

The Comparison of Adiponectin Level between Metabolic Syndrome Patients and Naïve Type 2 Diabetic Patients

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Abstract

Aim: To show the adiponectin concentration in metabolic syndrome which compared to naïve type 2 diabetic. **Method:** We conducted the adiponectin serum level cross sectionals from 16 metabolic syndrome patients (criteria from IDF 2005) and 16 naïve type 2 diabetic patients (criteria from WHO). For comparison adiponectin level between metabolic syndrome and diabetic patient were used t independent if the distribution we **Results:** The adiponectin serum level in metabolic syndrome patients is lower compared to naïve type 2 diabetic patients but the differences is not statistically significant (3.7413 ± 1.61 vs 4.7538 ± 2.09 ; $p= 0.135$). The adiponectin level has negative correlation with waist circumference ($r= -0.373$, $p= 0.035$), white blood cell ($r= -0.39$, $p= 0.027$) and positive correlation with HDL cholesterol ($r= +0.457$, $p= 0.009$) **Conclusion:** There was no significant differences of adiponectin level between metabolic syndrome and naïve type 2 diabetic, level adiponectin not only determined by blood glucose. The adiponectin serum is important marker, which can be used to measure inflammation level.

Keywords : Adiponectin, metabolic syndrome, naïve type 2 diabetes, inflammation

1. Introduction

Cardiovascular disease is the number one cause of death among patients with diabetes, and prevention is a major step in the management of diabetes at this time. Experts have long known that diabetes comorbid circumstances such as obesity, hypertension and hyperlipidemia in patients with type 2 diabetes they need to be treated to obtain better results. Group of insulin resistance, obesity, hypertension and dyslipidemia are also called "metabolic syndrome" (Sharpless, 2003).

Metabolic syndrome is a collection of risk factors that may predict the development of cardiovascular disease and type 2 diabetes in adults. This set of risk factors consist of: atherogenic dyslipidemia, hypertension, glucose intolerance, proinflammatory and prothrombotic state. Atherogenic dyslipidemia is a condition that includes an increase in triglycerides and apolipoprotein B, an increase of small LDL particles (small LDL) and decreased HDL. Although the underlying pathophysiology of metabolic syndrome remains unclear, but insulin resistance is thought to be central abnormalities in the pathogenesis of the metabolic syndrome (Shaibi GQ, *et al.* 2007; Blaka M, Elasy TA. 2006).

Obesity has long been recognized as a major risk factor for diabetes, but only recently the relationship between obesity and diabetes is starting to be explained. Adipose tissue not only serves as an energy storage organ but also as an organ of secretion. Protein - a protein produced by adipose tissue, most are proinflammatory, can explain the relationship between obesity and insulin resistance, type 2 diabetes and atherosclerotic disease (Duncan BB, *et al.* 2004; Arita Y, *et al.* 2002).

Adiponectin, a protein secreted by adipose tissue, has anti-inflammatory and metabolic effects are important in the role to prevent the development of diabetes. Some studies found that adiponectin is an important predictive marker for metabolic syndrome. Low plasma adiponectin levels are also predictive of insulin resistance and type 2 diabetes mellitus in adult individuals (Shaibi GQ, *et al.* 2007; Duncan BB, *et al.* 2004).

Hypoadiponectinaemia associated with insulin resistance, where the increase in the levels of circulating adiponectin in circulation will improve glucose levels and increasing fatty acid oxidation. Adiponectin can be considered as a marker for insulin sensitivity and the study - a prospective study found that hypoadiponectinaemia can predict the incidence of type 2 diabetes mellitus and coronary artery disease. In addition to the ability of adiponectin improve insulin sensitivity, the relationship between adiponectin and chronic inflammation, which is a characteristic of obesity, type 2 diabetes and cardiovascular disease, has also been investigated. In vitro, will inhibit the expression of adiponectin molecule - adhesion molecules on cells - endothelial cells, disrupt the function of macrophages and cytokines secretion from adipocytes (Herder C, *et al.* 2006).

