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CORRELATION OF SEVERITY OF CORONARY ARTERY DISEASE WITH INSULIN RESISTANCE IN PATIENTS UNDERGOING CORONARY ANGIOGRAM

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Abstract

Background and Objectives:
Diabetes mellitus is recognized as a major risk factor in the development of coronary artery disease (CAD). Insulin resistance (IR), which precedes and accompanies type 2 diabetes mellitus, has been suggested as a predictive marker for CAD severity. However, limited evidence is available linking IR with angiographic severity of CAD in the local population. The objective of this study was to evaluate the correlation between IR, measured using the HOMA-IR index, and the severity of CAD assessed by the modified Gensini score in patients undergoing coronary angiography.

Material & Methods:
This cross-sectional study was conducted at Department of Cardiology, PIC/ Quaid-e-Azam Medical College Bahawalpur, Pakistan over a six-month period. A total of 200 type 2 diabetic patients (age 35–75 years) undergoing coronary angiography were included. Insulin resistance was calculated using HOMA-IR. CAD severity was determined using the modified Gensini score. Chi-square test was applied to assess associations. P-value <0.05 was taken as statistically significant.

Results:
The mean age of the patients was 54.2±9.3 years, with 138 (69%) males and 62 (31%) females. The mean duration of diabetes was 8.1±6.2 years. The mean HOMA-IR score was 3.1±1.2. A significant positive correlation was observed between IR levels and CAD severity as assessed by the modified Gensini score ($p<0.01$). Patients with higher HOMA-IR scores had more severe, multi-vessel disease.

Conclusion:
Insulin resistance is strongly associated with the severity of coronary artery disease among type 2 diabetic patients. Measurement of HOMA-IR may be considered a useful, simple tool for risk stratification and early identification of patients at risk of severe CAD.

Keywords: Coronary artery disease, insulin resistance, HOMA-IR, Gensini score, type 2 diabetes mellitus

Introduction

Coronary artery disease (CAD) continues to be the leading cause of morbidity and mortality globally and its burden is projected to increase further in low- and middle-income countries [1]. The disease arises from atherosclerosis, a chronic inflammatory process characterized by lipid accumulation, endothelial dysfunction, and plaque formation within coronary arteries [2]. Diabetes mellitus has been consistently recognized as a major contributor to the development and progression of CAD, with diabetic patients demonstrating a two- to four-fold increased risk of cardiovascular events compared to non-diabetic individuals [3,4]. Among diabetic populations, premature, diffuse, and multi-vessel coronary involvement is frequently observed, which translates into poorer outcomes following revascularization [5].

A growing body of research has shifted attention from traditional risk factors, such as hypertension, dyslipidemia, and smoking, toward metabolic abnormalities that precede and accompany diabetes. Central to these is insulin resistance (IR), defined as a subnormal biological response to circulating insulin levels [6]. Insulin resistance precedes the development of type 2 diabetes and remains a persistent abnormality even after initiation of glucose-lowering therapies [7]. It is associated with endothelial dysfunction, impaired nitric oxide bioavailability, low-grade systemic inflammation, and pro-thrombotic states, all of which accelerate atherogenesis [8,9]. Consequently, IR has been proposed not only as a risk factor for CAD incidence but also as a determinant of disease severity [10].

Several large-scale cohort and angiographic studies have explored the association between IR and CAD severity. In the Insulin Resistance Atherosclerosis Study (IRAS), IR was independently associated with subclinical atherosclerosis as measured by carotid intima-media thickness [11]. Kruszelnicka et al. demonstrated in angiographic cohorts that while asymmetric dimethylarginine predicted CAD severity, insulin resistance had heterogeneous effects depending on patient subgroups [12]. Conversely, Ormazabal et al. found a strong linear correlation between homeostasis model assessment of insulin resistance (HOMA-IR) and angiographic burden of disease [13]. Similarly, studies in Asian cohorts suggest that IR amplifies the risk of obstructive multi-vessel CAD, particularly among younger and obese individuals [14,15].

The Gensini score, a validated angiographic tool that quantifies CAD severity by assigning weights to the degree and anatomical location of stenosis, has been widely used to investigate this relationship [16]. Some studies have confirmed a positive correlation between HOMA-IR and Gensini scores, suggesting that IR could serve as a simple biomarker for stratifying cardiovascular risk [17]. However, others report no clear association, highlighting the influence of ethnicity, genetic predisposition, and environmental factors [18,19]. This inconsistency underlines the need for region-specific research.

