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# JSMDC

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**Editorial Correspondence should be addressed to**  
Editor JSMDC  
Sharif Medical & Dental College  
Sharif Medical City Road,  
Off Raiwind Road, Jati Umra,  
Lahore 54000, Pakistan.

**Tel**  
(+92-42) 111-123-786

**Fax**  
(+92-42)37860122

**E-mail**  
editors@jsmdc.pk

**Website**  
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## Understanding the Monkeypox Virus: A Threat Worth Monitoring

Maria Aslam

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Monkeypox, a viral disease with origin dating back to the late 1950s, has garnered attention due to sporadic outbreaks and its potential for human-to-human transmission. Although relatively rare and less severe than smallpox, the monkeypox virus remains a significant concern, particularly in regions of Africa where it is endemic. This editorial aims to shed light on the monkeypox virus, its impact, and the need for continued vigilance in monitoring and managing this infectious disease.

Monkeypox is an emerging zoonotic disease with rising human outbreaks in recent years. The monkeypox virus played havoc in 2022 in both endemic and non-endemic countries.<sup>1,2</sup> The first human case of this zoonotic virus was documented in 1970 by the Democratic Republic of the Congo. Many human cases have been reported as a result of intermittent epidemics during the past 50 years, mostly in African nations.<sup>3</sup>

The Democratic Republic of the Congo (DRC), Cameroon, Central African Republic, Cote d'Ivoire, Gabon, Liberia, Nigeria, Republic of the Congo, and Sierra Leone are among the nations in Central and West Africa where monkeypox is endemic. The majority of infections are sporadic or relate to localized outbreaks.<sup>4</sup> International travel and importation of monkeypox virus-infected animals are the most common causes of outbreaks in non-endemic areas.<sup>5</sup> Instances in nations other than Africa were previously reported in the US, UK, Israel, and Singapore prior to 2022.<sup>6</sup> The case-fatality ratios for infections with the West African clade are commonly estimated to be between 3 and 6 percent, whereas the Central African clade has been linked to increased transmissibility and mortality. The only nation where both clades have been verified is Cameroon.<sup>3,7</sup>

Monkeypox can spread from animals to humans by close contact with the diseased animal or body fluids, contact with contaminated things, animal bites or scratches, ingestion of infected meat, direct contact

with an infected human, their respiratory secretions, skin or genitals lesions, and face-to-face contact.<sup>8,9</sup>

Clinical features of monkeypox are remarkably similar to those of chickenpox. However, monkeypox is clinically milder.<sup>4</sup> The fundamental distinction between monkeypox and chickenpox is the prevalence of lymphadenopathy, as 90% of monkeypox patients experience enlargement of their lymph nodes. The Varicella-zoster virus (VZV), which causes chickenpox, is most frequently mistaken for monkeypox. Both of these disorders have many similarities in terms of their clinical traits. Typically, the monkeypox virus takes 5 to 21 days to incubate.<sup>9</sup>

There are two distinct stages of monkeypox in humans i.e. prodrome and rash stage. Infection with the monkeypox virus causes headache, fatigue, fever with chills or sweats, muscle aches, sore throat, and lymphadenopathy.<sup>10</sup> The rash mostly emerges a few days after a fever and lymphadenopathy. The rash is characterized by lesions and typically begins on the face before spreading to the entire body. Plaque is replaced by papules, pustules, blisters, and scabs develop over the course of roughly 2-4 weeks, followed by shedding. Pneumonitis, keratitis, encephalitis, and subsequent bacterial infections are significant side effects of monkeypox.<sup>9</sup>

Currently, available laboratory tests for detection include polymerase chain reaction (PCR), enzyme-linked immunosorbent assay (ELISA), Western blot analysis or sequencing, and immunohistochemistry.<sup>11</sup> Monkeypox infection is confirmed by nucleic acid amplification testing (NAAT) by real-time or traditional PCR.<sup>4</sup>

Supportive therapy & bed rest are frequently adequate to treat the patient's symptoms because the sickness is typically moderate and self-limiting in nature. Analgesics, antipyretics, and antibiotics for secondary bacterial infections are part of supportive care. However, in extreme situations, hospitalization, antivirals, and specialized care may be required.<sup>11</sup>

Vaccination remains a vital tool in the prevention and control of monkeypox. The smallpox vaccine also provides cross-protection against monkeypox. It is effective in reducing the severity of the disease. Continued research into the development of more specific vaccines and antiviral treatments is necessary to enhance preparedness and response capabilities.<sup>10</sup>

According to Centers for Disease Control and

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*Sharif Medical & Dental College, Sharif Medical City,  
Sharif Medical City Road, Off Raiwind Road, Jati Umra,  
Lahore 54000, Pakistan.*

*Correspondence: Dr. Maria Aslam  
Head & Professor Department of Pathology  
Sharif Medical & Dental College, Lahore  
E-mail: mariaaslam77@outlook.com*

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Prevention (CDC), people should avoid close skin-to-skin contact with those who have monkeypox-like rashes and also avoid contact with objects and materials used by the patients, use alcohol-based hand sanitizers prior to eating and touching the face, and frequently wash their hands after using the restroom. The patient should be in isolation, keep lesions covered as much as possible, and wear a surgical mask.<sup>9</sup>

Monkeypox cases have substantially surged recently, raising serious concerns.<sup>12</sup> Considering the potential for international spread through travel and globalization, global collaboration and preparedness are paramount in addressing the monkeypox threat. Sharing of surveillance data, best practices, and resources among nations can help bolster prevention, detection, and response efforts. Strengthening healthcare systems, especially in affected regions, is crucial for effective control and management.

Monkeypox remains a significant concern due to its potential for human-to-human transmission and the challenges in diagnosis and management. Continued research, surveillance, and international collaboration are vital to effectively monitor and control the virus. Through heightened awareness, preventive measures, and a commitment to public health, we can mitigate the impact of monkeypox and safeguard communities worldwide.

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# Evaluation of Coronary Arteries Diameter using an Intravascular Ultrasound during Coronary Angiography in a Tertiary Care Hospital of Rawalpindi

Muhammad Kashif, Atif Nazir, Asim Javed, Muhammad Mohsin, Khawar Naeem Satti, Waleed Abbasi, Mohsin Shah

## ABSTRACT

**Objective:** To evaluate the diameter of coronary arteries using intravascular ultrasound (IVUS) in individuals presenting for coronary angiography.

**Methodology:** It was a cross-sectional descriptive study conducted at the Rawalpindi Institute of Cardiology, Rawalpindi from July to December 2020. A total of 80 patients with a normal segment on IVUS imaging and plaque burden less than 30% were enrolled in the study by non-probability convenient sampling. All these patients underwent IVUS during coronary angiography for guideline-directed clinical indication. Intravascular ultrasound images were taken from the left anterior descending artery (LAD), right coronary artery (RCA), and left circumflex artery (LCX), and their diameters were measured. Patient demographic details about age, gender, and risk factors for coronary artery disease such as body mass index (BMI), smoking, hypertension (HTN), & diabetes mellitus (DM) were noted. Data was analyzed using the Statistical Package for the Social Sciences (SPSS) version 25.

**Results:** The mean diameter of LAD was  $3.96 \pm 0.48$  mm, RCA was  $3.7 \pm 0.22$  mm, and LCX was  $3.4 \pm 0.43$  mm. There was a significant association of LAD, LCX, and RCA diameter with gender, males having a greater diameter than females. Similarly, HTN and DM had a significant association with LAD diameter. Smoking was also associated with LCX and RCA diameter ( $p$ -value=0.001). In addition, age was also significantly associated with RCA diameter ( $p$ -value=0.002).

**Conclusion:** The diameter of coronary arteries determined by IVUS was larger as compared to visual assessment on coronary angiography. So, intravascular ultrasound provides a better measurement of the size of coronary arteries. The diameter of LAD, RCA, and LCX was significantly associated with gender.

**Keywords:** Coronary arteries. Hypertension. Coronary angiography. Intravascular ultrasound.

## INTRODUCTION

Cardiovascular diseases (CVDs) are still a significant cause of premature mortality, disability-adjusted life years, and financial burden, globally.<sup>1</sup> The mortality rate attributed to CVDs has risen by 12.5% across the world.<sup>2</sup> Cardiovascular diseases account for 17.8 million deaths worldwide, annually.<sup>3</sup> Coronary artery disease (CAD) is responsible for a major proportion of mortality and morbidity attributed to cardiovascular diseases.<sup>4</sup> Almost 85% of the deaths caused by CVDs are due to ischemic heart disease and stroke.<sup>5</sup> The burden of CVDs is particularly high in low and lower-middle-income countries.<sup>2</sup> Evaluation of the severity of coronary artery disease has a crucial effect on the management and prognosis of the disease. The prevalence of CAD is high in the Asian population as compared to Caucasians. Almost one-fourth of the disease occurs in Asians less than 40 years of age. This refers to the

smaller size of coronary arteries in Asians, according to previous research.<sup>6</sup> Coronary angiography has been well recognized as a diagnostic modality to guide percutaneous coronary intervention (PCI) in CAD. But with the latest advances in intravascular imaging technology, optical coherence tomography and intravascular ultrasound are extensively used with angiography in guiding PCI.<sup>7</sup> Coronary angiography provides a two-dimensional image of coronary arteries. Imaging techniques are more feasible for direct vessel visualization and give a better estimate of plaque burden and vessel remodeling. In addition, better PCI outcomes are also attributed to intravascular imaging.<sup>8</sup> Determining the appropriate size for balloon dilation and stent size is an important step in planning the PCI procedure. It has been increasingly recognized that the original diameter of the vessel varies between IVUS analysis and assessment of conventional coronary angiography.<sup>9</sup>

The size of coronary arteries varies among individuals based on differences in age, gender, race/ethnicity, weight, the surface area of the body, left ventricular mass, and vasomotor tone.<sup>10</sup>

Different imaging modalities have long been used to assess vessel size, the severity of lesions, and plaque burden. Intravascular ultrasound provides an accurate assessment of vessel size. This study was

Sharif Medical & Dental College, Sharif Medical City,  
Sharif Medical City Road, Off Raiwind Road, Jati Umra,  
Lahore 54000, Pakistan.

Correspondence: Dr. Muhammad Kashif  
Medical Officer Department of Cardiology  
Rawalpindi Institute of Cardiology, Rawalpindi  
E-mail: kashifbbh@gmail.com

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planned to evaluate the size of normal coronary arteries by IVUS. The smaller diameter of coronary arteries presents a significant therapeutic challenge associated with difficulties in percutaneous coronary angioplasty and stenting. Smaller coronary artery diameter is also a poor prognostic factor for coronary artery disease. Data on normal diameters of coronary arteries adjusted for age, gender, and other factors may be useful to interventional cardiologists and cardiac surgeons in improving PCI & coronary artery bypass grafting (CABG), and preventing short & long-term complications associated with under or oversizing of coronary arteries.

### METHODOLOGY

It was a cross-sectional descriptive study conducted at the Rawalpindi Institute of Cardiology, Rawalpindi. A sample size of 80 was calculated using the standard deviation of the diameter of proximal LAD as 0.23 mm and 5% margin of error.<sup>11</sup> Patients with a normal segment on IVUS imaging and plaque burden less than 30% were enrolled in the study by non-probability convenient sampling. All these patients underwent IVUS during coronary angiography for guideline-directed clinical indication. The exclusion criteria included the patients with image distortion on IVUS due to artifacts and the absence of a normal segment in the desired segment. The patient demographic details about age, gender, BMI, smoking, and risk factors such as HTN & DM were noted on a proforma sheet. Informed consent was taken from the patients. Intravascular ultrasound images were taken at any time during the procedure at the operator's discretion after injecting 200 micrograms of glyceryl trinitrate. An IVUS catheter (Volcano Eagle Eye Short Tip) was introduced into the distal left anterior descending artery, left circumflex artery, and right coronary artery over a 0.014-inch guide wire. After optimal adjustment of gain and contrast, continuous ultrasound imaging was performed for better visualization of lumen-intima and medial-adventitial interfaces. Intravascular ultrasound images were taken from proximal LAD, proximal RCA, and proximal LCX. Only the healthy segments on IVUS imaging or segment with a plaque burden of less than 30% were part of the study. Measurements from proximal LAD (before the origin of large septal or diagonal), proximal LCX (before the origin of the first marginal branch), and proximal RCA (within the first 2 cm after its origin) were taken. The vessel diameter and luminal area of the artery at the given reference points were noted on IVUS images by defining the distance from media to media.

### STATISTICAL ANALYSIS

Data was analyzed using the Statistical Package for the Social Sciences (SPSS) version 25. The qualitative variables such as gender were presented as frequency and percentage. The quantitative variables, such as age and coronary artery diameter were expressed using mean and standard deviation (SD). The association of coronary artery diameters with various variables, such as age, gender, BMI, etc. was determined using an independent t-test and one-way Analysis of Variance (ANOVA). A p-value of  $\leq 0.05$  was considered significant.

### RESULTS

The mean age of the study participants was  $54.61 \pm 10.19$  years, with a minimum age of 34 years and a maximum age of 78 years. Majority of them (33.7%) were of the age group 51-60 years followed by 41-50 years (30%). Out of 80 study subjects, 55 (68.7%) were males and 25 (31.3%) were females. Fifty (62.5%) subjects were diabetic, 57.5% were hypertensive, and 38.7% were smokers. The mean BMI was  $27.31 \pm 3.23$  kg/m<sup>2</sup>. The minimum and maximum BMI were 21.3 kg/m<sup>2</sup> and 34.5 kg/m<sup>2</sup>, respectively. The majority of the participants (55%) had a BMI ranging from 25-29.9 kg/m<sup>2</sup> followed by 18.5-24.9 kg/m<sup>2</sup> (25%) (Table 1). The mean diameter of LAD was  $3.96 \pm 0.48$  mm, LCX was  $3.4 \pm 0.43$  mm, and RCA was  $3.7 \pm 0.22$  mm (Table 2). There was a significant association of LAD, LCX, and RCA diameter with gender, with males having a greater diameter than females. Similarly, HTN and DM had a significant association with LAD diameter. Smoking was also associated with LCX and RCA diameter with a significant p-value. In addition, age was also significantly associated with RCA diameter (Table 3).

