controlled Type 2 Diabetes Mellitus with Duration of Diabetes. (n=60)

Count		Diastolic dysfunction		Total
		Present	Not present	
Duration of diabetes	5-10 years	5	11	16
	10-15 years	14	5	19
	>15 years	18	7	25
Total		37	23	60

Table No.5: Chi-Square Test

	Value	df	Asymp. Sig. (2-sided)
Likelihood Ratio	8.458	2	.015
Pearson Chi-Square	8.552	2	.014
N of Valid Cases	60		

DISCUSSION

Diastolic dysfunction is a condition that is characterized by abnormal left ventricular relaxation and filling diastolic defect resulted due to ventricular wall stiffness. Patients with diabetes who have poorer glycemic control are more likely to experience significant diastolic dysfunction. Almost 30% of individuals with T2DM manifest impaired left ventricular diastolic function (LVDF) without demonstrated coronary artery disease (CAD) or hypertension. The E/A ratio, by both imaging modalities, was significantly lower in Type 2 diabetes mellitus (T2DM) vs normal glucose tolerance (NGT).[10] With statistically significant differences (p 0.05), diastolic dysfunction was discovered in 61.7% of the patients in our research who had HbA1c levels higher than 9%. These findings provide credence to the idea of a particular subclinical diabetic cardiomyopathy that may be influenced by glycemic management.[4] HbA1c level has a detrimental impact on the myocardium with left ventricular (LV) diastolic dysfunction.[11]

HbA1c is a good reliable marker for chronic glycemia and is associated with the long-term risk of diabetes complications, so it is currently considered the investigation of choice for monitoring and management of chronic cases of diabetes.[12] HbA1c level and duration of diabetes mellitus show a significant statistical difference, but not age or gender. Even an increase of 1% in HbA1c concentration was associated with (about 30% increase in all-cause mortality and 40% increase in cardiovascular or ischemic heart disease mortality, among individuals with diabetes.[13] These findings match the published data quite well.[14]

Similar to our work, people with diabetes frequently experience asymptomatic diastolic dysfunction. The severity of this dysfunction is connected with glycemic management and length of diabetes mellitus. Our investigation demonstrated that age and gender had no bearing on the occurrence of diastolic dysfunction. Similar findings were also published by Wojciech et al., who found that there were other causes for diabetic cardiomyopathy beyond smoking history, gender, age, blood pressure, and body mass index. [15]

It is also obvious that, diastolic dysfunction correlates well with diabetes duration and HbA1c. Diastolic dysfunction as being the cause of diabetic cardiomyopathy may be very helpful as the predictor of cardiac failure with preserved ejection fraction and medium to long-term mortality. Currently, the management options for a diastolic heart failure with normal systolic function are very limited.[16]

According to my research, diabetic individuals who have poor glycemic control are more likely to experience diastolic dysfunction.

CONCLUSION

Over 60% of poorly managed type 2 diabetic patients experience diastolic dysfunction, and this finding is correlated with HbA1c levels and the duration of diabetes mellitus but not with age or gender.

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

Comparison of Clinical Improvement with VS without Remdesivir Treatment in Hospitalized Patients with COVID-19

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ABSTRACT

Objective: To determine the role of remdesivir administered for treatment of hospitalized coronavirus disease 2019 (COVID-19) in terms of rapid clinical improvements.

Study Design: Retrospective comparative study

Place and Duration of Study: This study was conducted at the Department of Pulmonology and Covid-19 department, Recep Tayyip Erdogan Hospital Muzaffargarh from April 2020 to December 2021.

Materials and Methods: A total of 923 patients were enrolled in study. Clinical outcomes like hospital stay, ICU stay, mechanical ventilation time, discharge from hospital and duration of death after admission and mortality rate of patients treated with remdesivir and who were treated without remdesivir was taken from hospital record. Data was analyzed by using SPSS version 24.

Results: The mean length of stay of remdesivir patients was 8.19±5.71 days with 95% C.I (7.68-8.70) and non-remdesivir patients was 6.07±5.66 days with 95% C.I (5.54-6.60), and the difference was statistically significant, (p=0.000). The most common diagnosed complication in remdesivir patients was diabetes mellitus 7.6% and the second most common complication was sepsis 6.0%. Among total 14.8% of remdesivir patients needed to admit in ICU versus 14.9% with (p=0.980). Distribution of mortality was 39.5% of remdesivir patients versus non-remdesivir 26.3%.

Conclusion: Remdesivir is associated with poor clinical outcomes, mean hospital stay, ICU stay and death rate is higher in patients treated with remdesivir, as compared to those treated without remdesivir. Final outcome regarding discharge of patients is also better in without remdesivir group.

Key Words: Clinical outcomes, COVID-19, Death, Hospitalization, Remdesivir

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INTRODUCTION

Novel coronavirus, severe acute respiratory syndrome, was first identified in December 2019 as the cause of a respiratory disease designated coronavirus disease 2019, or Covid-19. Many therapeutic agents have been evaluated for the treatment of Covid-19, but no antiviral agents have proved to be efficacious[1].

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SARS-CoV-19 transmitted through respiratory droplets or direct contact from human to human, and has a median incubation period of 5.1 days and a basic reproduction number of 2.24–3.58[2,3]. The ongoing pandemic of severe acute respiratory syndrome coronavirus infections has led to more than 262,736,568cases and 5,229,500 deaths globally as of Nov, 2021[4,5]. Due to severity and expected high CFR of the pneumonia caused by SARS-CoV-19, it is important to find an effective drug treatment because supportive care and oxygen supplementation is not always enough[6].

Remdesivir, an inhibitor of the viral RNA-dependent, RNA polymerase was identified early as a promising therapeutic candidate for Covid-19treatment. Remdesivir is a monophosphoramidate pro drug of an adenosine analogue that has a broad antiviral spectrum including filo-viruses, paramyxo-viruses, pneumo-viruses, and corona viruses [7,8].

In a trial conducted in 2020 by WHO showed that remdesivir, hydroxychloroquine, lopinavir, and

interferon regimens had little or no effect on hospitalized patients with Covid-19, as indicated by overall mortality, initiation of ventilation, and duration of hospital stay. The UK-based RECOVERY (Randomized Evaluation of COVID-19 Therapy) trial showed that dexamethasone administration compared with placebo led to a significant reduction in mortality rate (22.9% vs 25.7%)[9]. Trials examining the benefit of different corticosteroids were stopped early after the results of RECOVERY led to corticosteroids being considered the standard of care. Whether there is additional benefit from using both remdesivir and corticosteroids requires further evaluation[10].

MATERIALS AND METHODS

It is a retrospective cohort study conducted at Department of Pulmonology and Covid-19 department, Recep Tayyip Erdogan Hospital Muzaffargarh. Non probability consecutive sampling type of sampling technique was used. Study was carried out after ethical approval from hospital ethical board. The inclusion criteria for this study was as follows; Patients with COVID 19 pneumonia with severe clinical status on day 1, Patients who received other medical standard care according to institutional guidelines, Patients with previously chronic lung disease like COPD, asthma and ILD evaluated on history and medical records, Both genders, 18 years to 80 years of age. The exclusion criteria was as follows; Patients who required ICU admission or mechanical ventilation on day 1, patients with COVID 19 pneumonia with mild to moderate disease, patients with ALT levels >5 times.

Previous data of COVID 19 patients from April 2020 to December 2021 was evaluated according to inclusion and exclusion criteria. Demographic variables like age, gender, BMI and previous clinical status like diabetes mellitus, hypertension, ischemic heart disease, asthma and chronic obstructive pulmonary disease was recorded on Performa. On day of presentation clinical severity of each patient was noted. Two groups were made for remdesivir and non-remdesivir. Every patient was followed for the primary and secondary outcome like length of hospital stay, ICU admission, recovery; complications of disease and death were recorded.

Data was analysed by SPSS 24. Quantitative variables like age BMI, length of hospital stay, was statistically analysed in mean and standard deviation. Qualitative variables like gender, presence of comorbidity, clinical severity on admission, event of ICU admission, complications of disease and mortality was analysed in percentage and frequency. Chi-square test was applied to check the significance. Length Of hospital stay, ICU admission, recovery, complications of disease and death was analysed in mean and standard deviation and independent t test was applied to check its significance. P value $\leq$0.05 was taken as significant.

RESULTS

Over the study period, 923 patients were admitted in Recep Tayyip Erdogan Hospital Muzaffargarh in Covid-19 ward. Out of these, 486 (52.7%) treated with remdesivir and 437 (47.3%) treated without remdesivir. The mean age of the remdesivir patients was greater than non-remdesivir patients and the majority of both the groups between 51-60 years. The mean CRP in non-remdesivir patients was greater than that of remdesivir patients, (p=0.040), but the same median was to be found. Most of patients of remdesivir and non-remdesivir patients were non-smokers, 464 (95.5%) and 404 (92.4%), respectively. Further, it was seen that very severe clinical stage of disease, 185 (38.1%), was statistically more common in remdesivir patients and least common, 115 (26.3%), in non-remdesivir patients.(Table. I).

Table No.1: Demographic characteristics of the patients

Variable	Hospital Treatment Remdesivir		P-value
	Yes, N (%)	No, N (%)	
Gender			
Male	268 (55.1)	264 (60.4)	0.106
Female	218 (44.9)	173 (39.6)	
Age			
Mean±S.D	56.63±13.25	54.37±16.77	0.023
<30 years	12 (2.5)	41 (9.4)	0.000
30-40 years	44 (9.1)	58 (13.3)	
41-50 years	80 (16.5)	74 (16.9)	
51-60 years	146 (30.0)	88 (20.1)	
61-70 years	129 (26.5)	88 (20.1)	
71-80 years	60 (12.3)	71 (16.2)	
>80 years	15 (3.1)	17 (3.9)	
CRP on admission			
Mean±S.D	37.41±46.17	44.10±52.91	0.040
Median± I.Q.R	32.00±51	32.00±64	
Smoking status			
Current smoker	5 (1.0)	13 (3.0)	0.069
Ex-smoker	17 (3.5)	20 (4.6)	
Non smoker	464 (95.5)	404 (92.4)	
Comorbidity			
Asthma	10 (2.1)	8 (1.8)	0.016
COPD	7 (1.4)	16 (3.7)	
Clinical stage of disease			
Severe	238 (49.0)	201 (46.0)	0.000
Very Severe	185 (38.1)*	115 (26.3)*	
P≤0.05 considered as significant, * standardized residual>1.96			

The mean length of stay of remdesivir patients was 8.19±5.71 days with 95% C.I (7.68-8.70) and non-remdesivir patients was 6.07±5.66 days with 95% C.I

(5.54-6.60), and the difference was statistically significant, (p=0.000).(Figure. I). The most common diagnosed complication in remdesivir patients was diabetes mellitus 37 (7.6%) and the second most common complication was sepsis 29 (6.0%). Only 72 (14.8%) of remdesivir patients needed to admit in ICU versus 65 (14.9%) with (p=0.980). Distribution of ICU stay was shown in figure. 2. 192 (39.5%) of remdesivir patients died versus non-remdesivir 115 (26.3%) (Table. 2).

Table No.2: Outcome representation of the patients

Outcome	Hospital Treatment Remdesivir		P-value
	Yes, N (%)	No, N (%)	
Length of hospital stay			
Mean±S.D	8.19±5.71	6.07±5.66	0.000
95% C.I	7.68 to 8.70	5.54 to 6.60	---
Median±I.Q.R	7.00±5.00	4.00±5.00	---
ICU admission			
Yes	72 (14.8)	65 (14.9)	0.980
No	414 (85.2)	372 (85.1)	
Length of ICU stay			
Mean±S.D	9.27±6.38	8.34±6.41	0.403
95% C.I	7.75 to 10.79	6.74 to 9.94	---
Median ± I.Q.R	7.50±9.00	7.00±9.00	---
Final outcome			
Death	192 (39.5)*	115 (26.3)	0.000
Discharge at room air	244 (50.2)	267 (61.1)	

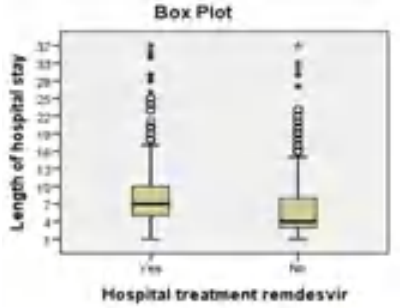

Figure No.1: Hospital treatment remdesvir with length of hospital stay.

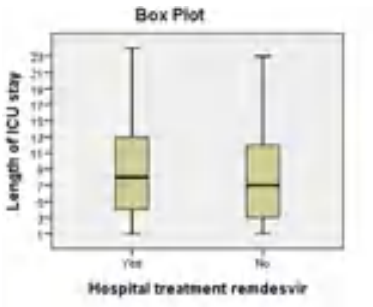

Figure No.2: Hospital treatment remdesvir with length of ICU stay.

DISCUSSION

In this comparative study 923 patients were admitted in COVID-19 ward in 1st 2days. Mean age of the remdesivir patients was greater than non-remdesivir patients and the majority of both the groups between 51-60 years. Male gender is dominant in our study. The mean CRP in non-remdesivir patients was greater than that of remdesivir patients, (p=0.040).

A study was conducted by Abd-Elsalam et al[11] in 2022 on 200 patients, remdesivir was given in 100 patients and 100 were treated without remdesivir. Mean hospital stay was higher in remdesivir group 12.37 ± 8.96 as compare to without remdesivir 16.72 ± 5.78, but mortality was found higher in remdesivir group 9% vs 7% respectively. It was reported in this study that mean CRP level is also associated with mortality. A study was conducted by Garibaldi et al[12] on 2483 COVID-19 patients, among them 342 patients were treated with remdesivir having median age of 60 years (IQR-46-69 years) and 55.3% were male. Mortality rate was 7.7% with 22 days duration.

In our study most common comorbidities were smoking, COPD. A study was conducted by Mozaffari et al[13] and observed similar findings as Diabetes, COPD, Obesity, cardiovascular disease, renal disease are common co morbidities. This study also favors use of remdesivir in COVID-19 patients as use of remdesvir improves the clinical outcomes and enhances the hospital stay. Another study by Wang et al[14] hastening recovery and reduction in mortality rate was observed but at day 29 there was not a significant improvement noted.

In our study Distribution of ICU stay was prolonged in remdesivir group. Among total 39.5% of remdesivir patients died versus non-remdesivir 26.3%. Further, 6.4% and 4.6% of remdesivir and non-remdesivir patient improved and discharged to home, respectively. In a study by Consortium et al[15] on benefits of remdesivir in mortality and recovery time and reported that a positive role in both outcomes. Another study by Kaka et al[16] showed positive role of remdesivir in mortality rate reduction and duration of death enhancement when compared with treatment without remdesivir patients.

Another randomized trial was conducted by Olender et al[17] and found 62% decrease in death rate within 14 days when compared with standard of care, 74.4% of remdesivir patients recovered within 14 days and in non remdesivir group 59% patients recovered and death rate was 7.6% and 12.5% respectively. A study by Elsawah et al[18] also reported similar findings that in patients with HFO requirements at baseline remdesivir reduced the risk of mortality at 14 days but at 28 days its role in mortality reduction and recovery benefits is not well documented.

In our study we used remdesivir for 10 days and at the end of study 50.2% patients discharged at room air mortality was 39.5%. A study was conducted by Goldman et al[19] on 397 patients in 2020 and reported that 52% patients were discharged from hospital and mortality was 11% with 10 days treatment. Another similar study was conducted by Spinner et al[20] on 584 patients and compared standard care treatment with remdesivir for 5 day and 10 days, at 28 day of admission death was observed in 2% of patients in patients with 10 days treatment plan.

A study by Terks et al[21] was completed in 2022 on 137 patients data form hospital record, remdesivir was given for 5 to 10 days and observed improvement in clinical outcomes in 75.9% patients and mortality was observed in 24.1% of patients. Mortality was higher in severe/critically diseased patients 34.8% than moderately ill patients 5.9%.

CONCLUSION

Remdesivir is associated with poor clinical outcomes, mean hospital stay, ICU stay and death rate is higher in patients treated with remdesivir, as compared to those treated without remdesivir. Final outcome regarding discharge of patients is also better in without remdesivir group.

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Original Article

Association Between Quality of Life and Severity of Disease in Newly Diagnosed Cases of Squamous Cell Carcinoma of Oral Cavity

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ABSTRACT

Objective: To evaluate the association between severity of squamous cell carcinoma and quality of life in patients
Study Design: Descriptive cross sectional study
Place and Duration of Study: This study was conducted at the Department of Oral & Maxillofacial Surgery, Jinnah Postgraduate Medical Centre, Karachi from July 2021 to January 2022.
Materials and Methods: Total of 161 Patients of squamous cell carcinoma diagnosed on biopsy samples were enrolled in study. Main variables of study were severity of disease (stage I, II, III, IV) and quality of life score (FACT H & N). SPSS Version 23 was used for data analysis. Variables were presented in form of mean SD and frequency percentages.
Results: One hundred sixty one patients were enrolled, in our study. The average age of the patients was 32.05±4.71 years. The average score for physical, social, emotional and functional well-being were shown in table. II. Further, the mean score for additional concerns, trail outcome index, FACT-G and FACT H&N was 25.02±4.76, 64.96±7.21, 86.81±13.01 and 112.92±23.84, respectively.
Conclusion: There is a strong association between quality of life (FACT H & N) score and severity of squamous cell carcinoma. Patients in advance stage of cancer (stage III and IV) were observed with more decrement in quality of life than early stages (I and II).
Key Words: Squamous cell carcinoma, Severity of disease, Quality of life, FACT H & N.

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INTRODUCTION

In head and neck region, Oral squamous cell carcinoma (OSCC) is one of the most common malignancies[1]. It is the 16th most common cancer in the world. According to a survey conducted in 2018, Pakistan is on number 2 in the list of highest rate of cancer of lip and oral cavity with the rate of 12.2/100,000[2].Cancer of the lip and oral cavity is the 2nd most common cancer in Pakistan and is the most common cancer in males.

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Total number of new cases in 2018 according to Globocan 2018 is 18881 which is 10.9% of all cancers in Pakistan[3].
90% malignancies of oral cavity are OSCC and sites can includes cancer of lips, cheeks, tongue, and floor of the mouth, hard palate, soft palate oropharynx, gingival and alveolar mucosa and tonsils[4]. Squamous cell carcinoma can also metastasize and involve other tissues or lymph nodes. The incidence rate that is estimated is about 48.1 per 100,000 populations per year. Progresses in a manner that normal mucosa first becomes dysplastic and then transformation from dysplasia to carcinoma in situ and lastly to advanced stage cancer. Major causal factors include consumption of alcohol, smoking, Areca nut containing products like betel quid (paan), gutka, paan masala, human papilloma virus 16 & 18, Epstein Barr virus (EBV) and betel nut chewing[5].
Doctors tend to underestimate the level of distress experienced by patients diagnosed with oral malignancies, result of which is inadequate treatment of these disorders. Proper treatment and evaluation of mental pain and agony is not only clinically effective but also cost effective[6].

Therefore early observation and management of psychological distress in patients with oral cancer should be of prime concern[7]. Decreased psycho-social wellbeing state of patients with this type of cancer can have influence on survival of patient and nutritional condition of the patient after he has been treated[8].

Better quality of life in patients is increasingly important in patients especially in oncology patients because of reduced recovery rate and inadequate expectancy of life survival[9]. For squamous cell carcinoma patients the main domain is achievement of quality of life with normal physical, psychological and social wellbeing. Main functional achievements are swallowing, breathing and hearing. Lack of social interaction is also a contributing factor in human life[10].

With this study we are aiming to identify the association between severity of disease and quality of life of squamous cell carcinoma patients which causing increased mental tribulation in patients with this type of cancer involving the oral cavity and trying to rectify them in order to increase survival rates and improve quality of life of patients suffering from oral squamous cell carcinoma.

MATERIALS AND METHODS

After seeking approval from the ethical committee of Jinnah Postgraduate Medical Centre Karachi and study period started from 15th July 2021 to January 2022. All the patients meeting the inclusion criteria were selected for the study after history and examination from the outpatient and in-patient department of Oral & Maxillofacial Surgery, Jinnah Post Graduate Medical Centre. Quality of life was assessed by using FACT H & N (Functional assessment of cancer therapy scale) scale in Urdu versions. As diagnosed cases of OSCC were selected so patients selected were explained about the study and were assessed on the day of diagnosis of OSCC. Non probability consecutive sampling technique was used. Patients with confirmed diagnosis of Oral Squamous cell Carcinoma by histological reports, age 18 years to 70 years old were included in the study. Post treatment patients of oral squamous cell carcinoma, psychiatric patients and having a second primary cancer were excluded.

After explaining study protocol, use of data for research and risk benefit ratio written consent was taken for the questions to be asked. All the findings were recorded in a specifically prepared case proforma and in the end the total scores was calculated. Interviewer bias was controlled with efficient and validated questionnaire selection with validated Urdu translation. Researcher was the sole interviewer.

Data entry and its analyzing were done in SPSS version 23.0.descriptive statistics were given for both quantitative and qualitative variables. For quantitative variables Mean ± S.D was calculated whereas calculation of percentages and frequency was done for qualitative variables. Qualitative data was assessed through chi-square test. Association between severity of disease and quality of life was assessed through Logistic regression and correlation between severity of disease and quality of life will be assessed through Bi-variate analysis. P value equal or less than 0.05 was considered as significant and confidence level of 95% was used for the study.

RESULTS

One hundred sixty one patients were enrolled, in our study. The average age of the patients was 32.05±4.71 years. Majority of the patients were (71.4%) between 26-35 years of age. There were (61.5%) males and (38.5%) were females. Majority of the patients (38.5%) had middle socio-economic status. Further, most of the patients (65.2%) were married. (Table. 1).

The average score for physical, social, emotional and functional well-being were shown in table. II. Further, the mean score for additional concerns, trail outcome index, FACT-G and FACT H&N was 25.02±4.76, 64.96±7.21, 86.81±13.01 and 112.92±23.84, respectively. (Table. 2).

Table No.1: Demographic and socioeconomic characteristics of the patients

Characteristic	Mean±S.D 32.05±4.71	N (%)
Age (years)		
18-25		12 (7.5)
26-35		115 (71.4)
>36		34 (21.1)
Sex		
Male		99 (61.5)
Female		62 (38.5)
Socio-economic status		
Low		48 (29.8)
Middle		62 (38.5)
High		51 (31.7)
Education level		
Middle		81 (50.3)
High		80 (49.7)
Marital status		
Married		105 (65.2)
Unmarried		56 (34.8)

Table No.2: Variables

Variable	Score	Mean ± S.D
PWB	0-28	17.91±2.15
SWB	0-28	22.94±3.22
EWB	0-24	18.12±1.14
FWB	0-28	21.69±3.42
Additional concerns	0-40	25.02±4.76
TOI	0-96	64.96±7.21
FACT-G	0-108	86.81±13.01
FACT-H&N	0-148	112.92±23.84

DISCUSSION

In our study mean age of patients was 30 years and range upto 65 years, a similar study was conducted by D'Souza et al[11] and reported age range 45 to 65 years. About 35% of patients diagnosed as grade III and IV disease. A study was conducted by Sharma et al[12] on quality of life in patients of squamous cell carcinoma of head and neck and concluded that severe disease (grade III and IV) is associated with reduced quality of life in all aspects, physical well-being to global well-being. In this study 35% patients of his study were having grade IV disease and 17 patients were having grade III disease.

A study was conducted by Visacri et al[13] in 2015 and observed a significant reduction in quality of life after start of treatment. As duration of treatment and stage of disease increases quality of life becomes more compromised. Another study was conducted by Abbas S et al[14] on factors affecting the quality of life in patients with squamous cell carcinoma and reported that advance stage of disease is the main contributing factor of reduction of quality of disease.

In a study by Terrel et al[15] reported 44% cases with stage IV cancer that were found with reduced quality of life, majority of patients were male in gender. Similarly in our study male gender is dominant but gender was not significant determinant of quality of life in our study. Lo et al[16] also determined similar finding that gender is not significant determinant of quality of life in squamous cell carcinoma patients.

Onakoya et al[17] reported in his study that mean score between both genders is not dominantly different but severity of disease has a strong association for all domains of quality of life. Like our study conclusion it was also observed that quality of life among younger patients generally affected specifically emotional and physical domain. Klein J et al[18] also reported that descending order of severity of disease is associated with significant decrease in quality of life in 7 domains out of 12.

Hammerlid E et al[19] in his study observed strong association between stages of disease and quality of life. Patients with small stage of disease I and II have better score as compared to the stage III and IV disease in all domains. Even after three years of diagnoses patients still suffering emotional limitation. Fang et al[20] also reported similar finding that late stage carcinoma even after surgical intervention associated with deterioration in quality of life. This condition is more severe when symptoms belong to head and neck or squamous cell carcinoma.

CONCLUSION

Our findings reveal that there is a strong association between quality of life (FACT H & N) score and severity of squamous cell carcinoma. Patients in advance stage of cancer (stage III and IV) were observed with more decrement in quality of life than early stages (I and II).

Recommendations: Oncologists and other medical professionals that are treating squamous cell carcinoma patients should consider impact of treatment on quality of life patients. All factors which are involved in hampering of quality of life in squamous cell carcinoma should be assessed and coped to improve the patients' satisfaction level.

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Original Article

Characteristics and Severity of CT Scan Involvement in COVID Pneumonia and its Value in Predicting the Outcome

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ABSTRACT

Objective: To evaluate the association of CT scan severity in-terms of severity score and characteristic of different lesions on admission in predicting the outcome of COVID pneumonia.

Study Design: Retrospective cross-sectional observational study

Place and Duration of Study: This study was conducted at the Department of Pulmonology, Recep Tayyip Erdogan Hospital, Muzaffargarh from May 2020 to December 2021.

Materials and Methods: Data of 209 patients was obtained from hospital record after clearance from hospital ethical board. Main variables of study were CT severity score, smoking status, total leukocyte count, lymphocyte count, ICU admission, LDH, CRP, ferritin, clinical stage of disease, mechanical ventilation and final outcome (discharge or death). SPSS version 24 was used for data analysis.

Results: ICU admission was needed in 11.8% mild disease stage, 16.9% in moderate stage and 20.0% in severe stage (P<0.001). Mechanical ventilation was given in 5.8% in mild, 10.8% in moderate and 8.0% in severe stage (P<0.001). In mild stage 58.8% patients discharged at room air, in moderate stage 78.5% and in severe stage 28.0% patients were discharged at room air (P<0.001). Death rate was high 40.0% in stage in which CT scan shows severe disease, in mild and moderate diseased stage death incidence was 17.7% and 4.6% respectively.

Conclusion: Computed tomography (CT) has an important role in diagnosis and assistance of clinicians during treatment of COVID-19 and it is a strong predictor of disease severity and final outcomes. Severity score predicted on CT scan is positively correlated with hospital stay, laboratory investigations and demand of oxygen.

Key Words: COVID-19 pneumonia, Clinical outcomes, Death, Severity of CT scan, Laboratory investigations.

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INTRODUCTION

The outbreak of the coronavirus disease 2019 (COVID-19) has spread rapidly throughout Wuhan (Hubei province) to other provinces in China and other more than 75 countries around the world[1,2], representing a significant and urgent threat to the global health. The clinical spectrum ofCOVID-19 pneumonia ranges from mild to critical cases, among which the diagnoses of ordinary, severe, and critical cases were all correlated with chest computed tomography (CT) findings[3,4].

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Previously published studies have described the general typical and atypical CT image manifestations[5], the time-course evolution of CT findings,[4] the correlation between CT features and clinical features[6], and evaluated the CT severity of patients with COVID pneumonia [7]. To reduce or eliminate the subjectivity in the qualitative and semi-quantitative visual evaluation of CT severity scores, quantitative approaches for assessing lung opacification percentage of the whole lung have been developed, such as deep-learning method, computer tool, or the calculation method of combing mean attenuation values and opacity volumes [8,9]. However, these quantitative analysis methods did not fully specify information characterising and quantifying different clinical stages with CT features.

High resolution CT scan chest is a common investigation to evaluate the extent of involvement and see the pattern of lesions in case of negative report of RT-PCR[10]. All the treatment strategies depend on clinical severity of COVID pneumonia[11]. So the study is designed to investigate the importance and value of CT scan severity and the characteristic of lesions in predicting the outcome of COVID pneumonia.

MATERIALS AND METHODS

After receiving clearance from our institutional review board, a retrospective cross-sectional observational research was conducted in hospitalized patients diagnosed with COVID-19 pneumonia in Recep Tayyip Erdogan Hospital Muzaffargarh from May 2020 to December 2021. Because there is no active intervention in this trial, informed permission was be required. Patients' privacy and confidentiality was protected in accordance with norms. The research was covering all COVID-19 pneumonia patients at our hospital who are 18 years or older (as defined by our operational criteria). Patients with COVID 19 pneumonia (as defined in operational definition) with non-sever and sever clinical status on day 1, received other medical standard care according to institutional guidelines, whose CT scan was done within three days of admission, both genders and 18 years to 80 years of age were included in the study.

Patients with previously chronic lung disease like COPD, asthma and ILD evaluated on history and medical records, required ICU admission or mechanical ventilation on day1 and patients on long term oxygen therapy were excluded from the study. Using a predetermined case report form, the hospital's Electronic Medical Records was utilized to collect and record important clinical and laboratory data. Demographic variables like age, gender, BMI and previous clinical status with given codes are code 1 is diabetes mellitus, code 2 is hypertension, code 3 is ischemic heart disease, code 4 is chronic obstructive pulmonary disease and code 5 is for other disease was recorded on Performa.

Patients with symptoms with Covid-19 e.g. fever, sore throat, cough, malaise headache, muscle pain, vomiting, diarrhea, loss of taste and smell without chest involvement i.e. dyspnea and abnormal chest findings were labelled as mild pneumonia.

Patients who have dyspnea with/without clinical signs of lower respiratory tract infection (crepitations, bronchial breathing) or have radiographic evidence of pulmonary involvement (ground glass opacities, infiltrates, consolidations) was labelled as moderate pneumonia.

Patients with COVID pneumonia and having oxygen saturation < 94% at room air or respiratory rate of over 25 breaths/min which can be maintained by nasal cannulation or simple face mask and there is no need for non-invasive ventilation, High flow nasal cannula, or mechanical ventilation were labelled as severe COVID pneumonia.

Ct scan severity score was measured by using percentages of anatomical structures of five lobes of lungs: 1:<5% involvement, 2: 5% to 25% involvement, 3: 26% to 49% involvement, 4: 50% to 75% involvement, 5: >75% involvement. Total CT score is the sum individual lobar score that can range 0 to 25 means no involvement to maximum involvement.

On day of presentation clinical severity of each patient was noted. CT scan of these patients was evaluated by consultant radiologist. CT scan severity score calculated visually, no of segments involved and types of radiological pattern. Every patient was followed for the outcome and event of ICU admission, mechanical ventilation and death was recorded. Radiological lesions were assessed on CT scan of COVID pneumonia by radiologist and characteristic of radiological lesions like consolidation, ground glass, infiltrates, reverse halo, crazy paving, effusion or pneumothorax / pneumomediastinum were noted of each patient. Primary outcome of this study is to evaluate the role of CT scan and characteristic radiological pattern in predicting the ICU admission, mechanical ventilation and death.

Data was analysed by SPSS 24, quantitative variables like age BMI, CT scan severity score, length of hospital stay, no of total segments involved and absolute lung volume of affected lung were statistically analysed in mean and standard deviation. Qualitative variables like gender, presence of co morbidity, clinical severity on admission, types of radiological pattern, event of ICU admission , mechanical ventilation and mortality was analyse in percentage and frequency. CT scan severity in-terms of score and absolute volume were compared in non-sever and sever COVID pneumonia. CT scan severity was compared between patients with and without event of ICU admission, mechanical ventilation and mortality. Independents t-test was applied to check the significance. Type of radiological pattern and CT scan severity score and its association with length. Of hospital stay, ICU admission, mechanical ventilation and death was analysed by regression. ROC of CT scan severity score for these events were calculated.

RESULTS

A total of 209 patients were analyzed, CT scan evaluation shows mild severity of disease in 34 (14.2%), moderate in 130 (54.4%) and severe in 75 (31.4%) of patients. Mean age of patients in three groups was 62.76±13.72, 52.83±13.52, 56.05±15.57 in mild, moderate and severe groups respectively (P<0.001). No patients were having age below 30 years, maximum age was observed in age group of 40-50 years and severe diseased patients. Male gender was dominant in all groups as 28 (82.4%) in mild, 69 (53.1%) in moderate and 38 (50.7%) in severe stage (P=0.004). In mild severity group no patients was smoker but in moderate and severe stage 8 (6.2%) and 8 (10.7%) were smoker. Mean TLC count was 16.49±5.18 in mild, 12.45±6.94 in moderate and 9.18±6.23 in severe stage (P<0.001). Lymphocytes count was 2316.98±18.21 in mild, 1409.31±10.1 in moderate and 1129.58±17.61 in severe stage (P<0.001).

Mean LDH at time of admission was 662.14±12.54 in mild disease, 517.11±12.1 in moderate stage and 697.33±6.41 in severe stage (P<0.001). Mean CRP in mild stage was 19.29±26.73, 10.61±12.25 in moderate and 32.98±7.12 in severe diseased stage (P<0.001). Mean serum ferritin was 324.71±42.1 in mild, 872.75±14.19 in moderate and 2854.29±25.11 in severe stage (P<0.00) (Table-1).

Clinically moderate disease was observed in 0% patients in mild disease in CT scan stage 33 (25.4%) and 0% patients in severe disease in CT scan stage, similarly severe clinical disease was observed in 22 (64.7%) mild disease stage, 81 (62.3%) in moderate stage and 38 (50.7%) in severe stage (P<0.001). ICU admission was needed in 4 (11.8%) mild disease stage, 22 (16.9%) in moderate stage and 15 (20.0%) in severe stage (P<0.001). Mechanical ventilation was given in 2 (5.8%) in mild, 14 (10.8%) in moderate and 6 (8.0%) in severe stage (P<0.001). In mild stage 20 (58.8%) patients discharged at room air, in moderate stage 102 (78.5%) and in severe stage 21 (28.0%) patients were discharged at room air (P<0.001). Death rate was high 30 (40.0%) in stage in which CT scan shows severe disease, in mild and moderate diseased stage death incidence was 6 (17.7%) and 6 (4.6%) respectively (Table-2). Correlation of final outcomes with findings of HRCT was shown in Table-III with statistically significant values (P<0.001).

Table No.1: Demographics and Special Investigations

Characteristic	CT scan severity			p-value
	Mild 34 (14.2%)	Moderate 130 (54.4%)	Severe 75 (31.4%)	
Age (years)	62.76±13.72	52.83±13.52	56.05±15.57	<0.001
<30	0 (0.0)	0 (0.0)	0 (0.0)	<0.001
30-40	0 (0.0)	22 (16.9)	8 (10.7)	
40-50	8 (23.5)	36 (27.7)	23 (30.7)	
50-60	6 (17.6)	30 (23.1)	22 (29.3)	
60-70	6 (17.6)	28 (21.5)	16 (21.3)	
70-80	14 (41.2)	6 (4.6)	6 (8.0)	
>80	0 (0.0)	8 (6.2)	0 (0.0)	
Gender				
Male	28 (82.4)	69 (53.1)	38 (50.7)	0.004
Female	6 (17.6)	61 (46.9)	37 (49.3)	
Smoking status	0 (0.0)	8 (6.2)	8 (10.7)	<0.001
TLC on admission	16.49±5.18	12.45±6.94	9.18±6.23	<0.001
Absolute lymphocytes on admission	2316.98±18.21	1409.31±10.1	1129.58±17.61	<0.001
LDH on admission	662.14±12.54	517.11±12.1	697.33±6.41	<0.001
CRP on admission	19.29±26.73	10.61±12.25	32.98±7.12	<0.001
Ferritin on admission	324.71±42.1	872.75±14.19	2854.29±25.11	<0.001

Table No.2: Clinical stages of disease and final outcomes

Characteristic	CT scan severity			p-value
	Mild 34 (14.2%)	Moderate 130 (54.4%)	Severe 75 (31.4%)	
CT scan severity	8.11±1.41	13.79±2.47	19.41±2.44	<0.001
Clinical stage of disease				
Moderate	0 (0.0)	33 (25.4)	0 (0.0)	<0.001
Severe	22 (64.7)	81 (62.3)	38 (50.7)	
Very severe	12 (35.3)	16 (12.3)	37 (49.3)	
ICU admission	4 (11.8)	22 (16.9)	15 (20.0)	<0.001
NIV	3 (8.8)	28 (21.5)	6 (8.0)	<0.001
Mechanical ventilation	2 (5.8)	14 (10.8)	6 (8.0)	<0.001
Final outcome				
Discharge at home	6 (17.7)	16 (12.3)	16 (21.3)	<0.001
Discharge at room air	20 (58.8)	102 (78.5)	21 (28.0)	
LAMA	2 (5.8)	6 (4.6)	8 (10.7)	
Death	6 (17.7)	6 (4.6)	30 (40.0)	

Table No.3: Correlation of final outcomes and findings of HRCT

Characteristic	HRCT chest pattern					p-value
	Consolidation 96 (40.2%)	Crazy paving 32 (13.4%)	Ground Glass 36 (15.1%)	Infiltrate 65 (27.2%)	Other 10 (4.2%)	
ICU admission	8 (8.3)	32 (100.0)	16 (44.4)	13 (20.0)	2 (20.0)	<0.001
NIV	18 (18.8)	6 (18.8)	8 (22.2)	8 (12.3)	2 (20.0)	<0.001
Mechanical ventilation	12 (12.5)	6 (18.8)	6 (16.7)	8 (12.3)	2 (20.0)	<0.001
Final outcome						
Discharge at home	8 (8.3)	0 (0.0)	8 (22.2)	16 (24.6)	8 (80.0)	<0.001
Discharge at room air	54 (56.3)	21 (65.6)	28 (77.8)	42 (64.6)	0 (0.0)	
LAMA	6 (6.3)	8 (25.0)	0 (0.0)	4 (6.2)	0 (0.0)	
Death	28 (29.2)	3 (9.4)	0 (0.0)	3 (4.6)	2 (20.0)	

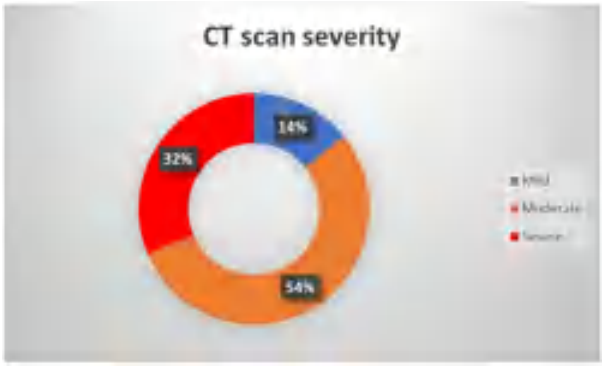

Figure No.1: CT scan Severity

DISCUSSION

World Health Organization recommended use of chest imaging as part diagnosis in COVID-19. Through quantitative assessment on CT chest severity of disease can be predicted[12]. In our study mean age of patients in three groups was 62.76±13.72, 52.83±13.52, 56.05±15.57 in mild, moderate and severe groups respectively (P<0.001), mortality rate was higher in severe stage of disease on CT chest. A study conducted by Francone et al[13] in 2020 was reported mean age of patients 63.2 ± 15.8, age range was 27 to 90 years, it was concluded that CT score above 18 is associated with increased rate of mortality.

