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Original Article

Correlation Between HbA1c Levels and Severity of Coronary Artery Disease

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ABSTRACT

Background: Glycated hemoglobin (HbA1c) is a reliable marker of long-term glycemic control and has been increasingly linked to cardiovascular risk. Its association with angiographic severity of coronary artery disease (CAD) remains clinically significant.
Aim: To evaluate the correlation between HbA1c levels and severity of CAD using the SYNTAX score in patients undergoing coronary angiography.
Materials and Methods: A cross-sectional study was conducted on 120 patients undergoing coronary angiography. Patients were categorized into three groups based on HbA1c levels: Group A (<6.5%), Group B (6.5–7.5%), and Group C (>7.5%). CAD severity was quantified using the SYNTAX score. Statistical analysis included ANOVA, Pearson correlation, and chi-square test.
Results: Mean SYNTAX scores increased significantly across HbA1c groups: Group A = 12.4 ± 5.8, Group B = 19.8 ± 6.5, and Group C = 28.6 ± 7.2 ($p < 0.001$). Triple-vessel disease was more common in higher HbA1c groups (28%, 52%, and 78% respectively). HbA1c demonstrated a strong positive correlation with SYNTAX score ($r = 0.71$, $p < 0.001$).
Conclusion: Rising HbA1c levels are associated with greater severity and complexity of CAD. HbA1c may serve as an effective adjunct marker for predicting CAD burden and improving risk stratification in clinical practice.

Keywords*: HbA1c, Coronary artery disease, SYNTAX score, Diabetes, Angiography, Atherosclerosis.*

INTRODUCTION

Coronary artery disease (CAD) remains the leading cause of morbidity and mortality worldwide, accounting for nearly one-third of all global deaths[1]. The burden of CAD is particularly high in developing countries, where rising urbanization, lifestyle changes, and increasing prevalence of diabetes have significantly contributed to accelerated atherosclerotic disease[2]. Diabetes mellitus, characterized by chronic hyperglycemia, is a well-established risk factor for both the development and progression of CAD, with diabetic patients exhibiting more diffuse, calcified, and multi-vessel coronary involvement compared to non-diabetics[3].

Glycated hemoglobin (HbA1c) is a reliable indicator of long-term glycemic control, reflecting average blood glucose levels over the preceding 8–12 weeks[4]. Beyond its role in diabetes diagnosis, elevated HbA1c levels have been shown to correlate with vascular complications, including nephropathy, retinopathy, neuropathy, and importantly, macrovascular events such as myocardial infarction and stroke[5]. Even modest elevations of HbA1c within the pre-diabetic range have been associated with increased cardiovascular risk, suggesting that HbA1c reflects cumulative glycemic exposure and underlying metabolic stress that may directly impact coronary vasculature[6].

From a pathophysiological perspective, hyperglycemia induces endothelial dysfunction, oxidative stress, non-enzymatic glycation of proteins, activation of inflammatory pathways, and lipid abnormalities—all of which contribute to atherosclerotic plaque formation and instability[7]. Chronic dysglycemia also enhances vascular smooth muscle proliferation, increases platelet activation, and promotes pro-thrombotic states, thereby exacerbating coronary disease severity[8].

The SYNTAX score, derived from coronary angiography, is a robust and widely accepted clinical tool for quantifying the anatomical severity and complexity of CAD[9]. It incorporates lesion characteristics, including location, morphology, and functional importance. Higher SYNTAX scores correlate with increased risk of adverse cardiovascular outcomes and help guide revascularization strategies, including percutaneous coronary intervention (PCI) vs coronary artery bypass grafting (CABG)[10].

Several studies have explored the association between HbA1c levels and CAD severity. Many authors have reported that higher HbA1c is independently associated with increased angiographic burden of disease, even in non-diabetic individuals[11–13]. However, findings remain inconsistent in different populations, possibly due to ethnic, lifestyle, and metabolic variations[14]. This underscores the need for region-specific research to better understand the predictive utility of HbA1c for CAD in diverse patient groups.

