

## ORIGINAL ARTICLE

## FREQUENCY OF ISCHEMIC MITRAL REGURGITATION AFTER ACUTE ST- ELEVATION MYOCARDIAL INFARCTION AT A TERTIARY CARE CARDIAC CENTER

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**Objectives:** Among the common complications of coronary artery disease (CAD) is the ischemic mitral regurgitation (IMR). Identifying IMR and assessing its severity is pertinent owing to its significance in post- myocardial infarction (MI) risk stratification. It is associated with a higher risk of heart failure and mortality. This study aimed to determine the frequency of IMR after the first acute ST-elevation MI (STEMI) in the Pakistani population.

**Methodology:** A cross-sectional observational study was conducted at NICVD, Karachi between January and July 2021. One hundred and ninety-five consecutive participants of first acute ST elevation MI who fulfilled the diagnostic criteria of IMR were included in the study. Demographic and clinical profile was recorded. All patients underwent echocardiography to grade the severity of IMR. Data was entered and analyzed using SPSS version 20.

**Results:** Of 195 patients, 141 (72.3%) were males. 77 (39.5%) were diabetic, 92 (47.2%) were hypertensive, 18 (9.2%) had dyslipidemia and 58 (29.7%) used tobacco. IMR was observed in 74 (37.9%) with mild in 50 (67.6%), moderate in 18 (24.3%), and severe in 6 (8.1%) patients. IMR was statistically significantly associated with duration of symptoms, type of MI, diabetes mellitus, hypertension, and tobacco use.

**Conclusion:** IMR was prevalent in more than one-third of patients presenting with acute ST elevation MI. Severity of IMR was moderate to severe in about one-third of the patients. IMR was found to be associated with duration of symptoms, type of MI, diabetes mellitus, hypertension, and tobacco use. Considering its prognostic role, assessment of IMR and its severity is necessary for appropriate management of patients.

**Keywords:** ischemic mitral regurgitation, echocardiography, Doppler, acute myocardial infarction

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### INTRODUCTION

Coronary artery disease (CAD) is among the most prevalent causes of global morbidity and mortality.<sup>1</sup> Despite advancements in diagnostic and therapeutic approaches, the burden of CAD has continued to rise, both in developed as well as developing countries.<sup>2</sup> In terms of ethnic backgrounds, population-based studies have shown that Asians are more vulnerable to myocardial infarction (MI).<sup>3</sup> Local studies have shown that the risk factors for MI are highly prevalent in the Pakistani population and that more than 30% of the population of age 45 years and above suffers from CAD.<sup>4</sup>

Among the common complications of CAD is Ischemic Mitral Regurgitation (IMR). IMR

particularly complicates myocardial infarction. It predominantly occurs in individuals who already have had an MI. IMR may also coexist with acute ischemia in which case it usually resolves once the ischemia settles.<sup>5</sup> Ischemic MR is defined as one that occurs secondarily to dysfunction of papillary muscle or abnormality of wall motion in the region of significant CAD.<sup>6</sup>

IMR is graded based on its severity into mild, moderate, and severe. Mild IMR is the most common.<sup>7</sup> It is reported that the incidence of MR is 50% in echocardiographic studies. Fazlinezhad et al. conducted a cross-sectional study in which 250 patients of first-time onset acute ST elevation MI (STEMI) were included. They reported that 45% of them had ischemic mitral regurgitation.<sup>8</sup>

We initiated this study to determine the frequency of ischemic MR after the first acute onset STEMI in the Pakistani population. Literature review on this subject revealed that there is a paucity of data both locally and internationally.<sup>9</sup> Identifying IMR and assessing its severity is pertinent owing to its significance in post-MI risk stratification. IMR occurring after MI is associated with a higher risk of other cardiac complications which may include heart failure and mortality. The commonness and severity of these complications proportionally increase with that of ischemic mitral regurgitation.<sup>11</sup> Hence it becomes pertinent to understand the underlying association between the two phenomenon to appropriately and timely diagnose IMR in these patients which ultimately will help in enhancing the overall prognosis and disease outcome.

