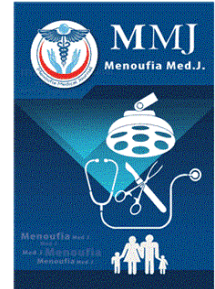




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ORIGINAL STUDY

Correlation Between Glycosylated Hemoglobin and Coronary Artery Disease Severity in Prediabetic Patients Using SYNTAX Score

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Abstract

Objectives: To assess the correlation between glycosylated hemoglobin (HbA1c), fasting blood glucose, and coronary artery disease (CAD) severity as measured by SYNTAX score (The SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery. Syntax score is a unique anatomical scoring tool to score complexity of coronary artery disease.) in prediabetic patients undergoing elective percutaneous coronary intervention.

Background: Numerous reports that prediabetes, a minimally aberrant glycometabolism, has an independent relationship with cardiovascular disease and that it reflects an escalation in the severity and complexity of CAD.

Methods: This cross-sectional study was conducted on consecutive sample of 92 prediabetic patients undergoing elective percutaneous coronary intervention in Cardiology Department of National Heart Institute (Egypt) in cooperation with Cardiology Department of Menoufia University hospitals, during the study period time from May 2022 to July 2023 and meeting the inclusion criteria.

Results: The mean hemoglobin (Hb) was 13.0 ± 1.7 , the mean fasting blood sugar (FBS) is 117.8 ± 6.1 , while the mean HbA1c was 6.1 ± 0.2 . The median (IQR) of the SYNTAX score among the studied patients was 6.5 (0–19). A low SYNTAX score was reported among 80.4% of the patients, an intermediate score was 9.8%, while a high score was reported at 9.8% of the studied patients. There is a significant positive correlation between number of vessel diseased (VD) and HbA1c, P less than 0.001. Also, there is a significant positive correlation between Hb, FBS, HbA1c, and SYNTAX score P less than 0.001. The median of the score was significantly higher among males, smokers, hypertensive patients, and those with positive family history for CAD P less than 0.001. No significant relationship was observed between the score and age P greater than 0.001. Linear regression for predictive factors of SYNTAX showed the number of VD was considered an independent predictor of the severity of CAD. Binary logistic regression Analysis showed the number of VD was the independent risk factor for the intermediate and high SYNTAX score among prediabetics, the presence of 3 VD and 4 VD increases the risk of getting intermediate and high SYNTAX score by 24.1 and 98.4 times, respectively.

Conclusion: In prediabetes, there is a strong positive correlation between Hb, FBS, HbA1c, and SYNTAX score with higher scores among males, smokers, and hypertensive patients. There is also a significant relationship between number of affected vessels and HbA1c. The number of VD was independent factor for getting high score of SYNTAX also increase severity of CAD.

Keywords: Coronary artery disease, Glycosylated hemoglobin, Percutaneous coronary intervention, Prediabetes, Severity score

1. Introduction

Diabetes mellitus (DM) particularly type 2 DM is related to a cluster of cardiovascular disease risk factors (CVD) [1]. Among people with diabetes, there is a prevalence of 60–70% for obesity, 75–85% for

hypertension, 70–80% for high low-density lipoproteins. The main cause of death in types 1 and 2 DM is coronary artery disease (CAD) [2]. DM is related to a two- to four-fold increase in cardiovascular mortality risk. Over 70% of persons over 65 years old with diabetes will die from heart disease or stroke [3].

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Prediabetes can be regarded as a path from normoglycemia to worsening dysglycemia that precedes diabetes. Specific definitions of prediabetes include poor glucose tolerance or impaired fasting glucose [4]. The American Diabetes Association defines impaired glucose tolerance as a plasma glucose value in the 2-h oral glucose tolerance test between 140 and 199 mg/dl (7.8–11.0 mmol/l). Blood glucose levels between 100 and 125 mg/dl (5.6–6.9 mmol/l) are considered impaired fasting glucose. In addition, a glycosylated hemoglobin (HbA1c) range of 5.7–6.4% (39–46 mmol/mol) is also indicative of prediabetes [5].

Globally, prediabetes prevalence is growing. In 2030, the number of people with prediabetes is projected to exceed 470 million. According to the American Diabetes Association, up to 70% of prediabetics will acquire diabetes in the future [6]. Numerous reports have shown that prediabetes, a minimally aberrant glycometabolism, has an independent relationship with CVD and that it reflects an escalation in the complexity and severity of CAD, leading to an increase in the number of small blood vessels and diffuse lesions. This contributes to the formation of unstable plaques [7].