### DISCUSSION

There is a wide variation in the diameter of coronary arteries across different populations.<sup>12</sup> Data regarding the size of coronary vessels is very limited among Pakistani population. The dilemma of the size of coronary vessels in the Pakistani population versus the western population has yet to be resolved. Many studies have reported the small size of coronary vessels in the Pakistani population. But in these studies, size was measured from patients undergoing CABG or from specimens taken from autopsy, which may be a reason for smaller coronary artery size.<sup>13</sup> In addition, coronary angiography is often used to estimate the diameter of coronary vessels which is less accurate and dependent on operator observation.<sup>14</sup>

In our study, the study participants had a mean age of  $54.61 \pm 10.19$  years, and 68.7% of them were males. Similarly, in a study done in Turkey, the mean age of the



**Table 1: Demographic Variables of the Study Subjects**

Demographic Variables		Frequency & Percentage
Age (Years)	31-40	9(11.3%)
	41-50	24(30%)
	51-60	27(33.7%)
	61-70	14(17.5%)
	71-80	6(7.5%)
Gender	Male	55(68.7%)
	Female	25(31.3%)
Diabetes Mellitus	Present	50(62.5%)
	Not Present	30(37.5%)
Hypertension	Present	46(57.5%)
	Not Present	34(42.5%)
Smoking	Smoker	31(38.7%)
	Non-smoker	49(61.3%)
BMI (kg/m <sup>2</sup> )	18.5-24.9	20(25%)
	25-29.9	44(55%)
	≥30	16(20%)

**Table 2: Diameter and Lumen Area of Coronary Arteries**

Coronary Artery Size		Coronary Artery		
		LAD	LCX	RCA
Diameter (mm)	Mean±SD	3.96±0.48	3.4±0.43	3.7±0.22
	Minimum Diameter	3.3	2.9	3.4
	Maximum Diameter	5.6	4.1	4
Lumen Area (mm <sup>2</sup> )	Mean±SD	13.09±2.9	11.8±2.13	13.44±2.04
	Minimum Lumen Area	9.3	9.3	10.42
	Maximum Lumen Area	21.1	16.1	17.1

**Table 3: Association of Various Variables with Diameter of LAD, LCX, and RCA**

Study Variables		LAD Diameter (mm)	p-value	LCX Diameter (mm)	p-value	RCA Diameter (mm)	p-value
Age (Years)	31-40	3.84±0.34	0.884	3.45±0.21	0.249	3.5±0.11	0.002*
	41-50	3.99±0.7		3.8±0		3.53±0.2	
	51-60	3.98±0.3		3.61±0.5		3.92±0.11	
	61-70	4.04±0.28		3.05±0.19		3.63±0.11	
	71-80	3.76±0.4		3.1±0		3.62±0.22	
Gender	Male	4.06±0.49	0.012*	3.85±0.2	0.001*	3.84±0.12	0.001*
	Female	3.66±0.27		3.07±0.15		3.44±0.05	
Diabetes Mellitus	Present	3.84±0.31	0.05*	3.4±0.46	0.82	3.73±0.24	0.496
	Not Present	4.11±0.61		3.45±0.21		3.65±0.17	
Hypertension	Present	4.06±0.52	0.03*	3.47±0.56	0.72	3.69±0.21	0.77
	Not Present	3.75±0.3		3.38±0.4		3.72±0.24	
Smoking	Smoker	3.94±0.52	0.843	3.86±0.22	0.001*	3.88±0.12	0.001*
	Non-smoker	3.97±0.45		3.15±0.28		3.58±0.18	
BMI (kg/m <sup>2</sup> )	18.5-24.9	4.01±0.74	0.684	3.05±0.19	0.108	3.7±0	0.636
	25-29.9	3.9±0.36		3.5±0.46		3.74±0.21	
	≥30	4.04±0.3		3.75±0		3.63±0.28	

\*Significant p-value

study subjects was  $57.3 \pm 11.4$  years, and 53.6% were males.<sup>11</sup> Ahmed et al. reported that the mean age of the participants was  $45.85 \pm 10.12$  years. The majority of them were males (73.3%).<sup>13</sup> In another study done in Pakistan, participants had a mean age of  $54.35 \pm 12.39$  years.<sup>15</sup> The mean BMI was  $27.31 \pm 3.23$  kg/m<sup>2</sup> in our study. The participants had a BMI of  $28.25 \pm 4.56$  kg/m<sup>2</sup> and a body surface area (BSA) of  $1.88 \pm 0.13$  m<sup>2</sup> in another study.<sup>11</sup> The results are similar to the present study. Ozdemir et al. reported mean BMI and BSA as  $29.0 \pm 5.3$  kg/m<sup>2</sup> and  $1.9 \pm 0.2$  m<sup>2</sup>, respectively in their study.<sup>16</sup> The BMI was less in other studies. The mean BMI was  $24.59 \pm 1.48$  kg/m<sup>2</sup> in a study by Raut et al.<sup>17</sup> The mean BMI was  $26.5$  kg/m<sup>2</sup> and BSA was  $1.81$  m<sup>2</sup> in another study.<sup>18</sup>

Our results showed that 62.5% of the subjects were diabetic, 57.5% were hypertensive, and 38.7% were smokers. The frequency of these risk factors was very high as compared to another study, in which HTN was present in 25.6%, smoking in 22.8%, hyperlipidemia in 12.9%, and DM in 7.7% of the study participants.<sup>16</sup> Kurt et al. reported HTN in 46.3%, DM in 12.2%, smoking in 43.6%, hyperlipidemia in 11.2%, and a family history of CAD in 11.2% of the participants.<sup>11</sup>

In our study, the mean diameter of LAD was  $3.96 \pm 0.48$  mm, LCX was  $3.4 \pm 0.43$  mm, and RCA was  $3.7 \pm 0.22$  mm. In a study by Ahmed et al. in Pakistan, computed tomographic (CT) angiography of coronaries was used to determine the diameter of coronary arteries. The mean diameter of the left main artery was  $3.96 \pm 0.585$  mm, LAD was  $3.62 \pm 0.515$  mm, LCX was  $2.99 \pm 0.629$  mm, and RCA was  $3.13 \pm 0.532$  mm.<sup>13</sup> In another study done in Pakistan, the size of the left main coronary artery (LMCA) was  $4.065 \pm 0.363$  mm, proximal LAD was  $3.559 \pm 0.33$  mm, proximal LCX was  $3.182 \pm 0.38$  mm, and proximal RCA was  $2.996 \pm 0.33$  mm as determined by coronary arteriography. Raut et al. reported the size of LAD, RCA, and LCX as  $3.27 \pm 0.23$  mm,  $3.2 \pm 0.37$  mm, and  $2.97 \pm 0.37$  mm, respectively.<sup>17</sup> These studies showed that the diameter of coronary arteries in our study was greater than in other studies. This might be due to the reason that intravascular ultrasound was used in our study to determine the coronary arteries' diameter. In contrast, coronary angiography or CT angiography was used in other studies.

Intravascular ultrasound provides a more accurate measurement of the size of coronary arteries. A study in India compared the diameter of coronary arteries measured by IVUS and coronary angiography. The size of LAD was significantly greater when measured by IVUS (3.71 mm) than by angiography (3.45 mm). Similarly, the diameter of LCX was 3.55 mm by IVUS and 3.16 mm by angiography. Right coronary artery dimensions were 3.85 mm and 3.27 mm by IVUS and

angiography, respectively.<sup>19</sup>

A study reported the size of LMCA, LAD, RCA, and LCX as  $4.5 \pm 0.9$  mm,  $3.5 \pm 0.7$  mm,  $3.8 \pm 0.8$  mm, and  $3.5 \pm 0.8$  mm, respectively in Caucasian men using coronary arteriogram. The diameter of LMCA, LAD, RCA, and LCX was  $4.6 \pm 0.9$  mm,  $3.5 \pm 0.8$  mm,  $3.5 \pm 0.8$  mm, and  $3.4 \pm 0.8$  mm, respectively in Asian men. No significant difference was found between the two groups. The study population had no history of CAD or its risk factors, and both groups were matched for age, weight, height, BMI, and body surface area.<sup>11</sup>

There was a significant association of LAD, LCX, and RCA diameter with gender, with males having a greater diameter than females in our study. In a study by Ozdemir et al., the diameter of LMCA and LCX were the same in both males and females. On the other hand, LAD and RCA diameters were significantly greater in males than in females.<sup>16</sup> A study conducted in Pakistan revealed that the size of coronary arteries is significantly associated with gender, BMI, and body surface area.<sup>13</sup> In contrast, the diameter of coronary arteries was not linked to BMI in our study.

Skowronski et al. enrolled an equal number of Caucasians and Asians in their study. Study participants were matched for age, gender, and BSA. The study reported that the luminal area and coronary vessel diameter are significantly larger in all the proximal segments of Caucasians as compared to Asians. The differences in the lumen area and diameter of the proximal segments of LAD were 13% and 6%, LCX were 14% and 8%, and RCA were 8% and 4%.<sup>20</sup> Another study also revealed that Caucasians had a larger diameter of coronary arteries than Asians. But when matched to body surface area, the difference was insignificant, suggesting that the smaller diameter of coronary arteries in the Asians might be attributed to their relatively small size.<sup>13</sup>

## CONCLUSION

The diameter of coronary arteries determined by IVUS was larger as compared to visual assessment on coronary angiography. So, intravascular ultrasound provides a better measurement of the size of coronary arteries. The diameter of LAD, RCA, and LCX was significantly associated with gender.

## LIMITATIONS & RECOMMENDATIONS

The study participants were recruited from a single tertiary care hospital in Pakistan, so these results cannot depict the overall Pakistani population. Further studies should be conducted by enrolling study participants from multiple healthcare institutions. The study had a small sample size, as IVUS is an expensive diagnostic modality. Future research should be done on a larger sample size.

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# Categorization of Histopathologic Subtypes of Lung Carcinomas using Immunohistochemistry in Small Biopsies at a Tertiary Care Diagnostic Center in Lahore

Babar Yasin, Zakia Wahid, Adeel Haider, Maimona Tabbsum, Najam-ud-Din

## ABSTRACT

**Objective:** To determine the frequency and distribution of different histological subtypes of lung tumors in small biopsies submitted at a tertiary care diagnostic center in Lahore.

**Methodology:** It was a descriptive cross-sectional study. This study included all computed tomography (CT)/ultrasound-guided core needle biopsies of suspicious lung masses recorded from 2021-2022 at Aznostics - The Diagnostic Center, Lahore. The study was approved by the Institutional Review Board and informed consent was taken. Total 66 core needle biopsies were performed in radiologically detected lung, mediastinal, hilar, and pleural masses. Histopathological analysis was performed, immunohistochemistry (IHC) was done where required, and data was analyzed.

**Results:** The study sample comprised of 66 cases, out of which 44(66.7%) were male patients and 22(33.3%) were female patients. The mean age was 64.4±13.34 years. The 51-75 year group constituted majority of the cases comprising 45(68.2%) cases. The male to female ratio was 2.5:1. Non-small cell lung carcinoma (NSCLC) comprised of 51(77.3%) cases & it was the predominant malignancy. Adenocarcinoma comprised of 34(51.5%) cases, and it was the most common subtype in both genders. All 3(4.5%) cases of small cell carcinoma were in males. In females the dominant subtype was adenocarcinoma [14(63.7%)]. High expression of cytokeratin 7 (CK7) and thyroid transcription factor 1 (TTF-1) was noted in adenocarcinoma and increased expression of p63 and p40 was seen in squamous cell carcinoma (SCC). Positive expression of synaptophysin was observed in 2 cases of small cell lung carcinoma.

**Conclusion:** Lung carcinoma is more prevalent in males and adenocarcinoma is the most common histologic subtype followed by SCC and small cell carcinoma. Females present at a relatively younger age with adenocarcinoma being the predominant histologic subtype. Immunohistochemistry of CK7, TTF-1, p63, and p40 can be helpful to classify difficult cases of NSCLC.

**Keywords:** Lung cancer. Immunohistochemistry. Molecular testing. Cytokeratin 7.

## INTRODUCTION

Lung cancer is a serious health concern and a major cause of cancer-related mortality. It is the second most commonly detected cancer around the world.<sup>1</sup> It is believed that the incidence of lung cancer is increasing steadily in Pakistan. According to the global cancer statistics 2020, it is predicted that incidence may rise to 19,140 new cases per year in 2040. It is the second most prevalent cancer in Pakistani males and it is ranked 2<sup>nd</sup> after breast carcinoma in females.<sup>2</sup> The dominant risk factor for lung carcinoma is tobacco smoking and variations in lung cancer incidence are closely related to the changing trends in cigarette smoking.<sup>3</sup> Majority of lung cancer patients present at an advanced and unresectable stage.<sup>4</sup> In such cases, primary pathologic diagnosis can only be made on small biopsy specimens obtained through bronchoscopic or ultrasound-guided percutaneous small biopsies and cytologic specimens.<sup>5</sup> Majority of these small biopsies can be differentiated into

malignant and benign lesions and cases of small and non-small cell lung carcinoma by using hematoxylin and eosin (H & E) stained slides. However, within the group of NSCLC, the accurate subtyping of the two most common histological types, adenocarcinoma (AC) and squamous cell carcinoma becomes difficult on H & E staining.<sup>6</sup> This categorization is highly important as it forms the basis for further molecular tests and choice of effective targeted therapy.<sup>7</sup> The judicious use of immunohistochemistry not only assists in further subtyping of lung cancer but is also required to rule out poorly differentiated lung carcinomas without clear and distinctive squamous or glandular differentiation on routine H & E morphology.<sup>8</sup> Histologic subtyping of lung carcinoma is vital as it forms the basis for molecular tests and the choice of personalized therapy. This study was planned to evaluate the frequency and distribution of various histological subtypes of lung cancer on IHC in both genders and different age groups in submitted small biopsies.

## METHODOLOGY

This descriptive cross-sectional study included all cases of suspicious lung lesions that underwent CT/ultrasound-guided core needle biopsy from 2021-2022 at Aznostics - The Diagnostic Center, Lahore. The study was approved by the Institutional Review Board and informed consent was taken. Computed

Sharif Medical & Dental College, Sharif Medical City,  
Sharif Medical City Road, Off Raiwind Road, Jati Umra,  
Lahore 54000, Pakistan.

Correspondence: Dr. Babar Yasin  
Consultant Histopathologist Department of Pathology  
Aznostics - The Diagnostic Center, Lahore  
E-mail: zahir3450@gmail.com

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tomography/ultrasound-guided core needle biopsies were performed on 70 radiologically detected lung, mediastinal, and pleural masses. Benign lesions, lobectomy, and pneumonectomy specimens were excluded and 66 cases were selected for the study. These biopsy cores were sent in 10% buffered formalin for histopathological analysis. The core tissues were fixed in formalin for 8-12 hours and processed for H & E staining. These sections were examined histologically and sent for special stains or IHC wherever required. The IHC markers chosen were based on histopathological features from a panel comprising of CK7, TTF-1, p63, p40, & synaptophysin. Immunohistochemistry was performed using Dako HRP-linked Detection System with 3,3'-diaminobenzidine (DAB) chromogen according to the instruction manual. Dark brown staining was considered positive. Histological types and subtypes of lung lesions were diagnosed based on 2015 WHO classification of lung tumors.<sup>7</sup>

### STATISTICAL ANALYSIS

Data was entered and analyzed in Statistical Package for the Social Sciences (SPSS) version 26. Descriptive analysis was performed on all the variables. Categorical variables were presented in the form of frequency and percentage, whereas quantitative variables like age were presented in the form of mean (SD). Chi-square test was applied to see the association between gender and age with the type of carcinoma. A p-value  $\leq 0.05$  was taken as significant.

### RESULTS

Out of a total of sixty six patients, 44(66.7%) were males and 22(33.3%) were females. The overall male to female (M:F) ratio was 2.5:1. The age ranged from 2 to 96 years with an average age of  $64.41 \pm 13.34$  years. The mean age for males and females was  $67.21 \pm 12.07$  years and  $58.82 \pm 14.25$  years, respectively.

Non-small cell lung carcinoma (comprising of adenocarcinoma and squamous cell carcinoma) was the most common diagnosis constituting 51(77.3%) cases and small cell carcinoma was seen in 3(4.5%) cases. Metastatic tumors were seen in 5(7.6%) cases and other

histological types were encountered in 7(10.6%) cases. The frequency distribution of different histological types of lung carcinoma is given in Table 1.

Maximum number of patients were seen in the age group of 51-75 years comprising 45(68.2%) cases. This was followed by 11(16.7%) cases in the age group above 75 years, and 10(15.1%) cases in the age group less than 51 years. The number of cases was almost double in males comprising of 44(66.7%) cases compared to females who constituted 22(33.3%) cases. However, an association of the tumor subtype with age and gender was not statistically significant, p-value=0.644 and p-value=0.096, respectively. The frequency distribution of lung tumors in both genders and different age groups is shown in Table 2 and 3.

Regarding the histological categorization of NSCLC, it was observed that adenocarcinoma is the common histological pattern in both genders as indicated in Table 3. Out of the total study sample, adenocarcinoma was reported in more than half 34(51.5%) cases followed by squamous cell carcinoma in 17(25.8%) cases.

As indicated in Table 3, a marked male predominance for SCC and small cell carcinoma was observed and 15 out of 17 cases of SCC were in males in comparison to 2 out of 17 cases in females. All 3(4.5%) cases of small cell carcinoma were reported in males only. However, the most prevalent cancer in females was adenocarcinoma comprising 14(63.7%) out of 22 cases in comparison to 20(45%) out of 44 cases in males.

