

The Relationship between Glycated Hemoglobin and Complexity of Coronary Artery Lesions Among Middle-Aged Patients with Diabetes Mellitus

Ahmed Mokhtar El Kersh, Mohamed Abd Elmoneim Salama*, HEND Mohammed Abdo Eldeeb

Cardiology Department, Faculty of Medicine, Menoufia University, Menoufia, Egypt

*Corresponding author: Mohamed Abd Elmoneim Salama, Mobile: (+20) 01062804181, E-Mail: dr.salam2022@gmail.com

ABSTRACT

Background: Microvascular angiopathies in DM patients are associated with elevated levels of glycated hemoglobin (HbA1c). However, the connection between HbA1c and the severity of CAD and coronary perfusion in DM patients remains obscure.

Objectives: Evaluation if there is a correlation between HbA1c levels and the complexity of coronary artery lesions, as measured by the Syntax score among middle-aged DM patients who have been referred for elective coronary angiography.

Patients and Methods: 50 patients with type 2 diabetes participated in this prospective, randomized clinical investigation. Patients who voluntarily had coronary angiography at 6th October Insurance Hospital, Giza, Egypt between April 2021 and January 2022 were evaluated for coronary artery blockage.

Results: Syntax score was highly statistically significant relation between Syntax score and HbA1c where Syntax score significantly increased among patients in group III (29.70 ± 5.14) than patients in group II (14.53 ± 4.42) and patients in group I (6.00 ± 2.66), ($P < 0.001$). Moreover, there were significant positive correlations between smoking and total cholesterol with Syntax score ($P < 0.05$). However, no significant correlations were found between Syntax score with age, sex, HTN, serum creatinine, LDL, HDL, and triglyceride of the studied patients, ($P > 0.05$). ROC curve analysis shows that, the best cutoff value of HbA1c in detection of severity disease using syntax score was ≥ 6.95 , with AUC=0.705, sensitivity 86%, specificity 73%, with significant level $p=0.016$

Conclusion: The severity of coronary artery lesions in diabetic patients was significantly linked with their HbA1c levels. Further, after accounting for other potential dangers, the HbA1c value was discovered to be a significant predictor of coronary artery lesion complexity.

Keywords: Coronary artery lesions, Diabetes mellitus, Glycated hemoglobin.

INTRODUCTION

High rates of coronary artery disease (CAD) and poor outcomes are both associated with diabetes mellitus (DM), a major risk factor for coronary heart disease⁽¹⁾. Indicative of 2- to 3-month mean blood glucose levels, glycated hemoglobin (HbA1c) is measured once a patient has been diagnosed with diabetes. Several benefits set HbA1c apart from the fasting blood glucose test: its repeatability is improved⁽²⁾. HbA1c can be measured even when the patient isn't fasting, and the panel specifically mentioned how much more practical it is, increased stability and decreased biological variation⁽³⁾. HbA1c, or glycated hemoglobin, is known to increase the likelihood that a person with DM may get microvascular angiopathies. Yet, it is still unclear how HbA1c relates to the degree of coronary perfusion as well as CAD in diabetic patients⁽²⁾.

Clinically, an individual's HbA1c level is used to evaluate the effectiveness of their long-term glucose management. Therefore, it is a reflection of how well diabetes people have managed their glucose levels over time. An HbA1c cutoff of 7 percent has been suggested by the American Diabetes Association for optimal cardiovascular benefit⁽⁴⁾, which represent potential predictive significance of HbA1c levels for cardiovascular disease risk assessment. Multiple prior research have shown that in those who have never had diabetes, HbA1c is positively linked with death and even preclinical cardiovascular disease⁽⁵⁾.

The risk of microvascular problems rises not linearly but exponentially with increasing HbA1c levels⁽⁶⁾. In contrast, research shows that a drop of just 1 percent in HbA1c, the risk of microvascular complications decreases by 37%, and the risk of any end point or mortality from diabetes decreases by 21%⁽⁷⁾.

Several prior researches have shown that HbA1c is positively correlated with mortality and even preclinical cardiovascular disease in individuals who do not have a history of diabetes⁽⁸⁾. HbA1c was found to be a significant predictor of future DM, CVD, and all-cause mortality by Selvin *et al.*⁽⁹⁾. Diabetes mellitus is also a major problem among the elderly population. Age also influences both HbA1c and diabetes risk. Iatrogenic hypoglycemia makes it challenging to achieve optimal glycemic control and HbA1c levels in the elderly⁽⁹⁾.

