

# Correlation of Glycemic Status with Angiographic Severity of Coronary Artery Disease in Acute Coronary Syndrome



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## ABSTRACT

**Background:** Cardiovascular disease (CVD) remains the leading cause of illness and death worldwide, placing a significant strain on healthcare systems. Its development is influenced by multiple factors, with major risk contributors including hypertension, dyslipidemia, diabetes mellitus (DM), and lifestyle-related behaviors. Among these, DM notably increases the risk of coronary artery disease (CAD), particularly acute coronary syndrome (ACS). Chronic hyperglycemia in DM accelerates atherosclerosis, thereby heightening the risk of vascular complications.

Given the intricate relationship between diabetes and CVD, assessing the influence of glycemic status on CAD severity is essential.

This study aims to evaluate the severity of CAD in diabetic, prediabetic, and nondiabetic patients presenting with ACS using the Gensini score, a validated angiographic tool for measuring disease severity.

**Aim:** To assess the severity of CAD in patients with ACS using the Gensini score, comparing disease severity among prediabetic, diabetic, and nondiabetic individuals.

**Materials and methods:** A 6-month hospital-based cross-sectional study was conducted at a tertiary care center from July to December 2023, involving 150 patients diagnosed with ACS who underwent coronary angiography (CAG). Data collection was carried out retrospectively (July to September 2023) from inpatient records and prospectively (October to December 2023) from patients meeting the inclusion criteria. Clinical parameters, including patient history, comorbid conditions, cardiac biomarkers, HbA1c levels, electrocardiography (ECG), echocardiography (ECHO), and angiographic findings, were analyzed. The severity of CAD was assessed using the Gensini score.

**Statistical analysis:** Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 22. Categorical variables were expressed as frequencies and percentages, with statistical significance determined using the Chi-square or Fisher's exact test. Continuous variables were represented as mean  $\pm$  standard deviation (SD) and compared using analysis of variance (ANOVA). Pearson's correlation was employed to examine associations between variables. Multivariate regression analysis was conducted to identify predictors of CAD severity (based on the Gensini score), adjusting for potential confounders such as diabetes duration (HbA1c  $\geq$ 6.5%), age, and other cardiovascular risk factors. A  $p$ -value of  $<0.05$  was considered statistically significant. Graphs were generated using Microsoft Excel and Word.

**Results:** The study analyzed 150 patients with ACS who underwent CAG, comprising 114 diabetic, 20 prediabetic, and 16 nondiabetic individuals. A male predominance was observed, with 100 male participants.

Diabetic patients exhibited the highest severity of CAD, with a mean Gensini score of  $49.08 \pm 39.67$ , followed by prediabetic patients with a mean score of  $24.48 \pm 41.42$ . Nondiabetic patients had the least severe CAD, with a mean Gensini score of  $0.94 \pm 2.56$ . Additionally, triple-vessel disease was more prevalent among diabetic individuals.

A significant positive correlation was observed between diabetes duration and CAD severity, indicating that prolonged diabetes exposure is associated with more extensive coronary artery involvement.

**Conclusion:** This study confirms that diabetes significantly exacerbates the severity of CAD, with diabetic patients exhibiting more severe CAD than prediabetic and nondiabetic individuals. Additionally, the findings demonstrate a direct correlation between diabetes duration and increased CAD severity.

The results emphasize the heightened risk of triple-vessel disease in diabetic patients, underscoring the necessity for targeted cardiovascular and diabetes management strategies to mitigate disease progression and improve patient outcomes.

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## INTRODUCTION

Cardiovascular disease (CVD) is the foremost contributor to both illness and mortality on a global scale.

Affecting  $>523$  million individuals, atherosclerotic conditions, notably ischemic heart disease and stroke, are the primary drivers of the CVD burden. Ischemic heart disease alone is linked to about half of all

CVD-related deaths, while ischemic stroke accounts for roughly another quarter.<sup>1</sup>

Diabetes mellitus (DM) is a major risk factor for cardiovascular conditions, including acute coronary syndrome (ACS). The link between these diseases is well established, as diabetes not only contributes to the onset of ACS but also exacerbates its outcomes. Individuals with diabetes face a two to four times greater risk of experiencing ACS events—such as non-ST-elevation myocardial infarction (NSTEMI) and ST-elevation myocardial infarction (STEMI)—primarily due to the accelerated development of atherosclerosis, endothelial dysfunction, and a prothrombotic state that result from chronic hyperglycemia and insulin resistance.