Immunohistochemistry was performed on 57(86.3%) cases. Adenocarcinoma showed a high expression of CK7 and TTF-1 in 31(81.5%) and 30(90%) cases, respectively. A positive staining pattern of p40 and p63 was observed in 8(66.7%) out of 12 cases and 7(87.5%) out of 8 cases of squamous cell carcinoma, respectively. There were 3 cases of small cell carcinoma and IHC was performed on 2 cases. Neuroendocrine marker synaptophysin was positive in both cases. The IHC profile of various histological subtypes is shown in Table 4. Hematoxylin and eosin and immunohistochemistry staining patterns in adenocarcinoma lung are shown in Figure 1.

**Table 1: Frequency Distribution of the Histological types of Lung Carcinoma**

Carcinoma	Frequency & Percentage
Adenocarcinoma	34(51.5%)
SCC	17(25.8%)
Small Cell Carcinoma	3(4.5%)
Metastatic Carcinoma	5(7.6%)
Others	7(10.6%)

**Table 2: Frequency Distribution of Histological Types of Lung Carcinoma according to Age**

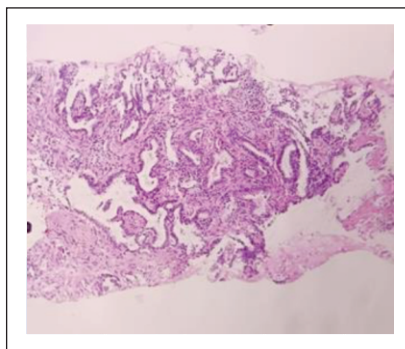
Carcinoma Type	Age Category (Years)			Total	p-value
	Less than 51	51-75	Above 75		
Adenocarcinoma	4(40%)	23(51.1%)	7(63.6%)	34(51.5%)	0.644
SCC	2(20%)	12(26.6%)	3(27.3%)	17(25.8%)	
Small Cell Carcinoma	0(0%)	3(6.7%)	0(0.0%)	3(4.5%)	
Metastatic Carcinoma	2(20%)	3(6.7%)	0(0.0%)	5(7.6%)	
Others	2(20%)	4(8.9%)	1(9.1%)	7(10.6%)	
<b>Total</b>	10(100%)	45(100%)	11(100%)	66(100%)	

**Table 3: Frequency Distribution of Histological Types of Lung Carcinomas according to Gender**

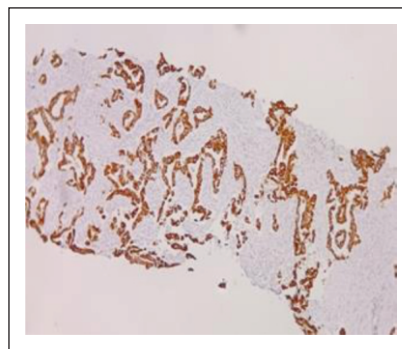
Carcinoma Type	Gender		Total	p-value
	Male	Female		
Adenocarcinoma	20(45.5%)	14(63.7%)	34(51.5%)	0.096
SCC	15(34.1%)	2(9.1%)	17(25.8%)	
Small Cell Carcinoma	3(6.8%)	0(0%)	3(4.5%)	
Metastatic Carcinoma	2(4.5%)	3(13.6%)	5(7.6%)	
Others	4(9.1%)	3(13.6%)	7(10.6%)	
<b>Total</b>	44(100%)	22(100%)	66(100%)	

**Table 4: Immunohistochemical Profile of the Different Histological Types of Lung Cancer**

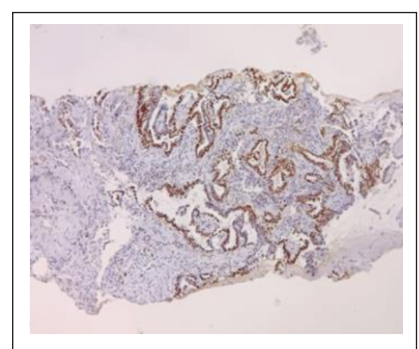
Markers	Histologic Subtypes					Total
	Adenocarcinoma	SCC	Small Cell Carcinoma	Metastatic Carcinoma	Others	
CK7	31(81.5%)	5(13%)	0(0%)	1(2.6%)	1(2.6%)	38(100%)
TTF-1	30(90%)	2(6%)	0(0%)	0(0%)	1(3%)	33(100%)
p40	4(33.3%)	8(66.7%)	0(0%)	0(0%)	0(0%)	12(100%)
p63	1(12.5%)	7(87.5%)	0(0%)	0(0%)	0(0%)	8(100%)



**a:** Adenocarcinoma, Acinar Pattern H & E



**b:** High Expression of Immunohistochemical Stain CK7



**c:** Positive Staining Pattern of Immunohistochemical Stain TTF-1

**Figure 1: Hematoxylin and Eosin & Immunohistochemistry Staining Patterns in Adenocarcinoma Lung**

## DISCUSSION

The present study gives a glimpse of the occurrence of different morphological subtypes of lung carcinomas in both genders and different age groups in submitted biopsies at a diagnostic center in Lahore. The average age at the time of diagnosis was 64.23 years, which was slightly higher in comparison to other regional studies which have shown a mean age of 58 years.<sup>9,10</sup> The reason may be that our study is single center based. In our study, females presented at a relatively lower mean age ( $58.82 \pm 14.25$  years) as compared to males ( $67.21 \pm 12.07$  years). This finding is in agreement with a study conducted by Bhatti et al.<sup>10</sup>

According to the available literature, smoking has a strong association with the development of lung carcinoma in both genders. Historically, it is believed that cigarette smoking is more common in males, hence lung cancer tends to display male preponderance.<sup>1,11</sup> In Pakistan, data regarding the prevalence and various histological subtypes of lung cancer is scarce. However, according to a nationwide survey, the prevalence of cigarette smoking is higher in males in comparison to females which is around 36% and 9%, respectively.<sup>12</sup> The findings in our study revealed that a large proportion of the cases of primary lung cancer (38 out of 54 cases) were seen in males. Females in contrast expressed a lower incidence (16 out of 54 cases). The average global gender ratio for male to female lung cancer is 1.9:1 which, however, varies from region to region.<sup>13</sup> In the current study, the gender ratio was slightly higher (2.5:1) than that in the world population. However, it is in tandem with other regional and local studies which show a gender ratio of 2.6:1 and 2.8:1, respectively.<sup>10</sup>

In our study, adenocarcinoma was the most common histological type comprising 34(51.5%) cases followed by SCC comprising 17(25.8%) cases and the least common morphological type noted was small cell cancer consisting of 3(4.5%) cases. Nath et al. also reported adenocarcinoma as the most prevalent histologic subtype in his study.<sup>14</sup> The recent global cancer statistics show a declining trend in the prevalence of SCC and a rise in the incidence of AC of the lung in both genders.<sup>15</sup> The declining incidence of SCC and small cell carcinoma around the world is considered to be due to the decrease in trends of tobacco smoking as SCC has a strong association with tobacco smoking.<sup>16</sup> On the other hand, the rising incidence of adenocarcinoma may be attributed to the change in cigarette designs, inhalation patterns, and rise in air pollution.<sup>15</sup>

A marked male preponderance was seen in our study for SCC (88.2%) and small cell carcinoma (100%). This observation is in agreement with other local and regional studies. A study conducted in India, reported that SCC lung was more common in males with a

gender ratio of 9.1:1.<sup>10</sup>

Substantial evidence suggests that the incidence of lung cancer in females is on the rise and adenocarcinoma of the lung is a frequent subtype. The reason for the rise in incidence is believed to be multifactorial, such as increase in smoking trend, more exposure to environmental toxins, and biomass exposure of females residing in rural areas.<sup>16</sup> Findings in the present study reveal that adenocarcinoma comprising of 14 out of 22(63.8%) cases was the most common subtype of lung cancer in females. This observation is in accordance with global statistics.<sup>15</sup>

Therapeutic decisions in precision medicine depend on accurate knowledge about tumor stage, genetic characteristics, and histological subtype of the tumor.<sup>17</sup> Therefore, the identification of histological subtypes is of crucial importance as therapeutic options for SCC and AC are different. Immunohistochemistry plays a vital role in the accurate categorization of NSCLC and thus in the decision about the choice of personalized therapy.<sup>6,18</sup> Further, since lung is a favored site for metastatic cancers, it is therefore important to rule out metastasis before considering it a primary lung malignancy.<sup>19</sup> In the current study, the high expression of CK7 (81.5%) and TTF-1 (90%) was seen in cases of AC which is in accordance with the observation made by Xu.<sup>20</sup> A positive staining pattern of p63 and p40 was observed in SCC cases. This observation is in agreement with the findings of another study.<sup>21</sup>

## CONCLUSION

Lung carcinoma is more prevalent in males and adenocarcinoma is the most common histological subtype followed by squamous cell carcinoma and small cell carcinoma. Females present at a relatively younger age and adenocarcinoma is the predominant histologic type in females. In males, SCC is the predominant subtype of lung carcinoma. Immunohistochemistry panel of CK7, TTF-1, p63, and p40 is helpful to classify difficult cases of NSCLC.

## LIMITATIONS & RECOMMENDATIONS

This was a single centered study with a small study sample, so results cannot be generalized to the entire Pakistani population. Further study with a larger sample size is recommended.

Immunohistochemistry can be useful in improving the diagnostic accuracy in difficult cases and further categorization of histological subtypes of lung cancer, so that therapeutic strategies may be tailored accordingly.

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## Frequency of Suicidal Intent in Patients with Epilepsy

Tehmina Mushtaq, Ayaz Muhammad Khan, Hassan Zulqernain Mahmood, Rabia Asghar, Muhammad Nasar Sayeed Khan, Muhammad Ali Awab Sarwar, Sarah Shirazi, Kanwal Iqbal

### ABSTRACT

**Objective:** To determine the frequency of suicidal intent in patients with epilepsy.

**Methodology:** This cross-sectional study was conducted at the Department of Psychiatry, Department of Neurology, and Department of Medical and Surgical Emergency, Services Hospital, Lahore from January to July 2022. The inclusion criteria were patients with epilepsy of both male and female gender, aged between 15-45 years. Total 226 patients fulfilling inclusion criteria were enrolled after informed consent. The patients were assessed for suicidal risk using Beck's suicide intent scale. The data was obtained by using a self-devised proforma. The patients scoring >15 were classified to have suicidal intent.

**Results:** In this study, out of 226 cases, 43(19.03%) were between 15-30 years of age, whereas 183(80.97%) were between 31-45 years of age. The mean age was 36.97±5.98 years. Among patients, 125(55.31%) were males, whereas 101(44.69%) were females. Out of 226 patients, 54(23.89%) patients showed suicidal intent. The frequency of suicidal intent in patients with epilepsy was 54 (23.89%).

**Conclusion:** The frequency of suicidal intent was higher in patients with epilepsy. Therefore, screening all epilepsy patients should be done for early diagnosis and treatment.

**Keywords:** Epilepsy. Suicide. Psychiatry.

### INTRODUCTION

Epilepsy, a chronic neurological disorder, is one of the world's oldest recognized conditions, with documented evidence dating back to 4000 BCE.<sup>1</sup> Every year, around 5 million individuals are diagnosed with epilepsy, and it affects 70 million people worldwide.<sup>2</sup> Suicidality, including suicidal ideation, suicide attempts, and completed suicide affects patients with epilepsy (PWE) with a higher frequency than in the general population.<sup>3</sup> Suicidal ideation is defined as "thoughts about self-harm with deliberate consideration or planning of possible techniques of causing one's own death", while suicide is "the act of intentionally causing one's own death" and the suicide attempt is "an attempt to end one's own life, which may lead to one's death".<sup>4</sup> Suicide is a global problem, with approximately 800,000 individuals dying from suicide every year, meaning that someone intentionally takes his/her own life every 40 seconds. Majority of completed suicides, approximately 78%, occur in low and middle-income nations.<sup>5</sup>

The lifetime prevalence of suicidal ideation has been reported to be 25% in PWE. Additionally, the risk of suicide is two to three times higher in epileptic patients without comorbid psychiatric disorders, and this risk increases by 12 to 32-fold in the presence of various

psychiatric disorders. Risk factors for suicide are multifactorial and include socio-demographic factors, genetics, age, gender, and psychiatric comorbidities. Suicide behavior is more common in monozygotic than dizygotic twins. Epileptic patients aged 30-64 years have been found to have a four-fold higher risk of completed suicide compared to those aged 10-29 years, while in terms of gender, men are twice as likely to commit suicide compared to women.<sup>6</sup>

Literature shows that the lifetime prevalence of depression in individuals with epilepsy is as high as 55%. Depression has a negative impact on the quality of life in people with epilepsy, and it is well documented that individuals with epilepsy and depression have a higher prevalence of suicide compared to the general population.<sup>7</sup> Certain antiseizure medications possess negative psychotropic effects, which may result in the onset of psychiatric symptoms such as suicidal ideation. However, these adverse effects are more frequently observed in patients with a history of psychiatric illness and/or a family history of mental health disorders.<sup>8</sup>

There are few researches available that show the definitive association of suicide and epilepsy in different cultures and socioeconomic settings. Also, there is limited data available regarding the prevalence of suicidal ideation and behavior in epileptic patients in Pakistan. We conducted this study to find out the suicidal risk in PWE in a tertiary care hospital of Pakistan. The study will help reduce mortality in patients with epilepsy, as early detection of suicidal intent can prevent it from progressing to suicidal attempts and completed suicide.

Sharif Medical & Dental College, Sharif Medical City,  
Sharif Medical City Road, Off Raiwind Road, Jati Umra,  
Lahore 54000, Pakistan.

Correspondence: Dr. Ayaz Muhammad Khan  
Head & Assistant Professor Department of Psychiatry  
Sharif Medical & Dental College, Lahore  
E-mail: dr.ayazmkhan@gmail.com

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## METHODOLOGY

This cross-sectional study was conducted at the Department of Psychiatry, Department of Neurology, and Department of Medical and Surgical Emergency, Services Hospital, Lahore from January to July 2022. Total 226 patients fulfilling inclusion criteria were enrolled by convenient sampling technique after informed consent. The inclusion criteria were patients with epilepsy of both male and female gender, aged between 15-45 years.

The exclusion criteria were patients with a history of mood disorder, psychotic disorder, anxiety disorders, and personality disorder prior to the onset of epilepsy, pregnant females (assessed on history), patient with a history of head trauma, and patients with a history of drug addiction. The calculated sample size was approximately 226 cases with a 6% margin of error, a 95% confidence level taking an expected percentage of suicidal risk among epileptic patients as 30%.

Epilepsy was defined as recurrent unprovoked seizures involving contractions of one or more parts of the body and at least two or more seizures, more than 24 hours apart.<sup>9</sup> Suicidal intent was assessed by Beck's suicidal intent scale developed by Aaron Beck. Beck's suicide intent scale contains 20 items each scoring from 1 to 3 points. The range was 15-45 and a score >15 was labeled as suicidal intent.<sup>10</sup>

## STATISTICAL ANALYSIS

Data was entered and analyzed with Statistical Package for the Social Sciences (SPSS) version 25.0. The quantitative data like age and Beck's score were presented as mean and standard deviation. The qualitative data like suicidal intent, gender, education,

and marital status were presented as frequency distribution. Data were stratified for age, gender, education, socioeconomic and marital status. Post stratification Chi-square test was used taking p-value  $\leq 0.05$  as significant.

## RESULTS

A total of 226 cases fulfilling the selection criteria were enrolled to determine the suicidal intent in patients with epilepsy. The mean age was calculated as  $36.97 \pm 5.98$  years. Age distribution showed that 43(19.03%) were between 15-30 years of age, whereas 183(80.97%) were between 31-45 years of age. Gender distribution showed that 125(55.31%) were males whereas, 101(44.69%) were females. Educational status showed that 61(27%) were illiterate, 103(45.57%) did middle, and 62(27.43%) did matric. Marital status showed that 145(64.16%) were married, 54(23.89%) were unmarried, and 27(11.95%) were divorced. Socio-economic status showed that 139(61.5%) had low socioeconomic status and 87(38.5%) had middle socioeconomic status.

