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Serum Lipoprotein Ratios as Markers for Insulin Resistance Among Non-Diabetic Acute Coronary Syndrome Patients with Impaired Fasting Glucose

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Abstract

Background Insulin resistance is a major risk factor in the development of cardiovascular diseases and type 2 diabetes mellitus. Some studies concluded that serum lipoproteins levels and hence lipoprotein ratios were altered in patients with insulin resistance.

Objective To identify the possibility of using lipoprotein ratios as markers for insulin resistance.

Methods A cross sectional study conducted in Baghdad (Medical City) and in Maysan (Al Shaheed Al Sadir Teaching Hospital) from February to December 2020. Eighty-three male and 51 female in Coronary Care Unit and Internal Medicine Wards patients were selected in the study group.

Results Lipoprotein ratios were significantly higher in individuals with homeostatic model assessment for insulin resistance (HOMA-IR) ≥2.5 as compared to subjects with HOMA-IR <2.5. There was a statistically significant association between lipoprotein ratios and insulin resistance when HOMA-IR ≥2.5 (P less than 0.05). Fasting insulin correlated significantly with lipoprotein ratios.

Conclusion Serum lipoprotein ratios and the best one is triglyceride/high density lipoprotein cholesterol could be used as markers for insulin resistance.

Keywords Lipoprotein ratios, insulin resistance, diabetes

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List of abbreviations: HDL-C = High-density lipoprotein cholesterol, HOMA-IR = Homeostatic model assessment for insulin resistance, LDL-C = Low-density lipoprotein cholesterol, TC = Total cholesterol, TG = Triglyceride

Introduction

Insulin resistance is a decrease in the biological response to the stimulation of insulin hormone in target tissues, which are mainly liver, muscle, and adipose tissue [(1)]. This pathological process usually impairs the glucose disposal (Insulin-Stimulated Glucose Disposal), which results in a compensatory elevation in the production of beta cell of insulin and increase in serum insulin [(2)]. Metabolic syndrome is a group of disorders that occurs at the same time, increasing the risk of heart diseases, stroke and type 2 diabetes mellitus [(3)].

Insulin resistance and dyslipidemia

Diabetic dyslipidemia is characterized by the lipid triad: high plasma triglycerides (TG), low high-density lipoprotein cholesterol (HDL), and high small dense low-density lipoproteins (sd LDL), in addition to excessive postprandial lipidemia [(4)]. Obesity is a global widespread epidemic and closely associated with the progression of coronary artery diseases and

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type 2 diabetes mellitus. Obesity has a great effect on lipoprotein profile and many systemic, endothelial disorders and vascular inflammation. Abnormal level of lipids and Apo lipoproteins may cause disruption in the production, catabolism and conversion, of lipoprotein particles [5,6].

The objective of this study is to identify the possibility of using lipoprotein ratios as markers for insulin resistance.

Methods

A cross sectional study conducted in Baghdad (Medical City) and in Maysan (Al Shaheed Al Sadir Teaching Hospital) from February to December 2020. All of the subjects were non-diabetic, impaired fasting glucose with acute coronary syndrome and the patients selected by convenient sampling (all patients presented during study visit and met the inclusion criteria). Lipid profile, fasting blood glucose (FBS), fasting insulin and HbA1c were measured for each participant. Immediate measurements of FBG, TG, HDL-C, Total cholesterol (TC), and LDL-C. The assay applied by automated method by using Abbott Architect C4000. Lipoprotein ratios: TG/HDL-C, TC/HDL-C, and LDL-C/HDL-C. Homeostatic model assessment for insulin resistance (HOMA-IR) was calculated by multiplying fasting insulin (µIU/mL) by FBG (mg/dL) divided by 405 [7].

Results

Eighty-three male and 51 female in Coronary Care Unit and Internal Medicine Wards patients were selected in the study group, from them, 17 patients less than 40 years, 45 patients between 40 to 60 years and the remaining above age of 60 with high HOMA-IR among males, and age group more than 60 years (Table 1).