In our study males were 82.4% in mild, 53.1% in moderate and 50.7% in severe stage. Dangis et al[14] conducted a study on impact of gender on severity of COVID-19 and reported that male gender is more vulnerable (93.4%) to disease which may be due to protective role of estrogen. Some other factors like stage of pandemic at the time of study, maturity of health facilities, co morbidities, also skill of health care facilitators and spread of disease in study area are also important[15].

In our study ICU admission was needed in 11.8% mild disease stage, 16.9% in moderate stage and 20.0% in severe stage. Death rate was high 40.0% in stage in which CT scan shows severe disease. Another similar study was conducted by Colombi et al[16] reported a positive association between severity of disease on CT chest and ICU admission, hospital stays and mortality. ICU mortality was 16% in Pan et al[17] also reported that CT findings along with clinically correlation are very helpful for physicians to treat early disease and rapid recovery.

In our study 10.7% smokers diagnosed as severe CT score and 6.2% as mild disease; mild disease was not diagnosed in any smoker. Guan et al[18] conducted a study and concluded that presence of co morbidities like smoking, hypertension yielded poor outcomes and prognosis. Increased number of comorbidities results in more poor outcomes. Serum ferritin was also found associated as in severe stage of CT score mean ferritin was 2854.29±25.11. Ferritin is an important marker and mediator of immune regulation its level have strong association with recovery of COVID-19[19].

Saeed et al[6] reported in a study that laboratory investigations significantly correlated with CT chest and demand of oxygen. Lymphopenia was observed 13.7%, 35.6% and 50.8% in mild, moderate and severe CT score stage respectively. These findings are identical with our results as we observed increased lymphocyte count in severe disease stage as compare to mild and moderate (<0.001). Similarly like our study Li et al[20] also reported increased CT score is associated with increased mortality.

CONCLUSION

Computed tomography (CT) have an important role in diagnosis and assistance of clinicians during treatment of COVID-19 and it is a strong predictor of disease severity and final outcomes. Severity score predicted on CT scan is positively correlated with hospital stay, laboratory investigations and demand of oxygen.

Author's Contribution:

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Final Approval of version:	Muhammad Aneel Razzaq

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

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Original Article

Efficacy of Modified Millard's Technique for Repair in Children Presenting with Cleft Lip in Jamshoro, Sindh

Shahzad Shaikh[1], Yasir Arafat Memon[2], Sadia Rasheed[3], Aamna Sanober[4], Rizwana Fazlani[4] and Samra Irshad[1]

ABSTRACT

Objective: To assess the efficacy of Modified Millard's technique for repair in children presenting with cleft lip
Study Design: Descriptive case series
Place and Duration of Study: This study was conducted at the Department of Plastic and Reconstructive Surgery, Liaquat University Hospital, Jamshoro from August 2016 to February 2017.
Materials and Methods: Patients of age from 3 months to 10 years of both gender and all 3 types of cleft lip (Incomplete, Complete and Microform) on clinical examination were included. Syndromic patients (with other clefts) on clinical examination, associated congenital anomalies including neural tube defect (on clinical examination) and anemic children (Hb<10mg/dl) were excluded. All children underwent cleft lip repair under general anaesthesia by a single surgical team. Millard classical repair consists of a straight line closure at vermilion. All the information was recorded in a pre-designed written questionnaire.
Results: Total of 80 children with cleft lips was included. The mean age of the children was 3.28±3.24 Years. There were 54(67.5%) male and 26(32.5%) female. Efficacy of Modified Millard's technique for repair in children presenting with cleft lip was 76.25% (61/80) children.
Conclusion: It is concluded that Modified Millard's Technique for cleft lips is an effective method to achieve better cosmetic outcome and a reliable & versatile technique associated with excellent surgical outcome.

Key Words: Cleft of lip, Cranio-facial malformations, Modified Millard's technique

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INTRODUCTION

A cleft of lip is a significant component of craniofacial malformations.(1) It occurs as a consequence of failure of fusion of maxillary process with median nasal process. Multifaceted genetic and environmental factors are involved in its etiology. Family history reveals in most cases of cleft lip, in our country, are associated with first degree cousin marriage.(2) The incidence of cleft lip is more common in males at a 2:1 ratio. Unilateral clefts with left dominance show a 2:1 ratio.

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Phenotypically cleft lip is classified into microform, complete and incomplete.(3) Repair of cleft lip is a demanding procedure for a Plastic surgeon. Aim of surgery is to compensate for the functional and aesthetic deformity of a lip.(4) Several different techniques and their modifications are used to repair unilateral and bilateral cleft lip including Millard technique, Mohler's, Nordhoff vermillion flap, Onizukatriangular advancement flap, Tennisson and Manchester procedure.(5, 6)

Modified Millard technique is used, at our set up, to repair all types of cleft lip. It is frequently being observed that different post-operative complications are seen with different frequency in different age groups. In under developed countries, like ours, patients frequently presents beyond the recommended age for cleft lip repair.(7)

The optimal, most agreed age for surgery of cleft lip is 10-12 weeks after birth.(8) Reports of early repair imply better aesthetic and functional outcome. Surgical correction of defect with late presentation is technically more demanding especially at teen age and puberty.(9) One study has showed that the efficacy of 72% was achieved with modified millard technique for cleft lip repair in children.(10) Therefore, the purpose of this study is to evaluate the efficacy of cleft lip repair, by Modified Millard technique. Literature has showed that

modified Millard technique is an effective method to achieve better cosmetic outcome. But no local evidence was available in this regard so we want to conduct this study to get local evidence. Repair of cleft lip is highly dependent on surgeon's experience. The results of this study will therefore enable practicing surgeon to counsel and undertake procedure with sufficient knowledge of expected complication in this particular age group.

MATERIALS AND METHODS

This descriptive case series was conducted from August 2016 to February 2017 at the Plastic & Reconstructive Surgery Department, Liaquat University Hospital, Jamshoro after getting the ethical approval from the research and ethics committee of LUMHS, Jamshoro. All patients aged from 3 months to 10 years of either gender and all 3 types of cleft lip (Incomplete, Complete and Microform) on clinical examination were included. Syndromic patients (with other clefts) on clinical examination, associated congenital anomalies including neural tube defect (on clinical examination) and anemic children (Hb<10mg/dl) were excluded. Sample size of 80 cases is calculated with 5% level of significance, 10% margin of error and taking expected percentage of efficacy i.e. 72% with Modified Millard's technique for repair of children presenting with cleft lip.

Written or informed consent was obtained from their parents. Demographic variables including age, gender, type of cleft defect, site of the defect was noted. Then all children underwent cleft lip repair under general anesthesia by a single surgical team having at least 4 years residency experience. Millard classical repair consists of a straight line closure at vermilion. After surgery, children were shifted to post-surgical ward and were followed-up there for 1 week. After 1 week, wound was examined and efficacy was labeled if there was no notch. Informed consent from patient's parents/guardians was sought. Confidentiality was maintained by securing the data in the locker and this was not shared with anyone else without permission of the patient.

The data was analyzed using SPSS version 21. Age was presented as mean ± SD. Gender, type of cleft defect, site of the defect and efficacy was presented as frequency & percentage. Data was stratified for age, gender, type of cleft defect and site of the defect. Post-stratification, chi square test was applied to compare efficacy. The p value ≤ 0.05 was taken as significant.

RESULTS

Total 80 children were included. The mean age of the children was 3.28±3.24 Years. Majority of patients were male compared to their counterparts. Unilateral site of defect was observed in most of the patients while regarding type of defect, most of them have incomplete defect. (Table I).

Table No.1: Distribution of Gender, Age, Side of defect (n=80)

		n (%)
Gender	Male	54(67.5%)
	Female	26(32.5%)
Age	Mean ±SD	3.28±3.24
	<1 years	30(37.50%)
	1-5 year	30(37.50%)
	6-10 year	20(25%)
Side of Defect	Unilateral	48(60%)
	Bilateral	32(40%)
Type of defect	Microform	21(26.25%)
	Incomplete	49(62.25%)
	Complete	10(12.5%)

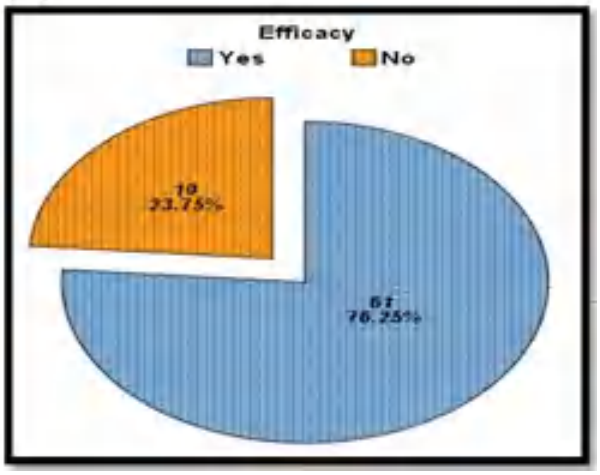

Figure No.1: Efficacy of Modified Millard's Technique for repair in children presenting with cleft Lip

Table 2 is presenting the stratification analysis of efficacy of modified MILLARD's technique for repair in children presenting with cleft Lip. There was no significant effect of age, gender, side of defect and type of defect on efficacy (Table 2).

Table No.2: Efficacy of modified MILLARD's technique for repair in children presenting with cleft Lip

		Efficacy of Modified Millard's Technique		P value
		Yes	No	
Age	Below 1 year	20(66.7%)	10(33.3%)	0.285
	1-5 year	25(83.8%)	5(16.7%)	
	6 -10 year	16(80%)	4(20%)	
Gender	Male	28(70.4%)	16(29.6%)	0.075
	Female	23(88.5%)	3(11.5%)	
Side of Defect	Unilateral	3$(70.8%)	14(29.2%)	0.163
	Bilateral	27(84.4%)	5(15.6%)	
Type of defect	Microform	15(71.4%)	6(28.6%)	0.675
	Incomplete	39(79.6%)	10(20.4%)	
	Complete	7(70%)	3(30%)	

DISCUSSION

One of the most common craniofacial developmental defects is cleft lip & palate.[11] According to reports, the prevalence of these anomalies varies by ethnicity, gender, and cleft type. The central 3rd of the face is distorted by the cleft & restoring the normal facial form is one of the primary goals for the reconstructive surgeon. Modern techniques in reconstructive surgery can make many abnormalities almost undetectable with the goal of restoring form and function. Early lip closure has been suggested to avoid unwanted anxiety and psychological effects on children and families.[12] The initial method developed by Millard for treating cleft lips.[13] The success of the Millard rotation/advancement approach in hiding incisions is demonstrated by the fact that 46% of North American surgeons claim to have used it without any modifications, and another 38% have done so while employing different modifications.[14]

Males are greater likely to have cleft lip with or without cleft palate & females are more likely to have isolated cleft palates, across different ethnic groups; the sex ratio changes depending on how to severe the cleft, additional abnormalities present, number of affected siblings in a family, ethnic origin, and perhaps the father's age.[15] The gender ratio for cleft lip even without cleft palate in white people is roughly 2:1. Cleft lip and palate in populations exhibits a considerable male excess, however, this excess is not limited to cases of cleft lip. [16] The male excess in cleft lip with or without cleft palate is noticeable in white populations as the severity of the defect increases and less noticeable when more than one child is affected in the family.[17]

In our study 80 children fulfilling selection criteria were enrolled. There were 67.5% male and 32.5% female. Our data showing predominance of male gender is supported by various studies. A local study, conducted by MM Elahi et al, reported male predominance in 117 cases of cleft palate from 61,156 live births. [18] The second most prevalent congenital abnormality is a single cleft lip (after club foot), accounting for about 13% of all congenital anomalies. The overall incidence of cleft lip with or without a cleft palate is approximately 1 in 750,000 live births. Unilateral clefts are 9.0 times common as bilateral clefts, and occur frequently twice on the left side than on right. [19]

In our study out of 80 patients we found Unilateral site of defect in 60% in which 13(16.3%) right and 35(43.8%) left. Overall prevalence shows 1 in 5000–6500 infants with bilateral clefts (BLC).[20] Bilateral cleft lip & palate has the potential to greatly change the shape and structure of the face. This malformation has serious psychosocial repercussions including aesthetic, eating, speech, and dental development issues.[21] In our study Bilateral clefts were observed in 40% cases. Around the world, the majority of surgeons employ rotation/advancement procedures in some capacity, Although there is no ideal method, Millard's rotation/advancement methodology was radically new, and several changes have been suggested to solve its shortcomings.[22,23] We found the efficacy of modified millard's technique for repair in children presenting with cleft lip was 76.25%.

A review study of outcomes of incision for primary repair of unilateral complete cleft lip in patients were carried out by Markus et al., using Millard rotation advancement technique and Pheiferwavy line incision.[24] They observed that there isn't a single method of cleft lip restoration that works in every circumstance. Individual clefts must be treated using a philosophy that includes ideas from several techniques and allows the surgeon to alter it as needed to meet a specific requirement.

CONCLUSION

The study concludes that Modified Millard's Technique for cleft lip is an effective method to achieve better cosmetic outcome & a reliable & versatile technique associated with good surgical outcome. Numerous techniques are employed with equivalent long-term outcomes, demonstrating the existence of multiple therapy options for permanent restoration.

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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

Practitioners' Perspective towards Association Between Periodontal Disease and Systemic Illness

Knowledge of Medical and Dental Practitioners about Periodontal Diseases

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ABSTRACT

Objective: To determine the knowledge of medical and dental practitioners about association of periodontal diseases and systemic illness.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the general dentists and general medical practitioners, and medical consultants from Khyber College of Dentistry, Khyber teaching hospital and Khyber medical college in Peshawar for 02 months from September to October 2022.

Materials and Methods: A cross-sectional survey was conducted via a self-designed, close-ended questionnaire on 76 medical and dental practitioners. The inclusion criteria were medical and dental practitioners who have more 5 years experience and both genders. The dental practitioners who had training or qualification in Periodontics were excluded. The questions asked were; systemic diseases may lead to periodontal disease, periodontal disease may lead to systemic diseases, is it a two-way process, periodontal disease is risk factor for medical conditions. Fisher exact was applied for comparison of awareness among practitioners.

Results: The males were 44 (57.89%) and females were 32 (42.11%). Half of the participants (n=38, 50%) know that 'systemic diseases lead to periodontal disease' and similarly 50% know that 'periodontal disease lead to systemic diseases'. The knowledge for two way relation between periodontal and systemic disease was found in 20 (26.32%). Statistical differences were found for knowledge about 'systemic diseases lead to periodontal disease' (p=0.042) and 'periodontal disease lead to systemic diseases' (p=0.042) among practitioners.

Conclusion: Dental and medical practitioners have less knowledge about association of periodontal disease and systemic illnes.

Key Words: Awareness, knowledge, association, periodontal disease, medical conditions

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INTRODUCTION

Periodontal diseases are usually due to gram negative bacteria and characterized by the loss of periodontal tissues.[1] Periodontal disease can be of two types; reversible or gingivitis and irreversible or periodontitis. The prevalence of periodontal disease is quiet higher and constituting a major health issue.[2]

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Many predisposing factors have been documented for periodontitis like improper oral hygiene, use of cigarettes, males gender, poor socioeconomic status and medical disorders.[3] The importance of periodontal health and their connection with overall health have been established.[4] Periodontal disease is assumed to have role in non-infectious disorders like diabetes, circulatory diseases, cancer and chronic respiratory diseases.[5]

A study was conducted at India on awareness about the effects of systemic disease on periodontal disease among internees. Their results shows that the level of awareness among medical internees was fair, poor and good in 67(47%), 60(42%), and 18(11%) respectively.[6] Another study reported that 56.7% faculty members were aware about that periodontal disease and systemic diseases has bidirectional relation and 39.3% know that periodontal disease risk factors for preterm low-birth weight infants.[7]

The knowledge about link of periodontal and systemic diseases is important to prevent complications. Periodontal disease is a preventable condition. There is lack of local research on this subject. This study will help to provide local baseline data. So this study was

conducted to determine the knowledge of medical and dental practitioners about association of periodontal diseases and systemic illness.

MATERIALS AND METHODS

A cross-sectional survey was conducted via a self-designed, close-ended questionnaire, in a non-probability, consecutive sampling technique. The calculated sample size was 76 by WHO calculator at 95% confidence level, 7% margin of errors and using 11% awareness about the association of periodontal disease and systemic conditions from previous study[6]. The participants of this study were registered general dentists and general medical practitioners, and medical consultants from Khyber College of Dentistry, Khyber teaching hospital and Khyber medical college in Peshawar. The inclusion criteria were medical and dental practitioners who have more than 5 years experience and both genders. The dental practitioners who had training or qualification in Periodontics were excluded.

A verbal informed consent was obtained from all participants after explaining the aims of the study. The participants of this study were approached personally. Questionnaires were given to all participants. The demographic data like age, gender and discipline (general medical, medical consultants and dental practitioners) were recorded. The questions asked were; systemic diseases may lead to periodontal disease, periodontal disease may lead to systemic diseases, is it a two-way process, medical conditions (diabetes mellitus, coronary heart disease, osteoporosis and pre-term labor) for periodontal diseases. The responses for all questions were recorded as know, don't know and can't say. Biases and confounders were controlled in the study by strictly following inclusion criteria.

The data analysis was conducted in SPSS 22. Descriptive statistics in the form of percentages along with frequency for qualitative variables and mean and SD for continuous data were calculated. The responses of awareness about the association of periodontal disease and medical conditions were compared among practitioners (dental, general medical and medical specialists) using Fisher exact test. The level of significance was $p \leq 0.05$.

RESULTS

The males were 44 (57.89%) and females were 32 (42.11%). Most frequent age category was 30-40 years (n=37, 48.68%) followed by 41-50 years (n=34, 44.74%). (Table 1)

Most of the participants were medical consultants (n=36, 47.37%) followed dental practitioners (29, 38.16%) and least were general medical practitioners (n=11, 14.4%). (Fig 1)

Table No.1: Frequency of gender and age group

	Characteristic	n(%)
Gender	Female	32 (42.11)
	Male	44 (57.89)
Age group (years)	30-40	37 (48.68)
	41-50	34 (44.74)
	51 & above	5 (6.58)

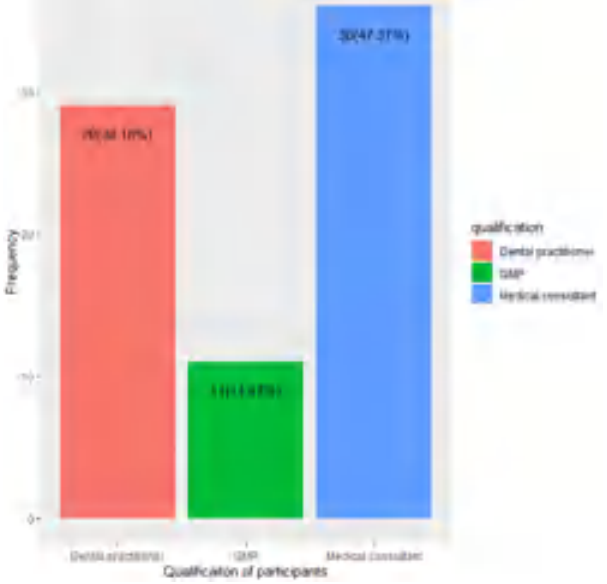

Figure No.1: Qualification of participants

Table No.2: Awareness about association between periodontal disease and systemic illness among medical and dental practitioners

variable	Characteristic	n(%)
Systemic diseases lead to periodontal disease	can't say	20 (26.32)
	don't know	18 (23.68)
	Know	38 (50.00)
Periodontal disease lead to systemic diseases	can't say	20 (26.32)
	don't know	18 (23.68)
	Know	38 (50.00)
Two way relation between periodontal and systemic disease	can't say	27 (35.53)
	don't know	29 (38.16)
	Know	20 (26.32)
Diabetes mellitus is risk factor for periodontal disease	can't say	3 (3.95)
	don't know	15 (19.74)
	Know	58 (76.32)
CVD is risk factor for periodontal disease	can't say	6 (7.89)
	don't know	23 (30.26)
	Know	47 (61.84)
Preterm labor is risk factor for periodontal disease	can't say	7 (9.21)
	don't know	28 (36.84)
	Know	41 (53.95)
Osteoporosis is risk factor for periodontal disease	can't say	7 (9.21)
	don't know	24 (31.58)
	Know	45 (59.21)

*CVD, cardiovascular disease

Table No.3: Comparison of association between periodontal disease and systemic illness among dental practitioners, general medical practitioner and medical consultants

variable	Characteristic	Dental practitioner, N = 29*	GMP, N = 11*	Medical consultant, N = 36*	p-value**
Systemic diseases lead to periodontal disease	can't say	6 (20.69)	3 (27.27)	11 (30.56)	0.042
	don't know	4 (13.79)	6 (54.55)	8 (22.22)	
	Know	19 (65.52)	2 (18.18)	17 (47.22)	
Periodontal disease lead to systemic diseases	can't say	6 (20.69)	3 (27.27)	11 (30.56)	0.042
	don't know	4 (13.79)	6 (54.55)	8 (22.22)	
	Know	19 (65.52)	2 (18.18)	17 (47.22)	
Two way relation between periodontal and systemic disease	can't say	9 (31.03)	3 (27.27)	15 (41.67)	0.26
	don't know	12 (41.38)	7 (63.64)	10 (27.78)	
	Know	8 (27.59)	1 (9.09)	11 (30.56)	
Diabetes mellitus is risk factor for periodontal disease	can't say	0 (0.00)	2 (18.18)	1 (2.78)	<0.001
	don't know	6 (20.69)	6 (54.55)	3 (8.33)	
	Know	23 (79.31)	3 (27.27)	32 (88.89)	
CVD is risk factor for periodontal disease	can't say	0 (0.00)	2 (18.18)	4 (11.11)	0.074
	don't know	11 (37.93)	5 (45.45)	7 (19.44)	
	Know	18 (62.07)	4 (36.36)	25 (69.44)	
Preterm labor is risk factor for periodontal disease	can't say	1 (3.45)	2 (18.18)	4 (11.11)	0.21
	don't know	12 (41.38)	6 (54.55)	10 (27.78)	
	know	16 (55.17)	3 (27.27)	22 (61.11)	
Osteoporosis is risk factor for periodontal disease	can't say	0 (0.00)	2 (18.18)	5 (13.89)	0.031
	don't know	11 (37.93)	6 (54.55)	7 (19.44)	
	know	18 (62.07)	3 (27.27)	24 (66.67)	

* n (%); ** Fisher's exact test; GMP, general medical practitioner

Half of the participants (n=38, 50%) know that 'systemic diseases can lead to periodontal disease' and similarly 50% know that 'periodontal disease lead to systemic diseases'. The knowledge for two way relation between periodontal and systemic disease was found in 20 (26.32%) participants. The knowledge about Diabetes mellitus, cardiovascular disease, Preterm labor and Osteoporosis to be risk factor for periodontal diseases were found in 58 (76.32%), 47 (61.84%), 41 (53.95%) and 45 (59.21%) respectively. (Table 2)

Statistical differences were found for knowledge about 'systemic diseases can lead to periodontal disease' (p=0.042) and 'periodontal disease can lead to systemic diseases' (p=0.042). For 'systemic diseases can lead to periodontal disease' the highest knowledge was found among dental practitioners (n=19, 65.52%) followed by medical consultant (n=17, 47.22%) and least among GMP (n=2, 18.18%). Similar results were found for 'periodontal disease can lead to systemic diseases'. The results were not non-significant for 'two way relation between periodontal and systemic disease'. The differences among different practitioners for diabetes mellitus (p<0.001) and osteoporosis (p=0.031) is risk factor for periodontal disease were statistically. Highest knowledge was found for 'diabetes mellitus is risk factor for periodontal disease' among medical consultants (n=32, 88.89%) followed by dental practitioners (n=23, 79.31%) and least among GMP(n=4, 36.36%). Similar results were found for 'osteoporosis is risk factor for periodontal disease'. (Table 3).

DISCUSSION

This survey was conducted to determine the knowledge of medical and dental practitioners about association of periodontal diseases and systemic conditions. Our findings showed about half practitioner have knowledge about association of systemic illness and periodontal disease. The level of relevant qualification has significant impact on this knowledge.

Periodontal disease is an infectious disease arising from interaction among host and pathogens. Bacteria come from oral cavity which is normal oral flora but when it cross oral mucosa and junctional epethelium it become pathogenic. Many risk factors have been reported for periodontal diseases like lack of proper oral hygiene measure, old age, hormonal changes in pregnancy and medical conditions.[8, 9]

Diabetes mellitus has many complication like neuropathy, vasculopathy and retinopathy. Periodontal diease is th sixth common complication of diabetes mellitus. Increase sugar level in blood lead to pathogen receptors expression, augment the pro-inflammatory response, promote bacterial replication and activation of osteoclasts. All these humoral changes lead to destruction of periodontium.[10] Association has been reported between cardiovascular disease and periodontitis.[11] Many chronic inflammatory diseases including periodontitis has been linked to cardiovascular disease. [12]

People usually neglect health of oral cavity and give priority to medical health only. It is usually

underestimated that oral disease can be deteriorating factor for general body health. So knowledge about the relation between systemic illness and periodontal health is of paramount importance.[13]

Our study showed that dental and medical practitioners limited have knowledge about the association of systemic disease and peridontal diseases. A study conducted in India on medical residents on association of systemic diseases and periodontal diseases and reported that medical residents have less knowledge. [6] Another study on medical faculty reported that 56.7% responded that the relationship between periodontal disease and systemic diseases is two way.[14] Another study by Vellayappan et al. on knowlesdge of medical practitioners about the effect of periodontal disease on body health showed that awareness was present in 79% participants.[15] In our study showed that awarness were more among dental practitioner followed by medical consultants and least among general medical practitioners. In this study we exclude periodontists and those who are working periodontics department. Previous study also reported that dental practitioners were more aware than medical practitioeners.[16]

This study have some limitation like unequal number of participants of various qualifications. This closed ended study and qualitative research with open ended quesitons can better explore this subject**.**

CONCLUSION

Dental and medical practitioners have less knowledge about association of periodontal disease and systemic illnes. Proper education is need to be given to all medical and dental practitioners about the link of oral and systemic diseaes to prevent its complications.

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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

Clinical Features, Risk Factors, Imaging Characteristics and Outcome of Cerebral Sinus Thrombosis

Mohsin Khan[1], Niama Khan[2], Nisar Ahmad Khan[3], Saif ud Din[1], Haidar Zaman[1] and Faizan Banaras[1]

ABSTRACT

Objective: To determine the presentation, clinical features, risk factors, imaging characteristics and outcome of patients with central venous sinus thrombosis.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Medicine in Ayub Teaching Hospital Abbottabad from March 2022 to October 2022.

Materials and Methods: All patients carrying the diagnosis (based on magnetic resonance venography) of cerebral venous sinus thrombosis (CVST) will be included in study. The patient with arterial stroke, arteriovenous malformation, intra and extra cerebral hemorrhages, space occupying lesions, septic meningoencephalitis and autoimmune encephalitis will be excluded from study. The data collection tool will be written questionnaire and data will be analyzed in SPSS version21.

Results: In present study 62patients met the inclusive criteria. The mean age of females was 30years and males was 40 years. The most common features of CVST were headache (93%), followed by Seizures. The most common potential cause was puerperium (64%). On MRV superior sagittal sinus was found thrombosed in 48% cases and left transverse sinus in 45% of cases. The mean duration of hospital stay was 10 days.

Conclusion: Majority of postpartum females have significantly high white cell count, although only 06 patients had history of localized infection. Most of patients presented with headache and seizures. Intra parenchymal bleed or superior sagittal sinus thrombosis is suspected in patients who presented predominantly with seizures. Superior sagittal sinus is most commonly thrombosed sinus (59%) in patients who presented with seizures. Prognosis of CVST is favorable than previously reported.

Key Words: Cerebral venous sinus, thrombosis, seizures, outcome, risk factors

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INTRODUCTION

Cerebral venous sinus thrombosis (CVST) is venous stroke caused by thrombosis of dural sinuses which lead to venous congestion, hypoxemia and brain injury. The prevalence of CVST is more common in Asia than the west. Its prevalence is 15% in young Asian population and account for 0.5 to 1.5% of all strokes [1]. Unlike arterial stroke the venous stroke, its presentation is highly variable. The presentation of CVST can be sub-acute i-e 2-28 days or chronic >30days.

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Sometime patient present only with chronic headache and in some cases, patient presents with coma. In present era due to great awareness and noninvasive improvement of radiological techniques now it is possible to diagnose CVST early [2]. The incidence of sinus thrombosis peaks in third decade of life with male to female ratio of 1.5:5 [3]. The risk factors vary according to age, demography and ethic group. In Asia pregnancy related causes are found to be most common cause while in European countries OCPs (oral contraceptive pills) were found to be most common culprit for CVST. In older age the most common cause of CVST is malignancy [4]. Currently, the magnetic resonance venography (MRV) is technique of choice for CVST while CT scan with contrast increases the sensitivity to 99% for sinus thrombosis and 88% for vein thrombosis [5]. The overall case fatality rate in CVST is 5-10% [6]. The factor responsible for poor prognosis is male gender, cancer, meningitis, hemorrhage and coma at presentation.

The present study updates the existing knowledge and creates local evidence for health care authorities. To the author's knowledge there is no regional data on CVST.

The study will serve as road map for further exploration of common risk factors.

MATERIALS AND METHODS

This cross-sectional study will be conducted in Ayub teaching hospital Abbottabad. The hospital provides tertiary care and encompasses Neuro ICU, Neurology ward and Neuro surgery unit. The study enrolled all patients who were diagnosed as a case of Dural sinus thrombosis on MRV from March 2022 to October 2022. The retrospective data through predesigned written questionnaire was obtained and the demography, predisposing risk factors and comorbidities were recorded. Moreover, necessary investigations which help in severity and diagnosis were also included. The laboratory investigations include complete blood count, erythrocytes sedimentation rate, C reactive peptide and coagulation profile. Radiological investigations include CT brain and MR Venography. The patients with arterial stroke, arteriovenous malformation, intra and extra cerebral hemorrhages, space occupying lesions, septic meningoencephalitis and autoimmune encephalitis were excluded from study. The institutional ethical committee approved the study with approval code/Ref.No.RC-2022/EA-01/058. The data will be analyzed in SPSS version 21 and variables with *P* value <0.005 will be considered as significant.

RESULTS

In current study almost 62 patients (n=62) were recruited from different medical departments. The mean age of sample was39.2±14, age ranges from 14 to 65. There was female gender preponderance with the 5:1 ratio. The first most common feature of CVST presentation was headache (58/62) followed by seizures (36), and Focal neurological deficit (22%), detail shown in fig1. The most common potential cause of CVST was puerperium 64% (40). The mean systolic blood pressure was137±27. 14 patients had underlying comorbidity. Hypertension was most common comorbidity recorded. Mean C reactive peptide (CRP) was 7 and d-dimer of 383 details shown in table1.

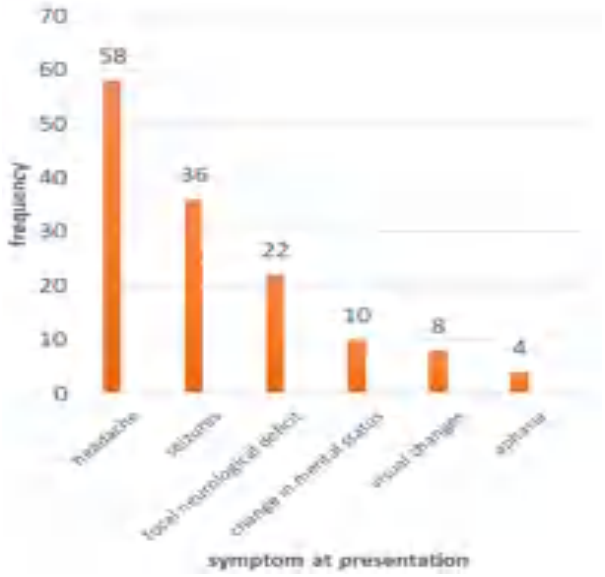

Figure No.1: Presentation of CVST

The CT of CVST was suggestive of ischemic venous infarct in 36 individuals (58%). The frequencies of cerebral venous sinus thrombosed in MRV were superior sagittal sinus 48.3% (30/62), left transverse 45.16% (28/62) and right transverse 41.9% (26/62). Single sinus was affected in 34 subjects; details shown in table 3. In isolated superior sagittal sinus thrombosis 87% (14/16) cases presented with seizures and headache, in isolated transverse sinus thrombosis 100% (18/18) patients presented with headache while, in superior sagittal and transverse sinus 67% (8/12) patients presented with focal neurological deficit and seizures. The mean duration of patient's hospital stay was 10 days.

Table No.1: Lab and Clinical Characteristic of Patients with CVST

Variables		Males	Females	P-value	Confidence interval (CI)
Age		40	30	0.00	-23— -04
Complete blood count	HB	15.2±1.3	11.7±2.5	0.04	-5.1 — -1.7
	WBCs	7.7±1.5	12.2±3.1	0.05	2.4 — 6.5
	Platelets	227±68	280±90	0.07	-8.0 — 113
CRP		7±1	9.0±7	0.001	0.2 — 12
D-dimer		200	429	0.17	-335 — 794
PT		15±2.5	16±3.1	0.76	-1.4 — 3.0
APT		32±0.2	36±1.1	0.12	2.2 — 6.2
Mean systolic blood pressure		140±20	137±28	0.47	-22 — 15.5
Mean diastolic blood pressure		84±10	85±13	0.37	-8.0 — 10.2
GCS		14±1	12±3	0.007	-4.0 — 0.03
Comorbidities		06	08	0.004	—
State of puerperium		—	40/52	—	—

Dehydration	00	32	0.001	—
State of pregnancy	—	10/52	—	—
Localized infection	00	06	0.32	—
Oral contraceptives use	—	04	—	—
History of previous DVT	02	02	0.119	—
Active Malignancy	00	00	—	—
History of Neurological trauma	00	00	—	—

Table No.2:Patients with details

Investigation	Characteristics	No
CT findings	Infarct	36
	Normal	22
	hemorrhage	02
MRV Findings	Single sinus involved	34
	2 sinuses involved	26
	3 sinuses or more involved	02
Frequency of sinus thrombosis on MRV	Superior sagittal	30
	R Transverse	27
	L Transverse	27
	Sigmoid	06
	Inferior Sagittal	04

DISCUSSION

The mean age of our cohort is 39 years with female gender preponderance. Women are significantly younger than males with the mean age of 30 and 40 years respectively. A multi-center study conducted in Pakistan by Khealani et al[7] reported mean age of 35 years with male and female mean age of 38 and 33 years respectively. The reason in age difference can be the cause related to CVST— Obstetric causes presented in younger age while infectious and malignancy related causes presented late [8]. The most common symptom at presentation is headache which is consistent with khealani et al and other international studies [8,9,10]. The male to female ratio is in accordance to De Bruijn SF et al[3]. Headache can be acute, sub-acute or chronic and it is due to intracranial hypertension. Usually, headache is diffuse and it is positional and get worsen with Valsalva maneuver [9]. Seizures followed by focal neurological deficit are 2nd and 3rd most common symptoms recorded in our study contrary to khalani et al which reported focal neurological deficit followed by seizures. There are multiple reasons for this, our cohort comprise most of females and obstetric causes are major risk factors of CVST in our cohort, it is well established that higher incidence of seizures observed in peripartum is up to 76% by one study [10]. Majority, 55% patients belong to far fang areas and they are late at presentation, as seizures are common at evolutionary stage of CVST [11]. Difference in Degree and number of sinus involvement also can be reason for late motor deficit and early seizures. In our study all patients having hemorrhagic transformation on CT have experienced seizures as a predominant symptom at presentation [12]. In the west 54% females have history of OCP use and onset of CVST [11] and some studies even state the risk of CVST increase up to 6-fold with the use of OCP [13]. The risk can be reached to 30 folds when BMI is >30 and concomitant use of OCP [4]. But surprisingly in our study only 04 females had history of OCP use. When compared with Khealani only 12% practiced OCP. This needs further exploration of risk factors in patients presented with CVST like hypothyroidism, hyperhomocysteinemia, hematological thrombophilia syndromes etc. Recently a study conducted by Bano S et al at Lahore reported that use of OCP is uncommon in Pakistan but no concrete reason explained [14]. In present study d-dimer is assessed in 21 patients, 18 showed high titer therefore the sensitivity of d-dimer is 86% and 3 patients represented false negative result. CRP level is accessed in 18 individuals, among which 08 had positive result[15]. So, sensitivity for CRP is 44.4%, 10 patients had negative results for CRP. The WBCS count of female are significantly higher than males, subtle infection in hospital can be the reason although only 06 females had history of localized infection in head and neck areas. Khealani et al reported infectious rate of 18% in patient presented with sinus thrombosis.