In individuals with stable CAD and ischemia, percutaneous coronary intervention (PCI) and coronary artery bypass grafting are alternatives for coronary revascularization. Americans and European guidelines show that treatment selection is influenced by patient preferences, comorbidities, and disease complexity [8].

Due to the yearly increase in the number of patients treated for CAD and the necessity of risk stratification and prognostic evaluations, various assessment techniques have been developed to assess patients' risk and predict their outcomes after therapeutic intervention [9]. The SYNTAX score is one of the most significant scoring systems that have been developed to date [10].

Since 2004, extensive research has been conducted on HbA1c as a predictor of CAD severity and cardiovascular mortality in non-diabetics. Numerous prior studies have demonstrated that increased HbA1c is linked to CAD severity, indicating that it might serve as a severity marker for CAD [10].

Thus, the study aimed to assess the correlation between HbA1c, fasting blood sugar (FBS), and CAD severity as measured by SYNTAX score in prediabetic patients undergoing elective PCI.

2. Patients and methods

This cross-sectional study was conducted on consecutive sample of 92 prediabetic patients undergoing elective PCI in cardiology department of

National Heart Institute in cooperation with the Cardiology Department of Menoufia University Hospitals, during a period time from May 2022 to July 2023.

Ethical consideration: Patients who decided to participate provided their signed informed permission after being told of the trial's advantages and risks and after receiving approval from the local ethics committee. The trial was registered with the local ethics committee of the National Heart Institute and Menoufia University Faculty of Medicine.

Inclusion criteria: Patients eligible for elective PCI, aged between 18 and 80 years old, and HbA1c ranging from 5.7 to 6.4% and normal kidney function.

Exclusion criteria: Previous diabetes diagnosis, current or past use of oral hypoglycaemic medications or insulin, fasting glucose of 126 mg/dl, 2-h postmeal blood glucose of 200 mg/dl in a previous oral glucose tolerance test, fasting for more than 10 h before coronary angiography, emergency PCI, abnormal haemoglobin, recent blood transfusion, erythropoietin medication history, or history of coronary artery bypass grafting.

Procedure: All patients were exposed to a thorough medical history, including age, sex, and risk factors for CAD (smoking, hypertension, family history of CAD), full clinical examination, and laboratory investigations (Hb, FBS, HbA1c). All individuals had coronary angiography via a femoral or radial route using the Judkins procedure. Multiple images of the left and right coronary systems were captured.

Coronary angiograms were analyzed by two experienced cardiologists to figure out CAD severity and affected vessel number. CAD severity was assessed using SYNTAX score according to the diagnostic algorithm. Briefly, each lesion causing 50% luminal blockage in arteries 1.5 mm was scored individually, and these scores were summed to calculate the SYNTAX score. This algorithm is available on the SYNTAX website calculator (<https://calculator.syntaxscore2020.com>).

The studied patients were divided according to their SYNTAX score according to SYNTAX trial I into three groups: Prediabetic patients with low scores was defined as less than or equal to 22. Prediabetic patients with intermediate scores as 23–32. Prediabetic patients with a high score of greater than or equal to 33 [11].

2.1. Statistical methods

The data was analyzed by SPSS (statistical package for social science) version 26.0 on IBM compatible computer (SPSS Inc., Chicago, IL, USA). The qualitative data was described as numbers and percentages. Quantitative data was described as mean \pm standard

deviation or median (IQR). Mann–Whitney *U* test and one-way-analysis of variance tests were used for quantitative data analysis after being tested for normality using Shapiro–Wilks test, assuming normality at *P* greater than 0.05. Correlation analysis was done using Spearman correlation test. Multivariate logistic regression analysis was done to assess the predictive factors for SYNTAX score. The accepted level of significance in this work was started at 0.05 (*P* < 0.05 was considered significant).

3. Results

Regarding Sociodemographic data, Risk factors, laboratory characteristics, and SYNTAX results of the studied group. This study showed that the mean age was 55.9 ± 10.9 years. They included 62 (67.4%) males and 30 (32.6%) females. 62% of the studied patients were smokers, 66.3% had hypertension, 27.2% had a family history of CAD, and 54.3% had a previous history of acute coronary syndrome or PCI. Also, the mean Hb of the studied patients was 13.0 ± 1.7, the mean FBS was 117.8 ± 6.1, while the mean HbA1c was 6.1 ± 0.2. Additionally, the median (IQR) of the SYNTAX score among the studied patients was 6.5 (0–19). Most of studied patients (80.4%) had low SYNTAX scores. Only 9.8% had intermediate score, while 9.8% had high scores (Table 1).