This angiographic score, called the Syntax score, ranks coronary artery abnormalities according to their severity and complexity⁽¹⁰⁾. Patients with a higher Syntax score are at much higher risk for major adverse cardiovascular events (MACE), and this system has been widely acknowledged as a CAD complexity marker with shown prognostic utility in a variety of clinical settings⁽¹¹⁾.

The greater risk of incapacitating and unpredictable hypoglycemia in elderly patients with DM must always be taken into mind when contemplating intensive medication to reduce HbA1c level. Clinical investigations have not conclusively

proved the benefits of tight glyceamic control in the elderly population⁽¹²⁾.

AIM OF THE STUDY

Our goal is to see if middle-aged DM patients referred for elective coronary angiography had higher HbA1c levels and more complex coronary artery lesions, as assessed by the syntax score.

PATIENTS AND METHODS

Several patients with type 2 diabetes participated in this prospective, randomized clinical investigation. Coronary angiography was performed on patients voluntarily to evaluate a possible blockage in their coronary arteries at 6 October Insurance Hospital, Giza, Egypt during the period study from April 2021 to January 2022.

Ethical consideration:

All participants signed a written informed consent that explains the aim of study before the study initiation. Approval was obtained from Ethical Committee on 6 October Insurance Hospital, Giza, Egypt. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

According to their HbA1c readings, patients were placed into one of three categories: Group I: included 23 patients Hb A1C<6.5%, **Group II:** included 17 patients with 6.5 = Hb A1C ≤8.5% and **Group III:** included 10 patients with HbA1c >8.5%.

Inclusion criteria: both sexes patients with type II diabetes mellitus aged 45-65 years, Patients who have symptoms or laboratory or other investigations indicative of ischemic heart disease (IHD), like ST alterations in ECG, or positive stress tests, wall motion as well as abnormality in echo.

Exclusion criteria: Patients with a history of coronary revascularization, those with unreliable laboratory results, or those with type I diabetes, hospitalized patients for whose post discharge HbA1c results were unavailable, subjects with age more than 65 years old, diseases of the heart, including heart failure, valvular heart disease of varied severity, and congenital heart defects, had a HbA1c beyond the normal reference range of 4.1–6.5%, which is the range for healthy, non-diabetic people.

The following procedures were performed on all research participants:

Complete history taking: assessment of the individual's history and potential risks factors.

Full clinical evaluation: General examination: included general appearance, built, decubitus and complexion. **Vital signs:** included blood pressure, pulse, respiratory rate, temperature. **Local cardiac examination:** included inspection, palpation, and auscultation.

Investigation: HbA1c, Kidney functions, including blood urea and serum creatinine using the open system autoanalyzer synchron CX5 (Beckman, USA) and lipid profile including Cholesterol, triglyceride (TG), low density lipoprotein (LDL), high density lipoprotein (HDL) using the open system autoanalyzer synchron CX5 (Beckman, USA).

Coronary angiography and assessment of syntax score: The Syntax score was created to provide a numerical value for the extent of damage to coronary arteries. The Syntax score is derived from the baseline diagnostic angiogram using the Syntax score algorithm described by **Sianos *et al.***⁽¹³⁾ and **Serruys *et al.***⁽¹⁰⁾. Individual coronary lesions responsible for at least 50% diameter stenosis in vessels 1.5 mm are scored separately and then added to yield the final Syntax score. The coronary angiograms were seen by two experts who were blinded to the patients' identities. The SYNTAX study defined the ranges of 0, 22, and 33 for "low," "mid," and "high" scores in Syntax⁽¹⁴⁾.

Statistical analysis

Results were tabulated and statistically analyzed using standard computer program using MICROSOFT EXCEL 2019 and SPSS V.25 program for MICROSOFT WINDOWS 10. Quantitative data was described using mean and standard deviation, whereas qualitative data was described using frequency and proportion. The mean is the sum of all observations by the number of observations. While the standard deviation is a measure the degree of scatter of individual varieties around their mean.

Analytical statistics: included Chi-Squared (χ^2), Kruskal Wallis test (K), The ROC (receiver operating characteristic) curve and the Pearson correlation. The significance level for the results was set at P value of 0.05, with lower or equal to P 0.01 being deemed high significant.

