Editorial

MONKEY POX, A NEW PANDEMIC ON THE MEDICAL HORIZON.

Asif Hussain

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Monkey Pox is a zoonotic disease caused by an enveloped DNA virus of the Orthopox virus family. The first human infection was discovered in 1970 in the African continent. The main source is wild rodents, but sporadic human cases were reported in Africa. The current spread of the virus across the globe involving more than 3000 cases so far, may be due to multiple reasons, including but not limited to changes in the virus biology, human behavior, fading immunity against smallpox, increase in international traveling, large gatherings with on-site unprotected sex, and relaxing of Coronavirus restrictions.[1]

The main transmission routes are respiratory droplets, skin contact with lesions, contact with animal secretions, contaminated fomites, and possibly sexual routes.[2] Sex-related transmission has not yet been established, although studies support the relationship. The virus had been detected in seminal fluid in many positive cases.[3] More cases are detected among those having men-to-men sex and are linked to large gatherings with on-site sex activities. Also, as the lesions are predominantly on the face, hands, genital & anorectal area, so can be confused with other sexually transmitted infections (STIs), especially when there are few or a single lesion. Safe sex practices, especially barrier methods such as condoms, are recommended up to 8 weeks after the resolution of the disease.[2,3]

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Cases have also been detected in heterosexual men; hence, it's not entirely a disease in homosexual men. Vertical transmission is also reported and newborns can contract the infection from the infected mother during birth. People at high risk of getting the infections are exposed to wild animals, immunocompromised, HIV-positive cases, people having other STIs, international travelers, and those having unsafe sex at large gatherings with on-site unprotected sex activities.[4,5]

Many cases are mild or even asymptomatic and may spread the disease. The most common presentation is a combination of constitutional symptoms, skin rash on face / hands / soles and acute lymphadenopathy: especially when someone has international travel history, large gatherings party with on-site sex, or exposure to cases or exposure to wild rodents. Skin rash starts as inflammation-related macules, which then accumulate further inflammatory fluid in the epidermis to progress as vesicles & then necrosis of the cells changes the inflammatory fluid to pus, now called a pustule. Pustules can rupture and make crusts / superficial ulcers. The face is involved in 95% of clinical cases, whereas 75% will involve hands and soles.[6] Oral mucosa is involved in 70% of clinical cases. The genital area is involved in 30-40% of cases and can be confused with other Sexually Transmitted Diseases such as Syphilis.

A single lesion may make it difficult to suspect the disease and confuse it with Syphilis. Often there are multiple lesions. The rash is less common on the trunk and central body. Genital involvement is more with those with men-to-men sex. Lymphadenopathy is a useful diagnostic clue

that helps differentiate monkeypox from other viral infections that can give similar rash, such as Measles, chicken pox, smallpox, etc. However, as the infection mainly comes from wild rodents, plaque or tularaemia should be kept in mind, which also causes lymphadenopathy. But plaque and tularaemia usually don't cause the typical rash caused by monkeypox. Associated symptoms and signs include constitutional symptoms, which may be mild or severe. Internal organ involvement is less common but a serious complication of the disease. It includes viral pneumonitis, myocarditis, encephalitis, hemorrhagic disease, and keratitis. Superadded bacterial infection is also common. The complications are more in immunocompromised patients, pediatric age and old age cases, pregnancy, and those with pre-existing comorbidities.[6,7] The virus is detected by a swab of the lesion/rash and PCR. Samples should be collected and transported with caution. Serological testing or antigen testing is not helpful due to the cross-reactivity of antigens and antibodies with other pox viruses of the Orthopox family. The smallpox vaccine will also affect serology.[8]

Vaccine & Treatment: High-risk people are offered the vaccine in developed countries, including the UK, Canada, and the USA. As smallpox and monkeypox are genetically similar, hence vaccines and antiviral for smallpox may also help for monkeypox as well.[9] Small Pox vaccine is effective for 85% of the cases and makes the disease milder. A new vaccine using the attenuated vaccinia virus is also available in a limited supply since 2019. There is no specific treatment for monkeypox. Antiviral drugs, including Cidofovir, binicidofovir, and tecovirimat, have been used with limited human data, but animal studies have shown hopeful results. Tecovirimat has a few side effects, a relatively safe drug available both as oral and intravenous preparations. Cidofovir is primarily used against cytomegalovirus (CMV) and has limited data for use against monkeypox with potential nephrotoxicity. Binicidofovir has a relatively better side effect profile than Cidofovir and is less nephrotoxic.[10] Antivirals are recommended for immunocompromised patients (transplant cases, those on biological drugs such as TNF inhibitors, those with systemic autoimmune disease, HIV and AIDs patients with low CD 4 counts, cancer patients, those receiving chemotherapy or radiotherapy, etc.), those with pre-existing skin diseases (eczema, psoriasis, or generalized skin diseases), or seriously sick patients with internal organ involvement or hemorrhagic disease, those with systemic sepsis, or high-risk cases such as pregnancy, children under eight years of age or those with comorbidities. Otherwise, the majority of the cases recover within 2-4 weeks. Immunoglobulins (IG) can be considered for post-exposure patients at very high risk of severe monkeypox diseases such as hematological malignancies or bone marrow transplant cases. Data for immunoglobulin use is limited.[9,10]

Healthcare professionals will need more education to manage these cases. Health awareness needs to be spread sensitively by targeted health education to increase enhanced reporting of the symptoms without stigma. Public health awareness in the community is of utmost importance to implement preventive measures without stigmatizing the disease and to avoid the undetected spread of the disease.[3,6]

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Original Article

FETAL OUTCOME AFTER EMERGENCY CESAREAN SECTION DUE TO NON-REACTIVE CARDIOTOCOGRAPHY

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ABSTRACT

Background: Cardiotocography (CTG) is one of the most popular methods of monitoring the fetus before and during birth. Non-sedative CTG at birth has been linked to meconium staining, low birth weight, and the need for prompt obstetric intervention for optimal outcomes for mother and fetus. The study aimed to assess the fetal outcome after emergency cesarean section due to non-reactive cardiotocography in females presenting at term for delivery.

Material and methods: This descriptive study corss sectional was conducted in Department of Obstetrics and Gynaecology, Jinnah Hospital, Lahore. The time allocated for the study was from 23-07-2015 to 22-01-2016. This study included 200 patients, including females, who underwent emergency cesarean section under spinal anesthesia by a single surgical team. After birth, Apgar score was assessed at 5 minutes of birth. If the score was <7 after 5 minutes, then a poor Apgar score was labeled.

Results: The mean age of the patients was 30.03±7.64 years. The mean gestational age was 38.75±1.65 weeks and the mean Apgar score was 7.56±1.41. According to parity distribution, 106 (53.0%) were nulliparous while 94 (47.0%) were multiparous. A good Apgar score was seen in 169 patients (84.5%) and a poor Apgar score was observed in 31 patients (15.5%).

Conclusion: The results of this study show that a cesarean section done only based on data attained via CTG monitoring does not create a great advantage for the welfare of the fetus. It is often falsely positive and needlessly surges the incidence of the cesarean section without maternal and fetal health benefits.

Key Words: Caesarean Section, Cardiotocography, Pregnancy

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INTRODUCTION

In many parts of the world, the total cesarean section rates have increased with time, especially in primigravidas. Future obstetric performance is dependent on the outcome of the first pregnancy. This aspect of women's health is not given appropriate significance, unfortunately. Factors implicated are the unavailability of health facilities, illiteracy, poor information about the significance of antental care and the non-availability of a proper referral system. Moreover, additional factors responsible for inadequate antenatal care include misapprehensions about the medical management of pregnancy and religious and cultural beliefs. In primigravidas, the cesarean section rate was more (57.5%) than in multigravidas (42.6%).[1]

Intrauterine fetal monitoring aims to identify fetuses at risk of injury as a result of asphyxia in the neonatal period and later in life. Fetal control with CTG was introduced in the 1960s. Although the beneficial effects of cardiotocography on neonatal outcomes have

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never been demonstrated, they are widely used.[2]

A reactive CTG on admission is less significant for undesirable fetal outcomes than CTG done before delivery. Therefore, it is sensible to encourage close fetal monitoring, and well-timed obstetric intervention for best maternal and fetal outcomes as a CTG at delivery is linked with reduced birth weight and meconium-stained liquor.[3]

One study reported that in emergency cesarean section cases due to non-reactive CTG, the poor Apgar score was 14.8%. This showed that non-reassuring fetal heart rate on CTG was not well-related to poor neonatal results. Not any substantial difference in immediate poor neonatal consequences was observed.[4] In another study, the poor Apgar score was 45.2% in cases who underwent emergency cesarean section due to non-reactive CTG. Monitoring by CTG is the non-invasive, economical, hands-on method that shows any variations in the FHR baseline, which can correlate to adverse fetal outcomes. Cesarean section conducted exclusively on data achieved via CTG monitoring would not produce significant advantages for fetal welfare (i.e., poor Apgar score), and the cesarean section rate is increased without advantages for mother and fetus.[5]

The rationale of this study is that a non-reassuring CTG at the time of delivery is linked with meconium-stained liquor, the need for prompt obstetric intervention for an optimal fetal status, low birth weight, and poor Apgar score after emergency cesarean section. It has been noticed that often prediction of CTG is found to be negative, as evident from one study which showed that in females who underwent emergency cesarean section due to non-reactive CTG, few neonates had poor Apgar scores. However, another study reported that the incidence of poor Apgar score was higher in females who underwent emergency cesarean section due to non-reactive CTG. Moreover, previous studies were conducted on small sample size, so we cannot rely on contradictory results. So, we conducted this study on a large sample size to achieve more précised results. This may help us, in the future, to plan better diagnostic methods for better fetal surveillance and optimal pregnancy outcome. The objective of the study was to analyze the fetal outcome after emergency cesarean section due to non-reactive cardiotocography in females presenting at term for delivery.

Operational Definitions

Emergency cesarean section: It was measured as if the female required delivery through an abdominal incision due to non-reactive CTG. Non-reactive CTG was labeled as follows:

1. Fetal initial heart rate (FHR) <100 or> 180 beats / min
2. Variability <5 ≥ 90 min
3. Atypical variable deceleration, late deceleration, single long delay> 5 min.
4. Lack of acceleration

The fetal outcome was measured in terms of:

Poor Apgar score: It was labeled if the Apgar score is less than 7 after 5 minutes of birth (Annexure-II)

MATERIAL AND METHODS

This descriptive cross sectional study was conducted department of Obstetrics and Gynaecology, Jinnah Hospital, Lahore.

The study was carried out over six months, from 23-07-2015 to 22-01-2016.

A sample size of 200 events was calculated in women undergoing emergency cesarean section due to non-reactive CTG, taking a 95% confidence interval, 5% error margin, and an expected weak Apgar score percentage of 14.8%.[4]

Non-probability, consecutive sampling was used.

Women between the ages of 18 and 40 who underwent emergency cesarean section due to non-reactive CTG (according to the definition of surgery).

Multiple pregnancies (on USG), abnormal presentation like macrosomia, non-cephalic presentation, or IUGR (on USG), women with PIH (BP> 140/90 mmHg), preeclampsia

(BP> 140/90, protein urea +1 rod method) and / or eclampsia (preeclampsia with convulsions), gestational diabetes (BSB> 186 mg / dl), cesarean delivery for other primary indications premature rupture of membranes [(PROM), placental abruption or placenta praevia or accreta, on clinical and USG examination] were excluded from the study.

Data Collection Procedure:

Following the approval of the hospital's ethics committee, 200 women who matched the selection criteria were retained in the labor room of the Lahore Jinnah Hospital, Obstetrics and Gynecology Department. Informed consent was obtained. Demographic data (name, age, gestational age, parity, and contact) were obtained. The women underwent emergency cesarean section under spinal anesthesia by a single surgical team. After birth, the Apgar score is estimated at 5 minutes. If, after 5 minutes, the score is <7, then the weak Apgar score is labeled (according to the operation definition). All this information was collected through a pre-prepared Proforma.

Data Analysis Procedure

The data were analyzed with SPSS 20 version. Quantitative variables such as age, gestational age, and Apgar score were calculated as mean and standard deviations. Qualitative variables such as parity and weak Apgar scores were calculated as frequency and percentage. The frequency is calculated for parity. Data are stratified for women's age and parity (nullipara/multipara). Chi-square test was used to compare the variables. p-value ≤0.05 was taken as significant.

RESULTS

A total of 200 patients were included in this study during the study period of six months, from 23-07-2015 to 22-01-2016.

Regarding age distribution, 105 patients (52.5%) were between 18-30 years of age, and 95 patients (47.5%) were between 31-40 years old (Table-1).

The majority of the patients, 161 (80.5%), had had gestational age between 37-40 weeks, and the remaining 39 (19.5%) patients' gestational age was 41-42 weeks (Table-2). According to parity distribution, 106 (53.0%) were nulliparous while 94 (47.0%) were multiparous (Table-3).

A poor Apgar score was observed in 31 patients (15.5%) and a good Apgar score was seen in 169 patients (84.5%) (Table-4).

The mean age of the patients was 30.03±7.64 years, the mean gestational age was 38.75±1.65 weeks, and the mean Apgar score was 7.56±1.41 (Table-5). Stratification about age and parity was carried out and presented in Tables 6 and 7.