From a pathophysiological perspective, diabetes tends to induce a more aggressive form of coronary artery disease (CAD), frequently affecting multiple vessels and leading to increased complications in ACS patients. Moreover, diabetics often have altered platelet function, which heightens their risk for thrombotic events. The presence of autonomic neuropathy in many of these patients can lead to “silent ischemia,” delaying both diagnosis and treatment. This delay is associated with poorer outcomes, including higher mortality rates, recurrent myocardial infarctions, and an increased incidence of heart failure.

On a global scale, diabetes represents a significant public health challenge. Currently, around 537 million adults between the ages of 20 and 79 years are living with the condition. According to projections by the International Diabetes Federation, by 2045 approximately 783 million adults—or one in eight—will be affected by diabetes.

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Diabetes creates a significant economic strain around the globe, with developing nations bearing the brunt of its impact. Approximately 75% of adults with diabetes live in low- and middle-income countries, which exacerbates the financial challenges these regions face.<sup>2</sup>

National Cholesterol Education Program's Adult Treatment Panel III guidelines<sup>3</sup> equate having diabetes with having CAD.

Diabetes damages the endothelium of blood vessels and leads to the formation of harmful glycation products, accelerating atherosclerosis. Compared to individuals without diabetes, those with the condition face an elevated risk of vascular complications that can affect major organs.<sup>4</sup>

The aging population globally is contributing to the increasing prevalence of CVDs. As individuals age, the risk of developing CVD significantly increases due to factors such as arterial stiffness, hypertension, and lifestyle changes. By 2050, it is estimated that nearly one in six people worldwide will be over the age of 65, exacerbating the global burden of CVD.<sup>5</sup>

Cardiovascular disease stands as the foremost contributor to both morbidity and mortality in individuals with diabetes.<sup>6,7</sup>

Among individuals with diabetes, major risk factors for CVD include high blood pressure, elevated cholesterol levels, hyperglycemia, and obesity.

Several studies have shown a direct link between chronic high blood sugar levels and cardiovascular complications in people with diabetes.<sup>8,9</sup>

Lifestyle choices that are within our control—such as consuming an unhealthy diet, remaining physically inactive, smoking, and drinking excessive amounts of alcohol—play a major role in the onset of CVDs. According to estimates from the World Health Organization, these behavioral risk factors are responsible for nearly 80% of cases of coronary heart disease and cerebrovascular disease.<sup>10</sup>

Cardiovascular diseases place a heavy burden on healthcare systems worldwide and also carry considerable economic consequences. In 2015, the global expenditure associated with CVD was estimated at around \$863 billion. This cost is projected to increase to approximately \$1 trillion per year by 2030, driven by rising healthcare expenses, reduced productivity, and the growing demands for long-term care.<sup>11</sup>

Women with diabetes experience a loss of the inherent protective advantage they usually have against developing CAD, making them more susceptible to the condition compared to women without

diabetes.<sup>12</sup> The Organization to Assess Strategies for Ischemic Syndromes study found that diabetic patients without any prior history of CVD experience long-term morbidity and mortality rates similar to those of nondiabetic patients who already have established CVD following hospitalization for unstable CAD.<sup>13</sup>

Diabetic patients experience a high mortality rate following their first myocardial infarction, with a significant number of these deaths occurring outside of hospital settings.<sup>14</sup>

These findings, along with the results of the INTERHEART study,<sup>15</sup> further reinforce the connection between diabetes and CAD. Despite extensive research, gaps remain in understanding how varying degrees of glycemic dysregulation (i.e., nondiabetic, prediabetic, and diabetic states) correlate with the angiographic severity of CAD in ACS patients. The Organization to Assess Strategies for Ischemic Syndromes (OASIS) study revealed that diabetic patients have similar cardiovascular outcomes as nondiabetics with a history of CVD, yet the specific differences in CAD severity between prediabetic and diabetic patients remain less explored. Furthermore, while studies such as INTERHEART have highlighted the global impact of diabetes on myocardial infarction, a more detailed analysis of angiographic severity based on glycemic status is needed. This study aims to fill these gaps by quantitatively evaluating CAD severity using the Gensini score,<sup>16</sup> an angiographic severity index, and analyzing how CAD severity differs between nondiabetic, prediabetic, and diabetic ACS patients. Through this analysis, we aim to offer new insights into the relationship between glycemic status and CAD, potentially guiding more tailored management strategies in clinical practice.