Pakistan is currently experiencing a diabetes epidemic, with prevalence rates among the highest in the world [20]. Despite this, there is a paucity of local data investigating the link between insulin resistance and angiographic severity of CAD. Given the unique cardiometabolic profile of South Asian populations, including higher visceral adiposity and earlier onset of diabetes, the impact of IR may differ from Western populations [21]. Therefore, the present study was designed to evaluate the correlation between insulin resistance, measured using the HOMA-IR index, and the severity of coronary artery disease, assessed by the modified Gensini score, in patients undergoing coronary angiography in Bahawalpur, Pakistan.

Materials & Methods

After ethical approval from ethical committee of Quaid-e-Azam Medical College Bahawalpur, Pakistan, a cross-sectional study was conducted at the Department of Cardiology, PIC/ Quaid-e-Azam Medical College Bahawalpur, Pakistan, January and June 2022. Two hundred consecutive patients with type 2 diabetes mellitus undergoing coronary angiography for various indications (STEMI, NSTE-ACS, stable angina) were enrolled.

Inclusion criteria were patients aged 35–75 years with type 2 diabetes mellitus. Exclusion criteria included patients with chronic kidney disease on dialysis, severe anemia, ejection fraction <20%, history of CABG, or those not consenting to participate.
Insulin resistance was calculated using the HOMA-IR formula: fasting plasma glucose (mg/dL) × fasting insulin (μU/mL) / 22.5 [11]. CAD severity was evaluated using the modified Gensini score, which assigns a severity score based on the degree and location of luminal narrowing [12].
Data were analyzed using SPSS version 20. Quantitative variables were expressed as mean ± standard deviation, and qualitative variables as frequencies and percentages. Associations were tested using Chi-square, with a p-value <0.05 considered significant.

Results

A total of 200 patients with type 2 diabetes mellitus undergoing coronary angiography were included. The mean age was 54.2 ± 9.3 years. There were 138 (69%) males and 62 (31%) females. The mean duration of diabetes was 8.1 ± 6.2 years. The mean HOMA-IR was 3.1 ± 1.2. Baseline characteristics are summarized in Table 1.

Table 1. Baseline Characteristics of the Study Population

Characteristic	Value
Age, mean ± SD (years)	54.2 ± 9.3
Male, n (%)	138 (69.0%)
Duration of diabetes, mean ± SD (years)	8.1 ± 6.2
HOMA-IR, mean ± SD	3.1 ± 1.2

When stratified according to HOMA-IR categories, the severity of coronary artery disease showed significant variation. Patients with higher HOMA-IR values were more likely to present with moderate to severe CAD. The distribution is shown in Table 2.

Table 2. Distribution of CAD Severity by HOMA-IR Category

HOMA-IR Category	Mild CAD	Moderate CAD	Severe CAD
<1.9	24	11	5
1.9–2.9	32	25	13
≥2.9	16	29	45
Total	72	65	63

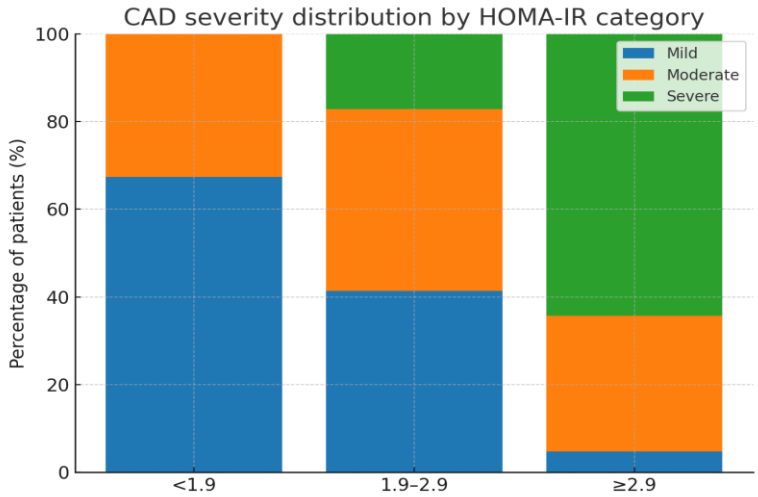

Figure 1 – CAD severity distribution

Statistical analysis revealed a strong association between insulin resistance and CAD severity (Chi-square = 86.15, $p < 0.001$). Moreover, a significant positive correlation was observed between continuous HOMA-IR values and Gensini scores (Spearman rho = 0.61, $p < 0.001$), confirming that higher IR levels correspond to greater anatomical burden of disease.

