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Impact of Treatment Delay on Mortality in ST-Segment Elevation Myocardial Infarction Patients with and Without Hemodynamic Instability

Asma Murtaza[1], Ambreen Haider[2], Ashok Kumar[3], Javed Khurshed Shaih[4], Javeria Amjad[5], Shahid Hussain Memon[6]

[1]Consultant Cardiologist, Department of Emergency Cardiology & Cath Lab, NICVD, Karachi
[2]Consultant Cardiologist, BMC for Boys LUKHS, Jamshoro
[3]Assiatnt Professor, National Institute of Cardiovascular Diseases (NICVD), Hyderabad
[4]Associate Professor, National Institute of Cardiovascular Diseases (NICVD), Sukkur
[5]Assitant Professor of Cardiology Indus Medical College T M khan, (Ex. Resident LUMHS)
[6]Associate Professor, Cardiology department LUMHS Jamshoro

Author`s Contribution

[1,2]Substantial contributions to the conception or design of the work; or the acquisition, [4,6]Active participation in active methodology, [2,3]analysis, or interpretation of data for the work, [5,6]Drafting the work or revising it critically for important intellectual content

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Address of Correspondent
Dr Ambreen Haider
Consultant Cardiologist, BMC for Boys LUKHS/ Jamshoro
ambreenambreen802@yahoo.com

ABSTRACT

Objective: To determine the frequency of mortality associated with delayed treatment time in ST-Segment Elevation Myocardial Infarction (STEMI) patients undergoing primary PCI, with and without hemodynamic instability.

Methodology: A descriptive cross sectional study was done at Department of Emergency Cardiology & Cath Lab, National Institute of Cardiovascular Diseases (NICVD), Karachi, Pakistan from June 2019 to December 2019. Patients between age of 30 to 70 years, both genders, presented with STEMI patients diagnosed undergoing primary PCI with treatment delay defined as the time > 90 minutes from admission to the hospital until the start of primary angioplasty were included. These patients were observed for 48 hours post PCI in ward to assess outcome in terms of mortality with respect to the hemodynamic instability. All the collected information was entered and analyzed using SPSS version 26.

Results: Overall mean of the patients was 55.2±9.5 years. Out of 153 patients, 105 (68.6%) were male while 48 (31.4%) were female. Positive family history was noted in 53 (34.6%) patients while 100 (65.4%) had no family history of heart disease. Mortality occurred in 10(6.5%) of the patients, which was higher among patients with unstable hemodynamics, old age (>50 years), males and smokers, while the findings were statistically insignificant (p>0.05). Likewise, diabetes, obesity, and family history showed no significant association with mortality (p>0.05).

Conclusion: Time to primary PCI is strongly associated with mortality risk with non-significant difference in stable versus unstable hemodynamic patients. Efforts to shorten door-to-balloon time should apply to all patients.

Keywords: Mortality, STEMI, Primary PCI, Hemodynamic Instability.

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Introduction

Acute STEMI presents suddenly and is associated with considerable mortality. Evidence from European research indicates that in-hospital mortality among STEMI patients ranges from 4% to 12%, while the mortality rate within one year is around 10%.[1,2] Pakistan, a developing nation in South Asia, has nearly two-thirds (67.5%) of its population residing in rural regions, where the burden of cardiovascular disease is particularly high.[3] Around 30% of individuals affected by heart disease in the country are older than 45 years.[3] Management of STEMI necessitates rapid revascularization of the culprit vessel, with percutaneous coronary intervention (PCI) within 120 minutes of first medical contact being the treatment of choice. For patients who are not suitable for PCI within this timeframe, fibrinolytic therapy may serve as an alternative, Achieving coronary artery perfusion without delaying is the cornerstone of life-saving therapy among patients with ST-segment elevation MI.[4] Given the strong

association between treatment delays and adverse outcomes, national guidelines in the United States highlights the specific time-to-treatment targets, beginning from the point of first medical contact.[4,5] The primary challenge in managing ST-segment elevation MI lies in delays to reperfusion therapy, since the greatest therapeutic benefit is achieved within the initial hours after symptom onset. Consequently, designing an optimal revascularization strategy that also considers the prevailing social and cultural factors is critically important.[6]

