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Predictive power of glycated hemoglobin in detecting severity of coronary artery disease in non-diabetic patients: A cross-sectional study in southern Iran

Shahin Abbaszadeh[(1)], Shideh Rafati[(2)], Daryoush Mamikhani[(1)], Mahdieh Emami[(3)], Nahid Shahabi[(1)]

Original Article

Abstract

BACKGROUND: The relationship between hemoglobin A1c (HbA1c) levels and coronary artery disease (CAD) severity is still a matter of debate in non-diabetic patients. This study aimed to determine the association between HbA1c and the severity of CAD in non-diabetic patients.

METHODS: The present cross-sectional study was conducted in 2018-2019 on 133 non-diabetic patients with stable angina, unstable angina, or myocardial infarction (MI). They were selected through systematic random sampling. The data were collected by taking a complete medical history, calculating the SYNTAX score, and measuring HbA1c.

RESULTS: A SYNTAX score of >22 was significantly correlated with age, left ventricular ejection fraction, HbA1c, and total cholesterol. The mean SYNTAX score was higher in male patients, those with HbA1c >5.6, and patients with a primary clinical presentation of MI. The association between the SYNTAX score and HbA1c was found to be statistically significant (r = 0.659; P < .001). The odds of having a SYNTAX score of >22 for those with HbA1c >5.6 was 5.48 times higher than for those with HbA1c ≤ 5.6 (odds ratio [OR], 5.48; *P* < .001). The odds of three-vessel disease in individuals with an HbA1c level greater than 5.6 were found to be 4.80 times higher than in those with HbA1c levels at or below 5.6 (OR, 4.80; *P* = 0.002).

CONCLUSION: The present findings showed that HbA1c has the potential to predict the severity of CAD in non-diabetic individuals. HbA1c, even at levels within the normal range, was significantly correlated with SYNTAX scores.

Keywords: Coronary artery disease; Glycated hemoglobin; SYNTAX score; Diabetes mellitus; Iran

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Introduction

Cardiovascular diseases (CVD) encompass a variety of disorders affecting the heart and blood vessels, and they collectively represent the leading cause of death worldwide. These diseases are responsible for approximately 17.9 million deaths each year[1]. Coronary artery disease (CAD) is associated with 17.8 million deaths annually and represents the most common form of CVD[2,3]. CVD is a significant contributor to mortality in Iran, and its prevalence is high in Hormozgan Province, Iran[4,5].

The development of non-invasive screening tools to detect CAD has been a focus of research, with new methods showing improved performanc[6]. However, clinicians currently lack unanimous agreement regarding the most precise methods for predicting fatal and non-fatal CAD-related outcomes. This situation creates an opportunity to evaluate

1- Cardiovascular Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
2- Social Determinants in Health Promotion Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
3- Independent Researcher, Private Clinic, Chalus, Iran
Address for correspondence: Nahid Shahabi; Cardiovascular Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran; Email: Nahid.shahabi68@gmail.com

supplementary biomarkers capable of identifying early metabolic alterations in atherosclerosis and CAD[7]. Hemoglobin A1c (HbA1c) is widely recognized as a crucial indicator of long-term glycemic control in individuals diagnosed with diabetes[8]. Elevated HbA1c leads to an increased risk of microvascular and macrovascular complications[9]. Lower HbA1c levels are associated with the reduction of these complications[10].

Previous studies have shown that higher HbA1c levels are an important risk factor for CAD and myocardial infarction (MI) in patients with diabetes[11,12]. HbA1c is a helpful prognostic tool for CAD, and this has been well investigated in patients with diabetes[13]. However, the association of HbA1c levels and CAD in non-diabetic patients is still unclear, especially in studies in which the SYNTAX score estimates the severity of CAD. The SYNTAX score is a scoring system based on coronary angiography that is utilized to assess the anatomical distribution of CAD and ascertain the complexity of lesions in the coronary arteries. It considers different characteristics of lesions such as bifurcation lesions, chronic total occlusions, thrombus, calcification, and diffuse small vessel disease[14]. The SYNTAX score is categorized into 3 main classes as follows:

