



Correlation of Glycosylated Hemoglobin and Complexity of Coronary Artery Disease among Aged ≥ 45 Years Population with Diabetes Mellitus

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Objective: Cardiovascular diseases are 1.7 times more prevalent in patients with diabetes mellitus. The aim behind this study was to examine the correlation of glycosylated hemoglobin and complexity of coronary artery disease among middle aged population with diabetes mellitus

Patients and Methods: This was a clinical prospective hospital-based comparative study carried out in the department of the cardiology department of Isra University Hospital Hyderabad for 10 months. 153 participants with diabetes mellitus having age ≥ 45 years both male and female and undergoing their first coronary angiography were included. Data were entered and analyzed by using Statistical Package for the Social Sciences version 21.0.

Results: A total of 153 patients were finally analysed. Patients were divided into two groups; group I (HbA1c $< 6.5\%$, normal) and group II (HbA1c $> 6.5\%$, impaired). The mean age was slightly higher in group II 54.60 as compared to group I 53.65 years, respectively. The Syntax score was

correlated with HbA1c levels in patients older than 45 years of age ($r = 0.001$; $p > 0.05$). Moreover, the higher HbA1c levels were observed in every three categories of Syntax score but they were insignificantly associated with each other in patients with diabetes mellitus and having age more than 45 years.

Conclusion: The HbA1c is insignificantly correlated with the complexity of coronary artery disease in diabetic patients having age more than 45 years. While only two factors, hypertension and increased triglycerides are significantly different among the HbA1c groups.

Keywords: SYNTAX score; coronary artery disease complexity; HbA1C; middle and old age group.

1. INTRODUCTION

Coronary artery disease (CAD) has now become the most prevalent non-communicable causes of morbidity and associated mortality and its prevalence ranges between 497 million to 550 million people worldwide and mortality projected from 12.1 million to 18.6 million from 1990 to 2019 [1]. While the actual burden of cardiovascular disease is undetermined in Pakistan but one national study conducted in Pakistan by Jafar TH has shown the prevalence of coronary artery disease was 26.9% and it was higher in women than men, 23.7% and 30.0%, respectively [2]. Type 2 diabetes mellitus is a chronic multi-systemic disorder and involvement of coronary and cerebral circulation is 1.7 times more prevalent and mortality rate increased 2 to 4 folds in diabetics than non-diabetics [3]. Glycated hemoglobin (HbA1c) is a determinant of average blood sugar levels over the preceding 2 to 3 months and in comparison to random blood sugar levels and fasting blood sugar levels it has several advantages including greater stability, easily available, and with less biological variability. Its prognostic value concerning to coronary artery and cardiovascular disease is studied in international studies and observed direct relation of increased levels of HbA1c with higher mortality rates in patients with coronary artery disease irrespective of age group but data is limited in Pakistan [4-6].

An angiographic based grading tool is designed called SYNTAX (synergy between percutaneous coronary intervention with TAXUS and cardiac surgery) scoring system to determine the complexity of coronary artery disease so the decision can be made regarding benefit and harm for coronary artery bypass grafting (CABG) vs. percutaneous coronary intervention (PCI) [7,8]. SYNTAX trial has shown that outcome of patients having SYNTAX score more than 34 are more likely to get benefited from CABG when a patient having multivessel or disease in left main (LM) [9,10] but to our best knowledge there is no

such study conducted in which the complexity of coronary artery disease was assessed in relation to HbA1c levels and patients having age more than 45 years. That is why, this study aims to fill the scientific gap present in this area of research so the cardiologist, interventionist, and surgeons would take advantage of the findings of our study.

2. PATIENTS AND METHODS

This was a prospective clinical single-center comparative study and was conducted in the department of Cardiology Isra University Hospital, Hyderabad. All the patients were enrolled through a convenient non-probability sampling technique. Keeping a 95% confidence interval, 6.5% margin of error and 17.5% prevalence of coronary artery disease (CAD) in Pakistan [11], the sample size of 153 was calculated using the world health organization (WHO) sample size calculator.