Mean Beck's score was  $16.86 \pm 4.6$ . The frequency of suicidal intent in patients with epilepsy was recorded in 54(23.89%) patients (Table 1). The data was stratified for age, gender, education, socioeconomic status, and marital status. No statistically significant correlation was found between suicidal intent and age, gender, educational status, socioeconomic status, and marital status (Table 2).

## DISCUSSION

Patients with epilepsy are more likely to suffer from psychiatric illnesses than the general population. The nature of the connection between epilepsy and mental

**Table 1: Frequency of Suicidal Intent in Patients with Epilepsy**

Suicidal Intent	Frequency & Percentage
Yes	54(23.89%)
No	172(76.11%)
<b>Total</b>	<b>226(100%)</b>

**Table 2: Stratification of Suicidal Intent with Demographic Factors**

Study Variables		Suicidal Intent		p-value
		Yes	No	
Age (Years)	15-30	10(4.43%)	33(14.6%)	0.92
	31-45	44(19.47%)	139(61.5%)	
Gender	Male	29(12.83%)	96(42.48%)	0.79
	Female	25(11.06%)	76(33.63%)	
Educational Status	Illiterate	14(6.2%)	47(20.8%)	0.84
	Middle	23(10.17%)	80(35.4%)	0.61
	Matric	17(7.52%)	45(19.91%)	0.44
Marital Status	Married	37(16.37%)	108(47.79%)	0.44
	Unmarried	11(4.86%)	43(19.03%)	0.49
	Divorced	6(2.65%)	21(9.3%)	0.83
Socioeconomic Status	Low	36(15.93%)	103(45.57%)	0.38
	Medium	18(7.97%)	69(30.53%)	

comorbidities is not well known, despite the fact that studies have demonstrated a substantial correlation between the two conditions. Due to this, psychiatric problems are frequently misdiagnosed and undertreated in PWE, resulting in an additional decline in the quality of life of patients.<sup>11</sup>

In this study, out of 226 cases, 43(19.03%) were between 15-30 years of age, whereas 183(80.97%) were between 31-45 years of age, and mean age was  $36.97 \pm 5.98$  years. Among patients, 125(55.31%) were males, whereas 101(44.69%) were females. The frequency of suicidal intent in patients with epilepsy was recorded in 54(23.89%). The findings of our study are in agreement with previous studies which reported that the prevalence of suicidal behavior in people with epilepsy ranges from 23.89-30%.<sup>12</sup>

Ding and colleagues looked at the relationship between the risk of suicidal behavior in people who have epilepsy and clinical characteristics that can increase or have been reported to raise the risk of suicidal behavior. There was a nine-fold increase in the risk of suicide associated with mental illness, and the use of antipsychotic medicines was associated with a ten-fold increase in relative risk. When compared with starting after 29 years of age, those having epilepsy before the age of 18 years were associated with a relative risk of suicide that was approximately 16 times higher.<sup>13</sup>

Another study reported that the risk of suicide increased with high seizure frequency and antiepileptic drug polytherapy. This was despite the fact that both of these factors increased the frequency of seizures. Epilepsy was seen to be associated with high rates of premature death.<sup>14</sup>

A recent systematic review concluded that the link between epilepsy and suicidality is complex, and epilepsy impacts various aspects of life, such as relationships with family and friends, employment, school, and leisure activities, leading to social and economic consequences. Furthermore, it has been reported that an increased risk of suicide in people with epilepsy is associated with various factors such as psychiatric risk factors, exposure to certain antiseizure medications, etc.<sup>15</sup>

People younger than 55 years old account for about half of all epilepsy-related fatalities, and the time period immediately after the initial diagnosis of epilepsy appears to be the most deadly of all. People who have epilepsy have a greater percentage of suicidal thoughts and suicide risk compared to the general population. Additionally, suicide is related with up to 5% of all deaths that are caused by epilepsy. Epilepsy patients who have passed away as a consequence of a suicide attempt can be the subject of case-control studies, which can provide significant information regarding risk factors.<sup>16</sup>

Harnod et al. evaluated the risk of attempted &

completed suicide in epilepsy patients in Taiwan. They concluded that Epilepsy is one of the independent predisposing factor for suicide attempt and therefore clinicians should also focus on the aspect of suicide in epileptic patients while treating them.<sup>17</sup>

Studies have shown that people with epilepsy have a higher risk of suicidality than the general population, and identified various risk factors for suicide in people with epilepsy, including a history of mental illness especially depression, use of antipsychotic medications, early onset of epilepsy, high seizure frequency, and use of multiple anti-epileptic drugs.

## CONCLUSION

A high proportion (23.89%) of patients with epilepsy had suicidal intent. The study also found that the majority of patients were between the ages of 31-45 years and there were a slightly higher proportion of males than females.

These findings emphasize the importance of identifying and treating mental illness in individuals with epilepsy to reduce the risk of suicidal behavior.

## LIMITATIONS & RECOMMENDATIONS

There are some limitations to the study that need to be acknowledged. Firstly, the study was conducted at a single center and may not be representative of the entire Asian population of patients with epilepsy. Secondly, the study relied on self-reported data, which may be subject to bias and may not accurately reflect the true prevalence of suicidal intent in patients with epilepsy. Additionally, the study did not take into account other factors that may contribute to suicidal intent in patients with epilepsy, such as the severity of their epilepsy, comorbid psychiatric disorders, and social support.

Therefore, while the study provides valuable insights into the frequency of suicidal intent in patients with epilepsy, further research is needed to better understand the underlying factors contributing to suicidal ideation in these patients.

It is recommended to screen all epilepsy patients for early diagnosis and treatment. This research has paved the way to carry out an epidemiological study to classify the etiology and endemic problems of different regions of Pakistan.

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# Fasting Lipid Profile in Pregnant Patients as a Predictor of Gestational Diabetes Mellitus

Anees Fatima, Nishat Akram

## ABSTRACT

**Objective:** To predict the risk of developing gestational diabetes mellitus (GDM) in early pregnancy by comparing the fasting lipid profile in pregnant patients with or without gestational diabetes during the second trimester of pregnancy.

**Methodology:** It was a cross-sectional study that was conducted in the Department of Gynecology & Obstetrics, Sharif Medical City Hospital, Lahore for six months from January to June 2021. A total of 385 patients were enrolled in the study. Out of 385 patients, 210(54.5%) women were with gestational diabetes mellitus (group A) and 175(45.5%) were without GDM (group B). A fasting lipid profile was performed by taking blood samples of patients. All samples were assessed for levels of total cholesterol (TC), triglyceride (TG) concentrations, low-density lipoproteins (LDL), and high-density lipoproteins (HDL).

**Results:** The mean age of the patients was 27.5±4.2 (group A) and 26.7±4.2 years (group B), respectively. The body mass index (BMI) was 29.4±3.6 in group A versus 25±3.5 in group B. The mean lipid profile in group A versus group B was; TC (177.1±21.3 versus 136.5±29.6, p <0.001), TG (186.3±23.9 versus 131.1±30.4, p <0.001), LDL (140.3±19 versus 96.3±23.1, p <0.001), and HDL (40.9±4.6 versus 44.3±23.9, p=0.044).

**Conclusion:** Hyperlipidemia is associated with GDM and identifies the need to evaluate maternal lipid profile in women with gestational diabetes mellitus during the antenatal period.

**Keywords:** *Gestational diabetes. Cholesterol. Triglyceride.*

## INTRODUCTION

Gestational diabetes mellitus is the most common medical disorder which affects 14% of pregnancies worldwide. An epidemiological transition towards sedentary lifestyle changes due to urbanization predisposes females not only to an increased prevalence of type 2 diabetes mellitus but also to GDM. Gestational diabetes mellitus is significantly prevalent in the South Asian region, however, in Pakistan, it mostly remains unnoticed. According to some studies conducted at small scale, the prevalence in Pakistan ranges from 3.3-8%.<sup>1</sup> Gestational diabetes mellitus is not only associated with adverse fetomaternal outcomes but also with long-term risk of type 2 diabetes mellitus, hyperlipidemia particularly obesity-associated GDM, cardiovascular disease (CVD) in the mother, and also diabetes mellitus and CVD in the child as well.<sup>2</sup> The major factors predisposing to this disorder include advanced maternal age, obesity, family history of diabetes, westernized diet, ethnicity, personal history of GDM, and diabetes mellitus. The major pathological dysfunction of this disorder is pancreatic  $\beta$ -cell disorder and or resistance to insulin which is directly or indirectly linked to predisposing factors as well.<sup>2</sup>

Physiologically, in normal pregnancy insulin resistance and lipid metabolism is altered, beginning at 24 to 28 weeks of gestation and this progresses in all trimesters. The major change observed is in triglycerides and cholesterol levels. Maternal physiological hypercholesterolemia is the mother's adaptive response to meet the growing cholesterol demand of the fetus during pregnancy. Gestational diabetes mellitus is also associated with both maternal and fetal adverse outcomes. The rate of pregnancy-induced hypertension, cesarean delivery, and macrosomia is high in patients with GDM.<sup>3</sup>

Dyslipidemia is a medical disorder which is characterized by high levels of low-density lipoproteins and triglycerides and low levels of high-density lipoproteins.<sup>4</sup> Cholesterol and low-density lipoprotein have a positive correlation with other hormones like thyroid stimulating hormone.<sup>5</sup> Serum lipid levels have also shown some correlation with raised blood pressure, especially in nulliparous women. In these women, lipid levels were found to be raised in patients with preeclampsia and eclampsia. Neonatal body weight is also positively correlated with maternal triglycerides level. Both fetal lipids and fetal growth are well predicted by maternal lipids in pregnancies with controlled diabetes.<sup>6</sup>

The rationale of our study was to compare the fasting mean lipid profile levels in pregnant females during their second trimester of pregnancy presenting with or without gestational diabetes. In routine, the lipid profile of females with hypertensive disorders is checked and cured if found deranged. But in pregnant females with GDM, work on lipid profile is scarcely studied. There is not much local evidence available in this regard.

Sharif Medical & Dental College, Sharif Medical City,  
Sharif Medical City Road, Off Raiwind Road, Jati Umra,  
Lahore 54000, Pakistan.

Correspondence: Dr. Anees Fatima  
Assistant Professor Department of Gynaecology & Obstetrics  
Sharif Medical & Dental College, Lahore  
E-mail: anees.fatima.dr@gmail.com

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Furthermore, the literature review highlights the ambiguity in understanding the relationship between the lipid profile of females with or without GDM. So, this study was conducted to confirm whether the lipid profile was deranged with GDM in patients of Pakistan. This study will help in early screening of lipid profile of GDM patients for their early detection, prevention, and timely management to prevent a bad obstetrical outcome.

### METHODOLOGY

It was a cross-sectional study conducted at Sharif Medical City Hospital (SMCH), Lahore in the Department of Gynaecology & Obstetrics for six months from January to June 2021. Ethical approval was taken from the ethical committee. The sampling technique was non-probability consecutive sampling. A sample size of 385 cases was calculated by the WHO sample size calculator.

All females in the Outpatient Department (OPD) of SMCH between 18-40 years of age with parity of <5 and 24 to 32 weeks of gestation were included in this study. Pregnant females with hypertension [blood pressure (BP)  $\geq 140/90$  mmHg], diabetes [glycosylated hemoglobin (HbA1c)  $>6.5$ ], patients on anti-hyperglycemic medication, obese females (BMI  $>35$  kg/m<sup>2</sup>), and females on lipid-lowering drugs or using statins before conception (on medical record) were excluded. Informed consent was taken from all patients. The demographic profile i.e., name, maternal age, and gestational age were noted. An oral glucose tolerance test (75 g OGTT) was done to diagnose gestational diabetes. It was diagnosed on the basis of a fasting plasma glucose level  $\geq 5.6$  mmol/L or 2-hour plasma glucose level of  $\geq 7.8$  mmol/L.<sup>7</sup> A venous blood sample was obtained under aseptic measures for a fasting lipid profile. All samples were sent to the laboratory for assessment of fasting lipid profile. Levels of total cholesterol, triglyceride concentrations,

low-density lipoproteins, and high-density lipoproteins were noted. All the information was noted on a proforma. Reference range for total cholesterol was  $<200$  mg/dL, triglycerides  $<150$  mg/dL, LDL  $<130$  mg/dL, and HDL between 35-55 mg/dL.<sup>8</sup>

### STATISTICAL ANALYSIS

Statistical Package for the Social Sciences (SPSS) version 21 was used for data analysis. Quantitative variables like levels of TC, TG, LDL, and HDL along with maternal age and gestational age were presented as means and standard deviations (SD). Frequency and percentages were calculated for patients with GDM. The mean TC, TG, LDL, and HDL of both groups were compared by using an independent t-test. A p-value  $\leq 0.05$  was considered as significant. Data was stratified on the basis of age, gestational age, BMI, and parity.

### RESULTS

Out of these 385 patients, 210(54.5%) were with GDM (group A) and 175(45.5%) were without GDM (group B). The mean age of the subjects in group A was  $27.5 \pm 4.2$  years and  $26.7 \pm 4.2$  years in group B. The mean gestational age was  $27.8 \pm 2.2$  weeks in group A and  $27.6 \pm 2.1$  weeks in group B, with a mean BMI of  $29.4 \pm 3.6$  in group A and  $25 \pm 3.5$  in group B.

Table 1 shows that group A patients had significantly elevated levels of TC, TG, and LDL as compared to group B patients. However, HDL levels were found to be lower in group A as compared to group B.

Stratification was done with regard to age, gestational age, BMI, and parity for TC, TG, LDL, and HDL. In group A, TC, TG, and LDL levels were significantly high as compared to patients in group B, when the data was stratified on the basis of gestational age (24-28 weeks & 29-32 weeks), age of the enrolled patients (18-30 years & 31-40 years), BMI (BMI  $<25$  kg/m<sup>2</sup> & BMI  $\geq 25$  kg/m<sup>2</sup>), and parity of the patient (primigravida & multigravida). However, HDL levels were found to be lower in group A (Table 2).