0–22: Low SYNTAX Score
23–32: Intermediate SYNTAX Score
≥33: High SYNTAX Score

Important predictors of cardiac mortality and major adverse cardiac events include SYNTAX scores, age, gender, smoking, diabetes, and acute coronary syndrome[15,16]. Limited research has been conducted on the correlation between HbA1c and CAD in non-diabetic patients, despite numerous studies that have established a connection between HbA1c and CAD severity in individuals with diabetes[17-19]. Conventional diagnostic methods for diabetes, such as fasting glucose levels or medical records, have been used in most previous studies. HbA1c has not been included in many studies to determine diabetes, leaving a gap in understanding its potential association with coronary artery lesions in non-diabetic individuals. In this study, we aimed to determine the association between HbA1c and CAD severity in non-diabetic patients. The severity of CAD was assessed using two distinct methods: the SYNTAX score and a traditional numerical approach that considers the number of vessels exhibiting luminal stenosis.

Methods

Study design and population

The present analytical cross-sectional study was conducted from September 2018 to September 2019 in Bandar Abbas, the capital city of Hormozgan Province in southern Iran.

A total of 133 non-diabetic patients visiting the angiographic center of Shahid Mohammadi Hospital in Bandar Abbas were included in this study. They were selected through systematic sampling. Therefore, every member of the population was listed with a number based on the angiographic center registry, but instead of randomly generating numbers, individuals were chosen at regular intervals. For example, all registered angiographic center patients admitted were listed in alphabetical order. From the first 10 numbers, we randomly selected a starting point: number 7. From number 6 onwards, every 10th person on the list was selected (7, 17, 27, 37, and so on), and we ended up with a sample of 133 people after recruiting participants based on inclusion and exclusion criteria.

Decisions about indications for diagnostic coronary catheterization and determination of clinical diagnoses—such as stable angina, unstable angina, and acute MI—were made by two experienced cardiologists based on the patient's clinical presentation, electrocardiogram characteristics, noninvasive test results, and cardiac biomarkers. According to the electrocardiographic definition, MI was classified as ST elevation or non-ST elevation MI.

The inclusion criteria were (a) visiting Shahid Mohammadi Bandar Abbas Angiography Center with a diagnosis of MI, stable angina, or unstable angina, and (b) informed consent to participate in the study.

Patients with a history of diabetes, those on diabetic medication, those with a fasting blood sugar of >126 mg/dL or postprandial blood sugar of >200 mg/dL, HbA1c ≥6.5%, a history of previous revascularization such as percutaneous coronary intervention or coronary bypass graft surgery, a history of hemoglobinopathies, anemia (Hb <11 mg/dL), recent blood transfusion in the past 3 months, and a history of splenectomy were excluded[20].

Measurements

A complete medical history, including age, gender, history of smoking, blood pressure, and

dyslipidemia, and a physical examination were obtained from all patients. All patients underwent coronary angiography. The number of occluded vessels, the severity of stenosis (>50% luminal stenosis of any epicardial coronary artery with a diameter of >1.5 mm), and the SYNTAX score were recorded by two experienced cardiologists who were unaware of patients' characteristics[14]. The results were categorized into No CAD (luminal stenosis <50%), single-vessel disease (SVD), double-vessel CAD (2VD), and triple-vessel CAD (3VD), and by SYNTAX score into low score (≤22) and intermediate to high score (>22)[21].

HbA1C was also measured in all patients using Sebia Capiflex 2 capillary electrophoresis (Sebia) and the results were divided into ≤5.6% or >5.6%.

Ethical considerations

After the researcher clearly explained the study's objectives to all participants, written consent was obtained that included all details about the research. Participation in the research was voluntary. The anonymity and confidentiality of the information collected from participants were preserved. This study was approved by the Ethics Committee of Hormozgan University of Medical Sciences (IR.HUMS.REC.1397.059).

Statistical analysis

Skewness and kurtosis values between –2 and +2 were considered acceptable to prove a normal distribution[22-24]. The normality of the dependent variable (SYNTAX score) was confirmed based on a skewness of 0.68 (standard error = 0.21) and a kurtosis of –0.15 (standard error = 0.41).

Continuous variables were described using mean and standard deviation as well as median (interquartile range [IQR]), and categorical variables were reported using numbers and percentages. A chi-square test was used to compare two categorical variables in a contingency table to determine whether there was statistical evidence of their association. The independent samples t-test was used to compare the mean scores of the two independent groups to determine whether they differ significantly from each other. Analysis of variance was used to check whether the difference between the mean scores of three or more groups was statistically significant. Scatterplots with Pearson correlation and regression linear were used to show the association between the SYNTAX score and HbA1c in non-diabetic patients.