The inclusion criteria for this study were all the patients undergoing first coronary angiography, both males and females, age more than 45 years, type 2 diabetes mellitus, and given informed & written consent before enrollment and the study was conducted in accordance with the Declaration of Helsinki Guidelines. Patients with renal impairment (Creatinine clearance < 60 ml/min), those who cannot proceed for further intervention (PCI/CABG), underlying end-stage liver disease, malignancy with life expectancy less than 1 year, and patients with history of coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) were excluded from the study.

Diagnosis of type 2 diabetes mellitus was made according to the American Diabetes Association (ADA) guidelines (2019) in which if a patient is having random blood sugar (RBS) ≥ 200 mg/dL or fasting blood sugar (FBS) level ≥ 126 mg/dL, or HbA1c level more than 6.5% [12] or any previously available medical record proving the

presence of diabetes mellitus and/or taking anti-diabetic medicines.

All the enrolled patients were then further evaluated by taking a detailed medical history, determination of renal function status, or any possible dye-induced reaction before undergoing coronary angiography. Coronary angiography was performed and interpreted by the interventional cardiologist who had at least 5 years of experience of doing such procedures after taking informed consent and explaining the risk associated with the procedure then Syntax score was calculated using the available online calculator <http://www.syntaxscore.com/calc/start.htm>.

Coronary angiography was performed based on certain indications; all the clinically stable patients with chest pain and/or non-invasive tests (exercise tolerance test [ETT] / myocardial perfusion scanning [MPS]) demonstrating myocardial ischemia. Department of Cardiology, Isra University Hospital, Hyderabad was the study center and used General Electrical (GE) machine for coronary angiography. The route of angiography (Radial/Femoral artery) was decided by the interventionist and the patient's combined decision.

All the collected data (baseline and clinical) were entered and analysed using Statistical Package for the Social Sciences version 21 (SPSS V.21).

By using the World Health Organization (WHO) criteria for the categorization of diabetes control based HbA1c, we have divided our patients into two groups; group I (HbA1c <6.5%, normal) and group II (HbA1c >6.5%, impaired). For taking the cut-off values of lipid profile parameters we have used ATP III lipid profile guidelines [13]. For the association between diabetic groups and demographical characteristics we have used the chi-square test/ fisher's exact and independent *t*-test, where appropriate. The correlation between HbA1c and Syntax score was assessed using ANOVA and Pearson correlation tests where needed and a p-value of <0.05 was taken as statistically significant.

3. RESULTS

A total of 153 patients were selected for this study. The overall mean ± SD was 54.28±9.55 years and among them the majority were males (70.6%, n = 108). The subjects were divided into two groups: group I (HbA1c <6.5%, normal) and group II (HbA1c >6.5%, impaired). Baseline and clinical data of the patients are summarized in Table 1. There were no significant differences in the proportion of age, gender, area of residence, marital status, addiction habits, total cholesterol, LDL cholesterol, HDL cholesterol, and syntax score. In contrast, hypertension and triglycerides were significantly different among the HbA1c groups, p<0.05.

