International Journal of Medical and Health Research
ISSN: 2454-9142
Impact Factor: RJIF 5.54
www.medicalsciencejournal.com
Volume 4; Issue 8; August 2018; Page No. 221-226

Impact of glycosylated haemoglobin (HBA1C) on acute coronary syndrome

Vivak Redkar[1], Danny P john[2*]
[1-2] Department of Medicine, Krishna Institute of Medical Sciences, Karad, Maharashtra, India
* Corresponding Author: Danny P john

Abstract
The median age for Acute Coronary Syndrome was 58.33 years for our study, and non-diabetics were 48.58 years for Acute Coronary Syndrome. The correlation between Diabetic (Group A), and Non-Diabetic (Group B) was observed in this study. The mean HbA1C was 6.5 percent in the non-diabetic community with a +0.6 SD, above the average value of regular ADA, that is to say 5.6 percent. Our research has showed that in all groups, males (diabetic and non-diabetic) are more prone to ACS. Few patients (diabetic) had a mean 298.83 BSL with ± 135.62 SD, meaning 8.06 ± 1.44SD with HbA1C>7 of 68% (34/50). In Group-B patients (non-diabetics) had mean BSL 277.44 with ± 124.9 SD in which mean HbA1C was 6.50 amongst 38% (19/50) have HbA1C >7. Hypertension is significant risk factor for ACS in diabetics with HbA1c >7 than non-diabetics. Comparing other co-morbidities, Ischemic Heart Disease, Strokes and Chronic kidney disease the P value between the two groups was not significant. In our study 15/50 (30%) diabetic patients and 7/50 (14%) patients had heart failure fallowing acute coronary syndrome. The results were evaluated using Chi-square, Students t-test, etc.

Keywords: acute coronary syndrome, heart failure, cardiac arrest, diabetes, hba1c, haemoglobin

1. Introduction
Elevated blood glucose concentrations in people with or without diabetes are normal and are related to an increased risk of death [1]. The amount of glucose molecules bound to haemoglobin is precisely determined by glycosylated haemoglobin. The glucose molecules of a red blood cell join hemoglobin and form glycosylated haemoglobin during a healthy life time of 120 days [2, 3].
Elevated levels of glucose in non-diabetic AMI patients are self-sufficient from individuals with mild or normal blood sugar levels with larger ischemic sizes as well as longer-term mortality. A major risk marker for long-term mortality in acute coronary syndrome patients is the glycometabolic condition at hospital admission.The risk factor for 'vascular conditions' in both micro-vascular and macro-vascular complications is expected to be significant for diabetes. The patient has opened diabetes well before macrovascular problems began [4]. A major contributing factor for cardiovascular disorder is hyperglycemia. The development of glyced proteins and advanced glycemic end-Products, functioning through enhanced endothelial breakdown, accelerates the cycle of atherosclerosis [5].
A significant increased risk of cardiac events and deaths is associated with HbA1c levels exceeding 7 percent [6-8]. This research aims to determine the association between HbA1c rates with diabetes and non-diabetic patients' incidence and complications.

1.1 Aims and Objectives
The present study was undertaken to find out the correlation between HbA1c levels and the severity and short term complications of Acute Coronary Syndrome (ACS) in diabetic and non-diabetic patients.

Literature Review
It is estimated that there is about 750g of hemoglobin in total circulating blood of a 70kg man that is destroyed destroyed each day. Dilute acid will readily split hemoglobin into the protein globin and its prosthetic group haeme (haematin). The hydrochloride of haeme called haemin can easily be prepared in crystalline form. Haeme is an iron porphyrine.
Globin, the protein moiety of hemoglobin, consists of 4 subunits i.e. it has the structure of a tetramer. Each subunit consists of polpeptide chains [9]. Two of the chains having identical amino acids composition are designated as α the other two; also identical with another are β chains. Adult human hemoglobin therefore possesses two alfa and two beta chains. Prospective Diabetes Study (UKPDS) indicated that HbA1c >7.0 % is associated with a significantly increased risk of both micro-vascular and macro-vascular complications, regardless of underlying treatment [10].
Further, HR figures for all-cause mortality for all trials in the HbA1c type have been published on a specific scale utilizing HbA1c<6.0 percent to act as comparison level for diabetes-free populations and HbA1c<5.0 percent to diabetes-free. A risk / protective factor to reference value has reciprocated HR estimate [11].
An earlier meta-analysis [12]. of a non-diabetes sample predicted an rise of cardio-vascular death of 5 percent by 1 percent in HbA1c rates, but the dose-response distribution was flat for HbA1c rates below 5.7 percent.

