ORIGINAL ARTICLE

JIACM 2024; 25 (3): 106-10

Association of HbA1c with Severity and Outcome of Acute Coronary Syndrome in Patients of Type 2 Diabetes Mellitus

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Abstract

Background: Diabetes is a major risk factor for acute coronary syndrome (ACS) and is associated with a poor prognosis in patients with an ACS. This study was conducted to analyse the association of HbA1c with severity of ACS in diabetic patients and the outcome post-ACS.

Material and Methods: Study was conducted at Department of Medicine and Cardiology in PGIMER, Dr Ram Manohar Lohia Hospital, New Delhi from November 2012 to February 2014. Consecutive diabetic patients who had ACS were selected. Study group consisted of 60 patients. Severity of ACS and the outcome post-ACS were analysed in different groups according to HBA1c levels. Severity of ACS was analysed by Killip class, TIMI score, 2D-ECHO findings and coronary angiography. Outcomes included in-hospital events (arrhythmias, CHF, pulmonary oedema, hypovolemic shock, reinfarction), re-hospitalisation and mortality within hospital stay and within one month of event. Statistical software package SPSS version 20.0 was used for analysis of data.

Results: Patients were divided into 2 groups according to HbA1c level, i.e., group 1 with HbA1c <8.5% and group 2 with HbA1c ≥8.5%. Severity of ACS was assessed by Killip classification, TIMI score and coronary angiography. In HbA1c group 2, the proportion of patients with Killip class 4 (45%) were significantly more in comparison to proportion of patients (5%) in HbA1c group 1 (p value <0.001). The proportion of patients with high-risk TIMI were significantly more in HbA1c group 2 (95%) in comparison to HbA1c group 1 (22.5%) (p value <0.001). The proportion of patients in HbA1c group 2 who had complications (85%) were significantly more in comparison to proportion of patients (27.5%) with complications in HbA1c group 1 (p value <0.001). In HbA1c group 2, the proportion of patients (45%) with re-hospitalisation/death within 1 month of event were significantly more in comparison to proportion of patients (17%) with re-hospitalisation/death in HbA1c group 1 (p value - 0.023).

Conclusion: In conclusion, HbA1c was an independent factor influencing the severity of ACS. Poor control of diabetes as shown by higher levels of HbA1c is associated with higher severity of ACS and more complications post-ACS.

Key words: Diabetes, acute coronary syndrome, HbA1c.

Introduction

Diabetes mellitus is a metabolic disorder characterised by hyperglycaemia, together with impaired metabolism of glucose and other energy-yielding fuels such as lipids and proteins. The number of people suffering from diabetes mellitus worldwide is increasing at an alarming rate, with a projected 366 million in 2030 in comparison to 191 million in 2000[1].

Diabetes is associated with both microvascular and macrovascular complications. Macrovascular complications start taking place long before the symptoms of diabetes appear[2]. It accelerates the process of atherosclerosis by the formation of advanced glycation end products, which increases endothelial dysfunction[3].

Hyperglycaemia is an independent risk factor for acute coronary syndrome syndrome (ACS)[4]. The term ACS includes ST elevation myocardial infarction, Non-ST elevation myocardial infarction and unstable angina. Epidemiologic evidence indicates that diabetes is a major risk factor for ACS and its burden contributed by diabetes is on the rise[5]. People with type 2 diabetes have a two-fold increased risk of ACS within the first five years of diagnosis, in comparison to the general population[6].

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The risk of having ACS in diabetic patients is equal to the risk in a non-diabetic individual having previous ACS[7]. The risk of death from coronary heart disease associated with type 2 diabetes is about 50 per cent more in women than in men[8].

Diabetes is associated with a poor prognosis in patients with an ACS having more acute glycometabolic disturbances which imparts a negative impact on outcome[9].

Thus, this study was conducted to assess the severity of ACS in diabetic patients and the outcome post-ACS.

The objectives of this study were: 1) To measure HbA1c in type 2 diabetes mellitus patients having a first episode of ACS, 2) Assessment of severity of ACS in patients of type 2 diabetic patients, 3) To study outcomes of ACS in type 2 diabetes patients.

Material and Methods

The study was conducted at Departments of Medicine and Cardiology in PGIMER, Dr Ram Manohar Lohia Hospital, New Delhi from November 2012 to February 2014. Consecutive ACS patients were selected from the patients attending the Medicine or Cardiology departments at Dr RML Hospital, New Delhi. The study group consisted of 60 patients. Valid written informed consent was taken from all patients prior to inclusion in the study.

