Original Article

Differences in symptoms and presentation delay times in myocardial infarction patients with and without diabetes: A cross-sectional study in Pakistan

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A B S T R A C T

Objective: A short pre-hospital delay, from the onset of symptoms to rapid initiation of reperfusion therapy, is a crucial factor in determining prognosis of myocardial infarction (MI). The purpose of this study was to evaluate symptoms and presentation delay times in MI patients with and without diabetes.
Methods: This cross-sectional study was conducted in 3 tertiary care hospitals of Pakistan over a period of 6 months. The study sample consisted of 280 consenting individuals diagnosed with ST-elevation MI (STEMI) or Non-ST elevation MI (NSTEMI), out of which 130 were diabetic and 150 were non-diabetic. Data was collected using a standardized questionnaire, investigating MI symptoms along with causes and duration of pre-hospital delay within 72 hours of admission.
Results: No significant difference was found in the intensity of chest pain between diabetics and non-diabetics. Atypical symptoms of MI such as anxiety ($p < 0.001$), cold sweats ($p = 0.034$) and epigastric pain ($p = 0.017$) were more frequently reported in diabetics. MI patients with diabetes had a significantly longer presentation delay time with 75% of the patients presenting after elapse of 3 h. Only a few patients reported to the hospital within an hour of onset of symptoms (n = 23, 8.2%), out of which majority were non-diabetics (n = 18). A majority of patients (n = 146, 52%) in both groups did not use emergency medical services.
Conclusion: This study provides an incentive for further research, aiming to reduce pre hospital delay along with investigating the effectiveness of emergency medical services.

1. Introduction

Myocardial infarction (MI) remains a leading cause of morbidity and mortality worldwide.[1] More than seven million people are reportedly diagnosed with MI each year,[2] with the incidence being the highest in South Asia.[3] Almost 90% of these cases are attributable to modifiable risk factors such as smoking, dyslipidemia, hypertension and diabetes.[2] Diabetes is a well-known coronary artery equivalent disease and a major cardiovascular risk factor.[4] Studies have shown that people with diabetes have a higher risk for MI[5,6] and twice the short- and long-term mortality after MI[7,8] than people without diabetes.

Presentation delay time is usually defined as time from symptom onset to arrival at hospital, and it can be divided into the patient decision phase, time to first medical contact (FMC) and the transportation phase. The time it takes for the person to decide how to interpret and respond to symptoms is considered to be the major contributor to pre-hospital delay.[9] Despite the importance of timely care seeking, more than 50% of MI patients delay their FMC by presenting to the hospital at least 2 h after the onset of symptoms, this delay is even longer among patients in the South Asian region.[10–12] Medical care seeking behavior has changed little over the past decades, even though numerous efforts have been made to educate the public about the detection of symptoms of MI and the benefits of immediate treatment. Literature shows that chest pain is a

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commonly experienced symptom but that several other symptoms also occur and that they vary in onset, nature, and intensity.[13–15]

Previous studies are inconclusive in establishing differences in symptoms and presentation delay times in diabetic and non-diabetic patients. Some research shows that patients with diabetes are more likely to present with atypical symptoms of MI[16,17] and have a longer delay time than patients without diabetes, both in ST-elevation MI (STEMI) and Non-ST elevation MI (NSTEMI).[18–20] However, others have found no such differences between the two groups.[21–24]

A short presentation delay, leading to prompt diagnosis and treatment of patients with MI can reduce mortality, improve prognosis, and shorten the hospital stay.[25–27] Therefore to improve outcomes, our study focuses on differentiating between the symptoms and presentation delay times in MI patients with and without diabetes in Pakistan, South Asia.

2. Method

This cross-sectional study was conducted over a period of 6 months, starting from 1st November 2015 to 30th April 2016, in 3 tertiary care hospitals of Karachi, Pakistan after approval from the institutional review board of Dow University of Health Sciences. All 3 hospitals are located in the center of the city, easily accessible to patients from all socioeconomic backgrounds. A total of 336 patients were approached, out of which 28 refused to give consent and the rest failed to fall in the inclusion criteria set for the study. The patients who fulfilled the inclusion criteria involved those diagnosed with STEMI or NSTEMI, those who were clinically stable and could answer the questions and those willing to contribute, with or without the help of family within 72 h of admission. STEMI and NSTEMI were defined following guidelines set by Circulation, Journal of the American Heart Association (ACS). STEMI was characterized by persistent elevation of ST segment along with subsequent elevation of biomarkers of myocardial necrosis and NSTEMI was characterized by elevation of biomarkers alone. No imputation method was used, only those applicants who fulfilled the inclusion criteria and had complete data were included in the study. While interviewing, same standard protocol was used to eliminate interviewer bias.

