

## A Study of Complications and in Hospital Outcome of Acute Myocardial Infarction in Diabetics and Non-Diabetics

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### ABSTRACT

**Background :** Diabetes mellitus is regarded as a major public health issue and the diabetics are known to have a two to four times increased coronary artery disease (CAD) risk, and CAD has been associated with elevated mortality in diabetics by two to three-fold as compared to non-diabetics. The present study was undertaken to compare the risk factors, complications and outcome of ST Segment Elevation Myocardial Infarction (STEMI) in diabetics and non-diabetics.

**Method :** Total 220 consecutive patients of STEMI were enrolled and divided into two groups of diabetics and non-diabetics. Various risk factors, complications and in hospital outcome were compared between the two groups.

**Results :** Out of 220 patients, 142(64.55%) were found to have diabetes and 78(35.45%) were non-diabetics. Dyslipidaemia (72.54%) and hypertension (39.44%) were the most prevalent risk factors amongst diabetics. 62.68% diabetics and 64.10% non-diabetics had Anterior Wall Myocardial Infarction (AWMI). Diabetics had a greater degree of LV dysfunction as was evidenced by higher on-admission Killip Class [99 (69.68%) of diabetics had Killip Class = 2]. Successful ST segment resolution 1-hour post thrombolysis was seen in 50% of diabetics. Heart failure (64.79%) and cardiogenic shock (39.44%) was the most common complication in diabetics. A total of 19 patients died, of them 15 (10.56%) were diabetics and 4 (5.13%) non-diabetics. Results of Binary Multiple Logistic Regression analysis showed that younger age < 50 years (OR=3.31, 95% CI 1.10-9.94, P=0.033), Male gender (OR=3.94, 95% CI 1.16-13.35, P=0.028), presence of Hypertension (OR=12.80, 95%CI 3.65-44.90, P=0.001) and tobacco consumption (OR=3.66, 95% CI 1.04-12.95, P=0.044) were independent predictors of greater mortality amongst the diabetics.

**Conclusion :** In patients with STEMI, presence of diabetes mellitus was associated with worse in-hospital outcome leading to increased mortality and complications as compared to non-diabetic patients.

**Keywords :** Diabetes mellitus; Mortality; ST Segment Elevation Myocardial Infarction; Dyslipidaemia; Killip Class; Thrombolysis; Cardiogenic shock

### Introduction :

is considered as a major health problem and an epidemic throughout the world. India is now facing a double epidemic of diabetes and coronary artery disease (CAD). As type 2 diabetes shares several risk factors in common with CAD, such as age, hypertension, dyslipidaemia, obesity, physical inactivity, and stress, an increase in the prevalence of diabetes indirectly implicates an escalating risk of CAD as well<sup>1,2</sup>. Diabetic subjects are known to have a two to four times increased CAD risk, and CAD has been reported to occur two to three decades earlier in diabetic subjects as opposed to their non-diabetic counterparts<sup>1</sup>.

However, the increased prevalence of CAD in diabetes has been attributed in large part to the acceleration of coronary atherosclerosis, which occurs at an earlier age and advances more rapidly to clinical cardiovascular events in individuals with diabetes than in those without diabetes<sup>3</sup>. Patients with diabetes are also prone to arterial thrombosis due to persistently activated thrombogenic pathways and impaired fibrinolysis<sup>4</sup>. Moreover, CAD in diabetes is often diffuse, with an increase in the number of affected vessels and in the incidence of moderate stenosis<sup>5</sup>. Detection of narrowing of the coronary lumen in patients with diabetes is often impaired by autonomic neuropathy, which can reduce the symptoms of ischemic CAD, delay its detection, and worsen the prognosis<sup>6</sup>. In addition, diabetic individuals are faced with increased restenosis and mortality rates following revascularization procedures<sup>7</sup>. Coronary artery disease accounts for more than 80% of all deaths and

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Received on 25th June 2021

Accepted on 30th June 2021

75% of all hospitalizations in diabetic subjects<sup>5</sup>. The impact of CAD on myocardial function in diabetes is also exacerbated by diabetic cardiomyopathies and altered metabolism of the myocardium<sup>8</sup>.

Despite modern therapies for CAD, diabetes confers a significant independent excess mortality risk. Given the increasing burden of cardiovascular disease attributable to diabetes, this study was therefore undertaken to compare the nature of in-hospital complications and differing outcome in patients of acute myocardial infarction in diabetics and non-diabetics. A better understanding of the same would help us to devise strategies for optimum management of this high-risk group of patients.