Table-1: Distribution of patients by age

Age (Year)	Number	Percentage
18-30	105	52.5
31-40	95	47.5
Total	200	100.0

Table-2: Distribution of patients by gestational age

Gestational age (week)	Number	Percentage
37-40	161	80.5
41-42	39	19.5
Total	200	100.0

Table-3: Distribution of patients by parity

Parity	Number	Percentage
Nulliparous	106	53.0
Multiparous	94	47.0
Total	200	100.0

Table-4: Distribution of patients by Apgar Score

Apgar Score	Number	Percentage
Poor	31	15.5
Good	169	84.5
Total	200	100.0

Table-5: Mean values of age, gestational age and Apgar score

Variables	Mean	S.D
Age (Year)	30.03	7.64
Gestational age (week)	38.75	1.65
Apgar score	7.56	1.41

Table-6: Stratification regarding age

Age	Poor Apgar score		Total	p-value
	Poor	Good		
18-30	15	90	105	0.618
31-40	16	79	95	
Total	31	169	200	

Table-7: Stratification regarding parity

Parity	Poor Apgar score		Total	p-value
	Poor	Good		
Nulliparous	18	88	106	0.539
Multiparous	13	81	94	
Total	31	169	200	

DISCUSSION

The aim of electronic fetal heart monitoring by cardiotocography was to identify fetuses affected by hypoxia during labor in a better way. Long-term neonatal outcomes did not show any benefit, and cesarean section rates increased by four folds.[6-8]

It shows that CTG understanding is sometimes erroneous, fails to predict early neonatal outcomes, is not consistent, and can be influenced by medicolegal claims. There was an increased incidence (15.5%) of the poor Apgar score (< 7) at term due to non-reactive cardiotocography in the current study, which was close to another study by Roy et al.[4]

In the current study, the Caesarean section rate was higher in primigravidas (53.0%) than in multigravidas (47.0%). These results are consistent with a study carried out by Naheed et al.[1]

Several questions have been raised regarding general anesthesia and induction-delivery interval because of their association with fetal acidosis and sedation. The patient was previously draped prior to the induction of anesthesia to keep the induction-delivery interval short, but it was horrifying for the patient. Nowadays, patient preparation and draping are performed after anesthesia induction at most western centers and tertiary care hospitals in Pakistan.[9]

CTG alone is not reliable for examining births by cesarean section, although it has emerged worldwide as a modern and non-invasive fetal monitoring method.[10] Other methods of detecting fetal distress may help reduce this trend, but CTG monitoring significantly increases the birth rate by cesarean section alone.[2]

Compression of the fetal head during a contraction causes early decelerations during the late first or second stage of labor. Generally, these decelerations are caused by mild transient hypoxia and are not associated with a poor fetal outcome. However, CTG must be observed for any variation in the deceleration pattern, followed by further tests of fetal wellbeing. No substantial difference was observed in five-minute Apgar scores, amongst two groups of fetuses with and without early decelerations, in two cohorts[11]

Late Decelerations are seen after the peak of uterine contractions, reaching the baseline at least 20 seconds after the contraction disappears. It derives its name "late" due to its delayed recovery to the baseline rate. An important cause is a uteroplacental insufficiency which is mostly associated with significant hypoxia.[11, 12]

Variable decelerations are due to umbilical cord compression. The conditions causing cord entanglement are the Umbilical cord around the neck, true knot in the umbilical cord, and prolapsed umbilical cord. Oligohydramnios may also cause repeated variable decelerations.

A study examined variable decelerations in fetal outcomes. Simple or typical variable decelerations were not always shown to be correlated with poor neonatal outcomes. Atypical or complicated variable decelerations were correlated with poor or adverse neonatal outcomes.[12,13]

Various research trials carried out at the Polizu Obstetrics and Gynecology Clinic in 2007 on the significance of CTG monitoring for identifying acute fetal distress established that there were various false-positive outcomes. CTG depicted fetal distress, and newborns scored an Apgar of 8–10, which resulted in an unnecessary cesarean section.[14,15] The results of our study are similar to these studies, as we also found that

CTG changes caused many cases of fetal distress, but the neonatal Apgar score was between 8 and 10. This suggests that the verdict to perform a cesarean section is centered solely on CTG changes (indicative of fetal distress), leading to an increase in the rate of a cesarean section without significant improvement in patient and neonatal outcomes.

CONCLUSION

Fetal distress (antepartum and peripartum) is a very important problem that cannot be ignored. This can lead to a rise in neonatal disease and death if not detected in time. Fetal heart rate monitoring with CTG is a simple, non-invasive, easy, and inexpensive method that detects changes in FHR. This research demonstrates that a cesarean section based only on data gained through CTG monitoring is not advantageous for the fetus's health. It is often a false positive and unreasonably raises the cesarean section rate with no benefit to the mother and fetus. Thus, other methods for assessing fetal wellbeing should be included before the decision to give birth by cesarean section, rather than relying solely on CTG.

AUTHOR'S CONTRIBUTION

AA: Data collection
SKK: Conception and planning
UA: Data collection
AZ: Literature review
SS: Interpretation of results
FN: Supervision

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Original Article

FREQUENCY OF UTERINE LEIOMYOMAS IN FEMALES PRESENTING WITH ABNORMAL UTERINE BLEEDING

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ABSTRACT

Background: Abnormal uterine bleeding (AUB), is defined as irregularities in the menstrual cycle with a change in recurrence, period, or quantity of bleeding. It is one of the most frequent gynaecological problems and around 10-30% of women in the reproductive age bracket are suffering from it. It accounts for about 1/3rd of all th walk-in gynaecological visits. The study aimed to determine the frequency of uterine leiomyoma in females with abnormal uterine bleeding in a tertiary care hospital.

Material and Methods: This cross sectional study was conducted in obstetrics and gynaecology department, Shalimar Hospital, Lahore from 1st October 2018 to 30th March 2019. A total of 130 females presenting with atypical uterine bleeding were taken in the study. Ultrasonography was done to determine the uterine fibroids. A Consultant Radiologist did ultrasound. Data was collected regarding uterine leiomyoma and was noted.

Results: The age bracket in the present study ranged from 18 to 40 years with mean age of 33.930±3.13 years, a mean weight of 77.738±7.11 Kg and a mean duration of complaining 4.453±0.96 months. Married females were 90% and unmarried 10%. Uterine leiomyoma was seen in 19.2% patients. 68% of uterine leiomyomas were of small size and 32% of large size. 48% of uterine leiomyoma were single and 52% were multiple.

Conclusion: In our Pakistani populace, the prevalence of uterine leiomyoma is approximately the same as reported in multiple studies for white females and increases with age and weight.

Key Words: Pregnancy, Menstrual Cycle, Leiomyoma

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INTRODUCTION

Abnormal uterine bleeding (AUB) is a comprehensive term that explains distortions in the menstrual cycle involving frequency, invariability, time period and quantity of flow other than pregnancy.

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Abnormal uterine bleeding (AUB), is described as a change in frequency, duration, or amount of bleeding. It is a common gynaecological problem in outpatient. It affects 10-30% of reproductive-aged females and accounts for about 1/3rd of all outpatient gynaecological visits.[1]

The irregular bleeding frequency can be frustrating and have adverse effects on a female's life. Abnormal uterine bleeding can cause mental, social, medical, and sexual issues in females; thus, sufficient and proper management is required.[2]

PALM-COEIN is a handy abbreviation coined by the International Federation of Obstetrics and Gynecology (FIGO) to categorize the causes of bizarre uterine bleeding. The initial part, PALM, defines anatomical issues for example polyps,

adenomyosis, leiomyomas and malignancy or hyperplasia. The second part, COEI, defines non-structural issues such as coagulopathies, ovulatory disorders, endometrial abnormalities and iatrogenic reasons. The N denotes "not otherwise classified."

Fibroids (leiomyoma) is the most commonly occuring tumor of females. In one study by the time a female reaches the age of 50, almost 70% of white females and upto 80% of African women will have at least one uterine fibroid in their life.[3] Worldwide, a lot of females are hesitant to show abnormal uterine bleeding (AUB) to their physicians, therefore it is vital to encourage to have a open discussion on bleeding problems. Medical professionals should inquire from females about their previous menstrual period, regularity, fertilization problems, contraception tools and general sexual health. If abnormal uterine bleeding is recognized at very initial period, then further history, physical examination, tests can be done.[4] Furthermore, proper awareness can be given and treatment plans can be devised. Females aged 45, or females below the age of 45 but at high risk for malignancy need endometrial sampling for assesment of AUB. Treatment relies on cause, inclination towards bearing a child and pre-existing medical issues.[5]

Fibroids are most commonly asymptomatic in most women while some females present with anaemia. In some females fibroids are linked with infertility, miscarriages, premature labour and failure of progression of labour. Fibroids can also cause aches, pains and pressure symptoms and sometimes urinary problems. In some conditions, fibroids of huge size may put undue pressure on the renal tract and pelvic vessles causing renal dysfunction and venous thromboembolism, respectively.[6,7] Fibroids were present in 64% of females with abnormal uterine bleeding compared to 28% without the disease.

In contrast, other studies failed to show any relation between fibroids and a worse bleeding pattern.[8] Most observational studies on this matter repeatedly yields conflicting results, but an interesting study showed the relationship of fibroids and endometrial function. This study has suggested a possible mechanism of the defective decidualization and haemostasis in the endometrium of females with fibroids and increased bleeding.[9] In a study by Qureshi FU, et al has showed that about 25% in females with AUB had one or more fibroids.[10] An identical study done by Ibrar F et al has showed the frequency of leiomyomas of about 7.4% in females with AUB.[11]

There is lack of data on this subject in our local population and insufficient research data is available. Only two studies have been done, and their findings cannot be generalized due to variability in results.[12] Therefore we have planned to evaluate the frequency of uterine leiomyomas in females who present with abnormal uterine bleeding in our local population. My study's results will help identify the actual morbidity of uterine fibroids in females with AUB in our local population.

The objective of the study was to find out the frequency of uterine leiomyomas in females who present with abnormal uterine bleeding in our local population at tertiary care hospital.

Operational Definitions:

Abnormal uterine bleeding is defined as bleeding with >80ml/cycle, excluding regular cyclic/menstrual patterns of bleeding. Blood was measured by using the difference of weight between soaked pads and dry pads, standardizing one millilitre blood to one gram.

Uterine leiomyomas were defined as when pelvic ultrasound reveals hypo echoic mass, and calcification as echogenic foci with shadowing cystic areas of necrosis. These were categorized as: - Number of leiomyomas: It was defined in terms of….

Single leiomyomas were defined as when ultrasound reveals one uterine leiomyoma (per operational definition).

Multiple leiomyomas were defined as when ultrasound reveals ≥ 2 uterine leiomyomas

(per operational definition).
Large leiomyomas were defined as when uterine leiomyoma sizes 6-10cm on ultrasound.
Small leiomyomas were defined as when uterine leiomyoma size 3-5cm on ultrasound.

MATERIAL AND METHODS

It is a cross sectional study conducted at Obstetrics and Gynecology Department, Shalimar Hospital, Lahore.
The study started on 1st October 2018 and finished on 30th March 2019.
Total sample size was 130 patients and calculation was done at 95% confidence level with 3.5% margin of error and expected frequency of uterine leiomyomas was 25%. Non probability consecutive sampling technique was used.
Females age 18-40 years presenting with abnormal uterine bleeding for three months or greater duration both married/unmarried were included in the study.
The patients with history of uterine surgeries on medical record, history of endometriosis on medical record and history of ovarian mass on medical record were excluded from the study.

DATA COLLECTION PROCEDURE

A total 130 patients from outpatients Gynaecology department of Shalimar Hospital, Lahore were included in the study as per inclusion criteria. Prior approval from ethical committee was taken. Consent was obtained from each patient and their confidentiality was ensured.
Data was collected for basic demographics (Age, marital status and complaint duration). An ultrasonography was done to determine the uterine fibroids. A consultant Radiologist did ultrasound. Data was collected regarding uterine leiomyomas and findings were noted on especially designed Performa by researcher herself.

DATA ANALYSIS

Data analysis was done with SPSS version 20. Frequency and percentage were calculated for marital status, uterine leiomyomas size and number. Mean ±SD was evaluated for quantitative variables such as age, weight and time duration of the bleeding. Effect modifiers like age, weight, marital status and duration of bleeding complaint was controlled by stratification. Post stratification chi square test was applied and $p \leq 0.05$ was taken as a significant value.

RESULTS

In this study patients were from 18 to 40 years age with mean age of 33.930±3.13 years, mean weight 77.738±7.11 Kg and mean duration of complain was 4.453±0.96 months as shown in Table-I. As shown in Table II, married females were 90% and unmarried 10%. Uterine leiomyoma was seen in 19.2% patients as shown in Table II. Regarding size of Fibroid as shown in Table-IV, 68% uterine leiomyoma were of small size and 32% of large size. 48% uterine leiomyoma were single and 52% were multiple as shown in Table-V. Data analysis showing Stratification of Uterine leiomyoma concerning age, weight, marital status and complaint duration are shown in Table-VI, VII, VIII and IX respectively.

Table-1: Mean ± SD of patients according to age, weight and duration of complaint n=130

Demographics	Mean ± SD
Age (years)	33.930±3.13
Weight (Kg)	77.738±7.11
Duration of complain (months)	4.453±0.96

Table-2: Percentage and Frequency of patients according to marital status n=130

Marital Status	No of Patients	Percentage
Unmarried	13	10%
Married	117	90%
Total	130	100%

Table-3: Percentage and Frequency of patients according to Uterine leiomyoma n=130

Uterine leiomyoma	No of Patients	Percentage
Yes	25	19.2%
No	105	80.8%
Total	130	100%

Table-4: Percentage and Frequency of patients according to Size of Uterine leiomyoma n=25

Size of Uterine leiomyoma	No of Patients	Percentage
Small	17	68%
Large	8	32%
Total	25	100%

Table-5: Percentage and Frequency of patients according to Number of Uterine leiomyoma: n=25

Number of Uterine leiomyoma	No of Patients	Percentage
Single	12	48%
Multiple	13	52%
Total	25	100%

Table-6: Stratification of Uterine leiomyoma concerning age.

Age (years)	Uterine leiomyoma		p-value
	Yes	No	
18-30	6(23.1%)	20(76.9%)	0.578
31-40	19(18.3%)	85(81.7%)	
Total	25(19.2%)	105(80.8%)	

Table-7: Stratification of Uterine leiomyoma concerning weight of Patient.