A consent form was signed by each participant. The questionnaire was translated into Urdu, which is the local language, for better understanding of the patient and to remove any miscommunications. Cardiologists well versed in both the languages and a person who had done a Masters degree in the local language along with a professional interpreter, sat down and translated the questionnaire with mutual consensus. In order to eradicate recall bias, frequent and recent questions were presented. The questionnaire was studied by three cardiologists of the involved hospitals to ensure it covered major aspects of patient information. Furthermore, a pilot study was conducted on 50 patients to validate the questionnaire and eliminate any ambiguity. These set of patients were ultimately included in the final sample of participants in the study. However, the pilot study has not been published anywhere.

The questionnaire had four domains; the first being background characteristics including age, sex, marital status, educational level, medical history, distance to the nearest hospital, smoking and alcohol habits. The second domain was typical and atypical symptoms, where the pain intensity was calculated using the Numeric Rating Scale (NRS-11). It is an 11-point scale ranging from zero to ten for patient self-reporting of pain, where zero is deemed as no pain and a rating of 7–10 is considered as severe disabling pain. The third included the causes of presentation delay to the nearest hospital. The presentation delay was recorded for four durations; <1 h, 1–3 h, 3–6 h and >6 h. Lastly, the fourth domain was mode of transport to the hospital. The records were collected for two groups, diabetics and non-diabetics.

Continuous data were presented as means and standard deviations while categorical data were presented as frequency and percentages. Differences in patients' demographics and clinical characteristics were compared between the two groups by applying chi-square test for categorical variables. Bar charts were used to represent continuous variables such as patient delay time. A 'p value' of less than 0.05 was considered to be significant. The data were entered and statistically analyzed using SPSS version 22.0 for Windows, developed by IBM Corporation (Armonk, New York, U.S.).

3. Results

Of the 280 patients included in the study, 130 (46.4%) were diabetic. The mean age of patients with and without diabetes was 67.3 and 66.9 years, respectively. A higher proportion of diabetic patients had hypertension (p = 0.03) and a positive family history of coronary artery disease (p < 0.001). More than two thirds of the whole study group lived more than 10 km away from the hospital without a statistically significant difference between the two groups (p = 0.60). Majority patients (n = 146, 52%) in both groups did not use emergency medical services. The demographic and clinical characteristics of the patients are shown in Table 1.

Table 1
Personal and medical history of myocardial infarction patients with and without diabetes.

|	Diabetic Status		p-value
	With Diabetes (n = 130)	Without Diabetes (n = 150)	
Age (years)	67 ± 9.2	67 ± 9.0	0.781
Males	88 (68%)	106 (71%)	0.590
Married	116 (89%)	132 (88%)	0.747
Hypertension	98 (75%)	95 (63%)	0.030
Smoker	30 (23%)	43 (29%)	0.288
STEMI	74 (57%)	87 (58%)	0.856
Distance to the hospital <10 km approximately	41 (32%)	43 (29%)	0.274
Education level			
Primary/No education	101 (78%)	108 (83%)	0.275
Secondary/Higher education	29 (22%)	42 (28%)	
Hyperlipidemia	64 (49%)	81 (54%)	0.426
Family history of CAD	81 (62%)	56 (37%)	<0.001
Renal failure	11 (8.5%)	7.0 (4.7%)	0.197
Alcoholic	9.0 (6.9%)	8.0 (5.3%)	0.578
Those who took an ambulance	71 (55%)	64 (43%)	0.046
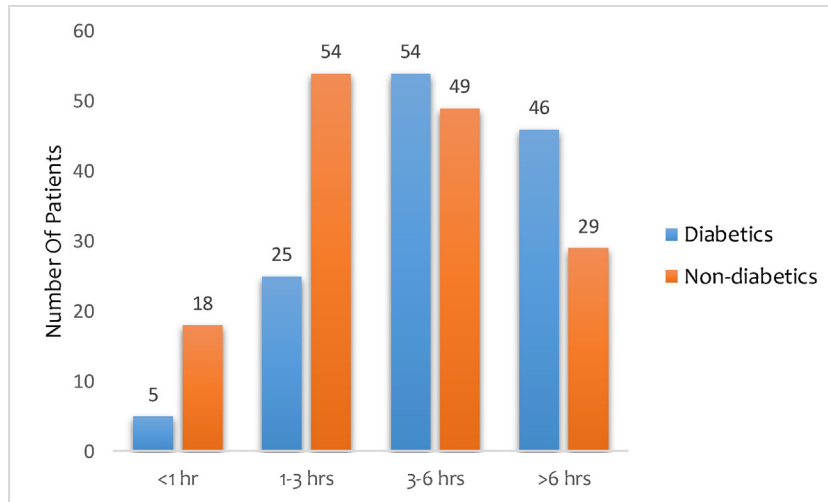
Fig. 1. Distribution of time from onset of symptoms to presenting to the hospital in patients with and without diabetes.

