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The Relation between Carotid Intimal Medial Thickness and HbA1c with The Severity of Coronary Artery Disease in Diabetic Patients

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ABSTRACT

Background: Research has demonstrated a link between glycated hemoglobin (HbA1c) levels and coronary artery disease (CAD). The HbA1c level can serve as a prognostic indicator for both the severity of CA in diabetic patients and the likelihood of future cardiovascular events. The severity of carotid artery disease can be assessed using Carotid Intima Medial Thickness (CIMT).

Objectives: This study aimed to examine the relationship between CIMT, HbA1c levels, and the severity of CAD in diabetic patients.

Patients and methods: Our prospective comparative study was carried out on 160 diabetic patients diagnosed with ischemic heart disease. They were recruited from Cardiology Department in Menoufia University Hospital during the period from September 2019 to March 2021. Full history taking, clinical examination, laboratory investigations, Conventional Echocardiography, Carotid ultrasonography, Coronary angiography and Gensini score were studied.

Results: CIMT was significantly higher in patients with high Gensini score than other groups ($p<0.05$). Regarding lipid profile, total cholesterol and LDL levels were significantly higher in patients with high Gensini score than in other groups ($p<0.05$). Similarly, HbA1c was significantly higher in patients with high Gensini score than in other groups ($p<0.05$). HbA1c and CIMT cut values (9.92 and 1.5 respectively) predicted high Gensini score with sensitivity of 71.8% & 80.2% respectively and specificity of 68.01, 70.91 respectively.

Conclusion: A significant positive association between CIMT and HbA1C was detected in diabetic patients and both were notably increased in diabetic patients with severe CAD measured with the Gensini score.

Keywords: Carotid intimal medial thickness, Coronary artery disease, Diabetes, Gensini score, Glycated hemoglobin.

INTRODUCTION

Coronary artery disease (CAD) stands as a formidable and pervasive cause of mortality across both industrialized and developing nations. Its development is multi-faceted, driven by a complex interplay of various established risk factors. These include, but are not limited to, a sedentary lifestyle, active smoking, diabetes mellitus (DM), hypertension (HTN), dyslipidemia, obesity, a pertinent family history, and underlying genetic predispositions [1]. The presence and accumulation of these factors significantly increase an individual's susceptibility to this debilitating condition.

A substantial and consistent body of epidemiological and clinical research has emphatically underscored the strong association between diabetes mellitus (DM) and both the incidence and progressive advancement of CAD [2]. This extensive evidence base, accumulated over decades, provides compelling proof that individuals with diabetes are at a significantly heightened risk for developing CAD and experiencing its more severe forms, highlighting DM as a critical, independent risk factor in cardiovascular pathology [2].

In this critical context of widespread cardiovascular morbidity and mortality, the CIMT has emerged as a widely accepted and rigorously validated surrogate marker. This non-invasive measurement provides a reliable indicator for the early detection and ongoing progression of atherosclerosis throughout the arterial system. Its significance lies in demonstrating a direct and statistically significant link to the actual presence and severity of CAD [3], making it an invaluable tool for risk stratification and monitoring in clinical and research settings.

HbA1c serves as a crucial and widely recognized measure, primarily quantifying the average plasma glucose concentration over extended periods, typically reflecting glycemic control over the preceding two to three months. Its formation is a continuous non-enzymatic glycation process, wherein hemoglobin molecules, specifically the beta-globin chain, undergo a stable attachment to glucose when exposed to plasma glucose. Consequently, as the average systemic glucose level rises, the fraction of hemoglobin that becomes glycated increases in a highly predictable and linear manner. This inherent and reliable property positions HbA1c as an invaluable biomarker for assessing long-term glycemic control, offering a more comprehensive picture than a single fasting or random glucose measurement, which can fluctuate acutely. It accurately reflects a patient's integrated blood glucose levels over the preceding three months prior to its measurement [4], making it an essential tool in diabetes management and cardiovascular risk assessment.

Beyond its well-known role in diagnosing diabetes, HbA1c is a highly useful index for identifying both glucose intolerance and persistent hyperglycemia, even in instances where fasting glucose concentrations might appear within normal limits. A well-established direct association exists between elevated HbA1c levels and CAD, further solidifying its utility as a valuable biomarker with significant prognostic implications. It

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can efficiently foresee the severity of coronary atherosclerosis among diabetic patients and forecast future cardiovascular events [5].

