Research Article

Study of plasma adiponectin level in patients with metabolic syndrome

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ABSTRACT

Background: The metabolic syndrome (MS) is a cluster of interrelated common clinical disorders, including hypertension, insulin resistance, glucose intolerance and dyslipidaemia, in addition to obesity. Central obesity accompanied by insulin resistance is a keyfactor in the development of metabolic syndrome (MS) and future macro vascular complications. Adiponectin is the most abundant peptide secreted by adipocytes, being a key component in the interrelationship between adiposity, insulin resistance and inflammation. Hypoadiponectimia has already been associated with the risk of the MS in several populations. Plasma adiponectin level was measured in the current study to clarify its role as a biomarker for metabolic syndrome (MS).
Methods: This study was conducted on 40 MS patients (Group I) compared with 20 age and sex matched healthy volunteers (Group II). All patients and controls were subjected to full medical history, clinical examination and laboratory investigations in addition to plasma adiponectin level.
Results: Plasma adiponectin levels were significantly lower in subjects with MS when compared with subjects with no diagnosis of MS. There was significant negative correlation between plasma adiponectin and age, waist circumference, body mass index, systolic blood pressure, diastolic blood pressure, fasting blood sugar, insulin resistance, serum insulin, and triglycerides. Also there was significant positive correlation between plasma adiponectin and HDL.
Conclusion: We conclude that adiponectin levels could help as a biomarker for cases of MS.

Keywords: Metabolic syndrome, Adiponectin, Insulin resistance, Lipid profile

INTRODUCTION

Metabolic syndrome is a cluster of risk factors for cardiovascular disease (CVD), including insulin resistance, obesity, hypertension, elevated triglycerides, and low levels of high density lipoprotein (HDL).[1] Metabolic syndrome is a strong predictor of type 2 diabetes, with an increased incidence rate of 5 to 7-fold. The risk of developing CVD is approximately doubled in the metabolic syndrome.[2]

Obesity, in particular visceral adiposity, is known to be associated with insulin resistance and a heterogeneous disorder, MS. MS is a cluster of interrelated common clinical disorders, including hypertension, insulin resistance, glucose intolerance and dyslipidaemia, in addition to obesity.[3] It has been shown that visceral fat deposits are more metabolically active than their subcutaneous homologues, being particularly involved in the development of diseases associated with obesity, such as MS, type 2 diabetes mellitus (T2DM) and coronary artery disease (CAD).[4]

White adipose tissue plays a key role as an organ secreting numerous bioactive molecules called adipokines or adipocytokines.[5] The number of identified

adipokines is permanently increasing, as well as their potential clinical diagnostic and prognostic value. These adipokines include mainly adiponectin,[5-6] adiponectin is the most abundant peptide secreted by adipocytes, being a key component in the interrelationship between adiposity, insulin resistance and inflammation. Central obesity accompanied by insulin resistance is a key factor in the development of metabolic syndrome (MS) and future macro vascular complications.

Adiponectin levels in plasma are inversely correlated with visceral adiposity. Lower levels of adiponectin were observed in patients with high blood pressure, hyperglycemia, low HDL-C, and hypertriglyceridemia, also in obese patients with MS.[7]

Adiponectin increases the sensitivity to insulin through several mechanisms. AdipoR1 and AdipoR2 are transmembrane receptors, whose carboxyl terminal group(C-terminal) is located outside the membrane, and the amino terminal group (N-terminal) inside.[8] When adiponectin attaches to its receptor it activates adenosine mono phosphate (AMP) kinase,[9-10] promoting so glucose uptake by muscles via intracellular translocation of the GLUT4 transporters. Simultaneously, it hampers gluconeogenesis by inhibiting the hepatic enzyme phosphoenolpyruvate carboxylase, inhibits the synthesis of fatty acids and stimulates their oxidation.[10-11]

Serum adiponectin is inversely related to body fat mass and to the degree of insulin resistance. Its concentration is particularly low in adults with T2DM or CAD. So it is accepted, that adiponectin ameliorates sensitivity to insulin and contributes to cardiovascular protection.[12-10] Low circulating levels, particularly of the high molecular weight (HMW) component,[13-14] are also a strong risk marker for the development of MS.