Weight (Kg)	Uterine leiomyoma		p-value
	Yes	No	
≤70	1(7.1%)	13(92.9%)	0.224
>70	24(20.7%)	92(79.3%)	
Total	25(19.2%)	105(80.8%)	

Table-8: Stratification of Uterine leiomyoma concerning marital status.

Marital status	Uterine leiomyoma		p-value
	Yes	No	
Unmarried	0(0%)	13(100%)	0.064
Married	25(21.4%)	92(78.6%)	
Total	25(19.2%)	105(80.8%)	

Table-9: Stratification of Uterine leiomyoma concerning duration of complain.

Duration of complain (months)	Uterine leiomyoma		p-value
	Yes	No	
3-5	20(16.9%)	98(83.1%)	0.038
>5	5(41.7%)	7(58.3%)	
Total	25(19.2%)	105(80.8%)	

DISCUSSION

The actual incidence of uterine leiomyomas (UL) in the common populace is unknown. There are various methods to find out the exact occurence of uterine leiomyomas (UL) in the general population such as targetted surveys, microscopic examination of surgical specimens obtained after hysterectomy, post-mortem of females who passed away unaware of any gynecological pathologies in them or any record of Pelvic ultrasonography, each method giving different results. Hence, the actual number of UL in general public is unknown.[13] Ultrasound imaging of female pelvic organs was introduced by Kratochwil et al in 1972.[14] In 1980, Muram et al devised a standard for uterine leiomyoma diagnosis with TVS defining it as a spherical mass being echogenically distinguished from the adjoining myometrium.[15] Ever since, TVS is considered the major, non-invasive, economically friendly and a global test for assessment of uterine pathologies, with extremely precise performance.[16] Ultrasound has a major drawback: it depends on the operator's expertise and the device's accuracy. To increase the precision in making uterine leiomyoma diagnosis, saline contrast-sonohysterography and 3-D ultrasonograms have been recommended, but both have conflicting outcomes sometimes. For routine detection of uterine leiomyomas 2-D pelvic ultrasonography remains the best method.[17,18] Endometrial sampling is advised in females younger than 45, facing unrestricted estrogen exposure, for example obese females and/or those diagnosed with polycystic ovarian syndrome (PCOS). This can also be done for the females who have had a failed treatment previously, or are suffering from unresolved bleeding.[19]

Some physicians advocate that Transvaginal ultrasound should be the first and foremost assessment test for AUB. In contrast, MRI should be done as a second test if the diagnosis is unsatisfactory or unclear. Delineation might affect patient treatment or a physician should suspect coexisting uterine myomas.

Magnetic resonance imaging is superior to ultrasound for myoma mapping and should be favored if a surgery is to be arranged. In this study, a 19.2% general prevalence of uterine leiomyomas was seen, with the greatest prevalence (20.7%) in females with weight >70 Kg, which supports the claim made with some other researches based on ultrasound diagnoses.[20] Many uterine leiomyomas were found in 52% of cases, less than that found in the surgical specimens and research by Cramer and Patel (84%).[21] In comparison to their findings, in this study only 32% patients had a uterine leiomyoma larger than 20 mm.[22] In a study by Qureshi FU, et al has showed the frequency of leiomyomas by 25% in females with abnormal uterine bleeding.[23] The research done by Ibrar F, et al has showed the frequency of leiomyomas by 7.4% in females with abnormal uterine bleeding.[24] The vast knowledge we have to date regarding the demographics and coexisting risk factors for developing uterine leiomyomas is largely extracted via results taken from the survey research done on large populations. There are certain menaces such as age, race, literacy factor, hormones, nutritional status, physical activity, oral contraceptives, labour, tobacco consumption and tissue injury that have been claimed to increase the risk factor for development of uterine leiomyomas, but there have been conflicting sequelea. Results of the present study agree with these findings reported by multiple ultrasound-based studies as our multivariate statistical analysis results also don't show any significant correlation between any demographic or clinical numerical and UL, except age which showed significant correlation.[25]

Abnormal uterine bleeding, especially menorrhagia is the commonest clinical feature of uterine leiomyoma. Uterine fibroids are monoclonal noncancerous growths of the smooth muscles of uterus. They are composed of large quantities of extracellular matrix, mainly collagen, fibronectin, and glycoproteins. The exact mechanism of their pathogenesis is unclear, there is a lot of research and clinical data that suggests that hormones specially estrogens and progestogens boost this tumor's growth, as the fibroids often appear during child-bearing years and rarely reported before menarche and if present, they regress in size after menopause.[26] They are generally classified by their site among the uterus layers (subserosal, intramural, or submucousal) and can be present singly or in multiple numbers. The precise mechanism of leiomyoma-linked bleeding is unknown, but submucous fibroids, vascular impairements, and dysfunctional endometrial hemostasis have been reported as potential liabilities. Even tiny little uterine leiomyomas not causing any pressure on the endometrial cavity may change myometrial blood supply and ability to contract. A study programmed by Benecke et al showed that intramural uterine leiomyomas may poorly affect the chances of conception.[15] In present study, menorrhagia had strong association with the abundance of uterine leiomyomas and not with the size of the largest fibroid, signifying that the symptoms are not the consequence of deformation of the myometrium and endometrial cavity. It was also found that the diversity of uterine leiomyomas was notably coupled to AUB (menorrhagia and metrorrhagia) as a presenting complaint. Management of the patient has to be customized according to the presenting complaint. Generally, it should be prioritized to treat AUB medically first before coming up with the surgical options.[27]

In acute AUB, hormonal therapies are given as a baseline treatment in the management as the first option. Intravenous (IV) conjugated estrogen, supported with oral contraceptive pills (OCPs), and oral progestins can also be included in the prescription as multiple options for treating acute AUB. Another

agent, named Tranexamic acid resists fibrin degradation and can be given as a supportive drug. The Uterine Balloon Tamponade (UBT) or a Foley bulb is a mechanical tool for treatment as it compresses the vasculature. Myomectomy is advised for the females who want to preserve their fertility. The biggest drawback of myomectomy is leiomyoma recurrence.[28] Within the following 5 years, more than one-third of these females who had myomectomy will need further surgery to manage uterine leiomyomas that may have newly formed. Laproscopic myolysis, uterine artery blockade by embolization, fibroid embolization and magnetic resonance-guided ultrasonograms are minimally invasive procedures for management of multiple Uterine fibroids. Still, these practices are rarely being performed currently. There is need of novel treatment strategies superior to surgical methods to tackle symptomatic uterine leiomyomas. lately, advancements in the scientific studies have probed new understanding on uterine leiomyomas biology.[29] We postulate that, in patients with more than one uterine fibroids and menstrual anomalies, every uterine fibroid can give rise to varying growth factors or numerous biological mediators that may collectively impose a negative effect on the myometrial and endometrial environment.[22] For patients with HMB as the major symptom of AUB, the levonorgestrel-releasing IUD has been reported to work wonders compared to other medical management approaches as it elevates the female's quality of life. Systemic progestogens and GnRH agonists can result in amenorrhea in up to 50% and 90% of females. In contrast to this positive effect, injectable progestogens have the adverse effect of causing Break through bleeding, and GnRH agonists can only be used for a 6-month course owing to their role in maintaining a low estrogen state.[29, 30]

A new category of medication called selective progesterone receptor modulators (SPRMs) has shown promising results for treatment of symptomatic fibroids. These restrict proliferation, down-regulate the growth factors and have an apoptotic potential that may reduce the growth mass and alleviate the symptoms.[17,20] Randomized clinical trials have established that the SPRM ulipristal can be an effective treatment modality as it decreases the episodes of menstrual bleed, retains normal levels of hemoglobin, and decreases the size of UL and alleviate leiomyoma-related symptoms.[18,19] GnRHa has been reported to decrease the size and mass of the UL when given before myomectomy or hysterectomy. Not only this but the patients also reported a lowered pelvic pain and improved hematocrit value. Also,the surgeons claim that giving GnRHa to the patient before the surgery has decreased table-time during surgery, and a wider fraction of hysterectomy patients had a small vaginal procedure rather than an abdominal surgery.[24,25] The sole goal for managing symptomatic uterus-related pathology is to reduce symptoms, as expectant management is apt for most asymptomatic leiomyomas.[28] In future, it is anticipated that noval treatment modalities for the management of uterine leiomyomas-associated symptoms will be devised, due to rising awareness about the functional facets and regulatory characteristics of leiomyoma morphology and uterine homeostasis.

CONCLUSION

In Pakistani population, the incidence of uterine leiomyoma is directly associated with/increases with weight, per the results reported in literature for White females. In females reporting with abnormal uterine bleeding, suspicion of multiple fibroids should arise and they must be carefully examined to look for multiple leimyomas during pelvic ultrasound testing. Additional investigation should be done to assess the morphology and association of symptomatics with multiple ULs versus single ULs, so that advanced and effective therapeutic strategies can be developed.

Disclaimer: None to declare.
Conflict of interest: None to declare

AUTHOR'S CONTRIBUTION

RB: Data analysis and interpretation with clinical significance
AN: Study design of research work and data collection
SS: Literature survey about the research project
SR: Data collection and acquisition of research work
DJR: Drafting the article, data editing and reference collection
RA: Data analysis with clinical significance and final approval of version

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Original Article

COVID 19 PANDEMIC IMPACT ON VARIATION OF DISEASE PATTERN ON HOSPITALIZATION OF ORAL AND MAXILLOFACIAL SURGERY PATIENTS

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ABSTRACT

Background: Because oral and maxillofacial surgery (OMFS) comprises airway and aerosol-generating operations, this study seeks to demonstrate that OMFS is a high-risk specialty, which may be exacerbated significantly during the coronavirus outbreak in 2019 (COVID-19). This comparative study aimed to investigate whether COVID-19 affected the illness patterns of OMFS inpatients and surgical procedures performed under general anesthesia.

Material and methods: The archival records related to patient's admission and operation theatre of OMFS patients who were admitted between January 2019 and August 2020. It was estimated and compared to the previous year's numbers the number of patients in total, the disease patterns they presented, and the fraction of patients who received imperative and non-imperative medical treatments between 2019 and 2020.

Results: They are based on 98 hospitalizations and 66 general anesthesia surgical operations during the research period. When comparing 2020 to the previous year, hospitalizations and procedures fell significantly ($p = 0.012$ and 0.007, respectively). Contrary to the previous year, cleft lip & palate and TMD, the number of malignancies grew dramatically and significantly. In 2020, the proportion of necessary services to non-essential services increased statistically significantly compared to the same year in 2019.

Conclusion: The findings of this study are among the pioneer in reporting data on the epidemiological effect of the corona pandemic on the OMFS illness pattern in Pakistan. A pandemic's impact on disease patterns and workload. Such pandemics impact patient care, education, and training on a long-term basis. In addition to other applications, health officials could use our findings to analyze resource mobility and optimize medical education and services.

Key Words: Oral Medicine, Oral Surgery, COVID-19

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INTRODUCTION

The coronavirus disease 2019 (COVID-19) has significantly impacted health care delivery.[1] Since the World Health Organization (WHO) declared the COVID-19 epidemic a global public health emergency, many healthcare strategies have been implemented worldwide. Combining the risk of COVID infection with a lack of medical resources has resulted in a drop in the number of elective surgeries performed in recent years.[2]

Medical care must be prioritized during a pandemic to avoid the medical system collapsing. During the 2014–2015 Ebola virus outbreak, systemic shortcomings contributed to an increase in fatalities from several diseases, including measles, malaria, HIV/AIDS, and tuberculosis.[3] To minimize increased morbidity and mortality due to insufficient or improper distribution of medical resources during an outbreak, key medical services must be maintained at all times during the outbreak

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period. According to the World Health Organization's recommendations, elective treatment priorities change with time and vary by nation. When contemplating alternative therapies, the World Health Organization states that the severity & longevity of the pandemic, the time frame of availability, and the non-availability of healthcare facilities in the affected area are some of the most crucial factors to consider.[4]

The citizens, medical professionals, and the government of Pakistan have been making joint efforts to maintain a reasonable level of control over the pandemic, despite the city's significant population mobility and congestion. Between January 1, 2020, and September 19, 2020, the Pakistan Department of Health reported cases of COVID-19. However, (2.1%) of the cases resulted in death, despite the vast majority being discharged following complete recovery. Intending to keep patient numbers under 1,000, the hospital's isolation ward was able to handle the majority of patients admitted or awaiting admission.[5]

Because oral and maxillofacial surgery (OMFS) involves airway and aerosol-generating procedures, this specialty is considered high-risk. In comparison, the effect of COVID-19 on inpatient illness patterns and procedures has not been identified in the OMFS. Even though the pandemic had a substantial impact on OMFS services globally, healthcare facilities in Pakistan have optimistically maintained essential and elective surgical treatments. This is an ideal way of examining OMFS service patterns changes over the COVID-19 timeframe. As suggested by the World Health Organization, health conditions and acute presentations needing time-sensitive care are not currently recognized as essential medical services in the OMFS area, owing to the absence of an acceptable, context-relevant definition.[4] This study aimed to determine the impact of COVID-19 on inpatient admission and the number of surgeries performed under general anesthesia. The researchers also wanted to identify the important OMFS services for future policy development and budget allocation.

MATERIAL AND METHODS

The study was conducted in the Department of Oral and Maxillofacial Surgery, Bakhtawar Amin Trust Teaching Hospital, Multan, after approval from the Institutional Review Board. Written informed consent was taken from each of the study participants. The findings of the research were divided into two categories. In the first segment, the researchers collected the inpatient admission data of the OMFS Unit. After that, the data regarding operating room procedures under general anesthesia by expert surgeons were collected. Apart from exodontia, complete information related to the following 08 variables were noted on specially designed proforma, i.e. (i) Dentofacial deformities (ii) Benign pathologies (iii) Malignancy (iv) Dentoalveolar diseases (v) Infections (vi) Cleft lip and palate (vii) Temporomandibular joint diseases (viii) Others.

