

## ASSOCIATION OF SERUM ADIPONECTIN LEVELS WITH METABOLIC SYNDROME RISK FACTORS IN MALAY ADULTS

Nur Firdaus Isa<sup>1,3</sup>, Laila Ruwaida Mohd Zainuddin<sup>2</sup>, Wan Manan Wan Muda<sup>3</sup>, Hamid Jan B. Jan Mohamed<sup>3</sup>

1 Department of Biotechnology, Kulliyah of Science, IIUM, Kuantan, Pahang, Malaysia.

2 School of Nutrition and Dietetics, Faculty of Health Sciences, Universiti Sultan Zainal Abidin (UniSZA), Gong Badak Campus, 21300 Kuala Terengganu, Terengganu, Malaysia.

3 Nutrition and Dietetics Programme, School of Health Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

**Abstract— Introduction:** This study aimed to investigate the relationship between serum adiponectin and metabolic syndrome in adults living in rural Malaysia.

**Methods:** A total of 299 Malay adults (men=124; women = 175) with a mean age 48.8 (11.7) years were recruited. Measurements for waist circumference and blood pressure were taken before drawing an overnight fasting blood samples. Biochemical tests for triglycerides, HDL cholesterol, glucose and serum adiponectin concentration were measured.

**Results:** Our results show that the adiponectin level in the subjects with metabolic syndrome was significantly lower than those without metabolic syndrome ( $p < 0.05$ ). Among the metabolic syndrome risk factors, adiponectin level was significantly associated with hypertriglyceridemia and reduced HDL cholesterol ( $p < 0.001$ ).

**Conclusion:** The outcome from this study which highlights the association of hypoadiponectinemia with risk factors of metabolic syndrome in Malay adults, suggests that the reduced level of adiponectin may play a pivotal role in the development of metabolic syndrome in this ethnic group.

**Keywords:** *adipokines, metabolic syndrome, obesity, dyslipidaemia, Asian*

### INTRODUCTION

Metabolic syndrome is an emerging public health concern worldwide. The risk factors of metabolic syndrome are central obesity, hypertriglyceridaemia, reduced high-density lipoprotein cholesterol (HDL cholesterol), hypertension, and hyperglycemia.<sup>1</sup> Based on the International Diabetes Federation (IDF) definition, the presence of central obesity with any two of the other risk factors is qualified for the diagnosis of metabolic syndrome.<sup>2</sup>

A comprehensive overview on metabolic syndrome pandemic in the America, Europe and India indicates that more than 20% of the adult populations have metabolic syndrome.<sup>1</sup> Several South East Asian countries such as Indonesia, Singapore and Thailand are actively involved in evaluating the metabolic syndrome.<sup>3-7</sup> There is growing interest in assessing whether metabolic syndrome is a health threat in our population. This is based on the accumulating reports documenting the occurrence of metabolic syndrome in Malaysia in various locations and sociodemographic background.<sup>8-11</sup> Since the metabolic syndrome pandemic is observed in diverse population therefore there is a pressing need to investigate the mechanism underlying metabolic syndrome as well as searching for robust and sensitive biomarkers to serve as a diagnostic tool for early detection of metabolic syndrome.

The underlying mechanisms for development of metabolic syndrome remain plausible. The accumulated evidence suggests that the reduced adiponectin concentration (hypoadiponectinemia) plays pathophysiologic role of metabolic syndrome. The inverse correlation between visceral adiposity and adiponectin concentration suggests that hypoadiponectinemia is unequivocally associated with central obesity, a principal feature for metabolic syndrome.<sup>12-14</sup>

Adiponectin, a type of adipose-specific serum protein can be found extensively in serum ranging from 1.9–17.0  $\mu\text{g/ml}$ .<sup>15</sup> It is expressed inversely to total fat, and acted not only as anti-diabetic but also as anti-inflammatory and anti-atherogenic agent.<sup>16</sup> In the last few years, a growing body of evidence suggests that adiponectin is a potential biomarker for the metabolic syndrome and its risk factors. The present study was designed to examine the association between serum

adiponectin level and metabolic syndrome or risk factors in the Malay adults in Malaysia.

