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Original Article

Serum adiponectin and resistin: Correlation with metabolic syndrome and its associated criteria among temiar subtribe in Malaysia

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ABSTRACT

Background and objectives: Metabolic syndrome (MetS) is characterized as a cluster of metabolic disorder including increased blood pressure, elevated blood glucose level, high cholesterol level and visceral fat obesity. Polypeptide hormones such as adiponectin and resistin play a significant role in glucose and lipids metabolism, liver and pancreas function. This study aimed to investigate the relationship between serum adiponectin and resistin with MetS criteria among Temiar subtribe in Kuala Betis.

Materials and methods: This cross sectional study involved 123 subjects from Temiar subtribe in Kuala Betis, Gua Musang, Kelantan. MetS criteria were measured according to standard protocol by modified National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guideline. Anthropometric and biochemical measurements were performed including serum adiponectin and resistin for every study subjects.

Results: Serum adiponectin was significantly lower in MetS subjects (7.98 ± 5.65 ng/ml) but serum resistin was found to be significantly higher in MetS subjects (11.22 ± 6.34 ng/ml) compared to non-MetS subjects with $p < 0.001$ and $p = 0.002$ respectively. Serum adiponectin was negatively correlated with most of the cardio-metabolic risk factors; BMI, waist circumference, systolic and diastolic blood pressure, fasting blood glucose, triglyceride and total cholesterol. Serum resistin was found to be positively correlated with BMI, waist circumference, fasting blood glucose and total cholesterol.

Conclusion: The difference in serum adiponectin and resistin level among MetS individuals indicated the potential of serum adiponectin and resistin to be used as a biomarker for the diagnosis of MetS among Temiar subtribe.

1. Introduction

Metabolic syndrome (MetS) has been a major burden to the public health and clinicians worldwide in the wake of urbanization and sedentary lifestyle. MetS confers a 5-fold and 2-fold risk of developing type 2 diabetes mellitus (T2DM) and cardiovascular diseases (CVD) respectively over the next 5–10 years [1]. MetS comprises the cluster of increased systolic and diastolic blood pressure (BP), elevated fasting blood glucose (FBG) level, high cholesterol level and visceral fat obesity. Principal contributors of MetS include urbanization, increasing energy intake, elevating obesity frequency and sedentary lifestyle. Prevalence of MetS is keep increasing throughout the world and its incidence is also increasing in developing regions. Relocation process to the more urbanized area is one of the factor, believed to be the cause for metabolic disorders among Temiar community. This has been shown by a study where the prevalence rate of diabetes and impaired glucose tolerance was higher in the relocation area compared to living in the forest [2]. The other study reported the prevalence of obesity, abdominal obesity, hypertension and T2DM was 16.8%, 38.4%, 29.6% and 4.6% respectively in Orang Asli population [3].

Adipose tissue acts as an active endocrine organ which involved in metabolic processes that secretes various regulatory mediator such as adipokines. Adipokines are the polypeptide hormones that

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have multi-directional effects on organism especially on a vital part of glucose and lipids metabolism, liver and pancreas function, and also in recovering tissue sensitivity to insulin. Therefore, defect in any process, may contribute to the progression of obesity-related diseases such as hypertension, atherosclerosis and T2DM, which subsequently lead to MetS [4–6]. Adiponectin is one of the adipokines produced by adipocytes that has an anti-inflammatory effect towards the cellular component of vascular wall [7]. Adiponectin sustains the regulation of carbohydrate and fat metabolism in insulin-sensitive tissues by playing a role as endogenous insulin-sensitizer [8]. Adiponectin also reduces the synthesis of glucose in liver, and increases the oxidation of fatty acid and glucose uptake in the muscle. The deficiency of adiponectin leads to insulin-resistance, obesity, T2DM and atherosclerosis [9,10]. Reduced serum adiponectin is usually observed in individuals with obesity, T2DM, insulin resistance and CVD [9,11]. Recent studies also suggested that increased serum adiponectin is inversely associated with the risk of MetS [12,13].