3.1. Presentation delay time

Patients with diabetes presented later than those without diabetes (Fig. 1). Majority (n = 54, 36%) of non-diabetics presented with a delay time of 1–3 h while the majority (n = 54, 41.5%) of diabetic patients had a delay of 3–6 h. Only a few patients reported to the hospital within an hour of onset of symptoms (n = 23, 8.2%), out of which most were non-diabetics (n = 18). Moreover, around 35.5% of diabetics presented with a noteworthy delay of more than 6 h as compared to nondiabetics (19.3%). Of the patients who presented after 6 h, majority (n = 66, 88.0%) did not believe that they were experiencing an MI (Fig. 2). However, this was more common among the patients with diabetes (n = 41, 54.7%) than those without diabetes (n = 25, 33.3%). The remaining patients stated self-medication (36.0%) and traffic (22.7%) as the main reason for the delay.

3.2. Symptoms

Chest pain was the most common symptom reported in both diabetics (n = 101, 77%) and nondiabetics (n = 130, 87%). However, patients with diabetes reported chest pain significantly less than those without diabetes (77.7% vs 86.7%, p = 0.049). The second,

third and fourth most common symptoms in both groups were cold sweats, dyspnea and nausea/vomiting followed by anxiety in diabetics and shoulder pain in nondiabetics (Table 2). However, anxiety (36.9% vs 18.0%, p < 0.001) and cold sweats (49.2% vs 36.7%, p = 0.034) were significantly more common in those with diabetes than without diabetes. Even though epigastric pain was the least common symptom reported by patients in both groups, a significantly higher number of patients with diabetes complained of it (11.5% vs 4.0%, p = 0.017). There was no significant difference in other symptoms such as jaw pain between the two groups (Table 2). There was also no difference in pain intensity in patients with diabetes (mean = 7.30) compared to those without diabetes (mean = 7.40). More than two thirds of the patients in both groups complained of persistent pain (70% diabetics vs 73% non diabetics) along with presence of more than one symptom (79% diabetics vs 81.5% non diabetics).

4. Discussion

We found that diabetics have a greater delay time between onset of symptoms and FMC when compared to nondiabetics. Around 75% of diabetics had a pre-hospital delay of more than 3 h; this finding is consistent with many similar studies.[18–20,28,29] At the
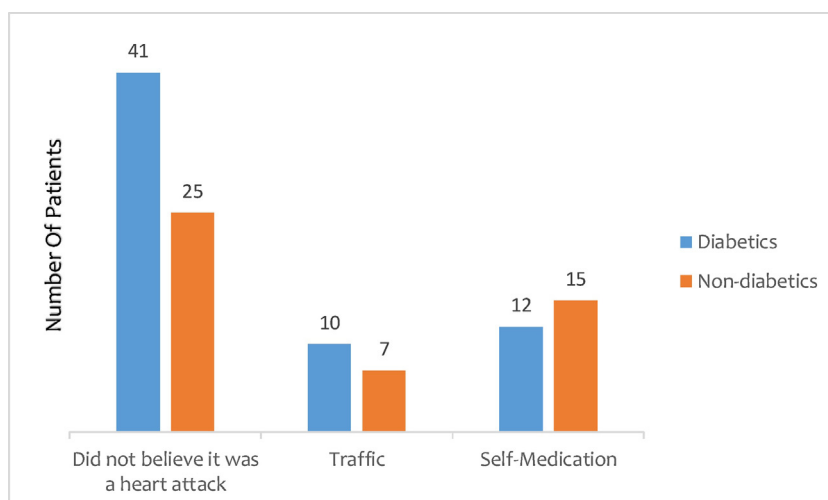

Fig. 2. Reasons of causing a delay of more than 6 h after the onset of symptoms in patients with and without diabetes.

Table 2
Symptoms experienced by myocardial infarction patients with and without diabetes.

	Diabetic Status		p-value
	With Diabetes (n = 130)	Without Diabetes (n = 150)	
Chest pain	101 (78%)	130 (87%)	0.049
Shoulder/arm pain	35 (27%)	50 (33%)	0.245
Epigastric pain	15 (12%)	6.0 (4.0%)	0.017
Jaw pain	32 (25%)	44 (29%)	0.376
Dyspnea	63 (48%)	76 (51%)	0.713
Nausea/vomiting	57 (44%)	52 (35%)	0.116
Anxiety	48 (37%)	27 (18%)	<0.001
Cold sweats	64 (49%)	55 (37%)	0.034
Pre-syncope	29 (22%)	28 (19%)	0.45
Pain intensity (out of 10)	7.3	7.4	0.81
Persistent pain	91 (70%)	109 (73%)	0.622
Patients complaining of more than one symptom	103 (79%)	122 (81.5%)	0.659

same time our finding is contrary to that of other studies which found that there was no difference in delay time between diabetics and nondiabetics.[22,30,31] According to the National Heart Attack Alert program, reperfusion therapy should be initiated within one hour of symptom onset, the objective being to decrease total ischemic time, which is the single most important factor in achieving the best possible outcome.[32] A majority of the patients presented to the hospital out of this time frame thereby making the goal of a total ischemic time less than one hour impossible.