AIM OF THE STUDY

The primary objective of this study was to evaluate the precise relationship between CIMT and HbA1c levels in relation to the severity of CAD specifically within the diabetic patient population to throw the light on the predictive value of these markers for cardiovascular risk in individuals with diabetes.

PATIENTS AND METHODS

This was a prospective comparative study carried out on 160 diabetic patients diagnosed with ischemic heart disease recruited from Cardiology Department in Menoufia University Hospital during the period from September 2019 to March 2021. All patients included in the study were selected according to the inclusion and exclusion criteria.

Inclusion criteria: Diabetic patients who were referred for coronary angiography in Menoufia University Hospital Cath. Lab fulfilling the following criteria: Age ≥ 18 years old. Diabetic patients: diagnosis based on (fasting plasma glucose ≥ 7.0 mmol/l (126 mg/dl) or 2–h post-prandial plasma glucose ≥ 11.1 mmol/l (200 mg/dl) or HA1c ≥ 6.5% (48 mmol/mol) or in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis and a random plasma glucose ≥ 200 mg/dL (11.1 mmol/L) **[6]**. Patients suspected to have ischemic heart disease according to clinical, ECG and echocardiographic criteria

Exclusion criteria: Renal impairment (Glomerular filtration rate less than 60 ml/min), severe liver disease, sepsis, coagulopathy, severe uncontrolled hypertension and Previous CABG.

Clinical criteria: Typical anginal pain and/or shortness of breath which increases with effort and relieved by rest ESC (According to chronic coronary syndrome ESC guidelines 2019).

ECG criteria: ST- segment deviation, inverted T wave or pathological Q wave.

Echocardiography criteria: Segment wall motion abnormality at rest.

Previous coronary angiography: Demonstrating atherosclerotic coronary artery disease or previous coronary intervention.

All patients included in this study were subjected to the following: A comprehensive full history taking was conducted, encompassing several key domains. **Personal history** involved gathering information on the participant's name, age, sex, address, current residence, occupation, marital status, and special habits, specifically focusing on smoking and alcohol consumption. **Past history** meticulously documented any prior medical diseases, detailing their nature, duration, specific treatments received, and any regular drug intake, including its regimen and duration. Finally, **family history** inquired about any similar medical conditions among immediate family members, aiding in the identification of potential genetic or familial predispositions. **Medical history:** presence of hypertension, DM (duration and medications) and dyslipidemia.

Clinical examination: Including general examination of pulse, blood pressure and respiratory rate and local examination of the heart to detect abnormal sounds or murmur.

Laboratory investigations: Including lipid profile (LDL, HDL, triglycerides and total cholesterol), HbA1c levels were quantitatively determined via a high-performance liquid chromatography (HPLC) method. The results were expressed in units consistent with the National Glycohemoglobin Standardization Program (NGSP) and the Diabetes Control and Complications Trial (DCCT). For values originally obtained using the Japan Diabetes Society (JDS) standard, an equivalent NGSP percentage was calculated using the conversion formula: HbA1c (NGSP) (%) = 1.02 * HbA1c (Japan Diabetes Society) (%) + 0.25% [7]. This standardization ensures comparability and consistency with international reporting guidelines. CBC, INR, serum creatinine and liver function test were determained. Conventional Echocardiography: A comprehensive transthoracic echocardiography was performed utilizing a GE Vingmed (Norway) system. This system was specifically outfitted with a harmonic M5S variable frequency (1.7 – 4 MHz) phased array transducer, ensuring high-resolution imaging capabilities. During the examination, patients were carefully positioned in the left lateral decubitus to optimize acoustic windows [8]. The conventional echocardiographic assessment incorporated various essential modalities, including M-mode for precise linear measurements over time, two-dimensional (2D) imaging for real-time anatomical visualization, and color Doppler for mapping blood flow patterns. Additionally, both pulsed-wave and continuous-wave Doppler techniques were employed to accurately quantify blood flow velocities and gradients. The M-mode: To measure LVEDD, LVESD and EF. 2D echocardiography to detect regional wall motion abnormalities.

