Pak **Heart J**

VARIOUS DELAYS AND ITS DETERMINANTS IN THE TIMELINE OF ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

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Contribution
Idea conceived by TA, SnK, and SA, study designed by SnK, SA, and MK, study execution and data collection was done by SnK, SA, MKB, ShK, MN, and MKh, manuscript drafted by SnK, SA, MK, KAK, and MN, manuscript was critical reviewed by MKB and TA, and study was supervised by TA. All the authors contributed equally to the submitted manuscript.

All authors declare no conflict of interest.

This article may be cited as: Khowaja S, Ahmed S, Ashraf T, Batra MK, Khowaja S, Nazir M, Khan M, Karim M, Khowaja KA. Various Delays and Its Determinants in the Timeline of ST-segment Elevation Myocardial Infarction. Pak Heart J 2021;54(01):18–24.
https://doi.org/10.47144/phj.v54i1.2059

ABSTRACT

Objectives: To assess the various delays in the timeline of STEMI, its determinants, and impact on in-hospital outcomes.

Methodology: In this study we included STEMI patients who were either presented late to ER or procedure was delayed. Pre-hospital delay was defied as chest pain (CP) to ER arrival time ≥120 minutes and hospital delay was defined as ER to procedure time ≥90 minutes. Reasons for pre-hospital and hospital delays and in-hospital complications and outcomes were recorded.

Results: A total of 103 patients, 72.8%(75) male, with mean age of 54.75±11.8 years were enrolled. Median duration between CP and ER arrival 240[420-144.5] minutes with ≥120 minutes for 89.3%(92). Procedure was performed in 120[180-60] minutes of ER arrival with ≥90 minutes for 61.2% (63). Pre-hospital delay was caused by unawareness of symptoms (53.3%) followed by unavailability of transportation (29.3%), while, hospital delayed was caused by unavailability of resources (69.8%). Pre-hospital delay of ≥360 minutes was associated with higher rate of LV thrombus, 21.4% vs. 1.3%; p<0.001, and in-hospital re-current ischemia, 32.1% vs. 12%; p=0.017.

Conclusions: In this study we observed that the most common causes of pre-hospital delay in our population are unawareness of symptomology and unavailability of transportation, while, the major cause of hospital delay was unavailability resources. Pre-hospital delay was associated with significantly higher rate of LV thrombus and in-hospital re-current ischemia.

Keywords: ST-segment Elevation Myocardial Infarction, presentation delay, pre-hospital delay, left ventricular thrombus

INTRODUCTION

Escalating health lost and mounting burden of cardiovascular diseases (CVD) especially in low-middle income developing countries, like Pakistan, is not only a public health issue but it also leads to reduction of around seven percent in countries gross domestic product (GDP).[1] Seventy-five to eighty percent of the global CVD deaths occur in this population.[1-5] Targeted interventions, advancement in methods of treatment, implementation of evidence based medicine, and rigorous processes of care resulted in improved survival and a significant reduction in cardiovascular morbidity and mortality in various parts of the world for the various presentations of CVD.[6,7]

However, ST-segment elevation myocardial infarction (STEMI) is the most lethal manifestation of ischemic heart diseases (IHD) resulting in increased cumulative major adverse cardiac events (MACE) irrespective of age, gender, or geography.[8] The earliest restoration of myocardium, pharmacologically or mechanically, remains the principal concern in the management of STEMI patients.[9] According to American college of cardiology guidelines of STEMI, after onset of chest pain the primary coronary intervention should be done within 12 hours.[10] It is well established that the time of presentation of STEMI from the onset of chest pain and timely treatment determines prognosis of patient.[11-15]

For a number of reasons the time between emergency room (ER) arrival and symptom onset was the primary concern among the cardiologists and efforts have made it possible to brought it down to less than 90 minutes of recommended cutoff in most of the situations.[10,16] However, up until recent years the scientific community was less attentive towards the pre-hospital delays. Various reasons for the pre-hospital delays were found to be lack of awareness and late recognition of cardiac symptomology, lack of financing, residence in remote areas, and unavailability of transportation.[14]

Although, it has been found that delayed presentation is associated with a multiple poor outcomes however, various delays and the reason beyond these delays have not been established in our population. Thus, in the present study, we assessed the various delays in the timeline of ST-segment elevation myocardial infarction (STEMI), its determinants and impact on in-hospital outcomes.