RESULTS

The current study shows that age of the studied patients mean value was (54.92±6.47 years), most of them (80.0%) were males, regarding hypertension 40 patients were hypertensive (80.0%) & only 10 patients were non-hypertensive (20.0%), regarding smoking 27 patients were smokers (54.0%) while 23 were nonsmokers (46.0%). Additionally, the mean of serum creatinine, total cholesterol, LDL, HDL, and triglyceride of the studied patients were 1.22±0.23 mg/dL, 160.40±17.37 mg/dL, 103.04±22.03 mg/dL,

41.80±5.95 mg/dL, 146.52±17.22 mg/dL, respectively (Table 1).

Table (1): Demographic, clinical data and Laboratory investigation of the studied patients.

| Variable | Mean ±SD | Median (range) |
|---------------------------|-----------------|-------------------------|
| Age (year) | 54.92±6.47 | 55.00. (45.00-67.00) |
| Sex | N | % |
| Male | 40 | 80.0 |
| Female | 10 | 20.0 |
| Smoking | | |
| Nonsmoker | 23 | 46.0 |
| Smoker | 27 | 54.0 |
| HTN (mmHg) | | |
| No | 10 | 20.0 |
| Yes | 40 | 80.0 |
| Variable | Mean ±SD | |
| Serum creatinine (mg/dL) | 1.22±0.23 | |
| Total cholesterol (mg/dL) | 160.40±17.37 | |
| LDL (mg/dl) | 103.04±22.03 | |
| HDL (mg/dl) | 41.80±5.95 | |
| Triglyceride(mg/dl) | 146.52±17.22 | |

HTN: Hypertension LDL: Low-density lipoprotein HDL: High-density lipoprotein

Moreover, there were no statistically significant relations between Hb A1C levels and smoking and HTN of the studied patients, serum creatinine, LDL, HDL and triglyceride (P>0.05). On the other hand, there is statistically significant difference between the 3 groups where total cholesterol was significantly increased among patients in group III (168.00±19.32 mg/dl) than patients in group II (166.18±15.42 mg/dl) and patients in group I (152.83±15.31 mg/dl), P=0.014, p value <0.05 (Table 2).

Table (2): Hb A1C levels in relation to demographic, clinical data and laboratory investigation data of the studied patients.

| Variable | Group I (n=23) | | Group II (n=17) | | Group III (n=10) | | K | P value |
|---|-------------------|-------|--------------------|-------|---------------------|--------|------------------|---------------|
| Smoking | | | | | | | | |
| Nonsmoker | 13 | 56.52 | 8 | 47.06 | 2 | 20.00 | X ² = | 0.153 |
| Smoker | 10 | 43.48 | 9 | 52.94 | 8 | 80.00 | 3.754 | |
| HTN (mmHg) | | | | | | | | |
| No | 6 | 26.09 | 4 | 23.53 | 0 | 0.00 | X ² = | 0.205 |
| Yes | 17 | 73.91 | 13 | 76.47 | 10 | 100.00 | 3.165 | |
| Serum creatinine (mg/dl) | Mean ±SD | | Mean ±SD | | Mean ±SD | | | |
| | 1.20±0.20 | | 1.23±0.27 | | 1.28±0.23 | | 0.423 | 0.658 |
| Total cholesterol (mg/dl) | Mean ±SD | | Mean ±SD | | Mean ±SD | | | |
| | 152.83±15.31 | | 166.18±15.42 | | 168.00±19.32 | | 4.702 | 0.014* |
| Post hoc: P1=0.013, P2=0.017, P3=0.779 | | | | | | | | |
| LDL (mg/dl) | Mean ±SD | | Mean ±SD | | Mean ±SD | | | |
| | 95.43±13.74 | | 109.94±13.05 | | 108.80±23.86 | | 2.726 | 0.076 |
| HDL (mg/dl) | Mean ±SD | | Mean ±SD | | Mean ±SD | | | |
| | 42.39±5.65 | | 41.29±3.26 | | 41.30±9.68 | | 0.204 | 0.816 |
| Triglyceride (mg/dl) | Mean ±SD | | Mean ±SD | | Mean ±SD | | | |
| | 146.65±7.61 | | 146.59±19.89 | | 146.10±27.72 | | 0.004 | 0.996 |

HTN: Hypertension K: Kruskal Wallis test X²: Chi square test,

LDL: Low-density lipoprotein HDL: High-density lipoprotein K: Kruskal Wallis test * significant (p value<0.05)

P1: group I compared group II, P2: group I compared group III, P3: group II compared group II

Furthermore, no statistical significant relations were found between syntax score and age, sex, smoking and HTN of the studied patients, P>0.05 (Table 3). Also, there were no statistically significant relations between syntax score and serum creatinine, total cholesterol, LDL, HDL, and triglyceride of the studied patients, P>0.05 (Table 4).