Carotid ultrasonography (Sonoace equipment), (7.5-MHz linear-array probe and a 3.5-MHz convex-array probe): The evaluation of carotid arteries was meticulously performed using a combination of bilateral, conventional ultrasound and Doppler ultrasound. This comprehensive assessment aimed to identify any significant stenosis and to precisely quantify the CIMT, which is characterized as the measurable distance between the lumen-intima and media-adventitia interfaces. To ensure consistency and accuracy, all ultrasonographic examinations were conducted using the

same scanner by a single, highly experienced sonographer.

During the sonographic procedure, subjects were positioned comfortably in a supine position, with their heads gently tilted backward to optimize the acoustic window and facilitate clear visualization of the carotid arteries. Once the carotid arteries had been successfully located and identified via initial transverse scans, the ultrasound probe was meticulously rotated 90 degrees. This rotation allowed for the acquisition of detailed longitudinal images of both the anterior and posterior arterial walls, crucial for comprehensive assessment. Furthermore, high-resolution images specifically targeting the internal carotid arteries (ICA) and the carotid bulbs [Structures anatomically distinct from the common carotid artery (CCA)] were also systematically obtained. These additional images were vital to enable the subsequent calculation of the plaque score (PS), which provides a more comprehensive and nuanced assessment of the overall atherosclerotic burden within the carotid system.

Coronary angiography: Coronary angiography was executed leveraging the standard Judkins catheterization technique. Following the angiography, the severity of coronary artery disease (CAD) was rigorously measured utilizing a modified Gensini score. To enhance the reliability and objectivity of this critical evaluation, the scoring was independently performed by two different expert interventional cardiologists, thereby accounting for and minimizing potential interobserver variability in the assessment of disease severity.

Gensini score System: This methodology is a sophisticated system that assigns a distinct **severity score** to coronary artery lesions, taking into account two critical factors: The **degree of luminal narrowing** and the **geographical importance** of the lesion within the coronary vasculature. According to this comprehensive scoring system, the narrowing of the coronary artery lumen is meticulously graded with specific point values:

- **1 point** is assigned for a luminal narrowing of ≤ 25%.
- **2 points** are attributed for a narrowing ranging from 26−50%.
- **4 points** are given for a more substantial narrowing of 51−75%.
- **8 points** are assigned when the narrowing reaches 76−90%.
- **16 points** denoted a severe narrowing between 91−99%.
- A maximum of **32 points** was allocated for a total occlusion of the coronary artery [9].

This detailed grading allowed for a precise and standardized quantification of coronary artery disease severity, which is crucial for both clinical assessment and research purposes.

Ethical consideration: All participants provided written informed consents prior to the study's initiation, after being thoroughly informed about its aim. Ethical approval for the study was secured from the Ethical Committee of the Faculty of Medicine, Menoufia University (IRB 11/2020 CARD19). The investigation rigorously adhered to the ethical principles stipulated by the Declaration of Helsinki throughout its entire execution. Consequently, the study's design and implementation were meticulously structured to safeguard participants' autonomy, uphold their privacy, and ensure stringent confidentiality, thereby fully aligning with the Declaration's core tenets and fostering trust in the research process.

Statistical Analysis

For the statistical analysis of the collected data, a comprehensive approach was adopted using MICROSOFT EXCEL 2019 for initial tabulation and the advanced statistical software SPSS V.25 program for MICROSOFT WINDOWS 10 for in-depth analysis. The methodology encompassed two primary types of statistical procedures. Firstly, descriptive statistics were employed to characterize the dataset: Quantitative variables were presented as the mean ± SD, while qualitative data were summarized using frequencies and proportions. Secondly, analytical statistics were utilized for inferential testing, including the Chi-square test (χ^2) for assessing associations between categorical variables, the Kruskal-Wallis test for comparing more than two independent groups on a non-normally distributed continuous variable, and Receiver Operating Characteristic (ROC) curve analysis to assess the diagnostic accuracy of continuous variables. A P-value ≤ 0.05 was uniformly predetermined as the threshold for establishing statistical significance, ensuring robust interpretation of the findings.