Resistin is secreted primarily by pre-adipocytes of abdominal localization and macrophages [14,15]. Insulin, glucose, growth hormone and thiazolidinediones are the example of resistin regulators [16–18]. Resistin exerts multiple functions in metabolism and physiological roles that related to inflammation, endothelial dysfunction, cardiomyocyte function and cholesterol metabolism [19]. Serum resistin was reported to be positively correlated with pro-inflammatory factors in several diseases such as atherosclerosis, renal disease and respiratory tract inflammation [20,21]. Resistin is also regarded as a potential risk factor and biomarker for MetS due to its association with obesity, inflammation, insulin resistance and comorbidities of CVD [22,23]. It has been supported by a clinical finding showing higher serum resistin in adults with MetS compared with their healthy counterparts [24]. Increased serum resistin is also found to be associated with increased obesity, visceral fat, insulin resistance and T2DM [25,26].

To date, there is no available data on the correlation between the concentration of serum adiponectin and resistin with MetS and its associated criteria among Temiar subtribe in Malaysia. Study on the association of serum adiponectin and resistin with MetS and its criteria is still deficient in Malaysia. Therefore, the present study is designed to investigate the relationship between serum adiponectin and resistin with MetS components among Temiar subtribe in Kuala Betis, Gua Musang, Kelantan.

2. Methods

2.1. Study design and population

This was a cross-sectional study conducted at RPS Kuala Betis, Gua Musang, Kelantan, located 30 km away from Gua Musang, involving Temiar subtribe. A total of 123 subjects were recruited in this study. This site was pragmatically selected as it represents Temiar subtribe population who has undergone urbanization and modern development. The inclusion criteria were individuals aged 18 years old and above, volunteered and agreed to participate in the study, completed the sociodemographic questionnaire, undergo the anthropometric measurements and clinical test, have no psychiatric illness, neurological deficit and body dysmorphic. Participants were given information on the purpose of the study and were pre-informed to fast for eight hours prior to screening. This study was approved by Universiti Sultan Zainal Abidin (UniSZA) Human Research Ethics Committee (UHREC), while a written permission was also obtained from Jabatan Kemajuan Orang Asli (JAKOA) and the head of each village to conduct the study. Written informed consent was obtained from all study subjects.

2.2. Anthropometric and biochemical measurements

Study subjects were evaluated for the anthropometric parameters, including body mass index (BMI), height, weight, waist circumference (WC) and blood pressure (BP). Weight and BMI were assessed in the upright position using an automated body composition analyzer (HBF-36, Karada Scan, Bioelectrical Impedance principle, Omron, Japan). WC were measured to the nearest 0.1 cm by using a non-stretchable measuring tape. BP was measured twice in 2 min apart on the right arm in sitting position, using an automated digital blood pressure monitor (Omron HEM-757, Japan). Twelve (12) ml of fasting venous blood sample were collected from the forearm of each subject. Fasting blood glucose (FBG) was measured using glucometer (ACCU-CHEK Performa, Roche, USA). Then, the blood samples were centrifuged at 4500 rpm for 10 min and stored at −20 °C until laboratory analysis. Serum samples were analyzed for lipid profile using automated chemistry analyzer (Olympus AU400 Chemistry Analyzer, USA) at Medical Campus, Universiti Sultan Zainal Abidin (UniSZA).

2.3. Metabolic syndrome definition

Subjects were diagnosed as MetS based on modified NCEP ATP III criteria. The modified NCEP-ATP III used in this study differs from the proposed NCEP-ATP III criteria. WC was lowered to ≥90 cm for male and ≥80 cm for female, while the fasting plasma glucose was decreased from ≥6.1 mmol/L to ≥5.6 mmol/L, with the inclusion of on treatment for high density lipoprotein-cholesterol (HDL-C) in the diagnostic criteria. An individual needs to fulfill at least any three risk factors to be diagnosed as MetS (Table 1).