Binary logistic regression was used to test the association between HbA1c and the SYNTAX score (≤22 and >22 as the binary dependent variable) after adjusting for the effects of other variables. Additionally, multinomial logistic regression was used to determine the association between HbA1c and the severity of coronary artery disease (CAD) with four levels—No CAD, single-vessel disease (SVD), double-vessel CAD (2VD), and triple-vessel CAD (3VD)—after adjusting for the effects of other variables. All analyses were done in STATA (version 15; StataCorp, 2017), and $P < .05$ was considered statistically significant.

Results

A total of 133 non-diabetic individuals were included in the final analysis. The mean age was 58.4 ± 12.3 years, and 64 patients (48.1%) were younger than 58 years. Ninety-two patients were men (69.2%); 67 patients were smokers (50.4%); 43 patients had dyslipidemia (32.3%), and 63 had hypertension (47.4%) (Table 1).

The mean and standard deviation of the SYNTAX score was 10.96 ± 9.35, and the median (interquartile range [IQR]) was 9 (14.75). The mean score of HbA1c was 5.38 ± 0.48, with a median (IQR) of 5.3 (0.6). The angiographic result of CAD severity as the number of diseased vessels was not statistically significant—No CAD (n = 29, 22%); SVD (n = 33, 25%); 2VD (n = 28, 21%); and 3VD (n = 43, 32%) (Table 1). The SYNTAX score of >22 was significantly correlated with age, left ventricular ejection fraction (LVEF), HbA1c, and total cholesterol. Compared with the No CAD group, the severity of CAD in categorical classification was significantly correlated with age, male gender, opium use, LVEF, HbA1c, serum Cr, and primary clinical presentation as MI (Table 1).

The mean SYNTAX score was higher in males compared to females, in patients with HbA1c >5.6% compared to patients with HbA1c ≤5.6%, and in patients with primary clinical presentation as MI (Table 2).

The correlation between the SYNTAX score and HbA1c was statistically significant ($r = 0.659$; $P < 0.001$). Also, the scatter plot showed a linear relationship between the SYNTAX score and HbA1c (Figure 1).

Table 1. General characteristics of participants in categories of the SYNTAX score and CAD