### Material and Methods :

The present prospective observational study was initiated after obtaining Institutional Ethics Committee (IEC) approval and written informed consent from all participants of the study. Total 220 consecutive cases of ST-Elevated Acute Myocardial Infarction admitted to the coronary care unit of a Tertiary Care Centre and who underwent thrombolysis during a period of 2 years from November 2018 to November 2020 were included in the study. The factors considered in the diagnosis were-

- 1) ECG changes i.e., ST - elevation = 1 mm in all leads other than leads V2-V3. For leads V2-V3: = 2 mm in men = 40 years, = 2.5 mm in men < 40 years or = 1.5 mm in women regardless of age<sup>9</sup> and
- 2) Elevated Cardiac Enzymes, CPK-MB and Trop-T levels, = 99 percentile of the upper reference limit<sup>10</sup>.

Patients of STEMI who were not thrombolysed, patients with type 1 DM, impaired glucose tolerance, old myocardial infarction, non-STEMI, unstable angina, valvular heart diseases, cardiomyopathy, any pre-existing systemic end stage disease and refusal of consent were excluded from the study.

The study participants were divided into 2 groups, Diabetics and Non-Diabetics. The diabetic arm included both known cases of Type 2 diabetes and

newly diagnosed cases having HbA1C more than or equal to 6.5<sup>11</sup>. All patients with HbA1C values less than 5.7 were considered as non-diabetic<sup>12</sup>.

All patients were interviewed as per the pre-set proforma. Relevant history was taken and careful physical examination with special reference to hemodynamic parameters as well as relevant investigations was done. 12-lead ECG, cardiac enzyme assay, echocardiography and Coronary angiography were done. 16 patients, which included 13 Diabetics and 3 Non-Diabetics, could not undergo coronary angiography due to poor general condition, early death or financial constraints. All patients, on admission, who fulfilled the criteria for thrombolysis, received thrombolytic therapy with the dose of 1.5 million units of Streptokinase diluted in 100 ml normal saline, over one hour. Over the course of the hospital stay, complications like Recurrent ischemic chest pain, Hypotension, Heart failure, Arrhythmias, Acute Pulmonary Oedema, Cardiogenic Shock, Ventricular septal rupture, Reinfarction and Thrombo- embolic phenomenon were observed for and treated as required. The socio-demographic profile, various risk factors, clinical and laboratory parameters and the observed complications were compared between the 2 groups and analyzed.

### Statistical Analysis :

Epi Info Software used for data analysis. Data analysis included the usual descriptive & univariate analysis. Discrete (categorical) variables were compared by Pearson Chi-Square test & for a continuous variable; student t-test was used. Unadjusted odds ratio with 95% confidence intervals (CI) was calculated & p values were computed. All p values were two-tailed & values < 0.05 were considered statistically significant. The Pearson correlation test was used to assess the correlation between the continuous variables.

### Observations and Results :

Out of total 220 patients, 142 (64.55%) were found to have diabetes and 78 patients (35.45%) were non-diabetic. The mean age of the patients was lower in the diabetic group. In both the groups' maximum

**Table 1 : Comparison of demographic data, time to presentation to the hospital and main presenting complaints between two groups**

Demographic data		Diabetics (n=142)	Non-Diabetics (n=78)	P-value
Age group (Years)	31-40	04 (80%)	01 (20%)	0.950
	41-50	43 (65.2%)	23 (34.8%)	
	51-60	39 (65%)	21 (35%)	
	61-70	41 (62.1%)	25 (37.9%)	
	> 70	15 (65.2%)	08 (34.8%)	
	Mean ± SD	55.7 ± 9.6	58.6 ± 10.7	
Sex	Male	78 (56.12%)	61 (43.88%)	0.001
	Female	64 (79.01%)	17 (20.99%)	
Time to presentation to the hospital (hours)	≤ 3	01 (0.70%)	19 (24.36%)	0.0001
	3-6	32 (22.54%)	11 (14.10%)	
	≥ 6	109 (76.76%)	48 (61.54%)	
	Mean ± SD	7.16 ± 2.19	5.65 ± 2.42	
Main presenting complaints	Chest pain	114 (80.28%)	76 (96.15%)	0.0012
	Dyspnoea	70 (49.30%)	38 (48.72%)	0.935
	Palpitations	61 (42.96%)	35 (44.87%)	0.784
	Syncope	16 (11.27%)	22 (28.21%)	0.001
	Nausea / vomiting	44 (30.99%)	31 (39.74%)	0.190
	Perspiration	116 (81.69%)	65 (83.33%)	0.760

Dyslipidaemia and hypertension were the most prevalent risk factors in the diabetic group as shown in **Table 2**.

