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Research Article

CORRELATION BETWEEN INSULIN RESISTANCE AND SEVERITY OF CORONARY ARTERY DISEASE IN NON-DIABETES

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ABSTRACT

Objective: There is an increased risk of coronary artery disease (CAD) in both diabetes and non-diabetes. Insulin resistance (IR) has been associated with the development of CAD in this both populations. However, there are not many studies on correlation between IR and severity of CAD in non-diabetes. This study aimed to establish a correlation between IR and severity of CAD in non-diabetic individuals.

Methods: A cross-sectional study of 79 consecutive non-diabetic patients undergoing coronary angiogram for evaluation of clinically suspected CAD at a tertiary care hospital in Mangalore, Karnataka, were recruited. Clinical history, anthropometric, and biochemical parameters were analyzed. IR was determined by homeostasis model assessment-IR (HOMA-IR). The severity of CAD was assessed by Modified Gensini score. A Pearson correlation was done to find out the relation between HOMA-IR and Gensini core.

Results: The correlation between log of HOMA-IR and severity of CAD as assessed by Gensini score ($r=-0.053$ and $p=0.64$) was not significant in non-diabetic patients. The correlations between severity of CAD and other known risk factors of CAD were also was not significant.

Conclusions: HOMA-IR is negatively associated with severity of CAD in non-diabetes.

Keywords: Insulin resistance, Coronary artery disease, Gensini score.

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INTRODUCTION

The major cause of death worldwide is coronary artery disease (CAD), and more than 60% of the global burden of disease (GBD) occurs in developing countries [1,2]. GBD 2010 study showed that death from CAD increased by 87.8% between 1990 and 2010 in South Asia, and a further rise by 50% is expected by 2030 [3,4].

The Chennai Urban Population Study showed that the total prevalence of CAD was 9.1% among South Indian subjects with normal glucose tolerance [5]. Cardiovascular diseases have a multi-factorial causation, [6] and insulin resistance (IR) is one such non-conventional risk factor that can explain a major part of the pathogenesis of CAD [7].

IR increases the risk of CAD in both diabetics as well as non-diabetics [8]. IR has also been identified as a factor in the development of atherosclerosis [9], and hyperinsulinemia has been associated with an increased death in CAD [10]. A significant positive linear correlation between IR and severity of coronary atherosclerosis has been shown in diabetics between the Indian populations [11]. However, there are not many studies in the same population that correlates the IR with the severity of coronary atherosclerosis quantitatively in non-diabetics. If we are able to establish a significant association between IR and severity of CAD, it would help us to identify the individuals who are likely to develop severe disease from the beginning itself.

In this study, IR is calculated by homeostasis model assessment-IR (HOMA-IR) [12] and is correlated with the severity of coronary atherosclerosis as assessed by Modified Gensini score following a coronary angiogram [13] in non-diabetic individuals.

METHODS

In this cross-sectional study, 79 consecutive non-diabetic patients who satisfied the diagnostic criteria as recommended by the American Diabetes Association [14] and undergoing coronary angiogram for evaluation of clinically suspected CAD at a tertiary care hospital were recruited. The patients aged between 45 and 65 years were recruited, as studies show that beyond 65 years of age, the extent and degree of CAD remain same in all the population [15]. Patients with Type 2 diabetes mellitus, on steroids, chronic kidney disease, and valvular heart diseases were excluded from the study. The study protocol was approved by the Institutional Ethics Committee. An informed consent was obtained from the study participants.

All the clinical findings were noted. Anthropometric measurements such as height, weight, waist, and hip circumference were noted as per standard norms [16]. Body mass index and waist-hip ratio were calculated. Biochemical parameters such as fasting blood sugar, fasting insulin, fasting lipid profile, glycated hemoglobin, and urine microalbumin were analyzed as previously described by Srinivasan *et al*. [11]. The degree of IR was measured by HOMA 2 computerized method [12]. In large epidemiological studies, the use of HOMA-IR has been shown to correlate well with the gold standard hyper-insulinemia euglycemic glucose clamp technique for the measurement of IR [17]. To achieve constant phase and to avoid changes in IR that may occur due to the burden of the disease and angiographic procedure, the blood test was done 2 weeks after coronary angiogram [18]. The Modified Gensini scoring method was used to assess the severity of CAD [13]. Gensini scoring was done by a cardiologist, who was blind to other parameters.

Statistical analysis

Data were expressed as mean±standard deviation. The correlation between these parameters was assessed by calculating Pearson's correlation coefficient. $p<0.05$ was considered statistically significant. HOMA-IR values were logarithmically transformed for analysis [12]. Data were analyzed using statistical software for the social sciences (SPSS version 15, Chicago, IL, USA).

RESULTS

The characteristics of the study population are shown in Table 1.

The mean age of the subjects was 57.36±8.08. The majority of the study population was males 64 (81%) and females 15 (19%). At the time of the study, 29 (37%) of the patients had been diagnosed with hypertension and were on antihypertensive treatment. The overall Gensini score ranged from 3 to 144 among non-diabetics.

The scatterplot representing the relation between Gensini score and IR in non-diabetic patients is shown in Fig. 1.

The correlation between log of HOMA-IR and severity of CAD as assessed by Gensini score (r=−0.053 and p=0.64) was not significant in non-diabetic patients.

The correlations between severity of CAD and other known risk factors of CAD were also not significant in non-diabetic patients (Table 2).

DISCUSSION

We have demonstrated the correlation between IR (HOMA-IR) and angiographic severity of CAD in 79 consecutive non-diabetic patients who underwent angiogram for the screening of clinically suspected CAD.

