Original Article

Association of HbA1c Levels with Complexity of Coronary Artery Disease in Diabetic Patients Presenting with Acute Coronary Syndrome

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ABSTRACT

Objective: To determine the association of Hemoglobin A1c (HbA1c) levels with the complexity of coronary artery disease (CAD) in diabetic patients presenting with acute coronary syndrome (ACS), in terms of higher synergy between percutaneous coronary intervention with taxus and cardiac surgery (SYNTAX) score measured during coronary angiography.

Methodology: This cross-sectional comparative study was conducted at Fauji Foundation Hospital, Rawalpindi from July to September 2025 after approval from the ethical committee of the institution. Patients were divided into two groups. Those with HbA1c ≤7% were labeled as group 1 and group 2 had patients with HbA1c >7%. After informed written consent, 122 confirmed diabetic patients who presented with ACS and underwent coronary angiography were included using non-probability convenience sampling. The SYNTAX score was estimated to determine angiographic disease complexity. The patients with scores of 0-22 were labeled as low risk, 23-32 as intermediate, and >32 as high-risk CAD. The blood samples of patients were taken and sent for HbA1c levels and fasting lipid profile. Data analysis was carried out with the Statistical Package for the Social Sciences (SPSS) version 26.

Results: When CAD risk categories were compared with HbA1c groups, the majority of the patients in group 1 (34.4%) and group 2 (24.6%) had low risk and intermediate risk CAD, respectively. There was a significant and moderate positive correlation (r=0.528) between HbA1c and SYNTAX scores (p-value=0.001). Only the lipid profile showed a significant relationship with CAD risk categories.

Conclusion: The majority of patients with HbA1c ≤7% had low-risk CAD, while patients with HbA1c >7% had intermediate-risk CAD. The SYNTAX score significantly increased with increasing HbA1c levels. In addition, the patients with intermediate and high-risk CAD also had dyslipidemia.

Keywords: *Glycated hemoglobin. Coronary artery disease. Acute coronary syndrome.*

INTRODUCTION

Cardiovascular diseases (CVDs) are a major contributor to deaths and disability, leading to 21 million deaths worldwide. Around three quarter of these deaths take place in low- and middle-income countries.[1] In South Asian countries, the burden of CVDs will double in the coming 20 years.[2] Similarly, diabetes mellitus (DM) is also rising globally, being most common in low- and middle-income countries. The reported prevalence of DM is 537 million across the world. In addition, these diseases are leading to a significant financial burden of healthcare costs. The United Nations Sustainable Development Goal is to decrease the deaths attributed to non-communicable diseases by one-third in these countries.[1,3]

Acute coronary syndrome (ACS) includes three fatal conditions: ST elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI), and unstable angina. There are various predisposing factors of ACS, such as hypertension, obesity, diabetes mellitus, and smoking.[4] In diabetic patients, coronary artery disease causes a significant proportion of mortality and morbidity.[5] It has been documented that not only the prevalence of CAD is higher in diabetic patients but DM is also linked with complicated CAD and bad prognosis. This link between DM and CAD is attributed to persistent hyperglycemia in diabetic patients. Hyperglycemia impairs the function of endothelial cells and causes inflammation, and accelerates atherosclerosis.[6]

Hemoglobin A1c (HbA1c) is the standard for monitoring and diagnosis of diabetes mellitus. Some studies have reported the positive relation of HbA1c with the severity of CAD. But others have not found any such association.[5] Diabetes mellitus is prevalent in Pakistan, reaching a frequency of 17.1%.[7] Understanding the relation between the two diseases has a great effect on global health owing to the higher prevalence of both diseases. This study was done to determine the association of HbA1c levels with the complexity of CAD indicated by the SYNTAX score in patients presenting with ACS who underwent coronary angiography. This study would provide insight into the possible relation between the two diseases and help in risk stratification for identifying patients at high risk.