Concerning correlation between SYNTAX score and age, Hb, FBS, and HbA1c of the studied group, the current study revealed that there was no significant correlation between SYNTAX score and age, *r* = 0.132. While, significant positive correlations were detected between Hb (*r* = 292), FBS (*r* = 281), HbA1c (*r* = 404), and SYNTAX score (Table 2).

The median score is significantly higher among males, smokers, hypertensive patents, and those with positive family history of CAD. No significant relationship was observed between the score and age or the presence of history of Acute Coronary Syndrome (ACS) or PCI. Most patients, 43.5% had normal coronary arteries, 19.5% had single vessel disease (VD), 13% had two- VD, and 12% had multiple -VD (3 or 4 vessels affected). There was a significant relationship between affected vessels number and SYNTAX score (Table 3). Additionally, there is a significant relationship was detected between affected vessels number and HbA1c, while there is no significant relationship was detected between the affected vessels number and FBS (Table 4).

Regarding the relationship between HbA1c by quartiles and patients' characteristics, the current study showed that the significant differences between the higher and lower HbA1c groups were associated with CAD severity as measured by mean SYNTAX

Table 1. Sociodemographic data, risk factors, laboratory characteristics and SYNTAX results of the studied group (N = 92).

Variables	Patients (n = 92) N (%)
Age/year	
Mean ± SD	55.9 ± 10.9
Sex	
Male	62 (67.4)
Female	30 (32.6)
	Values are expressed as mean ± SD or n (%).
Smoking	
Yes	57 (62)
No	35 (38)
Hypertension	
Yes	61 (66.3)
No	31 (33.7)
Family history of CAD	
Yes	25 (27.2)
No	67 (72.8)
History of ACS or previous PCI	
Yes	50 (54.3)
No	42 (45.7)
Number of affected vessels	
0	40 (43.5)
1 VD	18 (19.5)
2 VD	12 (13)
3 VD	11 (12)
4 VD	11 (12)
	Values are expressed as n (%)
Laboratory characteristics	
Hb	
Mean ± SD	13.0 ± 1.7
FBS	
Mean ± SD	117.8 ± 6.1
HbA1c	
Mean ± SD	6.1 ± 0.2
	Values are expressed as mean ± SD
SYNTAX results	
SYNTAX score	
Median (IQR)	6.5 (0–19)
Range	0–44
SYNTAX interpretation	N (%)
Low	74 (80.4)
Intermediate	9 (9.8)
High	9 (9.8)

Values are expressed as median (IQR) or n (%). Acute coronary syndrome, (ACS); coronary artery disease, (CAD); fasting blood sugar, (FBS); glycosylated hemoglobin, (HbA1c); hemoglobin, (Hb); percutaneous coronary intervention, (PCI).

Table 2. Correlation between SYNTAX score and age, Hb, FBS, and HbA1c of the studied group (N = 92).

Variables	SYNTAX score	
	r	P value
Age (years)	0.132	0.211
Hb	0.292	0.005*
FBS	0.281	0.007*
HbA1c	0.404	<0.001*

Fasting blood sugar, (FBS); glycosylated hemoglobin, (HbA1c); hemoglobin, (Hb).

r: correlation coefficient.

* Statistically significant at P value < 0.05.

Table 3. Relationship between SYNTAX score and characteristics of the studied group (N = 92).

Variables	SYNTAX score	
	Median (IQR)	P value
Sex		
Male	12.5 (2.3–24.6)	<0.001*
Female	0 (0–6.3)	
Smoking		
Yes	14.5 (3.4–25.3)	<0.001*
No	0 (0–10)	
Hypertension		
Yes	11 (0–23)	0.005*
No	0 (0–12)	
Family history of CAD		
Yes	20 (6.5–29.5)	<0.001*
No	3 (0–14)	
History of ACS or previous PCI		
Yes	6.5 (0–17.5)	0.900
No	7 (0–20)	
Number of affected vessels		
0	1.1 ± 6.3	<0.001*
1 VD	10.1 ± 5.2	
2 VD	16.8 ± 7.8	
3 VD	24.8 ± 7.4	
4 VD	9.6 ± 2.9	

Values are expressed as mean ± SD, median (IQR) or n (%).