**Table 1: Comparison of Lipid Profile in Pregnant Patients with and without Gestational Diabetes Mellitus**

Lipid Profile	Groups		t-value	p-value
	Group A with GDM (Mean $\pm$ SD)	Group B without GDM (Mean $\pm$ SD)		
Total Cholesterol (mg/dL)	177.1 $\pm$ 21.3	136.5 $\pm$ 29.6	15.572	<0.001*
Triglycerides (mg/dL)	186.3 $\pm$ 23.9	131.1 $\pm$ 30.4	19.882	<0.001*
Low-Density Lipoprotein (mg/dL)	140.3 $\pm$ 19	96.3 $\pm$ 23.1	20.457	<0.001*
High-Density Lipoprotein (mg/dL)	40.9 $\pm$ 4.6	44.3 $\pm$ 23.9	-2.019	0.044*

\*Significant p-value

**Table 2: Stratification for Age, Gestational Age, BMI, and Parity with regard to TC, TG, LDL, and HDL**

Variables		Groups	Mean±SD	p-value
Age (Years)	18-30	TC (mg/dL)	Group A 176.5±21	<0.001*
			Group B 135.1±28.8	
		TG (mg/dL)	Group A 185.3±24.1	<0.001*
			Group B 130.9±30.4	
		LDL (mg/dL)	Group A 142.5±19.1	<0.001*
		Group B 96±22.8		
	HDL (mg/dL)	Group A 41.1±4.5	0.067	
		Group B 44.8±25.6		
	31-40	TC (mg/dL)	Group A 179.3±22.3	<0.001*
			Group B 146.7±33.7	
TG (mg/dL)		Group A 190.3±22.9	<0.001*	
		Group B 133±30.9		
LDL (mg/dL)		Group A 131.8±16.1	<0.001*	
	Group B 98.7±25.4			
HDL (mg/dL)	Group A 40.4±4.9	0.472		
	Group B 41.3±4			
Gestational Age (Weeks)	24-28	TC (mg/dL)	Group A 175.6±20.8	<0.001*
			Group B 137.6±30.2	
		TG (mg/dL)	Group A 184.9±23.4	<0.001*
			Group B 130.1±31.5	
		LDL (mg/dL)	Group A 142.1±18.1	<0.001*
		Group B 96.4±23.9		
	HDL (mg/dL)	Group A 41.2±4.9	0.101	
		Group B 45.4±29.2		
	29-32	TC (mg/dL)	Group A 179.9±21.9	<0.001*
			Group B 134.4±28.6	
TG (mg/dL)		Group A 189±24.7	<0.001*	
		Group B 133.2±28.4		
LDL (mg/dL)		Group A 136.9±20.1	<0.001*	
	Group B 96.2±21.7			
HDL (mg/dL)	Group A 40.4±4	0.013*		
	Group B 42.2±4.3			
BMI (kg/m <sup>2</sup> )	<25	TC (mg/dL)	Group A 170.8±22.8	<0.001*
			Group B 131.8±27.7	
		TG (mg/dL)	Group A 179.9±25.9	<0.001*
			Group B 127.8±27.3	
		LDL (mg/dL)	Group A 140.6±13.9	<0.001*
		Group B 95.7±21.7		
	HDL (mg/dL)	Group A 40.3±4.2	0.421	
		Group B 45±30.5		
	≥25	TC (mg/dL)	Group A 178±20.9	<0.001*
			Group B 143.7±31.2	
TG (mg/dL)		Group A 187.3±23.5	<0.001*	
		Group B 136.2±34.1		
LDL (mg/dL)		Group A 140.2±19.6	<0.001*	
	Group B 97.3±25.1			
HDL (mg/dL)	Group A 41.0±4.7	0.002*		
	Group B 43.3±6.4			
Primigravida	TC (mg/dL)	Group A 178.2±19	<0.001*	
		Group B 143.7±29.5		
	TG (mg/dL)	Group A 188.2±27.2	<0.001*	
		Group B 131.9±30.1		
	LDL (mg/dL)	Group A 144.5±19.5	<0.001*	
		Group B 98.5±22.6		
HDL (mg/dL)	Group A 41.7±3.8	0.179		
	Group B 42.8±3.8			
Multigravida	TC (mg/dL)	Group A 176.8±21.9	<0.001*	
		Group B 134.4±29.5		
	TG (mg/dL)	Group A 185.8±23	<0.001*	
		Group B 130.9±30.6		
	LDL (mg/dL)	Group A 139±18.7	<0.001*	
		Group B 95.7±23.3		
HDL (mg/dL)	Group A 40.7±4.8	0.061		
	Group B 44.8±27.1			

\*Significant p-value

## DISCUSSION

In pregnant patients, metabolic changes occur throughout the pregnancy. In the first and second trimesters of pregnancy, lipogenesis occurs which leads to fat deposition, and during the last part of pregnancy, lipolysis is increased which leads to a drop in maternal fat stores.<sup>9</sup>

Even though the cause and aetiology of GDM is not yet clear, it somehow has similar pathophysiology as of type 2 diabetes. Because of the failure of pancreatic  $\beta$ -cells, both GDM and type 2 diabetes exhibit insulin resistance and deficient insulin production. Hyperlipidemia is associated with pregnancy-related complications in mothers and babies of these mothers showed high risk of atherosclerosis.<sup>10</sup> Another study indicated that the risk of GDM & hyperlipidemia was positively associated with maternal central obesity.<sup>11</sup>

In a study by Zhai et al., the association of hyperlipidemia & type 2 DM was observed. They concluded that glycemic control in type 2 diabetics was lower in patients with hyperlipidemia.<sup>12</sup>

Our study shows that in early pregnancy females with GDM have significantly elevated levels of TC, TG, and LDL, however, HDL levels were found to be lower as compared to women without GDM. After adjusting for potential confounders, we find that lean or obese women with higher TG concentrations are at an increased risk of developing GDM while lean women with high HDL were protected. Regarding total cholesterol and LDL levels, the results of our study are not consistent with Farsangi et al., who showed no change in the levels of TC and LDL in pregnant patients with GDM.<sup>13</sup>

Similar to our study, Asif et al. found that TC levels are higher in patients with GDM as compared to the controls.<sup>14</sup> Some case-control studies report an association between increased risk of GDM with higher TG concentration.<sup>15</sup> One of the South Asian studies also showed the altered selected lipid profile in patients with GDM. The study showed higher levels of triglycerides and lower levels of HDL in patients with GDM as compared to the control group.<sup>16</sup> However, Layton et al., exhibited no positive correlation between GDM and high lipid levels in pregnant patients.<sup>17</sup>

The association of metformin and insulin treatment on maternal serum lipid levels in patients with GDM was observed in another study. Their study showed that the levels of TG are higher in patients who were treated with metformin and insulin, and the increase was more in metformin-treated patients. More than 50% of patients were given metformin and the rise of total triglycerides was found to be one mmol/lit from the baseline value. The rise of 0.6 mmol/lit of total triglycerides from the baseline value was observed in patients who were given insulin.<sup>18</sup>

Closer investigations reveal that many reasons might

have contributed to these conflicting results including but not limited to different study designs, the basis of sampling and final sample size, differences in population features, cofounders, and different diagnostic criteria for GDM. A recent study by Wang et al. found that the lipid profile was dramatically different between patients with gestational diabetes mellitus and the control group. They found that the maternal TG, TC, LDL concentration, and the ratio of TG/LDL have been increased progressively throughout the pregnancy, however, HDL concentration showed a slight decrease in the third trimester. The study did not find any significant difference between the concentration of TC and LDL in all three trimesters in the GDM group and the control group.<sup>19</sup>

A study in Iran observed a relationship between dyslipidemia, gestational diabetes mellitus, and other maternal and neonatal outcomes. A significant relationship was found between hyperlipidemia and gestational diabetes mellitus, preeclampsia, cholestasis of pregnancy, and macrosomia. According to this study, dyslipidemia increases the chances of gestational diabetes mellitus by 4.1 folds.<sup>20</sup> The relationship between dyslipidemia and gestational diabetes was also studied in another research which showed that a lower level of plasma HDL was the most current lipid disorder followed by a high level of plasma TG in patients with gestational diabetes. Plasma HDL levels were found to be significantly decreased in patients who used insulin for the control of blood sugar as compared to the patients who did not use insulin.<sup>21</sup>

## CONCLUSION

Gestational diabetes mellitus is evidently associated with hyperlipidemia as evidenced by the significantly elevated total cholesterol, LDL, and triglyceride concentrations in pregnant patients with GDM. In early pregnancy, females with GDM have significantly elevated levels of TC, TG, and LDL. Therefore, fasting blood lipids should be considered in women during pregnancy for better antenatal care.

## LIMITATIONS & RECOMMENDATIONS

This study was conducted at a single hospital therefore, the diversity of the population lacks. A multi-centered study having adequate diversity in population characteristics can give more comprehensive results.

It is recommended that a fasting lipid profile should be done in the first trimester as it can help predict the risk of developing GDM at an early pregnancy stage.

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# Antibiotic-Impregnated Cement Coated Ilizarov Rod for Infected Non-Union of Femur

Muhammad Zafar Iqbal Shahid, Sohaib Inaam-Ullah, Naveed Ali Shair, Tahir Mehmood, Muhammad Iqbal, Mubashir Farhan

## ABSTRACT

**Objective:** To determine the effectiveness of antibiotic-impregnated cement coated Ilizarov rod for infected non-union of the femur.

**Methodology:** It was a prospective observational study conducted at the Department of Orthopedic Surgery Services Hospital, Lahore from December 2018 to December 2020. After approval from the Hospital Ethical Review Board, the study was conducted on 50 patients with infected non-union of the femur or established osteomyelitis of the femur after intramedullary (IM) nailing. Each patient underwent an X-ray of the shaft of the femur with hip and knee joint, both anterior-posterior (AP) & lateral views, complete blood count (CBC) with erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) as baseline investigations. The intramedullary nail was removed and irrigation with resident assessment instrument (RAI) system was done with 7-8 liters of normal saline. An Ilizarov rod of size 5 mm width and length equal to that of IM nail already introduced, was used. It was impregnated with bone cement coated with 2 g of vancomycin and 2 g of gentamicin.

**Results:** A total of 50 patients were enrolled in our study with a mean age of  $48.32 \pm 12.59$  years and a range between 40-70 years. Thirty eight (76%) were males and 12(24%) were females. In the initial culture, the *Staphylococcus aureus* was isolated in 30(60%) patients; *Escherichia coli* (*E. coli*) was present in 8(16%) patients, *Pseudomonas species* in 4(8%) patients, mixed infection in 4(8%), while in 4(8%) patients culture was negative. Vancomycin and gentamicin 2 g each were used with bone cement to impregnate the Ilizarov rods in all the cases. Thirty eight (76%) patients had discharging sinus at the time of presentation. In all these 38 patients, CRP & CBC with ESR returned to normal after 4 to 6 months. Thirty eight out of 50 patients showed signs of union radiologically after 5-6 months.

**Conclusion:** Antibiotic-impregnated cement rods are very effective in the treatment of infected non-union of the femur. It is a unique implant to control the infected non-union and provides stability for fracture union.

**Keywords:** Femoral fractures. Bone cement. Intramedullary nailing. Antibiotics.

## INTRODUCTION

Road traffic accidents (RTAs) are one of the most leading causes of bone fractures. As a result of an increase in the number of road traffic collisions, long bone fractures are common resulting in significant damage to soft tissue and bone, exposing the patient to risk of infection. The most common fracture encountered after RTA is that of femur bone.<sup>1</sup> Infections as a result of fractures can be highly debilitating and can cause complications which may ultimately lead to permanent functional loss or amputation.<sup>2</sup>

Intramedullary nailing is considered as the gold standard for the fracture of the shaft of the femur. Intramedullary nailing can be closed or open due to its biological and mechanical behavior. Delayed or inadequate treatment of infection allows the bacteria to spread resulting in diffuse infection. Systemic antibiotics cannot reach the interface of the implant because of the biofilm formed by bacteria.<sup>3</sup> After debridement, bacterial residues may remain in the

medullary canal or in the surrounding tissue resulting in the formation of biofilm which matures after 72 hours. The antibiotic resistance is further aggravated by osteonecrosis and poor blood supply. Various factors like bone loss, soft tissue loss, open fractures, and chronic osteomyelitis are reasonable for infected non-union. The benefits of antibiotics loaded materials are high local antibiotics concentration and elution, accurate positioning, low side effects, bone regeneration, and infection eradication because of the local antibiotics delivery system in loading doses.<sup>4</sup> The most common bacteria isolated from the infected fracture site culture is *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, and in rare cases there is mixed infection. Depending upon the progress of fracture union, the existing status of the bone, and the extent of infection, different treatment strategies are available.<sup>5</sup>

Infection is classified into 3 stages. Stage 1 is bacterial cellulitis and it occurs after 2-6 weeks. There is no need for wound exploration and surgical debridement in this stage. It usually resolves with a high dose of intravenous (IV) antibiotics. The second stage occurs 2-9 months after the surgery. There is wound discharge or wound necrosis with delayed wound healing at the operative site. If the implant is providing stability, there is no need for its removal. If it is unstable and bone infection is present, implant removal, wound debridement, stabilization of the fracture, and IV antibiotics for suppression of infection are required

Sharif Medical & Dental College, Sharif Medical City,  
Sharif Medical City Road, Off Raiwind Road, Jati Umra,  
Lahore 54000, Pakistan.

Correspondence: Dr Muhammad Zafar Iqbal Shahid  
Assistant Professor Department of Orthopedics  
Ameer Ud Din Medical College, Lahore  
Email: dr.zafar2014@gmail.com

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until the union is achieved. These infections can be treated successfully with antibiotic nails. In 3<sup>rd</sup> stage, established osteomyelitis in the medullary canal occurs after 9 months of initial treatment. In this stage, thorough wound debridement, removal of all dead and devitalized tissue with stabilization of fracture, and restoration of bone loss is required. In these patients, the implant is removed and Ilizarov is applied to stabilize the fracture especially when large bone defects are present.<sup>6</sup>

Infected non-unions are difficult to treat, antibiotic cement-coated rods have been shown to provide stability in non-union of bones. Antibiotic-impregnated polymethylmethacrylate (PMMA) nails provide local antibiotics, exhibit excellent osteogenesis, and have drug loading properties. These nails provide accurate positioning with less side effects and a longer duration of treatment.<sup>7</sup>

The antibiotics-impregnated PMMA rods can also be made from Ilizarov threaded rods, Ilizarov pins, intramedullary guide wires of 3 mm diameter, ball-tipped guide wires, Steinmann pins, Kuntscher nail (K-nail), and Kirschner wires (K-wires).<sup>8</sup> Antibiotic nails can be impregnated either with PMMA or calcium sulphate. Nails can also be coated with antibiotics and growth factors. The antibiotics usually used are vancomycin 2 grams and gentamicin 2 grams. The size of cement coated rod should be less than 1 mm than the last reamer used for reaming.<sup>9</sup>

It is difficult to treat infected non-union of bone fractures. So, the present study was conducted to find out the effectiveness of antibiotics impregnated cement coated Ilizarov rod for infected non-union of the femur. It will help surgeons in treatment of infected non-union of the femur.

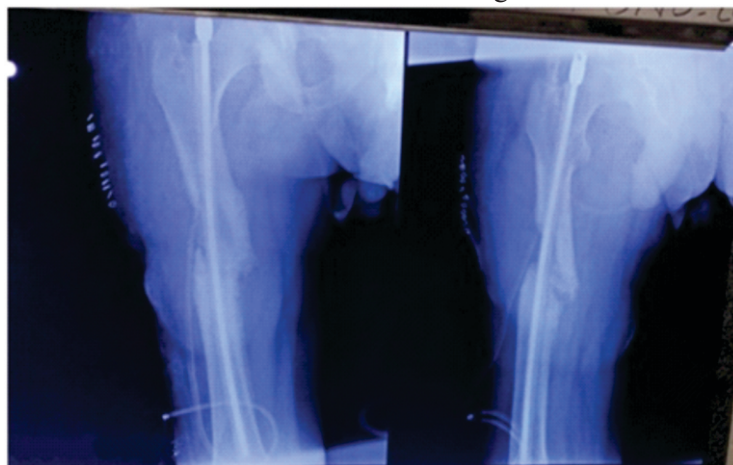
### METHODOLOGY

It was a prospective observational study conducted at the Department of Orthopedic Surgery Services

Hospital, Lahore from December 2018 to December 2020. After approval from the Hospital Ethical Review Board, the study was conducted on 50 patients with infected non-union of the femur or established osteomyelitis of the femur after intramedullary (IM) nailing. All patients presented with infected non-union of the femur, 4-7 months after the surgery and h clinical and radiological evidence of sepsis and infected non-union were included by consecutive sampling technique. A detailed history including comorbidities, number of surgical procedures to treat the infection, previous culture & sensitivity reports, antibiotics treatment, and previous hospital admission were taken from each patient under the study and noted on a proforma.

Written informed consent was taken from all the patients. Before the procedure, each patient underwent an x-ray of the shaft of the femur with hip and knee Joint, both AP & lateral views, CBC with ESR, and CRP as baseline investigations. The IM nail was removed, irrigation with the RAI system was done with 7-8 liters of normal saline. The medullary canal was reamed. The reamer head size used was decided preoperatively after information from the size of the implant already used for the initial surgical procedure. The size of the reamer head was 1 mm wide than the diameter of the antibiotic nail used (Figure 1). All sinuses and infected soft tissue were excised. Ilizarov rod of size 5 mm width and length equal to that of IM nail already introduced was used. It was impregnated with bone cement having high viscosity with 2 gram of vancomycin and 2 gram of gentamicin. All reaming material and necrotic material were sent for a culture sensitivity test. All patients under the study were given IV antibiotics according to the culture sensitivity report.