RESULTS

This study enrolled 160 diabetic patients diagnosed with ischemic heart disease, with a mean age of 54.85 ± 14.53 years. The cohort was comprised of 35.6% females and 64.4% males. Among these patients, 25% were smokers and 57.5% had a history of hypertension. In the current investigation, statistical analysis revealed no significant differences between the studied groups regarding age and sex ($p>0.05$). Similarly, anthropometric measurements showed no statistically significant differences in height, weight, and BMI between the groups ($p>0.05$). Furthermore, when comparing established cardiovascular risk factors, no statistically significant differences were found among the groups concerning hypertension, smoking status, and duration of diabetes mellitus ($p>0.05$), as detailed in table (1).

Table (1): Demographic data and risk factors comparison among the studied groups

Variable	cIMT						H	P value	95%CI	
	Group I cIMT <0.8 (n=56)		Group II cIMT, 0.8-1 (n=69)		Group III cIMT >1.01 (n=35)				Lower	Upper
Age/year										
Mean± SD	56.70±14.69		52.49±14.54		56.54±13.99		1.610	0.203	51.17	60.65
Range	35.00-80.00		35.00-80.00		35.00-80.00					
Sex, n (%)										
Male	32(57.14%)		44 (63.77%)		26 (74.29%)		X^2= 3.884	0.274	---	---
Female	24(42.86%)		25 (36.23%)		9 (25.71%)					
Weight/Kg										
Mean± SD	75.57±10.78		74.20±10.26		76.60±10.86		0.648	0.525	72.43	78.49
Range	65-100		65-100		65-100					
Hight/cm										
Mean± SD	167.20±7.67		170.93±8.50		169.43±9.43		3.031	0.051	170.74	180.40
Range	155-190		155-190		155-190					
BMI (kg/m^2)										
Mean± SD	22.63±3.29		21.73±2.94		22.63±3.01		1.660	0.193	21.46	29.20
Range	18.16-31.00		17.65-29.59		16.76-31.06					
BMI, n (%)										
<25 kg/m^2	36		47		27		X^2= 1.68	0.482	---	---
>25 kg/m^2	20		22		8					
Duration of DM/year										
Mean± SD	7.63±2.00		7.23±1.95		7.37±1.96		0.622	0.538	6.85	7.97
Range	5.00-10.00		5.00-10.00		5.00-10.00					
Smoking	19	33.93	14	20.29	8	22.86	X^2=4.253	0.235	---	---
HTN (> 140 mmHg)	33	58.93	37	53.62	22	62.86	**X^2**=0.893	0.827	---	---

BMI: body mass index **cIMT:** Carotid intima-media thickness test **DM:** Diabetes mellitus **HTN:** Hypertension **H**: Kruskal Wallis test **X^2:** chi-squared test.

No statistically significant difference was observed in serum creatinine levels across the studied groups (p>0.05). However, lipid profile analysis revealed that total cholesterol and LDL levels were significantly higher in patients with a CIMT greater than 1.01 mm compared to other groups (p<0.05). The study patients were subsequently categorized by Gensini score into three distinct groups: Group A comprised 46 patients (28.75%) with a low score, group B included 49 patients (43.2%) with a moderate score, and group C consisted of 65 patients (30.65%) with a high score (Table 2).

Table (2): Comparison of the laboratory investigations among the groups under study

Variable	cIMT			H	P value	95%CI	
	Group I CIMT <0.8 (n=56)	Group II CIMT, 0.8-1 (n=69)	Group III CIMT > 1.01 (n=35)			Lower	Upper
Creatinine (mg/dl) Mean± SD	1.03±0.20	1.13±0.27	0.99±0.21	1.755	0.176	1.00	1.13
HbA1c (%) Mean± SD	7.71±1.31	7.85±1.55	8.01±2.02	0.175	0.840	7.46	8.21
Total cholesterol (mg/dl) Mean± SD	201.11±30.70	209.57±8.71	216.89±7.97	2.741	**0.042***	198.45	222.11
LDL (mg/dl), Mean± SD	113.97±5.90	115.22±9.63	120.25±5.27	0.374	**0.032***	108.91	124.50
HDL (mg/dl) Mean± SD	61.11±15.93	61.54±14.62	66.46±16.87	1.482	0.230	60.02	64.90

Triglycerides(mg/dl) Mean± SD	247.63±8.25	254.75±9.82	271.89±9.81	0.794	0.454	241.97	270.04

HbA1c: Hemoglobin A1c **LDL:** Low density lipoprotein **HDL:** High density lipoprotein **cIMT**: Carotid intima-media thickness **H:** Kruskal Wallis test X^2: chi-squared test *****significant.