2.4. Determination of serum adiponectin and resistin

Serum adiponectin and resistin in plasma were measured using quantitative sandwich enzyme immunoassay technique (ELISA) assay kit (CUSABIO Human Adiponectin and Resistin, China) according to the manufacturer's instructions. Plasma samples were diluted into 1:3 ratios with dilution buffer. The lowest detectable amount of human resistin protein was 0.1 ng/ml having inter-assay variability of 5.1% and intra-assay variability of 2.8%. Aliquots of plasma were kept at −20 °C.

2.5. Statistical analysis

Clinical data and anthropometric values are presented as mean ± SD. Statistical analyses were performed using SPSS 24.0 statistical software package (SPSS Inc., Chicago, IL, USA). Comparison of variables between MetS and non-MetS were carried out using Student's t-test. Bivariate correlations were analyzed using Pearson's correlation coefficient. For all analyses, $p < 0.05$ was considered to indicate statistical significance.

3. Results

Forty nine (49) subjects consisting of 10 (20.4%) males and 39 (79.6%) females were diagnosed as MetS, with the mean age of 38.61 ± 12.67 years. The remaining 74 subjects, 27 (36.5%) males and 47 (63.2%) females were diagnosed as non-MetS with the mean age of 37.74 ± 14.19 years. MetS subjects were found to be significantly higher in BMI ($p < 0.001$), WC ($p < 0.001$), systolic BP ($p = 0.005$), diastolic BP ($p < 0.001$), elevated FBG ($p = 0.001$), triglycerides (TG) ($p < 0.001$) and total cholesterol (TC) ($p < 0.001$) compared to non-MetS subjects. Meanwhile, HDL-C ($p < 0.001$) was significantly decreased in MetS subjects compared to non-MetS subjects. Serum adiponectin was significantly lower in MetS

Table 1
Metabolic syndrome defined by modified NCEP-ATP III used in the present study.

Risk factors	Modified NCEP-ATP III
Metabolic syndrome criteria	At least any three risk factors
Central obesity – WC	Male: ≥ 90 cm, female: ≥ 80 cm
Raised BP	Systolic BP ≥ 130 and/or diastolic BP ≥ 85 mmHg or on treatment of previously diagnosed hypertension
Raised fasting plasma glucose	≥5.6 mmol/L or previously diagnosed type 2 diabetes mellitus
Raised triglycerides	≥1.7 mmol/L or specific treatment for this lipid abnormality
Raised HDL-C	Male: <1.03 mmol/L, female: <1.29 mmol/L or specific treatment for this lipid abnormality

WC: waist circumference, BP: blood pressure, HDL-C: high density lipoprotein-cholesterol.

Table 2
Anthropometric and biochemical parameters in MetS and non-MetS subjects (n = 123).

Variables	MetS (n = 49)	Non-MetS (n = 74)	*p*-value
Age (years)	38.61 ± 12.67	37.74 ± 14.19	0.126
Height (cm)	149.77 ± 18.2	153.87 ± 13.03	0.152
Weight (kg)	62.24 ± 14.07	60.38 ± 13.38	0.460
BMI (kg/m^2)	31.56 ± 4.14	22.51 ± 3.19	<0.001
WC (cm)	91.46 ± 12.89	74.91 ± 8.3	<0.001
Systolic BP (mmHg)	136.98 ± 21.23	126.67 ± 18.15	0.005
Diastolic BP (mmHg)	90.37 ± 13.1	81.33 ± 11.28	<0.001
FBG (mmol/L)	7.214 ± 3.37	5.62 ± 2.02	0.001
Fasting TG (mmol/L)	1.86 ± 0.63	1.29 ± 0.2	<0.001
Fasting HDL-C (mmol/L)	0.94 ± 0.35	1.42 ± 0.23	<0.001
Total cholesterol (mmol/L)	6.56 ± 3.15	4.83 ± 1.95	<0.001
Adiponectin (ng/ml)	7.98 ± 5.65	15.93 ± 7.17	< 0.001
Resistin (ng/ml)	11.22 ± 6.34	7.06 ± 5.64	0.002