Serial biochemical analysis i.e. CBC with ESR and CRP were conducted to judge bone infection. X-rays were used to monitor the treatment efficacy i.e., radiological reunion at 6 weeks, 12 weeks & 6 months.



**Figure 1: Antibiotic-Impregnated Nail of Study Participant**

### STATISTICAL ANALYSIS

Data was analyzed using Statistical Package for the Social Sciences (SPSS) version 25. Mean±SD was calculated for age and frequency & percentage for the quantitative variables such as gender, organism isolate, and radiological reunion.

### RESULTS

Fifty patients were enrolled in our study with a mean age of 48.32±12.59 years and age range between 40-70 years. Out of 50 patients, 38(76%) were males and 12(24%) were females. All these patients were having stage 2 infection and were infected 4-7 months after the surgery. In the initial culture *Staphylococcus aureus* was isolated in 30(60%) patients, *E. coli* was present in

8(16%) patients, *Pseudomonas species* in 4(8%) patients, mixed infection in 4(8%) patients, and culture was negative in 4(8%) patients. Vancomycin 2 gram and gentamicin 2 gram were used with bone cement to impregnate the Ilizarov rods in all the cases. Thirty eight patients had discharging sinuses at the time of presentation. In all these 38(76%) patients CRP & CBC with ESR returned to normal after 4 to 6 months. Thirty eight (76%) patients showed signs of union radiologically after 5-6 months. In the remaining 12 patients CBC, ESR & CRP returned to normal after 7 months but did not show any sign of union. In these 12 patients, the cement-antibiotic coated nail was removed and they underwent revised IM nailing after the removal of Ilizarov rods (Table 1).

**Table 1: Study Variables of Patients Included in the Study**

Study Variables (n=50)		Frequency and Percentage
Age (Years)	Mean±SD	48.32±12.59
	40-55	38(76%)
	56-70	12(24%)
Gender	Male	38(76%)
	Female	12(24%)
Organism Isolate After Culture	<i>Staphylococcus aureus</i>	30(60%)
	<i>E. Coli</i>	8(16%)
	<i>Pseudomonas species</i>	4(8%)
	Mixed Infection	4(8%)
	No Isolate	4(8%)
Radiological Reunion After 6 Months	Yes	38(76%)
	No	12(24%)

### DISCUSSION

Fractures of the femur are a very common complication post RTAs which mostly lead to infected non-union of the femur. These can be difficult to treat with a high risk of reinfection and persistence of non-union.<sup>10</sup> Standard protocols on custom-made implants coating strategies are scarce and available studies are limited. Some studies use antibiotics containing cement rods as a staged procedure while others use it as a simultaneous control of infection for achieving fracture union.<sup>11</sup>

The most common bacteria isolated in our study was *Staphylococcus aureus*. A study by Rupp et al., also reported the most common organism in infected non-unions being *Staphylococcus aureus*.<sup>12</sup>

In our study, vancomycin and gentamicin were used as antibiotics with bone cement. These are heat stable, broad spectrum, and are hypoallergenic. These also have no deleterious effects on bone healing and are good choices regarding their elution properties from

bone cement.<sup>13</sup> A study by Shukla et al., also used vancomycin, gentamicin along with tobramycin and cefazolin as antibiotics of choice.<sup>14</sup>

In this study, we used antibiotic-impregnated bone cement Ilizarov rods. It provided not only stability but also eradicated the infection. We achieved the union in 38 patients with this nail, while 12 patients had non-union. In twelve patients, the implant was removed and intramedullary interlocking nailing was done. Another study was conducted to observe the role of antibiotic cement-coated nailing in infected non-union fracture. It was concluded that antibiotic-coated nail has an advantage over external fixators and provides better patient compliance.<sup>15</sup> Another study was conducted to evaluate the role of antibiotic-impregnated rod in infected non-union of long bones. The study reported that this treatment modality cured infection in all 7(100%) patients and union was achieved in 5(71%) cases.<sup>16</sup> A study conducted in India pointed out that



antibiotic-impregnated nailing is a highly productive method in terms of finances and simplicity for the treatment of infected non-union of long bones.<sup>17</sup>

Koury et al. concluded that antibiotic-impregnated nails provide a useful & simple procedure for the treatment of bone sepsis. These techniques provide simultaneous stability, union, and control of infection. The use of threaded core provides a successful cement hold.<sup>3</sup> Another study was conducted on 21 patients with infected non-union fracture. They concluded that in infected non-union, both infection control and osseous union can be achieved in a significant number of patients with antibiotic-impregnated cement nails.<sup>18</sup> In 2019 Chavn et al. used antibiotic coated nails for patients with infected non-union fracture of the femur. They concluded that infection was controlled in 90% of the cases, while the union was achieved in 66% of the patients.<sup>4</sup> Pruthi et al. conducted a study on antibiotic-coated nails in infected non-union of long bones and they came to the conclusion that antibiotic coated nails not only provided mechanical stability but also delivered a high concentration of antibiotics for the control of infection.<sup>19</sup>

The management of postsurgical osteomyelitis and infected non-union involves a lot of factors and has several components.<sup>20</sup> The components include removal of the infected implant, thorough debridement of all devitalized tissue and bone, dead space management with local delivery of antibiotics for the control of infection, soft tissue coverage, and bone reconstruction.<sup>7,21</sup> Dar et al. conducted a study on antibiotic-impregnated cement-coated Ilizarov rods for the treatment of infected non-union of long bones. They showed that the implant is very effective in controlling the infection as well as fracture union, simultaneously.<sup>22</sup> In 2018, Cho et al. demonstrated that antibiotic-coated cement threaded hinged rod can be used as an effective intramedullary spacer and serves as a local source of antibiotic delivery, offers bone stability, and makes implant removal easier.<sup>8</sup> Antibiotic-coated nail is a simple, economical, less demanding, and effective procedure for treating the infection.<sup>20</sup> Patient compliance is good and it avoids the complication of an external fixator. Antibiotics used for nail coating should be broad-spectrum, hypoallergenic, and heat-stable.<sup>9</sup>

### CONCLUSION

Antibiotic-impregnated cement rod is very effective in the treatment of infected non-union of the femur. It is a unique implant to control the infected non-union and provides stability for fracture union.

### LIMITATIONS & RECOMMENDATIONS

The outcomes in our study were not compared with other surgical strategies for the management of infected

non-union. Although good results were achieved with this mode of treatment, still additional prospective studies with a large number of cases are recommended to confirm our findings.

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# Association of Severity of Coronary Artery Disease and HbA1c Levels in Patients with Acute Coronary Syndrome

Muhammad Umar Farooq, Iqbal Haider, Muhammad Mohsin, Khawar Naeem Satti, Sana Ahmed, Mueez Ehtizaz

## ABSTRACT

**Objective:** To determine the levels of glycosylated haemoglobin (HbA1c) among patients with acute coronary syndrome (ACS) and compare the severity of coronary artery disease (CAD) with glycosylated haemoglobin levels.

**Methodology:** It was a comparative cross-sectional study carried out in the Department of Cardiology, Rawalpindi Institute of Cardiology, Rawalpindi, from January to July 2020. After taking ethical approval and written informed consent, 100 patients with ACS were recruited by non-probability consecutive sampling. Glycosylated haemoglobin was measured using an immunoassay and patients were labeled as diabetic & non-diabetic. Coronary angiography was done and patients were categorized as having single vessel coronary artery disease (SVCAD), double vessel coronary artery disease (DVCAD) or triple vessel coronary artery disease (TVCAD), minor CAD or normal coronary arteries. The Statistical Package for the Social Sciences (SPSS) version 25 was used to analyze the data.

**Results:** Patients' mean HbA1c levels were  $7.52 \pm 2.69\%$ . Thirty seven patients were diabetic. When compared to non-diabetic patients, diabetic patients had significantly higher rates of TVCAD and DVCAD ( $p$ -value=0.00003). Single vessel disease and minor CAD were more frequent in non-diabetic patients. Single vessel disease was present in 5(13.5%) diabetic and 30(47.6%) non-diabetic patients. Minor CAD was found in 1(2.7%) diabetic and 8(12.7%) non-diabetic patients. This difference was statistically significant ( $p$ -value=0.001).

**Conclusion:** Diabetes mellitus significantly predicts the severity of coronary artery disease. The severity of CAD is greater in diabetic patients, with the majority of the patients presenting with TVCAD and DVCAD. In contrast, minor CAD or SVCAD is more common among non-diabetics.

**Keywords:** HbA1c. Coronary artery disease. Acute coronary syndrome.

## INTRODUCTION

Coronary artery disease is a significant contributor to mortality, morbidity, and financial burden globally. One hundred and ninety seven million cases of CAD were reported in 2019 leading to 17.8 million deaths across the world.<sup>1</sup> The mortality rate due to CAD rose by 21.1% in the last ten years.<sup>2</sup> The prevalence of CAD in Pakistan is reported to be 17%.<sup>3</sup> Diabetes mellitus (DM), the most prevalent chronic disease worldwide, is the most important predictor of CAD. The prevalence of DM is 451 million cases on the global scale and by 2045, it is anticipated to rise to 693 million. About 16.98% of Pakistanis had type 2 diabetes in 2017.<sup>4</sup> Even below the definition of overt diabetes, the risk of CAD increases with glucose intolerance. This is attributed to increased oxidative stress due to inflammation, increased glucose levels, and resistance to insulin in DM.<sup>5</sup> In diabetic patients, CAD is related to greater chances of major adverse cardiac events as compared to non-diabetic patients.<sup>6</sup> Glycosylated haemoglobin is a recognized indicator of long-term glucose levels in diabetic patients. A Sharif Medical & Dental College, Sharif Medical City, Sharif Medical City Road, Off Raiwind Road, Jati Umra, Lahore 54000, Pakistan.

Correspondence: Dr. Muhammad Umar Farooq  
Assistant Professor Department of Cardiology  
Rawalpindi Institute of Cardiology, Rawalpindi  
E-mail: hassan.elahi2009@gmail.com

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higher HbA1c level is linked to a higher risk of both microvascular and macrovascular complications. Studies have shown that good glycemic control (HbA1c <7%) results in lesser microvascular complications. Blood glucose levels correlate with CAD severity rather than random or fasting glucose levels.<sup>5</sup> Patients with elevated HbA1c levels are more likely to develop more severe CAD with multiple vessel disease.<sup>6</sup> Literature has reported that higher HbA1c is associated with increased stiffness & calcification in vessels and atherosclerosis. In patients with diabetes mellitus, it is an independent predictor of cardiovascular mortality and morbidity. It has been documented that a 1% increase in HbA1c results in a 30% rise in overall mortality and a 40% rise in cardiovascular mortality in diabetic patients. Patients with decreased HbA1c levels have fewer chances of developing macrovascular as well as microvascular complications.<sup>7</sup>

The present study aimed to establish the association between HbA1c level and the severity of CAD. The number of coronary arteries with significant CAD was used to determine the severity of CAD. Several studies have demonstrated an association between elevated levels of HbA1c and higher CAD severity, morbidity, and mortality but a few studies have also shown controversial results. This study will add useful information to the existing knowledge and aid in establishing a link between the severity of CAD and HbA1c levels in patients with acute coronary syndrome, particularly in our demographic region.

## METHODOLOGY

It was a comparative cross-sectional study carried out in the Department of Cardiology, Rawalpindi Institute of Cardiology, Rawalpindi in seven months from January to July 2020. The hospital ethics committee approved the study. One hundred patients were recruited in this study by non-probability convenient sampling after taking written informed consent. Patients of both genders presenting with ACS with ages ranging from 30-70 years were included. Patients with ACS had symptoms suggestive of CAD such as chest pain, palpitations, apprehension, shortness of breath, nausea, and sweating for >20 mins along with ischemic electrocardiogram changes and/or positive cardiac enzymes (troponin T and troponin I). The patients with ACS had either ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), or unstable angina. The study excluded patients with recent blood transfusion history, hemoglobinopathies, anemia, prior myocardial infarction, or coronary revascularization. Glycosylated haemoglobin was measured using an immunoassay. Coronary angiography was done during the hospital stay to define the severity of CAD. Patients were categorized as having SVCAD, DVCAD, TVCAD, minor CAD or normal coronary arteries based on the number of coronary arteries involved, and having significant CAD. Patient demographic details, history of risk factors of CAD like hypertension, smoking, dyslipidemia & body mass index (BMI), levels of HbA1c, and coronary angiography findings were collected on a predesigned proforma sheet.

Patients with HbA1c levels  $\geq 6.5\%$  were labeled as diabetics and those with HbA1c levels  $< 6.5\%$  were labeled as non-diabetics. A greater than 50% decrease in the luminal diameter of epicardial coronary arteries was considered to be significant CAD and less than 50% decrease was labeled as minor CAD.

## STATISTICAL ANALYSIS

Statistical Package for the Social Sciences (SPSS) version 25 was used to analyze the data. The mean and standard deviation (SD) for continuous variables including age, height, weight, and BMI were calculated using descriptive statistics. Frequency and percentage were calculated for categorical variables including gender, diabetes mellitus, hypertension, and smoking. The severity of CAD was calculated based on the number of coronary arteries having significant CAD on coronary angiogram. The association of severity of CAD was observed between the diabetic and non-diabetic patients by

Chi-square test. The association of the severity of CAD was seen with effect modifiers such as gender, body mass index, smoking, and hypertension by applying a poststratification Chi-square test. A p-value of  $\leq 0.05$  was taken significant.

## RESULTS

The age of the patients ranged from 30 to 70 years with a mean of  $52.14 \pm 10.76$  years. Distribution of patients according to age groups is shown in Figure 1. Out of 100 patients, 76(76%) were males and 24(24%) were females. Male to female ratio was 3.16:1. The mean BMI was  $26.27 \pm 2.57$  kg/m<sup>2</sup> with minimum and maximum BMI of 20 & 32 kg/m<sup>2</sup>, respectively. The mean ejection fraction (EF) of the patients was  $41.67 \pm 10.72\%$  with minimum and maximum EF of 20% & 80%, respectively. The patients' mean HbA1c value was  $7.52 \pm 2.69\%$ , while the lowest and highest values were 3.51% and 14.70%, respectively. Diabetes mellitus was found in 37(37%) patients and hypertension in 52(52%) patients. In our study, 47(47%) patients were smokers and 41(41%) patients had dyslipidemia. The family history of ACS was positive in 24(24%) patients.

Out of 100 patients, STEMI type of ACS was found in 79(79%) patients, NSTEMI was noted in 12(12%) patients, and unstable angina was found in 9(9%) patients. Thirty five percent of the patients had single vessel disease, 32(32%) patients had double vessel disease, and 21(21%) patients had triple vessel disease on angiography. Minor CAD was found in 9(9%) patients (Table 1).

In our study, in diabetic patients, TVCAD was found in 13(35.2%) patients, while in non-diabetic patients, TVCAD was found in 8(12.7%) patients. Double vessel disease was found in 17(45.9%) diabetic and 15(23.8%) non-diabetic patients. On the other hand, single vessel disease and minor CAD were more frequent in non-diabetic patients. Single vessel disease was present in 5(13.5%) diabetic and 30(47.6%) non-diabetic patients. Minor CAD was found in 1(2.7%) diabetic and 8(12.7%) non-diabetic patients. This difference was statistically significant (p-value=0.001).

With a significant p-value of 0.00004, the frequency of TVCAD and DVCAD was significantly greater in diabetic individuals (81.1%) compared to non-diabetic patients (36.5%). These results are shown in Table 2.

No significant difference existed in the frequency of TVCAD and DVCAD concerning gender, BMI, type of ACS, hypertension, and smoking (Table 3).