Materials and Method
This study was carried out in Krishna Institute of Medical Studies, Karad, Maharashtra. In this analytical study we

analyzed patients over the age of 18 with an Acute Coronary Syndrome diagnosis:

- Unstable Angina (UA)
- ST segment elevation acute myocardial infarction (STEMI)
- non-ST segment elevation acute myocardial infarction (NSTEMI)

3.1 Inclusion Criteria

- Age above 18 years
- Clinical History (with or without co-morbidities e.g. Ischemic Heart Disease, Diabetes Mellitus, Strokes, Peripheral Thromboembolic Diseases etc.)
- General and Systemic Examination
- ECG changes showing STEMI, non-STEMI and Ischemias
- Positive/ Negative cardiac markers for STEMI / NSTEMI and UA

3.2 Exclusion Criteria

- Patients in sepsis
- H/O Haemoglobinopathies
- H/O Or currently suffering from Hypothyroidism
- Chronic Alcoholic or Alcoholic Liver Disease

3.3 Study Design

The study comprised of 100 patients suffering from Acute Coronary Syndrome fulfilling inclusion / exclusion criterias.
They were divided in two groups:
(A) Diabetics
(B) Non-Diabetics.
The treatments will be given as per standard institute protocol and patients will be fallowed up till discharge and all complications like Cardiogenic shock, Heart failures, Arrhythmias, Accelerated Hypertension, Ketoacidosis will be noted.

All patients will undergo routine investigations including:

- Electrocardiogram
- Complete Blood Count
- HbA1c levels (on admission and irrespective of fasting status of the patient).
- Renal function tests
- Haemoglobin
- Chest x-ray
- 2D-Echocardiography for type of Ventricular Dysfunction (Systolic/ Diastolic)
- Random Blood Sugar Levels (on admission)
- CPK-MB

The samples will be collected after signing a consent for HbA1c levels.

3.4 Method

After the hemolysis of the entire blood test, gross hemoglobin and HbA1c levels are estimated. Colorimetrically, the total Hb is

Evaluated likewise HbA1c was determined Immunoturbidimetrically. The proportion of the two rates resulted in the final HbA1c figure.
HbA1c is assessed with latex particulate monoclonal antibodies. These antibodies bind HbA1c fragments of the beta-N-terminal. Remaining independent antibodies are mixed with a synthetic polymer that holds many versions of HbA1c 's beta-N-terminal form. The viscosity change is reverse proportionate to the concentration of connected glycopeptides and turbidimetrically analyzed at 552nm. For analysis a synthetic polypeptide consisting of the terminal N HbA1c structure has been utilized.
Reference method used for calculating HbA1c (%) from the HbA1c/Hb ratio is given below:
HbA1c (%) = (HbA1c/Hb) X 175.8 + 1.73

3.4.1 Analytical sensitivity

The detection limits for the assays are 9mg/dL for the Hb test and 0.4mg/dL for the HbA1c test. However, only results above 81mg/dL for the Hb test and above 1.3mg/dL for the HbA1c test are reported. The detection limit for the calculated HbA1c (%) result is 3% at a Hb concentration of 13.2g/dL in the sample.

Observations and Results

4.1 Statistics and Analysis

A Chi-square test (with adjustment where ever cell value was lower than 5) for association was used in statistical analyses. In order to compare the proportions, Z tests for the difference of two mean samples and two ratios have also been used. Using Taylor linearization series, standard errors were estimated. The student's test Unpaird 't' has been used to contrast the diabetes group's HbA1c values (< 7% and>7). The sample study was distributed in gender-based and age-based groups for diabetic and non-diabetic patients (Figure 1).