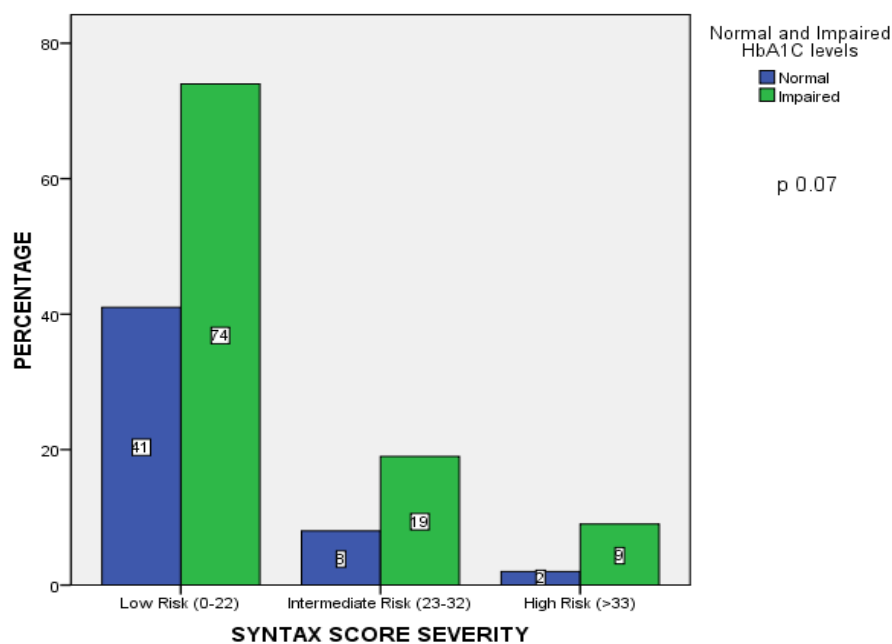


Fig. 1. Comparison between groups of HbA1c levels with severity of syntax score in diabetic patients aged ≥45 years (n = 153)

Table 1. Basic demographic and clinical characteristics of study subjects

Variables	HbA1c Groups		p value
	I (<6.5%) n = 51	II (≥6.5%) n = 102	
Age (Mean±SD) - years	53.65±9.67	54.60±9.53	0.56
Gender, %			
Male	68.6	71.6	0.42
Female	31.4	28.4	
Area of Residence, %			
Urban	54.9	64.7	0.08
Rural	45	35.3	
Marital Status			
Unmarried	21.5	17.6	0.77
Married	68.6	70.5	
Widowed	9.8	80.9	
Addiction			
Alcohol	5.8	5.8	0.88
Smoking	31.3	37.2	
Chewable tobacco	25.4	24.5	
Hypertension	27.4	32.3	0.003*
Total Cholesterol	135.92±34.93	137.16±37.27	0.84
LDL Cholesterol	91.45±24.95	90.97±24.89	0.91
HDL Cholesterol	27.45±6.72	26.99±7.08	0.7
Triglycerides	144.71±77.59	180.04±100.47	0.02*
Syntax Score	14.31±9.37	15.46±10.93	0.52

LDL: low density lipoprotein; HDL: high density lipoprotein

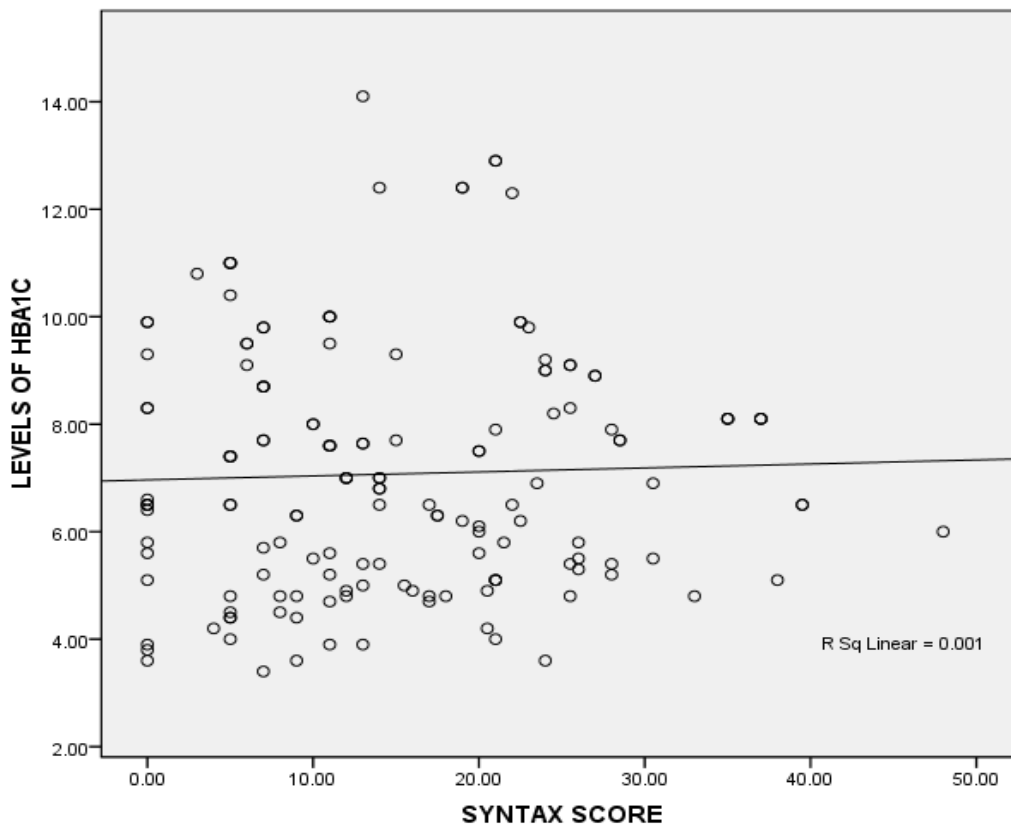


Fig. 2. Correlation Of Hba1c levels with syntax score in diabetic patients aged ≥45 years

