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TO STUDY THE LEVELS OF HBA1C AND IT IS PROGNOSTIC IMPORTANCE IN THE ACUTE CORONARY ARTERY DISEASE IN TYPE-2 DIABETICS POPULATION

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ABSTRACT

Background: It is believed that chronic hyperglycemia (assessed by glycosylated haemoglobin levels) is related to the development of microvascular disease. Since Mortality due to coronary heart disease is very high in diabetics, it is imperative to understand the relation of increased levels of HbA1c in patients of acute myocardial infarction.

Aims: To study the levels of HbA1c and it is prognostic importance in the acute coronary artery disease in type-2 Diabetics population.

Material And Method: The study was conducted on 60 patients admitted were divided into 2 groups of 30 patients each. Group A: Type 2 Diabetes Mellitus with acute myocardial infarction. And Group B: Non diabetic patients of age and gender matched with acute myocardial infarction as control in the department of medicine Rajindra Hospital and Govt. Medical college Patiala and the biochemical investigations were conducted in the department of biochemistry Govt. Medical college Patiala and the results were Statistically analysed.

Result: The mean value of HbA1c was found 8.27$\pm$ 1.22 % in the group A patients and mean value of HbA1c 5.79 $\pm$ 0.50% was found in the group B patients. Out of the 30 diabetic patients presenting with acute myocardial infarction, 23 (76.66%) had a poor glycemic control, as evidenced by HbA1c levels > 7%. Poor glycemic control among the diabetics (HbA1C > 7%) were found to have a significant positive correlation with Myocardial dysfunction (systolic and diastolic) and Heart failure

Conclusion: In conclusion, our study results show a significant association of glycemic control, measured by HbA1C levels. The Study shows that patients with DM when compared to non-diabetics have increased morbidity and severity after acute myocardial infarction.

Keywords: HbA1c (Glycosylated haemoglobin) Type 2 DM (Type 2 Diabetes Mellitus), ACS

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(Acute Coronary Syndrome), CAD (coronary artery disease), CPK-MB (Creatine Phosphokinase), ECG (Electrocardiography), MI (Myocardial Infarction), CHD (coronary heart disease), NSTEMI (non-ST elevation Myocardial infection.

1. INTRODUCTION

CAD has emerged as the single most important cause of death worldwide as well as in India. In 2013 CAD caused an estimated 7.5 million deaths worldwide accounting for 13.3% of all deaths. [1] CHD is a leading cause of morbidity and mortality in diabetes. Around 22-27% of patients admitted with acute coronary syndrome (ACS), have been reported to be presenting with established diabetes. [2-4] Chronic hyperglycemia has been hypothesized to contribute to CHD in diabetic as well as non-diabetic individuals, but there is a debate whether this relationship is independent of known CHD risk factors. [5]

Both type I and type II diabetes are powerful and independent risk factors for CAD, stroke, and peripheral arterial disease. Atherosclerosis accounts for virtually 80% of all deaths among diabetic patients. Prolonged exposure to hyperglycemia is a major factor in the pathogenesis of atherosclerosis in diabetics. Diabetic patients without prior MI have high risk of having myocardial infarction at rates comparable to non-diabetic patients with previous myocardial infarction. [6] A recent report has found that elevated HbA1c levels are also predictive for cardiovascular disease and mortality in patients without DM. [7] Every 1% increase in HbA1c is associated with a 20 to 30% increase in cardiovascular events, and all-cause mortality independent of diabetic status. Diabetic patients without history of MI have as great a risk for infarction as that in case of non-diabetics with a previous episode of MI. Diabetes mellitus (DM) is associated with a 2 to 4 fold increase in risk of cardiovascular disease.

Going by the aforced mentioned findings, Elevated HbA1c level is associated with higher risk of mortality in patients without recognized DM even after adjusting for other known risk factors but has neutral effect on mortality in patients with DM. [8] Keeping the fact in view, we intended to determine HbA1c levels as an independent predictor of morbidity and mortality in patients following acute MI. For this purpose, in our present study we analyzed prognostic significance of HbA1c in 60 patients with acute MI.

2. MATERIALS AND METHODS

60 patients were admitted in the Department of Medicine in the Rajindra Hospital, Patiala with diagnosis of acute MI, 50% of who were Diabetic (type-2 DM) and 50% Non-Diabetics were enrolled for the study Inclusion criteria: (i) Patients aged 35 to

75 years with acute MI, (ii) Documented cases of diabetes and those fulfilling the diagnostic criteria of diabetes were considered in the group A (Diabetics) and patients not fulfilling the set criteria for diabetics were considered non-diabetics and were taken in group B.