Table 1. Distribution of the study group by socio-demographic characteristics (age and gender)

Characteristics		HOMA-IR ≥2.5 (n=53) n (%)	HOMA-IR <2.5 (n=81) n (%)	Total	P value
Age groups (yr)	<40	6 (11)	11 (14)	17	<0.001
	40-60 years	18 (34)	27 (33)	45	
	>60	29 (55)	43 (53)	72	
Gender	Male	33 (62)	50 (62)	83	0.950
	Female	20 (38)	31 (38)	51	

* P ≤0.05 is significant

Regarding biochemical parameters; the mean±SD of fasting glucose of study group was 107.7±6.05 mg/dl. But fasting insulin level in insulin resistance group (HOMA-IR ≥2.5) was significantly high (12.0±1.80) µIU/mL. All types of cholesterol and HbA1c were significantly high except the HDL-C, which it was significantly low (Table 2).

There was a statistically significant association between lipoprotein ratios and insulin resistance. The ratios were higher among insulin resistant group than non-insulin resistant patients. P value for all was <0.05. (Table 3).

Table 2. Distribution of study group by biochemical parameters

Biochemical parameters	HOMA-IR ≥2.5 (n= 53) (Mean ± SD)	HOMA <2.5 (n= 53) (Mean ± SD)	Total (Mean ± SD)	P value
Fasting glucose (mg/dL)	107.6 ± 6.03	107.7 ± 6.09	107.7 ±6.05	0.885
Fasting insulin (µIU/mL)	12.0 ± 1.80	7.7 ± 1.14	9.4 ±2.56	<0.001
HbA1c %	6.1 ± 0.26	5.7 ± 0.35	5.8 ± 0.35	<0.001
Total cholesterol (mg/dL)	192.6 ± 26.74	166.9 ± 20.44	177.1 ±26.28	<0.001
LDL-C (mg/dL)	119.6 ± 25.13	109.1 ± 20.75	113.3 ±23.07	0.010
HDL-C (mg/dL)	46.0 ± 6.38	51.8 ± 3.43	49.5 ±5.58	<0.001
Non-HDL-C (mg/dL)	146.6 ± 28.02	115.0 ± 19.65	127.5 ±27.92	0.001
TG (mg/dL)	158.5 ± 19.25	119.8 ± 26.59	135.1 ±30.51	<0.001

* P ≤0.05 is significant

Table 3. Distribution of study group by lipoprotein ratios and HOMA-IR

Parameter	HOMA ≥2.5 (n=53) Mean±SD	HOMA <2.5 (n=81) Mean±SD	P value
T. Cholesterol/ HDL-C	4.2±0.86	3.2±0.39	<0.001
TG/HDL-C	2.5±0.67	2.1±0.45	<0.001
LDL/HDL-C	3.5±0.64	2.3±0.53	<0.001
Non-HDL-C/ HDL-C	3.2±0.86	2.2±0.39	<0.001

* P ≤0.05 is significant

To determine the efficiency of TC/HDL-C, LDL/HDL-C, TG/HDL-C and Non-HDL-C/HDL-C as markers of insulin resistance in non-Diabetic acute coronary syndrome patients. ROC curve was calculated as showed in figure 1.

The TC/HDL-C is sensitive and specific (77.4%, 81.5%), the cut-off value was ≥3.58, and area under curve (AUC) 0.888, while LDL/HDL-C has AUC 0.695 with cutoff value ≥2.41 and lower sensitivity and specificity 64.2%, 70.4% respectively. The TG/HDL-C is more sensitive and specific (90.6%, 80.2%), the cut-off value was ≥2.69 and AUC 0.910 as showed in table 4.