Variables	Syntax Score ≤22 (n=114)	Syntax Score >22 (n=19)	P value	CAD No CAD (n=29)	CAD SVD (n=33)	CAD 2VD (n=30)	CAD 3VD (n=41)	P value
Age (years)	57.09 ± 12.40	64.47 ± 9.68	0.015[a]	53.52 ± 12.28	54.45 ±11.10	61.13± 10.63	62.20±12.75	0.003[c]
Age<58 n(%)	59(44.4)	5(3.8)	0.040[b]	17(12.8)	20(15.0)	11(8.3)	16(12.0)	0.099[b]
Age≥58 n(%)	55(41.4)	14(10.5)		12(9.0)	13(9.8)	19(14.3)	25(18.8)	
Gender n(%)								
Female	38(28.6)	3(2.3)	0.180[b]	16(12.0)	6(4.5)	7(5.3)	12(9.0)	0.010[b]
Male	76(57.1)	16(12.0)		13(9.8)	27(20.3)	23(17.3)	29(21.8)	
Hypertension n(%)								
Yes	51(38.3)	12(9.0)	0.147[b]	9(6.8)	13(9.8)	16(12.0)	25(18.8)	0.060[b]
No	63(47.4)	7(5.3)		20(15.0)	20(15.0)	14(10.5)	16(12.0)	
Dyslipidemia n(%)								
Yes	33(24.8)	10(7.5)	0.062[b]	9(6.8)	8(6.0)	10(7.5)	16(12.0)	0.601[b]
No	81(60.9)	9(6.8)		20(15.0)	25(18.8)	20(15.0)	25(18.8)	
Smoking n(%)								
Yes	60(45.1)	7(5.3)	0.225[b]	10(7.5)	22(16.5)	15(11.3)	20(15.0)	0.091[b]
No	54(40.6)	12(9.0)		19(14.3)	11(8.3)	15(11.3)	21(15.8)	
Opium addiction n(%)								
Yes	31(23.3)	7(5.3)	0.417[b]	3(2.3)	14(10.5)	9(6.8)	12(9.0)	0.049[b]
No	83(62.4)	12(9.0)		26(19.5)	19(14.3)	21(15.8)	29(21.8)	
FBS(mg/dl)	102.86 ±11.12	107.36 ±10.48	0.102[a]	99.51 ± 10.08	105.48 ± 11.86	103.46 ± 10.73	104.78 ± 11.10	0.149[c]
Left Ventricular Ejection Fraction (%)	47.59 ± 8.31	42.89 ± 9.32	0.027[a]	51.55 ± 7.08	46.67± 7.87	44.67 ± 10.49	45.49 ± 7.56	0.007[c]
HbA1c (%)	5.28 ± 0.39	5.93 ± 0.28	<0.001[a]	5.01 ± 0.34	5.27 ± 0.37	5.43 ± 0.32	5.68 ± 0.42	<0.001[c]
HbA1c≤5.6 n(%)	91(68.4)	3(2.3)	<0.001[b]	27(20.3)	28(21.1)	23(17.3)	16(12.0)	<0.001[b]
HbA1c>5.6 n(%)	23(17.3)	16(12.0)		2(1.5)	5(3.8)	7(5.3)	25(18.8)	
Hemoglobin (mg/dl)	12.80 ± 1.42	13.52 ± 1.41	0.064[a]	12.38 ± 0.95	12.91 ± 1.49	13.14 ± 1.64	13.11 ± 1.48	0.141[a]
Serum Creatinine (mg/dl)	1.01 ± 0.35	1.10 ± 0.21	0.318[a]	0.92 ± 0.13	0.93 ± 0.17	1.06 ± 0.27	1.14 ± 0.51	0.016[a]
Total Cholesterol (mg/dl)	172.43 ± 40.70	191.84 ± 32.50	0.028[a]	160.06 ± 44.61	176.66 ± 40.31	176.63 ± 34.78	183.70 ± 38.68	0.108[a]
Triglyceride (mg/dl)	136.43 ± 57.95	129.94 ± 45.70	0.587[a]	144.55 ± 77.88	126.42 ± 54.35	136.26 ± 49.81	135.87 ± 43.67	0.660[a]
HDL-cholesterol (mg/dl)	41.30 ± 8.84	43.10 ± 6.50	0.398[a]	41.89 ± 8.39	40.42 ± 8.26	42.73 ± 11.50	41.39 ± 6.27	0.756[a]
LDL-cholesterol (mg/dl)	100.58 ± 34.79	114.63 ± 30.37	0.079[a]	88.03 ± 41.25	106.66 ± 32.86	103.93 ± 29.36	108.63 ± 32.06	0.072[a]
BMI (kg/m²)	24.63 ± 3.15	25.61 ± 3.25	0.216[a]	24.60 ± 2.77	24.11 ± 3.01	25.43 ± 3.24	24.93 ± 3.49	0.410[a]

FBS, fasting blood sugar; **HbA1c**, hemoglobin A1c; **BMI**, body mass index; **HDL**, high-density lipoprotein; **LDL**, low-density lipoprotein. Continuous variables were described using means and standard deviations (mean ±SD), and categorical variables were described using numbers and percentages (%). [a] Independent-samples T-test; [b] Chi-square test; [c] ANOVA test.

Based on the multivariable linear regression model, adjusting for age, gender, hypertension, dyslipidemia, smoking, opium addiction, total cholesterol, triglyceride, high-density lipoprotein, low-density lipoprotein, and body mass index, a 1% increase in HbA1c increased the mean SYNTAX score by 13.53 (unstandardized coefficient = 13.53; standardized coefficient = 0.647; $P < 0.001$).

Based on the binary logistic regression results (Table 3), after adjusting for other variables, the odds of having a SYNTAX score of >22 compared to having a SYNTAX score of ≤22, for those with HbA1c >5.6 was 5.48 times higher than for those with HbA1c ≤5.6 (odds ratio [OR], 5.48; 95% CI, 1.42-8.58; $P < 0.001$). Additionally, the multinomial logistic regression analysis revealed that after

