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Original Research Article

Role of HbA1c with mortality and severity among the patients of Acute coronary syndrome: a prospective study

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ABSTRACT

Background: Blockage of coronary artery lead to a reduction of blood flow towards heart resulting in Coronary Artery Disease (CAD). CAD leads to myocardial complications. CAD is one of the important causes of death all over the world including India. Diabetes mellitus is a risk factor for CAD. Reports have also shown to increase in cardiovascular morbidity among patients with glucose intolerance. In present study we tried to find the relationship of HbA1c levels with mortality, morbidity, and severity in Acute Coronary Syndrome (ACS).
Methods: Two hundred patients with ACS were studied from 2018 to 2019 at Gandhi Medical College and Hamidia Hospital, Bhopal. Following a thorough medical history routine medical examination including laboratory investigations was performed in all the patients. Electrocardiography (ECG), creatine phosphokinase-muscle/brain (CPK-MB), echocardiography and coronary angiography (CAG) was also done as part of this study.
Results: Mean age of the study cohort was 59.17±8.75 years. Out of 200 subjects, 110 (55%) were non-diabetic, 52 (26%) were diabetic, 38 (19%) had weakened glucose tolerance and 82 (41%) had hypertension. Left ventricular dysfunction (LVD) and heart failure (HF) were the common complications and were more prevalent among diabetic patients than the nondiabetics (p=0.009). HbA1c level (7.01±2.23) was high among subjects with complications than the subjects without complications (6.01±1.36).
Conclusions: The patients with DM have higher morbidity and mortality than the non-diabetic patients of ACS and therefore such patients should be screened for diabetes and glucose intolerance for better management of CAD.

Keywords: Coronary Artery Disease, Coronary Angiography, Diabetes Mellitus, Stress Hyperglycemia

INTRODUCTION

Coronary artery disease (CAD) has emerged as one of the major cause of death worldwide and in India. In 2013 worldwide mortality caused by CAD was estimated to 7.5 million which is around 13.3% of total deaths.[1] The seventh edition of International Diabetes Federation (IDF) Diabetes Atlas 2015 reported that globally around 415 million people are suffering from diabetes mellitus (DM) and this number is expected to rise to 640 million by 2040.[2]

Around 318 million people have impaired glucose tolerance and this number anticipated to rise to 482 million by 2040. DM is the most common chronic diseases in the world and the main reason for CAD.

Compared to non-diabetic person, diabetic patients have a double to fourfold high risk of mortality due to CAD.[2]

More than one third ACS patients are suffering from diabetes and these diabetic patients have worsened complications due to ACS.[3] The graded relationship of heightened risk observed in diabetics in the setting of ACS spreads up to glucose values in the range which is below the cut-off for diabetes. Diabetes is also reported as the reason of increased risk of heart failure among the ACS patients.[4] This study was conducted to assess and describe the relationship of HbA1c levels with mortality, morbidity, and complications among the ACS patients among the diabetics and impaired glucose tolerance subjects.

METHODS

This observational prospective study was carried out at the tertiary health center for a year from 2018 to 2019, on a sample of 200 ACS patients at Gandhi Medical College and Hamidia Hospital, Bhopal, India.

Patients with ACS symptoms within 24 hours and those who have given formal consent for participation in the study were included. Patient having other co-morbidities such as sepsis, hemoglobinopathy or chronic kidney disease (CKD) were excluded. After a detailed medical history and demographic details including age, sex, body mass index (BMI) and waist circumference, all the patients underwent a detailed medical examination and baseline investigations.

Subjects were also examined for HbA1c and dyslipidemia followed by ECG and CPK-MB were performed in all the subjects whereas CAG was performed in half of the subjects. The basis of HbA1c levels subjects were divided into diabetes (HbA1c ≥6.5%), prediabetes (HbA1c between 5.7 to 6.4%) and non-diabetics (HbA1c<5.7%).

All the data analysis was performed with the help of IBM Statistical Program for Social Sciences (SPSS) ver. 20 software. Quantitative data were expressed as mean whereas categorical data were expressed as a percentage. Chi-square test was used for comparisons between two groups for categorical variables and Student's T-test was applied on continuous variables. Level of significance was assessed at 5%.

RESULTS

Mean age of study cohort was 59.17±8.75 years with male preponderance (n=148). Based on the HbA1c levels subjects were divided into diabetes (n=52), prediabetes (n=38) and non-diabetics (n=110).

Eighty-two subjects were hypertensive. Out of 200 subjects, 113 (56.5%) had BMI >23kg/m^2, of these 42 (37.16%) were diabetics, 58 (51.32%) were non diabetic and 24 (21.23%) had impaired glucose tolerance.

A significant association was found between BMI and HbA1c; that means among the diabetes patients BMI and HBA1c were significantly high as compared to non-diabetic ACS patients (p<0.05). One hundred and four (52%) subjects had dyslipidemia out of that 71% of diabetic subject shad dyslipidemia, compared to 50% in pre-diabetic patients and 42% in non-diabetic subjects. This showed that dyslipidemia was more prevalent in diabetic than the non-diabetic (p-value 0.001) subjects who had ACS.