Inclusion criteria was newly or previously diagnosed type 2 diabetes patients having first episode of ACS.

Exclusion criteria were: 1) Previous history of congestive heart failure, 2) Recurrent episode of ACS, 3) Congenital heart disease or known cardiomyopathy. 4) Valvular heart disease. 5) Patient with known systolic dysfunction (LVEF <50%). 6) Echo findings of old scar or previous wall motion abnormality.

Acute myocardial infarction was diagnosed when symptoms were consistent with increase in cardiac enzymes – creatine kinase MB fraction >2 times upper limit of normal range or total creatine phosphokinase >2 times upper limit of normal range and/or positive troponin I or T results. ST segment elevation acute myocardial infarction was defined as persistent ST-segment elevation of ≥1 mm in 2 contiguous electrocardiographic leads or the presence of a new left bundle branch block in the setting of positive cardiac enzyme results.

Non-ST-segment elevation myocardial infarction was defined as occurrence of acute myocardial infarction in the setting of positive cardiac enzyme results with or without accompanying electrocardiographic changes other than ST-segment elevation[11].

Unstable angina was defined as cardiac enzymes negative for myocardial infarction and electrocardiographic changes: transient ST-segment elevation of ≥1 mm in 2 contiguous leads; ST-segment depression of ≥1 mm; new T-wave inversion of ≥1 mm; or pseudo normalisation of previously inverted T-waves[11].

Measurement of HbA1c was done according to the method used in our hospital. Bayer's $A1_c$ NOW$^+$ Monitor kit was used to assess HbA1c level.

Left ventricular ejection fraction was calculated by 2D-echocardiography and was assessed by modified Simpson's method from apical two chamber and four chamber views. LVEF was stratified as - 45 to 55% (mild), 35 to 45% (moderate), <35% (severe) dysfunction[12].

The severity of ACS was studied in the form of single vessel, double vessel or triple vessel disease, Killip13 class and TIMI score.

Killip classification was done as follows: class 1- no CHF, class 2-rales and /or increased JVP, class 3-acute pulmonary oedema, class 4-cardiogenic shock.

Outcomes studied included in-hospital events (arrhythmias, CHF, pulmonary oedema, hypovolemic shock, reinfarction), re-hospitalisation and mortality doing hospital stay and within one month of the ACS event.

Statistical analysis

All the data collected was entered in MS-Excel and statistical software package SPSS version 20.0 was used for analysis of data. Chi square test and Fischer exact test was used as test of association for qualitative variables. Statistical significance was accepted RA $p \leq 0.05$.

Results

Total patients included in the study were 60. A total of 37 (61.7%) patients were male and 23 (38.3%) were female. A total of 78% subjects were already diagnosed cases of diabetes and 21.7% subjects were newly diagnosed at the time of the event.

Patients were divided into 2 groups according to HbA1c level ie group 1 with HbA1c <8.5% and group 2 with HbA1c ≥8.5%.

Fig. 1 Shows distribution of patients according to age.

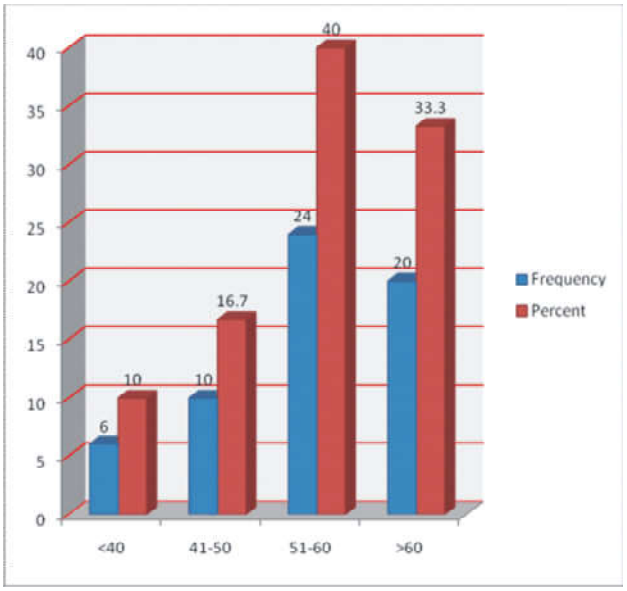

Fig. 1: *Distriution of patients according to age (n = 60).*

Table I: Association of HbA1c levels with Killip class (N = 60).