Exclusion criteria: (i) Age less than 35 years or more than 75 years, (ii) Patients with severe renal dysfunction, (iii) Patients with severe hepatic dysfunction and (iv) Patients with sepsis, hypothyroidism.

Method: A Detailed history and complete physical examination of the patients were carried out.

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Necessary investigations that is E.C.G, CPK- MB/, Cardiac Troponin levels, Echocardiography, Fasting/ random blood sugar, HbA1c, Lipid Profile were done in every patient. The patients were divided in two equal groups; Type 2 DM: Group A and Non-Diabetics: Group B

STATISTICAL ANALYSIS

Statistical analysis was carried out by using a computer based statistical analysis-based program, SPSS version 11.5. A p value of <0.05 was taken as significant. SPSS is a widely used program for statistical analysis in social science. It is also used by market researchers, health researchers, survey companies, government education researchers,marketing organizations, data miners. [9]

3. RESULTS

Results with broad analysis of this prospective case control study conducted over a period of two years, upon patients admitted with acute MI to Department of Medicine, Rajindra Hospital, Patiala are as under: -

The mean value of HbA1C was found 8.27 $\pm$ 1.22 % in the group A patients and mean value of HbA1C 5.79 $\pm$ 0.50% was found in the group B patients. Out of the 30 diabetic patients presenting with acute myocardial infarction, 23 (76.66%) had a poor glycemic control, as evidenced by HbA1C levels > 7%.

Table 1 shows the distribution of diabetics Group A patients, according to their levels of glycemic control.

	Group A		
HbA1c%	Males	Females	Total
6.5-7	4	3	7 (23.33%)
7.1-8.5	8	5	13 (43.33%)
>8.5	7	3	10 (33.33%)
Total	16	14	30 (100.0%)
Mean HbA1c%	8.27$\pm$ 1.22		

In the table-1: - Shows HbA1c levels ranged between 6.8% and 11%. Only 7 patients of the total 30 studied (23.33%), had good glycemic control (HbA1c<7%). 43.33% (13) of the patients had poor glycemic control, as seen by their HbA1c levels (7.1-8.5%). 33.33% (10) patients had very poor glycemic control as suggested by HbA1c >8.5%. The mean HbA1c in this group was 8.27 $\pm$ 1.22%.

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Table 2 shows the distribution of patients in the Group B according to their HbA1c levels.

	Group A		
HbA1c%	Males	Females	Total
<5.7	8	8	16(53.33%)
5.7-6.4	9	5	14 (46.66%)
Total	17	13	30 (100.0%)
Mean HbA1c%	5.79± 0.509		

In the above table-2 HbA1c ranged between 4.7% and 6.4%. Out of 30 Patients,16 Patients (53.33%) had HbA1c levels < 5.7% and 14 (46.66%) patients were having HbA1c between 5.7% - 6.4%. The mean HbA1c was 5.79 ± 0.509 %.

Table 3 shows the correlation between increasing duration of diabetes and presence of complications

	Complications			
Duration of Diabetes (in years)	Yes	No	Total	P value
0	0	4	4	0.004
<5	4	5	9	
5-10	7	0	7	
10-15	3	2	5	
>15	5	0	5	
Total	19	11	30	

In the above table-3 it was observed that as the duration of diabetes advanced, the complications occurring as the result of acute myocardial infarction increased and this correlation was found to be significant. (p value 0.004)

Table 4 shows the presenting symptoms of patients in both the groups

Symptoms	Group A (n=30)	Group B (n=30)	P value
Angina	11 (36.67%)	19 (63.33%)	0.039
Breathlessness	21(70.0%)	13 (43.33%)	0.037
Orthopnea	17 (56.67%)	7(23.33%)	0.008
Pedaledema	6(20.0%)	2(6.67%)	0.129
Cough	9(30.0%)	8(26.67%)	0.774

In the above table-4 many patients in both groups had more than one complaint at presentation. Angina was the most common presenting symptom in Group B and was present in 19 (63.33%) patients compared to 11(36.67%) patients in Group A. This difference between the two groups was very significant (p value 0.039). Breathlessness was the most common symptom in Group A, being present in 21 (70%) patients, versus only 13(43.33%) patients in Group B. This

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difference was statistically significant (p value 0.037). Orthopnea was also significantly more in Group A, compared to Group B (56.67% vs 23.33%) (p value 0.008). Pedal edema and cough were also more in group A as compared to B but the difference was not significant.

