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# Adiponectin Correlates in Malaysians: A Comparison of Metabolic Syndrome and Healthy Respondents

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**Abstract** Several studies have demonstrated that adiponectin has strong association with metabolic syndrome and its factors like obesity, insulin resistance, type 2 diabetes, dyslipidemia and coronary artery disease. A total 152 subjects were registered in this study. Among the respondents 76 were with metabolic syndrome (based on the criteria of the International Diabetes Federation (IDF) world-wide definition) and another 76 matching healthy respondents. The factors which were studied for possible differences and association include central obesity (body mass index (BMI) & waist circumference (WC), hypertension (systolic blood pressure (SBP), diastolic blood pressure (DBP), dyslipidemia (total cholesterol (Tc), high density lipoprotein Cholesterol (HDL-c), low density lipoprotein Cholesterol (LDL-c), Triglyceride (TG) and Adiponectin (AD), fasting plasma glucose and history of smoking. The data collected was statistically analyzed using SPSS statistical software version 12.0. Two tests were performed including paired t-test and Pearson correlation analysis. The collected data revealed some interesting differences for the healthy and metabolic syndrome respondents. There were significant ($P<0.01$) differences for central obesity and hypertension. There were also significant ($P<0.01$, $P<0.1$, $P<0.01$) differences for TG, HDL and fasting plasma glucose. More importantly, AD concentration was significantly ($P<0.05$) higher in normal healthy respondents. The AD showed strong negative association ($r = - 2.91$, $P<0.001$) with FBG and positive association ($r = 2.89$, $P<0.001$) with HDL-c. The present study provides baseline information on the predication of metabolic syndrome in Malaysian population.

***Keywords:*** *adiponectin, abdominal obesity, metabolic syndrome, hypertension, dyslipidemia*

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## 1. Introduction

According to the National Institute of Health (NIH) metabolic syndrome (MS) also called as dysmetabolic syndrome, hypertriglyceridemic waist, insulin resistance syndrome, obesity syndrome and Syndrome X. Whatever the name is it is often associated with abdominal obesity (AB) (visceral obesity) (OB). Indirectly, MS is the risk of having increased mortality and morbidity due to coronary artery diseases (CAD). Etiologically, it is closely associated with insulin resistance [1]. According to the definition of the International Diabetes Federation (IDF), for subjects to be defined as having the MS, must have visceral obesity plus any two of the four additional factors as shown in the Table 1 [2]. Clinically it has been demonstrated that LDL-lowering therapy can reduce major coronary events and coronary mortality [3]. A secondary target for the prevention of CAD after cholesterol–lowering is the management of MS which include abdominal obesity, dyslipidemia, glucose intolerance and hypertension. Although genetic factors, excess body fat particularly abdominal or visceral obesity are caused by over nutrition and physical inactivity [3,4,5,6]. Recent research studies indicate that adipose tissues produce various bioactive peptides called as adipokines which are believed to possess hormones like activities. The dysregulation of these adipokines in abdominal obesity may precipitate in the development of the metabolic syndrome [7,8,9]. Why adiponectin was chosen in this particular study? The lack of availability of adiponectin is considered key marker among the adipokines in the pathogenesis of metabolic syndrome [10,11,12,13]. Several studies have demonstrated that the adiponectin concentration in the blood is a useful predictor which exhibits stronger association with metabolic syndrome factors such as its decrease in obesity [14], insulin resistance [15], type 2 diabetes [16,17,18,19], dyslipidemia [20] and coronary artery disease [16,21]. Conversely, weight loss [22] and pharmacological improvement of insulin sensitivity [23] are associated with increased adiponectin levels. Lack of adiponectin results in an increased susceptibility to diet-induced insulin resistance [24]. Treatment of animals with adiponectin improved insulin resistance and other metabolic abnormalities associated with obesity and lipoatrophy [25,26].