Based on the above description, research on adiponectin levels in patients with metabolic syndrome and type 2 diabetes have not been studied recently. Therefore, the authors are interested in researching on adiponectin levels in patients with metabolic syndrome and type 2 diabetes mellitus patients, particularly patients with type 2 diabetes newly diagnosed (Naive DM).

2. Material and Methods

This study is cross sectional study between patients newly diagnosed DM who have met the WHO criteria and Metabolic Syndrome patients based on IDF 2005.

2.1 Subjects

Subjects were patients newly diagnosed DM and Metabolic Syndrome patients. 32 participants were recruited with inclusion criteria: 1. Patients with aged more than 18 years. 2. Have a complete personal data such as name, address, age, and phone number, or mobile phones. 3. Willing to participate in the study and signed a consent form after getting a description of the study (informed consent). Exclusion criteria : 1. Patients metabolic syndrome with fasting blood sugar > 126 mg / dl 2. Patients metabolic syndrome or newly diagnosed DM type 2 with heart failure, coronary heart disease, and kidney failure.

2.2 Treatment

This study was approved by the research ethics committee of the health sector Medical Faculty University of Sumatera Utara

Subjects were patients who went to the Division of Endocrinology and Metabolic Clinic and outpatient clinic at H Adam Malik Hospital, Medan. All subject done personal history, past medical history, and physical examination. All subjects fill the research approval letter

All subjects performed the measurement of waist circumference using the meter in a standing position and breathe as usual. Then examined the blood pressure in the sitting position of rest 10 minutes. Further examination were fasting blood sugar, lipid profile, ureum, creatinine, urinalysis, adiponectin levels and ECG. All subjects fasted for 8-10 hours.

2.3 Blood test

Blood sugar levels were measured by an enzymatic method (hexokinase) where the category that includes the components of the metabolic syndrome is when the fasting blood sugar > 100 mg / dl. Lipid profiles were measured by enzymatic method (CHOD-PAP) where a category that includes the components of the metabolic syndrome is when triglycerides > 150 mg / dl, HDL for men < 40 mg / dl and women < 50 mg / dl. The level of adiponectin conducted in the Clinical Laboratory Prodia using enzymatic methods EIA and ELISA

2.4 Statistical analysis

To compare the levels of adiponectin between the metabolic syndrome and patients newly diagnosed DM type 2 was used independent t test if the data is normally distributed both groups. If instead used the Mann Whitney test. We considered a value of $p < 0.05$ as significant. Data analyses were performed by using SPSS.

3. Result

Of the 16 patients with Metabolic Syndrome acquired 10 (62.5%) women and 6 (37.5%) were male. Ages ranged from 29 to 66 years with a median of 53.5 years and the largest age group in the group 50-59 years were 7 (43.75%) patients, followed by groups of 40-49 year 4 (25%) patients, a group of more than 60 years as much as 3 (18.75%) patients, and those less than 30 years and 30-39 years respectively of 1 (6.25%) patient.

Of the 16 patients with DM Naive acquired 10 (62.5%) women and 6 (37.5%) were male. Ages ranged from 34 to 68 years with a median of 46 years and the age group most in the group 40-49 years as many as 8 (50%) patients, followed by groups of 50-59 year 4 (25%) patients, and a group of more than 60 years and less than 40 years each in 2 (12.5%) patients. The baseline characteristics of the subjects by study group can be seen in table 1.

Table 1. The baseline characteristics of the subjects by study group

Variabel	Metabolic Syndrome	Naive DM
Sex		
Male	6 (37.5)	6 (37.5)
Female	10 (62.5)	10 (62.5)
Age (years)		
< 30	1 (6.25)	-
30 - 39	1 (6.25)	2 (12.5)
40 - 49	4 (25)	8 (50)
50 - 59	7 (43.75)	4 (25)
> 60	3 (18.75)	2 (12.5)