METHODOLOGY

This was a descriptive Cross sectional study conducted at a tertiary care cardiac center in Karachi, Pakistan. This study was commenced with the approval of the ethical review committee (ERC) of the hospital and verbal informed consent was taken from all the patients regarding their participation in the study and publication of data while maintaining confidentiality. Written consent was waived by the ERC due to observational nature of the study. Consecutive patients presented to the emergency room (ER) with the diagnosis of ST-segment elevation myocardial infarction (STEMI) and did not received thrombolytic therapy before arrival were included. Included patients were of either gender, aged between 18 to 80 years, had no prior history of IHD, and had not received any thrombolytic therapy prior to the arrival. All the included patients were either late presented to the ER or reperfusion (primary PCI) was delayed after ER arrival. Diagnosis of STEMI was made based on history, physical examination, and 12-Lead electrocardiograph (ECG) at presentation as per the ACC/AHA guidelines.[10] Patients with more than twenty minutes of typical radiating chest pain with ST-segment elevation in two or more contiguous leads or new LBBB were classified as STEMI. The timeline of STEMI was recorded as duration of chest pain (minutes), chest pain (CP) to emergency room (ER) arrival time (minutes), CP to first electrocardiography (ECG) time (minutes), CP to acute coronary syndrome (ACS) protocol time (minutes), ER to lab activation time (minutes), and total ischemic time (minutes) were recorded. Delay in arrival was defied as CP to ER arrival time of more than 120 minutes and delay in primary PCI was defined as ER arrival to lab activation time of more than recommended 90 minutes. Reasons of the pre-hospital and hospital delay were recorded for all the patients. Reasons for the delayed arrival were categorized as unawareness of symptoms, unavailability of transportation, unnecessary consultation by general physician or physician at non-cardiac facility, and financial issues. Reasons for the post arrival delay were categorized as

patients or attendants unwillingness or delay in given consent for the procedure, and unavailability of resources (unavailability catheterization laboratory due to running procedures).

The demographic details, symptoms on presentation, and risk factors of the patients were recorded. Type of MI on ECG and presence of left ventricular (LV) thrombus on echocardiography were recorded. The guideline-recommended ACS medication therapy, such as soluble aspirin, clopidogrel, unfractionated heparin, and glycoprotein IIb/IIIa inhibitor, were administered in ER and during the procedure. Primary percutaneous coronary intervention (PCI) procedures, within 12 hour of CP, were performed by consultant cardiologist in all the patients. Patients were kept under observation during their index hospitalization and length of hospital stay (LOS), and outcomes such as recurrent ischemia, re-infarction, sustained ventricular tachycardia, ventricular fibrillation, AVNRT/SVT/sinus bradycardia, heart failure/pulmonary edema, and cardiogenic shock were recorded.

Collected data were electronized on a data entry screen designed using CSPro 7.0 and after quality assessment collected data were converted to the SPSS format. Data were analyzed using SPSS version 21.0. Patients were categorized on the ER arrival cutoff of six hours (360 minutes) and outcomes were compared by applying appropriate Chi-square or Mann–Whitney U test over the significance criteria of p-value ≤ 0.05.

RESULTS

A total of 103 STEMI patients with either pre-hospital or hospital delay for the procedure. Majority, 72.8%, of the patients were male, mean age was 54.75 ± 11.8 years, and almost all, 98.1%, were married. The presenting compliant for almost all of the patients, 96.1% (99), was chest pain, 46.6% (48) had shortness of breath, 17.5% (18) of the patients had heart burn, and 6 (5.8%) patients presented with abdominal pain and syncope each.

The timeline of STEMI was recorded as; patient arrived to ER in median duration of 240 [420 - 144.5] minutes after CP, first ECG was obtained in 250 [444 - 171] minutes of the CP, ACS protocol was administered in 270 [487 - 181] minutes of the CP, procedure was performed in 120 [180 - 60] minutes of ER arrival, and median total ischemic time was 360 [690.5 - 259] minutes.