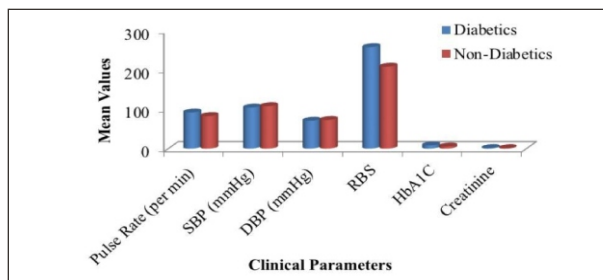
number of patients were in the age group 41-70 years, 86.6% in diabetics and 88.5% non-diabetics. Total numbers of males were 139 (63.20%) and total numbers of females were 81 (36.8%). Most of the patients (157; 71.4%) presented to the hospital = 6 hours. Significant number of diabetics had silent angina with/or angina equivalents. Chest pain and perspiration were the most common presenting features in both the groups as shown in **Table 1**.

Comparison of the on-admission parameters as depicted in **Figure 1** showed that diabetic patients with STEMI, had a higher mean pulse rate of 91.75 per minute as compared to the mean of 82.51 per minute in non-diabetics ( $p=0.0002$ ). Mean random blood sugar (RBS) and mean serum creatinine were also higher amongst the diabetics ( $p=0.001$ ). However, there was no statistically significant difference in either on-admission systolic blood pressure (SBP) or diastolic blood pressure (DBP) between the 2 groups.

**Table 2 : Various risk factors in diabetics and non-diabetics patients admitted with STEMI**

Risk factors	Diabetics (n=142)	Non Diabetics (n=78)	P-value
Smoking	28 (19.72%)	15 (19.23%)	0.930
Alcohol	10 (7.04%)	12 (15.38%)	0.048
Tobacco Chewing	26 (18.31%)	23 (29.49%)	0.057
Hypertension	56 (39.44%)	12 (15.38%)	0.001
Obesity	42 (29.58%)	24 (30.77%)	0.854
Dyslipidaemia	103 (72.54%)	23 (29.49%)	0.001
Family history	36 (26.76%)	29 (37.18%)	0.108

Diabetics had a greater degree of LV dysfunction as was evidenced by higher on-admission Killip Class. 99 (69.68%) of the 142 diabetics had a Killip Class = 2. Maximum number of patients had AWMI in both the groups, 62.68% diabetics 64.10% non-diabetics. Triglycerides, total cholesterol and LDL levels were higher in diabetics as compared to non-diabetics. Mean HDL was lower in the diabetics, (**Table 3**).

**Figure 1 : Various clinical parameters on-admission**

44.4% diabetics had moderate-severe LV dysfunction on 2D-Echocardiography as compared to 30.8% non-diabetics. The mean ejection fraction

was  $41.97 \pm 6.01$  for the diabetics and  $44.74 \pm 5.86$  for the non-diabetics.

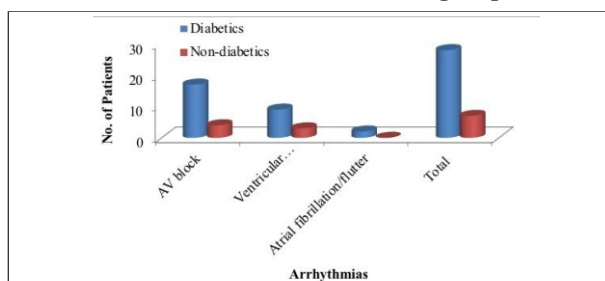
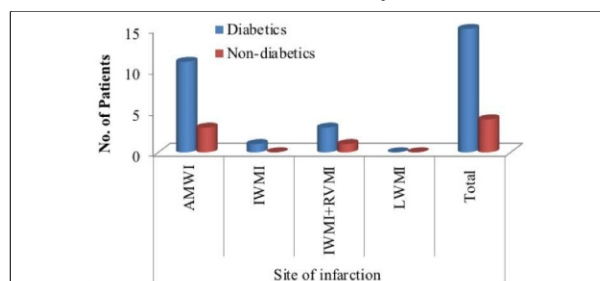
Successful ST segment resolution 1 hour after thrombolysis was seen in only 71 (50%) of the 142 diabetics as compared to 52 (66.67%) of the 78 non-diabetics, ( $p=0.017$ ). 85 (59.86%) diabetics developed diastolic dysfunction as compared to 31 (39.74%) non-diabetics, ( $p = 0.004$ ). Heart failure, development of cardiogenic shock and arrhythmias were more common complications in the diabetics as compared to non-diabetics with statistically significance difference, (**Table 4**).