Table 5 shows the changes in echocardiography in Group A and Group B

Echo Changes	Group A (n=30)			Group B (n=30)			P Value
	Total	STEMI	NSTEMI	Total	STEMI	NSTEMI	
MR	6 (20%)	6	-	3 (10.0%)	3	-	0.584
Systolic Dysfunction	19 (63.33%)	12	7	10 (33.33%)	6	4	0.071
Diastolic Dysfunction	22 (73.33%)	12	10	11 (36.67%)	7	4	0.004

In the above table-5 many patients had more than one abnormality on Echocardiography systolic and diastolic dysfunctions were more in Group A, when compared to Group B (19 vs 10, and 22 vs 11). The difference in systolic dysfunction between group A and group B was not statistically significant (p values 0.071). Whereas, the diastolic dysfunction was significantly more in group A as compared to group B (p values 0.004) Mitral regurgitation was present more in group A as compared to group B (6 vs 3), but it was not statistically significant.

Table 6 shows the impact of HbA1c on the cardiac complications in the Group A patients

Complications	6.5-7%(7)	7.1-8.5%(13)	>8.5%(10)	Total (30)	P value
Reinfarction	0(0.0%)	0(0.0%)	2(100.0%)	2(100.0%)	0.419
Arrhythmia	1(20.0%)	2(40.0%)	2(40.0%)	5(100.0%)	0.847
Myocardial rupture	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	-
Heart failure	1(9.09%)	4(36.36%)	6(54.54%)	11(100.0%)	0.039
Shock	1(16.67%)	2(33.33%)	3(50.0%)	6(100.0%)	0.666
Death	1(14.28%)	3(42.86%)	3(42.86%)	7(100.0%)	0.518

In the above table-6 many of the patients had more than one complication. Most of the complications were present in patients with HbA1c> 7%. Both of the patients with reinfarction had an HbA1c > 8.5%. 54.54% of patients with heart failure had poor glycemic control as they were having HbA1c >8.5%, whereas only one patient (9.09%) of heart failure had good glycemic control, with HbA1c < 7%. This correlation between poor glycemic control and heart failure was statistically significant (p value 0.039). However, there was no significant correlation between poor glycemic control (HbA1c > 7%) and cardiogenic shock in hospital death or arrhythmias.

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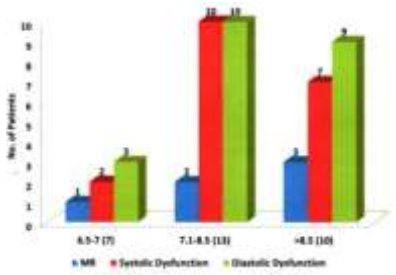

Figure 1 Shows the relationship between HbA1c levels and Echocardiography findings in Group A Patients

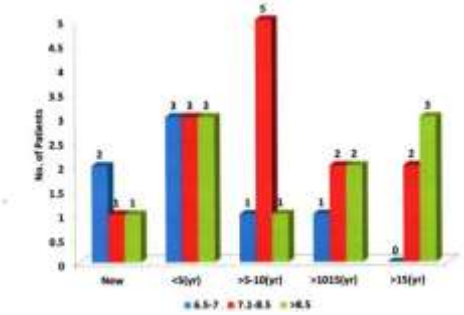

Figure 2 Shows the relationship between HbA1c levels and duration of diabetes in Group A Patients

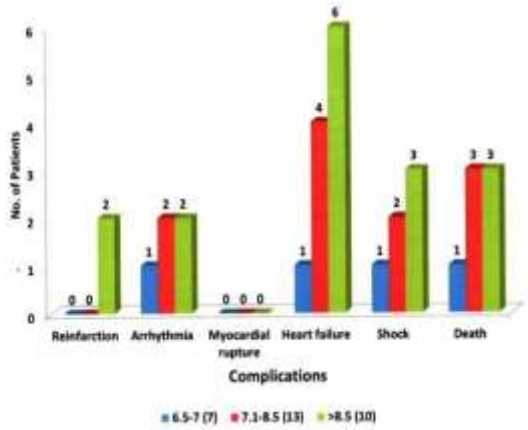

Figure 3 shows the impact of HbA1c levels on the cardiac complications

4. DISCUSSION

We observed that, 33.33% of the diabetics admitted with acute MI had diabetes for more than 10 years, all having HbA1c >7% with only 1 exception. The observation is in line with Saleem et al [10] who have stated that severity of CAD was correlated with the duration and poor control of DM as shown by higher levels of HbA1c. In our observations pertaining to the

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relationship between HbA1c and duration of diabetes, the mean HbA1c of patients was 8.01± 1.03% (less than 5 years diabetes), 8.42 ± 1.29%, (10 to 15 years) and 9.34 ± 1.86% (more than 15 years). The increasing (with duration) trend of mean HbA1c levels is in concordance to the study conducted by Yousefzadeh et al [11]in 2015.