Acute Coronary Syndrome (ACS).

Coronary artery disease, (CAD); fasting blood sugar, (FBS); percutaneous coronary intervention, (PCI).

* Statistically significant at P value < 0.05.

score, rate of positive family history, and number of diseased vessels, P less than 0.05 (Table 5). As regard syntax categories separately and patient characteristics, our study showed that FBS, HbA1c, the percentage of males, smokers, and those with positive family history were higher in those with intermediate and high SYNTAX score than those with low score, P less than 0.05. There was also a significant difference between those with intermediate and high SYNTAX score and those with low scores regarding the number of VD, with 50% of those with intermediate and high Syntax score had 4 VD versus 2.7% of those with low scores, P less than 0.001 (Table 6).

Multivariate linear regression was used to show the number of VD as independent predictor of the severity of CAD by the SYNTAX score among prediabetics (Table 7), and by binary logistic regression analysis, the number of VD was the independent risk factor for the intermediate and high SYNTAX II

score among prediabetics, the presence of 3 VD and 4 VD increases the risk of getting intermediate and high SYNTAX score by 24.1 and 98.4 times, respectively (Table 8).

4. Discussion

Worldwide, CAD is the main cause of death. Significant endeavors have been made to find innovative, noninvasive, and efficient CAD biomarkers, which may play a role in the CAD etiology or in the generation of risk factors that are predictive of disease severity [12]. Although DM is a prominent risk factor for CAD, new information is now available suggesting the need for a careful consideration not only of DM, but also of other disturbances of glucose metabolism, such as impaired glucose tolerance, which is now considered an independent risk factor for CVD morbidity and mortality [2].

In the last years, many studies have shown that HbA1c% is a better indicator of CAD presence and severity than other glycaemic variables. HbA1c% also reflects the glycaemic metabolic state in the preceding months [13]. So, it has been used to assess the efficiency of DM control [14]. Now, it has become one of the most used measures of chronic hyperglycaemia in epidemiological studies and clinical trials. In addition, HbA1C% level of 6.5% or more, is considered a diagnostic criterion for the presence of DM in a patient [15].

The present study demonstrated that the mean age was 55.9 ± 10.9 years. They included 62 (67.4%) males and 30 (32.6%) females. 62% of the studied patients were smokers, 66.3% had hypertension, 27.2% had a family history of CAD, and 54.3% had a previous history of acute coronary syndrome or PCI. In accordance with these results, Ekram *et al.* [16] reported that the age of the study participants ranged from 28 to 81 with a mean of 56.2 ± 11.6 years old. More than two-thirds (71.5%) of them were males. Hypertensive patients represented 53.7% of all study patients. As regards smoking, more than half (59.3%) of the patients were smokers. 19% of the patients has family history of premature coronary heart disease.

Our study showed that in prediabetes, the median of the SYNTAX score was significantly higher among males, smokers, hypertensive patients, and

Table 4. Relationship between both FBS, HbA1c and number of affected vessels of the studied group (N = 92).

	0 VD	1 VD	2 VD	3 VD	4 VD	P value
FBS	115.9 ± 6.8	119.6 ± 5.7	118.0 ± 4.7	119.8 ± 4.8	119.5 ± 5.0	0.093
HbA1c	6.0 ± 0.2	6.12 ± 0.23	6.10 ± 0.19	6.21 ± 0.14	6.17 ± 0.17	0.015*

Values are expressed as mean ± SD.

* Statistically significant at P value < 0.05.

Fasting blood sugar, (FBS); Glycosylated hemoglobin, (HbA1c).

Table 5. Relationship between HbA1c by quartiles and characteristics of the studied group (N = 92).