For the confirmatory diagnosis of CVST neuroimaging is considered as principal tool. Topographically the frequency of sinus thrombosis involved on MRV is in accordance to that reported by Khealani et al, the most commonly involved sinus is superior sagittal sinus, followed by transverse and sigmoid sinus. Our recorded frequency of sinus thrombosis is also in accordance to the study done in Lahore [9]. But a multicentered internal study in Argentina reported transverse sinus thrombosis and hemorrhagic finding as a common finding. The difference can be due to sample size and demographic variability with underlying risk factors [2]. We found 58% developed venous infarct on CT brain without contrast while Khealani reported 66%. The difference can be due to early diagnosis and older data reported by khealani et al. The mean duration of hospital stay is 10 days while Khealani recorded 9 days. There is no death recorded in our study population, the reason can be that our study sample lack factors associated with unfavorable outcomes like preponderance of male gender, coma at presentation, intracerebral hemorrhage, meningitis and cancer [5].

CONCLUSION

We have concluded that venous strokes are not uncommon in young females. CVST should be considered in differential diagnosis if young female is presented to hospital with particular headache and history of major predisposing event. Superior sagittal sinus is most commonly thrombosed sinus (59%) in patients who presented with seizures. The most common risk factor is puerperium in our setup. CVST with Hemorrhage on CT scan mostly presented with seizures. The most common sinus thrombosed is superior sagittal sinus. D-dimers are mostly positive but negative result cannot exclude the diagnosis of CVST. Further detailed should be obtained from females regarding infection as majority had significantly high WBCs count at presentation. OCPs use is uncommon practice in Pakistan. Prognosis of CVST is better than reported previously.

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

Prevalence and Pattern of Mandibular Fractures in Islamabad, Pakistan; A Retrospective Study

Muhammad Hashim Asad, Kalsoom Khan, Hina Rahman Sario, Salman Younas, Naveed Ahmed and Syeda Sameena Tasneem

ABSTRACT

Objective: To evaluate prevalence and pattern of mandibular fracture presented in various centers of oral and maxillofacial surgery of Islamabad region.

Study Design: Retrospective study

Place and Duration of Study: This study was conducted at the School of dentistry, Pakistan Institute of Medical Sciences Islamabad, KRL Hospital, Islamic international medical and dental college, Islamabad Medical and dental college Islamabad from July 2021 till March 2022.

Materials and Methods: Patient's having maxillofacial trauma was accessed from the record of different Oral and Maxillofacial Surgery hospital of Islamabad. During which 900 patients record was access among them 254 patients record was included due to having only isolated mandibular fracture. Data was entered and analyzed using SPSS v 23.0. Frequencies and percentages were calculated for fracture type, site, etiology and gender. Mean was described for age.

Results: The study revealed that among 254 patients, males in the age group of 21-30 years were in majority. Parasymphysis 43%, angle 30%, subcondylar 27 % and body of mandible fracture was 24%. Most common cause of trauma was the Road traffic accidents (79.9%).

Conclusion: From the present study we conclude that males belonging to the age group of 21-30 years are most frequently prone to mandibular fractures with highest mandibular parasymphysis fracture.

Key Words: Prevalence, Patterns, etiology, Facial trauma, Mandibular fractures.

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INTRODUCTION

World Health Organization reported that, around 1 million people losses life due to trauma and every year around 15 to 20 million population reported with injures in road traffic accidents(RTAs)[1]. Mandible fractures are the most common fractures of the facial skeleton due to its prominent position and mobility [2, 3]. Fractures of the mandible account for 36%-59% of all facial bone fractures.[2, 4] In spite of the mandible being the toughest and largest bone of the face, it is the 10th most commonly injured bone in the body[4],[2],[5].

The male/female proportion recorded for developed countries is around 3:1, while the male prevalence is more striking in developing countries [6]. However, in the latest reports the pattern is toward the equal gender proportion[7].

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These fractures could be classified according to severity as simple and compound, regarding the direction of fracture as favorable and non-favorable, with respect to type of fracture as greenstick, impacted, comminuted, and complex, regarding the teeth involvement in the fracture site as dentulous, partially edentulous, edentulous, and classification regarding the site of fracture as condylar, coronoid, ramus, angle, body, symphysis, parasymphysis of mandible[8].

The facial trauma specially mandibular which are categorically classified as: traumatic, iatrogenic and pathological fractures, among them traumatic etiology is the most cause[9]. The basic cause for facial trauma might be shifted from road traffic accidents to physical violence and from fall to sports trauma, in which alcohol consumption is the major contributing factor[10]. In spite of road traffic accidents (RTAs) and physical assault, such trauma can be occur due firearm incidents[2],industrial accidents and even attack by animals[5]. Road traffic accidents reported to be the main etiology for mandibular fractures in developing countries, which shows 60-80% of the cases with increase in mortality rates. Interpersonal violence account for about 10-20% cases followed by falls (5%) and other causes including sports injuries and industrial trauma[3]. In comparison, interpersonal violence and

sports are the main etiological factors for of mandibular trauma in developed countries[3]. In rare cases, mandibular fractures also occur secondary to certain diseases such as sarcomas, cystic lesions and metabolic diseases which are classified as pathological fractures[11].

Among the facial bones the mandible is the only mobile bone while the remaining facial skeleton is fixed [12]. Patients presenting with mandibular fractures may experience pain, edema, trismus, deranged occlusion, hematoma formation, lower lip paresthesia, ecchymosis and loose teeth [13]. Injuries related to mandibular bone can range from minimal head and facial lacerations to sever closed brain trauma [14]. Patients with fractures of lower jaw experience pain, trouble biting and talking, decrease mouth opening, unable to yawn properly and sleeping difficulty. A recent study on mandibular fracture patterns conducted in Peshawar, Khyber Pakhtunkhwa reported with common mandibular bone fracture as result of road traffic accidents among young male population[15].

Despite many published reports regarding mandibular fractures, there is a limited literature on the prevalence and importance of mandibular fractures in this region. With current evidence suggesting geographical variations in mandibular fracture patterns, there is a need to evaluate these patterns in Pakistan. This would provide evidence for maxillofacial surgeons to have an understanding of mandibular trauma in the population of this region. Hence, the primary objective of this retrospective study was to evaluate the prevalence and different patterns of mandibular trauma in Islamabad with respect to aid surgeons in anticipating the most probable site of fracture on presentation so as to help with treatment planning.

MATERIALS AND METHODS

A retrospective study was conducted from July 2021 till March 2022. Ethical approval was taken from competent authority of Ethical Review Committee of School of Dentistry Shaheed Zulfiqar Ali Bhutto Medical University Islamabad vide reference No.SOD/ERB/2021/116. Patient's having mandibular fracture was accessed from the record of different Oral and Maxillofacial Surgery centers of Islamabad. During which 900 patients record was access among them 254 patients record was included due to having only isolated mandibular fracture. The gender, age, etiology, type of facial trauma (single or multiple), site of mandibular fracture were retrieved from the patient records. The data was entered and analyzed through SPSS v 23.0. Frequencies and percentages were described for gender, etiology, fracture site and type. Mean and standard deviation were calculated for age.

RESULTS

This study included a total of 254 patient's record. All patients had fractured mandible. There were 230 (90.6%) males and 24 (9.4%) females. The mean age of the participants was 27.45 + 12.7 years. The most of these victims were up to 30 years of age (n = 161, 63.2%). Only 69 patients were above 30 year.

The most common etiology of mandibular fracture reported as a result of road traffic accidents (n = 203, 79.9%), followed by fall (n = 23, 9.1%) and assault (n = 12, 4.7%), as shown in table I.

Table No.1. Etiology of Mandibular Fractures

Etiology	Male	Female	No. of patients (%)
RTA	189(74.3%)	14(5.5%)	203(79.9%)
Fall	17(6.6%)	7(2.3%)	23(9%)
Assault	10(3.9%)	2(0.7%)	12(4.7%)
FAI	8(3.1%)	1(0.4%)	9(3.5%)
Occupational injury	7(2.7%)	0	7(2.7%)

The parasymphysis was the commonest fracture site (n = 110, 43%)., followed by the angle of the mandible (n = 77, 30%). Most of the parasymphysis fractures were only unilateral (n = 105, 41.3%).

Table No.2. Frequency of Mandibular Fracture Sites

Fracture site	Frequency of fracture (%)		
	Unilateral	Bilateral	Total
Condyle	10 (3.9%)	4 (1.6%)	14 (5.5%)
Sub condyle	49 (19.3%)	20(7.9%)	69 (27%)
Coronoid	4 (1.6%)	0	4 (1.5%)
Ramus	9 (3.5%)	0	9 (3.5%)
Angle	73 (28.7%)	4 (1.6%)	77 (30%)
Body	55 (21.7%)	6 (2.4%)	61 (24%)
Parasymphysis	105(41.3%)	5 (2%)	110 (43%)
Symphysis	40 (15%)		40 (15%)

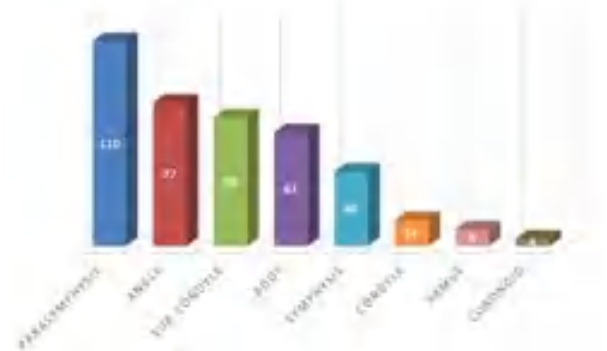

Figure No.1: Anatomical Distribution of Mandibular Fractures

DISCUSSION

In the maxillofacial region the mandibular bone is hardest and second most common site for fractures after the nasal bone owing to its relative protuberance in comparison to rest of the facial skeleton.[16,17] Mandibular trauma ranges from 15.5 to 59% of all the maxillofacial bone fractures [16]. Majority of mandibular fracture victims were males in this study with ratio of 3:1 male to female. This is in line with previous studies carried out in Pakistan and India, where the male to female ratio for mandibular fractures has been reported

to be 3.6:1.[4, 18] The mean age was 27.45 + 12.7 in our study with the peak age of fractures to be 18 years. These findings are consistent to previous studies which report mandibular fractures to be more common in males with age ranging from 15-25 years[4, 19].

We found RTA to be the leading cause for mandibular fractures from 79.7% (n=203) of the total fractures studied, followed by fall (9%), assaults (4.7%), FAI (3.5%) and occupational injury (2.7%). RTA accounting for majority of the mandibular fractures and our subjects mostly being young male patients could be associated with rash and careless driving of cars and motorbikes by these people. Moreover, since more RTA with fractures involve motorbikes, this also explains the large number of males in our sample, since motorbikes are primarily driven by males in Pakistan[20]. A study by Rashid et al reported that the leading cause of mandibular fractures is RTA in Pakistan which might be underage driving, over speeding, overloading of vehicles, poor condition of infra-structure and lack of traffic law implementation[4]. Impatience driving, driving after alcohol abuse, lacks of helmet use, and poor road conditions have been reported as some of the factors attributing to RTA in other parts of the world [16,21]. Previous epidemiological studies have reported RTAs and falls as the most common cause of mandibular trauma in developing countries [22]. However, physical violence has been reported as main cause of mandibular fractures in developing
countries [23].

The common anatomical fractures site either bilaterally or unilaterally was parasymphysis (43%), followed by angle (30%) and the subcondylar region (27%). Other fracture sites; condyle, ramus, body, coronoid and symphysis together accounted for (48.5%) of the fractures. Parasymphysis being the most common site of mandibular fracture has been reported in many studies [16,24] which is followed by symphysis and condylar fractures [25]. However a study by Iqbal et al stated that the combination fractures are the most common type of fracture followed by parasymphysis and condyle fracture [26]. We also observed that that RTA caused proportionally more concurrent mandibular fractures. Literature reports that the etiology and anatomic sites of mandibular fracture may be correlated and is evidenced by the fact that majority of parasymphysis fractures occur as a result of an RTA [4]. In this study fracture site varied with age and gender. The parasymphysis fracture with a small proportion occurring elsewhere in the mandible was reported in younger populations while in the older population of this study reported parasymphysis followed by angle and subcondyle fracture.

Our study had several limitations, as in this study data was collected retrospectively in which most of the patients data was incomplete. Furthermore, our study had a relatively smaller sample size with limited duration. Moreover, data for this study was only collected from the hospitals of Islamabad. Future studies should use a prospective, cohort study design with a larger duration and include multiple cities.

Keeping the findings of the study in mind, awareness programs should be executed to develop driving sense among the population and strict regulation of traffic guidelines must be implemented.

CONCLUSION

In this study we conclude that males belonging to the age group of 21-30 years are most frequently prone to mandibular fractures. The most common site of fracture is the parasymphysis followed by angle of mandible and most common cause being road traffic accidents (RTA) followed by history of fall and interpersonal violence.

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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

A Comparison of the Efficacy of Lycopene and Intralesional Steroids in the Management of Oral Submucous Fibrosis

Zehra Azher Jawa[1], Tauseef Zahra[1], Laila Azher Jawa[2] and Asif Nazir Ch[1]

ABSTRACT

Objective: The purpose of this study was to evaluate and compare the efficacy of oral lycopene with intralesional steroid injection and in combination.

Study Design: Randomized controlled trial study

Place and Duration of Study: This study was conducted at the Department of Oral and Maxillofacial Surgery (Surgical Unit 2), NID, Multan from May 2021 to February 2022.

Materials and Methods: Total 45 patients of OSF participated; three groups each containing 15 subjects were formed. Oral lycopene on daily basis was given to subjects in Group I, biweekly intralesional triamcinolone (40 mg/ml) was administered in participants of Group II and Group III received combination (biweekly steroid injection and daily lycopene) for a period of three months. Any increase in mouth opening and decrease in burning sensation of oral mucosa was noted monthly.

Results: Most of the participants in our study 60% were young male adults and 40% were females participated in our study also comes under the category of young adults. Therefore, the mean age of the subjects in this study was 27.9±3.1 years. There was significant increase in mouth opening in all groups with $p \leq 0.04$. Group III showed relatively increased mouth opening followed by group II and III. We noticed almost complete relief of burning sensation in subjects of all three groups, rapid decline in the burning sensation was observed in group I.

Conclusion: Combination of oral lycopene with steroid injection is more effective in minimizing the symptoms of OSF

Key Words: Trismus, Lycopene, Triamcinolone, Areca nut, Mouth opening, burning sensation

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INTRODUCTION

Oral submucous fibrosis is a chronic, incapacitating disease which is progressive in nature with a considerable increased risk of cancer[1]. This condition affects people of all age groups and both genders, more common in population of subcontinent and its migrants. Countries like Pakistan, India, Bangladesh and Iran are main victims and the reason of it is that habits like chewing areca nut, betel quid and tobacco are common among population of these countries. Above all of that what makes the situation worst is easy availability of these things in these countries. The dilemma is that mostly young adults are suffering from this premalignant condition.

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Schwartz (1952) was the first to account the cases and coined the term "atrophic idiopathica mucosa oris" to describe an oral fibrosing disease occurring in five Indian women from East Africa[2,3]. Latter Joshi termed the condition as oral submucous fibrosis[3].

Etiology of OSF is ambiguous, different risk factors like chewing areca nut, betel quid, and tobacco, intake of spicy food, nutritional deficiencies, genetics and collagen disorders have been recommended to be contributory[4]. This condition is characterized by stiffness of oral mucosa which differs in intensity. Fibroelastic transformation of juxta-epithelial layer occurs, chiefly Type I collagen with variable amounts of other types of collagen constitute fibrosis[5]. It occurs when the balance between synthesis and degradation of collagen is disrupted, which leads to an increase in the total amount of collagen over a period of time[6]. Initial outcomes of this disruption in collagen metabolism are restricted opening of mouth and burning sensation. Risk of developing oral cancer is its grave complication. Broadly two treatment modalities, conservative and surgical methods exist for treatment of OSF; yet significant component of the treatment is to quit the causative habits.

The medical treatment includes injection of steroids, hyaluronidase, placental extract, interferon-γ, collagenase, trypsin, moreover oral pentoxifylline, zinc

and lycopene. Among all of the above lycopene is more commonly used which is a natural pigment in plants and have the ability to reverse the pathogenesis of OSF[7]. Carotenoid drops the prevalence of premalignant lesions and cancer of oral cavity.[8]

MATERIALS AND METHODS

This study was conducted from May 2021 to February 2022 at department of Oral and Maxillofacial Surgery (Surgical Unit 2), NID, Multan. This study was commenced after clearance was obtained from the Institutional ethical committee. Forty five participants of either gender were randomly divided into three groups, each group had 15 subjects.

All the participants were informed about the study and consent was taken. Detailed medical history including the symptoms and history of associated habits such as chewing of areca nut, gutka, betel quid, smoking, pan-masala and alcohol drinking was recorded. Patients who had severe systemic diseases, active oral infections and allergies were excluded.

The premalignant potential of OSF was explained to all the participants and they were counseled and encouraged to quit the habit of chewing areca nut and all its form. They were also motivated to improve their oral hygiene.

Diagnosis was done according to clinical criteria like trouble in eating spicy food, restricted opening mouth, blanched oral mucosa and presence of fibrous bands on palpation. Buccal mucosa was common site.

The chosen participants included all age groups, both males and females and of all socioeconomic status. In our study youngest participant was 16-year-old boy and oldest was 65-year-old man. The number of males and females in our study were 27 and 18. The mean age in group I, II and III were 26.3, 29.8 and 27.5 respectively. Subjects in group I had to take 10mg of oral lycopene every day. On the other hand subjects in group II received intralesional triamcinolone (40 mg/ml) once in 2 weeks (Fig.1). The participants in Group III received intralesional triamcinolone biweekly and lycopene daily for a time period of three months.

In this study two parameters were analyzed, first parameter was to assess the improvement in mouth opening in millimeter (mm) and the second one was sensation of burning in oral mucosa which was recorded by visual analog scale (VAS).

The interincisal mouth opening was recorded using a standard steel scale. The distance between the upper and lower central incisal edges at maximal unaided mouth opening was measured (Fig.2). These two parameters were recorded before starting the treatment and then monthly for consecutive 3 months. Data was entered and examined using SPSS 22.0. ANOVA and Tukey's test for group comparisons were used.

RESULTS

In our study there were total forty five participants, age ranging from 16 years to 65 years. Most of the participants in our study 60% were young male adults and 40% were females participated in our study also comes under the category of young adults. Therefore, the mean age of the subjects in this study was 27.9±3.1 years. The gender distribution in each group is shown in Fig.5. Restricted mouth opening was the most common symptom among all the subjects which is followed by burning and sensation in the oral mucosa. In some patients other symptoms like pain, difficulty in swallowing, difficulty in speech and restricted tongue movements were also seen. In Groups I average baseline mouth opening was 18.13 mm, in group II, 18.07 mm and in group III it was 17.53 mm. The inter-incisor distance at the end of the study was 25.74 mm, 22.06 mm and 26.84 mm in Groups I, II and III with mean increase in mouth opening of 7.67 mm, 3.93 mm and 9.31 mm respectively as shown in Table 1.

At the end of the study there was mean decrease in burning sensation of 9.4, 8.5 and 9.6 in groups I, II and III accordingly, as shown in Table 2. No side effects to the treatment were found.

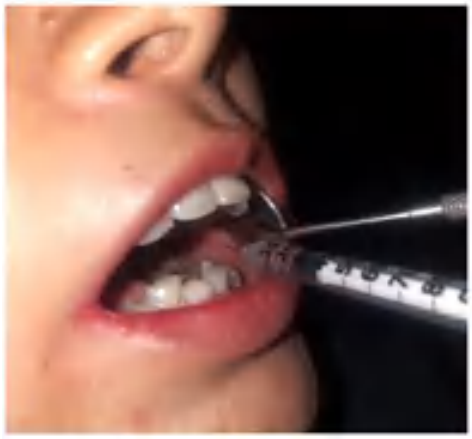

Figure No.1: Infiltration of Intralesional Steroid

Figure No.2: Measuring Interincisal Distance

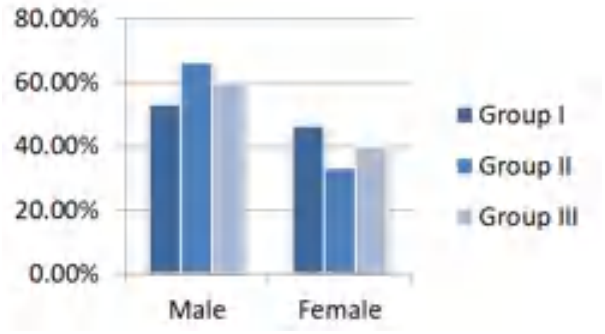

Figure No.3: Gender Distribution in Different Groups

Table No.1: Mouth Opening before and After Treatment (Mm)

Group	Baseline	After 1 month	After 2 months	After 3 months
I	18.13	19.50	20.44	22.06
II	18.07	20.40	23.30	25.74
III	17.53	20.56	23.52	26.84

Table No.2: Burning Sensation before and After the Treatment

Group	Baseline	After 1 month	After 2 months	After 3 months
I	10	3.5	2.1	0.6
II	10	6.3	4.4	1.5
III	10	4.6	2.1	0.4

DISCUSSION

OSF was defined by Schwartz as 'a chronic disease affecting any part of the oral cavity and sometimes the pharynx, associated with inflammatory reaction of juxta-epithelial followed by a fibro-elastic change of the lamina propria which leads to rigidity of oral mucosa and results in trismus. Oral submucous fibrosis (OSF) is a potentially precancerous condition, its prevalence is rising because of increasing habits like chewing areca nut, betel quid and tobacco. Various modes of treatment are present for managing OSF among which more common in practice are intralesional steroids and lycopene. There are various risk factors, but most important factor chewing areca nut in different forms such as pan masala, betel quid, gutka etc. There is substantial evidence present which indicates an important role of areca nut in the etiology of OSF[9,10,11]. Active ingredients in areca nut arecoline, arecaidine and tannin have capability to modulate metabolism of collagen. They stimulate fibroblast proliferation and disrupt normal collagen synthesis, leads to an increased fibrosis pointing towards a dose dependent relation between areca nut and causation of the disease[11,12]. Intralesional steroids hinder fibroblast proliferation of fibroblasts and syntheses of collagen[13]. Triamcinolone acetonide was chosen for the study as it has longer duration of action and less side effects[14]. Lycopene is a red carotenoid which is natural pigment widely found in red or pink fruits and vegetables, such as tomatoes, water melon etc and it is a potent quencher of singlet oxygen[15]. It has anti-oxidant and anti-carcinogenic properties[16]. It has also demonstrated benefits in cancers of the prostrate, pancreas and oesophagus[17].

In our study, there was a significant difference in improvement of mouth opening between the Group I and II ($p \leq 0.04$). In our study there was a significant increase in inter-incisal distance with the use of intralesional triamcinolone this is supported by the study conducted by Ameer et al[18]. But maximum decline in symptoms of OSF was noticed in group III which is similar to the study of Samuel HT[19]. Rapid reduction in the burning sensation was more in group I that could be supported by the study of Kumar et al[20].

CONCLUSION

There was rapid relief in the symptoms of OSF with combination therapy. Hence, it is more efficacious to use intralesional triamcinolone along with lycopene.

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

A Comparison of the Accuracy of the London Atlas and Demirjian Age Estimation Methods Based on Panoramic Radiography of Developing Teeth

Laila Azher Jawa[1], Zehra Azher Jawa[2] and Zubair Hassan Awaisi[1]

ABSTRACT

Objective: To compare two age estimation methods in children by using Demirjian's and the London Atlas of Tooth Development methods and to evaluate among these two methods which is more accurate.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Orthodontics at Nishtar Institute of Dentistry, Multan from May 2021 to February 2022.

Materials and Methods: To conduct this research we included OPGS of 100 children of 7 and 16 years of age group, proforma each patient was filled containing their date of birth and date of X-ray done. Then we assessed each radiograph to find out the developmental stage of tooth in respective region. Dental age estimation was calculated by using Demirjian and London Atlas methods and the difference and correlations between these two methods and chronological age was assessed. Differences and associations between two selected dental age estimation methods and chronological age were evaluated by paired t-test and Pearson's correlation analysis. P value ≤0.05 was considered as significant.

Results: In this study the mean chronological age evaluated was 10.23±2.7 years, while in London atlas method it was estimated as 10.11±2.91 and in Demirjian 10.44±2.5 years. In few number of individuals, Demirjian's method slightly over-estimated the age in females than males, while in London Atlas it underestimated the age in girls than boys, but the overall difference was not statistically significant. Both of the methods which we used in our study to determine dental age have no significant differences between them in terms of accuracy. P value for London Atlas was 0.14 and for Demirijian 0.15.

Conclusion: These two methods are reliable in estimating age of individuals of unknown chronological age.

Key Words: Age estimation, Dental age. Demirjian method. London Atlas of tooth development and eruption method, Chronological age

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INTRODUCTION

In different fields like in forensic and pediatric dentistry and also in orthodontics knowing exact age is of high importance. Tooth development is widely used in determining age and level of maturity. Age plays a critical role in orthodontic treatment planning, pediatric dentistry, surgeries[1,2]and also has a significant part in terms of legal perspective[3,4,5] and forensic dentistry[6].

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Different studies from time to time have shown that from living persons to dead, accurate estimation of age is very important. Ever since its importance was realized various methods and techniques were proposed by researchers and dentists to evaluate age with accuracy. Age simply can be chronological that is the age which can be easily calculated by date of the birth and then there is a biological age that can be assessed by secondary sexual characteristics, bone maturity and dental age. If in some instances chronological age is not known and accurate age estimation is required as mentioned earlier than there are different methods to assess age, among these techniques developmental and mineralization stages of teeth to estimate age can be used and it is the most practical option when correlated with the patient's chronological age. Another advantage of this method is that it is not afflicted by the environmental factors. Dental age estimation (DAE) method using radiographs are non-invasive, simple, fast and reproducible[7,8]. Demirjian method was developed on French-Canadian population in 1973 is the most

commonly used radiograph-based method till now[9,6]. The London Atlas[10] technique is another approach for age estimation, this method is founded on the developmental stages of crown and root of teeth and has specific reference material for age estimation from third molars. The accuracy of these methods with chronological age and with other methods were evaluated before in many studies in different population but in Pakistan only few numbers of studies have been conducted. In past few years many unfortunate events like plane crash to non-consented marriages of minors had occurred in Pakistan where age estimation was crucial to identify individuals from remains to solve the legal issue respectively.

"Age is just a number" is a famous quote but it is not just a number in much legal, medical, dental and forensic perspective, to identify age is an important component in making decisions to solve the problems, for treatment planning and etc. In orthodontics if accurate age of patient is known it helps to plan treatment, for example many orthopedic or growth modification appliances are only applicable up to specific age, after that certain age they are of no help. There is another advantage of finding dental age in orthodontics, if chronological age of patient is known and there is a difference of ±2 years exist between dental and chronological age than we can assess from these findings that patient is early grower or late grower, this helps in planning a treatment[11].

As the importance of accuracy in age estimation was understood, many dental age evaluation methods were assessed to find out which technique is most trusted. In our study we compared the two most accurate dental age estimation methods found in various studies, in this study we used the London Atlas technique and Demirjian's method to estimate age. In the present study we assessed and compared the accuracy of these two methods.

MATERIALS AND METHODS

Study was conducted from May 2021 to February 2022 at department of Orthodontics at Nishtar Institute of Dentistry, Multan. For the purpose of comparison and to find out the accuracy between the two methods of the dental age estimation, in this cross-sectional study we evaluated OPGs of 100 participants in their growing age of between 7 to 16 years. This study group consisted of 45 boys and 55 girls and they were divided into four groups according to age. Dental age was assessed by Demirijian's and London Atlas method. The chronological age was obtained by subtracting date on which OPG was taken with the date of birth of the individuals[12].

Differences and associations between two selected dental age estimation methods and chronological age were evaluated by paired t-test and Pearson's correlation analysis.

RESULTS

In the current study the known chronological age of the participants was registered, which was calculated by the method explained above and than we compared the calculated and documented chronological age of each participants with the dental age which was estimated by London Atlas and Demirijian's methods separately, then with each other. In this study the mean chronological age evaluated was 10.23±2.7 years, while in London atlas method it was estimated as 10.11±2.91 and in Demirjian 10.44±2.5 years. These results showed that overall there was no significant difference between the estimated mean ages. In few number of individuals, Demirjian's method slightly over-estimated the age in females than males, while in London Atlas it underestimated the age in girls than boys, but the overall difference was not statistically significant. The second method mentioned was simple and quick to apply and time saving with equivalent or has slightly more accuracy than demirijian in this specific study. In our study the results showed that in majority of the participants the frequency of deviation from chronological age lies within range of ±0.5 year as shown in table 1. P value was significant below 0.05. Pearson's correlation coefficient documented strong relation between chronological age and ages estimated by Demirijian and London atlas methods. No significant difference was detected between two methods and chronological age.

Table No.1: The frequency of deviation of ages evaluated by Demirijian's and London Atlas method from the chronological age

Chronological age	Gender	London Atlas			Demirijian's method		
		>1 y	-1 to +1	<-1year	>1 y	-1 to +1	<-1 y
7-9	Boys	1	2	2	3	1	1
	Girls	1	3	1	2	2	1
10-12	Boys	1	10	1	2	9	1
	Girls	2	12	4	3	13	2
13-15	Boys	4	16	1	2	18	1
	Girls	4	17	3	4	18	2
>15	Boys	2	3	1	2	2	2
	Girls	3	1	4	2	5	1

Table No.2: Ages estimated by London Atlas and Demirijian method and mean chronological age

Age	Boys		Girls		Total	
	Mean	SD	Mean	SD	Mean	SD
Chronological age	9.8	2.92	10.1	2.28	10.23	2.7
London atlas	9.7	2.32	10.2	2.7	10.11	2.91
Demirijian's method	9.6	2.39	10.21	2.7	10.44	2.5

In the above table it was observed that majority of deviation ranges between -1 to +1. Therefore, overall difference was not found to be significant. Deviation categorized by age and sex were also insignificant. Positive correlation was observed between chronological age and age estimated by the two methods.

DISCUSSION

Age determination is of a fundamental importance regarding many procedures including medical, legal and forensic perspectives and also plays a crucial part in dentistry as in treatment planning in orthodontics and pediatric dentistry and surgeries[1,2].

The estimation of age accurately of a person is of central significance in law when crimes were committed by minors, to rule out underage slavery and employment, to solve the issues related to child marriage and in identification of individuals in cases of mass calamity in forensic medicine. In recent years, in our country many cases have been reported regarding the abovementioned crimes. Many countries are facing an alarming expansion in crime rate committed by juveniles[6] and age forgery in sports[6] which has increased the demand to find out the accurate estimation of age, so that only those who are guilty of crime can receive punishment.

In various fields of dentistry dental age estimation has gained popularity due to its central importance in planning treatment, like in orthodontics, in pediatric dentistry, in forensic dentistry and in maxillofacial surgeries[1,2].

For the age estimation various methods have been proposed including height, weight, secondary sexual characteristics, bone and dental development[12]. Among these the one mentioned in last is commonly used. Dental development stages regarded as the most appropriate technique for determination of age because these stages are resistant to environmental changes unlike other methods which can be severely affected by intrinsic and extrinsic factors like hormonal changes, behavioral changes and socioeconomic conditions[12].

In our study for the purpose of comparison and to check the accuracy we selected two methods, one is Demirjian[9] method of dental age estimation which is simple, non-invasive and one of the oldest and the most widely used method[6]. The second technique is London Atlas method which we used in our study, it is also simple, novel, fast and accurate method that was developed by Alqahtani et al in 2010[12], also known as atlas of tooth development and eruption. The objective of our study was to establish a comparison between the two chosen methods and to assess the precision of the London Atlas and Demirjian age estimation methods and for this purpose we used panoramic radiographs of developing teeth.

According to the study done by Bianca Gelbrich[13]and coworkers, the London Atlas method provides more precise estimates of dental age. In our study the dental age estimated by London atlas method also showed more accuracy than demirjian but the difference between the two was not found to be significant enough. In comparing our study with other relevant studies like by Chhaparwal et al[3], a strong correlation between chronological and dental age estimated by Demirjian method was observed like in our study.

V. Jain et al[6]used the original Demirjian method in OPGs of 102 individual showed significant mean underestimation of age unlike our study, in which among sample few were overestimated but overall difference was not significant. In our study frequency of deviation of age estimation of London Atlas from chronological age was between +1 to-1, it was similar to the results found from the study conducted by Alshihri et al[14] in Saudi Arabian children and adolescents in which they used London Atlas method for age estimation, the majority (65.5%) of estimate frequency deviation was within 12 months of chronological age which was calculated. The current study demonstrated Demirjian's method to have accuracy in both genders similar to the study done by Javadinejad et al[1].

The main goal of our study was to investigate if any difference exists between dental ages estimated by the Demirjian and the London Atlas method and chronological age and how accurate the two methods were. The result of our study was similar to many studies like V. Jain et al[6], Alshihri et al[16]and Rezwana Begum Mohammed et al[15], they all documented that these age estimation methods are reliable and accurate. Similar to the study done in Sri Lankan population by S. Ranasinghein[16] which they compared three accuracy of the three dental age estimation methods including Demirjian and doccumented that all three methods are reliable and applicable. By comparing different studies we came to know that in each population different methods are more reliable and in our study both methods prove to be applicable and reliable in our population.

CONCLUSION

The present research showed that London Atlas and Demirjian's methods determine dental age of children and adolescents with acceptable accuracy. Both of the methods are simple but the one mentioned first was more easy and time saving and slightly more accurate than demirijian in this specific study.

Author's Contribution:

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Revisiting Critically:	Laila Azher Jawa, Zehra Azher Jawa
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Frequency of Metabolic Syndrome in Pre-Eclamptic Women Presenting at Tertiary Care Hospital, Hyderabad

Fahmida Parveen Memon, Ambreen Mughal, Shehzadi, Ruby and Nusrat

ABSTRACT

Objective: To determine the frequency of metabolic syndrome in Pre-eclamptic women presenting at Tertiary Care Hospital, Hyderabad.

Study Design: Descriptive cross sectional study

Place and Duration of Study: This study was conducted at the Department of Obstet and Gynae, Liaquat University of Medical and Health Sciences Hospital, Hyderabad from January, 2021 to December, 2021.

Materials and Methods: A total of 150 patients of age 20-40 years of any parity, presenting with preeclampsia 24-40 weeks of gestation were included. Patients with history of congestive cardiac failure, T2DM, CRF and history of hypo or hyperthyroidism were excluded. Metabolic syndrome was as defined according to NCEP, ATP-III criteria with abdominal obesity (waist circumference) for south Asian (>88 cm for women) plus any two of the following: Triglycerides > 150 mg /dl, HDL for women <50 mg/dl, Blood pressure >130/90 mmHg and Fasting blood sugar >110 mg/dl.

Results: Overall, 150 patients were included in our study. Out of these, 58 (38.7%) were suffered from metabolic syndrome (Figure. I). The average age, gestational age, BMI, fasting blood sugar, socioeconomic status and occupational status of metabolic syndrome and non-metabolic syndrome patients was almost equal, (p>0.050). Parity 0-2 was most common in non-metabolic syndrome patients, (p=0.002)

Conclusion: There is a high prevalence of metabolic syndrome in Preeclampsia women. Early diagnosis, compliance to preventive measure and treatment of underlying risk factors of metabolic syndrome can reduce its prevalence rate.

Key Words: Hypertension, Lipids, Metabolic syndrome, Obesity, Preeclampsia

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INTRODUCTION

Hypertensive disorders are major causes of maternal morbidity and mortality in pregnant women. Hypertension accounts for 5 to 10 percent of all complications of pregnancy[1]. In developing countries prevalence rate of preeclampsia has been increased from 1.8% to 16.7%[2]. Severity of hypertension or preeclampsia is strongly associated with perinatal outcomes and extent of different fetal injuries. Fetal growth retardation is main complication of preeclampsia due to the utero-placental vascular insufficiency which ultimately results in insufficient nutrition supply to the fetus[3].