**Table 1. International Diabetes Federation Metabolic Syndrome World-wide Definition**

| Central Obesity | Waist circumference –plus any two of the following |
|---|---|
| Raised triglycerides | ≥ 1.7 mmol/l (150 mg/dl) or specific treatment |
| Reduced HDL-Cholesterol | < 1.03 mmol/l (40 mg/dl in males)<br>< 1.29 mmol/l (50 mg/dl in females)<br>or specific treatment |
| Raised blood pressure | Systolic ≥ 130 mmHg<br>or Diastolic ≥ 85 mmHg<br>or treatment of previously diagnosed hypertension |
| Raised fasting plasma glucose | Fasting plasma glucose ≥ 5.6 mmol/l (100 mg/dl) or previously diagnosed Type 2 diabetes.<br>If > 5.6 mmol/l or 100 mg/dl, oral glucose tolerance test is strongly recommended but is not necessary to define presence of the syndrome. |

Adiponectin concentration in the blood is positively correlated to HDL-c concentration but negatively to insulin concentration [30]. Furthermore, the concentration in blood is reduced in obese and type 2 diabetes [31]. Adiponectin possibly has anti-atherogenic, insulin sensitizing, lipid oxidizing and vasodilating effects [33,34]. Plasma adiponectin is a useful biomarker for metabolic syndrome [35]. Therefore, this was an effort to study the association between adiponectin concentrations with the defined risk factors of metabolic syndrome in Malaysian population.

## 2. Methods

A Cross sectional comparative study was carried out in seven different polyclinics around Kuantan district which is the state capital of Pahang Malaysia. A total of 152 subjects were registered in this study. Among the respondents 76 were with metabolic syndrome (based on the criteria of the International Diabetes Federation (IDF) world-wide definition) and another 76 were matching healthy (control) respondents. The control group was selected from healthy individuals matching to the nearest possibility in particular in terms of age. According to World Health Organization (WHO) [36], health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity. Apart from age, the other matching factors included were gender, races and income etc. An informed consent was obtained from all respondents and were free to participate in this study. Prior data collection, the study protocol was approved from the relevant health authorities of the District Kuantan of Pahang state and the International Islamic University Malaysia Research Ethical Committee (IREC) which is a recognized body of the Ministry of Health, Government of Malaysia. Adult population aged 20 years and above who attend to Polyclinics Community in Kuantan during the study period for health examination. The subjects were randomly selected from those who visited the primary care clinics. All individuals who were consented and fulfilled the criteria were included in the study. Participants were included and considered suitable for inclusion in this study group if fulfilled the criteria of metabolic syndrome described by IDF as mentioned earlier [28]: Central obesity (ethnicity specific): waist circumference (WC) ≥90 cm (Asian male) or ≥80 cm (Asian female) and two or more factors as indicated in the Table 1. The participants were physically examined and some of the anthropometrics namely height, weight, waist circumference measured to the closest possible measurements with appropriate measuring tools along with some demographic information and of course blood pressure was recorded as well. Furthermore, the patients and the healthy respondents were requested to make an appointment for bloods sampling after overnight fasting. The collected blood was analyzed for serum lipid profile, serum adiponectin and fasting blood plasma glucose (FBG) test using appropriates commercial kits. The collected data was statistically analyzed by using SPSS statistical software version 15.0 for Windows using One-way ANOVA, Student t-test and Pearson correlation analysis. The differences were considered as significant at 95% confidence interval ($p<0.05$).

## 3. Results

The mean age of the respondents was 51 ± years majority of Malay ethnicity. Most of them were non-smoker (77.6%) and had history of hypertension (51%) and diabetes mellitus (46.4%) with a mean waist circumference of 89± cm and mean weight of 66.6 ± kg. Demographically, as indicated in the Table 2, the mean age of the MS respondents was 54 ± years old while the non-MS group was 48 ± years old. The number of current smokers in the MS group was less than in the non-MS (28 smokers and 06 smokers) as indicated in the Table 2.