Patients with metabolic syndrome had lower adiponectin levels compared with DM naive patients but the

difference was not statistically significant ($p = 0.135$). Compared with patients with diabetes, patients with metabolic syndrome have a systolic blood pressure, diastolic blood pressure, waist circumference, triglycerides and body mass index greater and have lower fasting blood sugar. The differences were statistically significant (Table 2)

Table 2. Comparison of sample characteristics between metabolic syndrome and naive diabetes patients

Variabel	Metabolic Syndrome X ± SD	Naive DM X ± SD	p
Age (years)	50.81 ± 9.76	48.31 ± 9.74	.474
Blood pressure			
Systolic (mmHg)	149.69 ± 31.75	124.38 ± 10.78	.007*
Diastolic (mmHg)	90.31 ± 15.76	75.94 ± 7.58	.003*
WC (cm)	106.66 ± 12.22	88.66 ± 12.08	.0001*
Hb (mg/dl)	13.906 ± 2.24	13.894 ± 1.19	.984
WBC (mg/dl)	10390 ± 2456.18	8527.5 ± 2874.57	.058
FBG (mg/dl)	98.75 ± 13.88	222.25 ± 110.64	.0001*
Lipid profile			
Cholesterol (mg/dl)	227.50 ± 36.37	233.63 ± 45.16	.676
LDL (mg/dl)	140.06 ± 28.38	164.31 ± 45.31	.080
HDL (mg/dl)	40.81 ± 9.29	43.31 ± 13.54	.548
Triglyceride (mg/dl)	235.25 ± 182.51	136.06 ± 56.39	.046*
BMI (kg/m ²)	31.71 ± 8.09	24.6244 ± 4.38	.004*
Adiponectin (µg/ml)	3.7413 ± 1.61	4.7538 ± 2.09	.135

Note: WC = waist circumference; WBC = white blood cell; FBG = fasting blood glucose; BMI = body mass index

Adiponectin levels in women is higher than men, but the difference was not significant ($4.4710 \pm 3.8750 \pm 1.60$ versus 2.07 , $p = 0.4$).

When divided by the reference value, from 16 patients with metabolic syndrome, gained as much as 6 study participants (37.5%) had higher levels of adiponectin lower than normal. The difference between low adiponectin levels in patients with metabolic syndrome were significantly different with adiponectin levels were normal. Whereas of the 16 patients naive DM, found as many as four study participants (25%) who had lower adiponectin levels, and the difference between the levels of adiponectin and HDL cholesterol found a statistically significant

Of the 16 participants of the metabolic syndrome that has three components were 7 participants (43.75%); which have 4 components were 7 participants (43.75%) and that has 5 components by 2 participants (12.5%). Lowest levels of adiponectin are owned by the participants with the 4 components of metabolic syndrome (Table 3).

Table 3. Comparison levels adiponectin based components of metabolic syndrome in patients with metabolic syndrome

Component	Participant (%)	Adiponectin (µg/ml)
3	7 (43.75)	4.56
4	7 (43.75)	2.89
5	2 (12.5)	3.85

Results of this study also found that adiponectin levels had a negative correlation with waist circumference (correlation coefficient ($r = -0.373$, $p = 0.035$), white blood cell ($r = -0.39$, $p = 0.027$) and had a positive

correlation with HDL cholesterol ($r = +0.457$, $p = 0.009$).

The results of this study also found that adiponectin levels had a negative correlation with body mass index, but showed no significant correlation ($r = -0.204$, $p = 0.262$).

4. Discussion

The prevalence of metabolic syndrome in the United States found an increase of 6.7% in the age group 20-29 years to 43.5% in the age group 60-69 year. (Ford ES *et al.* 2002). In this study also found an increased prevalence of metabolic syndrome than 6.25% in the age group below 30 years and 30 - 39 years to 43.75% in the age group 50-59 years. The highest prevalence of patients with metabolic syndrome obtained in this study are in the age group 50-59 years.

The results of this research to get the levels of adiponectin, metabolic syndrome patients were lower than naive patients with diabetes, but the difference was not statistically significant ($p = 0.135$). This may occur

because the metabolic syndrome patients obtained a state where an increase in systolic blood pressure, diastolic blood pressure, waist circumference, triglycerides and body mass index than patients naive DM.

