

## A Comparative Study to Assess the Efficacy of Streptokinase in Diabetic Versus Non-Diabetic Acute ST Elevation Myocardial Infarction Patients

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### Abstract

**Objective:** Prominent resolution in the ST segment elevation on electrocardiogram(ECG), thrombolysis at the infarction site restoring perfusion determines the effectiveness of the streptokinase therapy. Hypercoagulable states and lack of efficacy with streptokinase is seen in diabetics. This study aimed to assess the thrombolytic efficacy of streptokinase in diabetic vs non-diabetics patients.

**Methods:** A cross-sectional study was conducted at Cardiology Department of Allama Iqbal Memorial Teaching Hospital, Sialkot from 1st September 2019 to 30th April, 2020. Total 504 patients of which 185 diabetics and 319 non-diabetic were selected. All the patients presenting with first episode of acute ST-elevation myocardial infarction were thrombolysed with 1.5million units of streptokinase within 12hours from the onset of their typical chest pain symptoms. A complete record of ECG changes was kept before and 90 min after thrombolysis with streptokinase. Chi-square test was applied and p value <0.05 was considered significant.

**Results:** 89.19% diabetic patients had >70% resolution of ST segment changes in comparison to 95.61% non-diabetics. 16.76% of the diabetic patients had increased ST-segment elevation post thrombolysis (P-value 0.001). 8.11% and 10.81% reinfarction rates during hospital stay and at one month post-thrombolysis were recorded in diabetics. Reduced left ventricle Ejection Fraction was seen in 62.16% and 58.62% of the diabetic and non-diabetic patients(P-value<0.005).

**Conclusion:** Comparatively decreased efficacy of streptokinase is seen in diabetic patients with reduced resolution of ST-segment. In correspondence with reduced left ventricle EF, re-infarction and stroke episodes.

**Key Words:** Streptokinase, acute myocardial infarction, STEMI, diabetes mellitus, hypercoagulability, atherosclerosis.

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### Introduction

In Pakistan, one of the major cause of increasing mortality and morbidity is myocardial infarction

mainly due to atherosclerosis of the coronary arteries.<sup>1</sup> Acute myocardial infarction has mainly increased the death ratio in many world leading countries.<sup>2</sup> Majority of the population in Pakistan between 46-55 years of age are at risk of myocardial infarction.<sup>3</sup>

Diabetes mellitus is one of the main co-morbidities associated with myocardial infarction others being dyslipidemia, smoking, hypertension and previous episode of ischemic heart diseases.<sup>4</sup> High blood sugar or glucose levels in diabetics identifying poor glyce-mic control are important cause of hypercoagulable states in diabetic patients.<sup>5</sup> Therefore, hypercoagulable state risk is considered more common in diabetic population.<sup>6</sup> Also fibrinolysis is decreased in diabetics

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as a result of increased plasminogen activator inhibitor type 1, thus progressive thrombus formation and accelerated plaque formation.<sup>7</sup> This increases the incidence of myocardial infarction among diabetics as compared to non-diabetics. ST-segment resolution is a predictor to see the outcomes in myocardial infarction patients.<sup>8</sup> Early thrombolysis with streptokinase in acute stage of myocardial infarction to restore blood supply of the myocardial cells is the main goal. Significant ST segment changes on ECG after thrombolytic therapy is more economical for accessing the prognosis of the disease, comparatively to coronary angiogram. Increased mortality and morbidity is observed widely in diabetic patients post thrombolysis.<sup>9</sup>

Our study mainly aimed at assessing the efficacy and outcomes in diabetic patients receiving thrombolytic therapy with streptokinase in acute myocardial infarction and comparing the results with non-diabetic patients. The efficacy of streptokinase associated with diabetic population will be assessed by electrical parameters (ECG changes) >70% or <70% ST-segment resolution, relieve of typical chest-pain symptoms, raised CK-MB levels, number of re-infarctions or stroke episodes and left ventricle ejection fraction (E.F%) estimation through echocardiography post-thrombolysis. This will help choose different treatment options as coronary interventions in diabetic patients with associated morbidities especially acute myocardial infarction.