## METHODS

### Study subjects

This was a cross-sectional study involving a total of 299 Malay adults recruited from October 2008 to August 2009. This study was approved by the Human Research Ethics Committee of Universiti Sains Malaysia (USM/KK/PPP/JEPeM [205.4.(1.3)]). Written informed consent was obtained from all of the subjects. Each subject was interviewed using a structured questionnaire on demographic characteristics such as age, sex, and personal medical history. A qualified nutritionist measured height, weight and waist circumference using a portable bodymeter (Seca 206, Germany), body composition monitor (Tanita BC545, Japan) and non-elastic measurement tape (Seca 201, Japan). After 15 minutes of rest, blood pressure was measured twice by a trained laboratory technician using an automatic blood pressure monitor (Omron SEM-1, Japan). The general characteristics of the subjects were previously described.<sup>8</sup>

### Biochemical Tests

Peripheral venous blood samples were collected after an overnight fasting. Metabolic syndrome biomarkers such as fasting blood glucose, triglycerides and high-density lipoprotein cholesterol were assessed with commercially available reagents (Randox, UK) by using Vitalab Selectra E chemistry analyzer (Vitalab, Netherlands). Serum adiponectin concentration was determined by using the Human Adiponectin Enzyme-Linked Immunosorbent Assay (ELISA) kit (Chemicon, USA).

### Definition of Metabolic Syndrome

The following risk factors and criteria were used: central obesity (waist circumference; men  $\geq$  90 cm, women  $\geq$  80 cm) plus any two of the following: (1) raised triglycerides ( $>$  1.7 mmol/L (150 mg/dL) or specific treatment for this lipid abnormality); (2) reduced HDL-cholesterol (men  $<$ 1.03 mmol/L (40 mg/dL) or women  $<$ 1.29 mmol/L (50 mg/dL) or specific treatment for this lipid abnormality); (3) raised blood pressure ( $\geq$  130/85 mm Hg or treatment of previously diagnosed hypertension); (4) raised

fasting plasma glucose ( $\geq$  5.6 mmol/L (100 mg/dL) or previously diagnosed type 2 diabetes).

### Statistical analyses

Subjects with missing information in socioeconomic, anthropometric measurements and blood analyses were excluded from statistical analyses. Each variable was examined for normality of frequency distribution based on the histogram. Normally distributed data were expressed as mean (standard deviation or SD) and skewed data were expressed as median (Interquartile Range or IqR). The Mann-Whitney *U* test was conducted to study association of adiponectin concentration and metabolic syndrome or risk factors. The two-way ANOVA analysis of variance was applied to explore the mean differences of adiponectin concentration on status of metabolic syndrome or risk factors. Although this test requires the dependant variables to be normally distributed, however it is robust against violations of the assumption of the normal distribution (17). A 2-tailed value of  $p < 0.05$  was considered significant. All statistical analyses were performed using the Predictive Analytics Software (PASW Statistics 18.0) (SPSS Inc., Chicago, IL, USA).

## RESULTS

A total of 299 Malay adults mean (Mean age  $\pm$  SD:  $48.8 \pm 11.7$ ) of which 124 were men ( $49.8 \pm 11.7$ ) and 175 were women ( $48.6 \pm 11.8$ ) were recruited in this study. Clinical characteristics of metabolic syndrome among the subjects *i.e* the mean (SD) for waist circumference, systolic and diastolic blood pressures, glucose, triglycerides and HDL cholesterol, and median (IqR) for adiponectin concentration are presented in Table 1.

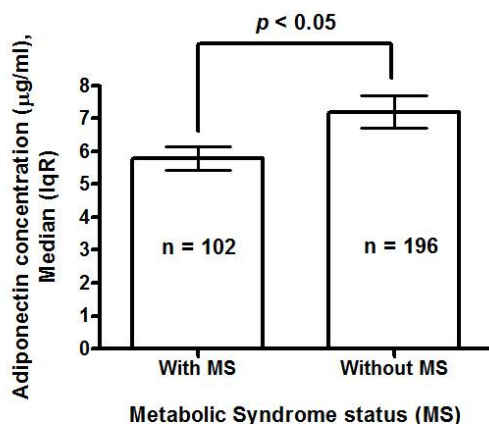
**Table 1.** General characteristics of the study subjects (n=299)

Characteristics	Mean	SD
Age (years)	48.8	11.7
Waist Circumference (cm)	83.8	11.3
Systolic Blood Pressure (mmHg)	134.8	23.1
Diastolic Blood Pressure (mmHg)	79.1	11.2
Glucose (mmol/L)	5.7	2.3
Triglycerides (mmol/L)	1.4	0.9
HDL cholesterol (mmol/L)	1.2	0.3
	<b>Median</b>	<b>IqR</b>
Adiponectin ( $\mu$ g/ml)	6.5	5.7

The association of adiponectin level with metabolic syndrome were examined using Mann-Whitney *U* test (Figure 1). The median (IqR) of adiponectin concentration among those with and without metabolic syndrome were 5.8 (3.7)  $\mu\text{g/ml}$  and 7.2 (6.8)  $\mu\text{g/ml}$ , respectively. The adiponectin level among those with metabolic syndrome was significantly lower than those without metabolic syndrome ( $p = 0.004$ ).