In 1995, a report was published on the proteins that produce adipocytes were found in serum (30 kDa). This protein is named adiponectin, or ACRP 30 (adipocyte complement-related protein of 30 kDa), GBP 28 (gelating binding protein 28 kDa) or AdipoQ. Adiponectin has the same structure with collagen and C1q and demonstrate the ability of a strong bond with collagen. (Kadowaki T *et al.* 2005).

The protective effect of the development of diabetes by high levels of plasma adiponectin has been shown in several studies involving observation of groups of different ethnicities, namely the Pima Indians, white European, Japanese, Asian Indian and African Americans. (Daimon M *et al.* 2003; Fernandez-Real JM *et al.* 2003; Gabir MM *et al.* 2000; Lindsay RS *et al.* 2002; Spranger J *et al.* 2003). The effect of decreasing blood glucose levels by adiponectin has been shown by the work of the AMP-activated protein kinase (AMPK). AMPK, which is the target of metformin and anti-diabetic drugs other as to which to transport glucose associated with physical exercise, is independent of insulin, which stimulates glucose transport. AMPK stimulates both catabolism of intra-cellular energy storage available, such as triglycerides, and extra cellular energy source that is independent of insulin, such as glucose. There are two adiponectin receptors that have been identified and found to be mediating the increase in fatty acid oxidation in muscle and increase glucose uptake in the liver. (Duncan BB *et al.*, 2004). Interestingly in this study found the opposite case, where the concentration of adiponectin correlate positively with fasting blood glucose levels, although not statistically significant ($r = +0.104$; $p 0.572$).

The synthesis of adiponectin has been known to decrease in individuals with coronary heart disease and endothelial dysfunction. Reduced adiponectin concentrations associated with the incidence of coronary heart disease (independent of diabetes met, BMI, dyslipoproteinaemia, hypertension, smoking). Kumada M *et al* who reported the findings indicate that individuals with hypo adiponectinaemia have a significantly higher risk for coronary heart disease independent of risk factors other. Kazumi *et al* get a negative correlation between adiponectin levels with an average of systolic and diastolic blood pressure (Kazumi T, *et al.*, 2002; Kumada M *et al.*, 2003). The results of this study also found a negative correlation between adiponectin levels with an average of systolic and diastolic blood pressure, although not statistically significant.

Increased number of white blood cells is a predictor of cardiovascular mortality independent of the effects of smoking and traditional risk factors other. Although still in the normal range, the number of white blood cells independently associated with mortality from coronary heart disease. Also found a significant positive relationship between the number of leucocytes and severity of atherosclerosis. Inflammation will provide a role for vascular injury, atherosclerosis and thrombosis. White blood cells, which is activated by cytokines, especially interleukin (IL) -6 and IL-8, is an important marker for these processes. White blood cells have contributed to the blood viscosity, releasing products that will lead to plaque rupture and thrombus formation and has a role in endothelial dysfunction. Adiponectin itself has been known to have anti-inflammatory properties (Ohshita K, *et al.*, 2004). The results of this study showed low levels of adiponectin are associated with an increased number of white blood cells, which is one of the inflammatory markers were significantly.

The strength of this study there are two things. First, the study participants suffering from metabolic syndrome is not a diabetic, so the possibility of bias from the results obtained adiponectin concentrations can be minimized. Second, participants with diabetes who participated in this study is that naive participants so that the bias that may arise due to taking diabetes medicines that can increase adiponectin concentrations can be eliminated.

The weakness of this study there are two things. First, participants with diabetes who participated this study there who have a large waist circumference and had dyslipidaemia, and hypertension, which can bring a bias in the results of this study. Second, a small number of study participants and therefore cannot describe the population as a whole

5. Conclusion

We found that Levels of adiponectin metabolic syndrome patients was lower than naive patients with diabetes but no significant. Require further study with a larger sample size to compare the strength of the results of this study.

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