Table 2. The mean of SYNTAX score in different groups

Variables	Syntax Score Mean	Standard Deviation	Standard Error	P value
Age (years)<58	10.12	8.82	1.10	0.322
Age (years)≥58	11.73	9.81	1.18	
Gender				
Female	7.51	7.64	1.19	0.004
Male	12.5	9.66	1.01	
Hypertension				
Yes	12.63	9.80	1.23	0.052
No	9.45	8.72	1.04	
Dyslipidemia				
Yes	12.0	9.55	1.45	0.379
No	10.46	9.26	0.97	
Smoking				
Yes	11.08	8.94	1.09	0.882
No	10.84	9.81	1.20	
HbA1c (%)≤5.6	7.46	7.12	0.73	<0.001
HbA1c (%)>5.6	19.38	8.75	1.40	
BMI(kg/m²)<24.9	11.18	9.66	1.13	0.771
BMI(kg/m²)≥25	10.70	9.04	1.15	
Clinical Presentation				
Stable angina	8.92	12.08	2.70	<0.001
Unstable angina	4.53	7.59	1.43	
NSTEMI	12.19	9.60	1.72	
STEMI	14.34	6.92	0.94	

HbA1c, hemoglobin A1c; **BMI**, body mass index; **NSTEMI**, non-ST elevation myocardial infarction; **STEMI**, ST-elevation myocardial infarction; The Independent Samples t Test was used to compare the means of two independent groups; The one-way ANOVA test was used to compare the means of four independent samples.

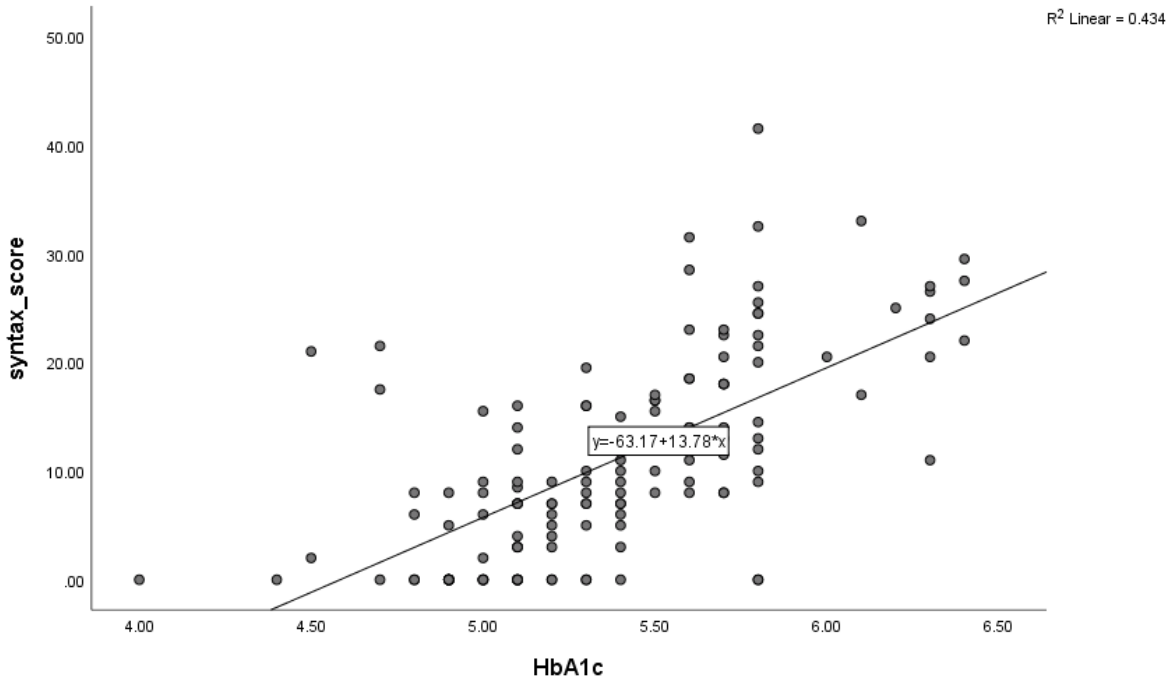

Figure 1. Scatter plot to show the relationship between SYNTAX score and HbA1c in non-diabetic patients.