## METHODOLOGY

A cross-sectional study was performed at the National Institute of Cardiovascular Diseases (NICVD), Karachi. The study was conducted between January and July 2021. The study was approved by the Ethical Review Committee of the hospital (ERC-50/2020). Verbal informed consent for participation was obtained from all included patients. In this study, we included patients to determine the frequency of IMR after the first acute STEMI presenting at the tertiary care cardiac center.

By taking the prevalence of ischemic mitral regurgitation of 45%,<sup>10</sup> with a margin of error of 7% and confidence interval of 95%, the sample size was calculated using the WHO software and it was 195 patients.

One hundred and ninety-five consecutive participants who fulfilled the diagnostic criteria were included. The inclusion criteria of was age group between 18-75 years, both gender, and patients presenting within 24 hours with acute STEMI. Patients were excluded if: they had a prior history of MI, prior cardiac surgery or percutaneous coronary intervention (PCI), known valvular heart disease, active pregnancy, or had a history of chronic kidney disease.

Demographic details like age (years), gender, residence (urban or rural), monthly household income (in Pakistani rupees), height (cm), and weight (kg) were obtained at the time of hospital arrival. Body mass index (BMI) was then calculated in kg/m<sup>2</sup> as follows; (weight in kg) / (height in m<sup>2</sup>). History of the patients was taken regarding the presence or absence of hypertension, diabetes mellitus, dyslipidemia, tobacco use, obesity, family history of premature CAD, and duration of symptoms.

Acute ST elevation myocardial infarction was defined according to the fourth universal definition of MI.<sup>11</sup> All patients underwent echocardiography performed by two experienced echocardiologists ( $\geq 5$  years' experience) in a blinded fashion, within 72 hours of hospitalization to limit inter-observer variability. The finding of ischemic MR was categorized as mild, moderate, and severe as per the grading classification outlined in the 2020 ACC/AHA guideline for the management of patients with valvular heart disease, e.g. moderate IMR was defined if the following criteria were fulfilled: regional wall motion abnormality with tethering of mitral leaflet, regurgitant volume < 60 ml, regurgitant fraction <50% or effective regurgitant orifice area < 0.4 cm<sup>2</sup> of the left atrium.<sup>12</sup> Echocardiography was performed on GE Vivid 7 and Phillips iE33x Matrix equipped with adult cardiologic probes.

Data was entered and analyzed using IBM SPSS for Windows version 20.0. Mean and standard deviation (SD) were calculated for continuous variables such as age, height, weight, BMI, and duration of symptoms of acute STEMI. Frequency and percentages were calculated for categorical variables like gender, residence, type of MI, hypertension, diabetes mellitus, dyslipidemia, tobacco use, obesity, family history of CAD, anemia status, occupational status, monthly household income, and ischemic mitral regurgitation (Yes/No). Stratification was done with regards to age, gender, residence, type of MI, hypertension, diabetes mellitus, dyslipidemia, tobacco use, obesity, family history of CAD, anemia status, occupational status, monthly household income, and duration of symptoms of ST-elevation MI to determine the effect of these on the outcome variable. Post-stratification Chi-square test or Fisher's exact test was applied and a p-value of  $\leq 0.05$  was taken as statistically significant.

## RESULTS

There were 195 individuals who met the inclusion criteria and were included after attaining consent. The mean age of the study sample was  $55.86 \pm 10.71$  years, while the mean duration of symptoms of ST-elevation MI was  $5.03 \pm 4.6$  hours. (Table 1) shows the descriptive statistics for continuous variables.

There were 141 (72.3%) were males. Out of 195 patients, 32 (16.4%) and 163 (83.6%) patients were in age group 25-45 years and 46-75 years respectively. Duration of symptoms of ST-elevation MI was up to 6 hours in 156 (80.0%) and more than 6 hours in 39 (20%).