## Methods

A cross-sectional study was conducted at the department of cardiology, Allama Iqbal Memorial Teaching Hospital, Sialkot. The data was collected over a period of eight months from 1st September, 2019 till 30th April, 2020 through electronic databases. After informed consent, 504 patients were carefully registered of which 185 were diabetics and 319 non-diabetics. After confirmation their data (including their complete medical or any surgical history) was entered on the computerized database. The inclusion criteria had patients (diabetics or non-diabetics) with first episode of MI, suffering from typical chest-pain for >30mins but <12hours, ST-segment elevation in concordant leads on ECG and were thrombolysed with streptokinase within 12 hours from onset of their symptoms. Pregnant females, those patients with any

contraindications to thrombolysis with streptokinase, other than ST-segment ECG changes, with chest pain for >12hours, having previous cardiac intervention or history of ischemic heart disease were in the exclusion criteria. The patients were divided into two groups i.e diabetics and non-diabetics. Only previously diagnosed diabetic patients (HbA1C levels >6.5%) were enrolled. The study is approved by research and ethics committee of KMSMC/AIMTH, Sialkot letter No.46/REC/KMSMC Date:04/01/2020.

An ECG was obtained on presentation and 90 minutes after streptokinase therapy for complete record. The outcome of thrombolysis with streptokinase in both the groups was assessed based on electrical parameters, relieve of patient symptoms, tachycardia episodes, reduction in left ventricle systolic function by calculating EF(%) on bedside echocardiography and post thrombolysis reinfarction or stroke episodes. The electrical parameters were assessed whether the patient had increased or persistent ST segment elevation, or had >70% decrease / resolution in ST segment elevation after administration of streptokinase, which is considered to be a successful reperfusion sign. ECG reporting was done by a single senior E.R doctor to avoid any discrepancies in interpretation. Similarly, continuous monitoring for any re-infarction (with raised Ck-MB levels or new concordant ST-segment elevations on ECG within 6 days of patients hospital stay) was done. Episodes of cerebrovascular accidents of the same patients were recorded easily due to re-admission of the patients to the same hospital. Regular follow-ups of all the enrolled patients were ensured every 1 month for first six months after their acute MI episode by repeated telephonic reminders and than updating their data on electronic data collection devices respectively.

The data were analyzed by using SPSS version 23. Mean and standard deviation were used to calculate quantitative variables as age. Both (male & female) genders were included as qualitative variables and were measured using percentages. Outcome variables for successful reperfusion were recorded and the results compared between diabetics and non-diabetics groups using Chi-square test. P-value of <0.05 was considered significant.

## Results

A total of 504 patients were enrolled, of which 185

were diabetics and 319 non-diabetics ,mean age in the diabetic group was 54±9.6yrs as compared to 57±13.3yrs in non-diabetics (table 1). Age range was between 44 to 64yrs in diabetics and 42 to 71yrs in the non-diabetic group. Among the diabetic group 90 (48.65%) were males and 95 (51.35%) were females whereas, the other comparative group of non-diabetics had greater number of males 232(72.72%) than 87 (27.27%) females with the significant P-value of 0.001. Average basal metabolic index (BMI) of 33.71±9 was calculated in diabetic population and 23.51±7.5 in non-diabetic group. According to the

**Table 1:** Baseline Characteristics of Patients

	Diabetics	Non-diabetics	p-value
<b>AGE</b>	54±9.6 (34.3%)	57±13.3(65.7%)	.082
<b>GENDER</b>			
Male	90 (48.65%)	232 (72.72%)	.001
Female	95 (51.35%)	87 (27.27%)	
<b>BMI</b>	33.71±9 (37.8%)	23.51±7.5(62.2%)	.603
<b>Cholesterol</b>	185.19±37.52 (35.0%)	170.81±38.34 (65.0%)	.037
<b>HbA1c</b>	9.65±2.66 (46.4%)	6.01±0.76 (53.6%)	.008

**Table 2:** Post Streptokinase Therapy Efficacy Determinants

	Diabetics		Non-Diabetics		P-Value
	count	%	count	%	
Symptoms relieved	98	52.97%	258	80.88%	.004
Inhospital rethrombolysis	15	8.11%	10	3.13%	.000
One month reinfarction	20	10.81%	15	4.70%	.004
One month stroke	3	5.0%	0	0.0%	.041
Six month reinfection	5	2.70%	0	0.0%	.280
Six month stroke	2	1.08%	0	0.0%	.447
St-Segment Elevation increased	31	16.76%	0	0.0%	
St-Segment Resolution >70%	165	89.19%	305	95.61%	.001
St-segment Resolution <70%	20	10.81%	14	4.39%	
CK-MB (raised)	8	4.32%	7	2.19%	0.063
Heart rate >100 bpm	80	43.24%	105	32.92%	0.013
Reduced LV ejection fraction	115	62.16%	187	58.62%	0.000

biochemical parameters significantly increased HbA1c values 9.65±2.66 were seen in the diabetics with P-value 0.008. Blood cholesterol levels were found deranged among the two groups. (table 1)