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Increased body mass index or obesity in women make them more susceptible to develop preeclampsia, number of studies have conducted and reported that obesity causes elevation in inflammatory markers, insulin resistance and cardiovascular diseases and enhance the probability of preeclampsia five times more[4]. Some other risk factors include multiple pregnancies, preexisting diabetes, null parity, renal disease, autoimmune disease older maternal age[5].

According to NCEP (National Cholesterol Education Program) presence of minimum three clinical features low high density lipoprotein, high triglycerides, abdominal obesity, increased fasting blood sugar and high blood pressure is a strong indicator of metabolic syndrome[6]. Late recognition of metabolic disease may lead to cardiovascular diseases and mortality. Researches on cardiovascular specialty have shown that deranged lipid profile directly influenced endothelial function, prolong dyslipidemia can cause endothelial dysfunction[7].

In recent literature it has been described that maternal pre-disposition towards preeclampsia may be predicted by monitoring change in lipid values[8]. Association between hypertension or preeclampsia and altered total cholesterol, high density lipids and triglycerides level is well documented[9]. Furthermore, it was also reported

that abnormal lipids may lead to increase in thromboxane and low prostaglandins. This change in antioxidants and lipid peroxidase level can cause preeclampsia in pregnant women[10].

The rational of this study was to determine the frequency of metabolic syndrome in pre-eclamptic women presenting at tertiary care hospital, a local study conducted in Pakistan at Jinnah Post Graduate Medical Centre showed the prevalence of recurrent pre-eclampsia 25.26% and the incidence of metabolic syndrome of 19.3%. Appropriate strategies may be planned in prevention and treatment of metabolic syndrome which may decrease frequency of pre-eclampsia in our population.

MATERIALS AND METHODS

Study was conducted at obstetrics and gynecology department of Liaquat University of medical and health sciences hospital Hyderabad from 20th January 2021 to 19th December 2021 in 6 months duration. This study was conducted after approval from ethical board of hospital. Age: 20-40 years, women of all parity with Pre- eclampsia, gestational amenorrhea of 24-40 weeks calculated by early scan of first trimester, raised blood pressure of at least 140/90 mmHg or more on two separate occasions, at least 4 hours apart in the presence of proteinuria were included. Non-consenting, inadequate information regarding Pre-eclampsia diagnosis in the medical record of the patient, pregnancy complicated by Pre-eclampsia before the established period of five years, critically ill patients, patients with history of congestive cardiac failure, known case T2DM, patients with history of chronic renal disease, patients with history of hypo or hyperthyroidism were excluded. Permission from the institutional ethical review committee was taken prior to conduction of study. Written informed consent was obtained from every patient.

Preeclempsia was diagnosed as per WHO guidelines, two consecutive reading of high blood pressure (≤140 systolic and 90 diastolic) with difference of at least four hours after gestation period of 20 weeks and presence of associated proteinuria (300mg or above protein in 24 hours urine collection).

Brief history of hypertension was taken. Five components of metabolic syndrome were assessed. Blood pressure was measured by the researcher using a standard mercury sphygmomanometer with different cuff size twice, repeated after five minutes and the mean systolic and diastolic blood pressure was used for analysis. For variable of obesity, BMI was calculated as weight in kilograms divided by the square of height in meters.

Abdominal (waist) circumference was measured by drawing a horizontal line above the upper most lateral border of the ilium and then cross the line to indicate the midaxillary line of the body. Measurement was made at the end of normal expiration at the nearest centimeter. Fasting blood sugar levels and lipid profile (after 12 hours of fasting) were taken after five ml of fasting venous blood sample withdraw from the anti-cubital vein of each participant after taking all aseptic precautions using sterile needles and syringes. Blood sugar and triglycerides were estimated by enzymatic method while high density lipoprotein (HDL) by precipitation method. Metabolic syndrome was as defined according to NCEP, ATP-III criteria with abdominal obesity (waist circumference) for south Asian (>88 cm for women) plus any two of the following: Triglycerides > 150 mg /dl, HDL for women <50 mg/dl, Blood pressure >130/90 mmHg and Fasting blood sugar >110 mg/dl.

Data was analyzed on SPSS version 16. Mean and standard deviation were calculated for age, parity, height, weight, BMI and gestational age. Frequency and percentage were calculated for socioeconomic status, occupational status, parity and metabolic syndrome (yes/no). P-value of ≤0.05 was taken as statistically significant.

RESULTS

Table No.1: Association of metabolic syndrome with demographic and baseline characteristics

Variable	Metabolic syndrome		p-value
	Yes, N (%)	No, N (%)	
Age (years)	28.29±4.59	27.34±5.05	0.250
Gestational age (weeks)	30.09±3.93	30.79±4.16	0.302
BMI (kg/m^2)	29.84±4.01	29.77±4.32	0.919
Fasting blood sugar (mg/dl)	101.37±14.26	101.75±13.71	0.872
Parity			
0-2	39 (67.2)	81 (88.0)	0.002
>2	19 (32.8)	11 (12.0)	
Socioeconomic status			
Lower	15 (25.9)	24 (26.1)	0.060
Middle	19 (32.8)	46 (50.0)	
Upper	24 (41.4)	22 (23.9)	
Occupational status			
Employed	33 (56.9)	66 (71.7)	0.062
Un-employed	25 (43.1)	26 (28.3)	

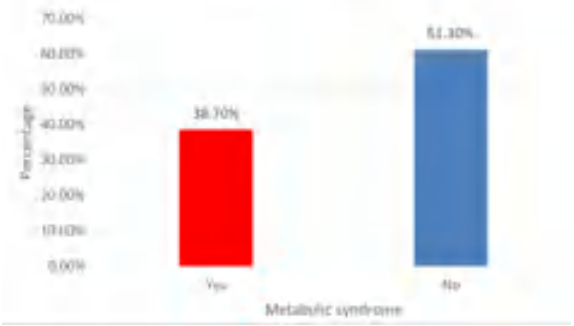

Figure No.1: Metabolic Syndrome Distribution

Overall, 150 patients were included in our study. Out of these, 58 (38.7%) were suffered from metabolic syndrome (Figure. I). The average age, gestational age, BMI, fasting blood sugar, socioeconomic status and occupational status of metabolic syndrome and non-metabolic syndrome patients was almost equal, (p>0.050). Parity 0-2 was most common in non-metabolic syndrome patients, (p=0.002) (Table. I).

DISCUSSION

Increase in blood pressure during pregnancy and insulin resistance has been described in numerous previous studies[11]. Preeclampsia accounts for upto 8% of total pregnancies and contributes to significant neonatal and maternal deaths. Treatment of underlying causes should be considered in start of pregnancy. In a study conducted by Mazar et al[12] reported that metabolic score or presence of insulin resistance, high blood pressure and deranged lipid profile is independent indicator of preeclampsia, association of these metabolic indicators with preeclampsia is approved.

In our study metabolic syndrome was observed in 38.7% of preeclampsia women and mean gestational age of patients was 30.09 ± 3.93 weeks that shows complications of end stage pregnancy. A study was conducted by Zain et al[13] reported 46.7% metabolic syndrome incidence and mean gestational age was 35.43 weeks in his study. Another study by Ray et al[14] concluded a positive correlation between preeclampsia and indicators of metabolic syndrome like maternal triglycerides.

Dane et al[15] conducted a study on 169 pregnant women and assessed indicators of metabolic syndrome in pre-eclamptic women after 32 weeks pregnancy. Results of this study show that values of indicators were higher in all parameters among preeclampsia women as compare to controls like mean blood pressure in cases was 135mmHg systolic and 90mmHg diastolic pressure, but in control group it was 100 mmHg (P < 0.001). In another study by Sibai et al[16] frequency of metabolic syndrome among women with preeclampsia was observed 27%.

In our study mean BMI of patients was observed 29.84±4.01 kg/m^2 among preeclampsia women. Beigh et al[17] also reported correlation between weight gain in pregnancy and development of hypertension and preeclampsia in late weeks of pregnancy. Metabolic syndrome was observed in 4.4% of preeclampsia women. Lorenzo et al[18] compared metabolic syndrome patients with healthy controls and reported that blood disorders are more common in women with metabolic syndrome (P<0.001).

Studies conducted by Gratacós et al[19] and Zahran et al[20] also examined preeclampsia patients and measured their metabolic syndrome indicators. Significant difference was observed between markers of these levels and women with severe hypertension (P<0.001). Triglyceride was found deranged in both studies which is strong indicator of metabolic syndrome.

CONCLUSION

Metabolic syndrome is highly associated with preeclampsia, early diagnosis, compliance to preventive measure and treatment of underlying risk factors of metabolic syndrome can reduce its prevalence rate.

Recommendations: Therefore, we recommend that there should be public screening and public awareness programs on national and regional levels to modify these factors and improve the mortality and morbidity of community due to heart diseases

Author's Contribution:

Concept & Design of Study:	Fahmida Parveen Memon
Drafting:	Ambreen Mughal, Shehzadi
Data Analysis:	Ruby, Nusrat
Revisiting Critically:	Fahmida Parveen Memon, Ambreen Mughal
Final Approval of version:	Fahmida Parveen Memon

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

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Original Article

Management of Hypertension before Surgeries of ENT & Eye

Can Unexpected Preoperative Hypertension be Managed by Reassurance and Anxiolytics and Avoid Postponement of Eye and ENT Surgeries?

Mohammad Mohsin Rana[1], Sajid Rashid Nagra[2], Muhammad Saleem Akhtar[1], Danish Gani[3], Zafar Iqbal Zafar[3] and Nauman Khalid[4]

ABSTRACT

Objective: To highlight the fact that single preoperative high reading of Blood pressure doesn't have any effect on the surgical outcome in non-cardiothoracic and major abdomino-thoracic surgeries. In common ENT and Eye surgeries this shall not be a reason for the postponement or delay in the procedures, most of these situations can be managed by reassurance and anxiolytics

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 Jan to June, 2022.

Materials and Methods: All subjects between 20-90 years of age of both sexes, presenting for pre-operative assessment before any planned Eye and ENT surgery were assessed by measuring their BP. If it was found to be above 140/90 mmHg, they were included in this study.

Results: Out of 288 patients, 25% (n 72) were found to have their BP above 140/90 mmHg. 42% (n 30) were known hypertensives, out of these 37% (n11) missed the morning dose of their antihypertensive medicine and were excluded from the study. Out of the remaining 61 when BP was rechecked after 30 minutes of reassurance and comfortable , stress free environment away from OT, 18 (29%)patients had BP reading below 140/90 mmHg.

Remaining 43 (70.49%) patients were given tablet Alprazolam 0.25 mg orally and reassured again. BP was checked after 1 hour. Majority 31 (72.5%) out of 43 responded to reassurance and anxiolytics and BP returned to below 140/90mmHg and were issued fitness for anesthesia and surgery. 12 patients didn't responded and their BP remained above the limit of 140/90mmHg and their surgery was postponed. Their BP didn't responded to either reassurance or anxiolytics.

Conclusion: A simple explanation and reassurance by hospital staff may be sufficient to smoothen the patient's anxiety. Missed dose of routine antihypertensive medicines shall be given in cases where only regional or local anesthesia is planned.

Key Words: Hypertension, pre-operative hypertension, Eye and ENT surgery

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INTRODUCTION

All routine pre-anesthetic assessments includes vital signs, most importantly BP and a normal or near normal BP is considered mandatory for anesthesia fitness. Many a time one is confronted with unexpected hypertension in previously normotensive or well controlled hypertensive on the morning of planned common Eye and ENT surgeries. It is one of the commonest reasons for a delay or even postponement of the procedure. This study was carried out to assess the contribution of anxiety and whether it could be controlled simply by reassurance and/or use of simple anxiolytics in these situations to avoid the postponements of the surgical procedures. Recent NICE guidelines reiterate the importance of the threshold of systolic 180 mm Hg and diastolic 110 mm Hg. The grade of HTN may not be applicable to the perioperative HTN as it differs in all three important aspects of underlying mechanism, treatment responsiveness and consequences depending on patient characteristics and invasiveness of surgical procedure. The American College of Cardiology/American Heart

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Association (AHA) guidelines do not even mention hypertension, probably because of lack of evidence of its influence on perioperative outcome. [1]

MATERIALS AND METHODS

All subjects between 20-90 years of age of both sexes, presenting for pre-operative assessment before any planned Eye and ENT surgery were assessed by measuring their BP. If it was found to be above 140/90 mmHg, they were included in this study. Consenting patients were referred to the physician for proper assessment and management prior to surgery. They were reassured by trained paramedical staff and BP was rechecked after 30 minutes. If it settled down to below 140/90 anesthetic fitness was issued by the concerned physician. If the BP stayed above the 140/90mmHg level tablet Alprazolam 0.25 mg was given with a small sip of water along with another session of counseling and reassurance, BP was reassessed after 1 hour, if it settled down to below 140/90 anesthetic fitness was issued by the concerned physician.

Inclusion Criteria: 20-90 years age, both sexes, presenting for eye and ENT surgery.

Exclusion Criteria: Known hypertensive who have missed the routine morning dose of antihypertensive medicine.

Seriously sick patient or terminally ill patient.

Secondary Hypertension and pregnancy

Major end organ disease, liver, kidney, heart, lungs

Hypertensive urgency and emergency

Sample Size and Sampling Technique: A minimum sample size of 196 patients was calculated to maintain a 5 percent margin of error, a 95 percent confidence interval and a 75 percent response distribution, using a raosoft sample size calculator.

Statistical Analysis: Data analysis was conducted using Microsoft Excel version 2016 and Statistical Package for Social Sciences (SPSS) software version 25. Descriptive statistics (i.e. frequency distribution, percentages, mean and standard deviations) were used.

Disclaimer: This is an observational study. No monetary compensation was given to the patients. Informed consent was taken. Confidentiality and personal grace are ensured in all the examinations and questionnaires. There is no monetary interest or conflict of interest for all the contributing authors**.**

RESULTS

During the study period 288 patients presented for surgery in Eye [(67%) (n 192)] and ENT [(33%) (n 96)] Departments. On preoperative assessment, 25% (n 72) were found to have their BP above 140/90 mmHg. 42% (n 30) were known hypertensive, out of these 37% (n11) missed the morning dose of their antihypertensive medicine and were excluded from the study as per exclusion criteria. The remaining 61 were referred to physicians for further management by reassurance and/anxiolytics. Only these 61 patients were enrolled in this limb of the study.

Table No.1: Demography N 61

Gender and Eye/ENT Surgery	Eye Males	Eye Females	ENT Males	ENT Females
< 40	N1 (1.64%)	N 0	N 0	N1 (1.64%)
40-60	N13 (21.31%)	N10 (16.39%)	N 2 (3.28%)	N 3 (4.92%)
60-80	N16 (26.23%)	N10 (16.39%)	N 3 (4.92%)	N 0 (%)
>80	N1 (1.64%)	N 0	N1 (1.64%)	N 0

Table No.2: Preoperative BP

Gender and Eye/ENT Surgery	Eye Males	Eye Females	ENT Males	ENT Females
< 40	n1 (1.64%) 170/100	N 0	N 0	N1 (1.64%) 165/100
40-60	N13 (21.31%) 150-195/80-105 Mean,180/99 Median,182/100 Mode, 190/100 Sd, 10.07/3.14	N10 (16.39%) 155-210/95-115 Mean, 179/99 Median,180/100 Mode, 190/100 Sd10.28/3.37	N 2 (3.28%) 155/85 Mean165/100 Median165/100 Mode165/100 Sd 0	N 3 (4.92%) 155-170/90-100 Mean,171/90 Median, 165/85 Mode, 165/85 Sd, 11.5/8.6
60-80	N16 (22.22%) 175-195/95-105 Mean,175/94.2 Median,175/100 Mode, 180/100 Sd,13.9/8.8	N10 (16.39%) 165-190/95-105 Mean,180/100 Median,175/100 Mode, 170/100 Sd, 18.4/5.9	N 3 (4.92%) %) 165-185/85-100 Mean, 160/93 Median,155/90 Mode, 155/90 Sd, 8.6/5.7	N 2 (3.28%) 190/100 Mean,190/100 Median,190/100 Mode,190/100 Sd, 0
>80	N1 (1.64%) 190/100	N 0	N1 (1.64%) 180/105	n 0

All these patients were properly assessed by the physicians and a team of trained staffed reassured them. When BP was rechecked after 30 minutes of reassurance and comfortable , stress free environment away from OT, only 18 (29.5%) patients had BP reading below 140/90 mmHg.

Table No.3-A: Non-Responders

Gender and Eye/ENT surgery	Eye Males	Eye Females	ENT Males	ENT Females
< 40	n 0	n0	n0	n 0
40-60	n 9 (14.8%) 150-195/80-105 Mean Median Mode SD	n 7 (11.5%) 155-210/95-115 Mean Median Mode SD	n 1(1.64%) 165-185/85-100	n 2 (3.28%) 155-170/90-100 Mean Median Mode SD
60-80	n13 (21.31%) 175-195/95-105 Mean Median Mode SD	n 7 (11.5%) 165-190/95-105 Mean Median Mode SD	n 2 (3.28%) 165-185/85-100 Mean Median Mode SD	n 0
>80	n1 (1.64%) 190/100	n0	n1 (1.64%) 180/105	n0

Table No.3-B: Responders to Reassurance

Gender and Eye/ENT Surgery	Eye Males	Eye Females	ENT Males	ENT Females
< 40	n 1 (1.64%)	n0	n0	n 1 (1.64%)
40-60	n 4 (6.56%)	n 3 (4.92%)	n 1(1.64%)	n 1 (1.64%)
60-80	n3 (4.92%)	n 3 (4.92%)	n 1 (1.64%)	n 0
>80	n 0	n0	n 0	n0

Table No. 4-A: Responders to Anxiolytics

Gender and Eye/ENT surgery	Eye Males	Eye Females	ENT Males	ENT Females
< 40	n 0	N0	N0	N 0
40-60	N 7 (16.28%)	N 5 (11.5%)	N 1(1.64%)	N 2 (3.28%)
60-80	N 8 (18.6%)	N 6 (13.95%)	N 2 (3.28%)	N 0
>80	N 0(1.64%)	N0	N 0(1.64%)	N0

Table No.4-B: Non-Responders

	Eye Males	Eye Females	Ent Males	Ent Females
< 40	N 0	N0	N0	N 0
40-60	N 2 (3.28%) 150-175	N 2 (3.28%) 145-190	N 0	N 0
60-80	N5 (11.5%)	N 1 (1.64%)	N 0	N 0
>80	N1 (1.64%) 180/100	N0	N1 (1.64%) 180/100	N0

Remaining 43 (70.49%) patients were given tablet Alprazolam 0.25 mg orally and reassured again. BP was checked after 1 hour. Majority 31 (72.5%) out of 43 responded to reassurance and anxiolytics and BP returned to below 140/90mmHg and were issued fitness for anesthesia and surgery.

12 patients didn't responded and their BP remained above the limit of 140/90mmHg and their surgery was postponed. Their BP didn't respond to either reassurance or anxiolytics.

DISCUSSION

The National Institute for Health and Care Excellence (NICE) guidelines 2019 serve as basis for managing hypertension in adults. Recently, the Association of Anesthetists of Great Britain and Ireland (AAGBI) and British Hypertension Society (BHS) produced joint guidelines for simplified anesthesia management and categorized hypertension into 1-4 grades. The cardiovascular risk factors especially metabolic syndrome mostly going unnoticed for a long period or under treated in diagnosed cases.[2] Naturally one must seek evidence of occult or evident coronary artery disease (Q waves or T wave changes or left ventricle hypertrophy on ECG) and evidence of heart failure and target organ damage before proceeding for surgery in known hypertensive patients.[3]

Central systolic BP may be up to 40mmHg lower than peripheral systolic BP while diastolic BP remains

relatively constant. Non-invasive tonometry using arterial flattening is reliable surrogate when applied to radial, carotid or femoral artery.[4]

Like in almost every other system BP control has its own "homeostasis" mechanisms intended to ensure a constantly adequate organ perfusion with ever-changing demands of different organs in response to physical or emotional stress and or sleep. Blood pressure variability (BPV) is determined by the individual reactivity of their cardiovascular control mechanisms and have role in predicting cardiovascular risk. The BPV shall be related with mean BP levels, average BP and standard deviation. The average of daytime and night-time Bp with SD corrected for the respective duration of day and night with preference for nocturnal BPV. The magnitude of nocturnal dipping and morning surge shall also be taken into account. Similarly day-by-day home BPV and clinic-within-visit and visit-to-visit BPV was found to have its role in prognosis and risk stratification. Compliance with antihypertensive medication definitely smoothens and blunts the BPV, expressed as the smoothness index, longer acting drugs have an edge.[5]

According to the editorial of The British Journal of Anaesthesia, 2017, hypertension impacts 1 billion adults across the globe affecting up to 80% of patients in the general population above 60.[6] Contrary to popular notion multiple Randomized Controlled Trials (RCT) collectively favor a higher BP target due to safety and improved outcome.[7] Like any other surgery non-ocular complications like bronchospasm, cardiac arrhythmia, labile BP, silent myocardial ischemia and hypertensive emergencies during cataract surgery, hypertensive patients are at a higher risk.[8]

In this study out of 288 patients, every 4th persons was referred to physicians for reassessment on the day of surgery when assessed preoperatively. All were either normotensive or well controlled hypertensives when assessed on the time of taking appointment for a planned ENT or Eye surgery. 11 (37%) patients who didn't took their routine dose of morning antihypertensive medicine were excluded. These patients missed the morning dose of their antihypertensive medicine as they were asked to come in fasting state or as per common belief that fasting is mandatory for each surgery.

The remaining 61 patients were properly assessed by the physicians and a team of trained staffed reassured them in a comfortable, stress free environment away from OT, in 18 (29.5%) patients BP settled down to normal BP reading i.e. below 140/90 mmHg. This strongly points out that this temporary rise in BP was simply anxiety response. All had clear cut evidence of anxiety manifesting as palpitation, tremors and cold sweaty palms. Though not formally calculated majority pointed out to the fear of surgery, claustrophobia of being alone in the OT, uncomfortable theaters waiting room temperature especially in when in OT dress and most importantly due to presence of unfamiliar theater staff who appeared quiet indifferent and non-sympathetic. White coat hypertension is a known phenomenon and OT atmosphere can augment these reactions.

Remaining 43 (70.49%) patients were given tablet Alprazolam 0.25 mg orally and reassured again. After 1 hour majority, 31 (72.5%) out of 43, responded to reassurance and anxiolytics. This clearly favour our point of view that one or even few preoperative readings in previously normotensive or well controlled hypertensive patients shall not be a reason for alarm and postponement of planned surgery. 12 patients didn't responded and their BP remained above the limit of 140/90mmHg and their surgery was postponed. Their BP didn't respond to either reassurance or anxiolytics. Perioperative use of beta blockers is being recommended in American College of Cardiology guidelines since 2014 for major non-cardiac and vascular surgeries.[3]

Preoperative HTN is responsible for about 10% of surgical cancellations and in excess of 10% of intraoperative interventions, this prompted AAGBI and BHS to issue guidelines for hypertension management before elective surgery. They even very boldly recommended not to routinely checked BP preoperatively in patients whose BP was below 160/100 mm Hg in the referral letter from primary care. The argument was that it's the long term baseline BP that has importance not the spot reading on the day of surgery. One can resort to acute lowering of BP to avoid cancellation, maintain effective use of the operating theatre space and other logistical reasons. Labetolol, esmolol, nicardipine, nifedipine, clevipidine and fenoldopam, can be used in such cases. One must be cautioned to neither overestimate the benefit nor underestimate the risk of acute blood pressure reduction. Overzealous attempts may lead to unintentional hypotension due to anesthetic and analgesic drugs interaction.[9,10]

CONCLUSION

The decision to postpone elective cataract surgery shall be individualized taking into consideration the comorbidities (diabetes mellitus, coronary artery disease, peripheral vascular disease, impaired renal function, smoking or dyslipedemia), general physical health, nature of surgical procedure and anesthesia. Inconvenience, anxiety, continuing risk of falls and accidents from delaying cataract surgery must therefore be weighed against the benefits of hypertension treatment. Anxiety and missing routine antihypertensive medications due to fasting on the day of surgery are the commonest reasons for preoperative high BP. Routine use of anxiolytics prior to surgery blunts hemodynamic liability. A simple explanation and reassurance by

hospital staff may be sufficient to smoothen the patient's anxiety. Missed dose of routine antihypertensive medicines shall be given in cases where only regional or local anesthesia is planned.

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Original Article

Effect of BMI on Nerve Conduction Velocities Among Healthy Individuals

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ABSTRACT

Objective: To evaluate the influence of BMI on Nerve Conduction Velocity (NCV), particularly in the peripheral sensory (ulnar) and motor (ulnar and peroneal) nerves of the upper and lower limbs among healthy individuals. As we know NCV is affected even by physiological factors.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Physiology department of Baqai Medical University, Karachi from January 2017 to July 2017.

Materials and Methods: Subjects included in this study were 500 healthy adult male and females of Gadap town, Karachi, age ranges between 18-45years. Power Lab was used to record the NCV after stimulation of ulnar and peroneal nerve at wrist and at lateral aspect of knee respectively. Obtained data and basic parametric values were calculated by using the 'Statistical package for Social science' (SPSS) software version 22.0.

Results: Results showed that, Ulnar sensory nerve have highest mean in obese class, than in overweight and among underweight samples, ($p=< 0.01$). It showed that, there were significant mean differences in ulnar sensory nerve with respect to BMI, Ulnar motor nerve were also found higher among obese class samples but these results were statistically insignificant, Peroneal motor nerves gave high mean among normal BMI samples, and underweight samples, these results were found statistically significant ($p=<0.02$).

Conclusion: The study showed inverse relationship of ulnar sensory, ulnar motor and peroneal motor nerve conduction velocity with body mass index (BMI).

Key Words: Nerve conduction velocity (NCV), BMI = Body mass index & Statistical package for social sciences (SPSS).

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INTRODUCTION

Nerve conduction study (NCS) is a test that commonly used to evaluate the patency of a nerve by examining the capacity of human motor and sensory nerves to conduct electricity. [1] In order to gauge how quickly electrical impulses travel through a nerve, nerve conduction velocity (NCV) tests are frequently conducted. [2] It is found to be a major tool in diagnosis of any damage or destruction that occurred in peripheral nerves.

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NCS is influenced by a number of factors, including age, gender, temperature, BMI, the proportion of upper to lower extremities, and a number of physiological factors, including the nerve's diameter, myelination, and internodal distance. As a result, there is no global standard reference value for any given nerve that can be taken into account due to climate variations around the world. As a result, various areas and laboratories utilize their own standard reference values. [3,4] By observing the generated response to electrical stimulation of the peripheral nerves, NCS is a crucial method for estimating peripheral nerve functioning.[5] Nerve impulses can be triggered by enough stimulation from an electrical stimulator. Electrical impulses will propagate at a rate of 100 m/s after a nerve fiber's action potential threshold is reached, albeit the velocity of the impulse varies depending on the diameter of the fiber, the degree of myelination of the nerve, and the temperature. [6,7] Conduction velocity and latency are NCS parameters that measure the speed of nerve impulse propagation. Any condition that results in demyelination of the nerve affects the conduction capacity of both the motor and sensory nerves.

Amplitude, which measures the quantity of active nerve fibers, is diminished under conditions that lead to axonal degeneration. [8]

The evoked response to electrical stimulation of peripheral nerves, which helps in determining the extent and distribution of the neuronal lesion and provides a measure of the degree of nerve damage by which demyelination and axonal degeneration can be distinguished between two major peripheral nerves, is recorded using the NCV, which is regarded as the gold standard in clinical assessment of motor and sensory functions. [9] The locations of the stimulation and recording sites as well as the distances between these locations are clearly described in normative papers. [10]

NCV has been used clinically for many years to determine the precise location and extent of the lesion in a single nerve and for differentiating disorders of the muscles and the neuromuscular junctions. It not only aids in localizing the sites of the lesions but also allows us to accurately characterize the functions of the peripheral nerves.[8,11] Poor physical function, which can result in diminished mobility, impairment, hospitalization, and mortality, is a result of poor strength in old age. Given its significant significance, it is imperative to look at the risk factors for deteriorating strength in older persons. Power Lab is the instrument utilized in the investigation. It is a piece of HTML-based software that manages experimental data sampling, digitization, and storage while enabling data editing and analysis.[4] Nerve conduction studies (NCS) can be used to assess the health and function of peripheral nerves. Demyelination and axonal degeneration are the two main kinds of peripheral nerve illnesses that are distinguished by NCS, which aids in determining the degree and distribution of neural lesions. [1] The procedures have been improved and standardized, making NCV a reliable test in clinical settings.

MATERIALS AND METHODS

This study was conducted in the Department of Physiology at Baqai Medical University, Karachi, from January 2017 to July 2017 utilising a comparative cross-sectional, analytical method using a non-invasive Power Lab 8/30 series with dual Bio-amplifier (AD Instruments Australia, Model No. ML870). The Baqai Medical University Ethical Committee gave their approval for this investigation. 500 local Gadap town inhabitants were the 500 subjects who were a part of this investigation.

Sample Technique: The sampling method used was practical sampling.

Electrophysiological Methods: The Power Lab, multichannel recording equipment for measuring electrical signals, was used for all of the testing. It features two-channel Bio-amplifiers for the best biological signal recording as well as an isolated stimulator for electrical stimulation of nerves and muscle. [4,10,11] Instead of using anatomical landmarks for near-nerve recording, the NDTF advises using the orthodromic technique, which involves conventional fixed distances and precise electrode placement. [13]

Analysis:

1. Two points A & B were marked at a measured distance between the elbow and the wrist, the stimulation, and the recording site.
2. The conduction velocities were obtained by stimulating the nerve at two different points at least 10 cm apart between marks A & B.
3. Conduction velocities were calculated by dividing the difference of latencies of two stimulating point by the distance between the stimulating and recording site (mark A & B), expressed in meters per second.
4. The peroneal nerve recording procedure was carried out using the same techniques as described before.
5. Enter the value of the latency in the table.
6. Onset latency or latency 2 (proximal) - latency 1 (distal) (m/sec).
7. The following formula was used to determine the nerve conduction velocity, which was given in meter/second;

$$\text{Velocity} = \frac{\text{Distance between stimulation sites (mm)}}{\text{Difference between latencies (m/sec.)}}$$

To convert mm into m, divided the value from 1000. Similarly for tenth of second, multiplied with 10.

RESULTS

Table No.1: Age and BMI distribution in males and females

Characteristics	Males (n=250) Mean ± SD	Female (n=250) Mean ± SD	p-Value
Age (Years)	31.04±2.48	29.70±3.39	0.0001
BMI Normal (18.5-24.9) Kg/m^2	21.8±1.76	22.2±1.79	0.012
BMI Underweight (<18.5) Kg/m^2	16.9±0.92	16.91±1.44	0.92
BMI Overweight (25-29) Kg/m^2	26.4±1.17	26.83±1.34	0.0001
BMI Obese (30-40) Kg/m^2	32.03±1.4	31.33±1.05	0.001

P<0.05 significant
P>0.05 non-significant

Table No.2: Mean Comparison of Nerves Responses with BMI

Nerve(s)	BMI CATEGORIZATION				p-value
	Normal (A)	Underweight (B)	Overweight (C)	Obese Class-I (D)	
	Mean ± SD	Mean ±SD	Mean ±SD	Mean ±SD	
Ulnar Sensory Nerve	55.99 ± 3.91	54.29 ±2.05	57 ± 4.3	58 ± 5.63	<0.01*
Ulnar Motor Nerve	54.13 ± 5.8	54.69 ±6.78	55.76 ± 6.19	57.1 ± 6.93	0.05
Peroneal Motor Nerve	48.72 ±4.2	50.2 ±4.57	48.12 ± 3.93	47.55 ± 4.99	0.02*

*p<0.05 was considered significant using ONE WAY ANOVA

DISCUSSION

Peripheral nerves are an excellent location to test nerve conduction velocities (NCVs). Nerve impulses can be triggered by enough stimulation from an electrical stimulator. A nerve fiber's electrical impulses will spread at a rate of 100 meters per second if the action potential threshold is crossed. [11] The velocity is a direct function of the myelination and fiber diameter.[12] In the past, numerous studies were conducted to assess the impact of body mass index on nerve speeds.[13] However, the majority of these studies were based on populations in the west. Therefore, the purpose of this study was to investigate how BMI affected the NCVs of the ulnar sensory, ulnar motor, and peroneal motor nerves in the local Gadap Town population.

The crucial technique of nerve conduction studies, which has received extensive validation, is employed in clinical practice.[14] Numerous investigations and reviews on nerve conduction studies that take into account the variables influencing nerve velocities have already been published. These variables were separated into biological variables (such as age, height, and gender) and physical variables that have an impact on the health of the nerve and the muscle.[15] We concentrated on the impact of BMI, one of the biological determinants, on NCV. As advised by the majority of neurophysiology laboratories, factors like temperature were maintained constant to limit findings variability.

A study was conducted[16] to ascertain the impact of BMI on NCV. The researcher came to the conclusion that there was no relationship between NCV plus H reflex latency and BMI. We observed a slowing of NCVs across various BMI categories.[17].

CONCLUSION

In summary, BMI can have an impact on conduction velocities. We noticed a slowing down of the typical motor peroneal nerves' speeds. There was a statistically significant decrease in Nerve Conduction Velocities with increasing BMI. The opposite outcome of the weaker sensory nerve is caused by other factors, such as age and gender, whose discussion is outside the scope of this article.

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Original Article

A Study of Prevalence of Urological Abnormalities Among Elementary and Secondary School Boys

Shoaib Rafique[1], Ahmad Bilal[2], Imran Hyder[2], Ammaar Rafique[3], Asif Hameed[1] and Muhammad Ayyaz Bilal[1]

ABSTRACT

Objective: To screen male school children to determine the prevalence of various urological abnormalities and offer appropriate advice to the parents of children in whom abnormalities would be detected.

Study Design: Descriptive / observational study.

Place and Duration of Study: This study was conducted at the Departments of Urology, Multan Institute of Kidney Diseases, Multan and NMCH, Multan from January 2014 to December 2017.

Materials and Methods: We studied 129 boys, aged 6 to 17 years, in four public sector elementary and secondary schools of the city. In addition to physical examination, all boys had ultrasonography of abdomen and pelvis done for detection of urological abnormalities.

Results: The mean age of boys was 13.12±2.017 years. Urological abnormalities were identified in 84 (68.9%) boys. The most common abnormalities included varicoceles in 26%, inguinal hernia 7.75%, undescended testis 6.97%, hydrocele 3.87%, epididymal cysts 3.87% and urolithiasis 3.87%. Other abnormalities identified included: unilateral renal agenesis, ectopic kidney, ureteropelvic junction obstruction, unilateral small sized kidneys, micropenis and hypospadiasis. None of the parents of these children were aware of identified abnormalities.

Conclusion: The present study has identified that a significant number of school boys have urological abnormalities. Three most common abnormalities were varicoceles, inguinal hernias and undescended testes. The renal abnormalities were identified in 9.3% boys. Careful screening of school children is necessary to avoid later complications.

Key Words: Congenital Anomalies of the Kidney and Urinary Tract (Cakuts), Cryptorchidism, Inguinal Hernia, Hydrocele, Varicocele, External Genitalia, Children

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INTRODUCTION

The urological abnormalities in school going boys are common and many remain undiagnosed. Timely diagnosis and treatment of these abnormalities is essential to prevent subsequent morbidity. The congenital urological abnormities are common and may involve either upper renal tract (kidney or ureter), lower urinary tract (bladder or urethra) or genitalia.

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In addition to congenital abnormalities, some acquired diseases like renal tract stones may develop, which also require appropriate timely management. Among the congenital abnormalities, inguinal hernia and hydrocele are common. The major complication of untreated inguinal hernia is incarceration. This condition requires an emergency surgery and can also lead to intestinal gangrene and gonadal atrophy[1]. In majority of hernias, concomitant hydrocele may be present. Most (60%) of the new hydroceles which appear after birth and before puberty are associated with a patent process vaginalis (i.e. communicating hydrocele). Hydroceles which appear during and after puberty are more commonly non-communicating. Cryptorchidism or undescended testis is a common congenital abnormality. Cryptorchidism is associated with subfertility in adulthood and 2 to 5 times higher risk of testicular germ cell tumors, however, this risk is positively correlated with age at surgery. It represents a failure of testicular descent which is dependent on the growth and hormonal function of the developing testis, its regulation of growth and function of gubernaculum[2]. Although most cases are isolated or non-syndromic, cryptorchidism may be associated with many other syndromes. Majority (75% to 80%) of undescended

testes are palpable and 60% to 70% are unilateral and are more often seen on right side[3]. Micropenis is a more common anomaly and a penis smaller than 2 SD (standard deviation) from the norm is considered as micropenis [4]. Micropenis has been attributed to a testosterone deficiency that result in poor growth of organs that are targets of this hormone. The varicoceles are common among adolescents. Because of progressive nature of disease, its prevalence increases with puberty. Akbay et al [5] investigated the prevalence of varicoceles in boys aged 2-19 years and reported that prevalence at age 2-10 years, 11-14 years, and 15-19 years was <1%, 7.8% and 14.1% respectively. Varicoceles may contribute significantly to the risk of subfertility in adulthood. The majority of varicoceles in children and adolescents are identified incidentally by medical practitioner or by patient on self-examination. Small number of adolescents (2-11%) present with scrotal discomfort [6]. Uncorrected varicoceles may result in testicular hypotrophy and adulthood subfertility. Recent studies report an increase in the incidence of congenital anomalies of the kidney and urinary tract (CAKUTs) and they are significantly associated with male sex[7]. Such abnormalities are present at birth, however, they may not become apparent until later in life. Renal stones in children are associated with significant morbidity. An increase in the incidence of urolithiasis in children and adolescents has been observed during last three decades[8]. Timely diagnosis and/or treatment of above mentioned conditions is important to avoid complications. Unfortunately, there is no health check system in Pakistan for the detection of these urological abnormalities in school children either before admission or during their school years.