Frequency distribution of MI type showed that out of 195 patients, 76 (39%) patients had anterior wall MI while 92 (47.1%) patients had inferior and posterior wall MI. Frequency distribution of IMR with the type of MI showed that out of 195 patients, 20 (10.3%) patients with anterior wall MI, while 47 (24.1%) with inferior and posterior wall MI had IMR. Distribution of severity of IMR among 74 patients with IMR was mild in 50 (67.6%), moderate in 18 (24.3%), and severe in 6 (8.1%) patients.

**Table 1: Descriptive statistics for continuous response variables**

	Mean ± SD	Median [IQR]	Min - Max
Age (year)	55.86 ± 10.71	55 [50 - 65]	25 - 75
Height (meter)	1.71±0.07	1.72 [1.68 - 1.76]	1.4 - 1.85
Weight (kg)	73.86 ± 11.57	75 [68 - 80]	1.73 - 100
Body mass index (kg/m <sup>2</sup> )	25.27 ± 3.36	25.25 [23.24 - 27.04]	16.14 - 36.98
Duration of symptoms STEMI (Hours)	5.03 ± 4.6	4 [2 - 6]	0.5 - 24

Table 2 shows the association of IMR with baseline demographic and clinical characteristics of the study sample.

Stratification analysis showed statistically significant association between ischemic MR and duration of symptoms, location of myocardial infarction, diabetes mellitus, hypertension, and tobacco use were observed with p-values of 0.001, <0.001, 0.019, 0.003, and 0.024, respectively. However, there was no statistical association of IMR with gender, age groups, body mass index, dyslipidemia, family history of CAD, obesity, and anemia.

**Table 2: Association of ischemic mitral regurgitation with baseline demographic and clinical characteristics of the patients**

	Ischemic Mitral Regurgitation		P-value
	Yes	No	
<b>Total (N)</b>	<b>74 (37.9%)</b>	<b>121 (62.1%)</b>	-
<b>Gender</b>			
Male	51 (26.2%)	90 (46.2%)	0.408
Female	23 (11.8%)	31 (15.9%)	
<b>Age group</b>			
25 to 45 years	10 (5.1%)	22 (11.3%)	0.393
46 to 75 years	64 (32.8%)	99 (50.8%)	
<b>Body mass index (kg/m<sup>2</sup>)</b>			
≤18.5	3 (1.5%)	1 (0.5%)	0.366
18.51 to 22.99	18 (9.2%)	24 (12.3%)	
23.00 to 27.49	39 (20%)	69 (35.4%)	
≥27.5	14 (7.2%)	27 (13.8%)	

<b>Duration of symptoms</b>			
Up to 6 hours	50 (25.6%)	106 (54.4%)	0.001
More than 6 hours	24 (12.3%)	15 (7.7%)	
<b>Type of Myocardial Infarction</b>			
AWMI	20 (10.3%)	56 (28.7%)	<0.001
IWMI	26 (13.3%)	42 (21.5%)	
LWMI	7 (3.6%)	20 (10.3%)	
PWMI	21 (10.8%)	3 (1.5%)	
<b>Diabetes Mellitus</b>			
Yes	37 (19%)	40 (20.5%)	0.019
No	37 (19%)	81 (41.5%)	
<b>Hypertension</b>			
Yes	45 (23.1%)	47 (24.1%)	0.003
No	29 (14.9%)	74 (37.9%)	
<b>Dyslipidemia</b>			
Yes	6 (3.1%)	12 (6.2%)	0.672
No	68 (34.9%)	109 (55.9%)	
<b>Tobacco use</b>			
Yes	29 (14.9%)	29 (14.9%)	0.024
No	45 (23.1%)	92 (47.2%)	
<b>Family history of CAD</b>			
Yes	4 (2.1%)	5 (2.6%)	0.681
No	70 (35.9%)	116 (59.5%)	
<b>Obesity status</b>			
Yes	14 (7.2%)	27 (13.8%)	0.572
No	60 (30.8%)	94 (48.2%)	
<b>Anemia</b>			
Yes	15 (7.7%)	14 (7.2%)	0.098
No	59 (30.3%)	107 (54.9%)	