According to the current European Society of Cardiology (ESC) STEMI guidelines, the recommended cut-off of 90 to 120 minutes from diagnosis to PCI mediated reperfusion, used to determine whether PCI or fibrinolysis should be performed, is derived from old reports registries and trials that employed treatment approaches different from those outlined in present guidelines.[7] However, many patients are unable to receive treatment within this recommended time frame due to several factors, most commonly geographic distance, the need for clinical stabilization prior to transfer, and delays during transportation. Among STEMI patients treated with primary PCI, those presenting with cardiogenic shock experience significantly worse outcomes when reperfusion is delayed, underscoring the urgent need for rapid revascularization in this high-risk group.[9] Furthermore, patients with hemodynamic instability or cardiogenic shock face a particularly poor prognosis, with in-hospital mortality rates often ranging from 40% to 60%, and therefore derive critical benefit from immediate culprit-vessel intervention whereas any delay in PCI markedly increases their risk.[10] Overall as per above literature the STEMI is a critical emergency where timely reperfusion is vital to reduce mortality, yet many patients particularly in resource-limited settings fail to receive primary PCI within the recommended 90 to 120 minutes. Additionally the impact of these delays is even more critical in patients presenting with hemodynamic instability or cardiogenic shock, who carry the highest risk of adverse outcomes. However, due to the lack of local evidence quantifying how treatment delays affect mortality in this subgroup compared to stable cases. Present study therefore conducted aims to provide context-specific evidence on how reperfusion delays influence mortality in STEMI patients with and without hemodynamic instability.

Methodology

This descriptive cross sectional study was conducted at department of Emergency Cardiology and Cath Lab, National Institute of Cardiovascular Diseases (NICVD), Karachi. Study duration was six months from June 2019 to December 2019. A sample size of 153 patients was calculated using frequency of mortality in delayed treatment among patients undergoing primary PCI (17.3%),[11] with margin of error (d)=6%, and confidence level (1-a)=95%. Non-probability, consecutive sampling technique was used. All the patients between 30 to 70 years of age, both genders, presented with STEMI patients diagnosed undergoing primary PCI with treatment delay defined as the time > 90 minutes from admission to the hospital until the start of primary angioplasty were included. Patients who underwent primary PCI and treatment delay in accordance with operational definition. All the patients with pre-hospital delay longer than 12 hours, transferred from other hospitals, renal impairment, creatinine values greater than 2.5 g/dl (this is to avoid the negative effects related to the contrast medium given in angiography), prior history of cardiac surgery and PCI, heart failure, if received thrombolytic therapy and patients had severe anemia (Hb< 7g/dl) were excluded. Informed written consent was taken after explaining the potential benefits and risks of the study. Those who gave the consent were only included in the study. All these patients underwent primary PCI under the supervision of senior registrar or consultant cardiology had 5 years of experience. These patients were observed for 48 hours post PCI in ward to assess outcome in terms of mortality with respect to the hemodynamic instability. Hemodynamic instability was defined operationally as the presence of all of the following clinical findings on assessment: an abnormal heart rate or arrhythmias, typical chest pain, cold extremities (hands, arms, legs, or feet) or bluish discoloration of these areas indicating peripheral cyanosis, and hypotension defined as a blood pressure less than 90/60 mmHg. All the collected information was noted and recorded in the Performa attached. Confounding, explanatory variables and biasness were controlled by strictly following inclusion and exclusion criteria. Data was analyzed by SPSS version 25.0. Mean ± Standard deviation were calculated for age and delayed treatment time. Frequency and percentage were calculated for gender, smoking status, diabetes mellitus, obesity, family history of heart disease, hemodynamic instability and outcome variable i.e. mortality (yes/no). Comparison between with and without hemodynamic instability was done for mortality due to treatment by using Chi-square test. Data was stratified for

effect modifiers / confounders like age, delayed treatment time, gender, diabetes mellitus, obesity, family history of heart disease and smoking status. Stratified groups were compared by using Chi- square test / Fisher Exact test as appropriate, taking $P \leq 0.05$ as significant.

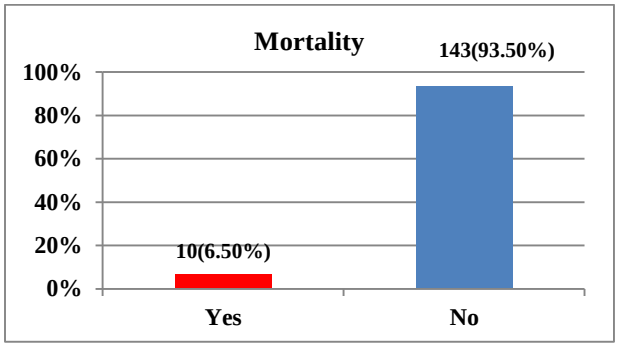
Results

Overall 212 patients were included after equally divided Overall 153 patients were included with a mean parental age of 55.2 ± 9.5 years. The mean delay time was 105.8 ± 12.4 minutes. Among the participants, 105 (68.6%) were male and 48 (31.4%) were female. Diabetes mellitus was present in 72 patients (47.1%), while 81 (52.9%) had no diabetes. Hypertension was reported in 60 patients (39.2%), whereas 93 (60.8%) did not have hypertension. Obesity was observed in 70 patients (45.8%), while 83 (54.2%) were non-obese. A positive family history was noted in 53 patients (34.6%), compared to 100 (65.4%) with a negative history. Smoking was reported by 63 patients (41.2%), while 90 (58.8%) were non-smokers. Regarding hemodynamic status, 40 patients (26.1%) were stable, whereas the majority, 113 (73.9%), presented with unstable hemodynamics. Table I