	HbA1c interquartile				P value
	<5.8 (n = 35)	5.9–6.0 (n = 18)	6.1–6.3 (n = 26)	>6.4 (n = 13)	
Age	56.7 ± 12.7	55.6 ± 9.2	56.8 ± 11	52.2 ± 7.2	0.610
Hb	12.8 ± 1.7	13.2 ± 1.7	13.2 ± 1.9	13.2 ± 1.3	0.758
FBS	116.5 ± 6.5	117.1 ± 5.4	118.3 ± 6.5	121.2 ± 3.0	0.098
SYNTAX score	5.2 ± 9.8	13.1 ± 10.4	16.3 ± 14.9	15.1 ± 12.0	0.002
SYNTAX interpretation, n (%)					
Low	33 (94.3)	15 (83.3)	16 (51.5)	10 (76.9)	0.066
Intermediate	1 (2.9)	2 (11.1)	4 (15.4)	2 (15.4)	
High	1 (2.9)	1 (5.6)	6 (23.1)	1 (7.7)	
Sex, n (%)					
Male	22 (62.9)	13 (72.2)	16 (61.5)	11 (84.6)	0.444
Female	13 (37.1)	5 (27.8)	10 (38.5)	2 (15.4)	
Smoking, n (%)					
Yes	17 (48.6)	12 (66.7)	17 (65.4)	11 (84.6)	0.122
No	18 (51.4)	6 (33.3)	9 (34.6)	2 (15.4)	
Hypertension					
Yes	18 (51.4)	14 (77.8)	20 (76.9)	9 (69.2)	0.117
No	17 (48.6)	4 (22.2)	6 (23.1)	4 (30.8)	
Family history of CAD, n (%)					
Yes	3 (8.6)	3 (16.7)	14 (53.8)	5 (38.5)	0.001
No	32 (91.4)	15 (83.3)	12 (46.2)	10 (61.5)	
Old CAD, n (%)					
Yes	15 (42.9)	9 (50)	19 (73.1)	7 (53.8)	0.128
No	20 (57.1)	9 (50)	7 (26.9)	6 (46.2)	
Number of VD, n (%)					
0	23 (65.7)	4 (22.2)	9 (34.6)	4 (30.8%)	0.027*
1 VD	5 (14.3)	5 (27.8)	4 (15.4)	4 (30.8)	
2 VD	4 (11.4)	5 (27.8)	1 (3.8)	2 (15.4)	
3 VD	1 (2.9)	2 (11.1)	6 (23.1)	2 (23.1)	
4 VD	2 (5.7)	2 (11.1)	6 (23.1)	1 (7.7)	

Values are expressed as mean ± SD, median (IQR) or n (%).

* Statistically significant at P value < 0.05.

those with positive family history of CAD. While there was no significant relationship between the score and age or the presence of either previous ACS or PCI. In a study by Omidi *et al.* [17] who studied the relationship between CAD traditional risk factors and disease burden as assessed by GENSINI score in a large cohort study and found a positive correlation between age, sex, DM, hypertension, positive family history of CAD and GENSINI score, they found no significant relationship between smoking and GENSINI score. On the other hand, Bhattacharya *et al.* [18] studied the relationship between CAD traditional risk factors and disease severity as assessed by SYNTAX score and reported an insignificant relationship between SYNTAX score and hypertension, smoking, or family history of CAD. Only age was found to have a significant positive correlation with SYNTAX score.

Concerning correlation between SYNTAX score and age, Hb, FBS, and HbA1c of the studied group, the current study revealed that there was statistically significant positive correlations were detected between Hb ($r = 292$), FBS ($r = 281$), HbA1c ($r = 404$), and SYNTAX score. In this context, Dutta *et al.* [19]

reported similar results. They evaluated the relationship between HbA1c% and CAD severity, using SYNTAX score, in nondiabetic patients and concluded that HbA1c% was significantly correlated with SYNTAX score (75). Also, in a study by Mirza *et al.* [20]. The study involved 322 patients without type 2DM with symptoms of chronic stable angina referred for conventional coronary angiography to evaluate the relation between HbA1c level and severity of CAD angiographically in non-diabetic patients with chronic stable angina, they found a positive correlation between CAD severity using SYNTAX score and HbA1c%. Also, Ekram *et al.*, 2018 [16] found a statistically significant positive moderate correlation between HbA1c% and SYNTAX score and a statistically significant positive moderate correlation was present between HbA1c% and a number of affected vessels. Considering this correlation between HbA1c% and SYNTAX scoring for CAD angiographic severity, In this context Arbel *et al.* [21] studied the correlation between SYNTAX score and gluco-metabolic markers, including fasting glucose, HbA1c%, and admission glucose levels, the only marker that was linked to higher SYNTAX score was

Table 6. Comparison between Low vs intermediate and high SYNTAX score regarding characteristics of the studied group (N = 92).

