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Original Article

Relationship between serum resistin concentrations with metabolic syndrome and its components in an Iranian population

Sedigheh Asgary [a,*], Seyyed Ziaedin SamsamShariat [b], Ahmad Ghorbani [b], Mahtab Keshvari [a], Amirhossein Sahebkar [c], Nizal Sarrafzadegan [a]

[a] Isfahan Cardiovascular Research Center, Isfahan Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
[b] Department of Clinical Biochemistry, Isfahan Pharmaceutical Sciences Research Center, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran
[c] Biotechnology Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

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ABSTRACT

Background: The aim of the study is to determine the association of resistin with each MetS component.
Methods: This study had a case-control design, and its data was retrieved from the Isfahan Healthy Heart Program (IHHP), Serum samples from 44 subjects with MetS (diagnosed according to the NCEP-ATPIII criteria) and 46 healthy controls were analyzed for resistin using enzyme-linked immunosorbent assay. Association between serum resistin and levels of total (TC), low- (LDL-C) and high-density (HDL-C) lipoprotein cholesterol, triglycerides (TG), fasting blood sugar (FBS), waist circumference, body mass index, and systolic and diastolic blood pressures was determined.
Results: Serum resistin levels were significantly higher in the MetS compared with control group (3.64 ± 1.63, $P = 0.040$). Serum levels of resistin were found to be significantly correlated with levels of TC ($r = -0.347$; $P = 0.027$) and LDL-C ($r = -0.311$; $P = 0.050$), but not other components of MetS including systolic and diastolic blood pressure, TG, HDL-C and FBS ($P > 0.05$) in the MetS group, after adjustment for age, gender and BMI. No significant correlation between resistin and MetS components was observed in the control group ($P > 0.05$).
Conclusion: Serum resistin levels are elevated in subjects with MetS and may be associated with the severity of this syndrome.

1. Introduction

Metabolic syndrome (MetS) is a group of risk factors that collectively predispose an affected individual to cardiovascular disease (CVD). Components of MetS include abdominal obesity, Type 2 diabetes, hypertension, hypertriglyceridemia and low serum high-density lipoprotein cholesterol (HDL-C) concentrations [1,2].

Visceral adipose tissue plays a pivotal role in the pathogenesis of MetS [3]. Adipose tissue is an active endocrine organ capable of producing several regulatory mediators named adipokines. Adipokines have been shown to be involved in several biological processes that determine cardiovascular risk, including inflammation, adipogenesis, lipid metabolism and oxidative stress [4,5].

Resistin is an adipokine with 114 amino acids, belonging to the resistin-like family of proteins [6]. Animal studies have suggested resistin as a link among obesity, insulin resistance, and diabetes [7,8]. Resistin levels have been shown to be positively correlated with pro-inflammatory factors in several diseases such as atherosclerosis, renal disease, and respiratory tract inflammation [9–12]. Owing to its close association with inflammation and comorbidities of CVD, resistin has been proposed as a potential risk factor and risk marker of MetS. This notion has been supported by clinical findings showing higher serum resistin levels in adults with MetS compared with their healthy counterparts [13]. There are also other reports indicating that increased serum resistin levels are associated with increased obesity, visceral fat [14,15], insulin resistance, and Type 2 diabetes [16,17], but these findings have not been consistent [18,19]. Owing to these inconsistencies [20], the association of resistin with MetS and its components has remained controversial. Therefore, the present study aimed to compare serum concentrations of resistin in Iranian subjects with

* Corresponding author. Tel.: +98 9133094145; fax: +98 33373435.
E-mail address: sasgary@yahoo.com (S. Asgary).

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and without MetS, and also determines the association between these concentrations and MetS components.

2. Methods

Serum samples for this study case-control study were obtained from the Isfahan Healthy Heart Program (IHHP) sample bank. The IHHP was a comprehensive community-based program for the prevention and control of CVD and promotion of healthy lifestyle. Complete information on sampling process has been reported elsewhere [21,22]. Blood samples of 90 subjects from IHHP were analyzed in this study, comprising 44 subjects with MetS (mean age 43.57 ± 11.27 years), and 46 subjects without MetS (mean age 36.39 ± 9.51 years). Selection of subjects was on a random basis using computer-generated random numbers. Diagnosis of MetS was made according to the criteria defined by the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATPIII). Diagnosis of MetS according to this criteria requires at least three of the followings: (I) Abdominal obesity (waist circumference ≥ 40 inches [men] or ≥35 inches [women]); (II) serum triglycerides (TG) ≥ 150 mg/dl; (III) serum HDL-C < 50 mg/dl [men] or < 40 mg/dl [women]; (IV) blood pressure ≥ 130/85 mmHg; and (V) fasting glucose ≥ 100 mg/dl. MetS group was further categorized into subgroups with ≤3 and >3 components.

The study protocol was approved by the Medical Ethics Committee of the Isfahan Cardiovascular Research Institute under the approval no. 91115.

