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SEVERITY AND FREQUENCY OF MITRAL REGURGITATION IN PATIENTS PRESENTING WITH ACUTE MYOCARDIAL INFARCTION

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Contribution
NMM conceived idea, planned study and did statistical analysis. AMB critically reviewed manuscript. ZI collected data. ASA, TJ drafted final manuscript. All authors contributed significantly to the submitted manuscript.

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ABSTRACT

Objectives: The aim of our study was to determine the frequency and severity of MR in patients presenting with STEMI after emergency reperfusion treatment with primary percutaneous coronary Intervention (P-PCI) or streptokinase (SK) during hospital stay.

Methodology: This cross-sectional study was conducted at National Institute of Cardiovascular Diseases (NICVD), Karachi for six month of duration from 1st August 2013 to 31st January 2014. Patients of both genders aged between 20-60 years presenting with STEMI who underwent emergency reperfusion therapy with primary percutaneous coronary Intervention (P-PCI) or streptokinase (SK) were included in the study. Descriptive analyses were performed for socieo-demographic characteristics while Chi-square test was applied for the association of different characteristics among various categories of mitral regurgitation.

Results: Total of 262 patients were included in the study with mean age of 53.9±7.1 years. Of them 68% of the patients were males. Mitral regurgitation (mild, moderated and severe) with different characteristics was found in 58% (152) patients .Elderly patients with acute inferior wall MI (IWMI) and those receiving SK were more likely to have MR. Furthermore patients with IWMI and those receiving SK were more likely to suffer from severe grade of MR ($p \leqslant 0.05$).

Conclusion: MR is a frequent complication of STEMI and it was more frequent in patients with IWMI or who received SK as a mean of emergency thrombolysis.

Key Words: ST Elevation Myocardial Infarction, Mitral Regurgitation, Streptokinase, Primary PCI

INTRODUCTION

Globally cardiovascular disease remains the leading cause of morbidity and mortality. Despite marked advances in the field of mechanical and pharmacological therapies for coronary artery disease there is a large gap in the utilization of these effective therapies.[1] Community incidence rates for STEMI have declined over the past decade, whereas those for Non–ST elevation ACS have increased. Currently, STEMI comprises around 25% to 40% of MI presentation.[2] The mortality rate in hospitals regarding STEMI is 5% to 6% while one year mortality rate is about 7% to 18%, which have decreased significantly because of a substantial increase in care of these patients that includes guideline directed medical treatment and interventions.[3] Even in United States, important regional differences exist in 30-day in hospital mortality and readmission rates of STEMI.[4]

Patients who survive an acute event of STEMI are at greater risk of future cardiovascular complications and mortality. Soon after the acute event, risk stratification can identify the patients who are at increased risk of recurrent events. In addition to the standard medical treatment these high risk patients require more aggressive management. Adverse risk factors affecting the mortality rate of patients with STEMI include ischemic mitral regurgitation (MR), recurrent myocardial infarction (MI), pump failure, arrhythmias, recurrent ischemia, hyperlipidemia and hyperglycemia.[5] Mitral regurgitation arises in many cases after ischemic myocardial changes despite anatomically normal mitral leaflets and chordae.[6] Mitral regurgitation itself is associated with an increased cardiovascular mortality after acute STEMI and may cause significant morbidity and a worse prognosis even when the regurgitation is mild or asymptomatic.[7,8]

Globally literature reported the prevalence of mitral regurgitation in the range of 10% to 50% in patients after acute STEMI.[8] Data from VALIANT trial showed that after STEMI the frequency of mild, moderate and severe mitral regurgitation was 40.7 %, 9.9 % and 2.8 % respectively.[8,9] It demonstrated that higher degree of mitral regurgitation is independently associated with an increased risk of overall mortality, cardiovascular mortality, and hospitalization for heart failure.[9] A study conducted in Lahore reported frequency of Doppler detected mitral regurgitation to be 65.2% after acute STEMI.[10]

Mitral valve itself is normal but abnormalities in left ventricular (LV) volume, function, and shape have led to mitral regurgitation.[11] In addition, ventricular dilatation results in annular enlargement, which further increases valve incompetency.[12] Conversions of the LV shape from an ellipsoid to a rounder sphere further exacerbates this problem. As volume overload is added to the pathophysiological process it further increases the annular dimensions and worsens the papillary muscle alignment further increasing the amount of leak and setting up a perpetual cycle. This cycle subsequently has important effects on LV geometry and pathophysiology of MR.[13] Although MR has often been viewed as an after load reducing lesion, the ventricular dilation associated with MR increases the radius term in the Laplace equation.[14] Thus, the effect of MR on LV geometry is to increase ventricular wall stress despite the unloading effect of the leak itself. Increased load further worsens LV performance, leading to further hemodynamic compromise. It is clear that acute MR worsens the prognosis, but it is unclear whether poorer outcome stems from the MR itself or is simply a marker for worsening LV function and heart failure.[15,16]