Adiponectin enhances insulin sensitivity by increasing hepatic insulin receptor substrate 2 (IRS-2) expressions via a macrophage derived IL-6-dependent pathway.[15] Thus, these multiple pathways confer to adiponectin a key role in ensuring an effective protection against the development of insulin resistance (IR).

Aim of the work: was to study plasma level of adiponectin to clarify its role as a biomarker of MS.

METHODS

Subjects and methods

This study was conducted on 40 MS patients (26 female and 14 male) their ages ranged between (44-60 years) with mean ± SD (51.90±5.48) and 20 healthy persons (10 female and 10 male) their ages ranged between (40-60 years) with mean ± SD (48.85±5.04) from the medical department in Al-Zhraa university Hospital (from January 2014 to September 2014). A written consent was obtained from all participants and approval of ethical

committee of faculty of medicine, Al-Azhar University was also obtained.

Diagnosis of MS was based on International Diabetes Federation (IDF) criteria for diagnosis of MS, which include any three or more of the following abnormalities:

1. Visceral obesity, defined as waist circumference ≥ 102 cm in men and ≥ 88 cm in women.

2. Fasting plasma glucose (≥100 mg/dl), or patient on hypoglycemic treatment.

3. Systolic blood pressure (SBP) ≥130 mmHg and/or diastolic blood pressure (DBP) ≥85 mmHg, or patient on antihypertensive treatment.

4. Serum triglycerides ≥ 150 mg/dl or patient on lipid lowering treatment and HDL-cholesterol < 40 mg/dl in men, and <50 mg/dl in women.

Exclusion criteria

Exclusion criteria for all groups were:

Chronic liver disease, chronic renal failure, patients on corticosteroid therapy, autoimmune disease and malignancy.

Methods

Patients were subjected to:

1. Carful history taking.

2. Full clinical examination including:

    -   Arterial Blood pressure: measurement using mercury sphygmomanometer.

    -   Body Mass Index (BMI): Body mass index was calculated based on formula; BMI = Weight (Kg) / Height (m^2).

    -   Waist circumference: measured at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest, using a stretch resistant tape.

The following laboratory investigations were done:

1. Fasting and 2 hours postprandial blood sugar.

2. Lipid profile (Total serum cholesterol, Triglyceride, HDL, Low Density Lipoprotein (LDL).

3. Fasting Serum insulin level.

4. Insulin resistance

5. Plasma adiponectin level

6. Serum uric acid

Five ml of fasting (12-16 hours) venous blood samples were taken from all subjects participating in the study and

divided into 2 parts: the 1st part was put in plain tube and left to clot and the blood was centrifuged at 3000xg for 15 minutes. Fasting blood glucose was determined immediately then the rest of the serum was stored at -20ºC for determination of lipid profile and insulin. The 2nd part was put in a tube containing EDTA and the plasma was separated by centrifugation at 3000xg for 15 minutes and stored at -20ºC for determination of adiponectin[16] and the kit was supplied from Genway Biotech Inc. (6777 Nancy Ridge Drive San Diego, CA, USA).

The determination of fasting blood glucose, serum uric acid and lipid profile were carried out on Dimension RxL Max analyzer (Siemens Healthcare GmbH-Henkestr. 127, 91052 Erlangen, Germany) by colorimetric techniques. Two hours post prandial a sample was taken for post prandial blood glucose determination on Dimension RxL Max analyzer.

Fasting serum insulin was determined using radio immuno assay.[17] Insulin resistance measured by (HOMA-IR) the homeostasis model assessment which was calculated using the following formula:[18]

$$\frac{Fasting\ glucose\left(\frac{mg}{dL}\right) \times Fasting\ insulin\left(\mu\frac{U}{mL}\right)}{405}$$

Statistical analysis

Data was analyzed by Microsoft Office 2010 (excel) and Statistical Package for Social Science (SPSS) version 16.

Parametric data was expressed as mean ± SD, and non parametric data was expressed as number and percentage of the total.