52.97% of the diabetics and 80.88% non-diabetics had their symptoms relieved with a significant P-value 0.004 (table.2). The incidence of re-infarction in diabetics during their hospital stay (<6 days) was 8.11% (P-value 0.000) and 10.81%(P-value .004) after one month. With regards to the electrical activity our results showed that 16.76% (P-value 0.001) of diabetics showed increased or persistent ST segment elevation. 95.61% of the non-diabetics in comparison to diabetics 89.19% had >70% reduction in the ST-segment post thrombolysis(P-value 0.001). About 10.81% diabetics in group 1 had <70% ST segment resolution after thrombolytic therapy. 43.24% diabetics had episodes of tachycardia (H.R >100bpm) and 62.16%(p value <0.005) had reduced left ventricular ejection fraction in comparison to 58.62% non-diabetic MI patients(table 2).

## Discussion

Thrombolysis with streptokinase is an effective and well known treatment option in patients presenting with acute ST-elevation myocardial infarction. Presence of associated co-morbidities or late (>12hours) presentation can affect the efficacy of streptokinase therapy<sup>10</sup>. All the patients in our study presented in >30mis from the onset of their symptoms but not more than 12 hours. Diabetes is one of the main risk factors associated with cardiovascular diseases.<sup>11</sup> Increased morbidity is associated with diabetic acute MI patients and reduce effect of streptokinase was seen in a research by varshit hathi.<sup>12</sup> This led us to make a hypothesis that diabetes solely may effect the efficacy and the outcomes of streptokinase therapy. Therefore, we conducted this study to assess the efficacy of streptokinase and compared the results specifically among diabetic and non-diabetic groups with acute ST-elevation myocardial infarction.

The mean HbA1c levels in diabetic population were 9.65±2.66 and 6.01±0.76 in non-diabetic group. HbA1c is one of the important biomarkers to diagnose diabetes and to monitor its prognosis.<sup>13</sup> Therefore, HbA1c is used as continuous risk measurement variable for coronary artery diseases. Post thrombolysis reduced or decreased ST-segment resolution is seen significantly in diabetic patients in comparison to non-diabetics.<sup>14</sup> This was quite similar to our study results where comparatively reduced ST-segment resolution was seen in the diabetic group, 10.81% of the diabetics had <70% resolution of ST-segment and 16.76%



showed persistently increased ST-segment elevations post thrombolysis (P-value 0.001). Significant resolution of ST-segment was seen in 95.61% non-diabetic group (P-value 0.001) with no persistent or increase elevations post thrombolysis.

Among diabetic patients 98(52.97%) had their typical chest pain symptoms relieved after thrombolysis with streptokinase whereas 258 out of 319 non-diabetics patients had their typical chest pain symptoms relieved with a significant p-value (0.004). 8.11% of the diabetics had re-infarction during their hospital stay and were re-thrombolysed with streptokinase in comparison to only 3.13% non-diabetics. According to our results the risk of stroke at one month in diabetics was 5% and 1.08% at six months with no episodes seen in the other comparative group. So was the risk of six month re-infarction which was common in diabetics. These results were consistent with the Framingham heart study, which proved after 20 years of trials that diabetic patients have two-fold to three-fold increased risk of clinical atherosclerosis and the cardiovascular disease mortality was greater for diabetic women as compared to diabetic men but after adjustment of other associated risk factors it was same for men and women.<sup>15</sup>

Similarly, other determinants as heart rate and effect on left ventricle ejection fraction after streptokinase therapy were assessed. Some researchers stated that patients with diabetes respond poorly after thrombolytic therapy.<sup>16</sup> As was seen in our study results 43.24% diabetics had episodes of tachycardia (heart rate >100bpm) and most of them 62.16% had reduction in their left ventricle ejection fraction in comparison to 58.62% non diabetic patients. The limitations to our study included that we collected data from only one center with patients belonging to same ethnic backgrounds. Moreover, poor compliance of patients with medication and sedentary life styles were noticed. Therefore, more attention is required for treating diabetic myocardial infarction patients. Other treatment options as coronary interventions may be considered in diabetic acute STEMI patients.

## Conclusion

In comparison to non-diabetics, decrease efficacy of streptokinase is seen in diabetic patients with reduced resolution of ST-segment. Post thrombolysis failure was correlated with reduced EF, re-infarction and stroke episodes.

**Conflict of Interest:** None

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#### **Authors Contribution**

**HZ:** Conceptionlization of Project

**RB:** Data Collection

**RN:** Literature Search

**IA,RN,CJI:** Statistical Analysis

**RN:** Drafting, Revision

**RN:** Writing of Manuscript