	SYNTAX score		P value
	Low (n = 74)	Intermediate and high (n = 18)	
Age	55.5 ± 11	57.3 ± 10.6	0.544
Hb	12.9 ± 1.6	13.7 ± 1.8	0.056
FBS	117.1 ± 6.3	120.7 ± 3.9	0.021
HbA1c	6.0 ± 0.2	6.2 ± 0.2	0.003
Sex, n (%)			
Male	46 (62.2)	16 (88.9)	0.030
Female	28 (37.8)	2 (11.1)	
Smoking, n (%)			
Yes	41 (55.4)	16 (88.9)	0.009
No	33 (44.6)	2 (11.1)	
Hypertension, n (%)			
Yes	46 (62.2)	15 (83.3)	0.088
No	28 (37.8)	3 (16.7)	
Family history of CAD, n (%)			
Yes	13 (17.6)	12 (66.7)	<0.001
No	61 (82.4)	6 (33.3)	
Old CAD, n (%)			
Yes	40 (54.1)	10 (55.6)	0.909
No	34 (45.9)	8 (44.4)	
Number of VD, n (%)			
0	39 (52.7)	1 (5.6)	<0.001
1 VD	18 (24.3)	0	
2 VD	10 (13.5)	2 (11.1)	
3 VD	5 (6.8)	6 (33.3)	
4 VD	2 (2.7)	9 (50)	

Values are expressed as mean ± SD, median (IQR), or n (%).

HbA1c%, while there was no correlation between admission glucose, FBS and SYNTAX score.

Concerning the relationship between SYNTAX score and characteristics of the studied group, Our study showed that there was a statistically significant relationship between the number of affected vessels and HbA1c% level in prediabetic patients. While no significant relationship was detected between the affected vessels number and FBS. In the same line, Cai *et al.* [22] studied the relationship

Table 7. Linear regression for predictive factors of SYNTAX score (N = 192).

	β	P value	95% CI	
			Lower	Upper
Sex	-0.093	0.382	-13.785	3.858
Smoking	-0.062	0.580	-8.678	9.244
Hypertension	-0.008	0.891	-0.489	9.186
Family history	0.068	0.310	2.244	13.466
Hb	0.021	0.746	-0.926	2.103
FBS	0.063	0.292	-0.144	0.660
HbA1c	0.121	0.066	-0.457	14.019
Number of VD	0.753	<0.001*	5.464	7.851

Confidence interval, (CI); Coronary artery disease, (CAD); fasting blood sugar, (FBS); Glycosylated hemoglobin, (HbA1c); hemoglobin, (Hb); VD, (vessel disease).

*Significant.

Table 8. Binary logistic regression for predictive factors of intermediate and high SYNTAX score (N = 192).

	OR	P value	95% CI	
			Lower	Upper
Sex				
Female	Reference			
Male	4.7	0.393	0.1	168.1
Smoking				
Nonsmoker	Reference			
Smoker	0.3	0.497	0.01	10.7
Family history				
No	Reference			
Present	3.4	0.200	0.5	22.6
VD				
0	Reference			
1	0.00	0.998	00	00
2	5.9	0.227	0.3	103.8
3	24.1	0.015	1.9	313.5
4	98.4	0.001	6.0	1607.2
FBS	1.2	0.091	0.97	1.45
HbA1c	30.6	0.211	0.14	6534

between HbA1c% and number of affected vessels in 573 nondiabetic patients undergoing coronary angiography and found that the number of affected vessels was correlated with HbA1c. Another study by Acar *et al.* [23] conducted on 469 consecutive patients admitted with a diagnosis of ACS. Of these, 250 patients were admitted at the first occurrence of ACS undergoing diagnostic coronary angiography. reported that in diabetic and prediabetic patients, the SYNTAX score was significantly higher than in controls, and the number of affected vessels, especially three VD, was more common in the prediabetics than nondiabetics.

Also, in a study by Ashraf *et al.* [24] who studied the relationship between HbA1c and CAD severity as measured by GENSINI score in 299 non-diabetic patients undergoing coronary angiography and they found that there was a significant increase in the prevalence of CAD and number of vessels involved as HbA1c increased. Dutta *et al.* [19] reported similar results and revealed a significant increase in the number of affected vessels in nondiabetic patients with increasing HbA1c% levels. Also, Sahal *et al.* [25] evaluated 480 nondiabetic patients who underwent coronary angiography and they found a positive correlation between CAD burden and HbA1c.