## DISCUSSION

From the results of this study, it is demonstrated that the overall frequency of ischemic mitral regurgitation (IMR) by transthoracic echocardiography in patients with the first acute STEMI and treated by primary PCI was 37.9%. The results compare well with published studies reporting frequencies of IMR between 28 to 45%.<sup>7,8,13</sup>

Barra et al. in their cross-sectional study of 796 patients that included 45.3% patients with STEMI and 53.9% patients with non-STEMI, showed no statistically significant relationship between the risk of developing IMR and the extent of myocardial necrosis in both STEMI and non-STEMI acute coronary syndrome. The overall prevalence of IMR in their work was reported as 45% which correlates well with our results.<sup>7</sup>

IMR does not result from structural damage to the mitral valve itself rather it is a sequela of increased tethering forces and reduced closing forces. Displacement of papillary muscle leads to more apical position of the leaflets and their coaptation point which results in increased tethering forces. Reduced contractility, intra-left ventricular dyssynchrony, and dyssynchrony of the papillary muscles leads to reduced closing forces. A mix of these mechanisms may be uniquely operative in causing IMR in either

inferior or anterior location of MI. These mechanisms account for the fact that the most common direction of jet in inferior STEMI is posterior, while in anterior STEMI it is central.<sup>10</sup>

The work of Kumanohoso and colleagues has demonstrated that there is a greater incidence of IMR with higher degree of severity in patients with inferior as compared to those with anterior wall MI. They explain their results with the mechanism associated with severe geometrical changes in the apparatus of mitral valve with greater posterior papillary muscle displacement which in turn is caused by left ventricular remodeling.<sup>14</sup> Razzak and colleagues in their work with 117 acute STEMI patients showed that inferior MI location was the major site in 53 (63.9%) patients causing IMR, while anterior MI was found in 26 (31.3%) patients.<sup>13</sup> The results of our study also corroborate with these findings and showed that out of 195 study patients, 47 (24.1%) patients with inferior/posterior wall MI while 20 (10.3%) patients with anterior wall MI had IMR.

Barra et al. found moderate to severe IMR in 14.6% of their patients.<sup>7</sup> Bursi et al. conducted a large community-based study of 1331 patients with incident MI. In their study, IMR was reported in 50% participants. It was mild in 38% and 12% had moderate to severe IMR.<sup>15</sup> Our study results revealed moderate IMR in 18 (24.3%) patients and severe IMR in 6 (8.1%) patients.

Studies have also demonstrated that the severity of IMR evolves over time as MI enters the sub-acute phase.<sup>16</sup> Nishino et al. conducted a study on 546 patients and examined the impact of successful emergency primary PCI in first-onset AMI on the frequency and severity of IMR through the disease course from emergency room to the early-to-late follow-up period. Non-total coronary artery occlusion at angiography and onset-to-reperfusion time independently predicted acute IMR improvement post primary PCI. IMR extent also evolves in the chronic stage of MI. This reflects the degree of left ventricular remodeling or reverse remodeling in the chronic phase post AMI. Age, left ventricular ejection fraction, and peak CK-MB were the independent predictors of IMR in the follow-up phase. Identification of clinically significant IMR in both acute and chronic phases of AMI deteriorated the overall prognosis after PCI significantly in both short as well as long term period.<sup>17</sup>