Around 55.3% (57) of the patients not only late presented (≥ 120 minutes) but also procedure was delayed (≥ 90 minutes). The most common reason for delay arrival after symptom was unawareness of symptoms (53.3%) followed by unavailability of transportation (29.3%), while, the most common reason for the delayed procedure was unavailability of resources (69.8%). Demographics, risk profile, presenting and procedure timing and causes of delay are presented in Table 1.

Table 1: Demographics, risk profile, presenting and procedure timing and causes of delay

Characteristics	Total
N	103
Gender	
Male	72.8% (75)
Female	27.2% (28)
Age (years)	54.75 ± 11.8
≤ 40 years	15.5% (16)
41 to 65 years	74.8% (77)
> 65 years	9.7% (10)
Symptom onset to hospital arrival	
Median [IQR] minutes	240 [420 - 144.5]
Pre-hospital delay (≥ 120 minutes)	92 (89.3%)
Causes of pre-hospital delay [N=92]	
Unavailability of transportation	27 (29.3%)
Unnecessary consultation	34 (37%)
Financial issues	2 (2.2%)
Unawareness of symptoms	49 (53.3%)
Hospital arrival to lab activation	
Median [IQR] minutes	120 [180 - 60]
Hospital delay (≥ 90 minutes)	63 (61.2%)
Causes of hospital delay [N=63]	
Unavailability of resources	44 (69.8%)
Patients unwillingness or delay consent	6 (9.5%)
Others	13 (20.6%)

Risk Factors	
Diabetes mellitus (DM)	41 (39.8%)
Hypertension (HTN)	52 (50.5%)
Dyslipidemia	10 (9.7%)
Chronic kidney disease (CKD)	4 (3.9%)
Smoking	37 (35.9%)
Family history of IHD	32 (31.1%)

IHD = ischemic heart disease, IQR = interquartile range

Type of myocardial infarction (MI) was anterior wall MI in 48.5% (50), inferior wall MI in 40.8% (42), and lateral wall MI in remaining 10.7% (11) patients. Majority, 68.9% (71), patients had multi-vessel diseases and 31.1% (32) had single vessel diseased. Left ventricular (LV) thrombus was seen in 6.8% (7) patients. Primary PCI was performed in 77.7% (80) of the patients who were arrived within 12 hours of CP. LV thrombus was more commonly seen in patients with CP to ER arrival time of more than 360 minutes, 21.4% (6) vs. 1.3% (1); p<0.001. A significantly higher CP to ER median time was observed for the patients with LV thrombus, 2160 [2940 - 480] vs. 210 [360 - 137] minutes; p=0.001.

Length of hospital stay and in-hospital outcomes stratified by duration between onset of chest pain and hospital arrival are presented in Table 2. Overall adverse in-hospital outcomes were tilted towards the late arrival with a significantly higher rate of re-current ischemia in patients with CP to ER time more than 360 minutes, 32.1% (9) vs. 12% (9); p=0.017. In-hospital mortality and re-infarction rates were zero (0%) for this cohort of patients.

Table 2: Length of hospital stay and in-hospital outcomes stratified by duration between onset of chest pain and hospital arrival

Characteristics	Total	Chest Pain to ER Arrival Time		p-value
		≤ 360 minutes	> 360 minutes	
N	**103**	**75**	**28**	**-**
Left ventricular (LV) thrombus	9.3% (7)	1.3% (1)	21.4% (6)	<0.001
Length of hospital stay (days)				
Mean ± SD	4.09 ± 2.06	3.91 ± 2.07	4.57 ± 1.99	0.129
Median [IQR]	4 [5 - 2]	4 [5 - 2]	5 [7 - 2.5]	
In-hospital outcomes				
Re-current ischemia	17.5% (18)	12% (9)	32.1% (9)	0.017
Sustained ventricular tachycardia	2.9% (3)	4% (3)	0% (0)	0.283
Ventricular fibrillation	2.9% (3)	2.7% (2)	3.6% (1)	0.808
AVNRT/SVT/sinus bradycardia	9.7% (10)	8% (6)	14.3% (4)	0.338
Heart failure/pulmonary edema	4.9% (5)	2.7% (2)	10.7% (3)	0.091
Cardiogenic shock	7.8% (8)	9.3% (7)	3.6% (1)	0.331

ER= emergency room, SD = standard deviation, IQR = interquartile range, AVNRT = atrioventricular reentrant tachycardia, SVT = supraventricular tachycardia