Given the rising prevalence of dysglycemia and CAD in our population, evaluating whether HbA1c correlates with the angiographic severity of CAD is clinically important. A simple, inexpensive marker like HbA1c, if shown to reflect CAD burden accurately, could serve as an additional risk-stratification tool to identify patients with potentially severe coronary artery involvement. Therefore, this study was conducted to assess the correlation between HbA1c levels and the severity of CAD measured by SYNTAX score in patients undergoing coronary angiography.

MATERIALS AND METHODS

Study Design and Setting

This hospital-based **cross-sectional observational study** was conducted in the Department of Cardiology at a hospital over a period of 12 months. Consecutive patients undergoing coronary angiography for evaluation of suspected or established coronary artery disease (CAD) during the study period were screened for eligibility. Institutional Ethics Committee approval was obtained prior to initiation of the study, and written informed consent was taken from all participants.

Study Population

A total of **120 adult patients** aged 30–80 years who underwent diagnostic or interventional coronary angiography were included. Patients were recruited irrespective of diabetic status as long as they met the study criteria.

Sample Size Justification

Based on previous studies showing correlation coefficients between 0.5 and 0.7 for HbA1c and CAD severity, a minimum of 100 subjects was required for 80% power and $\alpha = 0.05$. To enhance statistical reliability, **120 patients** were included.

Inclusion Criteria

1. Age between 30 and 80 years
2. Undergoing elective or emergency coronary angiography
3. Availability of HbA1c measurement within **7 days prior** to angiography
4. Willingness to participate and provide informed consent

Exclusion Criteria

1. Prior coronary revascularization (PCI or CABG)
2. Severe renal impairment (CKD Stage ≥4, eGFR < 30 mL/min/1.73m²)
3. Conditions affecting HbA1c accuracy (hemoglobinopathies, hemolytic anemia, recent blood transfusion)
4. Acute severe infections, inflammatory diseases, or malignancy
5. Pregnancy
6. Uninterpretable or poor-quality angiograms

These criteria ensured accurate assessment of both HbA1c and angiographic severity.

Grouping of Study Subjects Based on HbA1c

Patients were stratified into **three groups** according to HbA1c levels (as per ADA guidelines):

- **Group A:** HbA1c < 6.5% (Normoglycemia / well-controlled diabetes)
- **Group B:** HbA1c 6.5% – 7.5% (Moderately elevated)
- **Group C:** HbA1c > 7.5% (Poor glycemic control)

Each group included **40 patients**, providing adequate distribution for comparison.

Clinical Evaluation

All patients underwent complete clinical assessment including:

- Demographic data (age, sex, BMI)
- Cardiovascular risk factors:
  - Hypertension
  - Diabetes mellitus
  - Dyslipidemia
  - Smoking status
  - Family history of CAD
- Presenting symptoms (stable angina, acute coronary syndrome)
- Vital signs and systemic examination

Standard laboratory tests were performed:

- Fasting plasma glucose
- Lipid profile
- Serum creatinine and eGFR
- HbA1c (measured via High-Performance Liquid Chromatography)

Coronary Angiography Procedure

Coronary angiography was performed using standard Judkins technique via femoral or radial access by experienced interventional cardiologists.

Lesions ≥50% luminal stenosis in a major epicardial artery were considered significant. Angiographic images were evaluated in multiple projections.

Two independent cardiologists, blinded to the patients' HbA1c values, reviewed each angiogram.

Assessment of CAD Severity: SYNTAX Score

CAD severity was quantified using the **SYNTAX scoring system**, which grades:

- Number of lesions
- Anatomical location
- Degree of stenosis
- Total occlusions
- Bifurcations and trifurcations
- Calcification
- Tortuosity
- Thrombus burden

SYNTAX scores were categorized as:

- **Low:** 0–22
- **Intermediate:** 23–32
- **High:** >32

Inter-observer discrepancies >10% were resolved by consensus.

Definition of Vessel Disease

- **Single Vessel Disease (SVD):** One major epicardial artery with ≥50% stenosis
- **Double Vessel Disease (DVD):** Two arteries with ≥50% stenosis
- **Triple Vessel Disease (TVD):** Three arteries with ≥50% stenosis

Presence of left main coronary artery (LMCA) stenosis was counted as equivalent to double vessel disease.