MATERIALS AND METHODS

A team of urology departments of two hospitals of city visited four public sector elementary and secondary schools of the city. For the purpose of study one public sector elementary and three secondary schools of city were chosen. The public sector schools were chosen for the study as most children in such schools belong to low socioeconomic background and do not usually get medical checkup by qualified medical practitioners. The permission from the Institution's ethics committee and school authorities was obtained. One week before the visit of urology team to any particular school, one member of the team visited the in-charge of each school and briefed him about the purpose of study. The school in-charge was requested to nominate those classes which could easily be included in the present study without affecting the school examination schedule. Each school in-charge was handed over 100 formal consent forms and he was requested to distribute these to the students for obtaining formal permission from their parents for examination of their children by the urology team. Parents were also requested to provide information about the previous illness of their child. In addition, the school in-charge allowed the parents of children to visit school on the study day if they wanted to accompany their child during examination. Only those boys who brought written duly signed consent form from their parents were considered suitable for examination. The examination was conducted in a room which was specially prepared for this purpose. Each child was examined in turn by two qualified urologists under the observation of one professor of urology who had initiated the concept of the present study. History of any previous illness or any surgical intervention was obtained. A careful physical examination focusing on abdomen, groin, scrotum and penis of each participant was carried out. For detection of hernia, the boys were examined in supine and erect position both before and after straining (cough reflex). For identification of varicoceles, the boys were also examined in an erect position using Valsalva maneuver. The penile length and testicular volume was recorded. All findings were recorded in a specially designed proforma and any positive or suspicious cases were re-examined by the assistant professor of urology. After physical examination, each student underwent abdominal ultrasonography. The GE-Logic 200MD, ultrasound machine with convex probe frequency 3.5 Hz was utilized for examination. The findings were recorded in proforma. The parents of boys in whom urological abnormalities were identified were contacted and an appropriate advice on further investigations and treatment in each case was given. The data was analyzed using SPSS software.

RESULTS

Out of 350 children, the written permission from parents of 129 boys was received and only these boys were considered suitable for present study. The mean age of boys was 13.12±2.017 years (range 6 to 17 years). Abnormalities were identified in 84 (68.99%) of boys. The three most prevalent abnormalities were varicoceles, inguinal hernias and undescended testes [Table 1]. Varicocele was the most common abnormality identified in 34 (26.35 %) boys. Grade II and III left sided varicoceles were identified in 12 and 19 boys respectively and 3 boys had bilateral varicoceles. All boys with varicocele were asymptomatic. The mean age of boys with varicocele was 14.09±1.16years. Inguinal hernias were identified in 10 boys and they were equally distributed on left and right side. Nine boys had undescended testes. Their mean age was 11.33±2.87 years. Eight boys had unilateral undescended testis, while one boy had bilateral undescended testes. In one boy a unilateral small atrophic testis in scrotum was identified. Two boys had rather smaller sized testis. Hydrocele was present in 5 boys and they were mostly on left side. Epididymal cysts were observed in 5 boys and were

predominantly on right side. One boy had multiple scrotal sebaceous cysts and in one boy coronal hypospadiasis was present. Decrease in penile size greater than 2SD was identified in 4 boys.

Various abnormalities which were identified on ultrasonography of abdomen and pelvis included unilateral renal agenesis (2 boys), ectopic kidney in pelvis (1 boy), ureteropelvic junction obstruction (1 boy), unilateral rather small sized kidneys (2 boys), renal stones (4 boys), vesical stone (1 boy) and a solid renal mass in one boy.

Table No.1: Urological abnormalities identified in school boys

Total number of school boys N=129	
Abnormality identified	Number (%)
Varicocele Grade III left varicocele 19 Grade II left varicocele 12 Bilateral Varicocele 03	34 (26.35%)
Cryptorchidism Right side 07 Left side 01 Bilateral 01	09 (6.9%)
Unilateral Atrophic testis	01 (0.77%)
Decreased testes size	02 (1.55%)
Inguinal Hernia Right inguinal hernia 05 Left Inguinal hernia 05	10 (7.75%)
Hydrocele Right hydrocele 01 Left hydrocele 04	05 (3.87%)
Epididymal cysts Right epididymal cysts 04 Left epididymal cysts 01	05 (3.87%)
Scrotal sebaceous cysts	01 (0.77%)
Coronal hypospadiasis	01 (0.77%)
Decreased penile size (more than 2SD)	04 (3.1%)
Unilateral renal agenesis	02 (1.55%)
Ectopic kidney (pelvic location)	01 (0.77%)
Smaller size of kidney	02 (1.55%)
Ureteropelvic junction obstruction	01 (0.77%)
Unilateral Renal mass	01 (0.77%)
Urolithiasis Renal stones 04 Vesical stones 01	05 (3.87%)

DISCUSSION

The Inguinal hernias develop in 1% to 5% of children. They are more common in boys and have propensity for the right side[9]. A positive family history is an important risk factor for inguinal hernia development and recent studies indicate genetic predisposition with autosomal dominance to developing inguinal hernias [10]. In the present study the prevalence of inguinal hernias in boys was7.75%. Other studies [11,12,13] reported figures between 1.36% and 13. 44%. In the present study hydrocele was identified in 3.87% of boys. This figure is higher than those reported by other authors [13, 14, 15] which ranged from 0.23% to 1.5%. Approximately 1-9% of all male are born with at least one cryptorchid testis. Most of these cases will descend spontaneously and at one year of age approximately 1% of all male will remain cryptorchid [16]. In the present study the prevalence of cryptorchidism was 6.9% which is much higher than other published studies. O Adekanye et al [11] from Nigeria reported cryptorchidism in 0.9% of primary school boys. Studies from Iran [12] and Southern Jordan [13] reported prevalence of inguinal hernias in 1.12% and 2.12% boys respectively.

The prevalence of hypospadiasis has been estimated to be between 0.8 and 8.2 per 1000 live births [17]. In the present study one boy was found to have coronal hypospadiasis. Micropenis is defined as “a penis which is smaller than 2 SD (standard deviation) from the norm” [4]. Micropenis has been attributed to a testosterone deficiency that results in poor growth of organs that are the targets of this hormone. Nelson et al [18] reported that in the USA, the incidence of micropenis in male children born between 1997 and 2000 was as 1.5 in 10 000 male children.

In adults, the prevalence of varicocele is about 15% and the reported prevalence of clinically diagnosed varicocele in adolescents is 8% to 16% [19]. The varicoceles are predominantly left sided and it is thought to be due to a unique anatomy of left testicular vein. However, the identification of right sided varicoceles in boys is increasing. Kumnov et al [19] reported that most varicoceles appear after 10 years of age, progress through puberty, and peak at Tanner stage 3. The varicocele progression is thought to be related to the continuous or spontaneously induced spermatic vein pressure. Varicoceles may contribute significantly to the risk of subfertility in adulthood, however, their effects on paternity are unclear as population based studies indicate that 85% of men with varicocele have fathered children. Unilateral renal agenesis (URA) is more common than bilateral agenesis. The ultrasound screening of 280,000 school children in Taipie by Sheih et al [20] showed the incidence of URA to be 1 in 1200. A systematic review[21] estimated that the general incidence of URA is 1 in 2000. Usually it is an isolated event, however, it may be associated with other developmental defects. In the present study the prevalence of unilateral renal was 1.5%, however, no other abnormalities were identified in these boys. The kidney may fail to ascend in fetal life and may remain in an ectopic location. The ectopic kidney may be associated with other urological anomalies, most commonly vesicoureteric reflux[22]. Sheih et al [20] found renal ectopia in approximately 1 in 4000 school children. In the present study one boy

(0.77%) was identified to have an ectopic kidney located in pelvis. Ureteropelvic junction obstruction (UPJO) is a common abnormality in children and adolescents and is caused either by an intrinsic narrowing or extrinsic compression by lower pole vessel. UPJO has a reported incidence of 1 in 500 live births more commonly in males than females and more frequently found on the left side [23]. UPJO may be associated with other congenital malformations. Nearly 1/3rd of affected children will need surgical intervention[24]. In the present study, UPJO was identified in one patient. Renal stone disease in children is associated with significant morbidity, due to its recurrent nature and presence of underlying abnormalities. A true frequency of urolithiasis in children is not known, however, the studies indicate an increasing trend [8]. The characteristics of renal stone disease show a wide geographical variation. Delayed diagnosis can cause risks to kidney function. There is high prevalence of renal stones in Pakistan and prevalence of stone disease in children is not much known. In the present study, urolithiasis was identified in 5 (3.87%) boys. Four boys had renal stones and in one boy had vesical stone.

From review of published literature it appears that the prevalence of different urological anomalies in school children in various regions of the world varies. Many studies have focused on the abnormalities of external genitalia. In the present study the authors not only focused on the abnormalities of external genitalia but also utilized abdominal ultrasonography for detection of upper and lower renal tract anomalies and other conditions. The study revealed urological abnormalities in a large number of school boys. In addition, nearly all parents were unaware of their child's urological abnormalities which raises the need for better education in the community. The parents of all those boys in whom urological abnormalities were detected were contacted and were advised either follow-up, further investigations or treatment as was deemed necessary in each case.

CONCLUSION

The present study has identified that a significant number of school boys have urological abnormalities. Three most common abnormalities were varicoceles, inguinal hernias and undescended testes. The renal abnormalities were identified in 12 (9.3%) boys. Careful screening of school children for detection of urological abnormalities and periodic examination during the school years is necessary to avoid later complications. In addition, there is need for the better education and awareness in community for timely diagnosis and treatment of urological abnormalities.

Author's Contribution:

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Original Article

Role of Dapagliflozin in the Management of Body Mass Index (BMI) and Glycated Hemoglobin (Hba1c) in Obese Type 2 Diabetic Patients

Effect of Dapagliflozin on BMI and HbA1C in Diabetics

Awais Naeem[1], Fahad Naim[1], Nizamuddin[2], Irum Mehmood[2], Samiullah[3] and Tahira Abrar[2]

ABSTRACT

Objective: To evaluate the effect of Dapagliflozin on BMI and HbA1C in Type 2 Diabetic Patients
Study Design: Retrospective / observational study.
Place and Duration of Study: This study was conducted at the internal department of Medicine, Khyber Teaching Hospital Peshawar from August 2020 to July 2021.
Materials and Methods: Total 333 diabetic patients, with mean age of 45.66 years, were enrolled in the study. Average BMI was 32.8 while average HbA1C was 9.94% at the time of enrollment. After taking prior informed consent and documentation of the demographic profile of the patients, SGLT2 inhibitors (Dapa) 10 mg was given for the treatment of T2DM. The main aim was reduction in HbA1C and BMI. Both BMI and HbA1C level was recorded at 0 months and 6 months. The statistical analysis was done using SPSS version 22.0 and graph were constructed using GraphPad prism software
Results: In total 333 diabetic patients, 39.9% (133) were females and 60.1% (200) were males. The mean age was 45.66 ± 8.3 years. The mean HbA1c at initial enrollment was 9.94 ± 0.53% and at follow-up, it was 8.42 ± 0.74%. Similarly, the mean BMI was 23.8 ± 1.1 at the time of enrollment, which was reduced to 31.4 ± 1.2 after follow-up. Statistically significant difference was recorded between initial and follow-up HbA1c values with p-value and 95%CI <0.001, -1.5-1.5. Similarly, the mean BMI reduction was significant from 32.8 ± 1.1 to 31.4 ± 1.2 with a p-value, 95%CI <0.001, -1.4-1.2.
Conclusion: SGLT-2 inhibitor, dapagliflozin is a very good anti-diabetic drug with additional benefits of BMI reduction.
Key Words: Diabetes Mellitus, Glycated hemoglobin (HbA1c), SGLT-2 inhibitors, Body Mass Index (BMI), Dapagliflozin.

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INTRODUCTION

Diabetes is common metabolic disorder where Type-2 diabetes mellitus contribute more than 90% of all cases through the world[1]. Some of the recent figures taken from International Diabetic Federation (IDF) report, the situation is alarming, which the global prevalence of 10.5%, affecting more than 536.6 million people throughout the world. In 2045, it is expected to be 12.5%, with a total number of 783.2 million people[2]. In Pakistan, the prevalence is 30% affecting every third person with a total number of approximately 33 million adults[3]. Insulin deficiency due to any reason or insulin resistance or both usually lead into T2DM[4].

Obesity is another hug metabolic disorder, which is closely linked with T2DM. According to WHO, more than 1 billion people worldwide are obese, where 650 million are adults, 340 million are adolescents and 39 million are children and this number is still increasing very rapidly[5]. In Pakistan, the prevalence of obesity is more than 27.85%[6,7].

The target in the treatment of T2DM is to decrease HbA1C level, treat the comorbidities and prevent complications and the drugs which are commonly used for this purpose either increase the secretion of insulin or decrease the resistance to insulin. Some drugs uses

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both aforementioned mechanisms and some of the drugs decrease the absorption of glucose from GI tract[8].

The sodium-glucose transport 2 (SGLT-2) inhibitors, also known as gliflozin, and include Dapagliflozin (Dapa), Empagliflozin (Empa) and Canagliflozin (Cana) and Ertugliflozin (Ertu)[9]. They remove about 80 to 100 grams of glucose per day from the body by blocking its reabsorption through inhibition of SGLT2 receptors in the kidneys, thus decrease blood glucose level and as well as remove 320 to 400 kcal from the body leading to weight loss. We have used Dapagliflozin in our patients for the treatment of diabetes and observation of its impact on obesity[10,11].

Though SGLT-2 inhibitors have significant effects on weight reduction, but little is known about it especially at national level. To fill this gap, this study was conducted on these drugs to explore its effect on diabetes and obesity in Pakistani population.

MATERIALS AND METHODS

The study was carried out in the internal medicine department, Khyber teaching hospital Peshawar. The duration of study was 12 months (August 2020 to July 2021). Total 333 type 2 diabetic patients, who were overweight or obese, were selected. HbA1C level was recorded at 0 and 6 months. BMI was recorded at 0 and 6 months. BMI was calculated using weight and height as follows: BMI= weight (kilograms)/height (meters squared). BMIs were classified according WHO BMI classification10 and Asia-Pacific BMI Classification.

The group age were 31 to 60 years and out of all 333 patients, 39.9% (133) were females and 60.1% (200) were males. To avoid any confounders, all patients with some other major comorbidities like congestive cardiac failure, ascites, chronic renal failure and cirrhosis were excluded from the study as these conditions can affect weight due to fluid retention. The study design was descriptive prospective.

Data Collection: The project was approved by the Medical Research department KMC/KTH. Total 333 obese diabetic patients were enrolled in the study. After proper consent, demographic data including BMI was recorded using purposefully designed proforma and 5cc blood was withdrawn using 5cc disposable syringe and forward to KTH laboratory for HbA1c analysis. Dapagliflozin 10mg was prescribed to all the patients and were followed for 6 months. After 6 months, all the patients were re-interviewed, the demographics were recorded and HbA1c was repeated.

Data Analysis: The numerical values were expressed in mean ± SD while categorical variables were expressed in frequency and percentages. Independent sample t test was applied to determine gender based differences. t-test was applied to find the mean differences between initial HbA1c, initial BMI and HbA1c and BMI after follow-up. p-value <0.05 was considered significant. Data was analyzed using SPSS version 22.0.

RESULTS

This study enrolls 333 diabetic patients in which 39.9% (133) were females and 60.1% (200) were males. The mean age was 45.66 ± 8.3 years. Similarly, the mean HbA1c at initial enrollment and follow-up was 9.94 ± 0.53% and 8.42 ± 0.74% respectively. Similarly, the mean BMI at the time of enrollment was 23.8 ± 1.1 which was reduced to 31.4 ± 1.2 after follow-up. All the values are summarized in table 1 for detail overview.

Table No.1: Demographic Data of Enrolled Patients

Variable	Minimum value/No	Maximum value/%	Mean	SD
Female	133	39.9	-	-
Male	200	60.1	-	-
Age	31	60	45.66	8.32
Initial HbA1C	9.1	10.7	9.94	0.53
HbA1C after follow-up	7.1	9.9	8.42	0.74
Initial BMI	31.3	34.6	32.8	1.1
BMI after follow-up	28.8	33.8	31.4	1.2

To determine whether gender imparts any significant importance on study variables, independent sample t-test was applied. The result reveals that there were no statistical differences between age, initial HbA1c and BMI and values of HbA1c and BMI after follow-up in both genders. All the values were non-significant with p-values >0.05. Table 2 summarizes the details of all difference between variables based on gender.

Table No.2: Gender based differences between study variables

Variable	Gender	N	Mean	SD	t-value	p-value	95% CI
Age	Female	133	45.59	9.03	0.124	0.90	1.9-1.7
	Male	200	45.71	7.8			
Initial HbA1C	Female	133	9.9	0.53	0.29	0.76	0.1-0.13
	Male	200	9.9	0.53			
HbA1C	Female	133	8.4	0.74	1.09	0.27	0.07-0.25

after follow-up	Male	200	8.3	0.73			
Initial BMI	Female	133	32.8	1.1	0.34	0.83	0.22-0.27
	Male	200	32.8	1.14			
BMI after follow-up	Female	133	31.41	1.18	0.75	0.77	0.30-0.22
	Male	200	31.45	1.21			

The mean differences were recorded between initial HbA1c and HbA1c after follow-up and initial BMI and BMI after follow-up. The mean HbA1c at the time of enrollment of patients were 9.94 ± 0.53% while it was reduced to 8.4 ± 0.74%. Statistically significant difference was recorded between initial and follow-up HbA1c values with p-value and 95%CI <0.001, -1.5-1.5. Similarly, the mean BMI at time of patient enrollment was 32.8 ± 1.1 while after follow-up it was reduced to 31.4 ± 1.2. The results were found statistically significant with p-value, 95%CI <0.001, -1.4-1.2. All the values are given in table 3 and graphically shown in figure 1.

Table No.3: Mean differences between initial variables and after follow-up

Variable	Mean	SD	t-value	P-value	95% CI
Initial HbA1C	9.94	0.53	36.2	<0.001	-1.5-1.3
HbA1C after follow-up	8.4	0.74			
Initial BMI	32.8	1.1	20.6	<0.001	-1.4-1.2
BMI after follow-up	31.4	1.2			

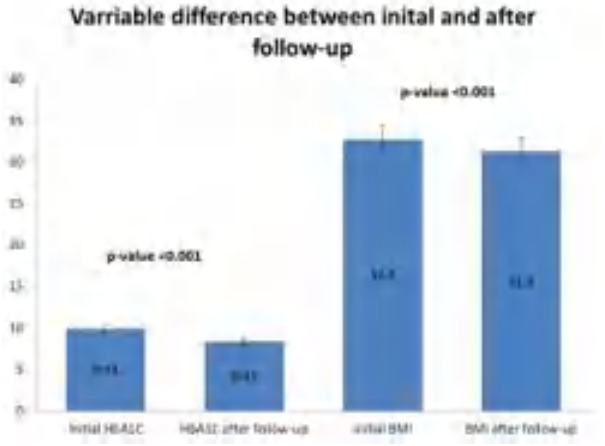

Figure No.1: Differences between HbA1c and BMI values at initial and after follow-up

DISCUSSION

In last decade, the treatment of Diabetes Mellitus is revolutionized and multidisciplinary approach is used to address the diabetes and prevent its complications. At the same time, treatment of co-morbidities like obesity, hypertension etc is also very important to prevent the grave complications, morbidity and mortality due to coexistence of these disease. So far, many drugs have been used, but SGLT-2 inhibitors may be considered as a magic bullet, as these drugs not only treat diabetes, but also can be used to treat the comorbidities and complications of diabetes. SGLT-2 inhibitors remove glucose from the body and thus reduce diabetes and decrease weight. These effects of one the most important drug in this class, named Dapagliflozin is evaluated in this study.

Our finding regarding the efficacy of Dapa on HbA1C is closed to the finding of a multi-center study conducted by Morieri ML et all, in Italy, where they have targeted the effect of Dapa on HbA1C and hypertension in diabetic patients. They have noted an average decrease of 1.20% in HbA1C level, which is close to our observed value of 1.52[12].

In another study conducted by Kudo T et all, in Japan, where .66% reduction in HbA1C was observed in diabetic patients with Standard dose of dapagliflozin, using it for good 12 months. This effect was comparatively less than the effect observed in our study, but was equally significant[13].

The effects of SGLT-2 inhibitors are also observed on the reduction of weight and BMI and now these drugs are the main weapon in the therapeutic armamentarium against obesity. In a study conducted by Iacobellis G and Gra-Menendez S, on the effects of dapagliflozin on epicardial fat thickness in patients with type 2 diabetes and obesity in, it was observed that there was a reduction of 3.5kg in weight and a reduction of 01 in BMI of T2DM patients[14]. These finding are closed to the finding of BMI reduction of 1.4% in these patients.

In another clinical trials, conducted by Oyama K et all, on the effects of dapagliflozin on Obesity, heart failure and renal dysfunction in type 2 diabetes mellitus patients, an average significant reduction of 1.8 in BMI was noted in these patients which is very closed to our finding of 1.4 in such patients. These finding in their clinical trials were different for different groups in term of BMI, where significant changes were observed in a group with very severely obsess patients[15].

CONCLUSION

The new drugs SGLT-2 inhibitors are safe and effective choice to treat and manage not only hyperglycemia but also delaying micro and macro vascular complications. These drugs also have positive impacts to reduce BMI.

Our findings need to be replicated in multicenter studies to endorse our findings.

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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 Among Positive PCR COVID-19 Patient's Clinical Outcome and Balanced Nutrition

Nutritional Status and Disease Outcome in Patients From Covid 19

Asya Tauqir

ABSTRACT

Objective: To study the nutritional status and disease outcome association in patients suffering from COVID 19.
Study Design: Cross sectional (Descriptive) study.
Place and Duration of Study: It was 6 months study after approval from research and ethical committee Women Medical and Dental College Abbottabad done on COVID-19 patients quarantined at different places in district Mansehra to check the COVID-19 being impacted by nutritional status on COVID-19 outcome in PCR positive patients. This study was conducted at the King Abdullah Hospital, Manshera from June 2021 to December 2021 (six months).
Materials and Methods: Cross sectional (descriptive) study was done on PCR positive sufferers quarantined at home and at different quarantine centers with complete SOPs and were assessed by anthropometric measurement and dietary assessment by FFQ and 24 hours dietary recall methods. A pre designed questionnaire was used for demographic variables. latest SPSS version was applied to rationalize statistical results.
Results: Results show the duration of the quarantine period and mean age of the patients 31 years and 7-14 days respectively, while standard deviation for age of the patients and quarantine period were 15.02, and 2.10 respectively. Std. Error of Skewness values for age of the patients and quarantine period were 0.17, and 0.79 respectively and 2-tailed significance show strong correlation
Duration of the hospital stay was recorded longer in 7 patients while shorter in 193 patients with 188 cases having quarantined at home and 12 at quarantine centers. Spearman's rho is significant for hospital admission history, fever and outcome of the disease while negative with heights and weights of the patients. Vitamin C & D serum levels were different in both males and females, while serum Ferritin levels, serum calcium and serum zinc levels showed strong correlation with immunity enhancement in favorable outcome of the COVID-19 patients and NRS score, duration of Quarantine period.
Conclusion: There is positive correlation between good nutritional status and decrease in quarantine period for COVID-19.
Key Words: Correlation, COVID-19, Nutritional status, PCR, Quarantine.

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INTRODUCTION

COVID-19 emergence is the result of the infectivity caused by SARS-CoV-2 early in Chinese atmosphere and grabbed the whole world turning into a pandemic infecting more than 650 million cases of COVID-19 around the world killing 6.6 million lives globally [(1)]. Many strategies have been implemented by countries in far east in their settings to control COVID-19 possibly can be an example for the global scenario turned out to be a major challenge for majority of the countries [(2)].

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The emergence of newly SARS viral strains has caused flu-like ailments, and many retrospective studies have emphasized to adopt protective measures to halt the spread of such strains .[(3)] The entire globe was not prepared well to face this calamity of COVID-19 pandemic [(4)].Micronutrients are responsible for immunity enhancement are the part of the balanced diets in daily life .Many vitamins like A, D, E, etc. Trace elements like zinc, iron are easily traceble in a fresh foods varieties based on animal and herbal sources, boost the body's capability to fight against illnesses [(5)]. Nutritional care is very much required during recovery time period of COVID-19 has turned out to be very meagre, although it is very vital to reduce recovery time and people's ability to join normal life sooner. Nutritional wellbeing is very vital to maintain skeletal muscle viability and protecting against metabolic disorders especially it becomes a serious issue when patients have to spend two weeks around in ICU.[(6).]

Similarity of the clinical picture of the COVID 19 to that viral pneumonia patients -causing respiratory failure is very much marked. It is well known that patients in ICUs require intubation for nutrition intake and chances of malnutrition become more elegant. Good physical belt and better nutritional status has effectively managed the prolong stay of patients in quarantine period, so good nutritional status can be very helpful in management of COVID 19 cases [7].

Patient's deterioration was very much observed in the early span of the pandemic caused by COVID-19 requiring immediate respiratory assistance. It was very less known about the role of the balanced and health nutrition to combat the fatal outcomes of this tragedy especially recovery time and people's ability to return in normal life again.[8]

MATERIALS AND METHODS

200 positive PCR patients were quarantined at home and at different quarantine centers with complete SOPs and were assessed by anthropometric measurement and dietary assessment by FFQ and 24 hours dietary recall methods. A pre designed questionnaire was used for demographic variables. DATA was analyzed by SPSS latest version. Interviews from patients were recorded to assess the mode of infection and exposure level including clinical picture of the patients as well. Patients in the research were included on the basis of having PCR positive results placed in different quarantine places in district Mansehra under strict SOPs.

RESULTS

Results show the frequency measures of different demographic variables of the study, in which majority of the patients were higher secondary passed (44.5 %). Gender results show for Male (119), female (81) respectively. Hospital admission results show 9 for admission in hospital while 191 were at home for quarantine.

Table 2 shows that serum vitamins level of the different vitamins including vitamin C, serum ferritin and zinc levels in the study group of the patients suffering from COVID-19 diseases. Vitamin D serum levels are different in both males and females serum vitamin C levels, serum Ferritin levels, serum zinc and calcium levels were correlated for immunity enhancement.

Table 3 shows the different micronutrients serum levels in COVID-19 Positive and Negative cases for each gender.

Table 4 shows correlation results of NRS score, MI and duration of Quarantine period which shows strong correlation between shorter quarantine period and normal BMI and NRS scores.

Table No.1: Frequencies of the socio-demographic variables

Educational Status	Frequency	Percent
Illiterate	6	3.0
Primary	67	33.5
Higher secondary	89	44.5
Graduate	12	6.0
Master	26	13.0
Gender of the Patient		
	Frequency	Percent
Male	119	59.0
Female	81	41.0
Hospital admission history		
Yes	9	4.5
No	191	95.0
Total	200	100
Duration of Hospital stay		
Long (more than 21 days)	7	3.5
Short (less than 21 days)	193	96.5
Mode of Quarantine		
At Home	188	94.0
At Quarantine center	12	6

Table No.2: Various micronutrients serum levels in Male and Female groups.

Serum Vitamins/Minerals Levels	Male	Female	P-Value (t-test)
Vitamin D serum levels (30–100 ng/ml)	21.8 ± 11.9	23.5 ± 14.3	0.007
Serum Vitamins C (0.2 - 1.1 mg/dL)	0.1 ± 0.2	0.1 ± 0.2	< 0.001
Serum Ferritin (24 to 336 ng/mL)	20.83 ± 10.97	23.50 ± 12.35	< 0.001
Calcium serum levels (8.6–10.3 mg/dl)	7.14 ± 0.19	7.50 ± 0.32	< 0.001
Zinc serum levels (70–127 µg/dl)	64.51 ± 14.10	76.66 ± 10.76	< 0.001

Table No.3: Serum levels of micronutrients in COVID-19 positive and negative cases for each gender.

Empty Cell		**Positive COVID-19**	**Negative COVID-19**	**p-value**
Vitamin D serum levels	Male	023.37 ± 14.04	023.92 ± 13.62	.050

Empty Cell		Positive COVID-19	Negative COVID-19	p-value
(30–90 ng/ml)	Female	20.82 ± 11.82	26.82 ± 15.41	0.00
p-value		.093	0.35	0.01
Vitamin C ((0.2 - 1.1 mg/dL)	Male	0.1 ± 0.2	0.2 ± 0.2	0.02
	Female	0.1 ± 0.2	0.2 ± 0.2	0.03
p-value		.083	.316	0.04
Serum Ferritin Level ((24 to 336 ng/mL)	Male	21.83 ± 10.97	23.50 ± 11.35	.001
	Female	20.50 ± 11.35	21.83 ± 11.97	.001
p-value		.073	.216	.001
Calcium serum levels (8.6–10.3 mg/dl)	Male	8.14 ± 0.19	9.15 ± .58	<.001
	Female	8.50 ± 0.32	9.43 ± .39	<.001
p-value		.059	.483	<.001

Table: 4 Correlation results of BMI, NRS score and duration of quarantine in COVID-19 patients

		Duration of Hospital stay	NRS score	Body mass index	PCR AFTER QUARANTINE	INITIAL PCRR ESULTS	Outcome
Duration of Hospital stay	Pearson Correlation	0.075	0.045	0.057	0.071	0.03	0.07
	Sig. (2-tailed)	0.015	0.07	0.07	0.04	0.03	0.07
NRS score	Pearson Correlation	0.00	0.07	0.07	0.06	0.03	0.07
	Sig. (2-tailed)	0.07	0.01	0.01	0.07	0.07	0.01
Body mass index	Pearson Correlation	0.00	0.00	0.02	0.01	0.01	0.09
	Sig. (2-tailed)	0.07	0.01	0.04	0.02	0.00	0.03
PCR AFTER QUARANTINE	P/Correlation	0.04	0.02	0.05	0.01	0.01	0.03
	Sig. (2-tailed)	0.07	0.03	005	0.02	0.00	0.07
INITIAL PCRR ESULTS	Pearson Correlation	0.05	0.37	0.03	0.03	0.01	0.00
	Sig. (2-tailed)	0.07	0.03	0.03	0.06	0.01	0.00
Outcome	P/Correlation	0.00	0.00	0.00	0.04	0.01	0.07
	Sig. (2-tailed)	0.00	0.00	0.00	0.015	0.02	0.07

P/correlation (Pearson correlation)

DISCUSSION

A strong association between exists between corona virus 2019 (COVID-19) infection and the measured nutritional status and. Clinical scenario contains hypertension, obesity, respiratory diseases, diabetics, cardiovascular patients, smokers, higher degree Organ Failure. Many studies have been done like assessment scores, and a series of laboratory tests for example

procalcitonin, lactate dehydrogenase-dimers, lymphopenia [9].

Allain et al rationalized the status of the nutrition in 372 confirmed admitted COVID-19 patients, while our study has included 200 confirmed cases of COVID-19 PCR positive patients' results, while Zhao et al included 67 critically ill patients but our study has not included any critically ill patient. Study by Zhao et al observed that 2 characteristics has directly affected COVID-19 patients at a invariable numbers including metabolism and immune response while in our study weights and daily caloric intake has played prominent role [9, 10].

NRS score has been considered by many studies to find out patient's nutritional status, as per recommendations by the clinical nutrition societies. The score ranges assesses severity of nutritional deficits by measuring ranging 0 to 7 (maximum, points value 3) It can measure illness severity (3 points maximally), with age points (maximum, 1 point). NRS score ≥ 4 for indoor patients and ≥5 for seriously ill-patients. NRS scores for 381 of 415 patients were collected in one study: while our study measured NRS score in 200 patients.94% of patients were facing developing hospital acquired malnutrition (≥3 points) [11].

Screening is a step one of vitamins remedy, only 25% of the study population had acquired vitamins provisions, a few COVID-19 patients have acquired probiotics in the form of remedy for diarrhea. It has been found that excessive NRS scores is associated with excessive [12].Many epidemiological studies have been done explaining the comparative analysis of mortality in Wuhan versus European settings due to COVID-19. Wuhan clinical groups have been coming across the ailment and the remedies to be applied. But vitamins role has not been evaluated. Interestingly it has been observed that the procalcitonin serum level became considerably correlated with the NRS scores [13].

The excessive malnutrition can be associated with prolongation of the illness, social apathy, isolation anorexia due to infection, dystocia, dyspepsia, dyspnea, confinement, stress, and organizational troublesome as it's been found in the shape of longer period in our research[14].One of the study carried by Rahman et al have located that further, lifestyles style, confined bodily pastime and shortage of social aid would possibly have relation with bad dietary consumption in infected population (Rahman et al., 2020, While our study has concluded that quarantine at domestic could be very good deal promising even as affected person recovered and became out to be a terrible PCR end result even as COVID-19 patients quarantined at quarantine facilities have confronted longer period to be terrible PCR possibly because of social apathy and tensioning conjunction with disturbed diets [14]. Malnutrition amongst older individuals is continually under identified and undertreated circumstance that results in underestimation of the aforementioned occurrence values. Relationship among COVID-19 patients final results and macro and micronutrients had been studied by Six different researches showing the decrease albumin levels to pre-albumin (Bedock ,2020), nutrition B12, Vitamin D, serum magnesium (Tan et al) even as our look at indicates no acute impact of use of multivitamins and minerals. All these vitamins have well-known immune modulatory outcomes, with advantages in infectious ailment [15].

The low serum level of vitamins is probably the main cause to the misbalance the immune system of the patients suffering with COVID infection patients which impact COVID 19 effects. In our study, daily caloric consumption and Fever has Sig. (2-tailed) correlation with 0.02 displaying excessive caloric consumption ensuing in alleviation in temperature, Duration of Hospital stay has week correlation with fever even as PCR after quarantine became strongly correlated with PCR [16].

Our study indicates Spearman's rho Correlational results of the study at wherein height has substantial correlation with caloric consumption, period of medical stay at hospital, negatively correlated with lower in caloric consumption ensuing in lengthen live, While in different research anthropometric measurements have now no longer been blanketed however NRS scores best .Our research bears few limitations, its consequences can't be generalized because the inclusion of very confined research applicable to the provision of nearby research [17]

CONCLUSION

It has been concluded in our study that PCR outcomes (after Quarantine) was directly related to good nutritional status and patients provided with balance diets recovered earlier and has lesser quarantined period and early PCR negative results.

Author's Contribution:

Concept & Design of Study:	Asya Tauqir
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Original Article

Representation of Clinical Manifestation of Mosquitoes-Borne Diseases

Humaira Zakir[1], Syed Muhammad Hasan[3], Asif Mashood Qazi[2], Riaz Ahmed Bhutto[4], Mataa-E-Masood[5] and Jarry Masood[6]

ABSTRACT

Objective: To evaluate the clinical manifestations of patients with mosquitoes-borne diseases

Study Design: Cross Section Study

Place and Duration of Study: This study was conducted at the Department of Medicine, Al-Tibri Medical Hospital, Isra University Karachi Campus from April 2022 to October 2022.

Materials and Methods: Study protocol was written and approval was taken from IREC, Total 100 numbers of patients with both genders were selected from Medicine OPD of Al-Tibri Hospital and were briefed about the study; written informed consents were taken. Diagnosed cases of malaria, dengue and dual dengue and malaria infection confirmed by serological analysis, patients with age of >18 and above were included in the study. Patients with negative serological markers and <18 years of age excluded from the study. Patient data was collected. Proforma was used for recording data and SPSS version 22 was used for data analysis.

Results: Total 100 numbers of patients the 57 were male and 43 were females. Mean age was 35.56 ± 1.23. Out of 100 patients 44% were in Group A, and 38% were included in Group B and 18% patients were included in group C as a diagnosed with both malaria and dengue

Conclusion: According to the study, the symptoms related to mosquitoes-borne diseases in all groups like fever, chills, vomiting, and conjunctivitis were reported. The percentage of severity in symptoms was recorded in Malaria and dengue patients as compare with dual infection. Low level of hemoglobulin and low platelet count were reported in all groups. Most of the symptoms and changes in hematological parameters were recorded in Malaria patients. In accordance with the results, mosquitoes-borne diseases need proper investigation and line of treatment along with preventive measures should be taken by Health care providers and ministry.

Key Words: Malaria, Dengue, Platelets, Geography, Virus, Signs, Symptoms, ELISA Test

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INTRODUCTION

Malaria and Dengue are two uncontrolled diseases, found in the region of Pakistan. This is a parasitic disease transmitted by Anopheles mosquito and the latter is a viral disease transmitted by Aedes mosquito[1]. In geographical area the basic cause of the dual impact of the disease cannot be ruled out. It's a challenging task to manage the dual presentation of the diseases and multiple symptoms[2]. The dengue virus is one of the common Flavivirus in human all around the world that creates the outbreaks of public health impacts. These mosquitoes-borne diseases can be happened simultaneously in human, so the differential diagnosis and management plan became so difficult to establish. Many of the reported cases about this concurrent disease were reported in Asia including Pakistan and India[3]. According to the studies the documented chills and high-grade fever are the common clinical presentation of the patients with associated symptoms like abdominal discomfort, vomiting and anorexia[4]. Most frequent findings for dengue are fever found in (100%) of the cases, myalgia (79-90%), rash (70-80%) along with the headache (68%) and in some of the cases nausea and diarrhea (37%)[1]. The management of mono effective patient and confections containing person are different, if they are not timely approachable then the condition can be fatal. The frequent documentation regarding the clinical presentation and the management are essential to spread the awareness among the public health workers before the uncontrolled endemic condition.