### Aim

The aim is to evaluate the severity of CAD in ACS patients by applying the Gensini score, and to compare the findings across prediabetic, diabetic, and nondiabetic groups.

### Objectives

- To assess CAD severity in ACS patients across prediabetic, diabetic, and nondiabetic groups by analyzing coronary angiography (CAG) results, utilizing the Gensini score and HbA1c levels.
- To determine the correlation between glycemic control and CAD severity.
- To analyze the relationship between diabetes duration and CAD severity in diabetic patients.

## MATERIALS AND METHODS

The study was conducted at Ramaiah Medical College and Hospital in Bengaluru, Karnataka, India. Data were collected over 6 months, from July to December 2023, using both retrospective and prospective methods. During the retrospective phase, patient records for those admitted with ACS who had CAG between July and September 2023 were examined. In the prospective phase, information was gathered from ACS patients who had CAG between October and December 2023.

### Study Population

A total of 150 patients over the age of 18 years who were diagnosed with ACS participated in the study. Based on their HbA1c levels, these patients were classified into three distinct glycemic groups:

- Diabetic: HbA1c  $\geq 6.5\%$ .
- Prediabetic: HbA1c 5.7–6.4%.
- Nondiabetic: HbA1c  $< 5.7\%$ .

### Exclusion Criteria

Patients presenting any of the following conditions were not included in the study:

- Prior diagnosis of CAD.
- Severe anemia.
- Renal failure.
- Chronic obstructive pulmonary disease (COPD).
- Malignancies.

### Clinical and Laboratory Assessments

All patients underwent comprehensive clinical evaluations, including:

- Physical examination.
- Cardiac biomarker analysis.
- Electrocardiography (ECG).
- Echocardiography (ECHO).

Diagnosis of ACS was based on ECG findings and biomarker analysis, classifying patients into the following subgroups:

- Unstable angina.
- NSTEMI.
- STEMI.

### Gensini Score Calculation and Coronary Angiography

Coronary angiograms were analyzed, and the extent of CAD was evaluated using the Gensini score,<sup>16</sup> which assigns severity points based on the degree of stenosis in various coronary artery segments. The Gensini score was derived by assigning a severity rating to each lesion according to the degree of luminal narrowing and then multiplying that rating by

a factor based on the lesion's location within the coronary arterial system.

Overall Gensini score was obtained by summing the individual lesion scores. A total score ranging from 1 to 40 signified mild atherosclerosis, while scores above 40 indicated severe atherosclerosis.<sup>17</sup>

The steps to calculate the Gensini score are as follows:

- Step 1: Each coronary lesion is given a severity score that reflects the extent of its luminal narrowing, with additional adjustments made for total occlusions or lesions with 99% obstruction that are supplied by collateral circulation (Table 1).
- Step 2: Each lesion's score is adjusted by a multiplier that reflects its position within the coronary arterial system (Table 2).
- Step 3: (1) Gensini score for each lesion is calculated by multiplying the severity score of the stenosis with the location's weight factor. (2) Gensini score is calculated as the sum of the severity scores of all the lesions.

The Gensini score serves as a comprehensive measure of CAD severity, with higher scores indicating a more advanced level of disease.

**Sample Size**

The sample size was determined using the correlation coefficient between the Gensini score and HbA1c, which was reported as 0.31 (i.e.,  $r = -0.31$ ) in the study by Muhammad et al.<sup>18</sup> Using a 95% confidence level and 90% power in the calculation, the minimum required sample size was found to be 105. When accounting for a 10% nonresponse rate, the adjusted sample size became 116 (105 + 10.5). Nevertheless, 150 subjects who met the inclusion criteria were ultimately enrolled and analyzed during the study period.

$$\text{Total sample size} = N = [(Z_{\alpha} + Z_{\beta})/C]^2 + 3$$

The standard normal deviate for  $\alpha = Z_{\alpha} = 1.960$

The standard normal deviation for  $\beta = Z_{\beta} = 1.28$

$$r = \text{correlation coefficient} = -0.31$$

$$C = 0.5 \times \ln [(1 + r)/(1 - r)] = 0.3205$$

$$N = 105$$

**Statistical Analysis**

Data were entered into Microsoft Excel, and statistical analyses were carried out using Statistical Package for the Social Sciences (SPSS) version 22 (IBM SPSS Statistics, Somers, NY, USA).