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METHODOLOGY

This cross-sectional comparative study was conducted at Fauji Foundation Hospital, Rawalpindi after ethical approval (Letter No. 981/RC/FFH/RWP, 30-06-2025) from July to September 2025. Patients were divided into two groups. Those with HbA1c ≤7% were labeled as group 1 and group 2 had patients with HbA1c >7%. The sample size of 61 for each group was calculated using 80% power, 5% margin of error, and the mean SYNTAX scores of 24.33±5.00 & 27.19±6.17 in diabetic patients with HbA1c ≤7% & HbA1c >7%, respectively.[8] After written informed consent, diabetic patients who presented with ACS and underwent coronary angiography were included using non-probability convenience sampling technique. The exclusion criteria were non-diabetic patients, patients who had previous percutaneous coronary intervention or coronary artery bypass grafting, severe renal or liver diseases, malignancy, and autoimmune disorders.

The medical history & previous laboratory reports of patients were used to confirm diabetes mellitus. The age, body mass index (BMI), and co-morbidities such as hypertension, smoking, dyslipidemia & family history of CAD were noted on a proforma. The blood samples of patients were taken and sent for HbA1c levels and fasting lipid profile. The lipid profile, which includes total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, very low-density lipoprotein (VLDL) cholesterol, and triglycerides, is considered normal when total cholesterol is less than 200 mg/dL, LDL cholesterol is less than 130 mg/dL, HDL cholesterol is greater than 40 mg/dL in men and greater than 50 mg/dL in women, triglycerides are less than 150 mg/dL, and VLDL cholesterol is between 5-30 mg/dL.[9]

The HbA1c levels of ≤7% showed good glycemic control and >7% was considered suboptimal and often categorized as poor glycemic control.[10] The patients with ACS were diagnosed on suggestive clinical history, raised troponin levels, and electrocardiogram changes.[11]

The patients then underwent coronary angiography and SYNTAX score was estimated to determine angiographic disease complexity. It was calculated by summing up the score given to individual lesions in the 16 segments of the coronary tree. Patients with >50% stenosis in coronary arteries of >1.5 mm diameter had significant CAD.[12] The range of SYNTAX score was from 0 to >60 and the higher scores meant more complex CAD. The patients with scores of 0-22 were labeled as low risk, 23-32 as intermediate and >32 as high-risk CAD.[13]

STATISTICAL ANALYSIS

Data analysis was carried out using the Statistical Package for the Social Sciences (SPSS) version 26. Numerical and categorical variables were expressed using mean±standard deviation and frequency (percentage), respectively. The association between categorical variables like CAD risk categories indicating disease complexity and HbA1c groups was determined using Pearson's Chi-square test. Similar test was used to compare demographic variables and other risk factors with HbA1c groups and CAD risk categories. Pearson's correlation was used to evaluate the correlation between HbA1c levels and SYNTAX scores of the participants. The p-value <0.05 was considered significant for both tests.

RESULTS

The average age of participants in our study was 54.3±9.35 years. Most of the patients (32.8%) were 51-60 years of age, followed by 41-50 years (28.7%) and >60 years (27.9%). Most of the patients (77.1%) were females. The mean BMI of the patients was 28.18±4.09 kg/m^2. Most of the patients (44.3%) were overweight, while 36.8% were obese. Out of 122 patients, 30.3% had hypertension, 41% had a deranged lipid profile, 14.8% were smokers, and 37.7% had a positive family history of CAD. There was no significant difference in demographic variables and co-morbidities between the two groups, showing no significant association of these variables with HbA1c (Table 1).

The statistically significant results of the association of CAD risk categories with HbA1c groups showed that the majority (34.4%) of the patients in group 1 had low risk CAD. However, most (24.6%) of the participants in group 2 had intermediate risk CAD indicating increasing complexity of CAD with increasing HbA1c levels (Table 2).