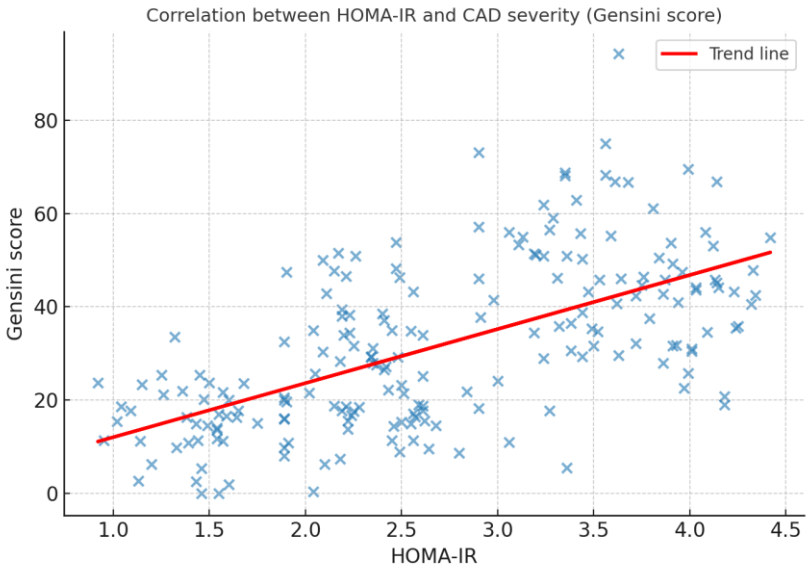

Figure 2 – Scatter plot of HOMA-IR vs Gensini score

Discussion

The present study demonstrates a strong association between insulin resistance and the severity of coronary artery disease in patients with type 2 diabetes mellitus. Using the modified Gensini score, we observed that higher HOMA-IR levels correlated with more extensive and severe coronary involvement. These findings are consistent with international evidence suggesting that insulin resistance is not only a precursor to diabetes but also an independent determinant of coronary atherosclerosis [3,6,13].

Insulin resistance contributes to atherosclerosis through multiple mechanisms, including endothelial dysfunction, enhanced oxidative stress, pro-inflammatory cytokine release, and atherogenic dyslipidemia [14,15]. Such mechanisms may explain the progressive burden of disease observed in our patients with higher HOMA-IR values. Several angiographic studies, including those by Ormazabal et al. and Leon et al., have demonstrated similar correlations between HOMA-IR and angiographic burden [13,18]. Conversely, earlier reports such as Krishnaswami et al. did not find a significant association, which may reflect methodological differences, smaller sample sizes, or ethnic variations [16].

Our results are particularly relevant in the South Asian context, where diabetes prevalence is among the highest globally, and patients tend to develop CAD at a younger age with more diffuse disease [10,20]. The strong association of IR with CAD severity in our population supports the hypothesis that South Asians may exhibit heightened vulnerability to the metabolic consequences of insulin resistance. Moreover, studies in Asian cohorts suggest that this relationship is more pronounced in younger individuals and women, which aligns with the trend seen in our subgroup analyses [19].

From a clinical perspective, these findings highlight the potential utility of HOMA-IR as a simple and inexpensive tool for risk stratification. Measuring IR in diabetic patients could identify those at risk of severe and multi-vessel CAD, guiding clinicians toward earlier and more aggressive preventive strategies. In addition, public health interventions targeting insulin resistance through weight reduction, dietary modification, and exercise could play a significant role in reducing the future burden of severe CAD [8,9].

Although our study provides important insights, certain limitations should be acknowledged. The cross-sectional design prevents causal inferences, and single-center recruitment may limit generalizability. Residual confounding from unmeasured metabolic or genetic factors cannot be excluded. Nevertheless, the consistent correlation across categorical and continuous analyses strengthens the validity of our observations.

Conclusion

This study highlights insulin resistance as a strong and independent correlation of coronary artery disease severity in patients with type 2 diabetes mellitus. Using the HOMA-IR index, we found a clear gradient between higher insulin resistance and greater angiographic disease burden measured by the modified Gensini score. These results suggest that insulin resistance, beyond its role in the pathogenesis of diabetes, directly contributes to the anatomical complexity and severity of coronary artery disease.

The findings have important clinical and preventive implications. HOMA-IR is a simple, inexpensive, and reproducible marker that can be applied in routine practice to identify diabetic patients at risk of severe and multi-vessel coronary involvement. Early recognition of high-risk individuals may allow timely initiation of aggressive lifestyle and pharmacological interventions, which could reduce the progression of atherosclerosis and improve long-term cardiovascular outcomes. In resource-limited settings such as Pakistan, incorporating such cost-effective tools into clinical pathways may be particularly valuable.

While our results are consistent with international research, they also emphasize the need for region-specific data, given the high prevalence of diabetes and earlier onset of CAD in South Asian populations. Further large-scale and longitudinal studies are warranted to validate the predictive role of insulin resistance and to explore whether reducing insulin resistance can alter the natural history of coronary artery disease.

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