**Categorical Data Analysis**

- Categorical variables were summarized by calculating frequencies and proportions.
- To assess statistical significance for qualitative data, either the Chi-squared test or Fisher's exact test (for 2 x 2 contingency tables) was used.

**Continuous Data Analysis**

- Continuous variables were presented as mean values along with standard deviations (SDs).
- For comparing the means across more than two groups, analysis of variance (ANOVA) was employed.
- The Pearson correlation coefficient was applied to investigate the relationships between continuous variables.

**Graphical Representation**

Various charts and graphs were created using Microsoft Excel and MS Word to visually represent the data.

**Statistical Significance**

A  $p$ -value of  $<0.05$  was regarded as statistically significant, in line with the assumptions underlying the statistical tests used.

**Multivariate Regression Analysis**

A multivariate regression model was developed to assess the relationship between diabetes duration (HbA1c  $\geq 6.5\%$ ) and various clinical and demographic predictors.

Variables included in the model are as follows:

- Dependent variable: Duration of diabetes (years).
- Independent variables:
  - Gensini score.
  - Age.
  - Gender.
  - Diagnosis.

**Table 2:** Calculation of the Gensini score. Step 2: a multiplying factor is applied to each lesion score based upon its location in the coronary tree

Segment	Right dominance	Left dominance
RCA proximal	1	1
RCA mid	1	1
RCA distal	1	1
PDA	1	1
PLB	0.5	0.5
Left main	5	5
LAD proximal	2.5	2.5
LAD mid	1.5	1.5
LAD apical	1	1
First diagonal	1	1
Second diagonal	0.5	0.5
LCx proximal	2.5	3.5
LCx mid	1	2
LCx distal	1	1
Obtuse marginal	1	1

**Table 1:** Calculation of the Gensini score. Step 1: a severity score is assigned to each coronary lesion based on the degree of luminal narrowing and adjustment for total occlusions or 99% obstructive lesions receiving collaterals

Degree of stenosis (%)	Receiving collaterals	Adjustment for collaterals	Severity score
1-25	-	0	1
26-50	-	0	2
51-75	-	0	4
76-90	-	0	8
91-99	No	0	16
99	Yes	-8	8
100	No	0	32
100	Yes and normal source vessel	-16	16
100	Yes and 25% stenosis source vessel	-12	20
100	Yes and 50% stenosis source vessel	-8	24
100	Yes and 75% stenosis source vessel	-4	28
100	Yes and 90% stenosis source vessel	-2	30

- CAG findings.
- HbA1c levels.
- Hypertension.
- Smoking status.
- Obesity.

The regression model aimed to identify significant predictors while adjusting for potential confounders. The following statistical parameters were computed:

- Unstandardized and standardized regression coefficients.
- T-values and corresponding p-values were calculated for every independent variable.
- % confidence intervals (CIs) for estimated coefficients.

Statistical analyses were carried out using SPSS version 22, ensuring the robustness and reliability of the results.

**Table 3:** Distribution of subjects according to HbA1c

	Frequency	Percentage (%)
Nondiabetic	16	10.7
Prediabetic	20	13.3
Diabetic	114	76.0
Total	150	100.0

HbA1c level of 6.5% or higher indicated diabetes; 5.7–6.4% indicated prediabetes; and below 5.7% indicated nondiabetes