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The purpose of the study to established the fact and figures regarding the diagnosis and the management of the mosquitoes-borne diseases, especially the co-manifestation of the diseases.

MATERIALS AND METHODS

Total 100 numbers of patients with both genders were included on the basis of non-probability convenient sampling from the department of Medicine at Al-Tibri Medical College and Hospital, Isra University Karachi campus. Ethical approval was taken by the concerned authority to conduct the cross-sectional study, the study was conducted from April 2022 to October 2022. All diagnosed cases of dengue and Malaria were included in this study, followed by the clinical representation, history and lab investigation including serology of dengue and, after taken a written concert the pre-designed proforma was filled by the investigators in OPD. Diagnosed cases of malaria, dengue and dual dengue and malaria infection confirmed by serological analysis, patients with age of >18 and above were included in the study. Patients with negative serological markers and <18 years of age excluded from the study. Proforma was used to document the symptoms similarly found in patients along with other associated complaints. For the purpose of data entry, we divided the patients into three groups:

Group A included Patients diagnosed with Malaria (IgM –ve and MP +ve)

Group B included Patients diagnosed with Dengue (IgM +ve and MP –ve)

Group C included patients had a dual manifestation of Dengue and Malaria (Dengue IgM +ve and MP +ve)

In some patients the ultrasound abdomen was done. CBC, LFTs, MP malaria and serology markers were done by ELISA test kit. The qualitative data was presented in the form of Frequency and percentage and data was analyzed through SPSS version 26.0.

RESULTS

From 100 numbers of patients the 57 were male and 43 were females. Mean age was 35.56 ± 1.23.

About 52% of the patients were educated

Out of 100 patients 44% were in Group A, and 38% were included in Group B and rest of the 18% were diagnosed as a dual malaria-borne diseases

Table 1 shows the frequency and percentage of symptoms-based representation of the patient among three different groups.

Table 2 shows the presentation of hematological parameters of the patients among different groups.

Table No.1: Shows the Frequency and Percentage of different pattern of clinical manifestations found among various groups

	Group A(n=48)	Group B(n=32)	Group C(n=20)
Fever	48(100%)	32(66.6%)	20(41.6%)
Body Ache	46(95.8%)	28(58.3%)	18(37.5%)
Rigors and Chills	32(66.6%)	18(37.5%)	8(16.6%)
Vomiting	39(81.2%)	20(41.6%)	6(12.5%)
Abdominal Pain	18(37.5%)	16(33.3%)	5(10.4%)
Rash	8(16.6%)	10(20.8%)	3(6.2%)
Conjunctivitis	48(100%)	27(56.2%)	15(31.2%)
Anorexia	45(93.7%)	30(62.5%)	17(35.4%)
Hepatomegaly	6(12.5%)	5(10.4%)	2(4.1%)
Splenomegaly	3(6.2%)	2(4.1%)	0(0%)
Bleeding Manifestation	16(33.3%)	51(31.2%)	9(18.7%)
Pleural Effusion	1(2%)	0(0%)	0(0%)
Others	1(2%)	0(0%)	0(0%)

Table No.2: Shows Frequency of Hematological parameters found in various

Investigation	Range	Remarks	Group A(n=48)	Group B(n=32)	Group C(n=20)
Hemoglobin (gm/dl)	3.6-16.6	>10	32	25	15
		7-10	14	6	4
		<7	2	1	1
Platelet count/mm3	5000-100,000	50,000-10,000	30	5	2
		20,000-50,000	14	18	14
		<20,000	4	9	4

DISCUSSION

The global advancement in clinical and laboratory infectious research vector-borne diseases continue to be a significant burden of disease worldwide[6,7]. Dengue and malaria are public health problems in mostly countries[8]. Actually water containers, storage places remains open or not fully covered so they serve as mosquito breeding sites in areas. In urban areas the disposed of unwanted containers also served as breeding sites and became the cause of disease outbreaks[9].

Hematologic abnormalities are well-known common clinical complications of these diseases and are frequently observed in patients with dengue and malaria infections. These complications also play important

roles in disease severity and fatality. It was reported that the risk of hematologic alterations, including thrombocytopenia, in dengue and malaria infections was associated with various clinical factors (e.g., immunity status, level of endemicity, demographic factors, individual hemoglobinopathy, and nutritional status of patients)[10].

In this study, we investigated platelet and hemoglobin levels of the patients to illustrate alteration patterns in patients with dengue, malaria and both that could be implied as a prognostic clue in the clinical differential diagnosis.

The clinical presentations of patients with dengue and malaria may mimic and overlap those of many other common infectious tropical diseases[11]. Our findings were consistent with previous reports indicating that this complication might be associated with thrombocytopenia[12]. The highlighted figures were seen as in group A (Malaria) fever and conjunctivitis were found in 100% patients, group B (Dengue) fever and anorexia were found in 66.6% and 62.5% patients respectively, and in group C (Malaria + Dengue) fever and anorexia were found in 41.6% and 35.4% respectively. Other parameters as shown in Table 2 represent less Haemoglobin level in Group A (Malaria) <7 in 2 patients, Platelet count <20,000 in Group B (Dengue) patients.

So as per this study it was seen that fever and body pain are common feature in all the three (A, B and C) groups. High fever may be the indication sign for Malaria[13], Dengue or both. By covering the water storage places and proper sewage systems may support in lowering the burden of these diseases in urban areas[14].

CONCLUSION

According to the study, the symptoms related to mosquitoes-borne diseases in all groups like fever, chills, vomiting, and conjunctivitis were reported. The percentage of severity in symptoms were recorded in Malaria and dengue patients as compare with dual infection. Low level of hemoglobulin and low platelet count were reported in all groups. Most of the symptoms and changes in hematological parameters were recorded in Malaria patients. In accordance with the results, mosquitoes-borne diseases need proper investigation and line of treatment along with preventive measures should be taken by Health care providers and ministry.

Author's Contribution:

Concept & Design of Study:	Humaira Zakir
Drafting:	Syed Muhammad Hasan, Asif Mashood Qazi
Data Analysis:	Riaz Ahmed Bhutto, Mataa-E-Masood and Jarry Masood
Revisiting Critically:	Humaira Zakir, Syed Muhammad Hasan
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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

Self-Management and Quality of Life Among Patients with Decompensated Liver Cirrhosis

Kiran Waris[1], Adnan Yaqoob[1], Hajra Sawar[1] and Sadia Khan[2]

ABSTRACT

Objective: To assess the effect of nursing intervention on knowledge about self-management and quality of life among patients with decompensated liver cirrhosis.

Study Design: Quasi-experimental study

Place and Duration of Study: This study was conducted at the Department of Gastroenterology, Bahawal Victoria Hospital Bahawalpur, Punjab, Pakistan from 1st April to 30th September 2022.

Materials and Methods: Thirty two who are diagnosed cases of decompensated liver cirrhosis, aged between 30 to 60 years of both genders were enrolled. After taking the informed consent from patient's intervention was given to patients as they were enrolled in study. The research scholar developed an interventional program. The post data was collected after the one month of intervention and was compared with pre-data to find out effect on knowledge about self-management and quality of life. Post assessment was done with the help of same questionnaires. Two questionnaires used for data collection Self-management knowledge questionnaire and CLDQ.

Results: Six (18.8%) were between the age group 21-40 years and 26(81.3%) were in the age between 41-60 years. Majority of the patients were females 17 (53.1%) were below primary education 21(65.6%). The findings revealed that there was a significant difference between the pre and the post interventional knowledge's score among patients regarding self-management and their Quality of life measure by CLDQ was also improved (p value <0.001).

Conclusion: The educational intervention has a positive effect on decompensated liver cirrhosis patients' quality of life and self-management skills. Moreover, the liver disease education intervention is beneficial in increasing patient and family knowledge.

Key Words: Liver cirrhosis, Patient care, Educational guidelines

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INTRODUCTION

Cirrhosis is a critical stage of liver scarring (fibrosis) caused by various forms of liver diseases and conditions, including hepatitis and chronic alcoholism. Any time the liver is injured, whether by disease, excessive alcohol consumption, or any other reason, it attempts to repair itself. This is how scar tissue develops. As cirrhosis progresses, scar tissue increasingly form, making it impossible for the liver to function. Advanced cirrhosis threatens life.[1]

In Pakistan, 60-70% of individuals have chronic liver disease, and 50% have hepatocellular carcinoma. Liver cancer is the sixth most prevalent disease worldwide, and it affects people in their fourth to fifth decades of life in Pakistan.[2] Pakistan is a developing nation with numerous causes and risk factors that contribute to liver disease, such as Hepatitis B and C. Other types of hepatitis also contribute to liver damage, 24% individuals die from bacterial peritonitis in DCLD, a late consequence of cirrhosis.[3]

Despite the fact that liver cirrhosis is an irreversible illness and the main cause of death. We can all have a role in reducing illness morbidity. Complications may be avoided by appropriate illness treatment and education.[4] There has been little studies on the disease burden of liver disorders in Pakistan, despite the fact that there are many review articles on the topic accessible worldwide.[5] In the last two decades, health-related quality of life has become an important additional outcome parameter. Quality of life is also increasingly recognized as an important outcome parameter in chronic diseases.[6] Self-management is described as dealing with the medical, emotional, and social difficulties of a chronic illness in daily life to achieve quality of life.[7] Self-management intervention have been comprehensively carried out to chronic disease educational programs, which are map up to slow down degenerated renal functions, rule out

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depression, and enhance quality of life.[8] Nevertheless, nurses must provide knowledge to patients regarding social support and assisted emotionally to live a healthy life, teachings on the medicine regimen, self- care activities, for the better self-management.[9]

Nurses play an essential role in interdisciplinary teams in many areas and the function of nurses in liver disorders is not specified; they work on the basis of their experience. The important thing to note is that nursing research in liver illness is very limited when compared to other chronic diseases. The commission's top suggestion, out of ten, is to enhance nurse education and training programs in the hematology department. Nurses have an important educational function.[10]

The current study is therefore designed to assess the knowledge of liver cirrhotic patients regarding self-management and quality of life. The study may have a variety of implications. Self-management is very important in chronic and lifelong diseases. Through this study patient will be able to manage the minor problems and frequent visits to hospital, ultimately knowledge about self-management will minimize the burden of health care department.

MATERIALS AND METHODS

This quasi experimental study was conducted at Department of Gastroenterology, Bahawal Victoria Hospital Bahawalpur, Punjab, Pakistan from 1st April 2022 to 30th September 2022. A total of 32 diagnosed cases of decompensated liver cirrhosis, aged between 30 to 60 years of both genders were enrolled. Patients were recruited by purposive sampling technique. After taking the informed consent from patient's intervention was given to patients as they were enrolled in study. The research scholar developed an interventional program. The intervention was developed by reviewing past and recent literature.[11-13] Procedure took 1 month, on each week 9 patients were enrolled. Time of educational sessions was different for patient to patient according to their level of understanding. Education was on nature of disease, complications of disease, diet, medications, knowledge about warning signs, how to self-manage the symptoms and about treatment and vaccinations. Booklets were handed over to each subject of study at the first contact between patient and the researcher. Intervention for each participant was completed in 8 weeks while overall intervention was completed in 12 weeks. The post data was collected after the one month of intervention and was compared with pre-data to find out effect on knowledge about self-management and quality of life. Post assessment was done with the help of same questionnaires. Two questionnaires used for data collection were:

I. Self-management knowledge questionnaire: The tool was consisting of total 13 questions with 3 or more options. Correct answer was scored as one score while wrong or don't know scored as 0. Less than 60% was considered as inadequate knowledge. The patients got 60% or more had adequate knowledge.

II. Chronic liver disease questionnaire: CLDQ comprises of 29 questions. Responses were recorded on 5 point Likert scale. Responses were **"all of the time"** to **"None of the time".** Score 1 was the most important while 5 was marked as least important. Results showed the worst to best quality of life.

Data was entered and analyzed by using SPSS 24. Normality was assessed through Shapiro Wilks test. Wilcoxon signed rank was applied to compare the scores of knowledge regarding self-management and CLDQ. P-Value ≤ 0.05 was considered as statistically significant

RESULTS

Six (18.8%) were between the age group 21-40 years and 26(81.3%) were in the age between 41-60 years. Majority of the patients were female 17 (53.1%) were below primary eduaction 21(65.6%), and majority of the patients were suffering from 1 to 5 years i.e. 16 (50.5%) whereas 15 (46.9%) patients had duration of 6 months to 1 year and the remaining 1 (3.1%) patients suffered from the disease for the period of more than 5 years (Tables 1-2).

Table No.1: Demographic information of the patients (n=32)

Variable	No.	%
Age (years)		
21 to 40	6	18.8
41 to 60	26	81.3
Gender		
Male	15	46.9
Female	17	53.1
Qualification		
Below Primary	21	65.6
Middle	9	28.1
High and above	2	6.3
Disease Duration		
6 months to 1 year	15	46.9
1 to 5 years	16	50.0
More than 5 years	1	3.1

Table No. 2: Comparison of pre and post intervention mean knowledge scores regarding self-management among patients with decompensated liver cirrhosis (n=32)

Variable	Pre-interven-tion median	Post-intervention median	z-value	p-value
Knowledge Scores	4.0	10.0	-3.861	<0.001

Overall pre-interventional median knowledge scores among patients with decompensated liver cirrhosis regarding self-management was 4.0 while, the post-

interventional median knowledge's scores were increased to 10.0. The findings revealed that there was a significant difference between the pre and the post interventional knowledge's score among patients regarding self-management as evident by ($p<0.001$). The overall pre-interventional median of CLDQ scores among patients was 54.5 while, the post-interventional median of CLDQ scores were increased to 114.0. The findings revealed that there was a significant difference between pre and post interventional CLDQ scores as evident by ($p<0.001$) [Table 3].

Table 4 shows that in the pre-interventional phase the majority of the patients had inadequate knowledge i.e. 27 (84.4%) while only 5(15.6%) patients had adequate knowledge regarding self-management. Whereas in the post-intervention phase there were 6(18.8%) patients had inadequate knowledge and remaining 26(81.3%) patients had adequate knowledge regarding self-management.

Table No.3: Comparison of pre and post intervention quality of life scores among patients with decompensated liver cirrhosis (n=32)

Variable	Pre-interven-tion median	Post-intervention median	z-value	*p*-value
Knowledge Scores	54.5	114.0	-4.938	<0.001

Table No.4: Comparison of pre and post interventional knowledge categories (n=32)

Knowledge Categories	Pre intervention	Post intervention
Adequate	5 (15.6%)	26 (81.3%)
Inadequate	27 (84.4%)	6 (18.8%)

DISCUSSION

Chronic disease self-management has been shown to be very beneficial for those dealing with chronic diseases to improve overall health and quality of life. However, self-management education is not tied to a specific time period or participation in a specific programme. In order for a patient to be in the best possible health, they need to develop a relationship with a nurse who can help them manage their chronic condition.

The results of current study revealed that, 6(18.8%) were between the age group 21-40 years and 26(81.3%) were in the age between 41-60 years. Majority of the patients were female 17(53.1%) were below primary education 21(65.6%). The findings revealed that there was a significant difference between the pre and the post interventional knowledge's score among patients regarding self-management and their quality of life measure by CLDQ was also improved ($p<0.001$). However, the findings of current study were comparable by the result of a pilot study conducted by Been[14] reveals that recipients who receive intervention admire the intervention, become more competent in solving their problems and social interactions. There was an improved quality of life among the intervention group and the nurse-led-self management approach was successfully accepted by patients and professionals as well.

Self-management initiatives significantly improved patients' quality of life, according to another study. Patient education, health-related quality of life, health status, and self-management abilities all show significant improvements.[15] In a different study, Beg et al. assessed the effect of an information booklet on patients with cirrhosis' level of knowledge. Understanding liver cirrhosis, complications, surveillance, self-management, and Treatment procedure were all part of the booklet's educational material. Results showed that the booklet considerably increased ability to enhance the knowledge of the condition.[16] In another study conducted on educational intervention by Goldsworthy et al[17] reported that the patient awareness and knowledge of liver cirrhosis was lacking at the start of the study but significantly increased following educational intervention. Furthermore, this study's educational intervention was a successful strategy for managing liver cirrhosis. The teaching instrument used was different, but the outcomes paralleled those of the current study. In a study, Kadokawa et al[12] investigated the efficacy of educational programmes for people with chronic liver illnesses. After attending classes, patients' and their families' knowledge levels dramatically increased, and the recovery rate was correlated with participation in the sessions. Overall, this study's findings indicated that the intervention improved the quality of life for patients with liver cirrhosis. Their attitude toward therapy can be more positive and have greater results through enhancing quality of life. Overall, the study's findings demonstrated that educational interventions greatly increased patient knowledge and may be applied as a practical way to raise awareness of patients with liver cirrhosis in clinical settings. In a study, Zandi et al[18] found that a self-care teaching programme and ongoing monitoring in cirrhotic patients for three months significantly improved quality of life.

CONCLUSION

The educational intervention may have a considerable positive effect on decompensated liver cirrhosis patients' quality of life and self-management skills. Patients' education, which can significantly alter their behaviours, management abilities, and quality of life, is greatly influenced by nurse's intervention. Moreover, the liver disease education intervention is beneficial in increasing patient and family knowledge.

Author's Contribution:

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Data Analysis:	Hajra Sawar, Sadia Khan
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Original Article

Behaviors and Barriers: Utilization of Intrauterine Contraceptive Devices (IUDs)

Saira Saeed[1], Zubaida Masood[3], Riaz Ahmed Bhutto[4], Rahila Imtiaz[6], Shahid Kamran[5] and Hina Khan[2]

ABSTRACT

Objective: To evaluate the behaviors and Barriers regarding the usage of intrauterine devices for the purpose of contraception**.**

Study Design: Observational study.

Place and Duration of Study: This study was conducted at the Al-Tibri Medical College and Hospital, Karachi from January 2021 to June 2022.

Materials and Methods: Total 100 numbers of married females with age of 20 and above from different communities and professions were included in the study after taking a verbal consent and ethical approval from the concerned authority. Those females were not willing excluded from the study. The samples were taking as non-probability convenient sampling. After explaining the importance of the study to the participants, the proformas were filled by the doctors. Descriptive data was represented as Frequency and Percentage.

Results: About 47% of females lie in 20-30 units of age Group, 27% from 31-40 years of age group and 26% from more than 40 years. Almost 45% were in >5-10 years of duration of marriage. 66 % educated, 64% presenting with less information of devices, 57% were not intended to use the contraception methods, and about 88-89% had a misinformation about the contraindications and benefits of method. 54% female's shows poor social support in this regards.

Conclusion: This study reveals the facts about the low interest of females towards the utilization of contraceptive devices or even other methods due to lack of information regarding benefits, side effects and services. Insufficient social and family supports especially from partner. Religious matters should be encounter. To cover all the aspects, awareness program and full support of their doctors, paramedics and health care workers can improve and correct the concept and minimize the fear and anxiety regarding the procedures.

Key Words: Contraception, Behaviors, Health Care

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INTRODUCTION

Now more than ever, the prevention of pregnancy still is considered a very important aspect of modern medicine [1]. This is more alarming when considering the rising global population worldwide, which is estimated to reach approximately 9-11 billion by 2050[2].

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Therefore, in this day and age population control and family planning has become even more critical to tackle the rising population, in a deflating economy, and a world at risk of food security [3]. With almost 70% of the population of Pakistan below the age of 30, a key concern for the green nation is population growth. Therefore, it is prudent that population growth must be reduced, with family planning being the most effective method to stagnate this growth [4]. Family planning is a dual effort by the couple to limit the number of children or space the birth of their children using various contraceptive methods [5]. It is damning to see that despite modern contraceptive methods available to reduce the number of abortions and limit both maternal and neonatal morbidity and mortality, family planning is still unmet in vast sectors of the developing world [6-8]. Now there are a vast array of devices available in the market that are build with the purpose of preventing contraception. One of them is the intrauterine contraception device (IUDs), which is by far the most widely used reversible contraception device, with 14.5% of women using it in the developing countries [9].

IUDs are highly effective in their function, with a failure rate estimated to be less than 1% [10]. IUDs are a safe, effective, and long-lasting form of mechanical and reversible contraception, and its use since the 1960s has now spread to be utilized as post-partum contraceptive agent as well[11]. Women need to have adequate awareness of contraception, how to carry it out, and how using it could impact their live and ultimately reduce the chances of unintended pregnancies[12]. A country like Pakistan, has very little education pertaining to family planning and contraception. With this in mind, a study was conducted to assess the behavior and barriers regarding utilization of intrauterine contraceptive devices.

MATERIALS AND METHODS

Total 100 numbers of married females were selected on non-probability convenient sampling. After taking an ethical approval from the concerned authority the study was conducted from January 2021 to June 2022 at Al-Tibri Medical College and Hospital and some other setups. After taking a verbal consent, all married females using or not using the intrauterine devices for the purpose of contraception were included in this study; proforma was filled by the doctor after explaining the importance of this survey. For statistical analysis the data was presented in the form of Frequency and percentage.

RESULTS

From 100 numbers of data, about 47% of females lie in 20-30 units of age Group, 27% from 31-40 years of age group and 26% from More than 40 years as shown in Table 1

Almost 45% were in >5-10 years of duration of marriage. 66 % educated, 64% presenting with less information of devices as shown in Table 1.

Table No.1: Percentage of demographic data of the study

Age	**%**	**Job**	**%**	**Source of Information**	**%**
20-30	47	House wife	41	Family	16
31-40	27	Laborer	20	Personal consultant	21
>40	26	Business	9	Media	22
Duration of marriage	**%**	Health professional	14	Friend	18
<5	28	Private employee	8	Health Workers	23
>5-10	45	Government Employee	5	Status of information	%
11-15	17	others	3	Good	21
>15	10	Gender of child	%	Enough	15
Religion	**%**	All Boys	24	Less	64
Islam	78	All Girls	25		
Others	22	Both	51		
Educated (Above matric)	Yes	66			
	No	44			

Table No.2: Percentage of Intended and non-intended reasoning among the participants

Intended		14%
Not Intended	Reasons	57%
	Fear/Anxiety	100%
	Fear of infertility	78%
	Husband factor	64%
	Family pressures	68%
	Fear of loss of uterus	68%
	Fear of side effects	81%
	Religious factors	58%
	Feeling ashamed	28%
Not know		29%

Table No.3: Percentage of Misperception / improper information of (IUDs) and Social Status

Information	
Definition	56%
Contraindication	74%
Usage	69%
Side effects	88%
Services	52%
Benefits	87%
Percentage of status of social support to the participants	
Good	23%
Normal	26%
Poor	54%

57% were not intended to use the contraception methods, and 29% not know about the methods as shown in Table 2.

About 88-89% had a misinformation about the contraindications and benefits of method. 54% female's shows poor social support in this regards as shown in Table 3.

DISCUSSION

This study suggests that there are multiple factors which are responsible for the uptake and continuation of Intrauterine contraceptives devices. One of them is the fear or anxiety in placing the Intrauterine Devices (IUDs), internally. Adult respondents who participated in this study's interviews who had never used an IUD but had heard of them all expressed a widespread concern of the device's internal implantation. Participants provided a variety of justifications for why they feared the IUD, some emotional and some more precise (e.g., fear or anxiety of pain and adverse effects of IUDs) (e.g., the idea of intervention from a foreign source). The key point made was that fear would be a significant deterrent to getting an Intrauterine Devices (IUDs).

Adult women have reported having IUD-related anxiety[13,14], which is probably related in part to a lack of knowledge of female anatomy. Participants' worries about the IUD's potential harm indicate that they do not fully comprehend the physical interactions between the private organs such as vagina, urethra, uterus, ovaries, and abdominal cavity.[15]

With a better understanding of anatomy, some worries that adults express, including pain during urine or intercourse, may be alleviated. Identifying the vagina in Contraception start with the uterus; educating teenage girls about their anatomy at the commencement of puberty may help to reduce misinformation. Young girls, who are still formulating their beliefs, might be more willing to change their minds than older women.[16, 17]

Additionally, we learned that "someone else" would choose the IUD as a contraceptive option. Although the interviewer did not specifically ask about the respondents' sexual preferences or whether they intended to use an IUD. But majority of them had responded that factors like language make the type of IUD ideal for the user themselves. Participants also stated that a potential Intrauterine contraceptive devices (IUD) user wouldn't routinely use condoms and would have already carried a pregnancy. This belief that women should use the IUD only after trying other methods of contraception may be the root of this idea. Contraception professionals have been shown to hold similar beliefs about IUDs. Participants noted that choosing an IUD would be hindered by their lack of control over its insertion and removal, albeit this concern was raised less frequently than fear. In addition, qualitative research has demonstrated that young women would have preferred or select IUDs more if there was a self-removal option, as Foster et al. demonstrated[18].

Themes from this study also point to a lack of obstacles to IUD use. It's interesting to note that young women didn't voice any worries about a higher risk of STDs with IUD use. In contrast, clinicians and adult women have raised worries regarding infection.[19,20]

Our study has a number of drawbacks. All female adolescents had not been represented in the study population. Since we restricted our recruiting to urban young females who had already heard of the IUD. However, in order for us to specifically examine teenagers' informed attitudes of IUDs, this inclusion criterion was necessary. For instance, young girls who enroll in any consultation program and seek care there may be more likely than other adolescents to think that the IUD is available there. Additionally, it's possible that adolescents from diverse backgrounds are not represented in the demographic analyzed, which includes minority, urban teenagers.[21]

Because of this anxiety, they are unable to see the IUD as a reliable method of birth control. Improved IUD education, counselling, and knowledge of female anatomy may ease these concerns[22]. We also discovered widespread myths regarding ideal IUD candidates (such age and parity), which need to be dispelled if the IUD is to be accepted as a reliable method of birth control for the majority of adolescents. By comprehending how adolescents see IUDs, clinicians may provide better contraceptive counsel on a little-used, very effective method. This study suggests that in order for women to accept the IUD as a credible source of contraception, clinicians must do a better job of explaining it in terms that everyone can comprehend.

CONCLUSION

This study reveals the facts about the low interest of females towards the utilization of contraceptive devices

or even other methods due to lack of information regarding benefits, side effects and services. Insufficient social and family supports especially from partner. Religious matters should be encounter. To cover all the aspects, awareness program and full support of their doctors, paramedics and health care workers can improve and correct the concept and minimize the fear and anxiety regarding the procedures.

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Original Article

Prevalence, Pattern and Factors Associated with Substance Abuse Among Young Adolescents in Malir Karachi, Sindh

Riaz Ahmed Bhutto[1], Razi Ullah Riaz[2], Shahid Kamran[3], Rakhshinda Younus[5], Nazia Qamar[6] and Pavan Kumar[4]

ABSTRACT

Objective: To find out the prevalence and pattern of substance abuse among young adolescents and the associated risk factors at Malir Karachi.

Study Design: Cross Sectional Study

Place and Duration of Study: This study was conducted at the Al-Tibri Medical College, Karachi from July 2021 to December 2021.

Materials and Methods: We have used the Self-Administered WHO Model Core Questionnaire to collect information on use of various substances among adolescents within Malir district Karachi. Data was analyzed by using SPSS version -25.

Results: A Total number of male adolescents were n=518 (100%) and no females were questioned due to socio-demographical environments and ethical view. Out of the 518 participants, 67 (12.7%) were addicted of Gutka, panmasla and mainpuri along with smoking, 108 (20.9%) used tranquillizers without a medical recommendation. 103 (19.9%) consumed cannabis and bhang. 18 (3.7%) young boys had tried heroin. 112 (21.6%) adolescents had used other opiate drugs their own on advice of friends for recreational purpose. Study showed significant positive but weak linear correlations between recreational and dependent use (r=0.161, p=0.003).

Conclusion: Study indicates a high prevalence of tobacco and inhalants use among adolescents in Malir Karachi.

Key Words: Substance, Substance Abuse; Prevalence; Factors; Young adolescents

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INTRODUCTION

Substance abuse is a convincing and out of control substance utilize. Substance abuse, also described as neurotic substance utilize, is characterized as an individual's inability to control his or her utilization of the substance, which over time presents obstacles in a man's life on the mental, social, academic, and professional levels[1]. The term of substance dependency or neurotic reliance has served as the foundation for the representation of substance addiction. It offers qualities like distraction, state of mind adjustment, resilience, withdrawal and practical impairment [2].

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Like different addictions, moreover, substance mishandle has been connected to an assortment of problems and issues. The use of alcohol, cigarettes, cannabis, and other psychoactive substances by young people worldwide is one of the most significant public health issues[3]. In Pakistan it is now growing problem. Before it was considered a problem of working and street children or children who were involving in substance trafficking business but it is currently affecting school going children as well. Researches in Pakistan have demonstrated that there is an expanding occurrence in the utilization of substances, and a diminishing age of onset, of these substances[4]. Most young children start their utilization of substances with cigarettes and later advance to more unsafe substances, for example, cannabis and cocaine[5]. Vartika Saxena in his research revealed a considerably higher prevalence of substance misuse among school-age teenagers from economically secure families who receive pocket money from their families and who develop a habit of substance abuse as their literacy levels rise. Most of them use drugs in the late afternoon or evening[6]. The majority of the illicit substances originate from the neighboring Afghanistan. As indicated by the UN estimate, 6.7 million individuals in the nation are substance users[7]. Substances of choice used are Supari, gutka, pan followed by hashish (cannabis), sedatives

and tranquilizers, opium, injecting drug use, ecstasy and solvent Abuse among school Children[8]. Researchers discovered that factors like joint families, parental control status, and employment status were associated with much greater levels of substance misuse[9]. Therefore this turns out to be more vital to analyze these elements in the quick changing social milieu.

A basic source of information to identify the high-risk pattern, example, and connections between drug use and sociodemographic factors is provided by understudy substance use research.

MATERIALS AND METHODS

It is a cross-sectional study. Young adolescents from public and private secondary schools, employed in private and public sectors, shops located in rural and urban areas of district Malir, Karachi were randomly selected for inclusion in the study. Study duration was from July 2021 to December 2021. Total 518 adolescents were selected by using simple random sampling technique. We have used the Self-Administered WHO Model Core Questionnaire to collect information. Inclusion criteria were adolescents from age between 11-20 years. Adolescents below 10 years of age or having any mental deformities, or unwilling to participate were excluded from study. All participants i.e. Parents/Guardian/Headmasters were asked for a written consent before participation in the study. Data was analyzed by using SPSS version 25.

RESULTS

Total number of male adolescents were n=518 (100%) who selected for study belong to Malir district including city, towns, and rural areas answered the questionnaire, majority among them were students, others were employed in various public and private institutions and shops, and no females were questioned due to socio-demographical environments and ethical view.

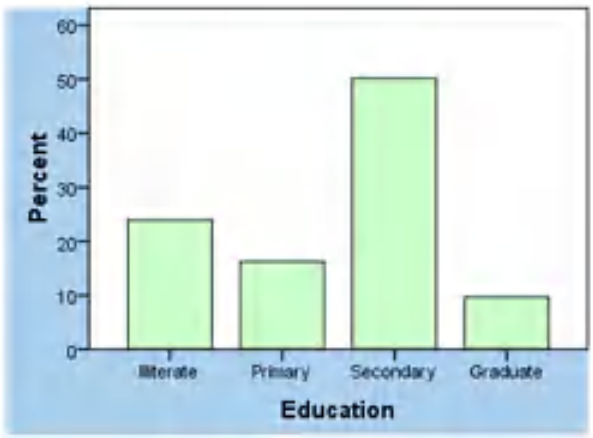

Figure No.1: Education Status of Study Participants

Study sample were distributed into two categories, having age less than 12 years and age more than 12 years. 15.16 ± 2.256(11-20). 96 study participants were unemployed or doing their own business, some of among them were doing nothing.

Educational, marital, occupation and residence status of the study samples was divided into different categories as shown in Table I and in Figure 1.

Table No.I: Socio-demographic Characteristics of Study Subjects (N = 518)

Variables		Frequency (n)	Percentage (%)
Age	15.16 ± 2.256(11-20)	518	-
Gender	Male	518	100
	Female	0	0
Education	Illiterate	124	23.9
	Primary to Matric	80	15.4
	Intermediate	264	51.0
	Graduate	50	9.7
Marital Status	Married	37	7.1
	Un-Married	481	92.9
Occupation	Students	364	70.2
	Unemployed	96	18.6
	Employed	58	11.2
Residence	City	178	34.4
	Town	218	42.1
	Rural	122	23.5

Majority of study participants' were having joint family system n=448 (86.5%). As regards to parent's education of participant, most of mothers were illiterate or middle standard education while majority of their fathers were matriculate, only 6 (1.1%) mothers and 27 (5.2%) of participants' fathers were higher education. Majority of respondent was starting smoking after 12 years of age and was taking one to five cigarettes daily, and 141 (27.2%) respondents has been smoking more than two years. 39 (7.5%) adolescents are regular and chain smokers. 67 (12.7%) were also addicted of Gutka, panmasla and mainpuri along with smoking, among them 48 (9.3%) study participants started taken chewing tobacco before age of twelve years. 110 (21.2%) respondents had had alcoholic drinks among them 28 (25.5%) adolescents had taken before age of 12 years. Of the responders, 108 (20.9%) used tranquillizers without a medical recommendation, among them 19 (3.7%) were having less than 12 years of age mostly taking tranquillizers by mean of eating, swallowing and in form of injection. Luckily only one individual had been taking amphetamine stimulants without prescription of doctor by mouth. When questioned about consuming of cannabis and bhang 103 (19.9%) accepted that they had tried these addictive, 11 of them had been taking six to nine days in a month in the form of eating or swallowing. It is contented to

know that only one respondent had used cocaine on insists of friends. It was shocked to learn that 18 (3.7%) young boys accepted that they have had tried heroin, one of them was less than 12 years of age they had taken it in form of smoking, sniffing and injection. 103 (19.9%) young boys had used opium after the age of twelve years, while 15 boys had used it below the age of twelve years. 112 (21.6%) adolescents had used other opiate drugs their own on advice of friends for recreational purpose and 66 (58.9%) are still using these drugs since more than one year, 3 to 5 days averagely per month in form of eating, smoking, sniffing and by means of other ways. 69 (13.2%) respondents acknowledged that when they wanted to pleasure themselves, they would periodically sniff glue, breathe aerosol spray, or inhale any other gases, sprays, or vapors from substances. The interviewees' most frequent justifications for using drugs were to fit in with their friends, to feel like an adult, and for recreational purpose. Any type of tobacco, inhalants, and opium and other opiate narcotics were the most frequently used substances among the participants (10.7%).