**Table 3 : Grading of LVF, Type of MI and Type of dyslipidaemia**

Parameters		Diabetics (n=142)	Non-Diabetics (n=78)	P-value
Grading of LVF according to Killip classification	Killip class 1	43 (30.28%)	53 (67.95%)	0.0001
	Killip class 2	27 (19.01%)	12 (15.38%)	
	Killip class 3	16 (11.27%)	03 (3.85%)	
	Killip class 4	56 (39.44%)	10 (12.82%)	
Type of MI based on the territory of infarction	AMWI	89 (62.68%)	50 (64.10%)	0.976
	IWMI	10 (7.04%)	06 (7.69%)	
	IWMI + RVMI	40 (28.17%)	20 (25.64%)	
	LWMI	3 (2.11%)	02 (2.56%)	
Type of dyslipidaemia [Mean (SD)]	Triglycerides (mg/dl)	174.35 $\pm$ 27.69	149.56 $\pm$ 19.88	0.0001
	Total cholesterol (mg/dl)	200.83 $\pm$ 24.94	178.68 $\pm$ 21.71	
	HDL (mg/dl)	48.65 $\pm$ 5.87	51.06 $\pm$ 7.62	
	LDL (mg/dl)	108.44 $\pm$ 15.19	95.29 $\pm$ 14.63	
Left Ventricular (LV) ejection fraction	Severe LV dysfunction (<30)	13 (9.15%)	04 (5.13%)	0.0011
	Moderate LV dysfunction (30-40)	50 (35.21%)	20 (25.64%)	
	Mild LV dysfunction (>40)	79 (55.63%)	54 (69.23%)	

**Table 4 : Comparison of the various complications in diabetics and non-diabetics**

Complications	Diabetics (n=142)	Non-Diabetics (n=78)	P-value	Risk of complications OR (95% CI)
Heart failure	92 (64.79%)	25 (32.05%)	0.001	3.9 (2.09-7.35)
Cardiogenic shock	56 (39.44%)	12 (15.38%)	0.001	3.58 (1.71-7.91)
Arrhythmias	28 (19.72%)	07 (8.97%)	0.037	2.49 (0.99-7.01)
Post infarction angina	40 (28.17%)	23 (29.49%)	0.836	0.94 (0.49-1.82)
Ventricular septal rupture	02 (1.41%)	00 (0.0%)	0.416	-
Intracranial Bleed	00 (0.0%)	03 (3.85%)	0.043	-
Ischaemic Stroke	03 (2.11%)	00 (0.0%)	0.267	-

**Figure 2 : Occurrence of various Arrhythmias in diabetic and non-diabetic group****Figure 3 : Association of site of infarction with mortality**

Coronary Angiography (CAG) showed that the diabetics had a more diffuse atherosclerosis with multi-vessel disease being present in 69% diabetics and 50.1% non-diabetics. A total of 19 patients died in our study, of them 15 were diabetics and 4 were non-diabetics. The diabetics were at 2.19 times increased risk of mortality as compared to non-diabetics [OR =2.19, 95% CI (0.66- 9.35)]. Amongst the 142 diabetics, Cardiogenic shock in 10 (7.04%) and ventricular arrhythmias in 4 (2.82%) were the most common causes of death while ventricular septal rupture (VSR) in 2 (1.41%) and CVE in 1 (0.70%) were the other causes of death. Amongst the 78 non-diabetics, 4 (5.13%) died, all because of cardiogenic shock. The causes of death in the 2 groups were similar with the data not showing any statistical significance ( $p>0.05$ ). Data comparing the site of infarction with mortality in the 2 groups was statistically insignificant ( $p>0.05$ ), (**Figure 3**).

Comparison of the on-admission RBS in the 2 groups with mortality showed that amongst the diabetics, mortality was associated with a higher mean RBS value of 338 as against 248.27 in the survivors, ( $P=0.0003$ ). The mean HbA1C was 9.73 amongst the diabetic non-survivors as compared to 8 in the diabetic survivors, ( $p=0.0001$ ). The duration of stay was more in the non-survivors in both the groups but relatively longer in the non-diabetics with statistical significance, (**Table 5**).