Table (3): Syntax score in relation to demographic and clinical data for the studied patients.

| Variable | Syntax score | | | | | | K | P -value |
|---------------------------------------|---------------------------|-------|---------------------------|--------|---------------------------|--------|---------------------------|----------|
| | Low N=36 | | Intermediate N=8 | | High N=6 | | | |
| Age(year) Mean ±SD Range | 55.83±6.49 45.00-67.00 | | 52.00±7.03 45.00-63.00 | | 53.33±4.89 48.00-60.00 | | 1.373 | 0.263 |
| Sex | N | % | N | % | N | % | X ² = 2.344 | 0.310 |
| Male | 27 | 75.00 | 7 | 87.50 | 6 | 100.00 | | |
| Female | 9 | 25.00 | 1 | 12.50 | 0 | 0.00 | | |
| Smoking | | | | | | | X ² = 5.325 | 0.070 |
| Nonsmoker | 20 | 55.56 | 1 | 12.50 | 2 | 33.33 | | |
| Smoker | 16 | 44.44 | 7 | 87.50 | 4 | 66.67 | | |
| HTN (mmHg) | | | | | | | X ² = 4.861 | 0.088 |
| No | 10 | 27.78 | 0 | 0.00 | 0 | 0.00 | | |
| Yes | 26 | 72.22 | 8 | 100.00 | 6 | 100.00 | | |

HTN: Hypertension K: Kruskal Wallis test * significant

Table (4): Syntax score in relation to laboratory investigation data of the studied patients.

| Variable | Syntax score | | | K | P value | 95% C | |
|--|--------------|---------------------|--------------|-------|---------|--------|--------|
| | Low N=36 | Intermediate N=8 | High N=6 | | | Lower | Upper |
| Serum creatinine (mg/dl) Mean ±SD | 1.20±0.22 | 1.28±0.30 | 1.28±0.19 | 0.537 | 0.588 | 1.16 | 1.29 |
| Total cholesterol (mg/dl) Mean ±SD | 157.94±17.18 | 163.25±8.28 | 171.33±24.37 | 1.704 | 0.193 | 155.46 | 165.34 |
| LDL (mg/dl) Mean ±SD | 100.69±22.51 | 111.25±8.19 | 106.17±3.92 | 0.814 | 0.449 | 96.78 | 109.30 |
| HDL (mg/dl) Mean ±SD | 42.03±4.87 | 39.63±3.70 | 43.33±2.27 | 0.754 | 0.476 | 40.11 | 43.49 |
| Triglyceride (mg/dl) Mean ±SD | 146.33±14.50 | 149.88±7.55 | 143.17±6.35 | 0.260 | 0.772 | 141.63 | 151.41 |

LDL: Low-density lipoprotein HDL: High-density lipoprotein, K: Kruskal Wallis test, X²: Chi square test, * significant.

Additionally, syntax score was highly statistically significant relation between Syntax score and HbA1C where Syntax score significantly increased among patients in group III (29.70±5.14) than patients in group II (14.53±4.42) and patients in group I (6.00±2.66), P<0.001 (Table 5).

Table (5): Hb A1C levels in relation to syntax score for the studied patients.

| Variable | Group I | Group II | Group III | K | P value |
|---------------------|------------------------------|--------------------|--------------------|---------|---------|
| Syntax score | | | | | |
| Mean ±SD | 6.00±1.32 | 14.53±3.42 | 29.70±5.14 | | |
| Median (range) | 6.00(1.00-9.50) | 13.00(10.00-22.50) | 29.00(23.00-38.50) | 130.925 | <0.001* |
| Post hock | P1<0.001, P2<0.001, P3<0.001 | | | | |

K: Kruskal Wallis test * significant

Moreover, there were significant positive correlations between smoking and total cholesterol with syntax score (P<0.05). On the other hand, there were no significant correlations between syntax score with age, sex, HTN, serum creatinine, LDL, HDL, and triglyceride of the studied patients, P>0.05 (Table 6).

Table (6): Correlation between syntax score with the studied parameters

| Variable | Syntax score | |
|---------------------------|--------------|---------------|
| | r | p-value |
| Age (years) | 0.171 | 0.235 |
| Sex (males) | -0.230 | 0.107 |
| Smoking | 0.282 | 0.047* |
| HTN (mmHg) | 0.186 | 0.195 |
| Serum creatinine(mg/dL) | 0.182 | 0.205 |
| Total cholesterol (mg/dL) | 0.319 | 0.024* |
| LDL (mg/dl) | 0.235 | 0.100 |
| HDL (mg/dl) | -0.008 | 0.956 |
| Triglyceride(mg/dl) | -0.039 | 0.788 |

HTN: Hypertension, LDL: Low-density lipoprotein HDL: High-density lipoprotein.