Looking at the anthropometric indices it was noted that the BMI and WC were significantly ($P<0.001$) lower in the Non-MS respondents compared to MS respondents. Similarly, the blood pressure both systolic and diastolic were significantly ($P<0.001$) lower in the Non-MS respondents compared to MS respondents (Table 3). On overall the body weights, heights and BMI were significantly associated with adiponectin concentration (Table 5). The blood plasma analysis of the respondents are shown in the Table 4 which reveals that FBG concentration was significantly (P<0.001) lower in the Non-MS respondents compared to MS respondents and surprisingly the TC & LDL-c were not different among the two groups of respondents. However, there seems to be a varied ratio of the cholesterol fractions which is evident from the concentration of HDL-c which was significantly (P<0.001) higher in the Non-MS respondents than the MS respondents. Triglyceride concentration in the circulation seems to be also significantly (P<0.05) lower in the Non-MS respondents compared to MS respondents. When the blood sample were assessed for AD it appears to be significantly (P<0.05) higher in the Non-MS respondents than the MS respondents (Table 4). The AD concentration was compared between MS and Non MS respondents using t-test for age, gender and smoking. These results suggest that age, gender and smoking do not affect AD concentration both in MS and non MS respondents Furthermore, Pearson correlation analysis was carried out to predict any possible association between the AD concentrations in the circulating blood with the other aforementioned parameters namely, BMI, waist circumference, blood pressure FBG and dyslipidemia. These results suggest that FBG and HDL-c significant association with AD. The FBG concentration had significant (r = - 2.91, P<0.001) negative association with AD. Interestingly, there was strong & positive association (r = 2.89, P<0.001) of HDL-c with AD.

**Table 2. Socio-demographic Profile of Respondents**

| Parameters | Metabolic Syndrome n=76 (%) | Mean ± SE | Non Metabolic Syndrome n=76 (%) | Mean ± SE | Significance Level |
|---|---|---|---|---|---|
| **Age** | 54(10) | 53.97 ± 1.15 | 48(12) | 48.29 ± 1.38 | (P<0.002 |
| **Gender** | | - | | | |
| **Male** | 29(38.2) | | 35(46.1) | - | P<0.328 |
| **Female** | 47(61.8) | | 41(53.9) | | |
| **Race** | | - | | | |
| **Malay** | 70(92.1) | | 65(85.5) | - | P<0.868 |
| **Non-Malay** | 6(7.9) | | 11(14.5) | | |
| **Current Smoker** | | - | | | |
| **Yes** | 6(7.9) | | 28(36.8) | - | P<0.000 |
| **No** | 70(92.1) | | 48(63.2) | | |

NS=Non Significant.

**Table 3. Anthropometric/Clinical Assessment of the Respondents**

| Parameters | Metabolic Syndrome (n=76) | Non-MetabolicSyndrome (n=76) | Significance Level (P) |
|---|---|---|---|
| **BMI** | 31.32 ± 5.58 | 22.48± 3.94 | 0.000 |
| **WC (cm)** | 101.8 ± 10.1 | 75.1± 9.5 | 0.000 |
| **Systolic BP (mmHg)** | 138 ± 16 | 120± 23 | 0.000 |
| **Diastolic BP (mmHg)** | 84± 10 | 77 ± 12 | 0.000 |

N= Number of Respondents

**Table 4. Biochemical Assessment of the Respondents**

| Parameters | Metabolic Syndrome (n=76) | Non Metabolic Syndrome (n=76) | Significance Level (P) |
|---|---|---|---|
| **FBG (mmole/l)** | 7.0 ± 2.5 | 4.7± 1.4 | 0.000 |
| **TC (mmoles/l)** | 5.39 ± 0.99 | 5.33 ± 1.11 | 0.757 |
| **HDL-c(mmoles/l)** | 1.22 ± 0.35 | 1.51± 0.47 | 0.000 |
| **LDL-c(mmoles/l)** | 3.51± 0.98 | 3.53 ± 1.11 | 0.932 |
| **Triglyceride(mmoles/l)** | 1.53 ± 0.89 | 1.07 ± 0.99 | 0.003 |
| **Adiponectin(mmoles/l)** | 11.64 ± 4.26) | 13.21 ± 3.88 | 0.019 |