**Table 4:** Distribution of subjects according to sex

	Frequency	Percentage (%)
Female	50	33.3
Male	100	66.7
Total	150	100.0

**Table 5:** Comparison of sex and CAG findings according to HbA1c

	Normal		Pre-DM		DM		p-value
	N	%	N	%	N	%	
Sex							
Female	6	37.5	11	55.0	33	28.9	0.069
Male	10	62.5	9	45.0	81	71.1	
CAG findings							
Double vessel disease	0	0.0	2	10.0	45	39.5	<0.001
Minor CAD	2	12.5	9	45.0	6	5.3	
Normal	14	87.5	2	10.0	0	0.0	
Single vessel disease	0	0.0	5	25.0	39	34.2	
Triple vessel disease	0	0.0	2	10.0	24	21.1	

N represents the total number of observations; Statistical test utilized: Chi-squared test of independence

## RESULTS

The study included 150 patients. Of them, 114 were diabetic, 16 were nondiabetic, and 20 were prediabetic (Table 3).

Out of the 150 patients enrolled in the study, 50 were female and 100 were male (Table 4).

Overall, male participants were more prevalent in the study. This trend was especially pronounced in the diabetic group, where males constituted 71.1% of the participants (Table 5).

Single-vessel disease occurred more frequently in diabetics (34.2%) than in prediabetics (25%). Additionally, triple-vessel disease was significantly more prevalent in the diabetic group compared to the nondiabetic group ( $p < 0.001$ ) (Table 5).

The majority of patients in the study were between the age-group of 61 and 70 years—30% (Table 6).

In this study, most patients diagnosed with ACS exhibited symptoms of unstable angina (Table 7).

The average age at presentation was higher in the diabetic and prediabetic groups, at 62.76 and 60.6 years, respectively (Table 8).

The diabetic group exhibited markedly more severe CAD, as reflected by a significantly higher average score.

The Gensini score of 49.083, compared to prediabetics 24.475 and nondiabetics 0.938.

**Table 6:** Distribution of subjects according to age-group

Years	Frequency	Percentage (%)
<40	7	4.7
41–50	22	14.7
51–60	43	28.7
61–70	45	30.0
>70	33	22.0
Total	150	100.0

The observed differences reached statistical significance, with a p-value of 0.001 (Table 9).

The longer a person has diabetes, the more severe their CAD tends to be (Fig. 1).

		Duration of diabetes
Gensini score	Pearson correlation	0.790**
	p-value	<0.001

\*\*Indicates significance

Among diabetic patients, the extent of CAD was significantly linked to the duration of their diabetes ( $p < 0.001$ ).

**Table 7:** Distribution of subjects according to diagnosis

	Frequency	Percentage (%)
STEMI	55	36.7
NSTEMI	23	15.3
Unstable angina	72	48.0
Total	150	100.0

ACS, acute coronary syndrome; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction

**Table 8:** Comparison of mean age according to HbA1c

		Age
Nondiabetic	Mean	53.13
	SD	11.165
Prediabetic	Mean	60.60
	SD	9.511
Diabetic	Mean	62.76
	SD	12.353
Total	Mean	61.45
	SD	12.193

p-value = 0.011; Statistical test utilized: ANOVA

Majority of patients had double vessel disease 31.3% (Table 10).

**Multivariate Regression Analysis**

Table 11 presents a summary of the findings from the multivariate regression analysis.

The dependent variable was the duration of diabetes years, defined as HbA1c ≥6.5. The independent variables included the Gensini score, age, gender, diagnosis, CAG findings, HbA1c%, hypertension, smoking, and obesity. The table provides unstandardized and

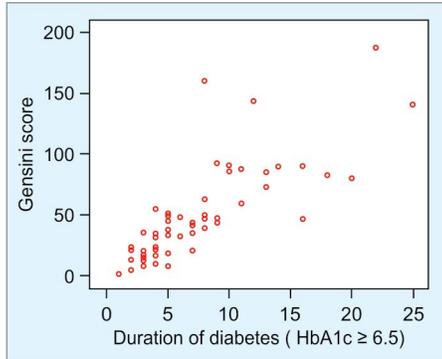


Fig. 1: Comparison of the duration of diabetes in years and the Gensini score

Table 9: Comparison of mean Gensini score according to HbA1c

		Gensini score
Nondiabetic	Mean	0.938
	SD	2.5617
Prediabetic	Mean	24.475
	SD	41.4213
Diabetic	Mean	49.083
	SD	39.6651
Total	Mean	40.667
	SD	40.8842

p-value = 0.001; Statistical test utilized: ANOVA

standardized coefficients ( $\beta$ ),  $t$ -statistics, significance ( $p$ -values), and 95% CIs.