Outcome Measures

Primary Outcome

- Correlation between **HbA1c levels** and **SYNTAX score**

Secondary Outcomes

- Comparison of SYNTAX scores among HbA1c groups
- Distribution of SVD, DVD, and TVD across groups
- Proportion of high SYNTAX score patients in each group

Statistical Analysis

All statistical analyses were performed using **SPSS 20.0**.

- Continuous variables were expressed as **mean ± SD**.
- Categorical variables were presented as **number and percentage.**
- **One-way ANOVA** was used to compare SYNTAX scores among the three HbA1c groups.
- **Pearson correlation coefficient (r)** was used to assess linear correlation between HbA1c and SYNTAX score.
- **Chi-square test** was applied to compare distribution of vessel disease (SVD, DVD, TVD) across groups.
- A **p-value < 0.05** was considered statistically significant.

RESULTS

The three HbA1c groups were comparable with respect to age, sex distribution, BMI, hypertension, dyslipidemia, smoking status, and blood pressure (p > 0.05). Only fasting plasma glucose differed significantly across the groups (p < 0.001), consistent with the increasing HbA1c categories as shown in Table 1

TABLE 1: Baseline Demographic and Clinical Characteristics

Parameter	**Group AHbA1c < 6.5%(n = 40)**	**Group BHbA1c 6.5–7.5%(n = 40)**	**Group CHbA1c > 7.5%(n = 40)**	**p-value**
Age (years) Mean ± SD	57.8 ± 9.2	58.4 ± 8.8	59.6 ± 9.5	0.62
Sex				
– Male	26 (65%)	25 (62.5%)	27 (67.5%)	0.84
– Female	14 (35%)	15 (37.5%)	13 (32.5%)	
BMI (kg/m²) Mean ± SD	26.1 ± 3.4	26.5 ± 3.7	26.8 ± 3.9	0.71
Hypertension	22 (55%)	24 (60%)	25 (62.5%)	0.78
Dyslipidemia	18 (45%)	20 (50%)	22 (55%)	0.63
Smoking status				
– Current smokers	12 (30%)	14 (35%)	15 (37.5%)	0.66
– Former smokers	8 (20%)	7 (17.5%)	6 (15%)	
– Non-smokers	20 (50%)	19 (47.5%)	19 (47.5%)	
Family history of CAD	10 (25%)	11 (27.5%)	13 (32.5%)	0.72
SBP (mmHg) Mean ± SD	134 ± 16	136 ± 15	137 ± 14	0.59
DBP (mmHg) Mean ± SD	84 ± 9	85 ± 8	86 ± 10	0.48
Fasting Plasma Glucose (mg/dL)	101 ± 16	132 ± 22	168 ± 34	<0.001*

Mean SYNTAX scores increased progressively from Group A to Group C. Patients with HbA1c > 7.5% had significantly higher SYNTAX scores compared to the other groups, with overall difference reaching statistical significance (p < 0.001) as shown in Table 2

Table 2: Comparison of SYNTAX Scores Across HbA1c Group

HbA1c Group	**n**	**SYNTAX Score Mean ± SD**	**p-value**
Group A (<6.5%)	40	12.4 ± 5.8	**<0.001***
Group B (6.5–7.5%)	40	19.8 ± 6.5	
Group C (>7.5%)	40	28.6 ± 7.2	

The proportion of single-vessel disease declined across the HbA1c groups, while triple-vessel disease showed a marked increase from Group A to Group C. The overall distribution of vessel involvement differed significantly among the groups (p < 0.001) as shown in Table 3

Table 3: Distribution of Vessel Disease

CAD Pattern	**Group A (n=40)**	**Group B (n=40)**	**Group C (n=40)**	**p-value**
Single-vessel disease	20 (50%)	11 (27%)	6 (15%)	0.01
Double-vessel disease	9 (22%)	8 (21%)	3 (7%)	**<0.001***
Triple-vessel disease	11 (28%)	21 (52%)	31 (78%)	0.12

A strong positive correlation was observed between HbA1c level and SYNTAX score ($r = 0.71$, $p < 0.001$), indicating increasing angiographic severity with higher HbA1c values as shown in Table 4