Killip class	HbA1c group 1 (<8.5%)	HbA1c group 2 (≥8.5%)	p value
1	22 (55%)	1 (5%)	**<0.001**
2	10 (25%)	6 (30%)	
3	6 (15%)	4 (20%)	
4	2 (5%)	9 (45%)	
Total	40	20	

Pearson's chi-square test.

Table I shows the association of HbA1c with Killip class. In HbA1c group 2 (i.e., HbA1c ≥8.5%), the proportion of patients in Killip class 4 (45%) were significantly more in comparison to proportion of patients in Killip class 4 in HbA1c group 1 (HbA1c less than <8.5%), i.e., 5%. (p value = <0.001).

Table II: Association of levels of HbA1c with TIMI score (N = 60).

TIMI score	HbA1c Group 1	HbA1C Group 2	p value
Low-risk (<4)	31 (77.5%)	1 (5%)	**<0.001**
High-risk (>4)	9 (22.5%)	19 (95%)	
Total	40	20	

Fischer's exact test.

Table II shows association of TIMI score with HbA1c. The proportion of patients with high-risk TIMI were significantly more in HbA1c group 2 (95%) in comparison to HBA1c group 1 (22.5%) (p value = <0.001).

Table III: Association of HbA1c with LVEF finding on 2D-ECHO (N = 60).

LVEF	HbA1c Group 1	HbA1c Group 2	p value
>55% (normal)	1 (2.5%)	1 (5%)	**0.002**
45 to 55% (mild)	1 (5%)	6 (30%)	
35 to 45% (moderate)	21 (52.5%)	11 (55%)	
<35% (severe)	17 (42.5%)	2 (10%)	
Total	40	20	

Fischer's exact test.

Table III shows association of HbA1c with LVEF finding on 2D-ECHO. Ejection fraction categories were divided in following way- EF >55% (Category 1), 45 - 54.9% (Category 2), 35 - 44.9% (Category 3) and <34.9% (Category 4). Maximum proportion of patients had LVEF of 35 - 45% in both HbA1c groups (p value: 0.002).

Table IV: Association of HbA1c with distribution of arrhythmia in study group (N = 60).

Arrythmia	HbA1c group 1	HbA1c group 2	p value
No	38 (95%)	13 (65%)	**0.004**
Yes	2 (5%)	7 (35%)	
Total	40	20	

Fischer's exact test.

Table IV shows association of HbA1c with arrhythmia events. Bradyarrhythmias and tachyarrhythmias were included in arrythmias. Proportion of patients who had arrhythmia in HbA1c group 2 (35%) were significantly more than proportion of patients in HbA1c group 1 (5%) who had arrhythmia (p value = 0.004).

Table V: Association of HbA1c with number of coronary vessels involved (findings of coronary angiography) (N = 60).

No. Of Coronaries involved	HbA1c Group 1	HbA1c Group 2	p value
0	1 (2.5%)	1 (5%)	**<0.001**
1	25 (62.5%)	0	
2	9 (22.5%)	11 (55%)	
3	5 (12.5%)	8 (40%)	
	40	20	

Fischer's exact test.

Table V shows association of HbA1c with number of coronary vessels involved on coronary angiography. In HbA1c group 2, maximum proportion of patients had double vessel disease (55%). Whereas in HbA1c group 1, maximum proportion of patients had single vessel disease (62.5%). The results were statistically significant (p value - <0.001).

Table VI: Association of HbA1c with complications occurring post-ACS (N = 60).

Complications	HbA1C group 1	Hba1c group 2	p value
No	29 (72.5%)	3 (15%)	**<0.001**
Yes	11 (27.5%)	17 (85%)	
	40	20	

Fischer's exact test.

Table VI shows association of HBA1c with complications that occur post-ACS. Heart block, cariogenic shock, heart failure etc were included as complications post-ACS. The patients who had at least one complication were included in the category of complication post-ACS.

The proportion of patients in HBA1c group 2 who had complications (85%) were significantly more in comparison to proportion of patients (27.5%) with complications in HbA1c group 1 (p value = <0.001).

Table VII. Association of HBA1c with outcomes of ACS within one month of event (N = 60).