**Key Findings**

- The Gensini score demonstrated a robust and statistically significant relationship with the duration of diabetes ( $B = 0.106, \beta = 0.803, p < 0.001$ ), suggesting a meaningful relationship between CAD severity and diabetes duration.
- Age also demonstrated a significant positive relationship ( $B = 0.115, \beta = 0.274, p < 0.001$ ). This finding suggests that increased age is correlated with a longer history of diabetes.
- Other variables, including gender, diagnosis, CAG findings, HbA1c, and hypertension, did not show significant associations ( $p > 0.05$ ).
- Smoking and obesity were not statistically significant predictors, with  $p$ -values of 0.171 and 0.283, respectively.

Table 11 highlights the importance of the Gensini score and age as key factors influencing the duration of diabetes. Although other variables did not reach statistical significance,

Table 10: Distribution of subjects according to vessel involved

	Frequency	Percentage (%)
Normal	16	10.7
DVD	47	31.3
Minor CAD	17	11.3
SVD	44	29.3
TVD	26	17.3
Total	150	100.0

Distribution of subjects according to vessel involved: DVD, double vessel disease; SVD, single vessel disease; TVD, triple vessel disease

the findings support the hypothesis that the severity of CAD, as measured by the Gensini score, is correlated with long-standing diabetes.

**DISCUSSION**

The study encompassed 150 patients with ACS who underwent CAG, including 114 diabetic, 16 nondiabetic, and 20 prediabetic individuals.

Consistent with other studies, diabetics comprised the majority of the study population. Our study revealed a preponderance of males among the study subjects. This finding aligns with previous research, such as that conducted by Roth et al.<sup>19</sup> and Maas and Appelman,<sup>20</sup> indicating a higher incidence of CVD in men compared to women.<sup>21,22</sup>

This study compared the mean age, sex, and type of ACS across each group. The study explored the correlation between glycemic status, measured by HbA1c, and the severity of CAD, evaluated employing Gensini score. The GUSTO-118 trial,<sup>21</sup> noted that diabetic patients were generally older than nondiabetic patients—a trend that our study similarly reflected.

The Gensini score, utilized in this study, provides a more detailed assessment of CAD by accounting for even minor lesions. Using the Gensini score to assess CAD severity, diabetic patients exhibited the highest mean score of 49.083, while prediabetic patients had a mean score of 24.475.

Coronary artery disease was least severe in people without diabetes, with an average score of 0.938. A study by Kumar et al.<sup>22</sup> found that diabetic patients experienced a higher degree of CAD severity than their nondiabetic counterparts. Additionally, their

Table 11: Multivariate regression analysis

Model	Coefficients <sup>a</sup>						
	Unstandardized coefficients		Standardized coefficients	t	Sig.	95.0% CI for B	
	B	Standard error	$\beta$			Lower bound	Upper bound
1 Constant	-5.715	2.315		-2.468	0.015	-10.307	-1.124
Gensini score	0.106	0.008	0.803	12.797	0.000	0.090	0.122
Age	0.115	0.021	0.274	5.392	0.000	0.073	0.157
Gender	0.154	0.581	0.013	0.264	0.792	-0.998	1.306
Diagnosis	0.064	0.341	0.011	0.189	0.850	-0.612	0.741
CAG findings	0.567	0.329	0.091	1.724	0.088	-0.085	1.219
HbA1c%	-0.240	0.131	-0.094	-1.827	0.071	-0.500	0.020
Hypertension	-0.766	0.556	-0.072	-1.377	0.171	-1.869	0.337
Smoking	1.178	0.666	0.093	1.767	0.080	-0.144	2.499
Obesity	0.608	0.563	0.058	1.080	0.283	-0.508	1.723