We found that CIMT was significantly higher in patients with high Gensini score than in other groups (p <0.05) (Table 3).

Table (3): Comparison of the studied patients concerning CIMT

Variables	**Gensini score**						**X^2**	**P value**
	Group A Low GS (n= 46)		**Group B Moderate GS (n= 49)**		**Group C High GS (n= 65)**			
	No.	**%**	**No.**	**%**	**No.**	**%**		
CIMT								
<0.8	15	32.61	19	38.77	22	33.85	1.660	0.193
0.8-1	20	43.48	20	40.82	29	44.61	0.622	0.538
>1.01	11	23.91	8	20.41	16	21.54	2.950	**0.028***

CIMT: Carotid intima-media thickness test **GS:** Gensini score **X^2**: Chi-square test **H:** Kruskal-Wallis test.

It was observed that no statistically significant difference existed among the studied groups concerning serum creatinine levels (p> 0.05). Conversely, within the lipid profile, both total cholesterol and low-density lipoprotein (LDL) levels were notably elevated in patients exhibiting a high Gensini score, in comparison with the other cohorts (p<0.05). Correspondingly, HbA1c levels were significantly higher in patients with a high Gensini score relative to the other groups (p<0.05). Analysis of the collected data revealed no statistically significant difference between the investigated groups with respect to serum creatinine levels (p>0.05). Conversely, within the lipid profile, total cholesterol and low-density lipoprotein (LDL) levels were significantly elevated in patients characterized by a high Gensini score when compared to the other cohorts (p<0.05). Consistent with these findings, HbA1c concentrations were also significantly higher in the group exhibiting a high Gensini score compared to the remaining study participants (p<0.05) as presented in table (4).

Table (4): Comparison between the studied patients as regard laboratory data

Variables	**Gensini score**			**H**	**P**
	Group A Low GS (n= 46)	**Group B Moderate GS (n= 49)**	**Group C High GS (n= 65)**		
Creatinine (mg/dl) Mean ± SD	1.14± 0.20	1.04± 0.17	1.03± 0.11	1.139	0.323
HbA1c (%) Mean ± SD	7.31± 1.17	8.03± 2.08	8.13± 2.07	2.641	**0.031***
Total cholesterol (mg/dl) Mean ± SD	204.45± 7.43	218.55± 8.05	208.23± 7.73	2.365	**0.047***
LDL (mg/dl) Mean ± SD	106.67± 4.11	119.13± 5.52	123.87± 5.22	0.105	**0.042***
HDL (mg/dl) Mean ± SD	60.53± 4.57	61.32± 6.49	66.08± 5.86	1.948	0.146
Triglyceride(mg/dl) Mean ± SD	247.79± 8.31	252.75± 9.31	268.14± 9.01	0.682	0.507

HbA1c: Hemoglobin A1c **LDL:** Low density lipoprotein **HDL:** High density lipoprotein **GS:** Gensini score **H:** Kruskal-Wallis test.

Our results showed that 9.92 and 1.5 were cut-off values for HbA1c and CIMT to predict high Gensini score with sensitivity of 71.8% & 80.2% respectively and specificity of 68.01, 70.91 respectively (Table 5 & figure 1).

Table (5): Cut-off values of total HbA1c and CIMT as predictors for high Gensini score

Variables	Area	Cutoff	Sens.	Spec.	95% C I	P value
HbA1C	0.596	≥9.92	71.8	68.01	0.506-0.687	0.044*
CIMT	0.573	≥1.50	80.2	70.91	0.476-0.670	0.049*

HbA1c: Hemoglobin A1c **CIMT**: Carotid intima-media thickness test **Sens.:** sensitivity **Spec.:** specificity