#### Discussion :

In present study the prevalence of diabetes in patients presenting with STEMI was 64.55% which is correlated with the study conducted by *Khan et al*<sup>13</sup> (51.6%) and *Hathi et al*<sup>14</sup> (52.8%). The high prevalence of diabetes in our study could suggest that diabetes mellitus is reaching potentially

**Table 5 : Association between various in hospital parameters and mortality**

Parameter	Outcome	Diabetics (n=142)	Non-Diabetics (n=78)	
On admission Hyperglycaemia (RBS in mg/dl)	Non- survivors (n=19)	338 ± 120 (n=15)	224.5 ± 120 (n=4)	0.0854
	Survivors (n=201)	248.27 ± 84.46 (n=127)	207.34 ± 41.39 (n=74)	0.0001
	P-value (by column)	0.0003	0.4228	-
Glycaemic Control (HbA1C)	Non- survivors	9.73 ± 1.59 (n=15)	-	-
	Survivors	8.0 ± 1.38 (n=127)	-	-
	P-value (by column)	0.0001	-	-
Mean duration of hospital stay (days)	Overall (n=220)	6.64 ± 1.93	5.97 ± 1.86	0.0138
	Non-survivors (n=19)	8.0 ± 2.36 (n=15)	12.25 ± 0.5 (n=4)	0.002
	Survivors (n=201)	7.07 ± 2.15 (n=127)	5.84 ± 2.35 (n=74)	0.003

Results of Binary Multiple Logistic Regression (MLR) analysis for predicting complications in diabetics showed that younger age < 50 years (OR= 3.31, 95% CI 1.10-9.94,  $P=0.033$ ), Male gender (OR=3.94, 95% CI 1.16-13.35,  $P=0.028$ ), presence of Hypertension (OR=12.80, 95%CI 3.65-44.90,  $P=0.001$ ) and tobacco consumption (OR=3.66, 95%CI 1.04-12.95,  $P=0.044$ ) were independent predictors of greater mortality amongst the diabetics.



epidemic proportions in India. In the younger age group STEMI was more frequent in diabetics. Diabetic females were 2.94 times more vulnerable for STEMI as compared to diabetic males. Risk of MI among female diabetics was 3.77 times more as compared to female non-diabetics. Also, the female gender appeared to play a protective role against MI in the non-diabetics. These findings are similar to the other studies<sup>13-15</sup>. The lesser mean age of diabetics in our study could be explained by the increasing prevalence of diabetes in the younger population due to accumulation of risk factors like, smoking, sedentary lifestyle, unhealthy food habits and obesity, besides the genetic and environmental factors. Diabetics presented to hospital much later than the non-diabetics which is correlated with previous study by *Hathi et al*<sup>14</sup>. The diabetic group, besides chest pain, is known to have atypical manifestations of myocardial ischemia such as nausea, vomiting, syncope, fatigue, confusion, dizziness or dyspnoea. A proportion of them do not have chest pain at all, and these taken together explain the delayed presentation to the hospital as compared to non-diabetics, as was the case in present study. 19.72% of the diabetics and 3.85% of the non-diabetics had absence of chest pain in the presence of objective evidence of STEMI. Thus, current study was similar to the previous studies<sup>16, 17</sup> on the subject.

In the diabetics, dyslipidaemia was the most prevalent risk factor followed by hypertension. The higher prevalence of dyslipidaemia could be explained by the increasing sedentary lifestyle, unhealthy dietary patterns, uncontrolled blood sugar levels and other socio-economic and genetic factors. Alcohol on the other hand was found to be a significant risk factor amongst the non-diabetic group. Similar studies<sup>13,14,18</sup> done in the past have identified the presence of these risk factors with varying proportions. The higher heart rate in diabetics could be explained by the impaired autonomic function in the diabetics, leading to greater sympathetic activity. This could also be because of reflex tachycardia, in response to greater incidence of complications like heart failure and cardiogenic shock in this sub-group. The greater

degree of renal impairment in the diabetics as evidenced by the higher creatinine values could be because of the underlying diabetic nephropathy. The diabetics also have diminished renal reserve and higher chances of precipitation of acute kidney injury with minimal insult.

The present study goes in accordance with the old studies<sup>15,18</sup> in terms of the higher on-admission Killip class in the diabetic subjects but is distinct in the much higher percentage of patients falling into this category. Poor access to healthcare facilities, late presentation and delayed treatment of our subjects could have been responsible for the difference in statistics. Similar to the previous studies<sup>15,19</sup> present study suggesting that the diabetics had greater chances of systolic and diastolic dysfunction even after adequate thrombolytic therapies, which portends a poor prognosis.