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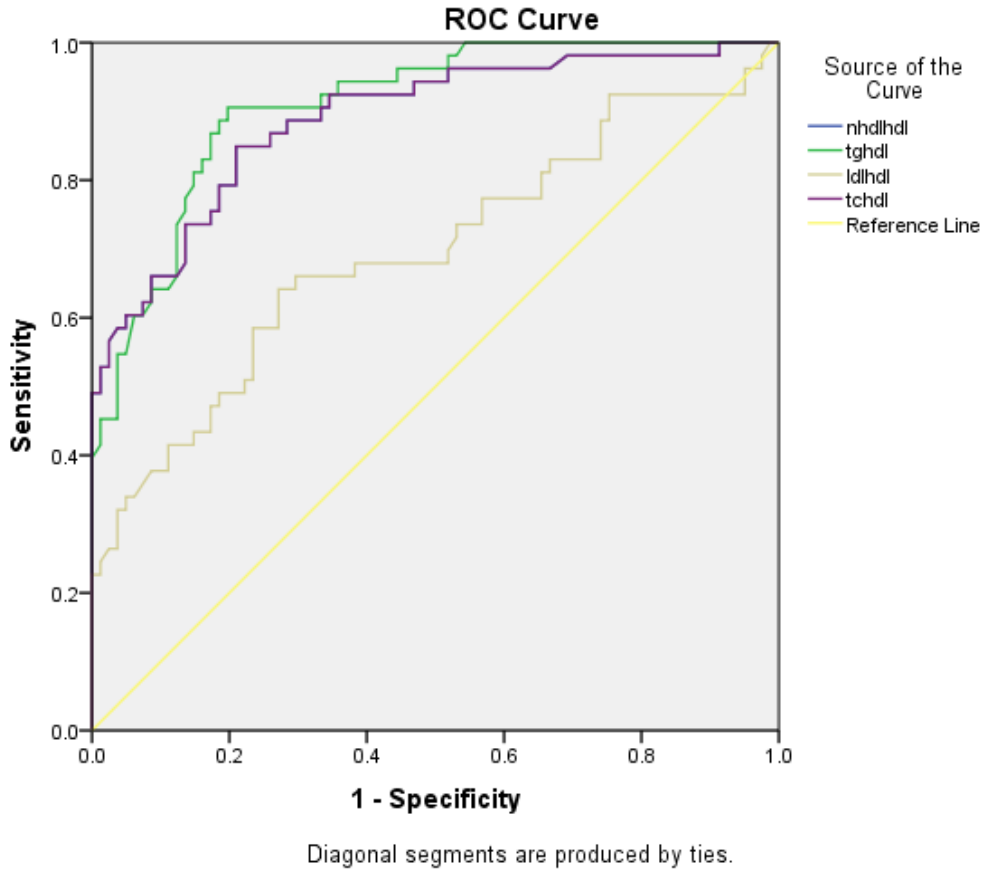

Figure 1. ROC Curves for the detection of insulin resistance in non-diabetic acute coronary syndrome patients

Table 4. Cut-off points corresponding to the highest percentage of sensitivity and specificity calculated from roc curves for the detection of insulin resistance in non-diabetic acute coronary syndrome patients

Lipid indices	Cut-off point	Sensitivity	Specificity	P value	AUC	95% CI
TC/HDL-C	3.57	77.4	81.5	<0.001	0.888	0.83-0.94
LDL/HDL-C	2.41	64.2	70.4	<0.001	0.695	0.59-0.79
TG/HDL-C	2.69	90.6	80.2	<0.001	0.910	0.86-0.95
Non-HDL-C/ HDL-C	2.57	77.4	81.5	<0.001	0.888	0.83-0.94

* P ≤0.05 is significant

Discussion

This study was conducted to determine the association between serum lipoprotein ratios and resistance to insulin in acute coronary syndrome patients with impaired fasting glucose.

In this study, there is significant association between age and insulin resistance, that defined as HOMA-IR ≥2.5 (p ≤0.05), this is different from results of another study from Rajappa et al. in 2014; who found that there is no significant association between them, while

the same study found that BMI, blood pressure and elevated waist:hip ratio were significantly associated with insulin resistance (p ≤0.01), the same as what found in this study [8].