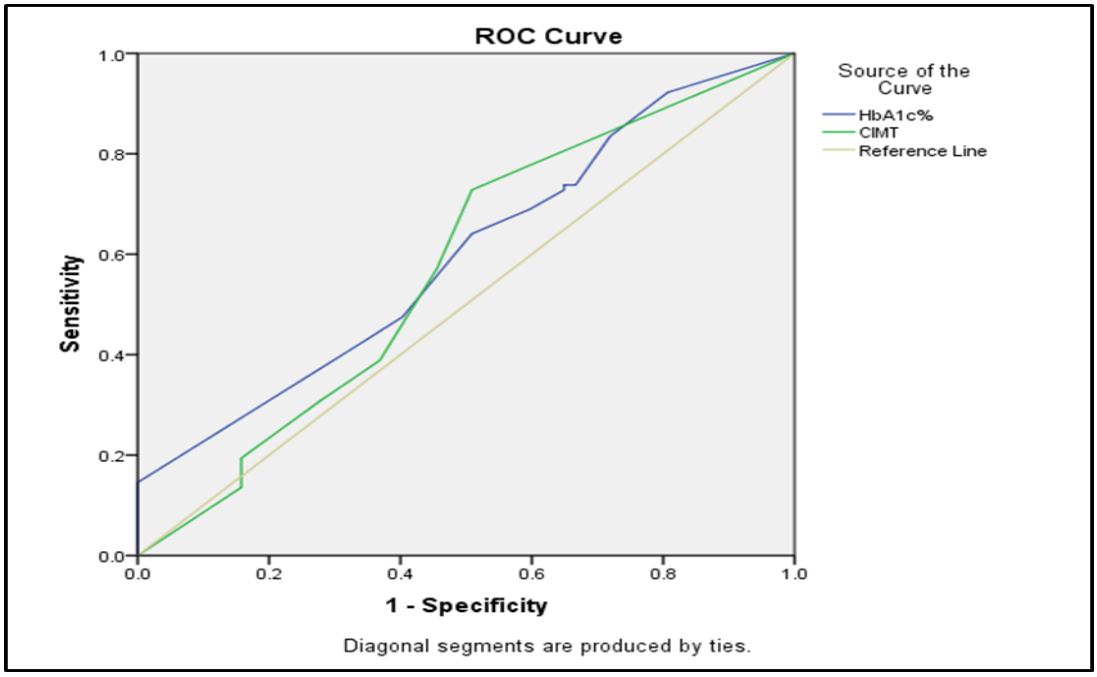

Fig (1): Cutoff values of total HbA1C and CIMT as predictors for high Gensini score.

DISCUSSION

The present study demonstrated a statistically significant positive correlation involving CC-IMT, an established non-invasive marker of atherosclerosis, and HbA1c, which is a crucial indicator of long-term glycemic control. This finding is consistent with the well-documented atherogenic effect of diabetes mellitus, though the precise strength of this association continues to be a subject of scientific debate. The rigorous methodology employed for CIMT quantification in our study further bolsters the credibility of this observed association. Diabetes itself is known to induce impaired endothelial function by reducing the bioavailability of nitric oxide produced by endothelial cells. This endothelial dysfunction has been explicitly demonstrated to correlate with HbA1c levels in diabetic patients [10]. Supporting our findings, previous research by **Kota *et al.*** [11] indicated significantly higher HbA1c levels in patients with increased CIMT.

Similarly, **Bulut and Avci** [12] concluded that HbA1c levels were independently associated with both internal carotid (IC-IMT) and common carotid (CC-IMT). Moreover, the study by **Di Pino *et al.*** [13] reported that patients with HbA1c values of ≥ 6.5% and even 5.7% to 6.4% exhibited greater IMT measurements compared to a group with HbA1c <5.7%. Furthermore, **Olt *et al.*** [14] firmly established CIMT as a reliable marker of subclinical atherosclerosis, closely associated with conventional cardiovascular disease (CVD) risk factors.

In our investigation, we also identified a statistically significant positive correlation between CIMT and both LDL cholesterol and total cholesterol levels. This observation reinforces the understanding that carotid IMT serves as a dependable measure of generalized atherosclerosis throughout the vascular system. A notable thickening of CIMT is consistently linked to an increased risk of ischemic events such as stroke and myocardial infarction, and it is also predictive of future coronary heart disease events, particularly in individuals with type 2 diabetes. In line with our results, **George *et al.*** [15] found a highly statistically significant association (P<0.001) between CIMT and both LDL and serum total cholesterol. A similar conclusion was drawn by **Bulut and Avci** [12], who reported an independent association between LDL levels and both IC-IMT and CC-IMT. Another study by **Abdeldayem *et al.*** [16] measured CIMT in adolescents with type 2 diabetes mellitus and found a positive correlation with cholesterol levels. Additionally, **Salonen and Salonen** [17], as well as **Kota *et al.*** [11], have demonstrated an association between total cholesterol and CIMT.