Most of the diabetics in our study, presented with breathlessness, while among the non-diabetics, angina was the most common symptoms at presentation (63.33%) as against only (36.67%) in case of diabetics. patients had angina. This difference between the two groups was statistically significant (p value 0.039). The difference may be because many diabetics

do not experience symptoms of ongoing myocardial ischemia because of the diabetic neuropathy. [12] Our observation regarding breathlessness and orthopnea being much more common among the diabetics is supported by a study conducted by Lewis et al [13]in 2003. The study reports that in patients with MI and without previous heart failure symptoms, diabetes was associated with a 42% increased risk of developing heart failure in comparison to those without diabetes. Similarly, a study by Murcia et al

[14]in 2004, showed that in stable patients with reduced LVEF following acute MI, the risk of developing symptomatic heart failure, after adjusting for co-morbidities, was 65% greater in case of diabetics.

According to study by Poirier et al

[15] in 2001, studies that left ventricular diastolic dysfunction is much more common in subjects with well-controlled type 2 diabetes. In our study, also, diastolic dysfunction was seen in a higher percentage of diabetics compared to non-diabetics. Systolic dysfunction was also present more in diabetics as compared to non-diabetics but not in a statistically significant proportion. This findings in agreement to the study conducted by Stone et al [16] (1989) who observed no statistically significant difference between number of diabetic and non-diabetic patients having systolic dysfunction and reduced ejection fraction admitted with acute MI.

Our study, brings out that myocardial dysfunction (systolic and diastolic) was significantly and positively associated with poor glycemic control (HbA1c >7%) among the diabetic patients. The finding is substantiated by Barzilay et al [17] (2004) who showed a positive correlation between high fasting blood sugar levels and higher incidence of congestive cardiac failure as well as by Bertoni et al [18] (2004) who found higher rates of heart failure in diabetics with poor glycemic control. In our study heart failure was nearly twice more common among diabetic patients when compared to the non-diabetic population. This is in agreement with the studies conducted by Dubey et al [19] (2016), Lewis et al [13] (2003), Murcia [14]et al (2004) and Stone et al [16] (1989). In our study, poor glycemic control (HbA1c> 7%) was found to have a positive and significant correlation with heart failure. However, this was in disagreement to the study conducted by Liu et al [8] (2011), Mc Ginn et al [20] (2011) in which there was no statistically significant difference in incidence of heart failure among diabetics and non-diabetics patients of post MI. Chowdhury et al [21] (1998), Rasoul et al [22] (2007) and Cicek et al [23] (2011) have suggested that HbA1c level was an important predictor of both in-hospital and long-term mortality

In the present study, all of the complications were found to be more in patients having HbA1c levels more than 7%. The facts find support from Khawetal [24] (2004), in the EPIC-Norfolk

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study, finding that people with HbA1c levels less than 5% had the lowest rates of cardiovascular disease and mortality. They proposed that the risk of cardiovascular disease increased with increasing levels of HbA1c, and that HbA1c is predictive of CAD even in non-diabetics. They found that persons with HbA1c less than 5% had the lowest rates of cardiovascular disease and mortality.

5. CONCLUSION

The study results show a significant association of glycemic control (measured by HbA1c levels) on the modes of presentation, and outcomes of acute myocardial infarction. The poor glycemic control among the diabetics (HbA1C > 7%) were found to have a significant positive correlation with Myocardial dysfunction (systolic and diastolic) and Heart failure This study in line with some earlier reports brings out that acute myocardial infarction can be the initial presentation of DM and there appears to be a graded rise in cardiovascular risk with increasing degrees of glucose intolerance. Our study also shows that patients with DM when compared to non-diabetics have increased morbidity and severity after acute MI. We conclude that every patient of acute MI should be screened for glucose intolerance and diabetes by testing for HbA1c levels. This will help in more informed prognosis and hence in charting a better treatment plan.

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