Studies do not preclude a potential for benefit from mitral valve repair or replacement in selected patients. Indeed, annuloplasty has been of benefit in some patients at least in terms of LV function. So far, virtually nothing is known about the mortality benefits of either therapy on this disease, data is awaited from on going randomized trials. In the future, it is likely that both restraint and valve surgery will be beneficial. The identification of patients who will benefit from such therapies have yet to be defined.[16] Thus, detecting and quantifying ischemic mitral regurgitation is essential, because its presence plays a vital role in post-MI risk stratification and management.[16]

Therefore the aim of our study was to determine the frequency and severity of mitral regurgitation post emergency reperfusion treatment during hospital stay, in patients presenting with acute ST elevation myocardial infarction in a tertiary care hospital at Karachi.

METHODOLOGY

This was a cross sectional study conducted in National Institute of Cardiovascular Diseases (NICVD), Karachi for six month of duration from 1st August 2013 to 31st January 2014. The patients were selected through non-probability consecutive sampling. We included all patients both male and female, between the ages of 20-60 years, presenting with the diagnosis of Acute ST elevation myocardial infarction (STEMI) who underwent emergency reperfusion treatment either with Primary PCI or Streptokinase within 3 days of admission. We excluded patients with prior diagnosis of MR complicating acute STEMI, patients having causes of Mitral Regurgitation other than acute STEMI and those who refused to provide informed consent. Sample size was calculated using WHO sample size calculator. Using 95% confidence level, anticipated population proportion (P) of severe mitral regurgitation in 2.8%[6] of acute ST elevation myocardial infarction and absolute precision (d) of 5%, the sample size for prevalence was estimated.

Mitral Regurgitation was taken as the backflow of blood into the left atrium (LA) from left ventricle (LV) in systole

(contraction of LV) through mitral valve on echo-cardiography. MR was graded as per echo findings i.e: **None:** Absent of backflow of blood from Left Ventricle to Left Atria

Mild MR: Presence of back flow of blood occupying less than 20% of Left Atrium

Moderate MR: Presence of back flow of blood occupying 20% to 40% of LA area

Table 1: Demographic details of the study population in tertiary care hospital, Karachi. (n=262)

Characteristics	Frequency (n)	Percentages (%)
Age		
20-40yrs	20	8
41-60yrs	242	92
Gender		
Male	178	68
Female	84	32
DM duration	100	38
<10yrs	52	20
=10yrs	48	18
HTN duration	146	56
<10yrs	88	34
=10yrs	58	22
Smoking duration	152	58
<10yrs	34	13
=10yrs	118	45
Length of stay in hospital		
1—4days	222	85
5—7days	38	14
>7days	02	1
Type of acute STEMI		
AWMI	170	65
IWMI	98	37
LWMI	12	5
Treatment Received		
SK	160	61
PPCI	102	39
MR		
None	110	42
Mild	112	43
Moderate	38	14
Severe	02	1

Severe MR: Presence of back flow of blood occupying more than 40% of the LA area

Acute ST segment Elevation Myocardial Infarction (STEMI) was defined as history of chest pain / discomfort for more 30 minutes; ST-segment elevation of more than or equal to 1 mm in two consecutive ECG leads and presence of elevated cardiac isoenzyme Troponin I of $>0.5\mu g/ml$.

Types of Acute STEMI defined as:

Acute Anterior Wall MI: ST segment elevation in anterior group of leads i.e. V1 - V6

Acute Inferior Wall MI: ST segment elevation in inferior group of leads i.e. II, III and aVF.

Acute Lateral Wall MI: ST segment elevation in lateral group of leads i.e. I, aVL, V5 and V6.

Patients were enrolled from Department of Adult Cardiology, NICVD. Informed consent was obtained from all the patients after explaining study protocol. The detailed history of chest pain, electrocardiogram (ECG) and serum Troponin I (TnI) level and type of acute STEMI as per operational definitions were noted. Patients underwent standard transthoracic 2-dimensional (2D) and Doppler echocardiography for diagnosis and grading of MR during the hospital stay.

Data was statistically analyzed by using statistical package for social sciences (SPSS) version 17. The descriptive analysis was performed by calculating frequencies and percentages of categorical variables (gender, diabetes mellitus, hypertension, smoker, type of acute STEMI, type and severity of MR and type of treatment received. Mean and standard deviation (SD) were calculated for continuous variables such as age of the participant, duration of smoking, HTN, DM and length of stay in hospital. To determine the association for the mitral regurgitation with different factors; duration of smoking, length of stay, type of STEMI, treatment received, age, gender, diabetes mellitus , duration of diabetes mellitus, hypertension, duration of hypertension; Chi-square test was applied and $p \leqslant 0.05$ was taken as significant.