ROC curve analysis shows that, the best cutoff value of HbA1c in detection of severity disease using syntax score was ≥ 6.95 , with AUC 0.705, sensitivity 86%, specificity 73%, with significant level 0.016 (**Table 7, fig 1**).

Table (7): ROC curve analysis of the role of HbA1c in detection of severity disease using Syntax score.

| AUC | Std. Error ^a | Asymptotic Sig. ^b | Cutoff value \geq | Sensitivity | Specificity | Asymptotic 95% Confidence Interval | |
|-------|-------------------------|------------------------------|---------------------|-------------|-------------|------------------------------------|-------------|
| | | | | | | Lower Bound | Upper Bound |
| 0.705 | 0.082 | 0.016 | 6.95 | 86% | 73% | .545 | .864 |

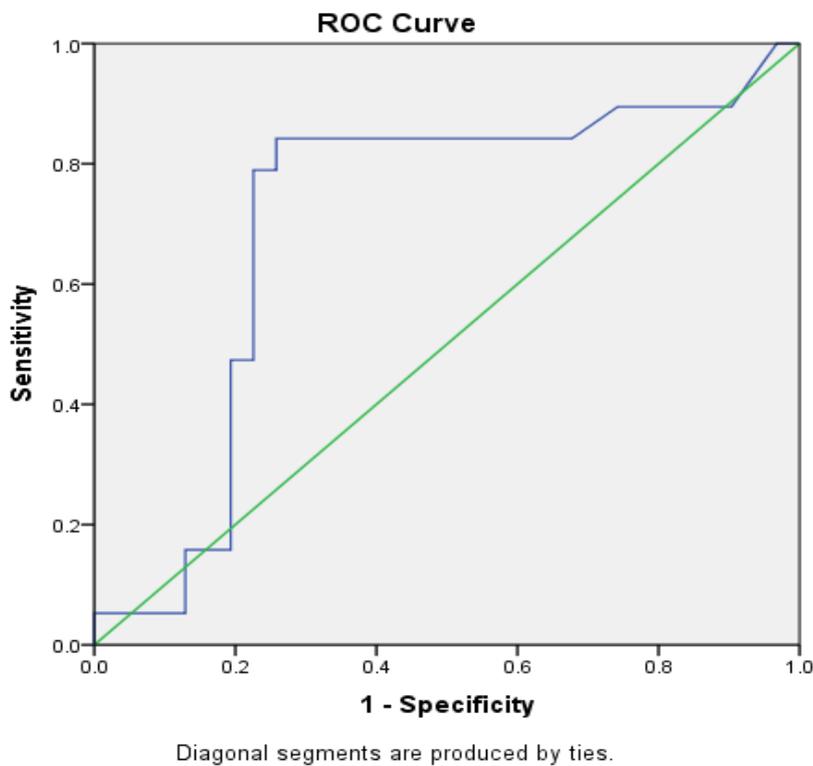


Figure (1): ROC curve analysis of HbA1c in detection of severity disease using Syntax score.

DISCUSSION

The prevalence of diabetes mellitus (DM) in the elderly is alarming. HbA1c and diabetes risk also fluctuate with age. Optimal glycemic control and HbA1c levels are difficult to attain in senior people due to the risk of iatrogenic hypoglycemia⁽¹⁵⁾.

In our study, the mean of age of the studied patients was (54.92±6.47 years), most of them (80.0%) were males. Also, no statistically significant relations were found between syntax score with age, and sex. In study by **Ma et al.**⁽¹²⁾ found that the average age of the 3805 participants in this study was 72.310.6 years. Subjects were categorised as belonging to Group I if their HbA1c levels were below 6.5%, Group II if their HbA1c levels were between 6.5% and 8.5%, and Group III if their HbA1c levels were over 8.5%. Clinical and laboratory patient features at baseline. When comparing male to female representation, we found no discernible trends. However, **Nabati et al.**⁽¹⁶⁾ observed the opposite: that men had a higher mean Syntax score than women did (9.29±10.34 and 6.98±9.97, P<0.001). In addition, patients beyond the age of 70 had higher Syntax scores than those under the age of 50 (12.04±11.56 and 4.13±7.20, respectively; P<0.001). For syntactic scores below 21, male participants were more common than female subjects (26.9% vs. 16.4%; P<0.001).