$p < 0.05$ was considered statistically significant based on independent *t*-test.
BMI: body mass index, WC: waist circumference, BP: blood pressure, FBG: fasting blood glucose, TG: triglyceride, HDL-C: high density lipoprotein-cholesterol, LDL-C: low density lipoprotein-cholesterol.

subjects (7.98 ± 5.65 ng/ml) compared to non-MetS subjects (15.93 ± 7.17 ng/ml) ($p < 0.001$). However, serum resistin was found to be significantly higher in MetS subjects (11.22 ± 6.34 ng/ml) compared to non-MetS subjects (7.06 ± 5.64 ng/ml) ($p = 0.002$) (Table 2).

Serum adiponectin was negatively correlated with most of the cardio-metabolic risk factors; BMI ($r = -0.443$, $p < 0.001$), WC ($r = -0.361$, $p < 0.001$), systolic ($r = -0.181$, $p = 0.045$) and diastolic ($r = -0.332$, $p < 0.001$) BP, FBG ($r = -0.278$, $p = 0.002$), TG ($r = -0.402$, $p < 0.001$), and TC ($r = -0.255$, $p = 0.004$). HDL-C was the only associated MetS component found to be positively correlated with serum adiponectin ($r = 0.342$, $p < 0.001$ (Table 3). On the other hand, serum resistin was found to be positively correlated with few cardiometabolic risk factors such as BMI ($r = 0.316$, $p < 0.001$), WC ($r = 0.233$, $p = 0.009$), FBG ($r = 0.292$, $p < 0.01$) and TC ($r = 0.216$, $p = 0.017$). HDL-C was negatively correlated with serum resistin ($r = -0.340$, $p < 0.001$). No significant correlation was observed between serum resistin with systolic and diastolic blood pressure and serum TG.

4. Discussion

The level of serum adiponectin was found to be lower in MetS subjects compared to Temiar subtribe without MetS (non-MetS) (Table 2). This was in agreement with the previous study conducted among São Paulo and Porto Alegre cohort where serum adiponectin was significantly lower in subjects diagnosed with MetS compared to non-MetS subjects [27]. A prospective cohort study of the rural area in Korea also found that baseline serum adiponectin concentration was significantly lower in subjects who developed MetS, compared to those subjects without MetS progression [28]. A similar finding was also observed with the other two previous studies where subjects with MetS have lower serum adiponectin compared to healthy individuals [29,30].

In the present study, a significant inverse correlation was observed between serum adiponectin and other MetS components such as WC, systolic and diastolic BP, FBG, TG and HDL-C (Table 3). The present study was in agreement with the other two previous studies involving Korean and Iranian population, which reported a negative correlation between serum adiponectin and BMI, WC, FBG, and TG [28,31]. The relationship of serum adiponectin with MetS components might be due to its function as a significant vasodilator. Adiponectin able to exert an antihypertensive effect, but hypoadiponectinemia may lead to arterial hypertension [32]. Previous study also showed that adiponectin plays an important role in chronic heart failure development and progression among patients with obesity [33].

HDL-C was found to be positively correlated with serum adiponectin. This was also in agreement with two previous studies which reported a similar finding of the relationship between serum adiponectin and HDL-C [34,35]. The prospective cohort study in rural Korea also reported that HDL-C was significantly decreased in subjects who developed MetS compared to those without progression of MetS [28]. The present study was also in concordance with the other studies conducted among elderly Koreans, Japanese and American adults which reported a systolic and diastolic BP were inversely correlated with serum adiponectin [34,36,37]. However, contradictory findings also have been reported by a previous study which they failed to find a significant correlation between serum adiponectin and systolic and diastolic BP [28].