Events	HbA1c group 1	HbA1c group 2	p value
No rehospitalisation/death within 1 mth	33 (82.5%)	11 (55%)	**0.023**
Rehospitalisation/death within one mth	7 (17.5%)	9 (45%)	
	40	20	

Pearson's Chi-square test.

Table VII shows association of HbA1c with outcomes of ACS within one month of event.

Outcomes studied were rehospitalisation (due to reinfarctions, arrhythmia, and congestive heart failure) or death post-ACS within one month of event.

In HbA1c group 2 the proportion of patients (45%) with rehospitalisation/death were significantly more in comparison to proportion of patients (17%) with rehospitalisation/death in HbA1c group 1 (p value = 0.023).

One patient died in HbA1c group 2.

Discussion

Total patients included in the study were 60. A total of 37 (61.7%) patients were male and 23 (38.3%) were female. Severity of ACS was assessed by Killip classification, TIMI score and coronary angiography.

In HbA1c group 2, the proportion of patients with Killip class 4 (45%) were significantly more in comparison to proportion of patients (5%) in HbA1c group1. Cubbon *et al*[16] showed similar observation of Killip class in patients with fresh ACS in diabetic patient *versus* non-diabetic patients with established past history of CVD.

TIMI score depicts risk of mortality in ACS patients and tells severity of event. The proportion of patients with high-risk TIMI were significantly more in HbA1c group 2 (95%) in comparison to HbA1c group 1 (22.5%).

Maximum proportion of patients had LVEF of 35 - 44% in both HBA1c groups. Vinita *et al*[17] also had similar finding in patients with acute cardiac stress, i.e., LVEF <50% was seen more in diabetics with HbA1c ≥7% in comparison to diabetics with HBA1c <7% (<0.0001).

In HbA1c group 2, maximum proportion of patients had double vessel disease (55%). Whereas in HbA1c group 1, maximum proportion of patients had single vessel disease(62.5%). In study conducted by Vinita *et al*[17] amongst patients with acute cardiac stress, triple vessel disease was seen in a significantly higher proportion of patients with poor glycaemic control (HbAlc > or = 7%) compared to patients with HbAlc level <7% (p value <0.001).

Post-ACS outcomes were analysed by inhospital events (arrhythmias, CHF, pulmonary oedema, hypovolaemic shock, reinfarction), rehospitalisation and mortality within hospital stay and within one month of event.

The proportion of patients in HbA1c group 2 who had complications (85%) were significantly more in comparison to proportion of patients (27.5%) with complications in HbA1c group 1. Complications like re-infarction were also seen more in diabetics with HbA1c ≥7% in study done by Vinita *et al*[17] (p value <0.032). Vinita *et al*[17] also showed that complications like heart failure was also seen more in diabetics with HbA1c ≥7% (p value <0.001).

In HBA1c group 2, the proportion of patients (45%) with re-hospitalisation/death were significantly more in comparison to proportion of patients (17%) with rehospitalisation/death in HbA1c group 1.

The strength of our study was that we studied both clinical and imaging laboratory parameters to assess the association of HBA1c with severity and outcome of ACS. Limitations of the study were a small sample size and short follow-up period.

In conclusion, HbA1c was an independent factor influencing the severity of ACS. Poor control of diabetes as shown by higher levels of HbA1c is associated with higher severity of ACS and more complications post-ACS.

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ANNOUNCEMENT

Mrs. Uma Bansal - Prof. B.C. Bansal Best Paper Award (Journal -2024)

Best Original Article – "Evaluation of Platelet Indices with Uncomplicated Essential Hypertension"- Dr. Aanchal Mangal, Dr. Yad Ram Yadav, Dr. Pawan Kumar, Dr. Sanjiv Maheshwari, Department of General Medicine, Jawahar Lal Medical College, Ajmer - 302015, (Rajasthan).

Best Review Article – "Hydroxychloroquine in Obstetrics: Newer Perspectives" – Dr. Nazia Parveen, Dr. Sandhya Jain, Department of Obstetrics and Gynaecology, University College of Medical Sciences and Guru Teg Bahadur Hospital, Dilshad Garden, Delhi - 110095.

Best Case Report – "The Bug Story: Melioidosis with Candidaemia" – Dr. Anusha Uddandam, Dr. Nandakrishna B, Dr. Vasudev Acharya, Dr. Cynthia Amrutha Sukumar, Department of Medicine, Kasturba Medical College, Manipal Academy of Higher Education, Manipal – 576104 (Karnataka).