Between 2019 and 2020, all the information available on the total number of patients admitted and the distribution of these patients among the categories described above were gathered and analyzed to highlight the heterogeneity of the disease pattern in the population. Since the World Health Organization categorized maxillofacial trauma, infection, and cancer as time-bound treatments, the WHO has advocated for their categorization as "essential medical services."[4]

Within 24 hours of surgery or hospitalization, COVID-19 RANA testing was done using a polymerase chain reaction test to determine positivity and negativity. Several criteria must be met before a patient can be considered for surgery. These include having no recent travel history within 14 days, no close contact with diagnosed cases, no typical symptoms consistent with suspected coronavirus infection, and confirmed negative PCR results. A minimum delay of 14 days was required for patients in close contact with confirmed cases unless they urgently needed life-saving emergency surgery at their admission.

IBM SPSS Statistics Version 26, which can be downloaded from the company's website, was used for all of the statistical analyses in this study. The binomial test was used to compare the proportions of patients who required critical

medical care and those who belonged to different groups of cases in the study. Using the Chi-square test, researchers could examine the proportions of vital medical services and separate case groups in the study population. Using the Bonferroni correction was necessary when there were multiple group comparisons. Two-sided values in all cases were taken. It was determined that the experiment was considered statistically significant if the p-value was ≥0.05.

RESULTS

Throughout the periods specified, a total of 124 people were hospitalized in 2019. A statistically significant decrease in hospital admissions was seen in 2020 (p = 0.012) compared to the previous year. At any point during the patient's hospitalization, there was no sign of COVID-19 infection or positive COVID-19 tests. A COVID-19 infection was not detected in any crew member during the experiment, and no one developed symptoms or tested positive (Figure 1).

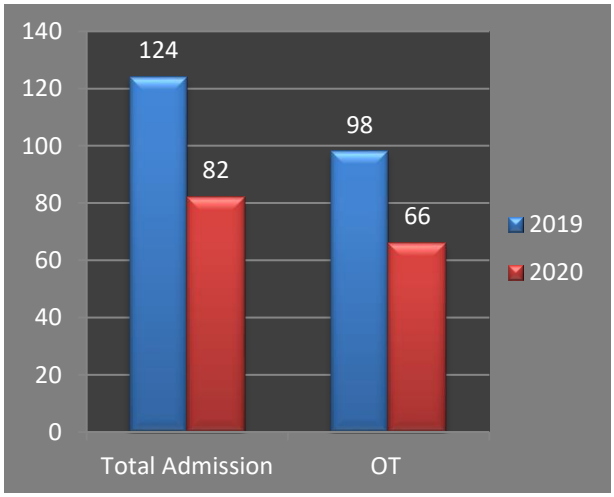

Figure 1: Number of inpatients admissions and surgically treated patients

The table 1 and 2 show the student numbers and percentages admitted to different groups. The proportion of patients hospitalized for cancer in 2020 was significantly higher compared to 2020 and 2019. On the other hand, there have been considerable reductions in admittance for dentoalveolar problems, diaphragm, and temporomandibular articular abnormalities. In addition, the admission rate for the category 'other' has significantly changed, mostly as the number of obstructive sleep apnea patients was reduced in 2020. In terms of patients hospitalized for an infection, benign disease, and dentofacial deformity. The proportions were unchanged between 2019 and 2020. A graph showing the percentage distributions in 2019 and 2020 for different admissions is available here.

Table 1: Frequency of dentofacial diseases presented

Causes	Admissions		p-value
	2019	2020	<0.05
Dental Deformities	27 (21.7%)	20 (20.4%)	<0.05
Benign Pathology	38 (30.6%)	31 (31.6%)	<0.05
Malignancy	13 (10.4%)	11 (11.22%)	<0.05
Dentoalveolar Disease	16 (12.9%)	13 (13.26%)	<0.05
Infections	12 (9.6%)	9 (9.1%)	<0.05
Cleft	5 (4.03%)	6 (6.1%)	<0.05
TMJ diseases	7 (5.6%)	6 (6.1%)	<0.05
Others(OSA, trauma, etc.)	6 (4.8%)	2 (2.04%)	<0.05
Total	124 (100%)	98 (100%)	

Table 2: Number of cases surgically treated during 2019 and 2020

Causes	OT		
	2019	2020	p-value
Dental Deformities	39 (31.45%)	27 (27.55%)	<0.05
Benign Pathology	42 (33.87%)	34 (34.69%)	<0.05
Malignancy	9 (7.25%)	19 (19.38%)	<0.05
Dentoalveolar Disease	14 (11.2%)	7 (7.14%)	<0.05
Infections	4 (3.2%)	9 (9.1%)	<0.05
Cleft	4 (3.2%)	0 (00%)	<0.05
TMJ diseases	7 (5.6%)	1 (1.02%)	<0.05
Others(OSA, trauma, etc.)	5 (4.03%)	1 (1.02%)	<0.05
Total	82 (100%)	66 (100%)	

DISCUSSION

Many patient management guidelines have been published since the discovery of coronavirus disease in the early stages of the pandemic in 2003.[6-8] It should be noted that this is the first comparative study to our knowledge that objectively demonstrates a significant decline in overall patient numbers, an increase in malignancy cases, and a significant loss in key medical services in the OMFS as a result of this pandemic.

Because personal protective equipment (PPE) reduced availability and a low number of training sessions provided to the OMFS staff, the overall number of patients operated on in the outpatient department declined from the period before to COVID-19, according to the study. Because of fewer surgeries and a drop in elective inpatient and outpatient treatments during the COVID-19 outbreak, admissions declined during the epidemic.

As a result of the COVID-19 epidemic, the number of persons in need of life-saving medical treatment increased significantly, with the proportion of people suffering from malignancies rising to an all-time high, particularly among the elderly. OMFS was first identified in China, where physicians divided patients into four severity levels based on their amount of disease progression. Injury to the upper respiratory tract, such as blood loss or obstruction of the upper respiratory system caused by tumors or infections, is a life-threatening illness that necessitates immediate medical attention.

Even though their vital signs are stable, some individuals require emergency surgery to resurrect them. An example of an emergency patient requiring immediate surgery is a fractured bone that has been closed. Patients with malignant tumors or recurrent infections are reviewed, followed by those requiring elective surgery for conditions such as cleft lip and palate, dentofacial abnormalities, or benign tumors.[9] As a result of our classification system, we discovered that cancer, infection, and trauma cases fell into the first three categories. In contrast, cases requiring "non-essential medical services" fell into the fourth category of elective surgery. A large number of people argued for assessing the risk of postponed surgery against the rehabilitative resources that would be necessary, as well as for prioritizing surgical procedures over non-surgical alternatives.[10,11]

Generally, when resources are limited, it is common to prioritize the most critical services first. The long-term consequences of this evolution will damage patient care, as will the education and training of surgeons and other medical professionals. It is anticipated that our data will be utilized to inform future policy decisions and resource allocation decisions, among other things.

Throughout the COVID-19 period, we employed patient care techniques comparable to those recommended by the OMFS and OMVID-19 in Spain.[12] In the OMFS Department's COVID-19-negative theatre, which the hospital had cleared before the surgery, the procedures were carried out at our hospital. Individuals were required to wear personal protection equipment (PPE) on the ward and in the outpatient department (OT) in accordance with World Health Organization (WHO) standards.[13,14] Therefore, according to Barca and colleagues, all instances treated in Italy between February 29 and April 16, 2020, were caused by cancer or trauma, in contrast to previous findings that all instances were caused by infection.[15] Beginning April 15, 2020, all elective non-emergency procedures in the United Kingdom will be suspended for three months, after which they will be reinstated on April 15, 2020.[16] According to the results of Maffia and colleagues' survey of OMFS surgeons, just 5.8 percent of OMFS physicians continue to conduct orthognathic surgery.[17]

Recognize and accept the limitations of a single-center study as they are presented here. Because of the small number of trauma patients at our center and in Pakistan, we have had trouble conducting statistical analyses on traumatology as a distinct category. Unexpectedly, the COVID-19 test returned a negative result in our study group, which was a disappointment. It will be more favorable to acquire more extensive and broadly applicable experience in managing OMFS patients if future multicenter research can be undertaken.

This will be especially true if future multicenter research can be conducted. We were solely interested in hospitalizations and procedures because those were the only things piqued our interest during our investigation. Suppose an outbreak persists for an extended period. In that case, outpatient management data will be required to guide outpatient therapies, which, if delivered promptly, may be essential in saving lives administered quickly.

CONCLUSION

COVID-19 data show that hospital hospitalizations and surgeries reduced dramatically between the COVID-19 and preCOVID-19 time periods. OMFS patients saw an increase in the number of malignancies and the need for further care, suggesting a statistically significant difference in the disease patterns of the two groups of patients. Furthermore, our findings suggest that adequate preparations can maintain non-essential medical services during a pandemic. Aside from the implications for patient treatment, education, and training, our findings have implications for OMFS policy and practice in various sectors, according to the authors.

AUTHOR'S CONTRIBUTION

MAK: Study conception, design, and data collection

MG: Design, data collection, and results interpretation

MRZ: Data Collection, Analysis, and manuscript writing

SA: Study conception, data analysis, writing, and review of the manuscript

MS: Study design, data collection, data analysis, review of the final draft

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Original Article

FREQUENCY OF INTRAUTERINE GROWTH RETARDATION IN GESTATIONAL HYPERTENSION IN PRIMIGRAVIDA TREATED WITH NIFEDIPINE VERSUS LABETALOL

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ABSTRACT

Background: It is estimated that about 6-8% of pregnancies are complicated by hypertensive pregnancy disorders, which cause the severe mother and fetal morbidity and death. The incidence of gestational hypertension is 6.3% worldwide. To treat hypertensive problems during pregnancy, several different medications have been employed.

Objective: The objective of this study was to assess the frequency of intrauterine growth retardation in gestational hypertension in primary gravida treated with nifedipine versus labetalol.

Material and Methods: This study was a randomized controlled trial carried out at Obstetrics and Gynecology department, Unit-III, Sir Ganga Ram Hospital, Lahore for six months from 26/09/2017 to 25/03/2018. In Group A patients were treated with Nifedipine whereas in Group B patients were treated with Labetalol. Within 30 minutes after delivery, a qualified operating room staff member assessed the newborn birth weight using weighing equipment that was set to zero before usage. By using IBM SPSS version 23, all the data was analyzed.

Results: Mean birth weight was lower significantly in patients in the labetalol group in comparison to the nifedipine group (2.3±0.3 Kg vs. 2.6±0.3 Kg with a p-value of less than 0.01). The frequency of IUGR was higher significantly in patients of the labetalol group in comparison to nifedipine (22.4% vs. 6.9% with a p-value of 0.018).

Conclusion: Nifedipine was found superior to labetalol in the treatment of patients with hypertensive disorder of pregnancy as its use was associated with significantly higher mean neonatal birth weight and significantly lower frequency of IUGR which recommends its routine use in future practice.

Key Words: Pregnancy, Intrauterine Growth Retardation, Hypertension

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INTRODUCTION

It is estimated that about 6-8% of pregnancies are complicated by hypertensive pregnancy disorders, which cause the severe mother and fetal morbidity and death.[1] Incidence of gestational hypertension is 6.3% worldwide.[2] The incidence of gestational hypertension is higher in Pakistan (10-12%).[3]The established risk factors for gestational hypertension include maternal age more than 35, body mass index greater than 24 and pregnancy complicated by gestational diabetes mellitus and renal diseases.[4]

Placental abruption, pulmonary oedema, renal impairment, elevated liver enzyme, uncontrolled blood pressure, thrombocytopenia, impaired coagulation profile, and maternal death are the known complications of gestational hypertension.[5] Labetalol, methyldopa, nifedipine, glycerol trinitrate, and other beta blockers are the

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drugs commonly used to treat this condition.[6] Because labetalol is more often used to treat gestational hypertension and is more efficient as compared to methyldopa and nifedipine at lowering blood pressure in people with gestational hypertension.[7]

Historically, methyldopa has been the medicine of choice for treating hypertension in pregnant women due to its efficacy and safety both for the mother and foetus as an anti-hypertensive agent, despite its slower onset of action and lower efficacy as a hypotensive drug. For the long-term management of hypertension during pregnancy, it remains the medicine of choice.[8] In comparison to other anti-hypertensive medications, labetalol provides excellent blood pressure management.[9] The availability of injectable and oral labetalol, as well as the fact that it begins working faster than methyldopa, are both advantages.[10-12] Nifedipine has long been regarded as a second-line medication even though its effectiveness has been well established.[13] This is due to its simple accessibility, quick commencement of the action, simplicity in oral administration, and adequate decrease in blood pressure. The choice of nifedipine over labetalol was recommended in current research that indicated labetalol usage was more often associated with intrauterine growth retardation.[14]

Giannubilo et al. in 2012 in a randomized controlled trial showed that the frequency of intrauterine growth retardation (IUGR) in gestational hypertension treated with nifedipine is lower as compared to those treated with labetalol (15.5% vs. 38.8%; $p<0.05$) respectively.[15] The results of this randomized controlled trial showed that the use of labetalol is associated with a higher frequency of IUGR as compared to nifedipine. Labetalol is routinely used as a preferable choice in patients with gestational hypertension.[16] There is no other local as well as international published data present on this topic. Repeating this research in the local population is necessary since it will enable us to choose the best anti-hypertensive drugs for these Patients.