Table 3
Correlation between serum adiponectin and resistin (ng/ml) with associated MetS criteria (n = 123).

Metabolic syndrome criteria	Serum adiponectin (ng/ml)		Serum resistin (ng/ml)	
	r	*p*-value[a]	*r*	*p*-value[a]
BMI	- 0.443	<0.001	0.316	<0.001
Waist circumference (WC)	- 0.361	<0.001	0.233	0.009
Systolic blood pressure	- 0.181	0.045	0.01	0.914
Diastolic blood pressure	- 0.332	<0.001	0.083	0.364
Fasting blood glucose (FBG)	- 0.278	0.002	0.292	<0.01
Triglycerides (TG)	- 0.402	<0.001	0.141	0.119
Total cholesterol (TC)	- 0.255	0.004	0.216	0.017
High density lipoprotein-cholesterol (HDL-C)	0.342	<0.001	- 0.340	<0.001

[a] Pearson's correlation.

The present study also demonstrated that the concentration of serum resistin was higher in Temiar subtribe diagnosed as MetS compared to non-MetS Temiar (Table 2). Our results were in concordance with the other studies conducted among Indian females and Iranian population (Singh et al., 2011; Asgary et al., 2014) [22,23]. A similar finding was also reported by a population-based study comprising of 1090 subjects [38].

Three components of MetS; WC, FBG, and HDL-C were observed to be significantly correlated in Temiar subtribe diagnosed as MetS when compared to non-MetS. Serum resistin was positively correlated with WC and FBG, whereas, HDL-C was found to be negatively correlated with the serum resistin (Table 3). No significant correlation was found between the concentration of serum resistin with the other three components of MetS; systolic and diastolic blood pressure and serum concentration of TG.

Previous studies reported that HDL-C, TG, WC, systolic and diastolic BP were significantly correlated with serum resistin [23,38]. In contrast, no significant correlation was observed between serum resistin with TG and systolic and diastolic BP in the present study. Our findings were in agreement with previous studies which failed to find any correlation between the concentration of serum resistin with lipid markers and also mediator of insulin resistance and MetS [20,39].

However, the present study was in agreement with a previous study involving Japanese population, where HDL-C was inversely correlated with serum resistin [40]. BMI was also observed to have a significant correlation with the concentration of serum resistin. A similar finding has been reported by previous study with serum resistin was found to be significantly elevated with increasing BMI [41].

Nevertheless, potential limitations of the present study have to be addressed. The response rate by the study population was low with some of them were refused to provide blood specimen, thus, contribute to the low response rate among this subtribe. We also could not ensure if the collected blood samples were fasting blood samples, even though they were pre-informed to fast for eight hours before screening. We realize that being a cross-sectional study, the predictive power to explore the possible relationship between serum adiponectin and resistin with the development of MetS in this subtribe cannot be ascertained.

Serum adiponectin was significantly decreased with MetS among the Temiar subtribe. However, serum resistin was significantly increased with MetS among this subtribe. Serum adiponectin was negatively correlated with most of the cardio-metabolic risk factors but serum resistin was found to be positively correlated with few cardiometabolic risk factors such as BMI, WC, FBG and TC. HDL-C was positively correlated with serum adiponectin and showed a negative correlation with serum resistin. The promising results shown by the present study proved that serum adiponectin and resistin have a potential to be used as a biomarker for the diagnosis of MetS among Temiar subtribe. It is imperative to suggest that an extensive study is warranted to further establish the association between serum adiponectin and resistin with the development of MetS and its risk factors in this particular subtribe.

Conflicts of interest

The authors whose names are listed certify that they have NO affiliations with or involvement in any organization with any financial interest or non-financial interest in the subject matter or materials discussed in this article.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2019.04.048.

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