We found that out of 200 ACS patients 56 (28%) patients had cardiovascular complications like left ventricular dystrophy (LVD), shock, heart failure (HF), and arrhythmia. Out of those having cardiovascular complications, 26 (46.42%) were non-diabetic, 18 (32.14%) were diabetic and 12 (21.42%) had impaired glucose tolerance.

Among the in-hospital complications, LVD [16 (30%)] and HF [14 (25%)] were the most common complications and were significantly higher among the diabetic subjects than the non-diabetics (p=0.009). Mean HbA1c level was more in patients having complications (7.01±2.23) than the patients without complications (6.01±1.36) (p=0.038).

Table 1: Comparing HbA1c with outcome

Category	Outcome		Total
	Death	Discharge	
Diabetics	3 (11.1)	24 (88.9)	27 (100)
Impaired glucose tolerance	1 (5)	19 (95)	20 (100)
Non-diabetic	4 (6.3)	59 (93.7)	63 (100)
Total	8 (7.3)	102 (92.7)	110 (100)

Data is expressed as no of patients (percentage)

The severity of CAD was evaluated in 100 subjects who underwent CAG. Multi-vessel disease connection was found significantly high in diabetic subjects as than the non-diabetic subjects. The mean HbA1c level was significantly higher in patients with the multi-vessel disease than those without multivessel disease (6.74% vs. 5.86%; p=0.048.)

DISCUSSION

Due to the availability of more advanced treatment and technology in cardiovascular disease (CVD) mainly in the ACS, a significant reduction in the morbidity and mortality is noted. But still, DM remains the major risk factors for the development of CVD in both patients with and without a prior history of myocardial infarction.[1,2]

According to Framingham Heart study findings, DM increases the age-adjusted risk for CVD two-fold among male and two-fold among the female population. DM is

also an independent risk factor among the patients having hypertension, smoking, hyperlipidemia and left ventricular hypertrophy.[5]

Meta-analysis of 13 prospective cohort studies by Selvin et al showed that for every 1% increase in HbA1c, the relative risk for any CVD was 1.18 (95% CI 1.10-1.26). Likewise with all other factors remains same, diabetic patients, have worse long-term outcomes after an acute coronary syndrome compared non-diabetic.[6]

Uncontrolled glycemia is an important factor for the development of diabetes-related complications and it also interferes with the treatment of ACS. Previous studies have also shown that despite the reversal in the hyperglycemia, a progression in diabetic vascular disease is reported. It may be because of the development of what is called metabolic memory. In the present study, we found that 26% without the history of DM had an HbA1c level of more than 6.4% means these subjects were diabetic. Similarly, 19% of patients had HbA1c in the impaired glucose tolerance range of 5.7 to 6.4%. Hence patients of DM can have macro-vascular complications of diabetes without having the traditional indications of DM and can directly present with them. This could be due to the majority of subjects' having type 2 DM are asymptomatic and can directly present with chronic complications, unlike type 1 DM. Above results are comparable to other studies like Khaw et al which also stated that myocardial infarction may be the initial manifestation of diabetes and there is graded rise in CVD risk with growing degrees of glucose intolerance below the definition of overt diabetes.[7]

Coutinho et al presented that there was a significant increase in the risk for a cardiovascular event with increasing glucose intolerance.[8] Juutilainen et al, recorded that diabetic patients without a history of myocardial infarction have a high risk of developing myocardial infarction as nondiabetic patients with previous myocardial infarction.[8]

Hyperglycemia during hospitalization in patients could be due to previously unidentified diabetes or that the stress of myocardial infarction increases or aggravates hyperglycemia. Thus, in the present study, we used HbA1c levels to categorize patients as diabetic, impaired glucose tolerance and nondiabetics which is HbA1c<5.7% normal; 5.7% to 6.4% impaired glucose tolerance; ≥6.5% diabetes.

We found the positive association between HbA1c levels and cardiovascular complications; 28% of patients had cardiovascular disease and LVD followed by HF were the most common one. These complications were more common in diabetics as than non-diabetic subjects. Similar observations were recorded by Mouhamad et al and Stone et al, that diabetic patients with ACS have a very poor prognosis.[9]

Iribarren et al in a prospective study with 48,858 adults having DM revealed that an increase of 1% HbA1c levels, increased the relative risk of HF by 8%. The clinical symptoms of an acute myocardial infarction are more severe in diabetic patients compared to the nondiabetics. Pulmonary edema and HF occurs considerably more in diabetics than the nondiabetics regardless of same infarct sizes and left ventricular ejection fractions, signifying that the left ventricle in diabetes cannot tolerate infarction properly.[10]

Cross-sectional nature and small sample size were the main limitations of the present study; a large randomized controlled trial is needed to strengthen the present study findings.

CONCLUSION

ACS can be the initial exhibition of DM, patients with DM have increased morbidity and severity after an ACS than the nondiabetic patients. This study concludes that a patient of ACS should be screened for glucose intolerance and diabetes by testing for HbA1c levels.

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