Stratification analysis of our study results showed statistically significant association between ischemic MR and duration of symptoms, location of myocardial infarction, diabetes mellitus, hypertension, and

tobacco use. Bursi et al. showed in their study that patients of IMR, of either grade of severity, were women, were older in age, had higher medical comorbidity, and were non-smokers.<sup>15</sup> Findings from the study by Barra et al. revealed being female, older age, comorbid diabetes mellitus, previously known CAD and LV dilatation were associated with an increased risk of IMR in echocardiography performed during hospitalization.<sup>7</sup>

Although IMR is more commonly seen in inferior STEMI and that with greater severity; its worse prognosis is seen in association with anterior STEMI as compared to inferior STEMI as studied by Mentias et al.<sup>10</sup>

There is evolving evidence that IMR is a strong predictor of risk after MI that provides prognostic value over other indicators of risk post MI.<sup>5,7,8,15,18</sup> IMR identification translates into adverse prognosis, higher post-MI mortality, in chronic heart failure patients and those who have undergone surgical or catheter revascularization.<sup>19</sup> Even mild IMR is known to increase mortality,<sup>22</sup> with a directly proportional relationship between severity and mortality.<sup>20</sup>

Lopez-Perez et al. found that moderate to severe IMR detected early with echocardiography independently predicted adverse long-term prognosis in STEMI patients treated with primary PCI. Even when effect modifiers were adjusted moderate to severe IMR sustained itself an independent predictor of all-cause mortality or admission due to heart failure during follow-up.<sup>21</sup>

Our study had few limitations: First, the presence of pre-existing MR before the index acute MI cannot be reliably excluded as data from a prior echocardiographic examination was not available for most of our patients; nonetheless, the reported frequency of IMR in our study exceeds what has been documented in the general population, hence it was most likely attributable to the acute MI. Second, the data presented in our study reported only on the frequency of IMR after acute MI; short-, medium- and long-term outcome data are not available for these patients. Third, our results cannot be directly deduced to other subgroup of acute MI patients such as those not receiving primary PCI.

As MR begets MR chronically through mechanisms of increased volume loading on the left ventricle and annular dilatation, therefore precise echocardiographic diagnosis and follow up are essential for targeted therapies.

## CONCLUSION

Ischemic MR is common and was prevalent in more than one-third of the patients presenting with acute ST-elevation MI. Moderate to severe grade of mitral regurgitation was found in about one-third of patients with IMR. Various clinical factors have been found to be associated with IMR; such as duration of symptoms, type of myocardial infarction, diabetes mellitus, hypertension and smoking status, which can play an important role in risk stratification and early prediction of this condition. These patients should be maintained in close follow-up after their discharge. These patients should also be offered more aggressive therapies to delay adverse left ventricular remodeling and alleviate the adverse prognostic impact of IMR.

## AUTHORS' CONTRIBUTION

KK and NUK: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. FQ, MTF, KIB, and PA: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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## REFERENCES