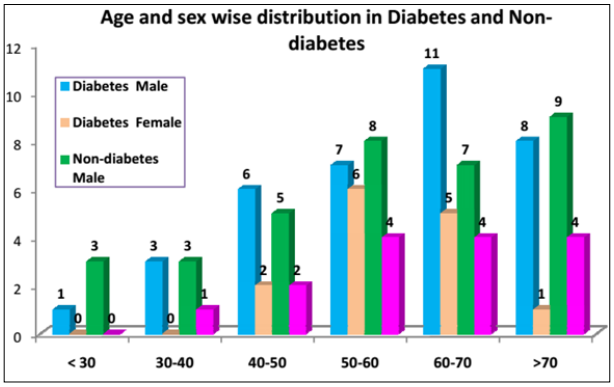

Fig 1: Age and sex wise distribution of Diabetes and Noncases under study

Co-morbidities were observed to be laying considerable impact on the outcomes of hypertension and ischemic heart disease (Figure 2).

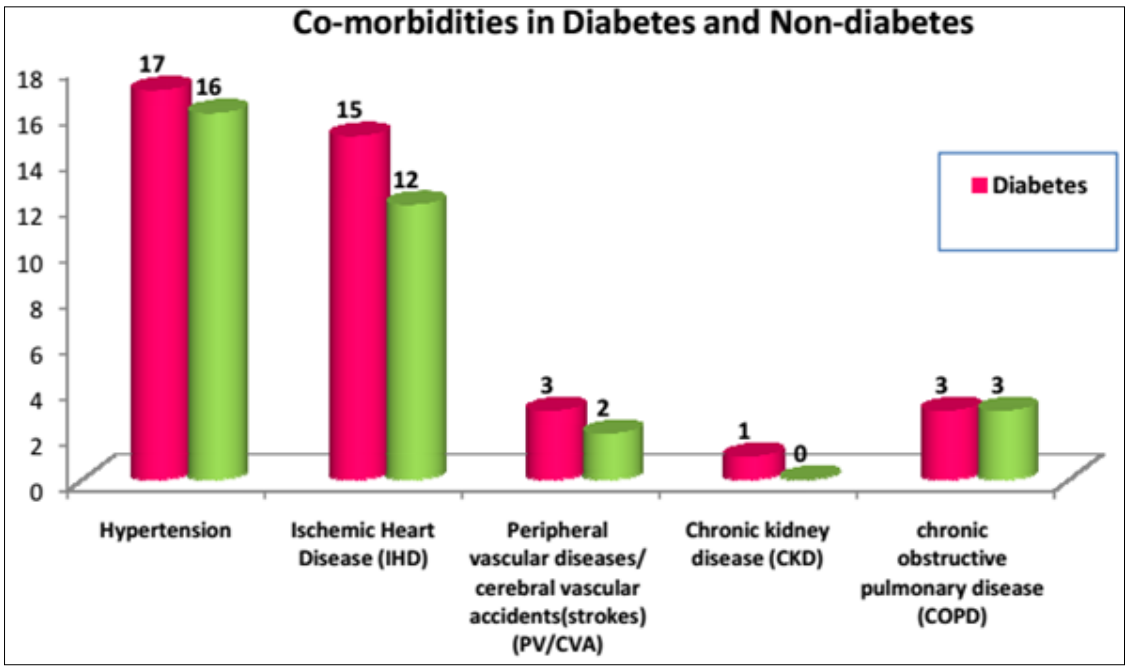

Fig 2: Co-morbidities in Diabetes and Non-diabetes cases

Results indicated that the Value of $\times^2$ = 1.071, d.f. =4, *p* = 0.4988, was significant. Applying a Z difference test among the two samples means produces a significant disparity between mean HbA1C, random BSL, and CPKMB parameters when diabetes group compared with Non-diabetes group (Table 1).