Table I: Demographic and clinical characteristics of the patients. (n=153)

Variables		Statistics
Mean age of the parents	Mean	55.2 years
	Standard deviation	9.5 years
Mean delayed time	Mean	105.8 Minutes
	Standard deviation	12.4 Minutes
Gender	Male	105,(68.6%)
	Female	48,(31.4%)
Diabetes mellitus	Yes	72,(47.1%)
	No	81,(52.9%)
Hypertension	Yes	60,(39.2%)
	No	93,(60.8%)
Obesity	Yes	70,(45.8%)
	No	83,(54.2%)
Family history	Positive	53,(34.6%)
	Negative	100,(65.4%)
Smoking	Yes	63,(41.2%)
	No	90,(58.8%)
Hemodynamic stability	Stable Hemodynamic	40,(26.1%)
	Unstable Hemodynamic	113,(73.9%)

Mortality was observed in 10 patients, accounting for 6.5% of the study population. Figure 1



Mortality was slightly higher in patients with unstable hemodynamics (7, 4.6%) compared to stable ones (3, 2.0%), though not statistically significant (p=0.512). Older patients (>50 years) showed higher mortality (6, 3.9%) than those aged 30–50 years (4, 2.6%) (p=0.422). Mortality was more frequent in males (7, 4.6%) than females (3, 2.0%) (p=0.614). With respect to treatment delay, 6 deaths (3.9%) occurred in patients treated within 90–120 minutes and 4 deaths (2.6%) in those treated after 120 minutes (p=0.602). Diabetes and obesity each accounted for 5 deaths (3.3%) among affected patients and 5 deaths (3.3%) among non-affected patients, showing no significant association (p=0.551 and p=0.516, respectively). A family history of disease was present in 3 deaths (2.0%) versus 7 deaths (4.6%) in those without (p=0.523). Similarly, smoking was linked to 6 deaths (3.9%) compared to 4 deaths (2.6%) in non-smokers (p=0.606). Table II

Table II: Incidence of mortality according to effect modifies. (n=153)

HEMODYNAMIC STABILITY		MORTALITY		P-value
		YES	NO	
Hemodynamic stability	Stable Hemodynamic	3(2.0%)	37(24.2%)	0.512
	Unstable Hemodynamic	7(4.6%)	106(69.3 %)	
Age groups	30 – 50 years	4(2.6%)	46(30.1%)	0.422
	>50 years	6(3.9%)	97(63.4%)	
Gender	MALE	7(4.6%)	98(64.1%)	0.614
	FEMALE	3(2.0%)	45(29.4%)	
Treatment time	90 – 120 minutes	6(3.9%)	87(56.9%)	0.602
	120 minutes	4(2.6%)	56(36.6%)	
Diabetes mellitus	Diabetic	5(3.3%)	76(49.7%)	0.551
	Non-diabetic	5(3.3%)	67(43.8%)	
Obesity	Obese	5(3.3%)	65(42.5%)	0.516
	Non-Obese	5(3.3%)	78(51.0%)	
Family history	Positive	3(2.0%)	50(32.7%)	0.523
	Negative	7(4.6%)	93(60.8%)	
Smoking	Smoker	6(3.9%)	84(54.9%)	0.606
	Non-Smoker	4(2.6%)	59(38.6%)	

Discussion

Early reperfusion remains the sources of STEMI management, and even uncertain delays can significantly impact survival of the patients. Although the advances in reperfusion strategies, the delay in the treatment continues to be a major factor of in-Hospital mortality, specifically among patients presenting with hemodynamic instability. Additionally, the association between treatment delay and baseline hemodynamic status has therefore emerged as a critical prognostic factor, since unstable patients face both higher risk and are more likely to get ischemic injuries. In this study, 153 patients were included, with a mean age of 55.2 ± 9.5 years and 68.6% were male while 31.4% were female. In line with this study, Zameer I et al[12] reported an average patient age of 53.2±15.5 years, and most of their patients were male (130, 91.5%). Comparatively, the mean age in this study was slightly higher than that reported by Ashraf S et al[13], where the mean age of patients was 46.62±9.76 years, with a consistent male predominance (75.27% males and 24.73% females). Overall male predominance in ST-elevation MI across the studies may because males have higher exposure to risk factors including stress, smoking, and unhealthy lifestyles, and may develop CVD at younger age than women compared to females.