MATERIAL AND METHODS

This study was a randomized controlled trial carried out at Obstetrics and Gynecology department, Unit-III, Sir Ganga Ram Hospital, Lahore. The study duration was six months from 26/09/2017 to 25/03/2018 after synopsis approval. The sample size was 116 cases (58 cases in each group), calculated by using 80% test power confidence interval of 95% and taking the projected frequency of IUGR among patients of gestational hypertension treated with nifedipine vs. labetalol to be 15.5% vs. 38.8% respectively.[15] The selection of participants was done by consecutive Non-Probability sampling. The inclusion criteria in our study were primary gravid patients with ages in the range of 18-35 years suffering gestational hypertension and patients willing to take part in our study whereas the criteria for exclusion were all the patients who were multipara as per history and clinical record, patients with twin pregnancy or having fetal anomaly (as per obstetric ultrasound), patients having liver disorder (bilirubin ≥1.2mg/dl) or renal disorder (serum creatinine ≥1.2mg/dl) as per history and clinical record, patients having anemia (hemoglobin ≤9g/dl) as per clinical record and patients having cardiac disorder (ejection fraction ≤40%) or diabetes (fasting blood glucose level ≥110mg/dl) based on history and clinical record. The study was explained, after taking approval from the ethical and research committee to all the patients from the outpatient department of Gynae Unit-Ill, Sir Ganga Ram Hospital, Lahore, and then informed consent was signed. By employing the lottery method, patients were randomized into two groups. In Group A patients were treated with Nifedipine whereas in Group B patients were treated with Labetalol. Nifedipine 20 mg or labetalol 100 mg (was given according to the group in which the patient was assigned) orally given twice daily to 12 hours apart and continuation of the same drug without overlaps with other medications until delivery. Within 30 minutes after delivery, a qualified operating room staff member assessed the newborn birth weight using

weighing equipment that was set to zero before usage. Infants were classified as having intrauterine growth retardation if their birth weight was below the 10th percentile for their gestational age.[17] All the data was recorded by using proper Performa. By using IBM SPSS version 23, all the data was analyzed. Numerical variables; age, BMI, duration of therapy, and neonatal birth weight have been presented by mean ±SD. Nominal variables; like intrauterine growth retardation have been presented as frequency and percentage. Chi-square test was applied for comparison of the frequency of intrauterine growth retardation amongst the study groups by considering a value of $p \leq 0.05$ as statistically significant. Stratification of data was done concerning age, BMI, and therapy duration to determine effect modifiers. Post-stratification chi-square test was employed by considering a p-value of ≤0.05 as significant statistically.

RESULTS

In the current research, a total of 116 patients (58 in each group) were enrolled. The overall mean (SD) age, BMI, and treatment duration were 25.6±4.4 years, 28.0±3.8 Kg/m^{2,} and 16.2±2.5 weeks respectively. In the current study, the mean age (SD) in group A was 25.8 (4.0) years while the mean age (SD) in the group was 25.3 (4.8) years. In group A, 31 (53.4%) patients were in the age group 18-26 years and 27 (46.6%) in the age group 27-35 years while in group B, 34 (58.6%) patients were in the age group 18-26 years and 24 (41.4%) in the age group 27-35 years (p=0.575). In groups A and B the mean BMI was 28.2±3.9 Kg/m^2 and 27.9±3.7 Kg/m^2 respectively. In group A based on BMI, the number of patients in 20-25, 25-30 and 30-35 Kg/m^2 were 18 (31.0%),20 (34.5%) and 20 (34.5%) respectively while in group B, the number of patients in 20-25, 25-30 and 30-35 Kg/m^2 were 18 (31.0%), 22 (38.0%) and 18 (31.0%) respectively (p=0.905). In group A, the mean treatment duration was 16.2±2.2 weeks while in group B it was 16.2±2.2 weeks. Based on treatment duration, the number of patients in a range of 13-17 weeks and 18-22 weeks was 41 (70.7%) and 17 (29.3%) respectively while in group B the number of patients in a range of 13-17 weeks and 18-22 weeks was 41 (70.7%) and 17 (29.3%) respectively (p=1.000). (Table 1) Mean birth weight was lower significantly in patients in the labetalol group in comparison to the nifedipine group (2.3±0.3 Kg vs. 2.6±0.3 Kg with a p-value of less than 0.01) (Table 2) The frequency of IUGR was higher significantly in patients of labetalol group in comparison to nifedipine (22.4% vs. 6.9% with a p-value of 0.018). (Table 3) Stratification of frequency of IUGR concerning age, BMI and therapy duration is given in Table 4.

Table-1: Baseline Characteristics of Study Groups

Characteristics	Nifedipine n=58	Labetalol n=58	p-value
Age (years)	25.8±4.0	25.3±4.8	0.517
• 18-26 years	31 (53.4%)	34 (58.6%)	0.575
• 27-35 years	27 (46.6%)	24 (41.4%)	
Duration of Treatment (weeks)	16.2±2.2	16.3±2.7	0.823
• 13-17 weeks	41 (70.7%)	41 (70.7%)	1.000
• 18-22 weeks	17 (29.3%)	17 (29.3%)	
BMI (Kg/m^2)	28.2±3.9	27.9±3.7	0.629
• 20-25 Kg/m^2	18 (31.0%)	18 (31.0%)	0.905
• 25-30 Kg/m^2	20 (34.5%)	22 (38.0%)	
• 30-35 Kg/m^2	20 (34.5%)	18 (31.0%)	

Table-2: Comparison of Mean Birth Weight (Kg) between the Study Groups

	Nifedipine n=58	Labetalol n=58	p-value
Birth Weight in Kg (mean±sd)	2.6±0.3	2.3±0.3	<0.001*

Table-3: Comparison of Frequency of IUGR between the Study Groups

Intrauterine Growth Retardation	Nifedipine n=58	Labetalol n=58	p-value
Yes	4 (6.9%)	13 (22.4%)	0.018*
No	54 (93.1%)	45 (77.6%)	
Total	58 (100.0%)	58 (100.0%)	

Table-4: Stratification of Frequency of IUGR between the Study Groups

Characteristics	Intrauterine Growth Retardation (IUGR)		p-value
	Nifedipine n=58	Labetalol n=58	
Age (years)			
• 18-26 years	2/31 (6.5%)	8/34 (23.5%)	0.057
• 27-35 years	2/27 (7.4%)	5/24 (20.8%)	0.164
Duration of Treatment (weeks)			
• 13-17 weeks	3/41 (7.3%)	9/41 (22.0%)	0.061
• 18-22 weeks	1/17 (5.9%)	4/17 (23.5%)	0.146
BMI (Kg/m^2)			
• 20-25 Kg/m^2	1/18 (5.6%)	3/18 (16.7%)	0.289
• 25-30 Kg/m^2	1/20 (5.0%)	5/22 (22.7%)	0.101
• 30-35 Kg/m^2	2/20 (10.0%)	5/18 (27.8%)	0.158

DISCUSSION

Even with all the progress in medical research, pregnancy-related hypertension remains a significant obstetrical concern. To treat hypertensive problems during pregnancy, several different medications have been employed. Beta-blockers, calcium channel blockers, a combination of alpha and beta blockers, and centrally acting alpha-agonist methyldopa are the medications that are most often utilized in Pakistan.

In the current study, the overall mean (SD) age, BMI, and treatment duration were 25.6±4.4 years, 28.0±3.8 $Kg/m^{2,}$ and 16.2±2.5 weeks respectively. Similar results were reported by Hossain et al. in 2011 who observed a mean (SD) age of 24±5.05 years amongst women presenting with PIH.[18] Another study done by Nazli et al. reported a mean age (SD) of 25.24±0.54 years among women at Khyber Teaching Hospital Peshawar.[19] Muhammad et al. in 2010 observed a comparable mean (SD) age of 24.8±4.1 years amongst pregnant women with IUGR and PIH presenting at Leady Reading Hospital, Peshawar.[20]

Our findings are comparable with the of Nazli et al. who reported a mean BMI of 29.27±1.12 Kg/m^2 in such women.[19]

In the present study, Mean birth weight was lower significantly in patients in the labetalol group in comparison to the nifedipine group (2.3±0.3 Kg vs. 2.6±0.3 Kg with a p-value of less than 0.01). Padmaja et al. (2017) reported a similar significant difference in the mean neonatal birth weight between women receiving nifedipine and labetalol (2.5±0.51 Kg vs. 2.4±0.6 Kg; p-value=0.07).[21] Similar observation was made by A Alam et al. in 2017 (2.9 Kg vs. 2.6 Kg; p-value=0.045).[22]

In the present study, the frequency of IUGR was higher significantly in patients of the labetalol group in comparison to nifedipine (22.4% vs. 6.9% with a p-value of 0.018). A previous study observed a similar prevalence of 5.7% for IUGR with nifedipine.[23] A similar frequency of IUGR with the use of labetalol has been reported by Munshi et al. (22.9%) and Cruickshank et al. (20.0%).[24,25] A study carried out by Giannubilo et al. reported a comparable difference in the prevalence of IUGR between labetalol and nifedipine (38.8% vs. 15.5%; p-value<0.05.[15] The current study is the first study on the local population that supports the previous studies on the supremacy of nifedipine over labetalol; nifedipine is associated with decreased frequency of IUGR in women with gestational hypertension. As mentioned earlier, the current practice is to use labetalol in pregnant women with gestational hypertension. However, in light of this evidence, nifedipine is better and should be preferred in future practices. One major drawback of the current research is that we did not compare the two groups on important measures of hypertension control and treatment-related problems, which should be

considered before any modification in practice is made. Future research should consider such a study.

CONCLUSION

Nifedipine was found superior to labetalol in the treatment of patients with hypertensive disorder of pregnancy as its use was associated with significantly higher mean neonatal birth weight and significantly lower frequency of IUGR which recommends its routine use in future practice.

AUTHOR'S CONTRIBUTION

UN: Main idea and article writing
RZ: Data collection
R: Data analysis
AA: Data analysis
SA: Literature review and discussion
HZ: Review of article

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Original Article

VITAMIN D AND MYOCARDIAL INFARCTION…IS THE LINK REAL?

Qanita Mahmud[1], Maryam Rao[2], Shumaela Kanwal[3], Tabinda Kazmi[4], Saman Saeed[5], Qudsia Waseem[6]

ABSTRACT

Background: Vitamin D has assumed even more importance in recent years because of its diversity of actions. One of the most recently discovered effects of vitamin D is on the vascular system, through which it can produce an impact on cardiovascular health. Multiple studies have been done in this regard, but it still requires further exploration. The objective of our study was to explore any existing association of vitamin D deficiency with myocardial infarction (MI) and to make a comparison of levels of vitamin D in patients with recent MI and healthy individuals.

Material and Methods: A comparative cross-sectional study was carried out in the Cardiology Department of Shaikh Zayed Hospital and Punjab Institute of Cardiology. The study measured serum Vitamin D levels in 64 participants belonging to two categories: patients with recent myocardial infarction and healthy controls. Serum vitamin D levels in both groups were compared.

Results: showed Serum Vitamin D was sub-optimal in all study participants, including myocardial infarction patients and the healthy controls. A clear association between vitamin D deficiency and myocardial infarction could not be seen. Mean±SD Vitamin D levels were 18±7.8ng/L in myocardial infarction patients and 19.1±9.3ng/L in healthy individuals. This study did not establish an association between myocardial infarction and vitamin D levels.

Conclusion: Our study failed to show a link between Vitamin D and myocardial infarction. Further exploration is needed in this regard.

Key Words: Vitamin D, Myocardial Infarction, Hypertension

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INTRODUCTION

Vitamin D is a versatile hormone that was first identified and named for its role in calcium metabolism in 1922.[1] Since then, innumerable skeletal and extra-skeletal effects of this hormone have been identified, and its deficiency has been associated with a potential risk for many ill conditions like increased risk of hypertension and other cardiovascular diseases, increased incidence of cancers, migraine, musculoskeletal pain, headache, autoimmune diseases, asthma, atopic dermatitis, neuropsychiatric conditions like dementia, depression or even schizophrenia.[1, 2]

Many cells in the human body possess vitamin D receptors (VDR), which are responsible not only for gene modulation and proliferation but also regulation of gene expression, immune function, and inflammation.[3] Studies indicate that vitamin D influences the expression of almost 3% of the human genome through vitamin D receptors. Vitamin D, directly or indirectly, affects cellular functions like cell growth, apoptosis, DNA repair, differentiation and metabolism of cells, transport across the cellular membrane, and oxidative stress.[4]

Besides other effects, vitamin D is also thought to affect lipid metabolism, thrombogenicity, fibrinolysis and

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regeneration and growth of smooth muscle cells and endothelial cells.[4,5] Vitamin D deficiency can be associated with an increased risk of atherosclerosis, cardiovascular diseases, and even post-acute coronary syndrome complications.[5] The mechanism underlying these involves the anti-thrombotic and anti-inflammatory effects of vitamin D. As a result, vitamin D deficiency has been found to promote chronic inflammation, atherosclerosis, arterial calcification, and endothelial dysfunction.[6] Another important mechanism linking vitamin D deficiency with the risk of cardiovascular diseases is the up-regulation of the renin-angiotensin system, thereby leading to increased extracellular fluid volume. It also causes an increase in the level of metalloproteinases which is a marker of myocardial remodeling.[3,5] Therefore, the dynamic effects of vitamin D cannot be denied. Despite all these observations, an association between vitamin D deficiency and myocardial infarction could not be established, and evidence of the beneficial effect of vitamin D supplementation in the treatment of cardiovascular disorders is still lacking.[1,3]

The deficiency of vitamin D is a global health problem. Studies indicate that vitamin D deficiency is around 40%, even in Europe.[6] Moreover, almost 13% are severely deficient there. This, combined with the multi-system effects of vitamin D, necessitates further studies to link its deficiency with possible health hazards.

This study aims to identify vitamin D levels in patients with myocardial infarction so that a possible association can be established between the two, and thereby, supplementation can be instituted to improve cardiovascular outcomes.

MATERIAL AND METHODS

This cross-sectional comparative study was carried out at Punjab Institute of Cardiology, Cardiology Department, Shaikh Zayed Hospital, and Physiology Department of Shaikh Zayed Postgraduate Medical Institute, Lahore, after seeking permission from concerned authorities. The study population was divided into two groups. One group (group A) included diagnosed patients with myocardial infarction above 40 years of age, and another (group B) included age and gender-matched healthy controls. However, patients with renal disorders or those on vitamin D supplementation were excluded from the study.