Table 1: Mean and SD values of various parameters In Diabetes and Non-diabetes cases

Parameters	Diabetes (n=50)	Non-diabetes (n=50)	Z test value	'p' value and result
	Mean ± SD	Mean ± SD		
HbA1C	8.06±1.44	6.50±1.01	6.69	p<0.01, highly significant
Random BSL	259.71±123.97	160.47±76.31	4.82	p<0.01, highly significant
CPKMB	81.75±24.49	65.19±25.24	3.33	p<0.01, highly significant

By applying Z test of difference between two sample proportions there is a highly significant difference between proportion of complications Arrhythmias, Cardiac Arrest and Shock when diabetes group compared with Non-diabetes group (i.e. (p<0.01) and no significant between proportion of complications Heart failure, Accelerated Hypertension, diabetic Ketoacidosis (p>0.05). Table 2 shows the outcomes (deaths and recoveries in diabetes and non-diabetes (also see Figure 3).

Table 2: Outcome in Diabetes and Non-diabetes cases

Outcome	Diabetes (n=50)	Non-diabetes (n=50)
Death	12(24%)	5(10%)
Recovered	38(76%)	45(90%)

Value of $\times^2$ = 3.470, d.f. =1, p= 0.0451, significant

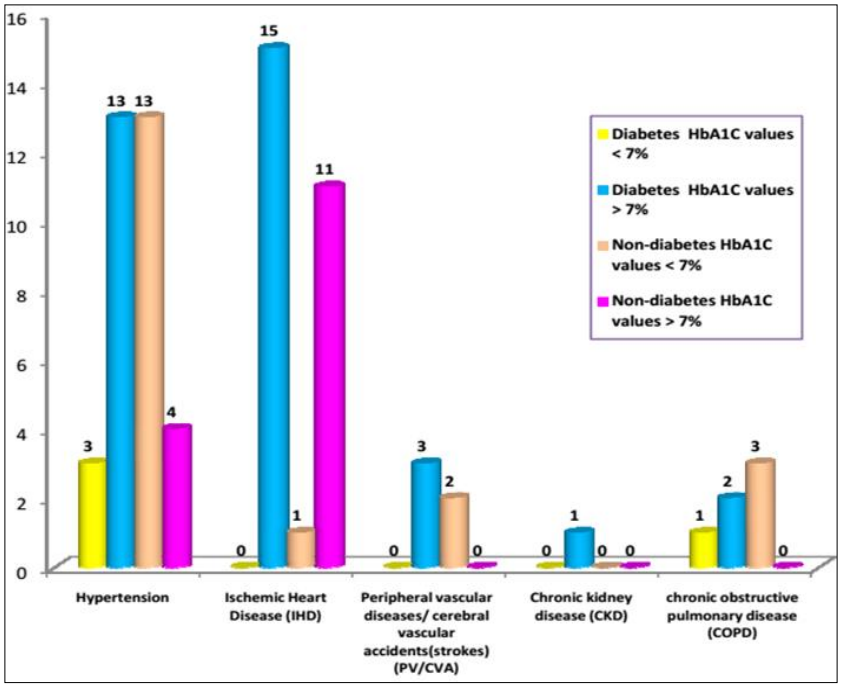

Fig 3: Impact of HbA1c on Acute Coronary Syndrome in Diabetes and Non-diabetes (Co-morbidities)

Table 3: Impact of HbA1c on Acute Coronary Syndrome in Diabetes and Non-diabetes (Diagnosis)

Diagnosis	Diabetes (n=50)		Non-diabetes (n=50)		P (for diabetic group only)
	HbA1C values		HbA1C values		
	< 7%	> 7%	< 7%	> 7%	
	No (%)	No (%)	No (%)	No (%)	
Unstable Angina (UA)	8(16%)	7(14%)	20(40%)	2(4%)	0.0210, Significant
STEMI	7(14%)	22(44%)	5(10%)	15(30%)	0.1182, Not Significant
NSTEMI	1(2%)	5(10%)	6(12%)	2(4%)	0.1496, Not significant
Total	16(32%)	34(68%)	31(62%)	19(38%)	

The unpaid 't' test is used because the mean value of the Random BSL and CPKMB are significantly different in diabetes with HbA1C < 7% compared with diabetes with HbA1C > 7%. This means that the average BSL and CPKMB is more in diabetes with HbA1C > 7% (Figure 3 and Table 3).