The Syntax score were correlated with HbA1c levels in patients older than 45 years of age (Fig. 1) ($r = 0.001$; $p > 0.05$). Moreover, the higher HbA1c levels were observed in every three categories of Syntax score but they were insignificantly associated with each other in patients with diabetes mellitus and having age more than 45 years (Fig. 2).

4. DISCUSSION

Coronary artery disease is the major cause of morbidity and mortality and when it is coupled with diabetes mellitus the poor outcome of such patients is expected earlier than non-diabetic patients. Besides other complications associated with diabetes mellitus, the development of complex atherosclerotic coronary artery disease now becomes the major concern. However, a previously conducted study by Ma J & colleagues [14] observed that higher HbA1c levels are associated with complex coronary artery disease which is contrary to our findings. The best possible reason could be the age factor as their study included older age group people (age >60 years) while our study also consists of middle-aged patients and majority belongs to age group <60 years. Secondly, the population they have selected in their study and even large sample size could play an important role in this regard. One mechanism behind this phenomenon could be the higher prevalence of diabetes mellitus in industrialized countries like China & Japan and are more prone to develop diabetes mellitus at an early age than in developing countries like Pakistan [15-17]. Due to the prolonged duration of diabetes mellitus they are more likely to have complex coronary artery disease and that is why our study's findings negate theirs. One another reason could be the presence of uncontrolled diabetes mellitus which is not mentioned in their study. As persistently higher blood sugar levels in a group of people may lead to unfavorable outcome.

SYNTAX score is widely used by interventional cardiologists and cardiothoracic surgeons to predict the severity/complexity of coronary artery disease and to determine the post-operative outcome of patients undergoing CABG or PCI. Literature from international centers shows favorable outcome of CABG if the Syntax score comes more than ≥ 34 [18-20]. In our study only 7.2% ($n = 11$) patients had Syntax score more than 34 and fall into high-risk Syntax score group while the majority had low (75.2%, $n = 115$) and intermediate (17.6%, $n = 27$) risk Syntax score,

respectively and when high-risk Syntax score patients were separately evaluated for correlation with HbA1c levels, we have observed an insignificant association. Only two factors hypertension and high levels of triglycerides were significantly different among groups of HbA1c. Patients with genetic predisposition of raised triglycerides and hypertension are more likely to have diabetes mellitus and comorbid are associated with uncontrolled blood sugar levels [21-23]. This could be the reason why triglycerides and hypertension were significantly observed in patients with HbA1c greater than 6.5%.

The principal findings of our study do not support the correlation of HbA1c levels with the complexity of coronary artery disease in middle-aged diabetic patients. Findings from most of the studies recommend control of HbA1c levels to reduce the risk of major cardiovascular events in diabetic patients [4,24,25]. KT Khaw et al. suggested that even 1% increase in HbA1c levels is associated with about an increase in 30% all-cause mortality and around 40% increase in cardiovascular and mortality associated with ischemic heart disease [20].

Our study has several limitations which should be considered. This study has a smaller sample size that would be associated with an insignificant association between HbA1c and the complexity of coronary artery disease. Second, our study did not represent those patients who already had CABG or PCI. Third, exclusion of patients who already had PCI or CABG (known patients of coronary artery disease) may produce different findings, as observed in our study. Therefore, inclusion of patients with known coronary artery disease, all age group people, and large sample size would be a better future approach to fill the huge scientific gap present in this area.

5. CONCLUSION

The HbA1c is insignificantly correlated with the complexity of coronary artery disease in diabetic patients having age more than 45 years. While only two factors, hypertension and increased triglycerides are significantly different among HbA1c groups.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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