Ethical approval was taken from the hospital ethical review committee prior to the commencement of the study.

RESULTS

A total of 262 patients were included in the study. Mean age of study participants was 53.9 ± 7.18 years with minimum of 27 years and maximum of 60 years. Out of total only 8% (20) of the patients were young i.e. in age group of 20-40 years and 92% (242) belonged to 41-60 years. Of them 68% were males. The demographic details of the study population are shown in Table1.

Frequency distribution of mitral regurgitation categories

Table 2: Frequency Distributions Among Types of Mitral Regurgitation MR with Different Characteristics in Tertiary Care Hospital in Karachi (n=262)

Variables	Mitral Regurgitation								P value
	None		Mild		Moderate		Severe		
	n	%	n	%	n	%	n	%	
Age									
20-40yeas	07	35	10	50	03	15	00	00	0.70
41-60yrs	103	43	102	42	35	14	02	01	
Gender									
Male	79	44	78	44	20	11	01	01	0.05
Female	31	37	34	41	18	21	01	01	
DM									
No	76	47	62	38	24	15	00	00	0.08
Yes	34	34	50	50	14	14	02	02	
Duration of DM									
<10yrs	24	46	22	42	04	08	02	04	0.001
>10yrs	10	21	28	58	10	21	00	00	
HTN									
No	48	41	58	50	10	09	00	00	0.17
Yes	62	43	54	37	28	19	02	01	
Duration of HTN									
<10yrs	44	50	28	32	14	16	02	02	0.04
>10yrs	18	31	26	45	14	24	00	00	
Smoking									
No	50	45	44	40	14	13	02	02	0.55
Yes	60	39	68	44	24	16	00	00	
Duration of smoking									
<10yrs	08	23	20	59	06	18	00	00	0.99
>10yrs	52	44	48	41	18	15	00	00	
Length of stay									
1-4days	110	50	112	50	00	00	00	00	0.001
5-7days	00	00	00	00	38	100	00	00	
>7days	00	00	00	00	00	00	02	100	
Type of STEMI									
AWMI	76	45	72	42	22	13	00	00	0.07
IWMI*	34	35	42	43	20	20	02	02	0.01
LWMI	08	66	02	17	02	17	00	00	0.24
Treatment received									
SK	50	31	84	53	24	15	02	01	0.001
PPCI	60	59	28	27	14	14	00	00	0.001

among different age groups showed in figure 1.

Of them 58% (152) developed mitral regurgitation:43% (112) had mild , 14% (38) had moderate and 1% (2) had severe mitral regurgitation. Males had slightly higher frequency of mitral regurgitation as compared to female: 44% had mild, 11% had moderate while 1% had severe mitral regurgitation ($p<0.05$). Among diabetic patient with more than 10 years history of; mild mitral regurgitation was found in 58% while 21% had moderate and none had sever mitral regurgitation, while those patients having history of DM less than 10 years mild, moderate and severe mitral regurgitation was found in 42%, 8% and 4% respectively ($p<0.05$). Similar trend was observed for duration of hypertension of more than 10 years with mitral regurgitation ($p<0.05$). There was significant association between severity of mitral regurgitation and IWMI and length of stay in

hospital ($p<0.05$). (Table 2)

DISCUSSION

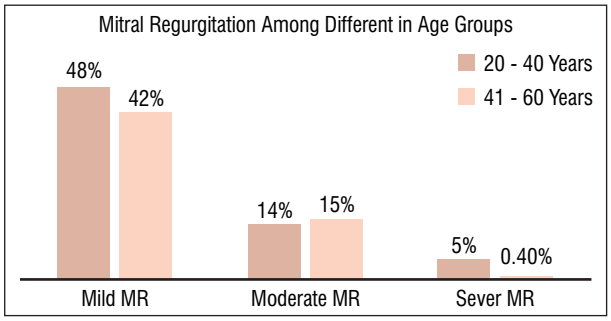
Mitral regurgitation is known to be a frequent complication of AMI. When present, it may exhibit a broad range of severity, from clinically evident and hemodynamically obvious to clinically silent and detected only as an incidental finding on catheterization or Doppler echocardiography.[17] Indeed, when it is sought by Doppler, MR has been reported to occur in up to 39% of patients with MI.[18] Papillary muscle dysfunction and associated dysfunction of the underlying ventricular wall are thought to be the most common cause of MR in post-AMI patients, and MR has generally been identified as a more frequent complication of inferior than anterior infarction.[19,20] Even MR may place an additional hemodynamic stress on the LV it was found that AMI patients with a murmur suggestive of MR had a 12-month mortality of 36% compared with 15% for patients without MR murmur.[21] However, correction for differences in baseline variables indicated that the presence of MR murmur was not an independent predictor of outcome. In contrast, Lehmann et al found that MR present on left ventriculography within 7 hours of MI was an independent predictor of survival at 1 year.[22] Another study found that moderately severe to severe MR appeared to be a likely independent predictor of impaired survival.[23] A study defined MR by physical examination and found it to be present in 17% of their patients with MI.[24] Patients with a systolic murmur had a 1-year mortality of 18% compared with 10% for those without a regurgitate murmur.