The mean HbA1c level of the patients was 7.8±1.10 and the mean SYNTAX score was 21.68±6.93. The Pearson's correlation coefficient was 0.528, indicating a moderate positive correlation between HbA1c & SYNTAX scores (p-value=0.001). This showed that as the HbA1c levels of participants increase, the SYNTAX score, indicating the complexity of CAD, also tends to increase (Figure 1).

When the CAD risk categories were compared with demographic variables and risk factors, only significant association was observed with lipid

profile. The majority (38.5%) of patients with normal lipid profile had low risk CAD indicating lesser complexity of the disease. Most of the patients with intermediate (20.5%) and high risk (9%) CAD had deranged lipid profiles (Table 3). The other factors, like age groups, gender, BMI, hypertension, smoking, and family history of CAD showed no statistically significant results.

Table 1: Association of Demographic Variables and Risk Factors with HbA1c Groups

Variables		Group 1 (HbA1c ≤7%) (n=61)	Group 2 (HbA1c >7%) (n=61)	Total	p-value
Age Groups (Years)	**≤40**	8(6.5%)	5(4.1%)	13(10.6%)	0.516
	41-50	20(16.4%)	15(12.3%)	35(28.7%)	
	51-60	18(14.8%)	22(18%)	40(32.8%)	
	>60	15(12.3%)	19(15.6%)	34(27.9%)	
	Total	61(50%)	61(50%)	122(100%)	
Gender	**Male**	12(9.8%)	16(13.1%)	28(22.9%)	0.389
	Female	49(40.2%)	45(36.9%)	94(77.1%)	
	Total	61(50%)	61(50%)	122(100%)	
BMI (kg/m^2)	**Normal (18.5-24.9)**	15(12.3%)	8(6.6%)	23(18.9%)	0.077
	Overweight (25-29.9)	29(23.8%)	25(20.5%)	54(44.3%)	
	Obese (≥30)	17(13.9%)	28(22.9%)	45(36.8%)	
	Total	61(50%)	61(50%)	122(100%)	
Clinical Presentation	**NSTEMI**	34(27.9%)	40(32.8%)	74(60.7%)	0.266
	STEMI	27(22.1%)	21(17.2%)	48(39.3%)	
	Total	61(50%)	61(50%)	122(100%)	
Hypertension	**Hypertensive**	17(13.9%)	20(16.4%)	37(30.3%)	0.554
	Non-Hypertensive	44(36.1%)	41(33.6%)	85(69.7%)	
	Total	61(50%)	61(50%)	122(100%)	
Lipid Profile	**Deranged**	24(19.7%)	26(21.3%)	50(41%)	0.712
	Normal	37(30.3%)	35(28.7%)	72(59%)	
	Total	61(50%)	61(50%)	122(100%)	
Smoking	**Smoker**	10(8.2%)	8(6.6%)	18(14.8%)	0.609
	Non-Smoker	51(41.8%)	53(43.4%)	104(85.2%)	
	Total	61(50%)	61(50%)	122(100%)	
Family History of CAD	**Positive**	21(17.2%)	25(20.5%)	46(37.7%)	0.454
	Negative	40(32.8%)	36(29.5%)	76(62.3%)	
	Total	61(50%)	61(50%)	122(100%)	

Table 2: Association of CAD Risk Categories with HbA1c Groups

CAD Risk Categories (SYNTAX Score)	HbA1c Groups		Total	p-value
	Group 1 (HbA1c ≤7%)	Group 2 (HbA1c >7%)		
Low Risk (0-22)	42(34.4%)	19(15.6%)	61(50%)	0.001*
Intermediate Risk (23-32)	14(11.5%)	30(24.6%)	44(36.1%)	
High Risk (>32)	5(4.1%)	12(9.8%)	17(13.9%)	
Total	61(50%)	61(50%)	122(100%)	