Further emphasizing this point, studies by **Baba *et al.*** [18] and **Bashir *et al.*** [19] investigated CIMT in patients with type 2 diabetes and consistently found that CIMT was more common in diabetic patients than in non-diabetics.

While **Okeahialam *et al.*** [20] compared CIMT among hypertensive, diabetic, and healthy individuals

and observed a tendency towards increased CIMT from normal in both hypertensive and diabetic groups (With diabetics showing a greater tendency) and the difference did not achieve statistical significance. Conversely, a systematic meta-analysis by **Brohall and Oden** [21] clearly indicated that diabetic patients exhibited greater CIMT than individuals in control groups. It's important to acknowledge, however, that some studies, such as those by **Byrkjeland *et al.*** [22] and **Gautam *et al.*** [23], showed no direct correlation between changes in LDL cholesterol and CIMT progression. These studies suggested that alterations in LDL cholesterol levels might be more strongly associated with changes in plaque characteristics rather than influencing the absolute progression of CIMT.

In the current study, HbA1c (With a cutoff value of 9.92%) and CIMT (With a cutoff value of 1.5 mm) were identified as the optimal predictors for a high Gensini score, which is a quantitative measure of coronary artery disease severity. These cutoff values demonstrated commendable predictive performance, yielding sensitivities of 71.8% and 80.2% respectively and specificities of 68.01% and 70.91% respectively. These findings are consistent with **Kapil *et al.*** [24] who determined that CIMT > 0.86 mm (AUC=0.642) and HbA1c > 6% (AUC=0.620) were the appropriate cutoff values derived from ROC curve analysis for predicting coronary artery disease (CAD) on coronary angiography. A study conducted by **Ayhan *et al.*** [25] in a Turkish population established an optimal cutoff value of 6.5% for HbA1c to predict severe CAD, achieving a sensitivity of 74.4% and a specificity of 75.1% on ROC curve analysis. In a similar vein to our results, **Kaya *et al.*** [26] reported a cutoff value of 6.0% for HbA1c that predicted severe atherosclerosis with a sensitivity of 54% and a specificity of 74%, additionally noting a correlation between HbA1c values and the Gensini score. Moreover, **Jia EZ *et al.*** [27], in a study involving Chinese subjects, found that the optimal cutoff value of HbA1c for predicting CAD was > 5.1%, with sensitivities and specificities of 72% and 75% respectively.

Comparable research that was conducted on an Indian population by **Dilley *et al.*** [28] revealed that HbA1c was significantly correlated with the prevalence of CAD, with an HbA1c value of > 5.6% predicting CAD with a sensitivity of 56% and a specificity of 67.6%. Similarly, **Kapil *et al.*** [24] independently correlated HbA1c with the presence of CAD on angiography, observing a cutoff value of 6% for HbA1c on ROC curve analysis for predicting CAD, which yielded a sensitivity of 39% and a specificity of 90%.

Our investigation revealed a statistically significant positive correlation between CC-IMT, a recognized noninvasive marker of atherosclerosis, and HbA1c, a crucial indicator of long-term glycemic control. This aligns with the understanding that diabetes mellitus exerts an atherogenic effect, directly impacting vascular health, although the precise strength of this association remains an area of ongoing discussion in the literature. This correlation is further reinforced by the meticulous methodology employed for CIMT quantification in our study. It is well-established that diabetes impairs endothelial function, largely by reducing the production of nitric oxide by endothelial cells, and this endothelial dysfunction has been consistently linked to HbA1c levels in diabetic individuals [10]. Supporting these observations, previous studies by **Kota *et al.*** [11] and **Bulut and Avci** [12] also found that higher HbA1c was significantly linked with elevated CIMT, including both internal and common carotid IMT. Moreover, **Di Pino *et al.*** [13] reported elevated IMT in patients with HbA1c levels ≥ 5.7% compared to those with lower levels, and **Olt *et al.*** **[14]** underscored CIMT as a marker of subclinical atherosclerosis linked to conventional cardiovascular disease (CVD) risk factors.