Table 3. The findings of binary and multinomial logistic regression models

Variables	Binary logistic regression Syntax Score>22		Multinomial logistic regression models					
			SVD		2VD		3VD	
	Odds Ratio (95% CI)	P value	Odds Ratio (95% CI)	P value	Odds Ratio (95% CI)	P value	Odds Ratio (95% CI)	P value
Age (years)	1.09 (1.01-1.17)	0.032	1.02 (0.97-1.08)	0.358	1.08 (1.03-1.15)	0.003	1.09 (1.02-1.15)	0.005
Gender (Reference: Male)								
Female	0.09 (0.01-0.96)	0.047	0.28 (0.06-1.30)	0.106	0.18 (0.04-0.85)	0.031	0.35 (0.07-1.73)	0.355
Hypertension (Reference: No)								
Yes	1.36 (0.29-6.30)	0.691	2.84 (0.73-11.12)	0.132	3.56 (0.95-13.34)	0.059	5.19 (1.29-20.86)	0.020
Dyslipidemia (Reference: No)								
Yes	1.42 (0.24-8.45)	0.695	0.33 (0.07-1.58)	0.170	0.60 (0.13-2.81)	0.524	0.39 (0.07-2.02)	0.267
Smoking (Reference: No)								
Yes	0.223 (0.04-1.15)	0.074	2.20 (0.55-8.71)	0.259	1.12 (0.28-4.53)	0.864	1.49 (0.36-6.15)	0.580
Opium addiction (Reference: No)								
Yes	1.49 (0.26-8.50)	0.650	2.28 (0.37-13.90)	0.369	2.45 (0.36-16.56)	0.356	1.47 (0.21-10.19)	0.695
HbA1c (Reference: ≤5.6)								
HbA1c (%)>5.6	5.48 (1.42-8.58)	<0.001	1.81 (0.24-8.88)	0.554	2.80 (0.37-21.27)	0.319	4.80 (1.25-7.16)	0.002
FBS(mg/dl)	0.961 (0.89-1.03)	0.961	1.04 (0.98-1.11)	0.168	1.01 (0.94-1.07)	0.839	1.01 (0.93-1.06)	0.995
Total Cholesterol (mg/dl)	1.06 (0.99-1.14)	0.084	1.11 (0.99-1.24)	0.071	1.13 (1.01-1.27)	0.032	1.19 (1.06-1.33)	0.002
Triglyceride (mg/dl)	0.99 (0.97-1.01)	0.320	0.97 (0.95-0.99)	0.019	0.97 (0.95-0.99)	0.022	0.97 (0.95-0.99)	0.006
HDL (mg/dl)	1.01 (0.89-1.13)	0.863	0.87 (0.76-0.99)	0.036	0.90 (0.79-1.03)	0.136	0.83 (0.73-0.95)	0.007
LDL (mg/dl)	0.956 (0.88-1.03)	0.238	0.92 (0.82-1.03)	0.192	0.89 (0.80-1.01)	0.069	0.86 (0.76-0.96)	0.010
BMI(kg/m²)	1.21 (0.95-1.55)	0.110	0.95 (0.77-1.17)	0.954	1.14 (0.93-1.40)	0.189	1.05 (0.85-1.30)	0.605

FBS, fasting blood sugar; **HbA1c**, hemoglobin A1c; **BMI**, body mass index; **HDL**, high-density lipoprotein; **LDL**, low-density lipoprotein. SYNTAX score ≤22 is the reference for the binary logistic model, and No CAD is the reference for the multinomial logistic model.

adjusting for other variables, the odds of 3VD compared to no CAD, for those with HbA1c >5.6 was 4.80 times higher than for those with HbA1c ≤5.6 (OR, 4.80; 95% CI, 1.25-7.16; $P = 0.002$).

Discussion

In our study, we evaluated the role of HbA1c in predicting the severity of CAD in non-diabetic individuals. The average SYNTAX score was higher in male patients, those with HbA1c levels exceeding 5.6, and those with a primary clinical presentation of MI. There was a significant direct correlation between HbA1c levels and SYNTAX scores ($P < 0.05$), indicating that HbA1c can be an appropriate predictor to assess the severity of CAD in non-diabetic patients.

A direct association exists between the level of HbA1c and the progression of coronary atheroma. This correlation remains unaffected by the presence of diabetes or other modifiable risk factors for atherosclerosis. This conclusion is drawn from a post hoc pooled analysis of data from seven prospective, randomized-controlled trials that utilized serial coronary intravascular ultrasonography (IVUS)[25]. There is also a moderate correlation between HbA1c and the degree of luminal stenosis in non-diabetic patients, using coronary CT angiography[7].

The SYNTAX score has been associated with

long-term outcomes, heart failure, and the ability to stratify patients according to their risk of cardiac death or major adverse cardiac events[26,27].