In our study, hypertension 40 patients were hypertensive (80.0%) & only 10 patients were non-hypertensive (20.0%), regarding smoking 27 patients were smokers (54.0%) while 23 were nonsmokers (46.0%). Also, there were no statistically significant relations between HbA1c levels and smoking and HTN of the studied patients, (P>0.05). In this concern, no statistically significant relations were found between syntax score with smoking, and HTN. In study by **Ma et al.**⁽¹²⁾ showed that the 3805 patients who made up the study population were split into three categories based on their hemoglobin A1c levels: divided into three categories: group I (HbA1c 6.5%), group II (6.5-8.5%), and group III (8.5+%). Clinical and laboratory patient features at baseline. Smoking rates and serum creatinine levels showed no discernible variations between the three groups. While **Ma et al.**⁽¹²⁾ did find a correlation between a higher HbA1c category and a greater prevalence of hypertension, they found no such correlation between the two variables and smoking. A greater HbA1c category was also strongly associated with a higher hypertension prevalence, according to research by **Ikeda et al.**⁽¹⁷⁾. However, **Nabati et al.**⁽¹⁶⁾ reported the opposite: that diabetics had a considerably higher syntactic Score than nondiabetics (9.79±10.60 and 7.47±9.92, respectively; P<0.001). Moreover, hypertension individuals had a considerably higher syntactic score than normotensive cases (9.25±10.59 and 6.81±9.43, respectively; P<0.001).

In our study, the mean of serum creatinine, was (1.22±0.23, mg/dL). Also, there were no significant relations between HbA1c and serum creatinine. However, no statistically significant relations were found between syntax score with serum creatinine. In study by **Ma et al.**⁽¹²⁾ found that there were no significant differences in the creatinine found among.

In our study, the mean of total cholesterol, LDL, HDL, and triglyceride of the studied patients were (1.22±0.23, 160.40±17.37, 103.04±22.03, 41.80±5.95, 146.52±17.22 mg/dL), respectively. Total cholesterol was significantly increased among patients in group III (168.00±19.32 mg/dl) than patients in group II (166.18±15.42 mg/dl) and patients in group I (152.83±15.31 mg/dl). On the other hand, there were no significant relations between Hb A1C and LDL, HDL, and triglyceride of the studied patients. In study by **Pacilli et al.**⁽¹⁸⁾ diabetes people aged 60 and up, when better glycemic management is associated with better intermediate and long-term clinical outcomes. However, there is not a straightforward connection between glycemic management and coronary atherosclerosis. Many unobserved variables of unknown significance may be at play. It's possible, for instance, that the progression of diabetes over time causes an increase in both coronary atherosclerosis severity and HbA1c levels. The atherosclerotic processes in type 2 diabetes have been linked to poor glycemic control, low-grade inflammation, and low HDL-cholesterol. In their investigation, **Ma et al.**⁽¹²⁾ found no statistically significant differences in creatinine percentages across the three groups.

In addition, the higher the HbA1c category, the more likely it was that the individual was male, had high blood pressure, had high levels of LDL cholesterol and triglycerides, and had low levels of good cholesterol (HDL). After controlling for confounding factors, **McNeely et al.**⁽¹⁹⁾ found no statistically significant correlation between HbA1c and either the presence or severity of coronary artery calcifications. Greater HbA1c was connected to a higher CAD diagnosis rate in women, but not in men, suggesting a potential gender difference in the association between the two variables. **Ikeda et al.**⁽¹⁷⁾ explored this topic and found that those with the highest HbA1c levels also had the highest proportions of LDL cholesterol and triglycerides and the lowest proportions of HDL cholesterol.

In our study, syntax score was highly statistically significant relation with HbA1c, Syntax score significantly increased among patients in group III (29.70±5.14) than patients in group II (14.53±4.42) and patients in group I (6.00±2.66). In study by **Koskinas et al.**⁽²⁰⁾ revealed that a total of 6081 patients were included in the current investigation, including 1310 people with diabetes (22 percent) and 4771 people who did not have diabetes and were not receiving medical treatment for it (78 percent). Most patients (4554, or

75%) were treated with cutting-edge DES. The median SYNTAX score was 11 (interquartile range: 7-18), and the mean was 13.18.7. In 5912 patients, nearly all (97%) had at least two years of follow-up data. In study by **Esper et al.** ⁽²¹⁾ at 5 years, there was less HCE in those who took either an angiotensin-receptor blocker or an angiotensin-converting enzyme inhibitor. After 5 years, the SS was linked to a higher risk of MACE and HCE, but it did not pose an increased threat on its own.