- Ralapanawa U, Sivakanesan R. Epidemiology and the magnitude of coronary artery disease and acute coronary syndrome: A narrative review. *J Epidemiol Glob Health* 2021 Jun; 11(2):167-177.
- Yusuf S, Rangarajan S, Teo K, Islam S, Li W, Liu L, et al. Cardiovascular risk and events in 17 low-, middle-, and high-income countries. *N Engl J Med* 2014 Aug 28;371(9):818-27.
- Sun VY, Liu C, Staimez L, Ali MK, Chang H, Kondal D, et al. Cardiovascular disease risk and pathophysiology in South Asians: can longitudinal multi-omics shed light? *Wellcome Open Res* 2021;20(5):255.
- Barolia R, Sayani AH. Risk factors of cardiovascular disease and its recommendations in Pakistani context. *J Pak Med Assoc* 2017;67(11):1723-1729.
- Piérard LA, Carabello BA. Ischaemic mitral regurgitation: pathophysiology, outcomes and the conundrum of treatment. *Eur Heart J* 2010; 31:2996-3005.
- Dudzinski DM, Hung J. Echocardiographic assessment of ischemic mitral regurgitation. *Cardiovasc Ultrasound* 2014; 12:46.
- Barra S, Providencia R, Paiva I, Gomes PL, Seca L, Silva J, et al. Mitral regurgitation during a myocardial infarction- new predictors and prognostic significance at two years of follow-up. *Acute Cardiac Care* 2012;14(1):27-33.
- Fazlinezhad A, Dorri M, Azari A, Bigdelu L. Frequency of ischemic mitral regurgitation after first-time acute myocardial infarction and its relation to infarct location and in-hospital mortality. *J Tehran Heart Cent* 2014;9 (4):160-5.
- Mengal MN, Badini AM, Iqbal Z, Achakzai AS, Jamali T. Severity and frequency of mitral regurgitation in patients presenting with acute ST-elevation myocardial infarction. *Pak Heart J* 2016;49(03):95-101.
- Mentias A, Raza MQ, Barakat AF, Hill E, Youssef D, Krishnaswamy A, et al. Outcomes of ischaemic mitral regurgitation in anterior versus inferior ST elevation myocardial infarction. *Open Heart* 2016;3(2): e000493.
- Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Fourth universal definition of myocardial infarction (2018). *J Am Coll Cardiol* 2018; 72(18):2231-44.
- Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin II JP, Gentile F, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease. *Circulation* 2021;143: e72-e277.
- Razak MNA, Khalil AS. The frequency of acute ischemic mitral regurgitation post-acute ST- elevation myocardial infarction. *IISR* 2017;6(11):1667-1672.
- Kumanohoso T, Otsuji Y, Yoshifuku S, Matsukida K, Koriyama C, Kisanuki A, et al. Mechanism of higher incidence of ischemic mitral regurgitation in patients with inferior myocardial infarction: Quantitative analysis of left ventricular and mitral valve geometry in 103 patients with prior myocardial infarction. *J Thorac Cardiovasc Surg* 2003; 125:135-143.
- Bursi F, Enriquez-Sarano M, Nkomo VT, Jacobsen SJ, Weston SA, Meverden RA, et al. Heart failure and death after myocardial infarction in the community: The emerging role of mitral regurgitation. *Circulation* 2005; 111:295-301.
- Abouomar MA, Shouib O, Hassan TM, Elsheikh A. Impact of percutaneous reperfusion on ischemic mitral regurgitation in patients presented with inferior ST elevation myocardial infarction. *J Cardiol Curr Res* 2021; 14(1):17-22.
- Nishino S, Watanabe N, Kimura T, Enriquez-Sarano M, Nakama T, Furugen M, et al. The course of ischemic mitral regurgitation in acute myocardial infarction after primary percutaneous coronary intervention: From emergency room to long-term follow-up. *Circ Cardiovasc Imaging* 2016;9: e004841.
- Bursi F, Enriquez-Sarano M, Jacobsen SJ, Roger VL. Mitral regurgitation after myocardial infarction: A review. *Am J Med* 2006; 119:103-112.
- Brescia AA, Watt TMF, Bolling SF. Ischemic mitral regurgitation: current understanding and surgical options. *Indian J Thorac Cardiovasc Surg* 2020;36(1):527-533.
- Sharma H, Radhakrishnan A, Nightingale P, Brown S, May J, O'Connor K, et al. Mitral regurgitation following acute myocardial infarction treated by percutaneous coronary intervention- prevalence, risk factors, and predictors of outcome. *Am J Cardiol* 2021; 157:22-32.
- Lopez-Perez M, Estevez-Loureiro R, Lopez-Sainz A, Couto-Mallon D, Soler-Martin MR, Bouzas-Mosquera A, et al. Long-term prognostic value of mitral regurgitation in patients with ST-segment elevation myocardial infarction treated by primary percutaneous coronary intervention. *Am J Cardiol* 2014; 113:907-912.

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