Our results also show that diabetics are less likely to experience chest pain and more likely to experience anxiety, cold sweats and epigastric pain in comparison to non-diabetics. Although lack of chest pain in diabetics has been reported in past studies,[16,17] others have shown that its presence is equally prevalent in both diabetics and nondiabetics.[23,33] Our study concurs with previous studies, which state that intensity of chest pain, when present, is approximately equal for both diabetics and nondiabetics.[23,34] The occurrence of cold sweats in diabetics in our study was found to be contrary to the findings of Karin et al.[34]

A greater pre-hospital delay in diabetics in contrast to non-diabetics can be attributed to a majority of them believing they were not having a heart attack (Fig. 2). This belief is most likely due to the appearance of the above mentioned atypical symptoms and the absence of crushing chest pain classically associated with MI. This can be due to diabetic autonomic neuropathy, which can reduce chest pain by decreasing stimulation of peripheral nerves. Central effects such as altered levels of pain perception and beta endorphin levels can also cause variation in symptomatology.[35]

The lack of alarming symptoms such as syncope can further contribute to the delay in seeking medical attention. Diabetics, especially long term diabetics, are known to adjust their perception of certain symptoms. Studies show that most diabetics downplay the appearance of atypical symptoms, such as nausea, epigastric pain and cold sweats, as symptoms of hypoglycemia or indigestion which can be remedied by medical treatment at home. The presence of anxiety can also affect the patient's decision making.[29] All these factors prevent the seeking of immediate medical attention and greatly increase morbidity and mortality as the optimum time of reaching emergency care (within 2 h) is exceeded.[25]

As our study shows, a majority of patients did not take an ambulance which further prolonged pre-hospital delay. Most of the patients lived more than 10 km away from the hospital, this coupled with the fact that most did not use an ambulance further prolonged pre-hospital delay. Effective use of ambulance services can reduce patient mortality as most deaths from MI occur in the pre-hospital phase. Ambulance services can detect, and remedy

fatal arrhythmias, which are common in the early stages of MI. The movement of ambulances is prioritized amongst city traffic, which helps reduce arrival time to the hospital.[36]

A lack of public awareness regarding the risk factors and symptoms related to MI in both diabetics and nondiabetics is responsible for reducing positive outcomes. This view is supported by a recent study done by Zuhaid et al., which concluded that the Pakistani public is poorly informed about the dangers of cardiovascular disease.[37] Therefore we recommend aggressive individualized counseling of patients at risk of MI, with particular focus on patients with significant co morbidities such as diabetes mellitus, hypertension as well as positive family history of CAD. Patients as well as their caretakers need to be made aware of both typical and atypical symptoms of MI; they should also be made aware of the urgency of seeking medical attention. The use of information technology can be used to improve health literacy and make it easier to contact ambulance services. The increased use of ambulances will decrease time spent in traffic and reluctance to visit the hospital. Electrocardiogram (ECG) should also be provided to all elderly patients who commonly present with atypical symptoms due to the high mortality associated with missed diagnosis of MI in this population.[38]

The primary strength of our study is that it is the first of its kind performed in Pakistan, where this subject is under researched. Our research is based on data collected from a variety of tertiary care hospitals in Karachi which helps to diversify our results. Efforts were also made to remove any form of bias. In spite of this our study has several limitations; firstly it does not take into account a diabetic patient's past history of glycemic control, time since diagnosis and medications used to control blood sugar. Secondly, it does not make distinctions between type 1 and type 2 diabetes. Thirdly, the patients' memories may have been influenced by sedatives and analgesia. Fourthly, a majority of the patients lived more than 10 km away from the location of the hospital, making it difficult to differentiate if the main cause of delay was transport or the decision-making time. Lastly, not all patients presenting to the hospital were included such as the ones who were not clinically stable enough to answer the questionnaire themselves within 72 h.

5. Conclusion

Our findings demonstrate that patients with diabetes experiencing a MI have a longer delay time in presenting to the hospital than patients without diabetes. Chest pain was the most common presenting symptom in both, however patients with diabetes had a higher incidence of epigastric pain. The number of symptoms and the intensity of chest pain was approximately the

same in both groups. This study provides an incentive for further research focusing on various methods to reduce pre-hospital delay. Furthermore, the effectiveness of improved patient education about their symptoms as well the use of emergency medical services in the advent of an MI can also be investigated.

Funding

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