<sup>a</sup>Dependent variable: duration of diabetes (years) (HbA1c ≥6.5)

findings revealed that the longer a patient had diabetes, the more severe their CAD became—an observation that concurs with the results of our study. The study by Sliema et al.<sup>23</sup> identified that longer durations of diabetes were associated with more extensive CAD, consistent with the findings of this study. A strong positive linear link was found between diabetes duration and the extent of CAD, as reflected by a Pearson correlation coefficient of 0.791 and a  $p$ -value < 0.001. In a similar study by Saleem et al.,<sup>24</sup> a direct linear correlation was identified between the duration of diabetes and the severity of CAD. A positive correlation between diabetes duration and CAD severity emphasizes the cumulative detrimental effect of long-term hyperglycemia on cardiovascular health. Chronic exposure to high glucose levels leads to increased atherosclerotic plaque formation, reduced arterial compliance, and heightened inflammatory responses, which contribute to more severe CAD over time.<sup>25,26</sup> HbA1c is a marker of long-term glycemic control but may not directly reflect acute plaque burden or coronary lesion characteristics.<sup>27</sup> For individuals with diabetes, intensive treatment approaches—including strict blood sugar regulation and the administration of medications such as sodium–glucose cotransporter-2 (SGLT2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists—have been found to lower the risk of cardiovascular events. Recent evidence further indicates that these treatments not only manage blood glucose effectively but also provide additional protection to the heart.<sup>28,29</sup> Recent clinical trials, such as EMPA-REG OUTCOME trial<sup>28</sup> and CANVAS program,<sup>30</sup> demonstrated that SGLT2 inhibitors (e.g., empagliflozin, canagliflozin) decrease major cardiovascular events, including myocardial infarction, in diabetic patients. Similarly, trials like LEADER<sup>29</sup> and REWIND<sup>31</sup> revealed that GLP-1 receptor agonists not only improve glycemic control but also reduce cardiovascular death and nonfatal myocardial infarction in high-risk patients. Given the study's findings of more severe CAD in diabetic patients, incorporating these novel agents into routine clinical practice could lead to significant improvements in long-term cardiovascular outcomes. These drugs not only address glycemic control but also act on mechanisms such as reducing oxidative stress, ameliorating endothelial dysfunction, and promoting favorable hemodynamic changes, all of which are crucial in slowing CAD progression.

Although medications are crucial for managing CAD in diabetic patients, lifestyle changes—such as improving diet,

increasing physical activity, and quitting smoking—remain fundamental for reducing cardiovascular risk. Lifestyle interventions can lower blood pressure, improve lipid profiles, enhance insulin sensitivity, and reduce inflammation, which collectively contributes to a slower progression of CAD.<sup>32,33</sup> Given the heightened risk of CAD in diabetic patients, early detection through regular cardiovascular screening is essential. Studies suggest that noninvasive tests such as coronary artery calcium scoring and carotid intima-media thickness measurements can identify subclinical atherosclerosis, enabling earlier intervention and more aggressive risk management.<sup>34,35</sup> Recent research is focusing on novel biomarkers, such as adiponectin, leptin, and advanced glycation end (AGE)-products, which may offer additional predictive power for CAD severity in diabetic patients. These biomarkers reflect the metabolic and inflammatory changes that drive both insulin resistance and atherosclerosis and may improve the risk stratification of diabetic individuals.<sup>36,37</sup> Beyond traditional cardiovascular risk factors, psychosocial factors such as depression, anxiety, and social isolation have been linked to worse outcomes in diabetic patients with CAD. Addressing mental health issues in these patients is crucial for enhancing treatment adherence and improving overall cardiovascular health.<sup>38,39</sup>

## Limitations of the Study

### Single-center Study

This research was performed at a single medical center, which may limit the generalizability of its findings to other populations. Factors such as regional differences, varying demographics, and distinct healthcare settings might affect how applicable the results are in different contexts.

### Reliance on HbA1c

The study measured glycemic status using HbA1c, which reflects long-term glucose control. However, HbA1c may not capture short-term fluctuations in blood glucose levels, which could also influence CAD severity.

Future research that addresses these limitations could significantly strengthen the validity and broader applicability of the findings.

## CONCLUSION

The study demonstrates that diabetes has a significant effect on CAD severity, with diabetic individuals showing more pronounced CAD than both prediabetic and

nondiabetic groups. The findings also indicate that the duration of diabetes correlates with increased CAD severity. These findings underscore the importance of integrated cardiovascular and diabetes care to reduce the elevated risk of adverse cardiac events in diabetics.

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