Beyond the parameters of glycemic control, the present study further revealed a statistically significant positive correlation between CIMT and both LDL cholesterol and total cholesterol. This compelling finding strongly reinforces the established concept of CIMT as a reliable and accessible non-invasive measure that accurately reflects the extent of generalized atherosclerosis throughout the systemic vascular tree. Crucially, an increased CIMT is widely recognized in clinical practice as a robust predictor of adverse future cardiovascular events, notably encompassing stroke and myocardial infarction, with particular prognostic significance in individuals diagnosed with type 2 diabetes. This specific observation from our study is consistent with and further corroborates findings from numerous earlier investigations in the field, for instance, **George *et al.*** [15] discovered a highly significant association between CIMT and LDL and total serum cholesterol (P<0.001). Similarly, **Bulut and Avci** [12] concluded that LDL levels were independently linked to both IC-IMT and CC-IMT.

Other studies by **Abdeldayem *et al.*** [16], **Salonen and Salonen** [17], and **Kota *et al.*** [11] have also reported positive associations between CIMT and cholesterol levels. Furthermore, research by **Baba *et al.*** [18] and **Bashir *et al.*** [19] highlighted that CIMT is more prevalent in diabetic patients compared to non-diabetics. While **Okeahialam *et al.*** [20] observed a trend toward increased CIMT in hypertensives and diabetics, this difference did not consistently reach statistical significance. Conversely, a systematic meta-analysis by **Brohall and Oden** [21] provided robust evidence that diabetic patients indeed exhibit greater CIMT than control groups. However, it's worth noting that studies by **Byrkjeland *et al.*** [22] and **Gautam *et al.*** [23] suggested no direct correlation between changes in LDL cholesterol and CIMT progression, implying that LDL cholesterol's impact might be more on plaque characteristics than on the absolute thickness of the IMT itself.

Crucially, in the current investigation, HbA1c (with a cutoff value of 9.92%) and CIMT (with a cutoff of 1.5 mm) emerged as the best predictors for a high

Gensini score, demonstrating strong predictive capabilities with sensitivities of 71.8% and 80.2% respectively, and specificities of 68.01% and 70.91% respectively. These findings align well with previously published literature regarding the predictive utility of these markers for coronary artery disease (CAD) severity. For instance, **Kapil *et al.*** [24] identified CIMT > 0.86 mm (AUC=0.642) and HbA1c > 6% (AUC=0.620) as significant cutoff values for foreseeing CAD on coronary angiography. In a Turkish population, **Ayhan *et al.*** [25] determined an optimal HbA1c cutoff of 6.5% for predicting severe CAD, achieving a sensitivity of 74.4% and specificity of 75.1%. Similarly, **Kaya *et al.*** [26] reported a HbA1c cutoff of 6.0% that projected severe atherosclerosis with reasonable sensitivity and specificity, noting a direct correlation between HbA1c values and the Gensini score. Further corroboration comes from **Jia EZ *et al.*** [27], who found an optimal HbA1c cutoff of > 5.1% for predicting CAD in Chinese subjects, with high sensitivity and specificity.

Dilley *et al.* [28] also underscored the significant correlation between HbA1c and CAD prevalence in an Indian cohort, identifying a > 5.6% HbA1c value as predictive. Lastly, **Kapil *et al.*** [24] independently correlated HbA1c with CAD presence on angiography, observing a 6% cutoff value that provided good specificity.

CONCLUSION

Our study definitively concluded a significant correlation between common carotid intima-media thickness (CC-IMT) and glycated hemoglobin (HbA1c) in diabetic patients. This finding underscored the strong link between long-term glycemic control and the progression of atherosclerosis. Furthermore, we observed that the levels of CIMT and HbA1c were significantly higher in diabetic patients with severe coronary artery disease (CAD) as quantified by the Gensini score. These findings underscore the key function of these two markers as indicators of both vascular damage and the extent of coronary atherosclerosis in individuals with diabetes.

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