A sample population of 32 myocardial infarction patients and 32 healthy control subjects were used to compare their vitamin D levels. Sampling was done based on a convenient, non-probability technique, and blood samples were taken from patients visiting the outpatient department after detailed history and examination. Informed consent was also taken from participants of the study. They were later informed of their serum vitamin D levels via mail. The study was completed in six months.

Estimating vitamin D levels was done using the ELISA technique after centrifuging and separating serum.

RESULTS

The study was conducted on 64 participants. Of these, 32 participants were myocardial infarction patients, and 32 were healthy controls. Results were analyzed using SPSS (version 20). Data for serum vitamin D levels were expressed in terms of Mean $\pm$ SD for both groups.

Among the two groups, variables were compared using a t-test. The deficiency of vitamin D was expressed in terms of percentage and frequency. Vitamin D levels were categorized for comparison with the help of a chi-square test.

The mean age for myocardial infarction patients and controls was 54.8±6.9 and 51.5±7.8 years, respectively. No significant difference was seen in gender distribution between the groups (p-value 0.174).

As shown in figure-1, body mass index ranged from a minimum of 22.7 to a maximum of 33.5 in the myocardial infarction group, which is quite comparable to BMI ranging from 19 to 33.5 in the healthy

control group. This difference was insignificant, with a p-value of 0.079.

A history of cardiovascular diseases in the family was seen for 8(26.7%) of healthy participants and 16(53.3%) cases of myocardial infarction patients.

As shown in figure-2, the mean vitamin D level was 18±7.8ng/ml in the myocardial infarction group and 19.1±9.3ng/ml in the control group. Therefore, no significant difference was found between the two groups, with a p-value of 0.997. For further analysis, vitamin D levels were divided into three categories, i.e., <15, 15-25, and ≥25, and a comparison was made using the chi-square test, as shown in Table 1. There were 13(43.3%) myocardial infarction patients with deficient vitamin D levels and the same number, 13(43.3%) of healthy participants, showed deficient levels. In short, no difference in vitamin D status was evident between the two groups, with a p-value of 0.997.

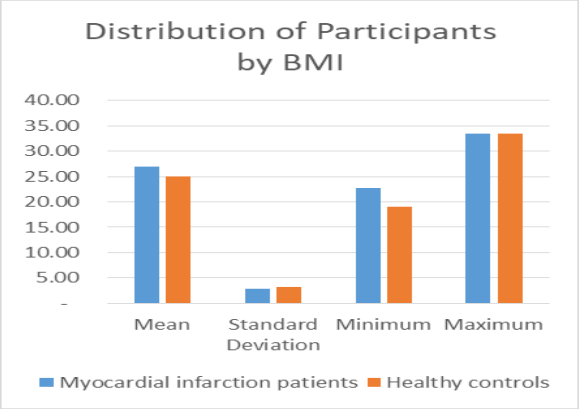

Figure-1: Comparison of groups participants according to BMI

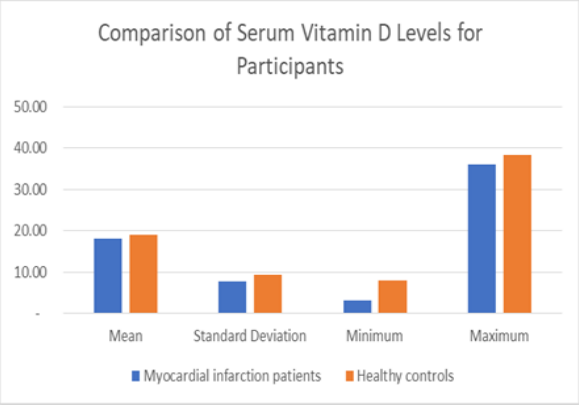

Figure-2: Showing comparison of Serum Vitamin D levels in two group

Table-1: Showing comparison of categorized vitamin D levels using the Chi-square test

	Serum Vitamin D Levels (ng/ml)			Total
	< 15 n (%)	15 - 25 n (%)	> 25 n (%)	
Group A	13 (43.3%)	11 (36.7%)	6 (20.0%)	30 (100%)
Group B	13 (43.3%)	12 (40.0%)	5 (16.7%)	30 (100%)

DISCUSSION

This study aimed to explore the physiological effects of vitamin D. A comparison of serum 25(OH)D levels was made between age and gender matched two groups, one of which included myocardial infarction patients and the other one consisted of healthy control subjects. Serum vitamin D levels were found to be comparably low in both myocardial infarction patients and healthy controls. In this study, the mean vitamin D level was measured to be 18±7.8ng/ml in myocardial infarction patients and 19.1±9.3ng/ml in healthy controls.

According to numerous studies, the optimal serum vitamin D level is more than 30 ng/ml. Adequate exposure to sunlight is very helpful for the dermal synthesis of vitamin D, but the presence of melanin in dark-skinned individuals necessitates more exposure for synthesis. That's why Asians of the Indo-Pak subcontinent need three times more exposure than Caucasians.[1,2] Worldwide, about 1 billion people suffer from vitamin D deficiency, while 50% of the global population is deficient in vitamin D.[3]

Different studies reveal variable data regarding the role of vitamin D in the development of coronary artery diseases. Some studies have attributed vitamin D receptor gene polymorphism, particularly the lack of Fok1, BsmI, and Taq1, as a risk factor for coronary artery disease. In contrast, others consider the role of Fok1 controversial in this regard.[4,5] Nevertheless, multiple mechanisms are responsible for linking vitamin D deficiency with coronary artery disease like its effect on the renin-angiotensin system, vascular compliance, hypertension,

parathyroid hormone regulation and glycemic control.[6,7]

One study conducted in 2018 in Iraq by Muhammed et al. led to the finding that vitamin D deficiency was prevalent in Iraq. Still, no statistically significant difference was found in vitamin D levels between patients with acute MI and healthy controls.[7] On the contrary, a study conducted in 2017 in Italy led to the notion that vitamin D is a cardiac risk factor and its deficiency is associated with worse short-term and long-term outcomes.[8] Similarly, a study conducted in Bangladesh in 2019 confirmed that vitamin D deficiency was considerably more severe in patients of acute myocardial infarction < 40years of age than in control subjects.[9]

A review based on numerous types of research was conducted in 2021, which led to the consistent finding that vitamin D deficiency was observed in almost 75%-90% of patients hospitalized with acute myocardial infarction.[10]

Another study in Egypt in 2020 concluded that primary percutaneous intervention was followed by better microvascular reperfusion in patients with normal vitamin D levels compared to those with abnormal vitamin D levels.[11] This showed that management outcome also improves with better vitamin D levels.

One study conducted in the USA in 2021 led to the finding that supplementation with vitamin D in vitamin D deficient patients with no prior history of myocardial infarction was associated with a significantly lower risk of mortality.[12] However, despite ample evidence on the importance of vitamin D as a regulator of multiple skeletal and extra-skeletal mechanisms, some studies still support that vitamin D must be considered a nutrient and not a medicine. Therefore, its supplementation is beneficial only when its deficiency has been established. Only then can its use as a supplement be justified, thereby causing a financial burden on society. In this regard, a consensus on the cutoff of deficiency also needs to be made, which can be followed universally.[13]

This study could not reveal an inverse association between serum vitamin D levels and myocardial infarction. However, a lot of ambiguous data on this topic needs further exploration.

CONCLUSION

This study led to the following conclusions:

Generally, our population is deficient/insufficient in vitamin D. Since serum vitamin D level is equally low in patients with myocardial infarction and healthy controls in this study, an association between cardiovascular diseases and vitamin D levels could not be established. Further large-scale studies are needed to explore the effects of vitamin D deficiency.

LIMITATIONS

Our study had a few limitations:

- The sample size was not large enough to give more accurate results.
- Ideally, all known risk factors for cardiovascular diseases must be excluded from the study to carry out a more reliable study. Our study did not remove this limitation.

AUTHOR'S CONTRIBUTION

QM: Conducted and presented the research. Also finalized the manuscript
MR: Designed the questionnaires and helped in the conduction of research
SK: Prepared the initial draft of the manuscript
TK: Helped in the conduction of research
SS: Helped in the conduction of research
QW: Reviewed the manuscript and improved it

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Review Article

VITAMIN D AND MALE FERTILITY

Maimona Tabbsum[1], Hamid Javaid Qureshi[2]

Abstract: Experimental and observational research found that males with vitamin D deficiency were likely to have testosterone deficiency or be at increased risk for it. Semen quality was also shown to be affected by low vitamin D levels, and it was the most consistent finding. It has been demonstrated that vitamin D directly affects spermatozoa and has a beneficial relationship with sperm motility. By describing experimental and clinical investigations in animals and humans addressing the link between testis function and vitamin D, the current review summarizes current information on the role of vitamin D in male fertility.

Keywords: Vitamin D, Semen quality, Spermatozoa, Male fertility

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INTRODUCTION

Vitamin D is crucial for maintaining bone metabolism and calcium homeostasis. Rickets in children and osteomalacia in adults can result from deficiency of vitamin D. Rickets was successfully eradicated from the world in the 1930s because of fortification of milk with vitamin D. However, up to 1 billion people worldwide still suffer from subclinical vitamin D deficiency, which is still very common in both industrialized and developing nations.[1]

A fat-soluble steroid, vitamin D, its source is either endogenous skin production or food (mainly oily fish, mushrooms and pharmaceutical supplements). When exposed to UV light, 7-dehydrocholesterol in the skin changes into pre-vitamin D. A heat-dependent process rapidly transforms pre-vitamin D into vitamin D (cholecalciferol). Passive diffusion causes dietary vitamin D and other lipids to be absorbed in the intestine.[2]

Vitamin D has received attention recently due to its pleiotropic effects, including endocrine, autocrine, paracrine, and activity on many target organs and systems.

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Its primary function is to control the homeostasis of calcium and phosphate, which aids in the mineralization of the bone. The parathyroid glands, skeletal system, kidneys, and gut are the main target organs of vitamin D. Thus, each of these organs is affected biologically by vitamin D in various ways. A healthy calcium-phosphorus balance is maintained by the intricate regulation of vitamin D metabolism. In actuality, vitamin D promotes calcium and phosphate absorption from the intestine, calcium retention, and phosphate excretion by the kidney, and changes the balance between bone production and resorption strictly on the level of circulating calcium. Vascular endothelium, pancreatic B cells, smooth muscle cells, monocytes and neurons have vitamin D receptors (VDR).[3]

According to the WHO, 60 to 80 million couples have infertility worldwide. Male factors cause nearly 50% of cases of infertility. Studies have revealed that mature spermatozoa, the prostate, and the testis have vitamin D receptors (sperm nucleus and neck). Infertile males who have oligo asthenozoospermia show a considerable increase in the mean sperm count and sperm motility following administration of vitamin D for 6 months.[4] Because the presence of VDR and the vitamin D metabolising

enzyme was shown in the spermatozoa and testis, it has been postulated that vitamin D shows a significant function in the male reproductive organs.[5] Semen and hormone production negatively impact hypovitaminosis D in humans and animals.[6]
Additionally, research on men having hypogonadism had mixed findings. According to several of them, men suffering from hypogonadism had relatively low levels of 25-hydroxyvitamin D3 in their blood than normal men.[7] Still, some studies could not find any association between hypovitaminosis D and hypogonadism.[8]
Interestingly, one study suggested a connection between increased vitamin D levels and hypogonadism.[9]
The interventional investigations did not even reach a consensus on this topic. The outcomes seem to be highly dependent on the duration of vitamin D administration. Short-term (3 months) and very short-term (4 days) supplementations could not affect the total testosterone levels in the blood.[10]
Otherwise, long-term, which includes 12 months of administration of vitamin D2 and D3 in males of different groups and different ages, can significantly increase total testosterone.[11]
Circulating 25-hydroxyvitamin D3 levels positively correlate with sperm count, progressive motility, total sperm motility, and normal morphology.[12] An observational study concluded that ionised calcium and vitamin D can affect testosterone bioavailability and quality of semen in infertile males because all those males with deficient vitamin D had significantly reduced progressive motility of sperm and the total number of motile sperm.[13] Studies have proposed that vitamin D plays a significant role in acrosome reaction. Hyperactivated motility and capacitation are a few Ca^{+2}-dependent activities. It also has been demonstrated that vitamin D affects sperm motility and survival. By controlling crucial processes, including cholesterol efflux and activating threonine and tyrosine residues on certain proteins, vitamin D governs sperm motility and survival. Serial vitamin D levels were favorably connected with normal morphology in normozoospermic males and with sperm motility in all patients.[14] Most research on the effects of vitamin D insufficiency has been done using mice models of the condition. In these mice models of vitamin D insufficiency, defective semen parameters have been demonstrated to be caused by vitamin D deficiency, including lower sperm count, motility, and a larger percentage of defective morphology.[15] Poor semen parameters and vitamin D insufficiency have very rarely been linked in human research.[16]
Semen samples were collected from 40 men from the general population to analyze in vitro response of sperm motility, intracellular calcium and mature spermatozoa's acrosomal reaction. Forty-five minutes of exposure to 1,25(OH)2D3 were given to the semen samples. Through the VDR-mediated release of calcium from those of intracellular calcium storage in this situation, 1,25(OH)2D3 raised intracellular calcium concentration in human spermatozoa, enhanced sperm motility and caused the acrosome reaction.[14] A condition that is sometimes disregarded, vitamin D insufficiency now affects over one billion individuals globally. Like many other nations, Pakistan has a vitamin D insufficiency problem affecting 53.5% of the population.[17]

CONCLUSION

Vitamin D deficiency might lead to subfertility in men by decreasing testosterone levels, sperm count, and sperm motility.