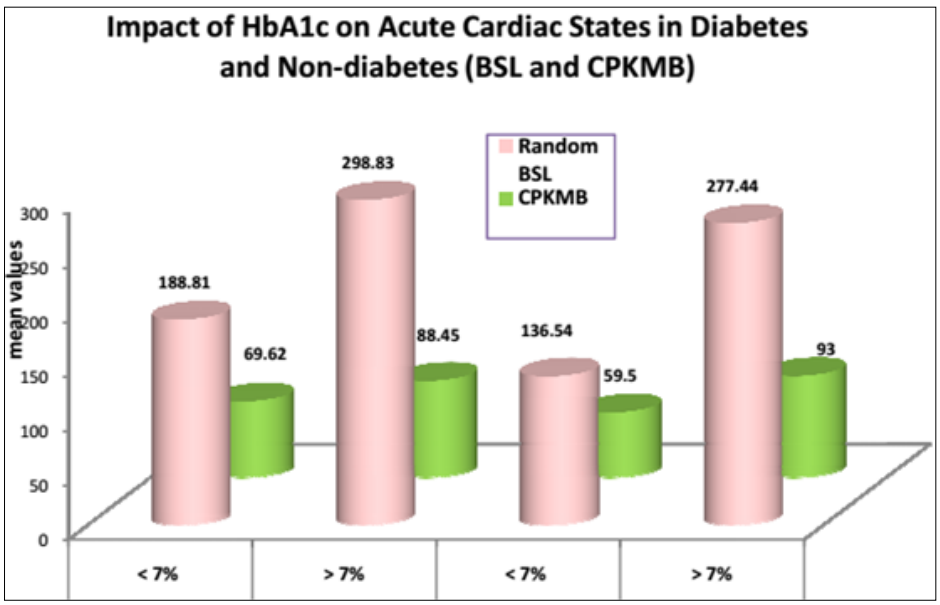

Fig 4: Acute Cardiac state and HbA1c effects on diabetic and non-diabetic patients

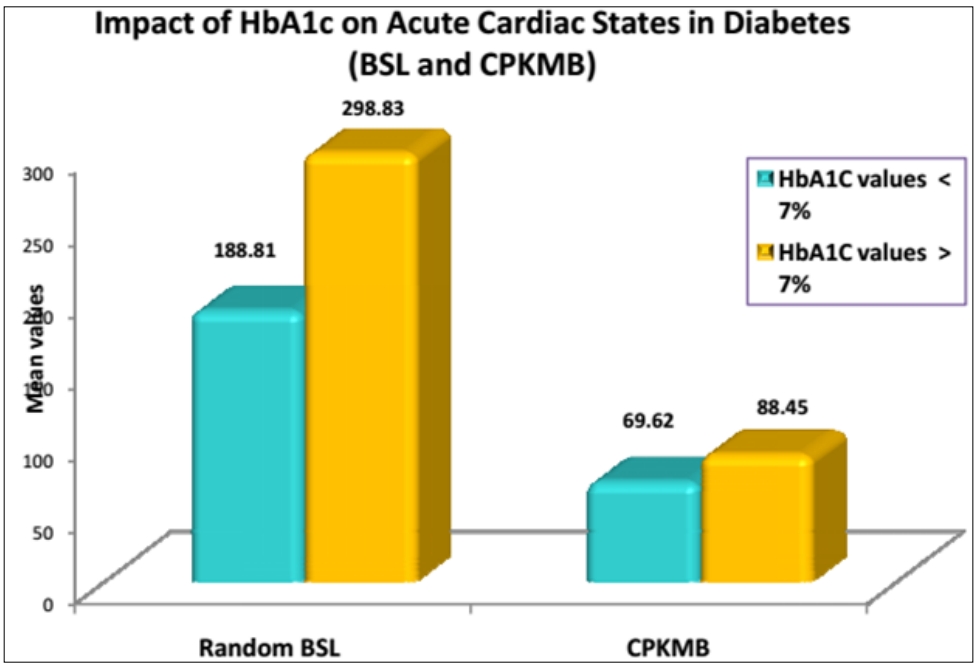

Fig 5: HbA1c and Acute cardiac levels in diabetic and non-diabetic cases

Application of Chi-square test shows that there is a highly significant association among diabetes and complications (Table 3).