Table 4: Correlation Between HbA1c and SYNTAX Score

Parameter	Correlation Coefficient (r)	p-value
HbA1c vs SYNTAX score	**0.71**	**<0.001**

DISCUSSION

In the present study, we observed a significant and progressive increase in the angiographic severity of coronary artery disease (CAD), as measured by the SYNTAX score, with rising HbA1c levels. Patients with HbA1c above 7.5% demonstrated the highest SYNTAX scores and the highest prevalence of triple-vessel disease. These findings reinforce the concept that HbA1c is not only a marker of glycemic control but also an indicator of cumulative vascular injury.

The strong positive correlation between HbA1c and SYNTAX score ($r = 0.71$) in our study aligns closely with earlier reports showing that chronic hyperglycemia accelerates atherosclerosis and contributes to more complex coronary lesions. Prasad et al. demonstrated that HbA1c was independently associated with severe CAD even after adjusting for traditional risk factors[15]. Similarly, Garg et al. found that HbA1c strongly correlated with multi-vessel involvement, especially in poorly controlled diabetics[16]. Our results are consistent with these findings, suggesting that HbA1c may serve as an accessible prognostic marker for CAD burden.

The high prevalence of triple-vessel disease in Group C (78%) observed in our study mirrors the results of Kim et al., who reported significantly higher angiographic disease load in subjects with elevated HbA1c irrespective of diabetic status[17]. Chronic hyperglycemia induces endothelial dysfunction, promotes oxidative stress, and enhances vascular inflammation, all of which accelerate plaque formation and complexity[18]. In addition, non-enzymatic glycation of vascular proteins increases arterial stiffness and promotes pro-thrombotic states that may explain the higher lesion complexity observed[19].

One important finding of our study is that even patients with HbA1c in the moderately elevated range (6.5–7.5%) showed significantly higher SYNTAX scores compared to those with HbA1c <6.5%. This supports the growing evidence that glycemic levels previously considered "acceptable" may already exert harmful vascular effects. A large meta-analysis by Selvin et al. showed that cardiovascular risk increases progressively with rising HbA1c, even within the pre-diabetic range[20]. Therefore, modest elevations in HbA1c may still represent unrecognized vascular damage.

Furthermore, our results demonstrate that higher HbA1c levels are associated with multivessel involvement rather than single-vessel disease. Liu et al. reported similar findings, highlighting that HbA1c was significantly higher in patients with three-vessel CAD compared to those with single or double vessel involvement[21]. This indicates that HbA1c may be a useful adjunct in identifying patients at risk of diffuse atherosclerosis.

The pathophysiological mechanisms explaining these observations are extensively documented. Hyperglycemia causes increased production of reactive oxygen species, activation of protein kinase C, and accumulation of advanced glycation end products (AGEs), which collectively contribute to endothelial injury[22]. Chronic metabolic stress also alters lipid profiles and increases platelet aggregation, leading to more aggressive and widespread atherosclerosis[23]. These mechanisms likely underlie the progressive increase in SYNTAX scores seen with rising HbA1c.

Our findings also have relevant clinical implications. Since HbA1c is inexpensive, widely available, and not influenced by acute stress or fasting status, it may serve as a practical tool for predicting the severity of CAD before angiography. Halkos et al. demonstrated that elevated preoperative HbA1c levels were associated with increased long-term cardiovascular events after CABG[24], highlighting its potential prognostic value beyond glycemic assessment. Incorporating HbA1c into clinical decision-making may therefore aid in early identification of high-risk patients requiring aggressive preventive interventions.

CONCLUSION

In this study, higher HbA1c levels were strongly associated with greater angiographic severity of coronary artery disease, reflected by significantly higher SYNTAX scores and a higher prevalence of multivessel involvement. HbA1c showed a robust positive correlation with CAD complexity, indicating that poor glycemic control contributes to more diffuse and severe coronary atherosclerosis. These findings suggest that HbA1c, an inexpensive and widely available biomarker, may serve as a useful adjunct for predicting CAD burden and aiding in early risk stratification, even among patients without known diabetes.

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