Additionally, **Ma et al.** ⁽¹²⁾ revealed that correlation between HbA1c and Syntax score was discovered. In addition, patients with a Syntax score of 23 or higher could be predicted to have a high HbA1c category all on their own. HbA1c was remained substantially correlated with Syntax score, according to research by **Pacilli et al.** ⁽¹⁸⁾.

In our study, it was shown that smoking and total cholesterol both were correlated with syntactic score ($P=0.05$). While no significant relationships were found between syntactic score and demographic variables such as age, sex, hypertension, serum creatinine, low-density lipoprotein (LDL), high-density lipoprotein (HDL), or triglyceride levels in the sample of patients investigated. In study by **Esper et al.** ⁽²¹⁾ found that having triglycerides below 150 mg/dl and being older than 70 were both protective against HCE over the course of 5 years. Additionally, **Ma et al.** ⁽¹²⁾ found that HbA1c and Syntax score are related. The higher categories of HbA1c still independently predicted individuals with a medium or high Syntax score after adjusting for age, sex, hypertension, smoking, cholesterol, and creatinine levels in a logistic regression analysis (Syntax score ≥ 23).

However, **Pacilli et al.** ⁽¹⁸⁾ shown that HbA1c is a strong indicator of the likelihood that an older diabetic individual will have advanced coronary artery lesions (Syntax score ≥ 23). Despite accounting for age, sex, and other cardiovascular risk factors such hypercholesterolemia, hypertension, and smoking, we observed that the HbA1c level is substantially related with the complexity of coronary lesions in this study. Our findings demonstrate that HbA1c significantly affects coronary artery lesion severity, even after controlling for other cardiovascular risk factors, age, and gender. After taking these into account, the correlation between HbA1c and Syntax score still remained.

In our study, AUC= 0.705, sensitivity 86%, specificity 73%, and significance level 0.016 all point to a threshold of 6.95 for HbA1c when detecting disease severity with the syntactic score. Similarly, to our results, **Ikeda et al.** ⁽²²⁾ a study comparing the predictive abilities of 1, 5-AG and HbA1c levels for CAD indicated that the former had an AUC of 0.67 (95% CI: 0.62-0.73, $p=0.001$), while the latter had an AUC of 0.63 (95% CI: 0.57-0.69, $p=0.001$). 1,5-AG cutoff value for CAD prediction was 11.90 ng/ml (76.2 percent sensitivity and 52.6 percent specificity). Both 1, 5-AG

and HbA1c were highly linked with the SS ($=0.27$, $p=0.001$ and $=0.23$, $p=0.001$, respectively), and the best cut-off value for HbA1c to predict CAD was 5.9% (60.5% sensitivity and 62.0% specificity).

CONCLUSION

From the results of our study, we concluded that the severity of coronary artery lesions in diabetic patients was substantially linked with their HbA1c levels. In addition, the HbA1c score remained a strong predictor of the complexity of coronary artery lesions even when other risk indicators were taken into consideration. In general, people with diabetes have a worse prognosis, but this can be mitigated with effective HbA1c treatment. HbA1c levels have shown promise as a predictor of the development of coronary artery disease with complex lesions. Patients with HbA1c levels that are closer to normal have a markedly reduced chance of developing complicated coronary artery lesions.

Financial support and sponsorship: Nil.

Conflict of interest: Nil.