N= Number of Respondents

## 4. Discussion

As mentioned earlier, that the anthropometric indices namely BMI and WC were significantly (P<0.001) lower in the Non-MS respondents compared to MS respondents. Similarly, the blood pressure both systolic and diastolic were significantly (P<0.001) lower in the Non-MS respondents compared to MS respondents. The correlation analysis reveals that weight height, WC and BMI are important indicators of MS maintaining normal BMI would increase adiponectin (Table 5). The FBG concentration was significantly (P<0.01) higher in MS respondents and surprisingly the TC & LDL-c were not different. However, there seems to be a varied ratio of the cholesterol fractions particulary, HDL-c. Triglyceride concentration in the circulation seems to be also was also higher in MS respondents. The present study might be of greater interest to the clinician/physicians working in this particular area of research and treatment of MS patients. When the blood sample were assessed for AD it appears to be significantly (P<0.05) higher in the Non-MS respondents than the MS respondents. The comparison was made by using an independent t-test of the AD concentration gender and smoking status. These results suggest that gender and smoking status does not have an effect on serum adiponectin level. The observed correlation (r = - 2.91, P<0.001) & (r = 2.89, P<0.001) FBG and HDL-c with AD indicates that in these MS patients it is one of the important determinants. The hypoadiponectinemia has previously been reported to be existed in the MS patients [10,11,35] and in the present study on the Malaysian population is no exception. Some other studies have also indicated that hypoadiponectinemia exhibits hyperglycemia [11,17,18,19] and low HDL-cholesterol [20] in MS patients. This means that there will be an increase in FBG with a negative association with AD, while a decrease in HDL-c with a positive association with AD in MS patients. The present study suggests that BMI and Waist circumference are important differentiating factors in the MS patients. In a multivariate regression model, significant independent associations have been noted for age (positive), gender (men higher than women), race or ethnicity (race), educational status (inverse), hypercholesterolemia (positive), concentrations of C-reactive protein (positive), physical activity (inverse), microalbuminuria (positive), and hyperinsulinemia (positive) [37]. However, they are not same in this population like gender, and hypercholesterolaemia. Adiponectin is suggested because of the mechanisms that it is involved in the signaling pathways that mediate the metabolic effects. It activate 5'-AMP-activated protein kinase (AMPK), stimulates phosphorylation of acetyl coenzyme A carboxylase (ACC), fatty-acid oxidation, glucose uptake and lactate production in myocytes, phosphorylation of ACC and reduction of molecules involved in gluconeogenesis in the liver, and reduction of glucose levels in vivo thereby directly regulating glucose metabolism and insulin sensitivity [38]. The present study might be an important step towards the assessment of MS prediction in patients by making use of anthropometry lipid profile.

**Table 5. Pearson Correlation Analysis of Adiponectin with the MS Factors**

| Parameters | r-value | Sig. Level | Parameters | r-value | Sig. Level |
|---|---|---|---|---|---|
| **Weight** | -0.232 | 0.004 | **FBG (mmole/l)** | -0.291 | 0.000 |
| **Height** | -0.201 | 0.013 | **TC (mmoles/l)** | 0.058 | 0.476 |
| **BMI** | -0.167 | 0.040 | **HDL-c(mmoles/l)** | 0.289 | 0.000 |
| **WC (cm)** | -0.225 | 0.005 | **LDL-c(mmoles/l)** | 0.011 | 0.299 |
| **Systolic BP (mmHg)** | -0.002 | 0.983 | **Triglyceride(mmoles/l)** | -0.148 | 0.345 |
| **Diastolic BP (mmHg)** | -0.046 | NS | | | |

NS=Non Significant
*=P<0.05, **=P<0.01, ***<0.001).

## 5. Conclusion

The sample size of the present study was very small and is surely not the representative of the whole country and has to be concluded with great caution. However, it does suggest that the adiponectin and fasting blood glucose & high density lipoprotein cholesterol concentrations can be used as predicators in the clinical assessments of metabolic syndrome apart from the parameters listed but still adiponectin is not an easily available option.

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