## DISCUSSION

The total serum adiponectin level observed in the Malay population is comparable with a study conducted among the Japanese, but lower than in other populations (Table 3). The adiponectin concentration reported among the Malays with metabolic syndrome was significantly lower than



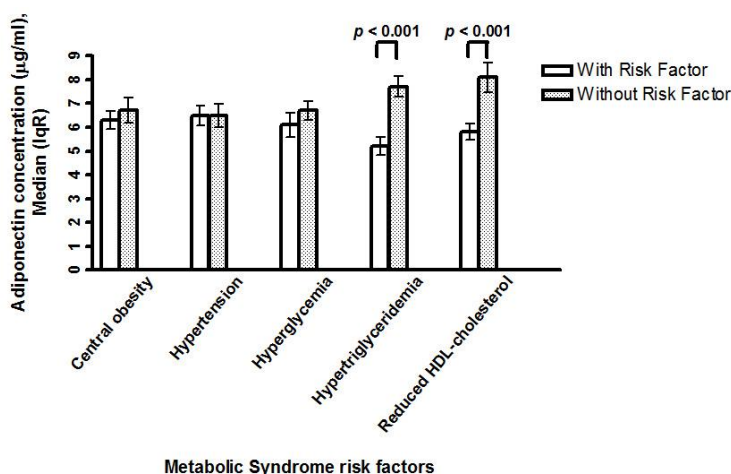
**Figure 1.** The median (IqR) of adiponectin concentration among subjects with and without metabolic syndrome (Mann-Whitney *U* test)

The association of adiponectin concentration with the individual metabolic syndrome risk factors is presented in Figure 2 and Table 2.

Subjects with high level of triglyceride (5.2  $\mu\text{g/ml}$ ) had significantly lower level of serum adiponectin than subjects with lower triglycerides (7.7  $\mu\text{g/ml}$ ) ( $p < 0.001$ ).

those without metabolic syndrome; this finding is in agreement with other reported studies.<sup>18,19</sup>

The Malay subjects with hypertriglyceridemia or reduced HDL cholesterol had significantly lower concentration of serum adiponectin concentration than those without them, respectively. The result is in accordance with



**Figure 2.** The median (IqR) of adiponectin concentration based on metabolic syndrome risk factors (Mann Whitney *U* test)

Similarly, subjects with reduced HDL cholesterol (5.8  $\mu\text{g/ml}$ ) had significantly lower concentration of serum adiponectin concentration than subjects with elevated HDL cholesterol (8.1  $\mu\text{g/ml}$ ) ( $p < 0.001$ ).

previous reports from various population such as Caucasian<sup>24</sup> and Japanese<sup>25</sup> and large-scale

**Table 2.** The association between metabolic syndrome risk factors with the adiponectin concentration

Risk Factors	Status	n (%)	Adiponectin (µg/ml) Median (IqR)	Z-stat <sup>a</sup>	p-value
Central obesity	With	146(48.7)	6.3 (4.6)	-0.931	0.352
	Without	153 (51.3)	6.7 (6.6)		
Hypertension	With	168(56.0)	6.5 (5.4)	-0.731	0.465
	Without	131 (44.0)	6.5 (5.6)		
Hyperglycemia	With	98(31.2)	6.1 (4.9)	-1.157	0.247
	Without	205 (68.8)	6.7 (5.8)		
Hypertriglyceridemia	With	87 (28.9)	5.2 (3.4)	-5.488	<0.001
	Without	212 (71.1)	7.7 (6.4)		
Reduced HDL cholesterol	With	196 (65.4)	5.8 (4.6)	-3.215	<0.001
	Without	103 (34.6)	8.1 (6.3)		

