Factors Associated with Pre-hospital Delay before Reperfusion Therapy in Patients with ST-Segment Elevation Myocardial Infarction

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ABSTRACT:

Introduction: Cardiovascular disease remains the main cause of death in the world, and myocardial infarction represents the main contributor to this mortality. Timely restoration of myocardial blood flow with reperfusion therapy is crucial. Pre-hospital delay is a major obstacle for early reperfusion therapy and has negative impact on mortality and left ventricle function. **Methods**: A prospective study was carried in cardiology unit of a medical college from August 2013 to December 2017. Cases of acute ST segment elevation myocardial infarction that have undergone thrombolysis were recruited. **Results**: Out of 450 patients with ST Elevation Myocardial Infection (STEMI), delayed presentation was seen in 288 (64%) for >6 hrs and 108 (24%) patients for >12 hrs. The duration from onset of symptoms to the presentation in the emergency room (pre-hospital delay) was 12.66 hrs (SD=14.19, range = 30 min to 72 hrs). The door to needle time was 54 min (SD=24) The major factors for pre-hospital delay were misinterpretation of symptoms (59%) and transportation problems (31%). **Conclusion**: Misinterpretation of symptoms remain the most common cause of delayed presentation. Health education for public awareness can reduce the delay. Extension of thrombolytic therapy to district hospital and primary health center level after basic training for medical officer with checklist and collaboration in form of telemedicine with referral cardiac center may have major impact on morbidity and mortality reduction in acute STEMI patients with early reperfusion therapy.

Keywords: chest pain, myocardial infarction, pre-hospital delay, thrombolysis

INTRODUCTION:

Non-Communicable Disease (NCD) is a leading cause of death worldwide. According to the World Health Organization (WHO), "40 million of the 56 million global deaths in 2015 were due to NCDs". Moreover, "48% of NCDs deaths in low- and middle-income countries in 2015 occurred before the age of 70".[1] Cardiovascular disease remains the main cause of death worldwide, and myocardial infarction represents the main contributor to this mortality. Annually, more than three million people suffer or die from ST Elevation Myocardial Infarction (STEMI) worldwide.[2] Treatment of patients with acute myocardial infarction (MI) is time related.[3] Delay of every minute after STEMI is associated with increasing mortality and morbidity.[4] Prehospital delay is a major contributor to the morbidity and mortality in MI.[5] A landmark study by De Luca et al. showed that every 30 minutes

prolongation in treatment delay was associated with a relative risk for 1-year mortality of 1.075. [6] Timely restoration of myocardial blood flow in STEMI optimizes myocardial salvage and reduces morbidity and mortality.[7,8]

Several factors contribute to pre-hospital delay such as age, gender, educational status, and clinical and psychological factors.[9] The total pre-hospital delay period consists of two components: Time taken by patients to recognize that their symptoms are serious and to contact medical help (decision time) and the time taken from requesting help to hospital admission (home-to-hospital delay). Despite quality improvement efforts to decrease the system delay in starting reperfusion treatment, some percentages of patients receive therapy outside the recommended time interval even in developed countries.[10] While the extent and the determinants of this delay have been well researched in the developed countries, it remains yet to be systematically identified in various developing countries like Nepal, and Nepalese studies are few in this regard. This study was carried out to determine pre-hospital delay and associated factors in patients with acute STEMI.

METHODS:

A hospital based prospective observational study was carried out in STEMI patients from August 2013 to December 2017. The study was conducted in cardiology unit, department of internal medicine, Manipal College of Medical Sciences, Phulbari-11, Pokhara.

The diagnosis of STEMI was done based on 2013 ACC/AHA guideline and thrombolytic agents were given according to patient party preference after they were given the option of both Streptokinase (STK) and Tenecteplase (TNK). Thromboytic agents were given in patients presented within 12 of chest pain or had clinical or electrocardiographic evidence of ongoing ischemia when given beyond 12 hrs.   Hypertension was defined according to JNC-7 criteria , Diabetes Mellitus based on 2013 ADA guideline and Dyslipidemia based on 2013 ACC/AHA guideline.