In VALLIANT trial it was found that among patients with LVSD, HF, or both after acute MI, the degree of MR at baseline was associated with worse LV function, greater LV enlargement and chamber distortion and worse mitral annular contraction.[9] Presence and grade of MR at baseline was significantly and independently associated with death and other adverse clinical outcomes.[9] Data from VALIANT trial showed that after STEMI the frequency of mild, moderate and severe MR was 40.7 %, 9.9 % and 2.8 % respectively, and in our study almost comparable results were found, frequency of mild, moderate and severe MR being 43%, 15%, 1% respectively. The low frequency of severe MR in our study may partially be explained by increased rates of Primary PCI.[9]

It has also been shown that MR has an independent prognostic value after acute and chronic MI.[6,25,27-29] In majority of the patients with MR following MI; MR is functional rather than due to abnormalities of the mitral valve apparatus itself.[27-29] And in these patients, the papillary muscles, chordae, and valve leaflets are normal, but changes in ventricular geometry displaces the attachments of the mitral leaflets to the papillary muscles and annulus thereby restricting their ability to close effectively at the annular level, with resulting decrease in the LV generated leaflet closing force.[30,31]

In our study worse MR was more common in older people, as has been shown in other studies[6,25,28,32-34] One of the study established the relationship between severity of MR and infarct location being more severe and more common in inferior wall MI.[27] Similarly, another study showed that even mild MR was associated with increased ventricular size, worse ventricular function, and alterations in ventricular geometry in patients with STEMI complicated by systolic dysfunction or heart failure.[28] And it was observed that MR in early post-infarct period was an independent and important predictor of death or development of HF following MI and even during the first month after MI , progression of MR was a potent predictor of subsequent outcome. In such patients accurate assessment of MR and its progression following MI may help to identify a particularly high-risk group who may benefit from aggressive adjunctive medical or surgical therapy.[35]

Figure 1: Frequency Distribution of Mitral Regurgitation (MR) Among Different Age Groups in Tertiary Care Hospital in Karachi (n=262)



LIMITATION AND FUTURE RECOMMENDATION

There were some limitations of our study. In our study we graded MR by color flow Doppler, mapping regurgitant jet expansion within the LA, a method that may have resulted in miscalculation of MR in some patients and more rigorous evaluation of regurgitant mitral lesions is possible using volumetric-based techniques such as proximal isovelocity surface area (PISA) method, but this is technically more challenging and less widely used technique. Nevertheless, the mitral jet area to LA ratio correlated well with effective regurgitant orifice area determined by the PISA method, in direct comparison of techniques in a single centre.[35]

This was a cross sectional study and hence an association between variables cannot be established (cause-effect relationship). We performed non probability sampling which might led to the under-representation or over-representation of a particular group within the sample. The data only reported in-hospital outcomes, hence medium and long

term outcomes of these patients were not available. The data reported only echo report within 3 days of hospital admission and not after discharge. However, the risk prediction models are based on early complications posed by MR in STEMI patients. Presentation of MR might be due to ischemic LV dilatation which may be the cause or consequence of ischemia and infarction, resulted in heart failure and increased morbidity and mortality.

Early recognition of this mechanical complication of STEMI is essential for timely management. In severe MR guidelines recommend early surgical intervention. In patients with STEM it is mandatory to rule out post MI complications, risk stratify the patient and select optimal management during the hospital stay and after discharge. With a thorough patient history, electrocardiographic monitoring, cardiac biomarker measurements and echocardiography one can assess the risk of death and recurrent events, from the time the STEMI patients arrive at the emergency department, throughout their hospitalization, and beyond. After echocardiography and risk assessment an early invasive-treatment with/ without surgery is strategy of most benefit to high risk patients with moderate to severe MR, whereas an early conservative strategy is recommended for low risk patients.

CONCLUSION

MR is a common complication of STEMI.It was more frequent in older patients, those with inferior wall MI or who received SK as a mean of emergency thrombolysis.

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