That is Arrhythmias, Heart Failure,Cardiac Arrest, Accelerated Hypertension, Shock and Diabetic Ketoacidosis is more in diabetes with HbA1C > 7%.

Table 4: HbA1c on Acute Coronary Syndrome effects in Diabetes and Non-diabetes (Complications)

Complications	Diabetes (n=50)		Non-diabetes (n=50)		p' value *
	HbA1C values		HbA1C values		
	<7%	>7%	<7%	>7%	
	No (%)	No (%)	No (%)	No (%)	
Arrhythmias	1(2%)	19(38%)	7(14%)	6(12%)	0.0001, highly significant
Heart Failure	1(2%)	14(28%)	4(8%)	3(6%)	0.0008, highly significant
Cardiac Arrest	1(2%)	15(30%)	1(2%)	4(8%)	0.0004, highly significant
Accelerated Hypertension	2(4%)	8(16%)	6(12%)	2(4%)	0.0445, highly significant
Shock	1(2%)	16(32%)	0	4(8%)	0.0002, highly significant

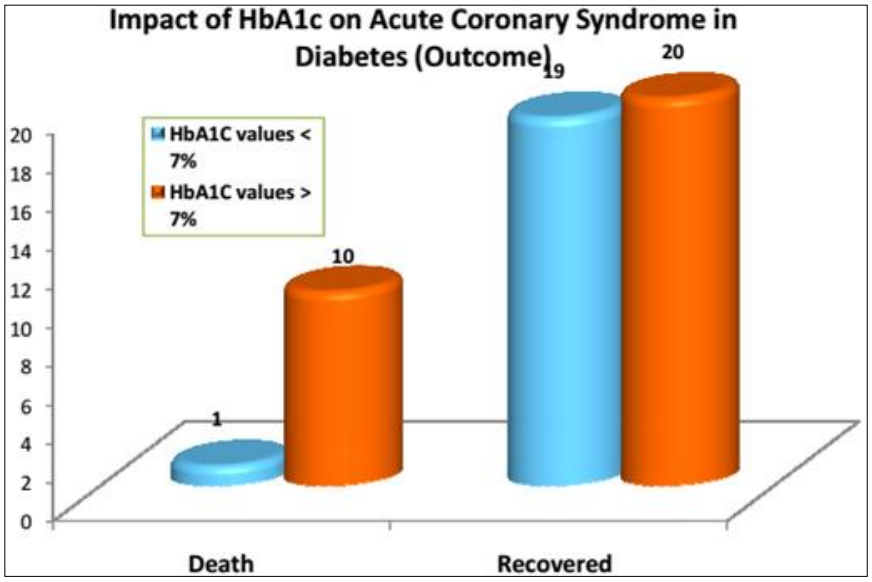

Fig 6: HbA1c and ACS outcomes

Table 5: Impact of HbA1c on Heart Failure

Hear Failure	Group. A (Diabetics)	Group. B (Non-Diabetics)
	HbA1C >7%	HbA1C >7%
Systolic Dysfunction	12 (85%)	0
Diastolic Dysfunction	2 (15%)	3 (100%)

Conclusion

According to our study, diabetics with HbA1C >7% have higher incidences of developing Heart Failures with systolic dysfunction fallowing ACS and non-diabetic patients are also at the risk of developing Heart Failure with diastolic dysfunction when HbA1C >7%. In diabetic group, 20 patients developed arrhythmias fallowing ACS. 95% of them had HbA1c >7%; And 13 non-diabetics in which 46% with HbA1c>7%. Tachyarrhythmias are predominantly seen in both the groups.

This study also showed that the complications of Acute Coronary Syndrome are more common and fatal in diabetics with poor glycemic control and HbA1C >7. High HbA1C >7 is also a significant marker in both the groups as predisposing factors for conditions which are associated with Acute Coronary Syndrome like Hypertension, Ischemic Heart Disease, Strokes and Chronic Kidney Disease and subsequently high incidence of complications of Acute Coronary Syndrome.

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