Our study demonstrated that higher HbA1c levels increase the odds of higher SYNTAX scores. By calculating the SYNTAX score, we evaluate the severity of CAD not only by measuring the luminal stenosis but also by considering the anatomical distribution of these stenoses and the complexity of atherosclerotic lesions, making the study results clinically more operational. There is growing evidence in the literature that shows a positive association between HbA1c levels and the severity of CAD in non-diabetic patients[7,18,28]. As the results of Kayali et al.'s study showed, HbA1c can be used as an independent marker to determine the probability and severity of CAD in non-diabetic patients. Additionally, HbA1c can be used as a valuable marker in primary care for predicting CAD[28]. Another study in the United States found that HbA1c is linked to a higher risk of coronary heart disease in seemingly healthy, non-diabetic individuals. The research suggests that HbA1c could be a significant early indicator of disease risk[29].

Cavero-Redondo et al. conducted a systematic review of 74 published studies and concluded that HbA1c is a reliable risk factor for all-cause and cardiovascular mortality in both diabetic and non-diabetic participants[30]. In contrast to our study, Habib et al. performed a linear regression analysis of HbA1c with the SYNTAX score. Their study revealed no statistically significant correlation between the SYNTAX score and HbA1c in 119 non-diabetic participants who underwent coronary intervention[17]. Moreover, another cross-sectional, prospective study in Karachi by Ul-Haque et al. on 177 diabetic and 378 non-diabetic patients showed no association between elevated HbA1c levels and a SYNTAX score of >22[31]. In these two studies, they did not consider a history of hemoglobinopathies as an exclusion criterion regarding their effect on the accuracy of HbA1c measurement. Only patients with acute coronary syndromes were included, the patients were overall younger than our study, and they also used HbA1c levels above 6.4 percent in their multivariate logistic regression for non-diabetic participants[31].

Overall findings indicate that HbA1c could potentially serve as a useful tool for assessing the risk and predicting the severity of CAD in individuals without diabetes, regardless of conventional cardiovascular risk factors. The results suggest that HbA1c could be used as a valuable marker in primary care to predict CAD and assess its severity, highlighting its potential role in identifying individuals at risk for cardiovascular disease. We propose conducting a longitudinal study to assess the predictive power of HbA1c levels for the progression of CAD and the benefits of early intervention in non-diabetic patients. Furthermore, we propose exploring the clinical implications of using HbA1c levels as a biomarker for CAD severity in non-diabetic patients, including the potential for personalized treatment strategies and improved patient outcomes.

Conclusion

In our study, we showed that HbA1c has the potential to predict the severity of CAD in non-diabetic individuals. HbA1c, even at levels within the normal range, was significantly correlated with SYNTAX scores. With the SYNTAX score, we can calculate the CAD extension through coronary arteries and the complexity of lesions, and also estimate its clinical impacts. This ability can enrich our knowledge of CAD severity beyond simply measuring the degree of luminal stenosis. We conclude that HbA1c can be used as an adjunct biomarker to predict CAD severity in non-diabetic patients, rather than as a surrogate marker. However, further research is required before this marker can be used for routine cardiovascular risk assessment in this population.

Strengths and Limitations

In the present study, we used standardized methods to measure HbA1c and the SYNTAX score. This ensured consistency and accuracy in the data collected. Additionally, we excluded patients with diabetes, hemoglobinopathies, and other conditions that could impact the results. This helped ensure that the findings were specific to non-diabetic patients. We used the SYNTAX score, which is a widely accepted measure of coronary artery disease (CAD) severity. This provided a relevant and meaningful outcome measure for the research. The current study encountered certain limitations. Initially, all individuals were enlisted solely from a single center, and the sample size was not particularly large.

Additionally, it is imperative to acknowledge that our findings do not establish a definitive cause-and-effect association. In other words, additional data is required to ascertain that elevated HbA1c levels escalate the severity of CAD in non-diabetic patients.

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Conflict of Interests

The authors declare no conflict of interest.

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Author's Contributions

SH.A was the principal investigator, conceived of the idea, shared in the practical work of coronary angiography, supervised the findings, and wrote the manuscript. SH.R shared the methodology structure and analytical plan. D.M & M.E collected patient data.NA performed manuscript preparation. All authors read and approved the final manuscript.

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