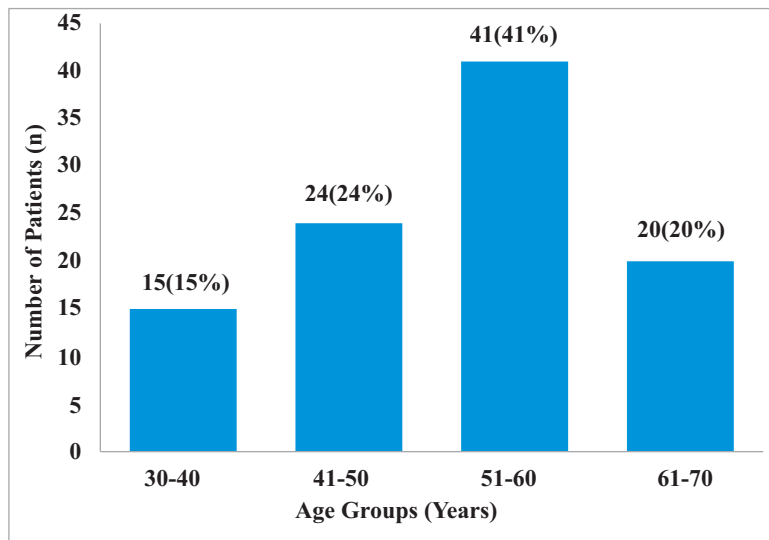


Figure 1: Distribution of Patients according to Age Groups

Table 1: Coronary Arteries Involvement in Diabetic and Non-Diabetic Patients

Angiographic Findings	Diabetic Patients	Non-Diabetic Patients	Total	p-value
TVCAD	13(35.2%)	8(12.7%)	21(21%)	0.0006*
DVCAD	17(45.9%)	15(23.8%)	32(32%)	
SVCAD	5(13.5%)	30(47.6%)	35(35%)	
Minor CAD	1(2.7%)	8(12.7%)	9(9%)	
Normal Coronaries	1(2.7%)	2(3.2%)	3(3%)	

\*Significant p-value

Table 2: Severity of CAD in Diabetic and Non-Diabetic Patients

Angiographic Findings	Diabetic Patients	Non-Diabetic Patients	Total	p-value
TVCAD & DVCAD	30(81.1%)	23(36.5%)	53	0.00003*
SVCAD & Minor CAD	6(16.2%)	38(60.3%)	44	

\*Significant p-value

Table 3: Association of Severity of CAD in Diabetic & Non-Diabetic Patients with various Parameters

Parameters		TVCAD & DVCAD		Total	p-value
		Diabetic	Non-Diabetic		
Gender	Male	21(39.6%)	20(37.7%)	41(77.3%)	0.14
	Female	9(17%)	3(5.7%)	12(22.7%)	
BMI (kg/m <sup>2</sup> )	<25	8(15.1%)	8(15.1%)	16(30.2%)	0.52
	≥25	22(41.5%)	15(28.3%)	37(69.8%)	
ACS Type	STEMI	24(45.3%)	19(35.8%)	43(81.1%)	0.52
	NSTEMI	5(9.4%)	2(3.8%)	7(13.2%)	
	Unstable Angina	1(1.9%)	2(3.8%)	3(5.7%)	
Hypertension	Hypertensive	21(39.6%)	16(30.2%)	37(69.8%)	0.97
	Normotensive	9(17%)	7(13.2%)	16(30.2%)	
Smoking	Smoker	9(17%)	12(22.6%)	21(39.6%)	0.101
	Non-smoker	21(39.6%)	11(20.8%)	32(60.4%)	

## DISCUSSION

Coronary artery disease is a leading factor in cardiovascular deaths worldwide. The predictors of coronary artery disease have been the subject of numerous investigations.<sup>8</sup> Diabetic people have 3-4 times increased risk of cardiovascular death.<sup>9</sup> In this study, we compared the severity of CAD in patients with and without diabetes.

In our study, patients had a mean age of 52.14±10.76 years, and 76% of them were males. In another study, patients had a mean age of 55.87±11.04 years and 67.08% were males.<sup>10</sup> In a study by Dar et al., patients had a mean age of 55.8±9 years with 85.1% males.<sup>11</sup> The mean EF of the patients was 41.67±10.72% in our study and 55.86±11.78% in another study conducted by Parkar et al.<sup>10</sup> Our results showed that 52% of the patients were hypertensive and 47% were smokers. Another study revealed that 41.42% of the patients had hypertension and 23.67% were smokers.<sup>10</sup> Thirty seven percent of patients had diabetes mellitus in our study. Similarly, another study reported that 41.8% of the patients were diabetic.<sup>11</sup> In contrast, 94.33% of the patients were diabetic in a study by Parkar et al.<sup>10</sup> The mean HbA1c was 7.52±2.69% in our study, 6.23±1.29% in a study by Basman et al., and 6.84±1.93% in another study.<sup>10,12</sup>

Out of 100 patients in our study, STEMI type of ACS was found in 79(79%) patients, NSTEMI was noted in 12(12%) patients, and unstable angina was found in 9(9%) patients. Another study also reported STEMI in majority of the patients (57.92%) followed by NSTEMI (30.33%) and unstable angina (9%).<sup>10</sup> Dar et al. reported STEMI in 80.77%, NSTEMI in 17.79%, and unstable angina in 1.44% of the patients.<sup>11</sup>

According to our findings, diabetic patients had significantly higher rates of TVCAD and DVCAD than non-diabetic patients (p-value=0.00003). In diabetic patients, TVCAD was found in 35.2% of patients while in non-diabetic patients, TVCAD was found in 12.7% of patients. Single vessel disease, however, was more prevalent in non-diabetics, and 13.5% of patients with diabetes and 47.6% of individuals without diabetes had single vascular disease. So, the severity of CAD and HbA1c levels were found to be positively correlated.

Another study reported that triple vessel disease was found in 45.4% of diabetic and 30.2% of non-diabetic patients with a significant p-value of 0.03. Single vessel disease was significantly more common in non-diabetics (11.6%) than diabetic patients (24.4%) (p-value=0.04).<sup>13</sup> Taimur et al. concluded that the chances of CAD were 6 times higher in diabetic patients than in non-diabetic patients. Thirty eight percent of diabetic patients and 22% of non-diabetic patients had triple vessel disease. Double vessel disease was seen in 26%

of diabetics and 20% of non-diabetics, whereas single vessel disease was present in 28% of diabetics and 18% of non-diabetics.<sup>14</sup> On the contrary, HbA1c was not linked to the severity of CAD as measured by the Gensini score, according to a study conducted by Wang et al.<sup>15</sup> Another study conducted in Karachi, Pakistan also reported that HbA1c levels did not significantly correlate with the severity of CAD.<sup>16</sup> In a study by Dar et al., there was a positive association between HbA1c levels and the Gensini score of severity of CAD was reported.<sup>11</sup> A positive correlation was also observed by Basman et al. and Yan et al.<sup>12,17</sup> Another study revealed that patients with diabetes mellitus have more severe CAD than patients without the disease.<sup>18</sup> A study was conducted in China to observe impact of diabetes mellitus and HbA1c level on outcomes of acute coronary syndrome. They concluded that diabetic patients with acute coronary syndrome were associated with increased major cardiovascular events and mortality.<sup>19</sup> Another study concluded that severity of CAD in diabetic patients is positively correlated with HbA1c levels.<sup>9</sup>

## CONCLUSION

Diabetes mellitus significantly predicts the severity of coronary artery disease. The severity of CAD is greater in diabetic patients, with the majority of patients presenting with TVCAD and DVCAD. In contrast, minor CAD or SVCAD is more common among non-diabetics.

## LIMITATIONS & RECOMMENDATIONS

The study compared the severity of coronary artery disease among diabetic and non-diabetic patients but didn't determine the severity of CAD in patients with impaired glucose tolerance. Furthermore, the duration of diabetes mellitus, glycemic control, and the association of HbA1c levels with various scores such as SYNTAX or Gensini scores were not studied. Further work is recommended to address these limitations.

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# Patient Satisfaction and Efficacy of Manual Vacuum Aspiration - A Safe Management Choice for First-Trimester Miscarriage

Lamia Yusuf, Natasha Bushra

## ABSTRACT

**Objective:** To determine the efficacy of manual vacuum aspiration (MVA) and the satisfaction regarding MVA in patients presenting with first-trimester miscarriage.

**Methodology:** This cross-sectional survey was conducted in the Department of Gynaecology & Obstetrics, Khawaja Muhammad Safdar Medical College, Sialkot. Permission from the institutional review board was taken. The sample size was 28 as calculated by an open epi calculator. Manual vacuum aspiration was offered to all women fulfilling the inclusion criteria. A self-administered questionnaire was given to patients to assess their satisfaction scores. The primary outcome was to assess the efficacy of the procedure defined as complete uterine evacuation without the need for further treatment (medical or surgical curettage). Secondary outcomes were the safety of the procedure and related complications including uterine perforation, bleeding, and patient satisfaction. The data obtained was evaluated using Statistical Package for the Social Sciences (SPSS) version 21.

**Results:** The mean age in the study group was 28.4±5.4 years. The efficacy of the procedure was 92.8% & the duration of the procedure was noticed as <10 minutes in 78.6% of patients. Blood loss was less than 100 mL in 78.6% of participants. The majority of patients (85.6%) were satisfied with the procedure.

**Conclusion:** Manual vacuum aspiration is an efficient treatment option in terms of complete uterine evacuation, blood loss, pain during & after the procedure, and patient's satisfaction. So, MVA is an acceptable, efficient, and satisfactory alternative method in patients with first-trimester miscarriages.

**Keywords:** Miscarriage. Early pregnancy. Patient satisfaction.

## INTRODUCTION

Miscarriage or abortion is defined as the natural death of an embryo before 24 weeks of gestation. It is the commonest presentation of the first trimester. The majority of miscarriages occur around 12 weeks mostly due to chromosomal abnormalities.<sup>1</sup> Bleeding, lower abdominal pain, and cramping are the usual symptoms of individuals with abortions or early pregnancy loss, but majority of patients remain stable. In uncomplicated pregnancy, further symptoms may vary from patient to patient. It may also include a loss or decrease or absence of pregnancy symptoms, such as decreased breast tenderness and/or nausea, and vomiting. Any patient with these symptoms must also be evaluated for ectopic pregnancy. The clinical scenarios that require treatment are of two types: missed abortion, that is, empty gestational sac or with an embryo without a fetal heartbeat, or incomplete abortion, that is, a significant amount of remains of trophoblastic tissue in the endometrial cavity. These situations are treated by different management forms, like using medications and vacuum aspiration or

surgical treatment. The choice of management is based primarily on the duration of pregnancy and age. This should be determined by asking last menstrual period of the patient and confirmed by a dating scan.<sup>2</sup> Sizes of retained products of conception also determine the choice of treatment, along with the preferences of the patient after appropriate counselling regarding the benefits and risks of all management options. Because of this, it is essential to have a thorough clinical history, gynaecological physical examination, and ultrasonography. Expectant management should be considered in pregnancies of less than 9 weeks or incomplete abortions without complications, allowing its natural course under observation, to confirm the complete expulsion of intrauterine contents. It is described that in a period of 7 to 14 days, in 75-85% of cases, there will be complete abortions without the need for procedures and without associated complications.<sup>3</sup> There are two basic treatment options for the management of abortions, or miscarriages; medical or surgical treatment. Medical treatment is in the form of prostaglandin E1 (misoprostol) and anti-progesterone (mifepristone). Surgical intervention is in two ways; conventional evacuation & curettage (E & C) and manual vacuum aspiration. Medical management has also been used as an alternative to surgical management and the most commonly used is misoprostol.<sup>4,5</sup> Surgical treatment is still an acceptable option by patients. It has few side effects like fever, hypersensitivity, diarrhea, etc.<sup>6</sup> Literature shows that both MVA and misoprostol are cost-effective and efficient methods for the termination of pregnancy, and MVA is

Sharif Medical & Dental College, Sharif Medical City,  
Sharif Medical City Road, Off Raiwind Road, Jati Umra,  
Lahore 54000, Pakistan.

Correspondence: Dr. Lamia Yusuf  
Associate Professor Department of Gynaecology & Obstetrics  
Khawaja Muhammad Safdar Medical College, Sialkot  
E-mail: doclamia@hotmail.com

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as an alternative to the conventional method of E & C. Manual vacuum aspiration was used first in China in 1958. It has numerous benefits, including the ability to be performed under local anesthesia, the ability to be used instead of standard electrical vacuum aspiration, the reduction of waiting time, and a shorter hospital stay. It has been deemed a secure and effective method of handling early pregnancy loss.<sup>7</sup>

In Pakistan, the public health sector is overburdened due to high rates of pregnancies (3.8%), inadequate use and non-availability of contraception methods, taboos against safe abortions, lack of trained staff, and poor understanding of legislation by health care providers. Due to the above-mentioned facts, it's high time to change the paradigm from the conventional method of E & C to MVA. So, this study aimed to find the efficacy of MVA as an alternative method and the satisfaction of patients associated with this procedure.

### METHODOLOGY

It was a cross-sectional study conducted in the Department of Gynaecology & Obstetrics, Khawaja Muhammad Safdar Medical College, Govt Sardar Begum Teaching Hospital, Sialkot. Before conducting the study, permission from the institutional review board (IRB) was taken. The duration of the study was 6 months after IRB approval. Non-probability sampling technique was used. The sample size of 28 was calculated by an open epi calculator.

The inclusion criteria for patient recruitment were missed miscarriage and incomplete miscarriage at gestational age (GA) <13 weeks. The patients excluded from the study were those with uterine anomaly, molar pregnancies, threatened miscarriage, and pregnancy. Patients fulfilling the inclusion criteria were selected from outdoor and emergency. Written and informed consent of patients was taken before the start of the procedure. The pros and cons of the procedure were explained to patients. Manual vacuum aspiration was offered to all women with first-trimester missed or incomplete miscarriage at GA <13 weeks. As per the protocol of The International Federation of Gynecology and Obstetrics, all women were administered 400 µg of sublingual misoprostol for cervical priming, 3 hours prior to the procedure with closed os. Manual vacuum aspiration was performed by applying local anesthesia, 10-20 mL of 1% lignocaine intracervical at 2, 4, 8, and 10 o'clock using a flexible Ipas EasyGrip Cannula attached to a 60 mL syringe (aspirator) with a double locking valve mechanism. Products of conception evacuated were sent for histopathology. Patients were kept in the labour room for 1 hour and later discharged. The primary

outcome measure was to assess the efficacy of the procedure defined as complete uterine evacuation without the need for further treatment, medical or surgical curettage. Secondary outcome measures included the safety of the procedure and related complications including uterine perforation, bleeding, pain, and infection. The duration of the procedure, blood loss assessed by the aspirator in the syringe, the need for further treatment medical or surgical curettage, and clinical complications were also evaluated. A self-administered questionnaire was given to patients to assess the satisfaction levels of the participants. The questionnaire included information regarding patients' satisfaction with the procedure on their personal assessment & pain, during and after the procedure. Percentages of the response of the patients were calculated using a Likert scale. Strongly agree and agree (1 & 2) were taken as satisfied, 3 was considered as uncertain, and strongly disagree and disagree (4 & 5) as being dissatisfied.

### STATISTICAL ANALYSIS

The data obtained were evaluated by using Statistical Package for the Social Sciences (SPSS) version 21. Quantitative variables like blood loss, change of procedure, uterine perforation, infection, and duration of procedure were measured as frequencies and percentages. Patients' satisfaction with the procedure and pain, during & after the procedure was also calculated as frequency and percentage.

### RESULTS

Out of 28 patients, 35.7% of patients belonged to the age group 20-25 years, 21.4% to the age group 26-30 years, 28.6% to the age group 30-35 years, and 14.3% to the age group >35 years. The mean age group in the study was 28.4±5.4 years. Among the patients, three patients were primigravida, five were para 1, six were para 2, four were para 4, six were para 4, and four patients were having parity of more than 5. The mean parity of the patients in the study was para 2. Almost 12% of patients had a history of previous abortions and 16% were without any history of abortions. Regarding their past history of use of contraception, 7% were previously using contraception and 93% were not using any contraception. Seventeen (60.7%) patients were illiterate and twenty seven (96%) were housewives. Manual vacuum aspiration was performed on 22(78.6%) patients upon indication of missed abortion and in 6(21.4%) patients, MVA was done for incomplete abortion. Efficacy was measured in terms of blood loss estimation, need for the switch of procedure, uterine perforation, and infection (Table 1).