Our study showed that the severity of CAD is not associated with IR in the non-diabetic population, which is similar to a study by Kruszelnicka *et al*. where no correlation was seen between the IR as measured by HOMA and Gensini score in 151 non-diabetic men [19].

Similarly, Vonbank *et al*. [20] reported no difference in HOMA-IR among 986 patients who underwent coronary angiography with varying severity of disease, irrespective of diabetes status and a study in 797 men by Solymoss *et al*. [21] found no association between the number of coronary arteries with >50% stenosis and fasting insulinemia, a surrogate marker for IR.

However, studies in smaller groups (n=38-83) found a positive relationship between angiographic CAD extent and IR as assessed by insulin suppression test or HOMA-IR [22-24].

Large data also suggest that IR has a pivotal role in atherosclerosis [25]. IR is closely related with an increased risk of cardiovascular disease [26]. The endothelial dysfunction which develops due to altered insulin signaling in the endothelial cells has resulted in the increased susceptibility to cardiovascular disease [26].

The third U.S. National Health and Nutrition Examination Survey III during a mean follow-up of 8.5 years found that there was independent association of HOMA-IR and mortality from cardiovascular events in non-diabetic adults [27]. Similar results were also obtained by a meta-analysis, which concluded that there 46% increase in the relative risk of symptomatic CAD per 1-SD increment in HOMA-IR [28].

In a cross-sectional study, a significant positive linear correlation between IR and severity of coronary atherosclerosis has been shown in diabetics between the Indian populations. In individuals with Type 2 diabetes mellitus, the evolution of insulin resistance is unique.

It precedes the onset of diabetes and remains fairly constant throughout the disease in spite of controlling for controlling for conventional risk factors [29]. In the U.K prospective diabetes study, the IR as measured by HOMA-IR method has been shown to be relatively stable during the many years of treatment even after with the conventional treatment of Type 2 diabetes mellitus, [30,31].

However, in non-diabetics, IR seems to be fluctuating, and that is why we were not able to appreciate the correlation with severity of CAD.

Table 1: Clinical characteristics of the study population (n=79)

Variables	Mean±SD
FBS	104.97±14.00
HOMA-IR	1.65±0.60
TC	171.82±50.87
TC/HDL ratio	4.36±1.40
LDL	115.50±45.56
HbA1C	5.58±0.33
Microalbumin	25.43±66.01
Waist circumference	75.87±26.60
BMI	24.34±3.58

HOMA-IR: Homeostasis model assessment-insulin resistance, TC/HDL: Total cholesterol/high density lipoprotein, LDL: Low density lipoprotein, HbA1c: Hemoglobin A1C, FBS: Fasting blood sugar, SD: Standard deviation, BMI: Body mass index

Table 2: Correlation between Gensini score, insulin resistance, and other conventional risk factors CAD

Variables	Gensini score	
	r value	p value
Log HOMA-IR	−0.053	0.645
TC	−0.003	0.979
LDL cholesterol	−0.066	0.565
HbA1C	0.063	0.584
TC/HDL	−0.111	0.3328
Microalbumin	0.219	0.052
Waist circumference	−0.156	0.171
BMI	0.030	0.794

HOMA-IR: Homeostasis model assessment-insulin resistance; TC/HDL: Total cholesterol/high density lipoprotein, LDL: Low density lipoprotein, HbA1C: Hemoglobin A1C, BMI: Body mass index, CAD: Coronary artery disease

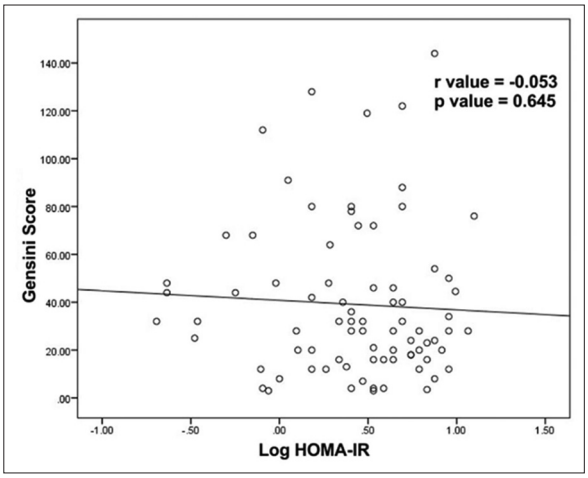

Fig. 1: Scatter plot showing, no correlation between severity of coronary artery disease (Gensini score) and log of insulin resistance (homeostasis model assessment-insulin resistance) in non-diabetes

Therefore, it is hypothesized that the morbidity is associated with elevated levels of HOMA-IR in non-diabetic CAD patients but not the severity.

Since major therapeutic decision depends on the severity of CAD, it is important to identify the factor responsible for severe CAD in non-diabetic individuals. But in this study, IR and other conventional risk factors of CAD were not associated with severity of CAD in non-diabetic patients. Thus, further prospective studies are needed to find out which of these risk factors is contributing to the severity of CAD in non-diabetic individuals.

LIMITATIONS

This study has several limitations, as this study included only patients with proven CAD, there is no control group. The study population and size were limited. The cross-sectional design and a single center study.

CONCLUSIONS

The findings of the study indicate that though HOMA-IR is not associated with severity of the disease in the non-diabetic population, and hence the role of insulin resistance leading to severe CAD would be limited in non-diabetes. More research is needed to study how IR influences coronary atherosclerosis in non-diabetics.

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