Table No.2: Comparison of Socio-Demographic Characteristics with prevalence of substance abuse

Characteristics		High Prevalence N (%)	Low Prevalence N (%)	Odds Ratio	95% CI	p-value
Age (year) (15.16 ± 2.256)	Less than 12 More than 12	8 (36.4) 19 (37.2)	6 (70.5) 14 (63.6)	1 0.83	- 0.29 2.16	0.05
Gender	Male Female	40 (39.6)	21 (20.4)	0.66	0.36 – 2.06	0.03
Education	Illiterate Primary to Secondary Intermediate Graduate	11 (17.7) 13 (32.5) 52 (39.4) 6 (64.0)	09 (82.3) 07 (47.5) 20 (40.4) 4 (26.0)	0.21 1 0.56 0.18	0.10 - 1.13 – 0.32 – 2.32 0.15 – 1.07	0.80
Marital Status	Married Un-Married	28 (34.3) 44 (39.3)	16 (65.7) 27 (60.7)	1 1.25	– 0.29 – 1.72	0.37
Occupation	Students Unemployed Employed	53 (26.4) 39 (67.2) 28 (57.1)	18 (53.6) 09 (32.8) 29 (43.2)	0.15 0.12 0.10	0.06 – 0.48 0.11 – 0.76 0.08 – 0.66	0.03
Residence	City Town Rural	51 (46.0) 43 (39.4) 48 (13.1)	48 (54.0) 26 (60.6) 33 (86.9)	0.58 0.73 1	0.25 – 1.31 0.36 – 1.71 –	0.26

Table No.3: Comparison of Socio-Demographic Characteristics with pattern of substance abuse

Characteristics		Recreational use N (%)	Dependent use N (%)	Odds Ratio	95% CI	p-value
Age (year) (15.16 ± 2.256)	Less than 12 More than 12	5 (16.4) 16 (37.2)	3 (54.5) 10 (33.6)	0.42 1.20	0.18 – 0.90 0.58 – 1.90	0.32
Gender	Male Female	60 (49.2) –	18 (22.1) –	0.50 1.19	0.22 - 1.51 0.59–1.96	0.65
Education	Illiterate Primary to Secondary Intermediate Graduate	15 (19.9) 23 (31.1) 41 (31.1) 8 (55.2)	13 (72.2) 10 (54.4) 24 (64.4) 3 (36.1)	1.61 0.67 0.65 0.36	0.80 - 1.22 0.31 - 1.82 0.27 – 1.55 0.17 – 1.41	0.45
Marital Status	Married Un-Married	28 (34.3) 44 (39.3)	16 (65.7) 27 (60.7)	0.95 0.47	0.41 – 1.85 0.19 – 1.22	0.22
Occupation	Students Unemployed Employed	73 (67.8) 53 (26.4) 39 (67.2)	45 (50.0) 18 (53.6) 09 (32.8)	0.93 1.20 0.16	0.57 – 1.22 0.60 – 1.91 0.15 – 0.92	0.46
Residence	City Town Rural	51 (46.0) 43 (39.4) 48 (13.1)	48 (54.0) 26 (60.6) 33 (86.9)	0.53 0.78 0.17	0.22 – 1.41 0.39 – 1.79 0.08 – 0.89	0.23

Table No.4: Comparison of Socio-Demographic Characteristics with factors associated with substance abuse

Characteristics		Good awareness about drug abuse N (%)	Bad awareness about drug abuse N (%)	Odds Ratio	95% CI	p-value
Age (year) (15.16 ± 2.256)	Less than 12 More than 12	19 (03.7) 171 (33.0)	89 (17.2) 239 (46.1)	0.38 0.36	0.16 – 1.22 0.19 – 1.37	0.98
Gender	Male Female	108 (20.8) -	410 (79.2) -	0.57 -	0.28 – 1.74 -	0.49
Education	Illiterate Primary to Secondary Intermediate Graduate	37 (07.1) 56 (10.8) 179 (34.6) 36 (07.0)	87 (16.8) 24 (04.6) 85 (16.4) 14 (02.7)	0.56 0.35 0.33 0.29	0.24 - 1.51 0.19 – 1.37 0.18 – 1.29 0.17 – 1.12	0.04
Marital Status	Married Un-Married	19 (03.7) 212 (41.7)	18 (03.6) 269 (51.0)	0.37 0.21	0.22 – 1.47 0.11 – 0.82	0.24
Occupation	Students Unemployed Employed	212 (40.8) 55 (10.7) 30 (05.8)	152 (29.4) 41 (07.9) 28 (05.4)	0.14 0.23 0.22	0.21 – 1.33 0.14 – 0.91 0.13 – 0.95	0.28
Residence	City Town Rural	116 (22.4) 112 (21.6) 43 (08.3)	82 (16.0) 106 (20.4) 79 (15.3)	0.20 0.32 1	0.15 – 1.01 0.17 – 1.11 –	0.18

Table No.5: Correlation of Age & Education with Adequate Knowledge about substance abuse

Characteristics	Total	Adequate Knowledge N (%)	In-adequate Knowledge N (%)	Adjusted OR (95% CI) *	p-value
Age (year)	Less than 12 More than 12	19 (03.7) 171 (33.0)	89 (17.2) 239 (46.1)	0.54 (0.23 – 1.56) 1	0.03 -
Education					
Illiterate	124	37 (07.1)	87 (16.8)	0.20 (0.09 – 0.54)	0.04
Primary to Secondary	80	56 (10.8)	24 (04.6)	0.88 (0.43 – 2.25)	0.20
Intermediate	264	179 (34.6)	85 (16.4)	0.59 (0.33 – 1.59)	0.14
Graduate	50	36 (07.0)	14 (02.7)	0.27 (0.12 – 0.75)	0.07

Association of socio-demographic characteristics with dependent variables was explored using Pearson's correlation analysis with a p-value of ≤ 0.05 and 95% of CI taken as significant. Occupation was showed good association with adequate education whereas age and residence was found to be positively associated with adequate practice pertaining to pattern and factors associated with substance abuse respectively as indicated in Table 2 to 4.

Univariate analysis of age and occupation indicated those participants of age group less than 12 years hardly have good awareness and age group above 12 years of age also was not statistically significantly associated with adequate awareness about drug abuse.

To determine the correlation between substance use and socio demographic factors, association analyses were performed. Adolescents from nuclear families showed a higher prevalence of substance use. None of the other demographic factors significantly correlated with the frequency of substance use among teenagers.

Following criteria were used to interpret correlations: Weak correlation is defined as 0.01 to 0.25, fair correlation as 0.25 to 0.50, good correlation as 0.50 to 0.75, and excellent correlation as 0.75 and beyond. This research revealed significant positive but weak linear correlations between recreational and dependent use ($r=0.161$, $p=0.003$). The study found that there is a substantial association between the utilization of awareness in this study and the relationship between recreational use and dependent use.

DISCUSSION

This survey is a self-reported questionnaire based study. Some of the respondents were hesitating to reply some questions and non-cooperative did not like to reply

properly though they voluntarily participated in survey without any fear or force. According to the study's findings, nearly half (51.8%) of the male teenagers admitted using one or more drugs at some point in their lives. Vartika Saxena in his study reveals that 46.9% prevalence of substance misuse among male adolescents, which is lower than the figures of 70.1% recorded. Although Juyal et al. observed a somewhat lower prevalence (45.8%) in their survey of intermediate school students in the same district four years back[11]. The high frequency of drug and cigarette use among youth could be due to a number of factors. Students have easy access to smokes and smokeless tobacco products, and using them is acceptable in society[11]. The significant conclusion in this study is that, compared to the results of the previous study, and over 50% of the respondents consumed solvents or other substances[12]. However, only 20% of the subjects admitted to drinking, which was quite high compared to earlier research from the region[13]. Very few teenagers in our survey admitted using heroin, cocaine, or amphetamines. Similar to the results of the last survey, nearly half of the individuals claimed to have started using drugs after the age of 12[14]. This reflects how easily drugs are accessible to young people, and drug usage during festivals may also contribute to the increase prevalence. Friends and acquaintances sell drugs including betel nuts, tobacco, cigarettes, marijuana, and locally brewed booze. This is most common specified reason. Few of them reported being to feel like adult and like the effects of substances[15]. However, experimenting with drugs for fun or out of curiosity can be extremely risky since recreational use can develop into more severe use and dependence. In comparison to other investigations, the majority of the respondents (62.9%) reported using drugs once or twice each month. Adolescents from nuclear families showed a higher prevalence of substance use[16]. Lack of parental supervision and a lack of family members who may provide support could be the cause[17]. The reason could be a lack of supervision by their parents and no support members in the family to talk about issues related to substance use as reported by subjects who had less than two siblings in the family. Schools are frequently acknowledged as key locations for initiatives aimed at preventing teen substance use. An essential factor of school health promotion is the substance use policy.

CONCLUSION

According to our research, Malir Karachi's youth use of tobacco and inhalants is highly prevalent. Adolescent substance use is linked to low educational levels and fewer family members. Friends are the main supplier of drugs and the people who introduce them to drugs. We cannot establish temporal or causal relationship in descriptive cross sectional study; therefore no critical conclusion can be expected.

Author's Contribution:

Concept & Design of Study:	Riaz Ahmed Bhutto
Drafting:	Razi Ullah Riaz
Data Analysis:	Riaz Ahmed Bhutto, Shahid Kamran, Rakhshinda Younus, Nazia Qamar, Pavan Kumar
Revisiting Critically:	Razi Ullah Riaz, Riaz Ahmed Bhutto
Final Approval of version:	Riaz Ahmed Bhutto

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

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Original Article

Hepatitis B in Khairpur Sindh

Frequency of Hepatitis B in Civil Hospital District Khairpur Province of Sindh, Pakistan

Sarmad Saeed[1], Shehzad Tariq[2], Farukh Imtiaz[3], Bakhtiar Ahmed[5], Shaista Khan[6] and Shams un Nisa Najiah[4]

ABSTRACT

Objective: Viral hepatitis B stays to be a chief health problem in Pakistan's Sindh province which encourages retrospective evaluation of the current frequency of its occurrence.

Study Design: Prospective study

Place and Duration of Study: This study was conducted at the Civil Hospital district Khairpur, Sindh province of Pakistan in period of 15 years from Jan 01, 2007 to Aug 30, 2021.

Materials and Methods: A total of 860,470 individuals of both sexes were screened for HBsAg in Civil Hospital Khairpur, encompassing the period of 15 years. HBsAg as a marker of HBV was considered in all serum samples which were tested using the Roche COBAS CORE HBsAg-II EIA system. SPSS version 23 was used for data entry and analysis.

Results: The prevalence of Hepatitis B (HBV) was analyzed over the period of fifteen years (2007-2021), in our study. In 2007, (16.0%) HBV was reported. It was seen that the prevalence of HBV were more than ten percent from 2007-2011. In 2012, it was (6.4%). But, after 2015, HBV was gradually decreasing. Therefore, in 2021, only (4.2%) was observed. The Linear forecasting trend line showed the decreasing trend.

Conclusion: HBsAg positivity in Khairpur has steadily decreased in frequency from 16% positive cases in 2007 to 4.2% positive cases in 2021.

Key Words: HBsAg, Frequency, Khairpur, Sindh, Pakistan.

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INTRODUCTION

Hepatitis B virus infection is one of the prominent public health issues. It is a leading reason of Chronic Liver Diseases (CLD) [1].According to WHO estimation, "296 million people were living with chronic hepatitis B infection in 2019, with 1.5 million new infections each year. Same year hepatitis B resulted in an estimated 820,000 deaths, mostly from cirrhosis and hepatocellular carcinoma (primary liver cancer)."[2]

The worldwide prevalence of hepatitis B virus varies broadly, with frequency fluctuating from 0.1% to 20%.[3]While high prevalence regions include China, parts of the Middle East and sub-Saharan Africa with hepatitis B positive cases is >8%, and low prevalence regions includes the United States, Northern Europe and Australia where rate is <2% hepatitis B positive, Intermediate prevalence with 2% to 7% hepatitis B positive cases is reported, in Japan, the Indian subcontinent, and parts of central Asia.[4,5,6,7]

Pakistan lies in the intermediate prevalence zone of hepatitis B while carrier rate is 3-4%. Hepatitis B is evolving into a big health problem.[8] Recent observations of chronic hepatitis, Hepatocellular carcinoma and cirrhosis from various regions of Pakistan showed 20-30% hepatitis B positivity in HCC patients.[9]As such viral diseases required substantial amount of resources[10] from health budget which ultimately increases the burden on government expenditures. Moreover further resources are used to restrain diseases and mortality rate.Hepatitis B can transmit vertically during pregnancy and cause early chronic liver disease. It is imperative to keep the close watch on the trends of viral diseases.

We wanted to check the trend of hepatitis B over last 15 years in our Outpatient department where the patients are from all ethnic and age groups visit, and are from numerous parts of Pakistan. We also wanted to endorse our opinions as regards to practices of these regions

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which can be responsible for an increase in spread of this viral hepatitis.

MATERIALS AND METHODS

The current study was conducted at The Civil hospital Khairpur. Data on blood immunological reactions had been collected since 2007.All samples were collected according to the protocols approved by the institutional ethical review board.A total of 860,470 people screened for HBsAg at Civil Hospital Khairpur in the serology laboratory during the period of 15 years from Jan 01, 2007 to Aug 30, 2021; out of which 456,049 were females (53%) and 404,421 were males (47%).

The subjected people were from the broad population group which includes women undertaking prenatal blood screening, children, and students, hospitalized patients with dysfunctional or regular liver functions, blood donors, professional health workers, doctors and folks completing foreign-travel visa requirements.

All candidates were screened for hepatitis B surface antigen HBsAg, Blood samples of about 5 ml blood from grown-ups and 1-3 ml from children and infants was taken in one-use sterile syringes, and readily shifted into sterile test tubes which were clot at room temperature, later at 1000rpm centrifuged for around 16 mins, and the buoyant serum on time removed from the debris and crammed cells. Evidently hemolytic samples which may cause false positive test outcomes were rejected.

Samples were tested using the HBsAg II EIA (Roche) solid phase qualitative enzyme immunoassay in the COBAS CORE analyzer. Manufacturer's instructions were strictly followed while performing the assays. Samples which were at or above the threshold value for HBsAg test were taken as reactive and the tests were repeated two times for further verification. In situation of repetitively positive results in two out of three analyses, confirmation test was implemented. Clienteles were self-driven or were routine appointments, and beyond taking gender and age, no attempt was feasible to acquire some history of first contact or probable cause of infection related with HBsAg positive patients as it was retrospective study.

A electronic data sheet was used for record examination and statistical analysis; all data were evaluated with SPSS23.0.We calculated prevalence of viral markers in total people screened positive with HBsAg (with 95% confidence interval (CI)) from total screened samples for each year to assess the frequency of infection in blood samples per year. Prevalence percentage was defined as number of seropositive people divided by total number of people for each year. To determine the infection trend in population, frequencies were plotted as the Linear forecast.

RESULTS

The prevalence of Hepatitis B (HBV) were analyzed over the period of fifteen years (2007-2021), in our study.In 2007, (16.0%) HBV was reported. It was seen that the prevalence of HBV were more than ten percent from 2007-2011. In 2012, it was (6.4%). But, after 2015, HBV was gradually decreasing. Therefore, in 2021, only (4.2%) was observed. The Linear forecasting trend line showed the decreasing trend. (Table. I). (Figure. I).

Table No.1:

Sr. No	HBV Year	HBV Total Screened	HBV Positive cases	HBV Positive (%)
1	2007	15077	2407	16.0
2	2008	13297	2059	15.5
3	2009	25583	2020	7.9
4	2010	13533	1448	10.7
5	2011	16873	1984	11.8
6	2012	22111	1408	6.4
7	2013	20868	1518	7.3
8	2014	26427	2647	10.0
9	2015	23135	1858	8.0
10	2016	56507	3790	6.7
11	2017	99885	5323	5.3
12	2018	138993	7874	5.7
13	2019	141987	5309	3.7
14	2020	135476	5322	3.9
15	2021	110718	4657	4.2

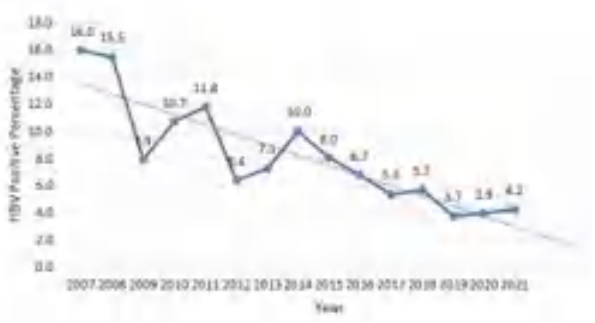

Figure No.1: Trend of HBV

DISCUSSION

This retrospective study (2007–2021) encompasses significant results showing that compared to previous years, the HBV infection rates have decreased substantially in patients visiting Khairpur civil hospital [Table 1]. HBsAg positivity among blood samples was around 16% during the years 2007 and 2008, which later decreased to 7.9% in 2009, following years it surged to 11.8% in 2011 but after 2014 there is steady downward trend, in 2021 it was 4.2%.

The outcomes of following study revealed a more protruding decrease in HBV positivity rate among the masses when the data of 15 years are plotted in linear forecast [Figure-1]. These promising results can be attributed to following factors. During the period 15 years there is relative improvement in drinking water by water filtration programs and increased access to better sanitation facilities. Also awareness of people about infectious diseases and prevention measures increased in the public with following measures.During our study period certain procedures incorporated into practice by health care authorities to avert the spread of hepatitis infections. These include encouraging the use of disposable syringes, hygienic practices and strict vaccination programs.

In our country, "Hepatitis B vaccine was first integrated in Pakistan's EPI (expended program on immunization) in 2001 as a tetravalent vaccine (with DPT) and later replaced with the pentavalent vaccine (DPT, HBV, Hib) given at 6, 10 and 14 weeks without a birth dose".[11] Other corresponding studies also validate our findings such as in 2006 studies Yousfani S et al.[12] observed 12.6% HBsAg positive cases, in 2008 studies 7.39% and 6.2% positive cases were observed by Malik N et al.[13] and Mujeeb SA et al.[14] while in 2009 4.6% positive cases were reported by Junejo SA et al.[15]

In 2021, Asghar MS et al.[16] observed Hepatitis B positive in 3.96% cases from 964 samples.Another study in 2021 by Khan MI et al.[17] observed from 119,263 people the overall frequency of hepatitis B was 1.42%. Similarly 1.7% of 1769 pregnant females screened for hepatitis B seropositivity in 2022 study by Ehsan A et al.[18]

Although these numbers are promising still, "in Pakistan, there are estimated 7-9 million carriers of hepatitis B virus (HBV) with a carrier rate of 3-5%."[19,20] This is quite a lot of patients.To fight the virus is however, requires strong political commitment in implementing health policies and improving health infrastructure. While it is imperative to employee multisectorial engagement through education and awareness on public and private level is also required.In our study, no difference among genders could be observed.

CONCLUSION

Our study encompassing 15 years (2007–2021) in which total of 860,470 people screened. Our finding reveals that there is downward trend in hepatitis B positive cases in Civil hospital Khairpur.

Recommendations: Further studies recommended investigating risk factors and common modes of transmission and awareness programs are required to further decrease its incidence.

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

Comparing the Efficacy of Standard Triple Therapy with Proton Pump Inhibitor and Vonoprazan and Amoxicillin Dual Therapy for Helicobacter Pylori Eradication

Muhammad Mumtaz Ather[1], Muhammad Tahir[2], Talha Rasheeq[2], Shahid Mukhtar[3], Aamena Gardazi[3] and Muhammad Ibrahim[4]

ABSTRACT

Objective: To compare the effectiveness of dual therapy with amoxicillin plus vonoprazan and standard triple therapy with amoxicillin, clarithromycin and proton pump inhibitor in terms of *H Pylori* eradication.

Study Design: Randomized controlled trial study

Place and Duration of Study: This study was conducted at the Department of gastroenterology in Bakhtawar Amin Medical & Dental College, Multan, from October 2021 to September 2022.

Materials and Methods: A total of 84 patients diagnosed as positive for Helicobacter Pylori infection through stool antigen test. Grouping of patients was done by lottery method in group A and B. In group A Vonoprazan and amoxicillin was given and in group B Amoxicillin with clarithromycin and proton pump inhibitor (PPI) were given. Main variables of study were Stool antigen (positive/negative), Bloating, diarrhea and nausea vomiting. SPSS version 24 was used for data analysis.

Results: The average age of Group A and Group B was 39.12±3.22 years and 38.51±2.84 years respectively. Male proportion is higher in both groups. In Group A, 71.4% patients had negative HP stool Ag and 59.5% patients had negative HP stool Ag, in Group B. (p>0.050). The prevalence of diarrhea, nausea vomiting and bloating in both the groups were 14.3% vs. 9.5%, 16.7% vs. 14.3% and 16.7% vs. 2.4 respectively (p>0.050).

Conclusion: Vonoprazan and amoxicillin dual therapy is better as compare to conventional triple therapy for h pylori eradication. In this era of rapidly developing antibiotic resistance, use of Vonoprazan based dual therapy for h pylori eradication is potentially new 1st line treatment.

Key Words: Helicobacter Pylori, Proton Pump Inhibitors, Amoxicillin, Clarithromycin, Vonoprazan

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INTRODUCTION

Helicobacter pylori also named as H pylori is a microaerophilic gram negative bacteria that can cause gastric mucosa inflammation is the main cause of peptic ulcer disease in the world[1].

It lives in form of colonies in gastric mucosa and responsible for gastric diseases like lymphoma of lymphoid tissue, adeno-carcinoma of gastric region and chronic gastritis[2]. Prevalence rate of h pylori varies from 30 to 50 percent in developed countries and 85 to 95 percent in developing countries[3].

Eradication therapy is recommended in patients with evidence of h pylori active disease; number of antibiotics is in practice for the treatment of h pylori[4]. Some of these regimens like triple therapy with PPI and combination of two antibiotics like amoxicillin with metronidazole or clarithromycin have high eradication rate and considered as best eradication therapy[5]. After decreased in eradication efficacy of these treatment plans other therapies have been practiced[5].

Failure to maintain PH above 7.5 and development of resistance against antibiotics are during treatment period is main reasons of decreased in efficacy[6]. Maintenance of high pH is achieved by using double dose of PPI in all treatment regimens[7]. Since the day of PPI efficacy was approved over non PPI treatment use of antisecretory medication along with antibiotics is recommended. Among antisecretory drugs Vonoprazan potassium based acid blocker is common[8].

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Vonoprazan works on contending potassium on luminal side of cells in parietal region and inhibit the HK ATPase and thus prevent the acid excretion[9]. Vonoprazan is more potent that can inhibit acid secretion as compare to PPIs, other advantages include less anti secretory variation, rapid onset and greater tolerability and safety[10]. Main reason behind failure of eradication therapy is local resistance against antibiotics like resistance against clarithromycin was reported 43.9% in a study conducted by Alavifard et al[11].

Since the day of Vonoprazan was used as an alternative of proton pump inhibitor in eradication of h pylori no local study available on this topic before, so this study will be a new gate towards this latest dual therapy and will fulfill this local reference gap.

MATERIALS AND METHODS

Study completed in the department of gastroenterology in Bakhtawar Amin Medical & Dental College, Multan, from October 2021 to September 2022 in one year. After the ethical approval from the ethical review board of hospital data collection was done. Written consent was obtained from the patients after detailed information about the purpose of study and ensuring confidentiality of data. Sample size was calculated by using WHO sample size calculator with 95% confidence interval, 80% power of study, 83.9% eradication with clarithromycin amoxicillin and PPI and 93.5% with Vonoprazan and amoxicillin. Diagnosed patients of H. Pylori infection with C13 urea breath test and campylobacter test were included in the study. Patients with age less than 18 years, allergic to study drugs, breast feeding or pregnant women, alcohol or drug addict, patients with history of previous partial gastrectomy, history of H. Pylori eradication therapy, using psychiatric medicine and malignant neoplasm were excluded from the study.

Endoscopy for upper GI to examine the stomach, esophagus, and duodenum and C13 breath test were taken. A specimen for biopsy of the antrum and corpus of the stomach was taken. Grouping of patients was done by lottery method as group A and B. Patients in group A were given Vonoprazan 20 mg twice daily and one gram amoxicillin was given twice in a day for 14 days. In the B group 20 mg omeprazole (proton pump inhibitor) twice in a day plus one gram amoxicillin twice in a day and calithromycin 500mg twice in a day for fourteen days. Patients were asked for adverse effects and compliance. Adverse effects may include bitter taste, abdominal pain, abdominal bloating, epigastric pain, general weakness , constipation, diarrhea, dizziness, loss of appetite, headache, nausea, skin eruptions, mucosal ulcer, vomiting and sleeping tendency. Termination of therapy was considered when compliance was less than 80%. Response of the therapy was evaluated after 4 weeks of stop of therapy and stool Hp antigen test was used for confirmation. Data analysis was performed on SPSS version 24, variables were classified as numerical (age) and categorical (stool antigen, bloating, diarrhea, nausea vomiting) and represented in form of mean ± SD and frequency percentage. Chi square and t-test were applied to observe association among outcomes. Significant probability value was taken as ≤ 0.05.

RESULTS

Overall, 84 patients enrolled and study patients were equally divided into two groups; Group A and Group B. The average age of Group A and Group B was 39.12±3.22 years and 38.51±2.84 years, respectively. There were more males than females in both the groups (Table. I). In Group A, 30 (71.4%) patients had negative HP stool Ag and 25 (59.5%) patients had negative HP stool Ag, in Group B. (p>0.050) (Figure. 1). The prevalence of diarrhea, nausea and bloating in both the groups were almost equal, (p>0.050) (Table. 2).

Table No.1: Demographic variables among groups

Variable	Group		p-value
	Group A, N (%)	Group B, N (%)	
Age (years)	39.12±3.22	38.51±2.84	0.616
Sex			
Male	30 (71.4)	28 (66.7)	0.637
Female	12 (28.6)	14 (33.3)	

Table No.2: Helicobacter pylori eradication and adverse events of the study groups

Variable	Group		p-value
	Group A, N (%)	Group B, N (%)	
HP stool Ag			
Negative	30 (71.4)	25 (59.5)	0.362
Positive	12 (28.6)	17 (40.5)	
Diarrhea	6 (14.3)	4 (9.5)	0.500
Nausea/vomiting	7 (16.7)	6 (14.3)	0.763
Bloating	7 (16.7)	1 (2.4)	0.026

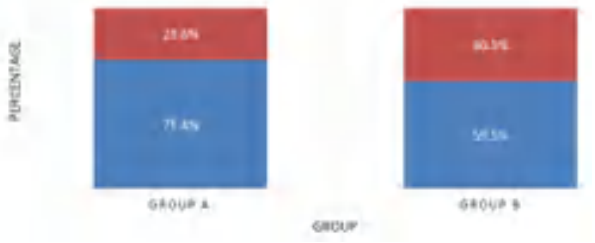

Figure No.1: Helicobacter Pylori Eradication

DISCUSSION

In our study in A group mean age of patients was 39.12±3.22 years and in B group mean age was 38.51±2.84 years, male ratio of patients is higher in both groups. A study was conducted by Suzuki et al[12] conducted a study to compare dual therapy with

Vonoprazan and triple therapy with clarithromycin mean age range of patients was 20 to 79 years in both groups. Eradication of h pylori after 7 days was observed 84.5% in triple therapy and 89.2% in dual therapy. Vonoprazan is not an antibiotic; its role in eradication is because of ability to maintain gastric pH.

In our study 59.5% patients with clarithromycin group have cure rate and in dual therapy 71.4% patients have cure rate. Graham et al[13] reported that cure rate with dual therapy (vonoprazan and amoxicillin) is 80% in patients with clarithromycin resistance. Addition of clarithromycin in dual therapy is associated with 12% cure rate remaining 88% patients used clarithromycin without any benefit. A study by Zuberi et al[14] on comparison of dual therapy with Vonoprazan and amoxicillin with triple therapy by adding clarithromycin and reported 93.5% cure rate with dual therapy and 83.9% by adding clarithromycin.

Adverse effects like bloating, diarrhea and nausea vomiting were also associated with eradication therapy in our study in Vonoprazan group minimal side effects observed. Qiu-Ju Lyu et al[15] conducted a study on this topic and shown minimum incidence of adverse effects in Vonoprazan group. Sakurai et al[16] also conducted similar study and reported higher tolerability with less adverse effects incidence in Vonoprazan group as compare to triple therapy with amoxicillin, PPI and clarithromycin.

In a report by Ozaki et al[17] in 2018 on comparison of Vonoprazan based triple therapy and proton pump based triple therapy and reported more than 90% eradication in Vonoprazan group and 80% in proton pump based triple therapy. Ouyang et al[18] also conducted a study on efficacy of Vonoprazan and reported that H pylori eradication rate with Vonoprazan is acceptable, it is safe to use and limits the unnecessary use of antibiotics. Vanoprazan can be used as an alternate to other regimens of H pylori eradication.

Furthermore, in United States and European countries efficacy of Vonoprazan based triple therapy was observed similar to triple therapy with proton pump inhibitors and its role in eradication of H pylori infection is also well accepted. These observations also support the use of Vonoprazan based eradication therapy in European and American region even in clarithromycin resistant population[19,20].

CONCLUSION

Vonoprazan and amoxicillin dual therapy is better as compare to conventional triple therapy for h pylori eradication. In this era of rapidly developing antibiotic resistance, use of Vonoprazan based dual therapy for h pylori eradication is potentially new 1st line treatment. Its use in terms of eradication rate and adverse effects is acceptable.

Limitations: Single center study with small sample size and poor compliance of patients are main limitations of our study.

Recommendations: More research with on larger number of patients or meta-analysis are recommended to evaluate the role of Vonoprazan with amoxicillin in h pylori eradication.

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

Effect of Bilateral Nasal Packing on Systematic Blood Pressure in Patients Treated with Septoplasty

Bilateral Nasal Packing for BP with Septoplasty

Sadaf Raffat Mustaf[1], Wajih-ud-Din Shinwari[2], Fatima Usman[3], Amir Akbar[4], Muhammad Jamil[5] and Muhammad Aslam Khan[1]

ABSTRACT

Objective: To find the Effect of bilateral nasal packing on systemic blood pressure in patients treated with septoplasty.

Study Design: Retrospective study

Place and Duration of Study: This study was conducted at the Department of ENT, Hitec Institute of Medical Sciences Taxila Cantt from 1st July 2021 to 30th June 2022.

Materials and Methods: One hundred patients were enrolled and divided into two groups depending upon the opted procedure they underwent. Fifity cases were enrolled in Group I where no nasal package was inserted while in other 50 patients from Group II conventional-anterior nasal packaging was introduced. All patients were kept on twenty four hours ambulatory monitotring of blood pressure pre septoplasty and post septoplasty on day two. A complete dempgraphic, clinical details of each patient were documented on a well structured quationnire.

Results: Most of the patients were male (54%) and 44% of the study participants were females. Total of 42% of the patients were in the age group of 20-30years. Fifty-five percent of male participants and 44% of female underwent nasal packing. Significant difference was observed in blood pressure with nasal packaging. Blood pressure was 118/75 before surgery and it was 130/90 after surgery.

Conclusion: Systolic and diastolic blood pressure was different before and after surgery with nasal packing.

Key Words: Nasal congestion, Obstruction, Well-being, Hypoxemia

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INTRODUCTION

Nasal airway blockage and congestion is one of the main problem which faced commonly by otorhinolaryngologists. Besides affecting financial and physical problem, it also poses serious detrimental challenge to the well-being of the person. Nose performs various important functions for human body including warming, air filtration and humidification.[1-4]

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Nasal airway blockage is observed in more than half of the patients but this situation is more frequently observe in pathological situations.[5]

Each side of nose show different nasal obstruction due to difference in nasal mucosa and this is becoming more obvious with the passage of time. Patient naturally shifts to oral breathing due to nasal blockage that in return alters arterial blood gases and respiratory mechanics.[6-8]

The unilateral nasal blockage is more commonly experienced by the patients and also increase the total airway resistance. Respiratory functions appeared to be altered in majority of the cases and hypoxemic state occurred in patients. Nasal packing after nasal surgery is considered as a standard protocol of the treatment. Studies also highlighted that, hypoxemic state also experienced in patients after nasal packing.[9-11] Certain methods have been employed including electric cautery, silver nitrate cautery and thermal cautery but did not prove successful results.

Nasal packing requires various treatment protocol that needs to be effectively performed during the procedure. This technique requires ribbon gauze with decongestant and anesthesia. This technique also needs a focused light source for nasal dressing and nasal speculum. Ceiling and floor also needs to be effectively pressed against each other. Few sides are also reported with

nasal packing such as neurogenic syncope, lacrimation from the eyes, necrosis, headache and decrease drainage from nasal ducts. Long term use of nasal packing also sometime leads to an infection especially if it kept consecutively for more than 48 hours. In present study, patients undergone for septoplasty were studied to find their effect on systolic and diastolic blood pressure. This study also helps to find the frequency of intra-nasal packing complications.

MATERIALS AND METHODS

This prospective study conducted at Department of ENT, Hitec Institute of Medical Sciences Taxila Cantt from 1st July 2021 to 30th June 2022 and 100 patients were included. The inclusion criteria was based on the fact that nasl asputum was conducted in them in addition to the septoplasty post their clinical evaluation. These patients sample size was generated through WHO sample size calculation using 80% power of test and 95% confidence of interval. The patients were further divided into two groups depending upon the opted procedure they underwen. Fifity cases were enrolled in Group I where no nasal package was inserted while in other 50 patients from Group II conventional-anterior nasal packaging was introduced. All patients were kept on twenty four hours ambulatory monitotring of blood pressure pre septoplasty and post septoplasty on day two. A complete dempgraphic, clinical details of each patient were documented on a well structured quationnire. Data was analysed using SPSS verion 26.0 inform of frequecnies and percentages. Chi sqaure analysis tool was applied with a p value <0.05 taken as significant.

RESULTS

Most of the patients were male (54%) and 44% of the participants were females. Total of 42% of the patients were in the age group of 20-30years followed by 39% and 19% in 31-40 and >40years age group respectively. The rural patients in this study group were 56% (Table 1).

More number of male participants were under-went nasal packing. Fifty-five percent of male participants and 44% of female underwent nasal packing (Table 2).

No significant difference was observed in blood pressure without nasal packaging. Systolic and diastolic blood pressure was almost same even before and after surgery (Table 3). Significant difference was observed in blood pressure with nasal packaging. Systolic and diastolic blood pressure was different before and after surgery. Blood pressure was 118/75 before surgery and it was 130/90 after surgery (Table 4).

Certain complications were also observed in patients with nasal packaging after surgery. High incidence of hemorrhage was observed in patients followed by septal perforations and vestibulitis (Fig. 1).

Table No.1: Demographical detail of patients (n=100)

Variable	No.	%
Gender		
Males	56	56.0
Females	44	44.0
Age (years)		
20-30	42	42.0
31-40	39	39.0
>40	19	19.0
Residency		
Rural	56	56.0
Urban	44	44.0

Table No.2: Groups and gender-wise distribution of patients (n=100)

Gender	Nasal Packing (n=50)	Without Nasal Packing (n=50)
Males	28 (55.56%)	28 (55.56%)
Females	22 (44.44 %)	22 (44.44 %)

Table No.3: Comparison of before and after surgery results of blood pressure without nasal packaging (n=50)

Characteristics	Before Surgery	After septoplasty 2nd day	P-Value
Mean systolic BP	118.66	118.76	>0.05
Mean diastolic BP	75	75.1	>0.05

Table No.4: Comparison of before and after surgery results of blood pressure with nasal packaging (n=50)

Characteristics	Before Surgery	After septoplasty 2nd day	P-Value
Mean systolic BP	118.96	130.16	>0.05
Mean diastolic BP	75	90.2	>0.05

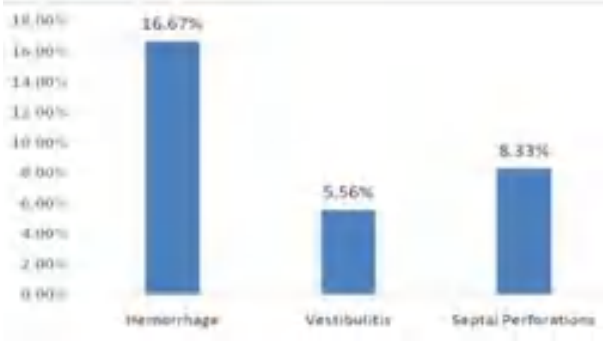

Figure No. 1: Prevalence of complications associated to nasal packaging

DISCUSSION

Nasal airway blockage is a common problem faced by the patients and more frequently referred in ENT clinics. Various treatment methods have been designed for treating nasal airway blockage. It not only alters the normal functions of breathing but also pose serious challenge to the functions of nose including air filtration and humidification of air. Endoscopic therapies for nasal airway treatment have widely been accepted worldwide. Nasal packing become the most cost-effective and reliable source for treating epistaxis. Complications and side-effects are also associated with the nasal packing method such as lacrimal canal blockage, excessive lacrimation and mucociliary disruption. Present study was designed to determine the difference in systolic and diastolic blood pressure among patients who underwent for septoplasty.[12-14]

In present study, majority of the study participants were males and they were in the age group of 21-30 years. Few number of patients were also present in >40 years' age group. Result of present study was comparable with already available data.[15,16] Patients of nasal packing group had elevated systolic and diastolic blood pressure and considerable difference was observed before and after surgery with nasal packing. Other studies also tried to establish the relation and difference in blood pressure values in septoplasty patients with nasal packing. Similar results were observed in those studies.[17,18]

Side effects and complications were also reported in previous literature. Study conducted by Gupta showed that, sleep problems, elevated blood pressure and drop in oxygen saturation were more frequently associated with nasal packing.[11] Nasal discomfort, sleep disturbance and dysphagia were reported by another study.[19] In present study, hemorrhage was reported as a main complication in 16% of the patients followed by septal perforations and vestibulitis, also showed more pain and suffering among patients with nasal packing.[20-22]

CONCLUSION

Nasal packing is a good approach for nasal blockage treatment and it's prevalent in ENT settings. Present study suggested that, this procedure shouldn't be the first choice of ENT for cardiac patients. Systolic and diastolic blood pressure was also different before and after surgery with nasal packing.

Author's Contribution:

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Original Article

Ultrasound Findings of Neck in Paediatric Patients with Hypothyroidism in Tertiary Care Hospital

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ABSTRACT

Objective: To evaluate ultrasonographic features of hypothyroidism in children at tertiary care hospital.
Study Design: Prospective cross sectional study
Place and Duration of Study: This study was conducted at the Department of Paediatrics, Children Hospital, Pakistan Institute of Medical Sciences, Islamabad from 1st January 2022 to 30th June 2022.
Materials and Methods: Fifty children who were less than 12 years with hypothyroidism were enrolled. The children with comorbid conditions and not willing to participate were excluded. The medical reports of children presenting with hypothyroidism and swelling in front of neck were evaluated after their consent by ultrasonography.
Results: The mean age of patients was 5.91±2.24. There were 27 (54%) were males and 23 (46%) were females. Fourteen (28%) had hypogenous type of echotexture, 2 (4%) had normal type of echotexture and 34 (68%) had heterogeneous echotexture. Majority of the participants had cyst i.e. 31 (62%) and 33 (66%) had lymphadenopathy. There was insignificant association of lobe size with age ($p>0.05$).
Conclusion: Ultrasound scanning is a non-invasive, widely accessible, and less expensive technique for diagnosis of thyroid disorder. In the investigation and treatment of thyroid problems, thyroid ultrasonography has become a well-known and effective tool.