In all patients, time of delay was established since the onset of symptoms associated with myocardial infarction and the arrival to the emergency department whether they received medical care elsewhere or not. The cases of STEMI who were eligible for thrombolysis were included in this study. STEMI cases not eligible for thrombolysis, who had undergone primary angioplasty or unable to tell exact timing of chest pain and who presented without chest pain but having angina equivalent symptoms were excluded from the study. In all patients, clinical evolution follow-up was made until discharge.

The data was collected as per the attached proforma. Semi structured questionnaire was used to interview the patient. Collected data were entered into a master chart prepared in Microsoft Excel 2007 which was checked, verified and converted into SPSS 18 version for statistical analysis. Descriptive statistics like mean, percentage, frequency, standard deviation was used to describe characteristics of collected data. Chi-square was applied to find association between prehospital delay with socio-demographic characteristics and cardiac risk factors. P value less than 0.05 was considered statistically significant.

The study was approved by the Ethical Review Committee (ERC) of Manipal College of Medical Sciences, Nepal. The participants were informed about the purpose of the project, their right to decline participation and to withdraw at any stage of the study. Verbal consent was obtained from the participants. The confidentiality was maintained by removing personal identifiers and information was only used for purpose of the study.

RESULTS:

Altogether 450 STEMI-diagnosed patients were interviewed from August 2013 to December 2017 giving a response rate of 100%.

Mean age of the patients was 60 yrs (SD=13.02). There were 319 (70.89%) male and 131 (29.11) female patients. Mean duration of prehospital delay was 12.66 hrs (SD=14.19). In nearly one fourth of the cases, delay was more than 12 hrs as shown in Table 1.

Several risk factors of MI were present in the patients. Their frequency and percentages are shown in Table 2. More than 2/3rd were smoker and majority (52%) had hypertension.

More than half (54.7 %, n=246) of the patients were treated with tenecteplase as a thrombolytic agent whereas 45.3% (n=204) were treated with streptokinase. Mean door to needle time was 54 minute (SD=24).

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Table 1: Prehospital delay in the study population (n=450)

Duration	n	%
< 1 hr	3	0.67
1 to 6 hrs	159	35.33
7 to 12 hrs	180	40
>12 hrs	108	24

Table 2: Exposure of MI patients to risk factors (n = 450)

Characteristics		n	%
Smoking	Yes	312	69.3
	No	138	30.7
Hypertension	Yes	234	52
	No	216	48
Diabetes Mellitus	Yes	72	16
	No	378	84
Dyslipidemia	Yes	72	16
	No	378	84
Alcohol	Yes	102	22.7
	No	348	77.3

Association between pre-hospital delay and various factors is shown in Table 3. It shows that there was a significant association of prehospital delay with age-group and sex of the patient but not with cardiac risk factors like diabetes, hypertension, hypercholesterolemia, smoking, and alcohol intake. Further analysis of relationship between delay and age-group with Bonferroni correction revealed that the relationship was significant with the age group more than 65 yrs. This suggests that the people above 65 yrs of age were more likely to be brought to hospital earlier (within 12 hrs) as compared to other younger age groups.

Table 4 shows the major factors for pre-hospital delay. The most common factor was misinterpretation of symptoms as acid peptic disease (APD) followed by transportation problems.

Table 4: Factors causing pre-hospital delay (n=450)

Factors	n	%
Misinterpreted as APD	266	59.1
Transportation delay	140	31.1
Inter-hospital delay	31	6.9
Reperfusion decision delay	13	2.9

DISCUSSION:

More than fifty percentage of the patients age ranges from 45-65 yrs with mean of 60 yrs (SD=13.02) which is similar to the study by Perkins-Porras L. et al,[11] Beig JR. et al,[12] and Ribeiro S. et al,[13] where mean age was 59 (SD=11.2), 57.6 (SD=10.5), and 62 yrs (SD=13.64) respectively. Whereas, a study conducted in China reported the mean age of the patient was found to be 65.68 yrs (SD=12.68).[14]

Table 3: Association between prehospital delay and different risk factors (n = 450)