REFERENCES

1. **Emara A, Samy N, Hammad A (2017):** Relationship between glycated haemoglobin and complexity of coronary artery disease in diabetic patients. *J Cardiol Therapy*, 5(1): 693-696.
2. **He D, Kuang W, Yang X et al. (2021):** Association of hemoglobin H (HbH) disease with hemoglobin A1c and glycated albumin in diabetic and non-diabetic patients. *Clin Chem Lab Med.*, 59(6):1127-1132.
3. **Fahad S, Rashied R, Jaffal W (2021):** Using of Glycated Albumin Rather than Glycated Hemoglobin for assessing Glycaemic Control in Hemodialysis Patients with Type II Diabetes Mellitus. *Medico Legal Update*, 21(1): 860-865.
4. **American Diabetes Association (2006):** Diagnosis and classification of diabetes mellitus. *Diabetes Care*, 29(1): 43-8.
5. **Levitan E, Liu S, Stampfer M et al. (2008):** HbA1c measured in stored erythrocytes and mortality rate among middle-aged and older women. *Diabetologia*, 51: 267-275.
6. **Bjerg L, Gudbjörnsdóttir S, Franzén S et al. (2021):** Duration of diabetes-related complications and mortality in type 1 diabetes: a national cohort study. *Internat J Epidemiol.*, 50(4):1250-1259.
7. **Chilton R (2020):** Effects of sodium-glucose cotransporter-2 inhibitors on the cardiovascular and renal complications of type 2 diabetes. *Diabetes, Obesity and Metabolism*, 22(1): 16-29.
8. **Sarwar N, Aspelund T, Eiriksdóttir G et al. (2010):** Markers of dysglycaemia and risk of coronary heart disease in people without diabetes: Reykjavik prospective study and systematic review. *PLoS Med.*, 7: e1000278. doi: 10.1371/journal.pmed.1000278.
9. **Selvin E, Steffes M, Zhu H et al. (2010):** Glycated hemoglobin, diabetes, and cardiovascular risk in nondiabetic adults. *N Engl J Med.*, 362: 800-811.

10. **Serruys P, Onuma Y, Garg S *et al.* (2009):** Assessment of the SYNTAX score in the Syntax study. *Eur Interven.*, 5: 50– 56.
11. **Serruys P, Onuma Y, Garg S *et al.* (2010):** 5-year clinical outcomes of the ARTS II (Arterial Revascularization Therapies StudyII) of the sirulimus-eluting stent in the treatment of patients with multivessel de novo coronary artery lesions. *J Am Coll Cardiol.*, 55: 1093-1101.
12. **Ma J, Wang X, Wang Y *et al.* (2014):** The relationship between glycosylated hemoglobin and complexity of coronary artery lesions among older patients with diabetes mellitus. *PloS One*, 9(3):91972. <https://doi.org/10.1371/journal.pone.0091972>
13. **Sianos G, Morel M, Kappetein A *et al.* (2005):** The SYNTAX score: an angiographic tool grading the complexity of coronary artery disease. *Eur Interven.*, 1(2): 219–227. 14.
14. **Morice M, Serruys P, Kappetein A *et al.* (2010):** Outcomes in patients with de novo left main disease treated with either percutaneous coronary intervention using paclitaxel-eluting stents or coronary artery bypass graft treatment in the Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery (SYNTAX) trial. *Circulation*, 121: 2645–2653
15. **Capucho A, Chegão A, Martins F *et al.* (2022):** Dysmetabolism and Neurodegeneration: Trick or Treat. *Nutrients*, 14(7):1425. <https://doi.org/10.3390/nu14071425>
16. **Nabati M, Moosazadeh M, Soroosh E *et al.* (2020):** Correlation between overweightness and the extent of coronary atherosclerosis among the South Caspian population. *BMC Cardiovascular Disorders*, 20(1): 1-11.
17. **Ikeda N, Iijima R, Hara H *et al.* (2012):** Glycated hemoglobin is associated with the complexity of coronary artery disease, even in non-diabetic adults. *J Atheroscl Thromb.*, 19(12):1066-72.
18. **Pacilli A, De Cosmo S, Trischitta V *et al.* (2013):** Role of relationship between HbA1c, fibrinogen and HDL-cholesterol on cardiovascular disease in patients with type 2 diabetes mellitus. *Atherosclerosis*, 228(1):247-8.
19. **McNeely M, McClelland R, Bild D *et al.* (2009):** The association between A1C and subclinical cardiovascular disease: the multi-ethnic study of atherosclerosis. *Diabetes Care*, 32(9):1727-33.
20. **Koskinas K, Siontis G, Piccolo R *et al.* (2016):** Impact of diabetic status on outcomes after revascularization with drug-eluting stents in relation to coronary artery disease complexity: patient-level pooled analysis of 6081 patients. *Circulation Cardiovascular Interventions*, 9(2): e003255. doi: 10.1161/CIRCINTERVENTIONS.115.003255.
21. **Esper R, Farkouh M, Ribeiro E *et al.* (2018):** SYNTAX score in patients with diabetes undergoing coronary revascularization in the FREEDOM trial. *J Am Coll Cardiol.*, 72(23 Part A): 2826-37.
22. **Ikeda N, Hara H, Hiroi Y (2014):** 1, 5-Anhydro-D-glucitol predicts coronary artery disease prevalence and complexity. *J Cardiol.*, 64(4):297-301.