**Significant p-value*

Table 3: Association of CAD Risk Categories with Lipid Profile

Lipid Profile	CAD Risk Categories (SYNTAX Score)			Total	p-value
	Low Risk (0-22) n=61	Intermediate Risk (23-32) n=44	High Risk (>32) n=17		
Deranged	14(11.5%)	25(20.5%)	11(9%)	50(41%)	0.0002*
Normal	47(38.5%)	19(15.6%)	6(4.9%)	72(59%)	
Total	61(50%)	44(36.1%)	17(13.9%)	122(100%)	

**Significant p-value*

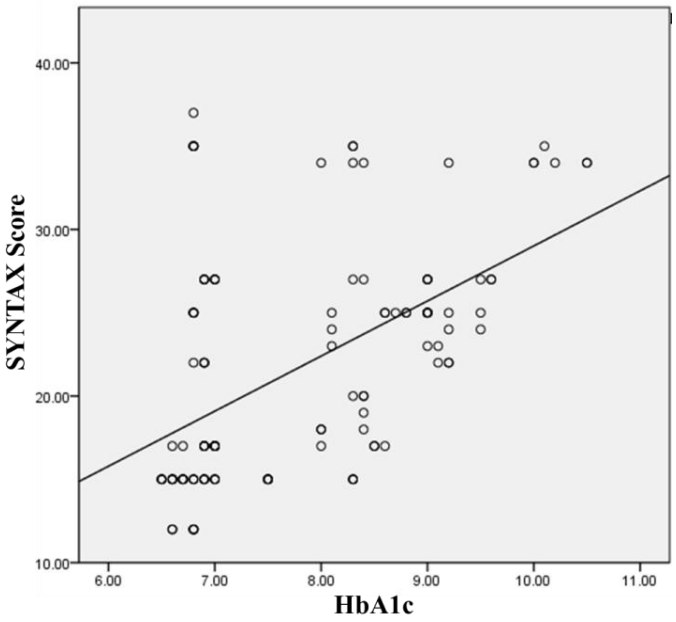

Figure 1: Scatter Plot showing a Positive Association between HbA1c and SYNTAX Score

DISCUSSION

The variation in blood glucose levels strongly influences the development of CAD. Hemoglobin A1c is a prognostic indicator of glycemic control in diabetic patients and can predict the complexity of CAD. Therefore, it is mandatory to monitor HbA1c levels continuously for risk assessment of patients.[14,15]

The average age of patients in our study was 54.3±9.35 years, with the majority (77.1%) of females. However, the age groups and gender did not differ significantly when compared with HbA1c groups and CAD risk categories. In a study done by Rashid et al., the mean age was 58.77±18.24 years with 60% males. In contrast to our results, the mean age of their participants had a statistically significant association (p=0.06) with CAD severity where increased severity was shown by older ages. The gender didn't show any such association.[16] Qadir et al. observed that 56.6% of their patients were males and the average age was 57.54±3.47 years.[17] A study from China showed that the average age of their participants was 65 years with 64.3% females. The age and gender didn't differ significantly when compared with adverse cardiac events indicating the complexity and severity of CAD in diabetic patients.[18] The average age was 57.6±9.5 years in another study with 65% males.[19] Patients had an average age of 54±10.2 years with 79.8% males in another study conducted in Karachi, Pakistan. But neither age nor gender had any statistically significant association with the prediction of CAD severity.[20]

Our results revealed that the mean BMI of the patients was 28.18±4.09 kg/m^2. Most of the patients (44.3%) were overweight, while 36.8% were obese. There was no significant association between BMI and HbA1c groups and CAD risk categories. Jiao et al. showed that the mean BMI of participants was 24.9±2.4 kg/m^2 and BMI and disease severity/complexity in diabetic patients had no significant association (p>0.05).[17] Another study reported that BMI had no statistically significant role in the prediction of CAD severity.[20] The risk factors profile of the current study showed that 30.3% of the patients were hypertensive, 14.8% were smokers, 41% had a deranged lipid profile, and 37.7% had a family history of CAD. None of these risk factors showed a statistically significant association when compared with HbA1c groups or CAD risk categories except lipid profile. The majority (38.5%) of patients with normal lipid profile had low risk CAD indicating lesser complexity, while most of the patients with intermediate (20.5%) and high risk (9%) CAD had deranged lipid profiles. Rashid et al. observed in their study that there were 73.77% hypertensive, 44.89% smokers, and 56.88% patients with dyslipidemia. These risk factors showed no significant relationship with the severity of CAD.[16] Similar to our results, Garg et al. observed that a deranged lipid profile was significantly related to CAD severity.[19] The most common risk factor in a