<sup>a</sup>Mann-Whitney *U* test

nationwide studies such as Rancho Bernardo Study<sup>26</sup> and KORA Survey 2000.<sup>27</sup> Although the exact crosslink between adiponectin and lipid metabolism remains unknown, it was proposed that adiponectin acts with HDL cholesterol in reverse cholesterol transport and involved in hepatic lipase activity.<sup>28</sup>

HMW is thought to be the active form of the adiponectin, and is implicated in the progression of metabolic syndrome.<sup>30,31</sup> Lara-Castro and the group reported that the reduced concentration of HMW adiponectin was associated with measures of central fat distribution, rather than the total adiponectin that

**Table 3.** Adiponectin concentration of Malay population and other populations

Population	Scope of the Study	Study Subjects	Adiponectin Concentration (µg/ml)
Malays <sup>This study</sup>	Metabolic Syndrome	Men and Women	6.5
Indonesian <sup>[7]</sup>	Metabolic Syndrome	Men	3.1
Japanese <sup>(20)</sup>	Healthy Young Adults	Men	6.4
Non-Hispanic White <sup>(21)</sup>	Pre-menopausal	Women	12.4
Hispanic <sup>(21)</sup>	Pre-menopausal	Women	9.5
Taiwanese <sup>(22)</sup>	Hyperglycemia	Men and Women	7.8
African Americans <sup>(23)</sup>	Insulin Resistance	Men	12.9
		Women	14.3

The finding from this study whereby hypoadiponectinemia is significantly associated with hypertriglyceridemia and reduced HDL cholesterol, suggests that an increased in adiponectin level could have protective effect via promoting HDL cholesterol and reducing the triglycerides.

We found no significant association between adiponectin with central obesity which appears to be in contradiction with the previous reports.<sup>24,29</sup> Such conflicting finding could be attributed by the adiponectin multimeric forms. Serum adiponectin exists as a trimer; low molecular weight (LMW) hexamers, medium molecular weight (MMW) and high molecular weight (HMW) multimerics. The

were commonly investigated by many researchers.<sup>32</sup> As findings from this study found no significant association between adiponectin and central obesity, it was proposed that adiponectin, specifically the total adiponectin measured during the course of the study, was not responsible for the association with central obesity in Malay population. Perhaps future investigation of HMW would provide more conclusive perspective.

Circulating adiponectin levels have been studied for their role in different ethnic groups which suggests that adipose tissue mass or distribution may be attributed by ethnic variation.<sup>33</sup> Since the present study displayed no significant association between

adiponectin and central obesity, further studies on the influence of Malay ethnic factor perhaps could explain the discrepancy.

The adiponectin concentration found in Malay subjects with hypertension was similar to those without hypertension. To our knowledge there are limited studies associating adiponectin and hypertension as compared to other risk factors. Besides, a number of studies purposely examined hypoadiponectinemia and hypertension in selected patients with other abnormalities for example in patients with essential hypertension; a form of high blood pressure with no identifiable cause or among obese participant.<sup>34,35</sup>

The association of hypoadiponectinemia and type 2 diabetes has been demonstrated as early as 2000.<sup>36</sup> Adiponectin is regarded as an insulin sensitizer that enhances insulin sensitivity by increasing fatty acid oxidation and inhibiting the hepatic glucose production.<sup>37</sup> Several studies carried out in diverse population show that diabetic subjects experience hypoadiponectinemia as compared to their nondiabetic counterparts.<sup>38-40</sup> We found no significant difference of the adiponectin level between hyperglycemic and non-hyperglycemic in our studied subjects. Increasing the sample size and expanding this cross-sectional study to a cohort study with longer follow-up may fill in the gaps.

Here we report the association of adiponectin levels in the Malay ethnics in Malaysia and its association with metabolic syndrome risk factors. The study population was selected from a rural area, thus the result may not be generalised to Malays living in urban Malaysia due to differences in socioeconomic status. A nationwide multicentre study involving not only Malay ethnics but also Indian Malaysian and Chinese Malaysian may provide perspective into the role of adiponectin in the development of metabolic syndrome in Malaysian. Studies have suggested that adiponectin can be a promising therapeutic agent for metabolic syndrome and its risk factors. Increasing circulating adiponectin concentration or enhancing adiponectin signalling through its receptors could promisingly tackle the root that cause the metabolic syndrome.<sup>41</sup> Although the claims excited many researchers, future investigations taking the ethnic differences into account, are required to support the matter.

### Conflicts of Interest

The authors declare there is no conflict of interest regarding this research

### Acknowledgment

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