Heart failure 3.9 times, cardiogenic shock 3.58 times and arrhythmias was 2.49 times more common in the diabetics as compared to non-diabetics. Also all the types of arrhythmias, namely, Atrioventricular block (AV Block), Ventricular tachycardia / fibrillation and Atrial flutter / fibrillation were all observed more frequently in diabetics than the non-diabetics. These findings are in accordance with earlier studies<sup>13,14,&19</sup>. Patients with diabetes have a more depressed left ventricular systolic function, decreased renal function and an increased prevalence multivessel disease or left main coronary artery disease. Also, patients with DM tend to receive incomplete revascularization. These poor clinical conditions and incomplete revascularization could also affect the high incidence of complications in patients with diabetes. The lower incidence of post infarct angina in diabetics could be because of decreased pain threshold and autonomic dysfunction. Comparison of the findings in coronary angiography (CAG) showed that the multi-vessel disease was present in 69% diabetics and 50.7% non-diabetics. Single vessel disease was seen in 49.3% non-diabetics and in 31% diabetics. Thus, the diabetic patients with STEMI tend to have a more diffuse atherosclerosis involving multiple coronary arteries.

Comparison of mortality data, diabetics were at 2.19 times increased risk of mortality as compared to non-diabetics. This observation was similar to that observed in previous studies<sup>13,14,18,&19</sup>. However, there were non-significant differences in mortality based on territory of infarction. Also, the causes of death were similar in both the groups. Early mortality could be higher among patients with diabetes because of impairment of regional left ventricular function in noninfarct-related areas and other factors intrinsic to diabetics, such as diastolic dysfunction and myocardial fibrosis, and the greater risk of development of arrhythmias and sudden cardiac death. Amongst the non-survivors, the stay was prolonged in both the groups as compared to the survivors. The early death amongst the diabetics as compared to non-diabetics could be explained by the greater incidence of arrhythmias and sudden cardiac death amongst this sub-group. It could also be because of the greater severity of the various complications amongst the diabetics. The mortality was associated with a higher mean on-admission RBS value and this is similar to the study done by *Schiele et al*<sup>20</sup>. Comparing HbA1C with the outcome in the 2 groups, the mean HbA1C was 9.73 amongst the diabetic non-survivors as compared to 8 in the diabetic survivors, with statistical significance. Our findings were similar to the old studies<sup>21, 22</sup> on the subject.

### Conclusion :

STEMI occurs at a younger age in diabetics. Women with diabetes lose most of the inherent protection against coronary artery disease when compared to non-diabetics. Painless myocardial infarctions were far more common in diabetics compared to non-diabetics. Heart failure and cardiogenic shock were three to four times more common and more severe in subjects with diabetes than in non-diabetics. This was more than to be expected from the size of the infarction. Life threatening ventricular arrhythmias and heart blocks were two to three times more common among diabetics compared to non-diabetics. In hospital mortality due to myocardial infarction in diabetics was two to three times higher than in non-diabetics.

Thus, in patients with STEMI, presence of diabetes mellitus was associated with worse in-hospital outcome leading to increased mortality and complications as compared to non-diabetic patients.

### Implications of the Study :

In developing countries due to lack of early detection, the acute coronary syndrome may be considered as one of the presentations of diabetes mellitus. Furthermore, HbA1c could be considered as a marker of the presence and burden of coronary artery disease. Morbidity and mortality remain high in diabetic patients with STEMI than in those without it, even after thrombolysis. It reinforces the importance of vigorous preventive measures by lifestyle advice and drugs in these patients. A long-term, intensive approach consisting of behaviour modification and pharmacologic therapy aimed at multiple risk factors is necessary and may result in reduction in cardiovascular complications in patients with diabetes. Behaviour strategies should focus on avoidance of a sedentary lifestyle and unhealthy dietary patterns and abstinence from alcohol and all forms of tobacco. Strategies such as peri-infarction metabolic control and primary angioplasty need to be considered. Research on methods to reduce the influence of diabetes on coronary artery disease is the need of the hour to save the lives at significant risk. Novel targets for diabetes management in patients with coronary artery disease must be identified and tested.

### Limitations of the Study :

- Ours was a small single centre study with a limited number of patients, so a larger multi-centre study would be required for the extrapolation of results to a larger population.
- The study was limited to the hospital stay only, follow up of these patients was not done and so the long-term complications may have been missed.

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