AUTHOR'S CONTRIBUTION

MT: Literature survey
HJQ: Proof reading

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Case Report

DENGUE HEMORRHAGIC FEVER

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ABSTRACT

Dengue fever is an airborne viral infection transmitted by the Aedes mosquito with various presentations, from a simple flu-like illness to hemorrhagic manifestations. Hemorrhagic complications can vary from simple rashes to GIT bleeding, hematuria, and severe bleeds in the brain. Here is a case of 24 years old Umer Ayub with dengue fever along with its hemorrhagic manifestations and decompensated shock state who was intubated and put on a ventilator, given 16 blood transfusions, but later his labs improved, he was extubated and recovered well from a condition which has mortality rate above 95%.

Key Words: Dengue Fever, Infection, Liver Failure

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INTRODUCTION

Dengue fever is an airborne viral infection caused by the Aedes aegypti mosquito, which can be a potentially life-threatening infectious disease with a wide spectrum from mild to severe. It has 4 different serotypes, which are DEN-1, DEN-2, DEN-3 and DEN-4. Poor sanitary conditions and unhygienic measures are leading causes of the excessive proliferation of mosquitoes and dengue infections. In mild cases, there can be fever, retro orbital pain, rash, muscle aches, nausea and vomiting; in severe cases, there can be bleeding from the nose, gums and GIT, organ failure and plasma leakage due to immune response triggers.[1]

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However some other complications include encephalopathy, myocarditis, pancreatitis, liver failure, acute kidney injury, splenic rupture and muscle hematoma.[2,3]
All these complications are rare but can be prevented if diagnosed earlier.

CASE PRESENTATION

The patient named Umer Ayub,24 years of age presented to the emergency department of Farooq hospital Westwood branch with a GCS of 3/15 in a gasping state and Blood pressure of 40/20mmHg. He was immediately shifted to ICU and electively intubated and ventilated
Baseline labs showed hemoglobin of 2.5 and a Platelet count of 14000.He suffered from severe dengue hemorrhagic fever, decompensated shock and leakage phase. He also suffered from Multi-organ failure with acute liver injury, acute kidney injury, altered state of consciousness, and lower respiratory tract infection (Aspiration Pneumonia). In addition, he had severe coagulopathy with INR over 3.

Sr No.	Investigation/units	1st day	5th day	Last day
1.	F.D.Ps D-dimer ug/dl	2.92		
2.	CRP mg/dl	7.57		
3.	Hemoglobin g/dl	5.6	10.3	11.5
4.	WBC 10/l	20	17.7	12.4
5.	Platelets 10/l	55	21	89
6.	PT sec	32	16	15
7.	INR sec	3.08	1.29	1.19
8.	APTT sec	>1	42	38
9.	ALTu/l	122	140	58
10.	ASTu/l	171	189	43
11.	ALPu/l	110	203	256
12.	Total proteing/dl	3.5	4.8	5.9
13.	UREAmg/dl	52	36	
14.	Creatinine mg/dl	12	1.0	
15.	Sodium (Na) mmol/l	133	140	133
16.	Potassium(K) mmol/l	145	4.2	3.8
17.	Iron ug/l	68		
18.	Ferritin ug/ml	3268		
19.	TIBC ug/dl	156		

Patient remained on Ventilator for 7 days. During this time, he received 16 Blood transfusions and 4 FFP transfusions.

Revolade (eltrombopag) and oprelvekin (IL 11 agonist) were used to stimulate rapid platelet production along with octreotide and omeprazole infusion to reduce GI bleeding.

On 7th Day, he was gradually weaned from the Ventilator and successfully extubated. Now patient is vitally stable, and his platelet counts are recovering; his liver function, kidney function tests and blood counts are normal. He had severe lower GI bleeding which continued persistently for 5 days despite all resuscitative measures.

The patient remained on triple inotropic supports, including morphine, dopamine and phenylephrine. In addition, the patient underwent a Colonoscopy which showed a massive lower GI Bleed from above the level of caecum. Plan was to do CT angiography of mesenteric vessels. However, it couldn't be done due to the patient's unstable condition. On the 6th day the bleeding stopped spontaneously and the patient showed signs of recovery. This patient recovered from a condition with more than 95% mortality.

DISCUSSION

DHF is categorized as DF associated with a decrease in the platelet count, plasma leakage and hemorrhagic manifestations. DF is a mosquito-borne tropical infection with an increasing number of cases yearly. In the 1950s, the approximated cases recorded per annum to the World Health Organization (WHO) was almost 900 among the enlisted countries. It has been reported that the occurrence of DF has remarkably risen with an estimated rate of 0.5 million diagnosed patients outlined in the year 2000 whereas 3.3 million patients reported in 2015.[5] DF febrile phase starts with sudden rise in body temperature, headache, body aches and retro-orbital pain continues for 2-7 days which is accompanied by plasma leakage in defervescence stage of 3-4 days. Bleeding-related symptoms of DHF usually initiate in the defervescence phase.[4] DHF is categorized into 4 different grades owing to the severity of the clinical features.[6,7] Grade I shows a positive tourniquet test involving no bleeding. Grade II shows bleeding, including ecchymosis, nose bleed, GIT hemorrhage, blood in urine, menorrhagia, or even bleeding into vital organs such as the brain and pulmonary system. Grade III indicates hypotension with a feeble pulse causing cardiac compromise. Grade IV involves features of shock. In this case report, the patient belongs to the grade IV category DHF because he had hypotension, plasma leakage and decompensated shock leading to multiorgan failure.

The exact mechanism of bleeding is not clearly understood and is believed to be caused by multiple etiological factors. However, plasma leakage is considered crucial in hemorrhagic episodes in DHF. Several studies suggested that the plasma leakage is due to the release of numerous inflammatory mediators such as interleukin (IL)-2, IL-4, IL-6, IL-8, IL-10 and interferon (INF)-γ which cause endothelial damage that

leads to increase in vascular permeability and activation of the coagulation pathway, platelet activation and fibrin breakdown ultimately causing Dengue shock syndrome (DSS).[8-10]

The mainstay of treatment in bleeding events in DHF is to compensate for the depleted intravascular volume. Unstable patients require aggressive and urgent treatment. They should be immediately transferred to the intensive care unit (ICU) and intravenous fluids should be given immediately. Blood pressure, heart rate, respiratory rate, oxygen saturation, and urine output should be monitored every 15 minutes. Fresh frozen plasma should be administered in case of active bleeding manifestations. If the platelets count is less than 20,000 without bleeding or 21,000-40,000 with bleeding then the platelets shouldbe transfused.

CONCLUSION

DHF is a fatal condition but curable if diagnosed and treated earlier. The mainstay of the treatment in severe cases is to replenish the fluid loss and intravascular volume along with blood transfusions and fresh frozen plasma. The delay in diagnosis and treatment can lead to an increased mortality rate in patients with DHF.

AUTHOR'S CONTRIBUTION

ZJ: Original idea, data collection and writing the case report
UF: Review of literature
SK: Data collection

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Qualitative Research

CAUSES OF RESISTANCE TO SOCIAL DISTANCING IN THE WAKE OF THE COVID-19 OUTBREAK IN PAKISTAN. A QUALITATIVE STUDY IN LAHORE, PAKISTAN

Malik Moazzam Elahi[1], Muhammad Ishaq[2], Nauman Ali Chaudhary[3], Muhammad Salman Butt[4]

ABSTRACT

Background: The study aimed to understand the reasons for resistance or a casual approach among people of Lahore towards COVID-19 guidelines of social distancing.

Material and Methods: An exploratory research design and qualitative research methodology was selected for this study based on the philosophical foundations of interpretivism.

Fifteen participants living in Lahore who were aware of the preventive measures against COVID-19 in general and social distancing were interviewed. Purposive sampling was utilized to short-list and approach the participants. The data collected, was analyzed using Graneheim and Lundman's approach.

Results: Through the qualitative data analysis, four major themes were derived, namely Knowledge about COVID-19 and Social Distancing, Role of socio-religious values; Role of Education; Nature of Work and attitudes toward social distancing.

Conclusion: The study concludes that most of the people were aware of the disease and adhered to SOPs about social distancing; however, a low literacy rate in certain segments of the population, preferring religious and cultural values and practices over SOPs, led some people to resist social distancing.

Key Words: Covid-19, Social Values, Attitudes, Awareness

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by a novel coronavirus, known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; formerly known as 2019-nCoV), initially defined as a result of an eruption of respiratory disease in Wuhan City, Hubei Province, China. The WHO first announced that on Dec 31, 2019.[1]

On Jan 30, 2020, the WHO declared the outbreak of COVID-19 as a global health emergency. On Mar 11, 2020, the WHO declared COVID-19 as a global pandemic, the first of its kind since the 2009 declaration of an H1N1 influenza pandemic. The SARS-CoV-2 disease was referred to as COVID-19 by the WHO, an acronym derived from the Coronavirus Virus 2019.[2] The name was chosen to avoid stigmatizing the virus's source regarding cultures, geography, or animal associations.

Long-term growth trajectories of the countries could have been affected by the decisions taken then by the countries and their funding. The United Nations mobilized the UN system to support national authorities

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in developing public health preparations and response planning to the COVID-19 crisis through its 131 country teams surveyed 162 countries and territories.[3] The impact of COVID-19 on the immediacy of the socio-economic crisis in The UN's Framework for the Immediate Socio-Economic Response warned that the COVID-19 pandemic is far more than just a health crisis.[3] Although the effects of the pandemic will vary in different countries, poverty and inequalities will most likely increase globally. The loss of several lives due to the pandemic caused permanent and lasting damage to the global society and economies.[4] Water contamination, runoff from sewage, climate change, degradation of the ozone layer, global warming, loss of groundwater levels, environmental and ecosystem changes, and arsenic pollution were all environmental concerns.[5]

COVID-19 has also caused several countries to implement various strategies, such as lockdown and social distancing, to mitigate the effects of the virus.[3] Practicing social distance means remaining as far as possible at home and away from others to prevent COVID-19 spread. Social distancing has been used since the beginning of the nineteenth century, indicating "the extent to which people and particularly people from social groups (such as race, ethnicity, class, and gender) accept or reject the social interaction"[6] Social distancing had been considered as the first line of defense in humanity's fight against the latest Coronavirus. To prevent community transmission, all local and central governments worldwide literally imposed a ban on the movement of their citizens outside their homes.[5] The evidence supports that the virus of COVID-19 can be contained and restricted to a certain extent by practicing social distancing. However, successfully implementing social distancing would require public support.[7]

Banning religious, sports, and commercial events also caused global economic challenges for developing nations like Pakistan. Pakistan faced the unique challenge of being sandwiched between the severely infected borders of COVID-19, such as China and Iran.[8] Furthermore, COVID-19 significantly impacted Pakistan through different aspects such as economic, religious, social, educational, and health.[9] The condition due to the coronavirus pandemic has also been alarming in Pakistan because of its weak healthcare infrastructure, poor sanitation, inadequate access to health services, and dramatic growth in local cases in a population that is larger than the combined population of Italy and Iran.[8]

Pakistan, since the outbreak of the coronavirus pandemic, is also included among the 180+ countries which have faced considerable challenges in the various sectors.[10] Due to this, the country put efforts into mitigating this health emergency and minimizing the economic loss extent through the method of social distancing policy in the country.[11] The spread of the disease within and into the country was similar to that of the global context as most of the cases in the world's urban population at 4.2 billion occurred in the metropolitan cities, which was similarly the case in Pakistan in which 40% of people live in cities.[12]

According to the Government of Pakistan (2020), the fatalities in Pakistan reached 6,342. It had 299K confirmed cases of Covid-19 till then; however, many remained unreported. Similarly, the government's estimate suggested that the mortalities in Pakistan could rise to 58,000 and could lie anywhere between 5 to 10% of this number. It was the healthcare system. It was forecasted to be overwhelmed.[13] Disease prevention is not just dependent on the system of sound health but also is concerned with the policies involving the population segments confronting the factors that create the condition of the spread of the disease, such as social distancing. Certain segments of the population, such as the unprivileged and those earning daily through odd jobs, remained at high risk of the disease due to their reluctance to maintain social distancing.[13]

The government of Pakistan on the federal and provincial levels had shown a great lack of coordination during the implication of the policies like the lockdown for the prevention of the Covid-19 spread.[14] The provincial governments focused on preventing the disease rather than the economic loss. In contrast, the federal government focused on minimizing the loss to the country's economy and ensuring that most of the population of Pakistan, which was dealing with poverty, did not die of hunger due to the country's economic collapse.[15] The government of Pakistan was restricted in its ability to deal with the pandemic emergency due to the country's social, political, and cultural practices.[16] The culture of Pakistan also plays a significant role as an obstacle in maintaining social distancing.[8] Most people in Pakistan follow religion blindly; specifically, people with low literacy rates in Pakistan have developed a belief that Covid-19 is a conspiracy made by the infidels against Muslims.[17] Due to these circumstances, people have shown immense resistance to the lockdown and are reluctant to follow the social distancing policy, specifically during religious occasions such as prayers.[18] In addition to the resistance from the religious sector of the society, poverty within the country was also observed as the significant cause of the resistance to the guidelines of social distancing provided by the government.[19] Unfortunately, there had been a casual approach toward social distancing.[20] Therefore, the reason for executing this study was to gain insight into the concept of Covid-19 with consequences and study its impacts, specifically in Pakistan.

MATERIAL AND METHODS

An exploratory research design and qualitative research methodology were selected for this study based on the philosophical foundations of interpretivism. In this research, people living in urban centers or cities were selected as the population of the study. The criterion for the inclusion had basic knowledge about the preventive measures against covid-19 in general and social distancing in particular. Purposive sampling, accessorized with convenience sampling, was used to short-list the participants.