2.1. Biochemical and anthropometric measurement

Blood samples had been obtained by venipuncture after a 12–14 h fast. Fresh serum samples were used to measure total cholesterol (TC), TG, LDL-C and HDL-C. Measurements of resistin levels were carried out on frozen (−78 °C) plasma. All analysis were performed at the Central Laboratory of the Isfahan Cardiovascular Research Center. Enzymatic methods with commercial kits were used for the measurement of lipid profile parameters [23]. Serum resistin levels were measured using enzyme-linked immunosorbent assay (ELISA) with a commercial kit (Phoenix Pharmaceuticals Inc., USA). The lower detection limit of the assay was 0.0625 ng/ml. Intra- and inter-assay coefficients of variation for the assay were 3% and 10%, respectively.

Anthropometric measurements were conducted using calibrated instruments and standard protocols. Measurement of height was done with bare feet by a metal ruler; and measurement of weight with a calibrated scale in light clothing. Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared. Measurement of waist circumference was done at a level midway between the lower rib margin and iliac crest [24].

2.2. Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD). Between-group comparisons were made using independent samples *t*-test. Bivariate correlations were assessed using Pearson's correlation coefficient. Multiple linear regressions analysis was used to determine the impact of MetS components (TC, TG and HDL-C, FBS, systolic blood pressure and diastolic blood pressure) on serum resistin concentrations, after adjustment for age, BMI and gender. For the regression analysis, serum resistin concentrations were log-transformed and entered into the model as the dependent variable. Data analysis was performed using SPSS 15.0 (SPSS Inc., USA). Statistical significance was assumed at a two-sided *P*-value of <0.05.

3. Results

There were 44 adult subjects in the MetS group, with an age range of 25–64 years, including 26 (59.1%) males. Control group comprised 46 healthy adults with an age range of 25–58 years, including 28 (54.3%) males.

As expected, subjects in the MetS group had elevated serum levels of TC (< 0.001), TG ($P < 0.001$), LDL-C ($P = 0.017$) and FBS ($P = 0.019$), and reduced HDL-C ($P = 0.004$) compared with subjects in the non-MetS group. Likewise, anthropometric indices (BMI [$P = 0.005$] and waist circumference [$P < 0.001$]), systolic ($P < 0.001$) and diastolic ($P < 0.001$) blood pressures were significantly higher in the MetS compared with control group (Table 1).

Plasma resistin levels were significantly higher in the MetS compared with non-MetS group (3.64 ± 1.63 ng/ml vs 3.04 ± 1.01 ng/ml; $P = 0.040$) (Table 1). Serum levels of resistin were found to be significantly correlated with levels of TC ($r = -0.347$; $P = 0.027$) and LDL-C ($r = -0.311$; $P = 0.050$) in the MetS group, after adjustment for age, gender and BMI. However, no significant association with the above mentioned parameters was observed in the non-MetS group ($P > 0.05$) (Table 2). With respect to systolic and diastolic blood pressure, and serum concentrations of TG, HDL-C and FBS, no significant correlation with resistin levels was observed in either of the studied groups.

A subgroup analysis was performed to compare serum resistin concentrations between subjects with ≤3 vs those with >3 components of MetS. A significantly higher concentration of resistin was found in the latter group (2.92 ± 0.69 [>3 MetS components] vs 0.190 ± 1.11 [≤3 MetS] $P = 0.05$) (Fig. 1), suggesting a plausible association between serum resistin levels and severity of MetS. Nevertheless, no significant correlation was found between

Table 1
Comparison of clinical and biochemical parameters between metabolic syndrome and non-metabolic syndrome groups.

Characteristics	Non-metabolic syndrome ($n = 46$)	Metabolic syndrome ($n = 44$)	*P*-value
Age (years)	36.39 ± 9.51	43.57 ± 11.27	0.020
Sex (female%)	18(41.9)	21(45.7)	0.651
Log Resistin (ng/ml)	3.04 ± 1.01	3.64 ± 1.63	0.040
Waist-C (cm)	90.93 ± 12.19	99.76 ± 9.41	<0.001
BMI (kg/m^2)	25.85 ± 3.96	28.31 ± 3.95	0.005
TC (mg/dl)	185.61 ± 32.64	216.11 ± 39.93	<0.001
TG (mg/dl)	107.72 ± 39.73	241.95 ± 35.69	<0.001*
HDL (mg/dl)	43.70 ± 8.170	38.34 ± 8.95	0.004
FBS (mg/dl)	86.70 ± 7.79	93.89 ± 18.78	0.019
SBP (mmHg)	109.34 ± 10.15	122.62 ± 15.73	<0.001*
DBP (mmHg)	72.66 ± 7.07	79.57 ± 9.85	<0.001*
LDL (mg/dl)	120.37 ± 27.82	129.40 ± 34.09	0.017

Waist-circumference (Waist-C), body mass index (BMI), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL), fasting blood glucose (FBS), systolic blood pressure (SBP), diastolic blood pressure (DBP). The results are expressed as mean values ± standard deviation (SD). *P*-values are significant $P < 0.05$. T test and Mann-Whitney test (for multiple comparison) was used.

* Mann-Whitney Test