study was smoking (44.5%), followed by hypertension (42%), family history of CAD (37%), and dyslipidemia (10%). These risk factors didn't serve as significant predictors of CAD severity.[20]

Our results revealed that most of the ACS patients (60.7%) presented with NSTEMI. More than half of the patients presented with NSTEMI (52.1%), followed by STEMI (25.2%) and unstable angina (22.7%) in another study done by Habib et al. Similar to our results, clinical presentation wasn't related to CAD complexity.[20] However, a previous study observed that patients with STEMI presentation had more complex disease indicated by higher SYNTAX scores ($p<0.05$).[21]

The current study reported statistically significant results of the association of CAD risk categories with HbA1c groups. The majority (34.4%) of the patients in group 1 had low risk CAD. However, most (24.6%) of the participants in group 2 had intermediate risk CAD indicating increasing complexity of CAD with higher HbA1c levels. Another study showed that the patients with higher HbA1c levels had significantly increased complexity/severity of CAD indicated by higher Gensini scores.[16] Similar results were shown by another study, which revealed that HbA1c was a significant predictor of the severity of coronary artery disease and major adverse cardiac events.[18] Garg et al. revealed a significant association between HbA1c in diabetic patients and severity of CAD, where 41.7% of the patients with HbA1c >10.5% had triple vessel CAD.[19] Our study showed a significant and moderate positive correlation of HbA1c and SYNTAX scores. Similar results were reported in a study by Xu et al., where HbA1c and SYNTAX scores were significantly & positively correlated in diabetic patients.[8] The study by Dar et al. also found a significant correlation between HbA1c and Gensini scores showing increasing complexity of CAD with higher HbA1c levels.[22] Habib et al. conducted a study on non-diabetic patients with ACS and did not find any significant correlation between HbA1c and SYNTAX scores.[20]

CONCLUSION

The majority of patients with HbA1c ≤7% had low-risk CAD, while patients with HbA1c >7% had intermediate-risk CAD. Our study also found a significant, moderate positive correlation between HbA1c and the complexity of coronary artery disease (indicated by SYNTAX score) in diabetic patients presenting with ACS. The SYNTAX score significantly increased with increasing HbA1c levels. In addition, the patients with intermediate and high-risk CAD indicated by higher SYNTAX scores also had dyslipidemia.

LIMITATIONS & RECOMMENDATIONS

This study had a few limitations: cross-sectional design, non-probability convenience sampling technique, and single-institution research. The study did not evaluate the association of higher HbA1c in diabetic patients with complications of CAD, such as cardiac mortality and major adverse cardiovascular events. In the future, multi-centered studies should be conducted with follow-up of the patients to assess long-term complications.

Diabetic patients with higher HbA1c levels should be considered at higher cardiovascular risk as higher HbA1c is linked with higher SYNTAX scores, indicating complex CAD. The need for strict glycemic control in diabetic patients should be emphasized to reduce cardiovascular risk.

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Authors' Contributions:
U.S: Assisted in patient recruitment and data acquisition, analyzed data, and drafted the manuscript.
I.A.K: Contributed to study design, data interpretation, and critical revision.
S.A: Conceived and designed the study.
K.R: Performed statistical analysis and literature review.
T.M: Assisted in data collection and manuscript formatting.
F.U: Supervised the study, validated results, and approved the final manuscript.

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