Regarding the relationship between HbA1c by quartiles and patients' characteristics, the current study showed that the significant differences between the higher and lower HbA1c groups were associated with CAD severity as measured by mean SYNTAX score, rate of positive family history, and number of diseased vessels, P less than 0.0. This result is matched with Dutta *et al.* [19] who found that CAD severity by SYNTAX score as well as

number of vessels involved was significantly different among quartiles (P values < 0.001 and < 0.001 , respectively). Increase in HbA1c level was strongly correlated with disease severity and higher SYNTAX score. A significant increase was noted in the mean number of diseased vessels (P value < 0.001) as HbA1c level increases. The mean SYNTAX score was also significantly increased with increased HbA1c levels (< 4.8 , $4.8–5.1$, $5.1–5.6$ and 5.6 to < 6.5 , respectively). In SYNTAX subgroups (< 23 , $23–32$ and > 32), mean HbA1c values were 4.9 ± 0.4 , 5.7 ± 0.3 and 6.0 ± 0.92 , respectively.

Regarding the relationship between our studied patients characteristics and SYNTAX score categories, the current study demonstrated that the FBS, HbA1c, the percentage of males, smokers, and those with positive family history were higher in those with intermediate and high SYNTAX score than those with low score, P less than 0.05. There was also a significant difference between those with intermediate and high SYNTAX score and those with low score regarding the number of VD, with 50% of those with intermediate and high SYNTAX score had 4 VD versus 2.7% of those with low score, P less than 0.001. In this context, in similar study by Garg *et al.* [26] who found mean SYNTAX score was significantly increased with increasing HbA1c level $9.9\% \pm 12.2\%$, $12.9\% \pm 12.7\%$, $15.4\% \pm 15.2\%$, $19 \pm 15.5\%$ in patients with HbA1c levels less than 5.5%, 5–5.7%, 5.8–6.1%, and greater than 6.1%, respectively, with P trend less than 0.001.

Concerning to Linear regression for predictive factors of SYNTAX score, the current study showed that, the number of VD was considered an independent predictor of the severity of CAD while sex, smoking, hypertension, Hb, FBS, and HbA1c are cofactors. After Binary logistic regression for predictive factors of intermediate and high SYNTAX score, the data revealed the number of VD was the independent risk factor for the intermediate and high SYNTAX score among prediabetics, the presence of 3 VD and 4 VD increases the risk of getting intermediate and high SYNTAX score by 24.1 and 98.4 times, respectively. In our study, as in line with previous studies, there was a strong relationship between HbA1c level and CAD in prediabetic patients, but after multivariate regression analysis, HbA1C not was independent predictor for CAD severity. In a study by Wang *et al.* [27] in the literature with 292 patients, it was aimed to correlate the severity of CAD with HbA1c value, and however, it was found No significant relationship between GENSINI score and HbA1c; thus, it is stated that HbA1c Cannot be used as an independent marker for CAD severity.

Also, a study by de Carvalho Cantarelli *et al.* [28] aimed to evaluate independent predictors of multi-vessel CAD in Brazil and assessed the association between cardiovascular risk factors and CAD extent, as assessed by coronary angiography. After multivariate analysis, Multivessel CAD in Brazil is associated with traditional risk factors for atherosclerosis, except for smoking. Age, diabetes, and chronic renal failure were the strongest predictors for multivessel CAD assessed by coronary angiography.

4.1. Conclusions

Smoking, hypertension, family history of CAD, and history of old CAD were risk factors for CAD in prediabetic patients. Prediabetic patients showed advanced CAD and increased levels of HbA1C. There was a significant positive correlation between Haemoglobin, FBS, HbA1c, and SYNTAX score. HbA1c is significantly associated with the SYNTAX score which reflect the severity and complexity of coronary lesions in CAD patients with and without diabetes. There was significant high SYNTAX score in males, smokers, hypertensive patient, and those with positive family history, however no significant relationship between the score and age or the presence of old CAD. there was a strong relationship between HbA1c level and CAD in prediabetic patients. The number of VD was independent factor for getting high score of SYNTAX also increase severity of CAD.

Ethics information

Patients who decided to participate provided their signed informed permission after being told of the trial's advantages and risks and after receiving approval from the local ethics committee. The trial was registered with the local ethics committee of the National Heart Institute and Menoufia University Faculty of Medicine.

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Conflicts of interest

There are no conflicts of interest.

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