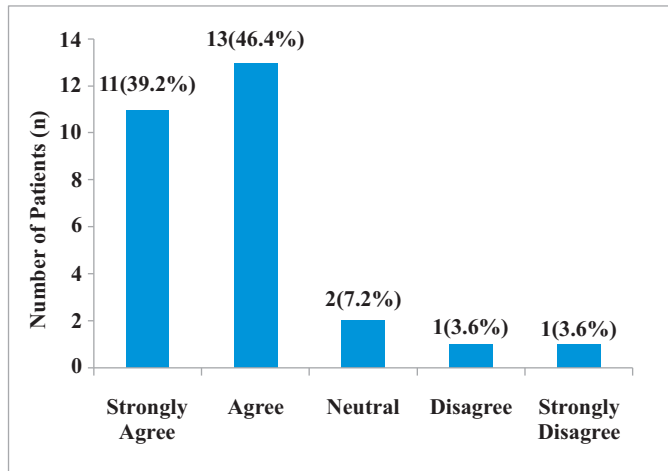
Patients' satisfaction with the procedure and pain

during & after the procedure was measured. We found that 25(90%) participants agreed that there was no pain during the procedure and 26(92.8%) participants were of the opinion that there was no pain after the procedure.

Twenty four (85.6%) patients were satisfied with the procedure, two (7.2%) patients were not satisfied and 2(7.2%) were uncertain. Satisfaction scale with the procedure is shown in Figure 1.

**Table 1: Efficacy of Manual Vacuum Aspiration**

Variables		Frequency & Percentage
Blood Loss (mL)	≤100	22(78.6%)
	>100	6(21.4%)
Change of Procedure	Yes	2(7.2%)
	No	26(92.8%)
Uterine Perforation	No	28(100%)
Infection	No	28(100%)
Duration of Procedure (Minutes)	≤10	22(78.6%)
	>10	6(21.4%)



**Figure 1: Satisfaction of the Study Participants with the Procedure**

**DISCUSSION**

Miscarriage for any couple is an emotional and distressful event. The treatment offered to these patients should be effective, humane, and without any effect on future fertility. Management of miscarriages is a huge burden on busy hospitals and it is encountered at all levels of healthcare facilities. Manual vacuum aspiration is generally, an acknowledged method of evacuation of the uterus after missed miscarriage, incomplete abortion, persistent gestational sac, and even in endometrial biopsy as an OPD procedure with little or no complications, especially when performed by trained health professionals and within a controlled environment.<sup>8,9</sup>

In this study, the efficacy and satisfaction of MVA in patients presenting with first-trimester miscarriage was determined. The efficacy was measured by the amount of blood loss. We found less than 100 mL of blood loss in 78.6% of cases. A study by Achkzai et al. in 2020 concluded that MVA had better outcomes than the conventional E & C in terms of blood loss as well as

uterine perforation.<sup>10</sup> In our study, an important parameter was uterine perforation, which was not noted in any patient. Another study was conducted at the University of Port Harcourt Teaching Hospital to evaluate the efficacy and complications of manual vacuum aspiration. Three hundred & twenty patients were treated with MVA. No complication was seen in any patient. So, MVA is a highly safe and effective procedure. The soft and flexible structure and easy to handle quality of the cannula of MVA are responsible for the safety of the procedure.<sup>11</sup> A study was conducted by Shaheen et al. to compare the efficacy of MVA & medical treatment in the management of miscarriage. They concluded that MVA is a better treatment option as compared to medical treatment.<sup>12</sup>

Another study was conducted in Hayatabad Medical Complex to evaluate the efficacy of MVA and conventional evacuation and curettage. A total of 160 patients were enrolled and categorized into MVA and E & C group. They reported 97.5% efficacy of MVA and 92.5% in E & C. Complication rate was 7.5% in MVA

& 30% in E & C group.<sup>13</sup>

In our study, 25(90%) and 26(92.8%) participants agreed that there was no pain during and after the procedure, respectively and 24(85.6%) patients were satisfied with the procedure. In a study conducted by Arif et al., 200 patients with missed or incomplete abortions at 6-12 weeks are enrolled. These patients were divided into MVA & oral misoprostol group. They concluded that in the MVA group, efficacy was 88%, feasibility was 95%, and patients' acceptability was 97% whereas, in the sublingual oral misoprostol group, efficacy was 64%, feasibility was 68%, and patients' acceptability was 70%.<sup>14</sup> Another study was carried out to determine patients' satisfaction with MVA. They reported that the patients were highly satisfied with MVA.<sup>15</sup> Another study reported that 84.2% of study participants were satisfied with MVA. They also found low pain score during and after the procedure.<sup>16</sup> Thus, with careful patient selection, trained health professionals, and effective counselling of patients, MVA can be used to achieve better results, reduce complications, and follow-ups.

### CONCLUSION

Manual vacuum aspiration is an efficient treatment option in terms of complete uterine evacuation, blood loss, pain during & after the procedure, and patient's satisfaction. So, MVA is an acceptable and satisfactory alternative method in patients with first-trimester miscarriages.

### LIMITATIONS & RECOMMENDATIONS

The limitation of this study was that this study was carried out in one center only, large multi-centered trials will help in establishing the efficacy of MVA, and the satisfaction regarding the procedure by the patients will also be better assessed.

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# Family Resilience in Pakistani Families having Children with Autism

Naila Aslam, Iffat Rohail

## ABSTRACT

**Objective:** To determine the resilience in families having Autistic children in Pakistan.

**Methodology:** A quantitative cross-sectional descriptive study was done involving 150 Pakistani families who had children with Autism spectrum disorder (ASD). Data was collected through a purposive convenient sampling technique. Family Resilience Assessment Scale was used to calculate the results.

**Results:** Descriptive statistic was used to analyze the data. The results indicated that only 4% of families of children with Autism exhibit high family resilience. A moderate level of family resilience was involved in 72.7% and 23.3% of families showed a low level family resilience. According to the results, family resilience indicated a significant relationship with education (p-value=0.000), gender (p-value=0.003), and family system (p-value=0.048).

**Conclusion:** Families of children with Autism have a moderate level family resilience. Also, parental education, family system, and gender are interdependent on each other for determination of the level of family resilience towards Autism.

**Keywords:** Family support. Autism. Resilience.

## INTRODUCTION

Autism spectrum disorder is defined as a neurodevelopmental disorder categorized by a lack of communication, portraying repetitive behaviors, and restricted interests.<sup>1</sup> The incidence of ASD diagnosis increased from 0.07% in 2009 to 0.23% in 2017, with a higher increase in girls, and in children aged 2-5 years at the time of diagnosis. Literature shows that the prevalence of ASD in South Asia is up to one in 93 children. Parents of children with autism spectrum disorder experience unique challenges in terms of understanding the disorder, the child's needs, management of their behaviors as well as increased parental stress.<sup>2</sup> Stress and well-being of the parents having children with autism spectrum disorder have always been a major concern in the family. The severe increase in the stress level causes more anxiety and depression in parents and family of child with ASD. Mothers are more likely to be affected by depression as compared to the fathers of children with ASD. There have been certain reasons for parents' suffering from stress at different levels. The most significant is the difficulty in availing diagnostic services and lack of proper counseling sessions with health care providers. In addition, ASD austerity and verbal intelligence quotient in the child can be extremely challenging for the parents to adhere with.<sup>3</sup> Resilience is frequently

described as a dynamic process that includes helpful environment adaptation. A person's ability to succeed in the face of adversity can be attributed to their resilience, which can involve the cumulative influence of their individual attitudes, beliefs, and skills.<sup>4</sup> It is essential for the whole family and community to contribute their efforts to increase resilience. Family resilience boosts healthy family functioning with the inclusion of independent constructs and shielding against hardships.<sup>5</sup>

Currently, there are several factors which incorporate resilience amongst the families/parents of children diagnosed with ASD. Major factors that impact family resilience are social influence and support, financial challenges, awareness and contemplating ASD by parents, and concerns about the child's outlook. However, both family and personal resilience are correlated so much so that several factors incorporated with resilience in parents are also deemed to be reflected in family resilience and cohesiveness.<sup>6</sup> According to Walsh Family Resilience Framework, nine key processes have been determined. These are further categorized into three dimensions dealing with the functioning of the family: family's assimilated belief systems, family configuration, and process of communication and problem-resolving techniques. The first dimension, family assimilated belief systems includes making sure that the family must have common sense-making efforts. A positive approach is one of the essential attributes in availing family resilience. Transcendence and spirituality ultimately assist in developing common efforts to eradicate detrimental challenges.<sup>7</sup>

Family resilience can only be beneficial if collaborative work is conducted towards building shared beliefs and strategies. The second dimension i.e. family

Sharif Medical & Dental College, Sharif Medical City,  
Sharif Medical City Road, Off Raiwind Road, Jati Umra,  
Lahore 54000, Pakistan.

Correspondence: Ms. Naila Aslam  
PhD Scholar Department of Psychology  
Foundation University, Islamabad  
E-mail: nailabhatti89@hotmail.com

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configuration, includes transactional processes which assist in strengthening, flexibility in the family while resolving problems, a firm belief in cohesion, availability of economic resources along with social support. There could be essential factors in contributing to the effective responses in order to overcome the aversive challenges. Lastly, the third dimension mainly focuses on communication strategies and resolving problem processes which involves clarity in their stance, ability to express emotionally, and resolving problems, collectively.<sup>8</sup> Considering the negative impacts, it is pertinent to understand that adaptation of positive thinking and resilience are mandatory for the parents of children with ASD while bringing up their child. It shall be beneficial for both parents and children with ASD in the long term to overcome the forthcoming challenges. So, this study was planned to observe family resilience in Pakistani families of children with ASD.

### METHODOLOGY

The present study was conducted at the Department of Psychology, Foundation University, Islamabad. The study was approved by the Board of Advanced Studies and Research. A descriptive research design was used to gather information about the family resilience levels in families who had children with Autism. The study was done in Islamabad and Rawalpindi region and data was collected through a purposive convenient sampling technique, where selection was focused on participants with pertinent characteristics that were associated with the research subject. A total of 150 parents participated in the study. Families having children with Autism but without physical disabilities were included. Families with Autistic children with physical disabilities and multiple disorders were excluded from this study.

Participants fulfilling the inclusion criteria were contacted through educational institutions situated in Islamabad and Rawalpindi. Willing participants were briefed about the nature of the study, and written consents were taken. Families were free to leave the study at any stage if they didn't feel comfortable. Demographic information was taken from the participants. Family resilience was measured by the family resilience assessment scale developed by Sixbey. It's a 5 point Likert scales with ranges between strongly agree to strongly disagree. Participants who scored 66-125 were considered to have low family resilience, 126-205 scores meant moderate family resilience, and scores 216-316 indicated a high level of family resilience.<sup>9</sup> It was a validated scale with Cronbach alpha value of 0.94.

### STATISTICAL ANALYSIS

Statistical Package for the Social Sciences (SPSS) version 25.0 was used to analyze the data. Descriptive statistics were applied on data to analyze and evaluate the family resilience level. Chi-square test was used to analyze the association between the degree of family resilience and demographic data. A p-value of  $\leq 0.05$  was taken as statistically significant.

### RESULTS

The results indicated that 72.7% of participants had moderate family resilience towards their Autistic child. Data analysis indicated that family resilience had a significant progressive relationship with three demographic variables, i.e. education (p-value=0.000), gender (p-value=0.003), and family system (p-value=0.048). However, there was no relationship with the levels of family resilience and child's perceived Autism (p=0.375) (Table 1).

**Table 1: Association of Demographic Variables with Family Resilience of the Study Participants**

Demographic Variables		Low Family Resilience	Average Family Resilience	High Family Resilience	p-value
Respondent's Education	Below Master's	20(13.3%)	62(41.4%)	3(2%)	0.000*
	Master's	15(10%)	47(31.3%)	0(0%)	
	Above Master's	0(0%)	0(0%)	3(2%)	
Family System	Joint Family	16(10.7%)	58(38.6%)	6(4%)	0.048*
	Nuclear Family	19(12.7%)	51(34%)	0(0%)	
Gender	Male	15(10%)	19(12.7%)	0(0%)	0.003*
	Female	20(13.3%)	90(60%)	6(4%)	
Child's Perceived Autism Levels	Mild Autism	19(12.7%)	55(36.7%)	6(4%)	0.375
	Moderate Autism	11(7.3%)	38(25.3%)	0(0%)	
	High Autism	2(1.3%)	10(6.7%)	0(0%)	

\*Significant p-value

## DISCUSSION

Raising a child with a disability is a big challenge and families have to show resilience in this stressful situation.<sup>9</sup> In this study, we observed family resilience among families of child with Autism. Our results showed that 72.7% of participants had moderate family resilience towards their Autistic child.

Another study reported that 79.5% of the families exhibited high resilience whereas 19.3% of the families have shown moderate resilience.<sup>10</sup> According to another study, individuals tend to consider their family to have the capacity to overcome their difficulties in adverse conditions, however, they also believe the fact that their family does not possess the ability to create maximum protective factors to eradicate the difficult situations or risk factors. There are several protective factors and risk factors for resilience. Risk factors have the potential of enhancing the difficulties and maintenance of resilience in the family.<sup>11</sup>

Our results also show that a correlation exists between the degree of family resilience and demographic variables like gender (p-value=0.003), family system (p-value=0.048) & education (p-value=0.000).

It was found by Hendrayu et al. that the gender of the child does not determine the level of family resilience and it has no co-dependency on the respective factor. It was also shown that the education, age of parents, and marital status can result in establishing differences in perceiving family resilience.<sup>12</sup> In another study conducted by Al-Jadiri et al., data of 151 children with ASD was analyzed. They reported low family resilience in 32% of families and it was associated with low-level family support.<sup>13</sup> Another study conducted by Zhao et al., observed relationship between family support and resilience. They reported that neighborhood support was significantly associated with family resilience.<sup>14</sup>

A study conducted by Ghanouni et al. & Afifi et al., reported that the stress levels of parents were negatively associated with family resilience, whereas monthly income was positively associated with parental resilience. They also concluded that no significant correlation was found between child and parental age and resilience.<sup>4,15</sup>

In our study, no correlation of severity of child's Autism and resilience was found (p-value=0.375). On contrary, other studies suggested a negative correlation between severity of ASD and family resilience.<sup>4</sup> According to Sixbey, life experiences play a vital role in constituting family resilience as the family grows older. Moreover, these experiences can also aid in increasing the resilience in the family with the passage of time.<sup>9</sup> Depending on the factors such as age, self-esteem, social orientation and interactions, achievement motivation, social comprehension, and cognitive and emotional development, children also

significantly contribute in developing family resilience.<sup>16</sup>

Our results show that education has an impact on developing efficient family resilience in family with ASD (p-value=0.000). For instance, an individual with a master's level education has the capacity to endure more family resilience as compared to a person with a lower level of education. According to Ungar and Theron, education can play a significant role in achieving higher levels of family resilience, for instance, if higher education is pursued then attaining a good level of family resilience becomes imminent.<sup>2,17</sup>

## CONCLUSION

Families of children with Autism have a moderate level of family resilience. Also, parental education, family system, and gender are interdependent on each other for determination of the level of family resilience towards Autism.

## LIMITATIONS & RECOMMENDATIONS

The study sample was not too large to generalize the results and sample consisted of one particular disability. Future studies are recommended to compare the family resilience in families with different disabilities. It is recommended to strengthen family resilience in Autistic families through public awareness and counseling sessions.

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## **Sharif Medical & Dental College**

Sharif Medical City Road, Off Raiwind Road, Jati Umra, Lahore 54000, Pakistan.

Tel: +92-4237860101-4 Fax: +92-4237860122 UAN- 042-111-123-786

E-mail: [editors@jsmdc.pk](mailto:editors@jsmdc.pk) Web: [www.jsmdc.pk](http://www.jsmdc.pk)