Given the need for immediate data collection to improve the patient care process and the limitations of face-to-face contact, data were gathered through 15 semi-structured in-depth telephone interviews at a convenient time for the participants during March and April 2020. The study used the primary method to obtain data through in-depth interviews. The data were collected during the first lockdown in 2020, from April 2020 to July 2020, to explore the factors for resistance against social distancing measures. Fifteen in-depth interviews were conducted with the participants living in Lahore who were aware of the spread of Covid-19 and the social distancing of SOPs as a precautionary measure against its spread.

Verbal consent was obtained and the study's goals were explained to the participants. On consent from the participants, a feasible time for the interviews was scheduled. The interview process continued until saturation was achieved and no further data themes emerged. The interview length was based on the participants' desires and experiences. The interview data was preserved by recording the interviews of the participants.

DATA ANALYSIS

Graneheim and Lundman's method was used for the analysis of data. Each interview data was transcribed into text. After numerous reviews, codes were extracted from the data. After the generation of codes, the participants were consulted, and the codes were verified accordingly. The codes were then categorized according to their relevance to reaching the participants' agreement, and the themes embedded in the data were generated.

ETHICAL CONSIDERATIONS

The research had been conducted according to the ethical guidelines, keeping in mind the human subjects involved in this research for

interview purposes. A consent form had been signed to obtain participants' informed consent. Moreover, all the information/data collected from secondary sources were cited systematically.

RESULTS

Fifteen participants participated in the study, of which five participants were females, and ten were males. The minimum age limit was 23 years, and the maximum was 49 years, giving the average age of 34.2 of the study participants (Table 1).

Table 1: Demographic characteristics of the Participants (N=15)

Participants	Age (Years)	Gender	Residence
1	23	Female	Lahore
2	25	Female	Lahore
3	25	Male	Lahore
4	26	Male	Lahore
5	30	Female	Lahore
6	32	Male	Lahore
7	34	Male	Lahore
8	36	Male	Lahore
9	36	Male	Lahore
10	37	Female	Lahore
11	38	Male	Lahore
12	40	Male	Lahore
13	40	Male	Lahore
14	42	Female	Lahore
15	49	Male	Lahore

The data codes were categorized into four major themes (Table 2). Major themes are explained under.

Table 2: List of themes and major codes

Themes	Major codes
1. Knowledge about COVID-19 and Social Distancing	The participants highlighted their knowledge of COVID-19 and social distancing measures against the spread of the pandemic.
2. Role of socio-religious values	The participants showed the influence of socio-cultural factors on their attitudes towards social distancing practices The respondents also mentioned a stronghold of religious values on the decisions of the people around them and their practices.
3. Role of Education	The level of education and the concept of COVID-19 The level of education and the attitude towards social distancing
4. Nature of Work and attitude towards social distancing	Types of work and effects on the attitudes of people

Knowledge about COVID-19 and Social Distancing

The concepts of COVID-19 from the perspective of 15 participants living in Lahore who were aware of the spread of COVID-19 and social distancing as a precautionary measure against its spread were examined through interviews. They were asked about the concept of Coronavirus. Most of the participants were well aware of Coronavirus and had a basic concept about it. 12 out of 15 participants knew about the global effects of the disease and the means of its spread. One of the participants stated that: *"It is a very dangerous and contagious virus. It has spread around the globe within a few months. Hundreds of people have died because of this virus. It spreads through the touch and droplets from sneezing and*

coughing. I know about this mostly through media and social media. People also talk about this."

However, not all the respondents had basic knowledge about COVID-19; 3 out of 15 participants had a very different perception of the virus. These participants' ideas were contrary to the facts about the virus. One of the participants stated that:

"I heard from people about this disease that spreads through the bats, and whoever gets affected develops a condition of worms in their body. Some say one experiences high fever and flu."

It can be examined from this statement that despite a lot of awareness campaigns, few people still had a misconception about the spread of the disease as the interviewee heard from people the cause of the disease is bats.

Role of Socio-Religious Values

Most individuals in Pakistan blindly follow the path of religion, and this aspect is considered common in people with a literacy rate, which has resulted in people believing that COVID-19 is a conspiracy developed by infidels against Muslims.[17] The responses from the interview participants were analyzed to identify the role of religious factors in the spread of Coronavirus. One of the participants of the study recorded the response:

"Well, if a virus has to attack, it can attack anywhere. Though I have seen a lot of people in countryside areas, where my work is, people have such views as well".

Another respondent recorded the response:

"Yes, I believe these things (diseases or other evils) do not attack where God's name is spoken. We conducted a milaad (congregational gathering) at our home recently during lockdown for the blessings by God".

The aspect of perception also played a key role because most respondents mentioned that attending funerals is mandatory because of the emotions attached to the event. The responses highlight that prayers such as Jumma and funeral prayers were considered necessary by the participants. Most participants did not refrain from these congregational prayers, even being aware of the threats of the pandemic. Rather, these participants believed that proper SOPs maintaining social distancing should be implemented in these gatherings.

Participants were asked about the socio-cultural practices of greetings like handshakes and hugs in resisting the commitment to follow social distancing. During the interview, one of the respondents specified how he faced difficulty in avoiding physical contact due to the cultural value of shaking hands:

"Yes, with friends, I have avoided as there is no compulsion with friends. We can say that I will not do this because of Coronavirus. But keeping a distance of 6 feet is nearly impossible. One cannot talk to a person properly at this distance."

It had been identified that the respondent was bound by cultural values of shaking hands on greetings even though the pandemic of COVID-19 was going on in Pakistan, and the cultural values like living in a joint family and proximity restricted the individuals within one household to maintain social distancing during the pandemic of COVID-19 in Pakistan.

To find out the role of age of the participants on their attitude towards social distancing practice, respondents were asked about their practice of social distancing with their elders and how the elders in their families follow the SOPs.

Most of the participants were of the view that keeping their distance from their elders was not considered important by them. Moreover, keeping a physical distance was not only seen as difficult but also disrespectful. In the words of one of the participants:

"If we will not receive the greetings of our elders (tap on head or shoulders), it will be considered disrespectful."

The responses obtained from the participants from both higher and lower age ranges showed a somewhat similar response. They had been reluctant to adopt the social distancing measures.

Level of Education And Attitudes Towards Social Distancing

Education played a major role in developing people's attitudes towards social distancing. The participants living in Lahore were aware of the spread of COVID-19, and social distancing was a precautionary measure against its spread. Those with an education level higher than matriculation tend to show more willingness to follow social distancing measures. The response of one of the participants interviewed detailed that:

"As my husband's sisters are educated (intermediate), they are always more concerned about precautions from coronavirus. They counseled my mother-in-law and father-in-law to stay at home".

The statements by the interviewees show that individuals with a lower level of education tend to be more negligent in their adherence to keeping social distance during the pandemic.

Nature of Work (Occupation) And Attitudes Towards Social Distancing

Through interviews with the participants, the researcher also tried to find the relation between work and attitudes toward social distancing. On asking about following the SOPs of social distancing at work during the outspread of Coronavirus, one of the respondents stated that:

"No, sir, I have been working part-time at a packaging factory with over 70 workers, and none of them wears masks or keeps a distance from each other. They eat together and do handshakes and hugs as normal. Even managers there do not follow any precautions."

The above response from one participant evaluates that even though the government directed the organizations to follow preventive measures and SOPs to build the habit of social distancing among the workforce, the factories and organizations have been ignoring such protocols. The statements depicted the attitude and seriousness of the participants in following social distancing about the nature of their work. Most participants seemed to have made an excuse for their work to resist the measure of social distancing against the spread of the pandemic.

DISCUSSION

The pandemic of COVID-19 was a fatal outbreak in the past, such as Ebola, etc. In Pakistan, the spread of COVID-19, especially in the urban population, was rapid; therefore, it was essential that the urban population gets aware of the concept of COVID-19 and social distancing. The research investigated that the people living in Lahore city of Pakistan know that COVID-19 is a very dangerous and contagious virus and spreads through touching, sneezing, and coughing. Moreover, they were aware that the most common symptoms of the disease were dry cough, difficulty breathing, and chest congestion. However, few of them believed that the inception of the disease was from bats, whereas the research by UNDP (2020)(1) proved that there was no close physical contact between humans and bats; therefore, it was not the origin of COVID-19.

Social distancing was important in decreasing the second wave of COVID-19 in Pakistan. Due to the weakened healthcare system in Pakistan, it was vital for the people of Pakistan to understand the concept of social distancing and practice it.[21] The current research analyzed the views of 15 participants living in Lahore. It was aware of the spread of COVID-19 and social distancing as a precautionary measure against its spread, regarding social distancing by conducting interviews. The responses showed that most participants had basic knowledge about the concept, ways, and reasons for practicing social distancing during the pandemic. The participants knew that maintaining a distance of 3-6 meters from each other is termed social distancing. In addition, there should be an avoidance of physical contact, such as handshakes and hugs, to reduce the spread of the virus. However, despite being aware of the concept of social distancing and its use in mitigating the novel Coronavirus, a sense of carelessness was observed in the participants'

responses towards strictly following the practice of social distancing.

In line with the study's objectives, one of the important aspects was to look into the source of information. The statements from the research participants revealed the role of media in spreading information about COVID-19 and the practice of social distancing as its major deterrent. The respondents' statements highlighted that news and television perform a major role in informing people regarding the issues of COVID-19 and its repercussions. The response from the research participants suggested that television was an important medium in developing awareness among individuals regarding the news and updates related to COVID-19 and the importance of social distancing during the spread of the virus. Furthermore, the responses can be decoded to gain insights that the automated messages are also crucial during the spread of the virus, which are responsible for generating automated government messages regarding COVID-19 during phone calls. These responses also highlighted that social media is the most used platform to gain information relevant to the spread of the virus and its impact on the economy and people. The statements recorded by the participants highlighted the importance of electronic media in Pakistan, which is the most informative platform for indigenous people.

To reach one of the objectives of this research to determine whether socio-cultural values are making it challenging for authorities to implement social distancing measures in Pakistan, the participants were interviewed to explore the effects of socio-cultural and religious values on their attitudes towards practicing social distancing during the pandemic. The response of several participants revealed that citizens living in outskirt areas of Lahore tend to believe that COVID-19 only affects the people from the elite class, and the people lying in the middle class and lower class are unaffected by COVID-19. Furthermore, the analysis findings suggested that most participants were reluctant to avoid and educate others about the greeting ways of handshakes and hugs. Similarly, the responses also indicated that due to socio-cultural factors, people living in close proximity and joint families were also unable to maintain social distancing to prevent the spread of COVID-19 in Pakistan. Furthermore, the findings comprehended that lack of trust by the people in the government and inadequate measures by authorities to prepare the population for the pandemic created major challenges for them in implementing the protocol of social distancing within Pakistan.

The participants' responses also suggested that people have developed the idea that diseases such as COVID-19 have no impact on religious congregations. Additionally, some participants refuted the virus's existence by highlighting that none of the individuals in their social circle had come in contact with it and that everyone in the country was behaving like normal; therefore, the virus did not exist.

By analyzing the participants' responses, it could be distinguished that some participants did not believe in the existence of Covid-19 and that it was just a hoax by the government and other non-Muslim individuals to diminish the population of Muslims so that they could rule over the world. Therefore, it can be analyzed from the study that religious, social, cultural, and perception were the most important factors influencing the public's approach towards social distancing.

From the data analysis, it was noted that the respondents' education level played a vital role in developing their attitudes towards social distancing. Participants with lower literacy levels responded more inclined to believe in the misinformation and the conspiracy theories resulting in a non-serious attitude toward social distancing. The respondents' feedback of the study highlighted the careful reaction of the people following their association with their level of education towards their family and their support for the social distancing policy.

While analyzing the role of gender in the development of the respondents' attitudes, the researcher found that gender played a

significant role in following the SOPs to mitigate the spread of COVID-19. This response of the male participants put light on the perception about the social distancing practice critical to the male population in Pakistan, which is considered primarily responsible for earning in the families, are burdened with various work duties, and have to abide by them to keep their jobs. Women have been more attentive to the risks linked with COVID-19 and the benefit of social distance practice due to their association with television, social media, and other media channels than men.

Through the analysis of the data extracted from the interviews of the respondents, it was derived that the nature of work also plays a significant role in the practice of social distancing during COVID-19. A significant number of participants believed that proper SOPs especially social distancing, cannot be followed due to their nature of work. The participants' responses contemplated that the nature of work, such as in dairy shops, faces complexities when workers use SOPs like wearing a mask in the workplace as it affects their efficiency level, which restricts the managers from incorporating the basic protocol of COVID-19 at the workplace. The responses specified that an organization held the capacity to follow the basic protocol of COVID-19. But, the nature of work and the people managing the organization were the main determinants that affected the practice of social distancing within the various workplaces across Pakistan.

The responses from the participants further revealed that conspiracy theories also played a major role in the casual approach toward social distancing. Furthermore, it was also noted by the researcher that the factor of age does not have a significant impact on the transformation of attitudes of people towards social distancing measures or about the pandemic in general.

CONCLUSION

Regarding people's attitude when it comes to practically applying the practice of social distancing, the level of education or literacy rate was a major determinant. Individuals with a better educational background were refraining from social gatherings and ensuring social distancing. However, at the same time, smaller family gatherings were still being conducted for weddings and other functions, which completely violated government restrictions.

The results show that even some people organized religious gatherings to reduce the negative effects of the disease. Similarly, certain cultural values in Pakistan often indicate some form of physical contact, a major socio-cultural factor in non-compliant behavior among people. In terms of age, the older population was more liable to disregard COVID-19 threats by claiming them to be conspiracy theories and a way for non-Muslims to diminish the Muslim population of Pakistan. Lastly, the findings showed that most people were aware of the disease and adhered to SOPs about social distancing. However, a low literacy rate in certain population segments, preferring religious and cultural values and practices over SOPs, led some people to resist social distancing.

AUTHOR'S CONTRIBUTION

MME: Main author, data collection, and conducted the fieldwork
MI: Research supervisor
NAC: Reviewed the methodology
MSB: Reviewed the paper for grammatical mistakes

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