Key Words: Thyroid disorder, Children, Ultrasonography, Diagnosis

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INTRODUCTION

Globally, the second most prevalent endocrine disorder in children, after diabetes, is thyroid disease, which has a significant share of pediatric endocrine disorders.[1] The clinical effects of thyroid disease depend on the age of the infant or child because of the developmental and organ- or tissue-specific effects of thyroid hormone on tissue maturation. Thyroid disorder in infants and children causes metabolic disturbances and also impairs growth and development.[2]

Tri-iodothyronine (T3), thyroxine (T4), and thyroid-stimulating hormone (TSH) circulating levels are unbalanced as a result of a variety of disorders defined by hypothyroidism or hyperthyroidism.[3] A central abnormality of hypothalamic-pituitary function can directly or indirectly cause thyroid dysfunction.

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Hypothyroidism can permanently impair a child's intellectual abilities if it is not diagnosed and treated in the early stages of childhood. Over time, it can also affect skeletal maturation and growth.[4] The spectrum of iodine deficiency disorders in children and adolescents includes goiter, subclinical hypothyroidism, poor mental function, delayed physical development, and increased thyroid gland susceptibility to radiation.[5] Children seem to suffer more frequently from thyroid diseases.[6] Compared to adults, there are significant differences in the etiology, prevalence, clinical presentation, and clinical outcomes of thyroid problems in children and adolescents.[7] Early diagnosis of thyroid disease is very important for a child's growth and development. Currently, ultrasonography in addition to clinical examination and thyroid function testing is the preferred approach for thyroid diagnosis.[8]

Thyroid imaging is recommended as part of newborn screening or when there is a palpable thyroid mass in children and adolescents to detect congenital hypothyroidism.[9] However; imaging plays an important role in the diagnosis of thyroid disease in pediatric patients. Radionuclide scintigraphy and ultrasound are the two main imaging modalities used to diagnose thyroid disease. The aspiration of nodules found can also be guided by ultrasound. Because scintigraphy provides functional information and ultrasound provides anatomic information, they complement each other. Ultrasonography is a first-line diagnostic tool for

lymphadenopathy and thyroid abnormalities in pediatric patients.[10]

In children, the size of the thyroid gland varies with age and is related to body surface area, height, weight, and age. Visual indicators of thyroid gland enlargement include anterior convexity rather than the normal isthmus's concavity, narrowing of the trachea, and greater isthmus thickness.[11-13] According to Chang et al, 14% of pediatric patients who showed no uptake on scintigraphy had a thyroid gland they were found in the correct location on ultrasound. If the thyroid is found in normal position, greater diagnostic power is available to determine aetiology, decision of discontinuation of treatment, and prognosis.[14] Ultrasound can also be used to ensure a newborn with congenital hypothyroidism has a normal thyroid in the correct location. Ultrasound has been increasingly utilized for evaluation of the thyroid structure. It is a useful adjunct to clinical exam to evaluate thyroid size and anatomy and to detect nodules. Therefore, this study was designed to evaluate ultrasonographic features of hypothyroidism in children at tertiary care hospital. It will help us to correlate possible underlying cause of hypothyroidism with ultrasonographic findings so that early evaluation and intervention can be done for better outcome of this condition.

MATERIALS AND METHODS

This prospective cross-sectional study was conducted at the Children Hospital, Pakistan Institute of Medical Sciences, Islamabad. After the approval of Ethics Committee, 50 children who were less than 12 years with hypothyroidism were enrolled. The Children with comorbid conditions and not willing to participate were excluded. The medical reports of children presenting with hypothyroidism and swelling in front of neck were evaluated after their consent by ultrasonography and findings were collected. Data was entered and analyzed by SPSS 25.0. Chi-square test was applied to find out significant association between categorical variables.

RESULTS

The mean age of patients was 5.91±2.24. There were 27 (54%) were males and 23 (46%) were females. As far as size of right lobe was concerned, there were 1 (2%) patients whose lobe size was below average, 10 (20%) were had normal and 39 (78%) patients were had above average. Whereas, 4 (8%) patients had left lobe size below average, 5 (10%) patients had normal lobe size and 41 (82%) had left lobe size as above average. Fourteen (28%) had hypogenous type of echotexture, 2 (4%) had normal type of echotexture and 34 (68%) had heterogeneous echotexture. Majority of the participants had cyst i.e. 31 (62%) and 19 (38%) were not having cyst. Almost 56% patients had focal lesions and 66% patients had lymphadenopathy (Table 1). Both left and right lobes are insignificantly associated with age (p>0.05) [Tables 2-3).

Table 1: Demographic and clinical features of pediatric patients (n=50)

Variable	No.	%
Age (Years)	5.91±2.24	
Gender		
Male	27	54.0
Female	23	46.0
Lobe size (right)		
Below average	1	2.0
Normal	10	20.0
Above average	39	78.0
Lobe size (left)		
Below average	4	8.0
Normal	5	10.0
Above average	41	82.0
Echotexture		
Hypogenous	14	28.0
Normal	2	4.0
Heterogeneous	34	68.0
Cyst		
Yes	31	62.0
No	19	38.0
Focal Lesion		
Yes	28	56.0
No	22	44.0
Lymphadenopathy		
Yes	33	66.0
No	17	34.0

Table 2: Association of age and lobe size (right) of pediatric patients

Age	Right Lobe			Chi square	P value
	Normal	Above average	Below average		
< 7 years	4	25	-	3.307	0.191
≥ 7 years	6	14	1		

Table 3: Association of age and lobe size (left) of pediatric patients

Age	Left Lobe			Chi square	P value
	Normal	Above average	Below average		
< 7 years	2	25	2	0.919	0.632
≥ 7 years	3	16	2		

DISCUSSION

Since ultrasound was first utilized as a new diagnostic tool for thyroid diseases in the 1960s, however it was evolved into a significant component to the examination.[15] It is common practice to employ thyroid

ultrasonography as a first-line diagnostic method for identifying and classifying nodular thyroid disease. Ultrasound scanning is a non-invasive, widely accessible, and less expensive technique for diagnosis of thyroid disorder. Furthermore, in cases of thyroid disease, real-time ultrasound imaging helps in planning diagnostic and therapeutic interventional procedures. A blood test or a radioactive isotope uptake test is typically necessary to evaluate thyroid function, which includes whether the thyroid gland is underactive, hyperactive, or functioning normally. This is the main limitation of ultrasonography in thyroid scanning.[16]

The results of current study showed the demographic and clinical features of pediatric patients. The mean age of patients was 5.91±2.24. There were 27 (54.0%) were males and 23 (46.0%) were females. These findings were compared with literature.[15,16]

The findings of an observational study reported that the majority of individuals with abnormal thyroid hormone levels belonged to the 0-1 year age group, followed by 9–12 years, according to demographic data on these patients. The total male to female ratio was 1:1.2, but as patients got older, the female majority of cases increased gradually, reaching 1:2.5 in the age group of 9-12 years.[17] However, a study revealed that thyroid issues are well recognized to be more prevalent in women of all ages.[18] Previous research in Indian children have shown that there are more females than males in these populations.[19]

In the present study it was reported that out of 50 patients, 14 (28%) had hypogenous type of echotexture, 2 (4%) had normal type of echotexture and 34 (68%) had heterogeneous echotexture. Majority of the participants had cyst i.e. 31 (62%) and 19 (38%) were not having cyst. Almost 56% patients had focal lesions and 66% patients had lymphadenopathy. In a study conducted in Japan conducted a study on 3 centers which includes children range from 3-18 years. The results of the study revealed that 56.88% have thyroid cysts and 1.65% have thyroid nodules.[20] Another study conducted in Nagasaki also reported that thyroid cysts was present in 42.51% and thyroid nodules in 0.73% of the children.[21] The use of US to assess thyroid structure has increased. To assess thyroid size and structure and find nodules, it is a helpful alternative to clinical examination. In autoimmune thyroiditis (AIT), diffuse echogenicity or the presence of micro nodules are commonly reported findings and are considered reliable indicators of AIT. US has also been useful in identifying patients at risk for developing hypothyroidism in patients with AIT.[22]

CONCLUSION

The important function that thyroid hormones play in fetal and early neonatal brain development and their effects on growth and development in the first two decades of life. In the investigation and treatment of thyroid problems, thyroid ultrasonography has become a well-known and effective tool. Not only radiologists, but also endocrinologists and surgeons who use advanced ultrasound techniques in their routine clinical and surgical practice are fond of these techniques.

Author's Contribution:

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Data Analysis:	Nighat Haider
Revisiting Critically:	Tanzeela Awan, Nighat Haider
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Original Article

Safety of SOF for Chronic Hepatitis C in CKD

Efficacy and Safety of Sofosbuvir (SOF) - Based Regimen for Chronic Hepatitis C Infection in Chronic Kidney Disease (CKD) Patients

Noman Kareem Qureshi[1], Farooq Ahmed[2], Munazza Nazir[3], Misbah Farooq[4], Mehreen Toufique[5] and Muhammad Rathore[6]

ABSTRACT

Objective: Sofosbuvir (SOF) is mostly eliminated via the kidneys. Patients with varied pretreatment estimated glomerular filtration rates (eGFR) were studied to determine the effectiveness and safety of SOF-containing regimens in chronic Hepatitis C patients.

Study Design: Cohort study

Place and Duration of Study: This study was conducted at the AJKMC, Muzaffarabad from 01.01.2020 to 30.06.2020.

Materials and Methods: Patients over the age of 18 in Pakistan who have been diagnosed with chronic HCV and whose eGFR is below 60 mL/min/1.73 m^2 are included. Between 01/01/2020 to 30/06/2020, they were treated at hospital for chronic hepatitis C with SOF-based antiviral medication. Laboratory tests, an abdominal sonogram, and a clinical evaluation were performed on every patient. For the latter, CBC, transaminases, bilirubin, albumin, HCV viral load, HBsAg, creatinine, fasting plasma glucose, alpha-fetoprotein, pregnancy tests, and hemoglobin A1c were measured.

Results: An initial eGFR was calculated in 100 subjects (3a genotype): The eGFR levels of 75 patients were below 30 while those of 25 patients were over 30. SVR was achieved in 90% of patients with SOF-based regimen. In 7% of the patient's adverse effect after SOF-based regimen was observed mainly due to worsened renal functionalities.

Conclusion: Treatment based on SOF proved effective and safe, causing very mild adverse effects. Larger research is still required to confirm these findings, however.

Key Words: Hepatitis C, Chronic Kidney Disease, Antiviral, Sofosbovir

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INTRODUCTION

Sofosbuvir (SOF) is the cornerstone of various FDA-approved oral hepatitis C regimens. Extremely large amounts of SOF are converted to active component GS-461203 and then dephosphorylated to the inactive component GS331007[1].

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In patients with an estimated glomerular filtration rate (eGFR) of 30 ml/min/1.73 m^2, the systemic exposure to SOF was 170% greater and the systemic exposure to GS-331007 was 450% higher than in those with normal renal function[2,3]. Therefore, individuals undergoing hemodialysis or those with an eGFR of 30 ml/min/1.73 m^2 or less should not take SOF. Patients with renal failure, such as those on dialysis, have a high unmet need for hepatitis C virus (HCV) therapy alternatives. Currently, glecaprevir, pibrentasvir, elbasvir, grazoprevir and ritonavir with or without dasabuvir are the only all-oral regimens authorized by the FDA for treatment in individuals with severe renal impairment. The risk of developing CKD and progressing to end-stage renal disease (ESDR) is higher in people with HCV infection, according to large-scale population observational studies[4,5]. This is due to the fact that HCV infection can cause renal dysfunction either directly, through cryoglobulinemic vasculitis and glomerulonephritis, or indirectly, through hepatic cirrhosis and related problems of portal hypertension. It is reasonable to anticipate an increase in the usage of SOF in patients with mild to severe renal impairment

because to the high demand and lack of viable alternatives[6]. In light of the aforementioned literature, the purpose of the present research was to assess the effectiveness and safety of SOF-based DAAs in CKD patients with chronic HCV infection.

MATERIALS AND METHODS

This is a cohort study. Patients over the age of 18 in Pakistan who have been diagnosed with chronic HCV and whose eGFR is below 60 mL/min/1.73 m^2 are included. Between 01/01/2020 to 30/06/2020, they were treated at hospital for hepatitis C infection with SOF-based antiviral medication. The potential for harm was outlined in detail, and patients signed a document giving their consent to publish their anonymous data in scientific journals. Laboratory tests, an abdominal sonogram, and a clinical evaluation were performed on every patient. For the latter, CBC, transaminases, bilirubin, albumin, HCV viral load, HBsAg, creatinine, fasting plasma glucose, alpha-fetoprotein, pregnancy tests, and hemoglobin A1c were measured. If a patient's serum creatinine was greater than 1.2 mg/dL, their eGFR was determined using the CKD-EPI equation. The fibrosis severity was determined by calculating a value of FIB-4. When other diagnostic options were unavailable or inconclusive, cirrhosis was diagnosed based on a FIB4 >3.25 value, an ultrasound image suggestive of cirrhosis, or a fibroscan result of 12.5 kPa. According to the established protocol, patients with hepatitis C infection were given SOF-based treatments. Those with an eGFR between 30-60 mL/min/1.73 m^2 (Stage III renal disease) and those with an eGFR of 30 mL/min/1.73 m^2 or less were considered to have stage IV or V renal disease. Both groups took 400 milligrams of SOF, but the first took it once daily and the second took it every other day. Dialysis patients received 400 mg of SOF an hour before their dialysis session. The following methods were used to track the efficacy and safety of SOF-based treatment plans: The patients were kept under observation (a) clinically for side effects, hepatic decompensation signs, and revaluation of possible medication interactions; and (b) laboratory-wise at weeks 12, and 24. (to test for SVR). In the lab, complete blood count, creatinine, eGFR, and a biochemical profile of the liver were measured. There was a follow-up assessment of viral load 12 weeks after therapy had ended. When HCV RNA levels dropped below the cutoff for detection (15 IU/mL), SVR was regarded to have been achieved. SPSS version 26 was used for the statistical analysis. Calculations were presented as means and standard deviations for numerical data, while percentages and raw numbers were used to represent categorical information. The means of quantitative variables were compared using a matched pairs t test. A value of p 0.05 was deemed as statistically significant.

RESULTS

Treatment effectiveness in relation to pre-treatment patient characteristics 90% of the study population showed a SVR (90 out of 100 participants). Viral responses were analyzed in light of demographic characteristics. A number of factors were found to be significantly associated with non-response, including dialysis use, treatment history, albumin levels, hemoglobin levels, and other parameters (Table 1).
Decompensated cirrhosis (Child B) was found in 19 patients, or 19%, and SVR was achieved in 16 patients, or 84.25%. Fortunately, nobody experienced any major side effects. 35 patients (35%) were on dialysis. thirty of them achieved SVR (85.7%), and 3 patients (8.5%) withdrawn treatment due to worsened renal function.
Patients' clinical features during treatment and relation with renal impairment.

Table No.1: Treatment success according to patient features and treatment protocol at the outset

Parameters	Sample size (n=100)	Treatment outcomes		
		SVR	Non-SVR	P value
Gender				
Male	65	59	6	
Female	35	31	4	
Age (Mean)	57.43	57.08	48.9	0.04
Age (Median)	55	55	45	
BMI	27.13	27.09	25.32	0.17
Viral Load (Mean)	4.56	4.43	0.56	0.01
Creatinine	1.7	1.7	1.7	-
eGFR	50.12	50.12	39.17	0.19
Dialysis	35	30 (85.7%)	2(6%)	-
Bilirubin	0.76	0.8	0.26	-
Albumin	4.5	5	3	0.49
ALT	36.4	33.8	22.7	0.009
Hemoglobin	13.2	13.8	11.1	0.37
AFP	6	5	19	.755
FIB-4	2.3	2..5	2.7	.231
Liver stiffness (kPa)	17.1	17.4	20	0.22
Cirrhosis by sonograph	1043	977	45	0.00
Previous decompensation				
Ascites	35	33 (94%)	2 (6%)	
Hepatic encephalopathy	6	5 (83%)	1 (17%)	
Oesophageal varices	15	14 (93%)	1 (7%)	
Treatment regime				
SOF+DAC	55	51 (92.7%)	4 (7.3%)	
SOF+VEL	45	39 (86.7%)	6(13.3 %)	

According to the KDIGO criteria, the patients were split into two groups. Patients have renal disease of stage IV or V were categorized into group with eGFR <30 mL/min/1.73 m^2, while the patients with stage III renal disease were categorized into eGFR ≥30 mL/min/1.73 m^2. A statistical variation was in the SVR was observed in both groups. About 68% participants achieved SVR in eGFR <30 mL/min/1.73 m^2. While 97% participants in eGFR ≥30 mL/min/1.73 m^2 achieved SVR.

SVR and Treatment regimens. In terms of the employed regimens, In Table 1. 92.7% SVR was achieved in the participants with SOF+DAC. 96.7%, SVR was achieved in regimen cohort of SOF+VEL.

Treatment failure and adverse effect In the 10 patients who had treatment failure, 2 patients (2%) did not attain a negative viraemia at the conclusion of the course of therapy, 1 patient (1%) relapsed, and 7 patients (7%) stopped the course of therapy due to side effects. The primary adverse event that required therapy cessation in individuals with renal impairment were worsening of kidney's functioning (7 patients).

Table No.2: Characteristics at baseline and the rate of SVR in relation to the degree of renal impairment

	eGFR ≥30 mL/min (n = 75)	eGFR <30 mL/min (n = 25)	P Value
Gender			
Male	50	15	
Female	25	10	
Age			
Mean	58.75	51.23	0.30
Median	59	54	
BMI			
Mean	28.23	27.12	0.105
Median	27	26	
Viral Load (Mean)	$0.51x10^6$	$0.38x10^6$	0.15
Creatinine	1.5	6.32	0.23
Dialysis	23	7	-
Bilirubin	0.88	0.85	0.205
Albumin	3.21	4.1	0.119
ALT	39	43	
Hemoglobin	12.91	13.2	0.45
AFP	6	6	0.50
FIB-4	2.89	1.76	0.022
Liver stiffness (kPa)	13	19.02	0.001
Cirrhosis by sonograph	920	132	0.001
Previous decompensation			
Ascites	29	6	
Hepatic encephalopathy	1	5	
Oesophageal varices	2	13	
Treatment regime			
SOF+DAC	36 (48%)	14 (56%)	
SOF+VEL	39 (52%)	11 (44%)	
Treatment response			
SVR	73 (97%)	17 (68%)	
Non-SVR	2(3%)	8(32%)	

DISCUSSION

Contrary to the widespread global practice of SOF limitation, several recent studies have shown the safety and effectiveness of SOF-based regimens in renal impairment participants. This trial observed at the effectiveness and safety of treating patients with chronic HCV who also had mild to severe chronic kidney disease. Twenty-five percent of patients with severe renal impairment and seventy-five percent of individuals with less severe renal illness obtained SVR. Finding that SOF generates about the same amount of active intracellular metabolites regardless of renal function may explain the high SVR rate.[7] High rates of SVR were also seen in a study of the safety and effectiveness of full dosage SOF in 29 patients with severe renal failure conducted by Cox-North et al[8]. In their phase II research of 59 patients with chronic HCV and ESRD on hemodialysis dialysis, Borgia et al. similarly showed an SVR rate of 95% after treatment with open-label full dosage sofosbuvir/velpatasvir for 12 weeks[9]. Among 28 patients with HCV G1 and stage 3 CKD, Shin et al. observed an SVR rate of 85.7% after evaluating the effectiveness and safety of full-dose SOF. Maybe that's because their research included more participants who already had cirrhosis and were on treatment than ours did[10]. A comparable SVR rate of 83% was seen by Saxena et al. in patients with an eGFR of 45 mL/min when using full-dose SOF-based regimens. The relatively high rate of treatment discontinuation owing mostly to adverse effects may account for their lower SVR[11].

Only 10% of patients in our study had treatment failure (non-response plus discontinuation), and no baseline factors were found to be associated with treatment failure in the subgroup of patients with severe renal impairment. According to the trials, patients who had never received treatment before enrolling in the DAA study did slightly better than those who had previously failed on Peg-IFNRBV medicine. SVR rates in cirrhotic patients range from 33% to 100%, and are heavily determined by the level of severe fibrosis[10].

7 people in this research (7%) dropped out of therapy due to adverse side events. Treatment termination was most common due to worsening renal functions in the subgroup of individuals with severe renal impairment. The frequency with which studies document unwanted outcomes varies widely. All patients getting RBV in Cox-North et al. study reported increased anemia, but no treatment dropouts (8). However, 79/1789 (4%) of participants in the well-known TARGET research by Saxena et al., reported stopping treatment due to adverse effects; 6% of these were considered to be "severe."[11] Paradoxically, the treatment completion rate

of SOF-based therapy in our study was higher than that observed with the use of renal disease-specific regimens, such as paritaprevir/ ritonavir/ ombitasvir+ dasabuvir ribavirin in the ERCHIVES study[12], in which only 69% (38/55) of patients with stage 4 0r 5 CKD completed therapy; or grazoprevir/elbasvir in the C-SURFER study. The latter included things like patients passing away, being lost to follow-up, refusing treatment, doctors dropping them, and patients leaving because of doctors' aggressive behaviours[13].

A total of 56 patients (56%) in our research had decompensated cirrhosis (Child B), and 93% of them achieved SVR. There were no severe adverse effects recorded. Seven patients (14.9%) with decompensated cirrhosis and ascites were included in Singh et al studies on the effects of full dosage SOF in patients with severe renal impairment. At the completion of therapy, 100% of their patients were responding well, and SVR was attained in 95.7%. In the pre-dialysis group, therapy did not improve hemoglobin or estimated glomerular filtration rate[14].

Hemodialysis patients in this trial had an SVR of 85.7%, with 5% dropping out due to anemia. This figure is much lower than that found by Agarwal et al., who evaluated the effectiveness and safety of SOF-based treatment in a group of 62 patients on maintenance hemodialysis. He found an SVR of 95.2% in his research[15]. There were no treatment discontinuations due to adverse events, however the majority of patients in the RBV group (n = 23; 56%) needed an increase in the erythropoietin dosage. Present study hemodialysis cohort was small, and the discrepancy IN SOF dose may explain the decreased SVR rate. Patients in the earlier trial were given RBV and SOF every day, but our hemodialysis patients only got medication every other day before their hemodialysis sessions. Several recent studies confirmed that the effectiveness of SOF decreases with decreasing dosage[16,17].

CONCLUSION

This study suggests that SOF-containing regimens are effective and safe for the treatment of those with chronic HCV who have moderate to severe renal impairment, as well as those who have hepatic decompensation. Patients with an eGFR 30 mL/min/1.73 m2 have been shown to benefit from taking sofosbuvir every other day. To underline safety issues and alter the prevailing thinking, however, prospective studies are required.

Author's Contribution:

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Original Article

Menstrual Patterns of Reproductive Age Group Women and Their Association with Thyroid Dysfunctions

Amina Bibi, Tabassum Ali, Tariq Mahmood and Sara Gul

ABSTRACT

Objective: This study was designed to evaluate the menstrual cycle patterns including cycle-specific characteristics and explore their relationship with thyroid hormones by measuring the levels of urine hormones in premenopausal women.

Study Design: Prospective Cohort Study

Place and Duration of Study: This study was conducted at the District Head Quarter Hospital Swabi from August 2021 to August 2022.

Materials and Methods: This prospective cohort study was conducted to evaluate the menstrual patterns and thyroid association among reproductive women. Data was collected by a pre-designed questionnaire and clinical diagnosis of thyroid performed by physicians. Menses were defined as two consecutive days of bleeding proceeding by three consecutive days of spoting. For monitoring, menstrual cycle patients were asked to submit their first urine void sample and kept their daily menstrual diaries for at least three menstrual cycles. We used univariate analysis for the distribution of each hormone. The log method was used to transform the TSH into a normal distribution. A linear mixed random effect model was used for those results reporting single outcomes.

Results: This study recruited 140 women with irregular menstrual patterns. Out of 140, a total of 52 cases of oligomenorrhea, 12 cases of neuropathic, 43 cases of polymenorrhagia, and 33 cases of menorrhagia were detected. These women reported a total of 423 cycles. We recruited cases between the age range of 18 to 45 years. A high association was observed between total T4 and Pd3G and E13G throughout the follicular and luteal phases. At various timeframes, we observed a high association of total and free T3 with high E13G concentrations. These T3 levels were also associated with Pd3G.

Conclusion: We observed that thyroid hormone levels were associated with several menstrual cycles. Across the menstrual cycle, a positive correlation between T4 and T3 indicates the effect of hormones on the female reproductive system.

Key Words: Menstrual cycle, Thyroid dysfunctions, Hormones

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INTRODUCTION

Menstrual cycle function plays an important role in reproductive health and fertility. The menstrual cycle is defined by the complex endocrine axis which is responsible for controlling ovaries and endometrium and represents the underlying hormonal milieu of the reproductive system of women. Therefore, the mestrual cycle is a major indicator of reproductive health and provides a pathway for epidemiologic research.[1,2]

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The Gonadotropins network and sex steroid hormones constitute the hypothalamic-pituitary-gonadal system. This system controls thyroid functions.[3] However, the association between thyroid functioning and female reproductive physiology is still debatable. The incidents of thyroid disorders are more prevalent in females than males. Thyroid disorders fluctuate the estrogen levels affect the menstrual patterns leading to menopause.[4] Incidents of menstrual disturbances are more highly reported in women suffering from hypothyroid and hyperthyroid than in euthyroid women.[5] Previous studies observed oligomenorrhea and menorrhagia in patients of hypothyroid whereas hypomenorrhea is highly reported in hyperthyroid women.[6-9] However, associations between thyroid disorders were found in clinical-based studies while very limited research reported an association with thyroid hormones. Furthermore, these studies were based on self-reported menstrual outcomes and integrated different outcomes as menstrual "disturbances" or "irregularities.[8,10] Therefore, the results of these studies are not strong enough to clarify the relationship between menstrual

patterns and thyroid functions. To fill this gap this study was designed to evaluate the menstrual cycle patterns including cycle-specific characteristics and explore their relationship with thyroid hormones by measuring the levels of urine hormones in premenopausal women.

MATERIALS AND METHODS

This prospective cohort study was conducted to evaluate the menstrual patterns and thyroid association among reproductive women in Gynaecology Department of DHQ sawabi hospital from August 2021 to August 2022. For this study, all the premenopausal women were eligible however, lactating or pregnant women were excluded. All the participants who were currently on thyroid medication were also excluded. Data was collected by a pre-designed questionnaire and clinical diagnosis of thyroid performed by physicians. This pre-designed questionnaire entailed information on thyroid medication used by participants and the menstrual cycle. Menses were defined as two consecutive days of bleeding proceeding by three consecutive days of spoting. For monitoring, menstrual cycle patients were asked to submit their first urine void sample and kept their daily menstrual diaries for at least three menstrual cycles.[11] Three menstrual cycles were defined as weeks for oligomenorrhea while diaries enlisted information about cramps, bleeding, stress, medication, and exercise habits. Urine samples were used to measure the estrogen and progesterone metabolites, estrone 3-glucuronide (E13G), and pregnanediol 3-glucuronide (Pd3G) within 17 days of the ovulation window. For measuring these parameters we used double-antibody time-resolved fluoroimmunoassays. At the research laboratory of our institution we analyzed the thyroid-stimulating hormone (TSH), total and free thyroxine (T4), and total and free triiodothyronine (T3) by using an immunoassay analyzer. For this purpose, the blind control method was used to strengthen the results. The self-reported bleeding intensity was measured by using a scale ranging from 0 to 4 grades throughout menses. We used the definition of Baird et al[12] for hormonal outcomes.

Statistical Analysis: All the data from the questionnaire and laboratory tests were transferred to the excel sheets for performing statistical analysis. We used univariate analysis for the distribution of each hormone. The log method was used to transform the TSH into a normal distribution. A linear mixed random effect model was used for those results reporting single outcomes. This linear effect model helps us in measuring individual correlations among multiple menstrual cycles per woman. We adjusted age and thyroid hormones as fixed effects for measuring the association between each thyroid and menstrual cycle outcomes. Coefficient Beta analysis was used for comparing the 3-day GM outcomes while the medium was treated as a reference because a previous study mentioned that both hypothyroid and hyperthyroid patients suffer from menstrual cycle disruption. An association between thyroid hormones and E13G and Pd3G was observed by fitting the linear mixed model. All these tests were performed by using the statistical package for Social Science (SPSS) version 23.0.

RESULTS

This study recruited 140 women with irregular menstrual patterns. Out of 140, a total of 52 cases of oligomenorrhea, 12 cases of neuropathic, 43 cases of polymenorrhagia and 33 cases of menorrhagia were detected. These women reported a total of 423 cycles. We recruited cases between the age range of 18 to 45 years. Women with experience of 1-2 (45%) pregnancies had high irregular menstrual patterns than others. We observed that 55.7% were obese, 63.5% never do any kind of exercise and 44.2% had moderate levels of stress. Detailed findings were presented in Table 1. In table 2, we presented different mean levels of total triiodothyronine, thyroxine, and Thyroid-stimulating hormone concerning the menstrual cycle, bleeding length, bleeding intensity, follicular phase length, and luteal phase. We observed that bleed length decreased with age obese women had longer cycles than others. We observed high FSH in women aged 41–54. No association of thyroid hormones was found with cycle length. However, we observed a significant association of free T4 levels with decreased cycle length. This association was observed due to variations in follicular phase length. No association of thyroid hormones was found between bleeding intensity while body mass index was independently associated (Table 2). Correlation Beta analysis was performed in table 3. A high association was observed between total T4 and Pd3G and E13G throughout the follicular and luteal phases. At various timeframes, we observed a high association of total and free T3 with high E13G concentrations. These T3 levels were also associated with Pd3G.

Table No.1: Characteristics of premenopausal women

	Total number of participants	Mean TSH (µIU/ml)	Mean Total T4 (µg/dl)
Age			
41-45	19 (13.5%)	1.56	9.7
36-40	40 (28.5%)	1.68	9.2
31-35	33 (23.5%)	1.6	9.33
26-30	28 (20%)	1.31	9.71

18-25	20 (14.2%)	1.41	8.26
Parity			
0 prior pregnancies	56 (40%)	1.29	8.6
1-2 prior pregnancies	64 (45.7%)	1.65	9.1
3 or more prior pregnancies	20 (14.2%)	1.54	9.2
Body Mass Index			
Normal	24 (17.1%)	1.59	8.8
Overweight	39 (27.8%)	1.41	9
Obese	78 (55.7%)	1.29	9.4
Weekly excercise			
0 times	89 (63.5%)	1.33	9.3
1-3 times	31 (22.1%)	1.59	8.78
> 3 times	20 (14.2%)	1.48	8.9
Stress			
Low	29 (20.7%)	1.52	8.9
Moderate	62 (44.2%)	1.41	8.35
High	49 (35%)	1.41	9.86

Table No.2: Clinical presentation of Thyroid hormones

	Mean Cycle length	Mean bleeding length	Mean bleeding intensity	Mean follicular phase length	Mean luteal phase length
Total tri-iodothyronine					
High	30.5	5.6	2.2	16.4	12.6
Medium	31	5.6	2.2	18.1	12.9
Low	29.1	5.7	2.3	17	13.4
Total thyroxine					
High	30	5.6	2.2	16.3	12.7
Medium	30.9	5.7	2.3	18.1	13
Low	30	5.6	2.2	16.3	13.1
Free triiodothyronine					
High	30.7	5.9	2.3	17.7	12.6
Medium	30.4	5.6	2.2	17.2	13.1
Low	29.6	5.4	2.2	16.6	13.2
Free thyroxine					
High	32.1	5.7	2.2	19	13
Medium	31.1	5.7	2.2	17.9	13
Low	28.2	5.5	2.3	15.4	12.9
Thyroid-stimulating hormone					
High	29.7	5.6	2.1	16.7	12.9
Medium	30.5	5.6	2.2	17.5	13
Low	30.4	5.7	2.3	17.5	12.9

Table No.3: Coefficient beta analysis

	FSH (mIU/mg Cr) in early follicular	FSH (mIU/mg Cr) in late luteal	Pd3G (µg/mg Cr) luteal phase	Pd3G (µg/mg Cr) in mid luteal phase	E13G (ng/mg Cr) in follicular phase	E13G (ng/mg Cr) in luteal phase
Total triiodothyronine						
High	-0.1 (-3.8, 3.6)	-0.6 (-3.9, 2.8)	1.0 (-1.6, 3.5)	1.2 (-1.0, 3.4)	9.2 (-1.5, 19.8)	6.6 (-1.3, 14.5)
Medium	7.5 (5.0, 10.0)	4.3 (2.1, 6.5)	9.8 (8.1, 11.5)	8.4 (6.9, 9.8)	35.5 (29.6, 41.5)	28.7 (23.4, 34.0)
Low	1.9 (-1.1, 4.8)	1.6 (-1.1, 4.2)	-0.8 (-3.1, 1.5)	-1.0 (-2.8, 0.7)	-2.9 (-10.5, 4.7)	-4.0 (-11.1, 3.1)
Total thyroxine						

High	1.0 (-1.4, 3.3)	0.7 (-1.3, 2.7)	2.2 (0.7, 3.8)	2.2 (1.0, 3.4)	7.4 (2.3, 12.4)	3.2 (-2.0, 8.4)
Medium	8.1 (6.0, 10.2)	4.8 (2.9, 6.6)	9.5 (8.1, 10.9)	7.9 (6.7, 9.0)	34.3 (29.4, 39.2)	28.5 (23.9, 33.2)
Low	-0.8 (-3.5, 1.8)	-0.9 (-3.3, 1.4)	-1.4 (-3.2, 0.4)	-0.9 (-2.3, 0.6)	-0.6 (-6.8, 5.5)	-0.9 (-7.1, 5.2)
Thyroid-stimulating hormone						
High	-0.7 (-3.1, 1.7)	-0.4 (-2.6, 1.7)	0.7 (-1.0, 2.4)	0.6 (-0.8, 2.0)	-3.5 (-9.0, 2.0)	-0.3 (-5.5, 5.0)
Medium	8.4 (6.4, 10.3)	4.9 (3.1, 6.6)	9.6 (8.2, 11.0)	8.2 (7.1, 9.4)	38.0 (32.7, 43.3)	30.1 (25.7, 34.4)
Low	0.2 (-1.3, 1.7)	0.0 (-1.4, 1.3)	-0.2 (-1.3, 0.8)	-0.2 (-1.1, 0.7)	1.0 (-5.0, 7.0)	-0.9 (-4.1, 2.4)

DISCUSSION

In this prospective cohort, thyroid hormones were examined to evaluate their effect on menstrual patterns. In this study, we found a positive association of high T4 with elevated levels of Pd3G and E13G throughout the menstrual cycle while low T4 levels were correlated with Pd3G, especially at the follicular phase. Meanwhile, several times during the menstrual cycle, we observed a positive correlation of total and free T3 with Pd3G and E13G levels. We observed that T4 was associated with the length of the menstrual cycle and similar findings were observed while adjusting the covariates. In the current study associations between cofounders and hyperthyroidism were observed in 3-day hormonal outcomes. Evaluation and interpretation of thyroid hormones and their association with menstrual cycle function are hard. However, many clinical studies observed menstrual disruption in women suffering from thyroid disorders. One of the studies observed elevated estrogen levels during pregnancy which leads to boosting total T4 due to thyroxine-binding globulin (TBG).[13]

In the current study, serum samples were collected before monitoring the menstrual cycle. These serum samples were used to measure the thyroid hormones so there is a great possibility that enhanced levels of pre-existing TBG increased the T4 concentration and resulted in a positive correlation of E13G and Pd3G. Therefore, we failed to produce meaningful results to explain the relationship. Comparing our results with International literature one previous study revealed high free T4 in the progesterone therapy group than in the placebo group.[14] This study observed a positive correlation between progesterone and thyroxine due to similar metabolic pathways. Both of these hormones are involved in maintaining basal temperature and energy expenditure. Albumin is the main carrier of both these hormones however, only 10% thyroxine was transported by albumin.[15] The positive correlation between T4 and E13G was observed in our study. These results are parallel to the previous studies which observed increased plasma estrogen levels in hyperthyroid women during their menstrual cycle.[16,17] One of the hypothesis claim that elevated T4 hormones also enhanced the sex hormones binding globulin.[5] These sex hormones enhanced estrogen levels and reduced clearance rates.[17] In hyperthyroid women, many studies reported increased amounts of androgen production and estrogens. Our study revealed similar results despite the variations in sample size as the study design. Similar levels of thyroid hormone and urinary estrogen metabolites were observed[18] but our study shows contradictory results when measuring plasma or serum estradiol concentrations.

Previous studies also reported the influence of behavior and environmental toxicants that affect thyroid functions. A disturbance in thyroid functions also menstrual cycles and the reproductive system.[19,20] However, in this study, BMI was not strongly associated with thyroid functions. In the current study, 89% of participants were exposed to persistent organic pollutants (PBB). These results were detected in their blood samples. These results indicate a direct and causal relationship between thyroid hormones and menstrual patterns when compared with other studies. This prospective cohort study monitored many menstrual cycles and has an edge over other self-reported studies. Observations over multiple cycles reduced the chances of misclassification and validate the results. However, our study has many limitations including a small sample size. In our study, we also observed two perimenopause cases. One of the women had a small menstrual cycle while one was amenorrhea however both these cases showed hormonal evidence of ovulation and eliminating both findings does not affect our overall results. We did not measure serum reproductive hormones. Our study was not able to detect the independent association of thyroid hormones due to low statistical power.

CONCLUSION

In conclusion, we observed that thyroid hormone levels were associated with several menstrual cycles. Across the menstrual cycle, a positive correlation between T4

and T3 indicates the effect of hormones on the female reproductive system.

Author's Contribution:

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