In this study, according to the hypothesized risk factors, the 47.1% of patients had diabetes, 39.2% had hypertension, 45.8% were obese, 34.6% had a positive family history, and 41.2% were smokers. Consistently Ashraf S et al[13], reported that the among 88 patients (47.3%) had diabetes, 85 (45.7%) patients were hypertensive, and 55 (29.6%) were smokers. in the comparison of this study Khowaja S et al[14] reported that the 39.8% of patients had DM, 50.5% had hypertension, 9.7% had dyslipidemia, 3.9% had chronic kidney disease, 35.9% were smokers, and 31.1% had a family history of IHD. On the other hand et al[15] demonstrated the most common risk factors were male gender (90.3%), obesity (48.3%), use of tobacco (45%), and a positive family history in 48.4% of then patients.

The outcome point there was observed in 10 patients, accounting for 6.5% of the study population. In the supporting to our observation, Ashraf S et al[13] found that patients admitted later after the onset of symptoms faced significantly higher in-hospital mortality rates. Consistently Jollis JG et al[4] reported that the adjusted in-hospital mortality was lower among patients treated within target times, with those achieving first medical contact to laboratory activation ≤20 minutes (3.6% vs 9.2%; adjusted OR 0.54) and first medical contact to device ≤90 minutes (3.3% vs 12.1%) indicated the significantly improved outcomes compared with those treated beyond time goals. Overall, 2.4% of patients died during hospitalization, with mortality significantly higher in the non-reperfusion group (5.3%) compared to those who received reperfusion therapy (2.1%) (P<0.001). On the other hand Nepper-Christensen L et al[16] observed that the prolonged symptom-to-primary PCI time correlated with an increased incidence of adverse clinical events among STEMI patients, particularly when the delay surpassed 12 hours. Delays in the diagnosis or inaccuracies may arise due to an incomplete medical history or difficulties in eliciting a precise description of the symptoms among patients. Thus, obtaining a comprehensive history and maintaining clear, detailed communication are crucial for recognizing the multifaceted presentation of ACS symptoms, which can facilitate the diagnosis early and accurately.[17] Clinically assessment focused should include both a concise medical history and an evaluation of presenting symptoms to ensure rapid direction toward the appropriate management strategies. Clinical examination must be systematic assessing all major pulses, measuring blood pressure in arms, auscultating cardiac and pulmonary sounds, and examining for indicators of heart failure or the instability in the circulation. Furthermore the patients should be questioned about the nature and pattern of chest pain, accompanying symptoms, cardiovascular risk factors or history, and any recently used drugs.[17]

Furthermore, the mortality was slightly higher in patients with unstable hemodynamics (7, 4.6%) compared to stable ones (3, 2.0%), though not statistically significant (p=0.512). Consistently Rubartelli P et al[18] reported that the after controlling for GRACE risk score tertiles and angiographic success, the Cox regression analysis identified comorbidity-related delays [HR 2.19] and hemodynamic instability [HR 2.05] as the strongest independent determinants of mortality among patients of reperfusion delay in the ST-elevation MI**.** supporting to this series Kochan A et al[9] reported that the patients with cardiogenic shock (CS) more frequently exceeded guideline-recommended first medical contact-to-device times (76.6% vs 54.1%, P < 0.001), and between 60–90 minutes, each 10-minute delay increased absolute mortality by 4%–7% in CS patients versus <0.5% in those without CS. In aligns to this study Scholz KH et

al[19] found that the patients with CS wihtout out-of-hospital cardiac arrest, every additional 10 minutes of treatment delay was linked to 3.31 extra deaths per 100 individuals undergoing PCI and such effect of delayed intervention on mortality was markedly greater than that observed in OHCA patients with shock (2.09) or without shock (1.34), and in hemodynamically stable individuals [(0.34) P-0.0001]. Additionally, in aligns to this study Ullah R et al[20] also reported that the in-hospital mortality was 29.8% in study population and showed a highly significant association with mitral regurgitation p-0.0001. Overall, delays in treatment, particularly among patients presenting with hemodynamic instability, were associated with increased mortality risk. However, the limited existing literature exploring this specific cause of mortality and few significant limitations of this study, like small sample size and relatively lenient sample selection criteria, indicating further larger scale and multicenter studies to confirm these findings and to guide evidence-based clinical management in this high-risk population.

Conclusion

In hospital mortality among STEMI patients was relatively low 6.5% and was not significantly linked to treatment delay. It was slightly higher in patients with unstable hemodynamics and in older age groups, without statistical significance, likely due to the limited number of deaths. These results suggest that while treatment delay and baseline risk factors remain important considerations, hemodynamic instability at presentation continues to be the strongest clinical marker of adverse outcomes. Due small number of events highlights the need for further larger multicenter studies to better define the independent predictors of mortality and to explore how treatment delays interact with hemodynamic status in determining prognosis.

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