Characteristics		Prehospital delay		Stats
		< 12.66 hrs n (%)	≥ 12.66 hrs n (%)	
Age (yrs)	< 45	39(81.3)	9(18.8)	$X^2 = 6.3$, df = 2 p = 0.043
	45 - 65	180(78.9)	48(21.1)	
	> 65	120(69)*	54(31)*	
Sex	Female	78(60.5)	51(39.5)	$X^2 = 21.51$, df = 1 p < 0.001
	Male	261(81.3)	60(18.7)	
Smoking habits	Yes	240(76.9)	72(23.1)	$X^2 = 1.38$, df = 1 p = 0.24
	No	99(71.7)	39(28.3)	
Hypertension	Yes	174(74.4)	60(25.6)	$X^2 = 0.25$, df = 1 p = 0.62
	No	165(76.4)	51(23.6)	
Diabetes	Yes	54(75.0)	18(25.0)	$X^2 = 0.005$, df = 1 p = 0.94
	No	285(75.4)	93(24.6)	
Dyslipidemia	Yes	57(79.2)	15(20.8)	$X^2 = 0.68$, df = 1 p = 0.41
	No	282(74.6)	96(25.4)	

* Statistically significant cell

Nearly 1/4th (24%) of the patients duration of pain (prehospital delay) was >12 hrs and mean duration was 12.66 hrs (SD=14.19) which is similar to the study from Mexico.[15] While a study conducted in China confirmed about the mean delay of 23.58 hrs (SD=85.09) which is relatively higher than the present study.[14] The present study revealed the median duration of prehospital delay is eight hrs which is comparatively higher than other studies where lesser median delay times were reported in Korea (2.5 hrs),[16] Beijing (2.3 hrs),[17] and Chennai (three hrs).[18]

The present study highlights the door to needle time was 54 min (SD=24) which is comparable to the study from South India and Beijing which depicted the median door-to-needle time were 75 and 82 min respectively.[19,20] However, few studies showed significantly lower door to needle time i.e 40 min and 34 min respectively.[12,21] The current study enlightened the most commonly used thrombolytic agent was tenecteplase (TNK) 54.7%. Nevertheless, the study conducted in Mexico confirmed streptokinase as a most commonly used lytic agents in 67% of cases.[15]

Age has been shown to be a determinant of increased prehospital delay in many studies;[22,23] the present study also showed significant association between age-group and prehospital delay. There was significant association between sex of the patient and prehospital delay which is analogous with the result acquired in several studies by Ribeiro S. et al, Taghaddosi M. et al, Angerud KH. et al with a higher proportion of female with longer pre-hospital delay.[13,22,23] The reason being females could not directly activate the transportation system and they had to first inform their husband or family in most cases and then only process of transportation started. While divergent result was obtained in a study by Banos-Gonzalez et al,[15] Farshidi H. et al,[24] and George L. et al,[25] where no significant association was found between sex and prehospital delay. There were no significant associations with other cardiac risk factors such as diabetes, hypertension, hypercholesterolemia, smoking habits similar to the study from London.[11] In contrast to this, some studies have reported the presence of diabetes was associated with increased delay.[12, 25]

The major factors for pre-hospital delay were misinterpretation of symptoms (59%) and transportation delay (31%) due to difficult geographical location and non-availability of ambulance or other vehicles alike to the results from Mumbai with misinterpretation of symptoms (45%) and transportation problems (27%).[21] A study conducted in London figured out the decision time constituted 60% of the total pre-hospital delay period, home-to-hospital delay accounted for 40%.[11]

Limitations:

This study has some limitation. Although every effort was made to interview patients soon after admission, data may have been affected by recall bias. We could not assess other component of pre-hospital delay like cardiovascular history, patient's attribution of symptoms, clinical and proximal factors, and time of admission, symptom onset and call for assistance. Only the cases of acute ST segment elevation myocardial infarction that have undergone thrombolysis were recruited. Only survivors could be interviewed thus factors that influenced delay in individuals who did not survive ACS may not have been captured.

CONCLUSION:

Majority of cases in our study presented out of window period of six hours. Misinterpretation of symptoms remain the most common cause of delayed presentation. Health education for public awareness can reduce the delay. Extension of thrombolytic therapy to district hospital and primary health centre level after basic training for medical officer with checklist and collaboration in form of telemedicine with referral cardiac centre may have major impact on morbidity and mortality reduction in acute STEMI patients with early reperfusion therapy.

Conflict of interest:
Authors declared that no conflict of interest exists.

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