In this study, about 62% of those with HOMA-IR ≥2.5 and 61.7% from other group were males, according to another study (Ray et al., 2015), 76.9% of insulin resistant group and 78.4% from other group were males [9].

In comparison with another study (Ormazabal et al., 2018) [1] who found that there was significant association between insulin resistance and CAD, this may be due to future development of CAD in follow up. The study of (Rajappa et al., 2014) who found that family and personal history of CAD are significantly associated with insulin resistance (p <0.01) [8].

The HOMA-IR is a good marker for insulin resistance in both patients and healthy individuals as it not required more than single measurement of fasting serum glucose and fasting serum insulin levels. Insulin resistance, in this study was identified as HOMA-IR ≥2.5, if less they considered sensitive to insulin without regard to the participant's gender. HOMA-IR is a commonly used measure to estimate insulin resistance. However, there were few studies focusing on the use of it in predicting the Framingham risk score (FRS). In one study, (Lu et al., 2020), participants who have elevated HOMA-IR levels were with higher capability to develop high FRS if compared with those had low levels of HOMA-IR. With adjustment for risk factors, such as sex, age class, BMI, tobacco smoking, the fasting sugar level, and blood pressure through multiple logistic regression statistical models, HOMA-IR also significantly associated with high FRS. These results may indicate that HOMA-IR is risk factor for high levels of FRS. They concluded that the power of HOMA-IR in identification of individuals with an elevated FRS. But, the lower specificity and low area under the curve, HOMA-IR using alone for prediction of high FRS was restricted [11].

In this study, there was significant difference in mean Total cholesterol, TG, HDL-C and LDL-C between the insulin resistant group and non-insulin resistant group, this is exactly similar to the results of International Scholarly Research Notices study (Rajappa et al, 2014) [8]. Fasting insulin level was significantly different between the two groups by the use of independent sample t test, this is similar to another study, (Johnson et al., 2010), who found that from individuals had fasting insulin level of >9 µIU/mL. In spite of presence of several methods for evaluation of insulin resistance, they are not cost effective and consume more time, the serum lipoprotein ratios (especially TG/HDL-C) can be used by physicians to classify patients into insulin resistant or sensitive [12]. The study of (Giannini et al., 2011) found that the relationship was statistically significant in white overweighted children but not significant in Hispanic individuals and African-American, the study found that TG/HDL-C ratio was significantly associated with the resistance to insulin in Korean individuals and the obese South-East Asian Immigrants [13].

In this study, serum lipoprotein ratios (TG/HDL-C, TC/HDL-C, LDL/HDL-C and Non-HDL/HDL-C) were higher among patients with insulin resistance than other group, and the difference is statistically significant. This is similar to the results of another study from India (Ray et al, 2015), in which, ninety participant who were known non-diabetic patients, with impaired fasting glucose level admitted to the hospital with ACS, lipoprotein ratios were higher in patients with HOMA-IR index ≥2.5 significantly, if compared to participants with lower index <2.5. The study of (Ray et al., 2015) also found that TG/HDL-C and TC/ HDL-C were significantly correlated with fasting insulin [9], this is similar to what found in this study, but In this study, fasting glucose and LDL-C were not correlated significantly with fasting insulin, this may be due to selection of impaired fasting glucose patients. According to another study (Kheirollahi et al., 2020) from Iran, on 305 individuals, the both groups, the insulin-resistant and the insulin-sensitive, diagnosed by the HOMA-IR were different in the levels of TG/HDL-C, TC/HDL-C ratios [14].

There is significant association between increased serum lipoprotein ratios and insulin resistance among the study group and are correlated significantly with fasting insulin. Serum lipoprotein ratios are cost effective and

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not time-consuming method for prediction of insulin resistance.

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Author contribution

Dr. Issa: Data collection, writing, and analysis. Dr. Rasheed: study deign, editing and revision.

Conflict of interest

None.

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