DISCUSSION

The primary purpose of STEMI management is the restoration of myocardium, hence, time to treatment determines the prognosis of STEMI patients.[9,11-15] Therefore, in this study our aim was to assess the various delays in the timeline of STEMI and to understand the associated reasons for these delays. In this study of STEMI patients with either pre-hospital or post arrival delayed treatment, a significant number of patients had both pre-hospital and post arrival delay. Pre-hospital and post arrival delay were observed in 89.3% and 61.2% of the

patients respectively, while 55.3% of the patients had both pre-hospital and hospital delay in treatment. The most common reason for pre-hospital delay of patient was unawareness of symptoms (53.3%) and the most common cause of hospital delays were due to unavailability of resources (69.8%). Pre-hospital delay of more than 6 hours was found to be associated with significantly higher rate of LV thrombus, 21.4% vs. 1.3%; p<0.001, and in-hospital re-current ischemia, 32.1% vs. 12%; p=0.017.

With the recognition of impact of total ischemic time (TIT) on outcomes of STEMI patients, strategies for the reduction of TIT are in the limelight, pre-hospital delays are the major determinants of the prolonged ischemia.[16] A study conducted by Pereira et al.[17] concluded that advance age (≥75 years), symptom onset in late hours (after midnight), and primary care unit before PCI capable hospital (first medical contact) were the key predictors of pre-hospital delay. Also sociodemographic factors, such as gender, age, education, and socioeconomic class, appeared to play role in pre-hospital delay of patients.[18] Shahin et al.[19] observed that the TIT was longer for unstable patients (resuscitated), patients presenting on weekends and late hours. However, the primary focus of this paper was door to balloon (DTB) time and acknowledge that the DTB time is only the climax of the STEMI timeline for the ultimate results appropriate measures are needed along the timelines of entire healthcare chain.

Park YH, et al.[20] reported pre-hospital delayed associated with in-hospital mortality and level of education, late hours (after midnight) symptom onset, use of private transportation, and triage via non-cardiac center were the key determinants of pre-hospital delay. They further reported that only 7% of the patients ware of symptomology of acute myocardial infarction and more than three fourth of the patients were triage via non-cardiac centers causing a significant delay in presentation. No decline has been reported in age adjusted monthly pre-hospital delay trend and there is a lot more room for improvement especially for female and elderly patients.[21] Manzo-Silberman et al.[22] investigated the increased female mortality and its linkage with presentation delay and reported that it was reassuring to observe no significant difference in system delays for female, however, increased pre-hospital delay was observed to be associated with female gender but higher mortality rate for female was not solely explained by delay presentation.

LV thrombus formation after acute MI is not that uncommon and its predictors and reduced LV ejection fraction (EF), anterior wall MI, and large infarct size are the key predictors of LV thrombus formation.[23] In our study LV thrombus formation was found to be associated with pre-hospital delay. These findings of our study were align with a past study by Jadoon RJ et al.[24], that early hospitalization leads to reduced risk of LV thrombus formation.

Hence, with unawareness of acute myocardial infarction symptomology as a leading cause of pre-hospital delay in our population, it is important to educate our common masses regarding call for help time. This would be the starting of race against time in timeline of STEMI along the resource limited healthcare chain. The second challenge in the sequence is transportation, increased access to the 24/7 on-call ambulatory services and finally availability of resources (limited number of available catheterization laboratories) and reduction in patients to doctor and patients to facility ratio should be the prime objective of health care system.

Single center experience is the key limitation of this study, as study center provides 24/7 free of cost primary PCI services, therefore, despite being a low-middle income population the financial constraints are not surfaced. Secondly, smaller sample size limit us from the subgroup analysis such as gender and age.

CONCLUSION

In this study we observed that not only the pre-hospital delay but also system delay are the major challenges in the timeline of STEMI. The most common cause of pre-hospital delay in our population was patients' unawareness of symptomology and unavailability of transportation, while, the major cause of system delay was unavailability resources. Pre-hospital delay was associated with significantly higher rate of LV thrombus and in-hospital re-current ischemia. Therefore, improving awareness, transportation facilities, and availability of resources should be our focused strategies to shorten the STEMI timeline.

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