Comparing the mean ± SD of 2 groups was done using paired and unpaired student's t test

Measuring the mutual correspondence between two values was done using the Spearman correlation coefficient.

P value > 0.05 is considered non-significant
P value < 0.05 is considered significant
P value < 0.01 is considered highly significant.

RESULTS

Our study was conducted on 60 subjects, classified as 2 Groups:

Group I: included 40 MS patients (26 female and 14 male) their ages ranged between (44-60 years) with mean ± SD (51.90±5.48) and Group II: included 20 healthy volunteers served as controls (10 female and 10 male) their ages ranged between (40-60 years) with mean ± SD

(48.85±5.04) from medical department in Al-Zhraa university Hospital (from January 2014 to September 2014).

Comparison between results of the studied groups

The mean age has no significant difference in MS group compared with control group. There was highly significant increase in mean of waist circumference, BMI, SBP and DBP in MS group compared with control group (Table 1).

Table 1: Comparison between group I (MS) and group II (control) as regard demographic data.

| Parameters	group I	control	P value	Sig
No.	40	20		
Sex♂/♀	26 female & 14 male	10female &10male		
Age(years) (mean ± SD)	51.90±5.48	48.85±5.04	0.038	NS
Body Weight (kg)	87±13.83	60.40±6.23	0.000	HS
Height (cm)	164.65±6.74	166.50±5.36	0.254	NS
Waist circumference (cm)	115.20±13.80	86.90±6.10	0.000	HS
Body Mass Index (kg/m²)	32.62±4.09	22.22±1.66	0.000	HS
S.B.P. (mmHg)	139.5 ±19.34	109.5 ±9.99	0.000	HS
D.B.P. (mmHg)	85±7.51	73 ±8.01	0.000	HS

There were highly significant decrease in mean plasma adiponectin and highly significant increase in mean serum insulin, mean insulin resistance, mean fasting and mean postprandial blood glucose in MS group compared with control group (Table 2 and Figure 1 – 3).

Table 2: Comparison between group I (MS) and group II (control) as regard plasma adiponectin, serum insulin, insulin resistance, fasting and postprandial.

Parameters	Group I	control	P value	Sig
Adiponectin (µg/ ml)	5.40 ±1.09	9.26 ±1.09	0.000	HS
Serum insulin (µIU/ml)	29.69±7.25	10.09±2.22	0.000	HS
Insulin Resistance	9.42±3.40	2.16±0.55	0.000	HS
F.B.S. (mg/dl)	127.80 ±25.60	86.55±7.34	0.000	HS
Postprandial B.S (mg/dl)	176.65±47.91	116.45±8.19	0.000	HS
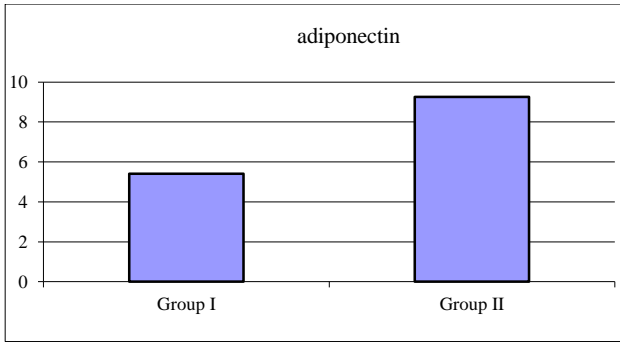
Figure 1: Comparison between MS Patients (Group 1) and Control (Group II) as regard to Plasma Adiponectin level.
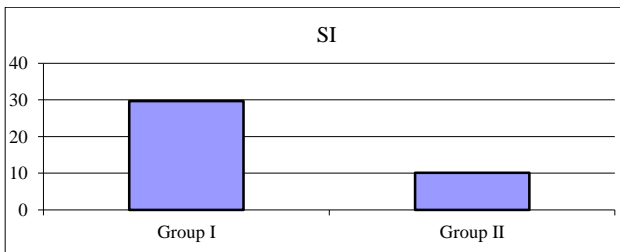
Figure 2: Comparison between MS Patients (Group 1) and Control (Group II) as regard to Serum Insulin level.
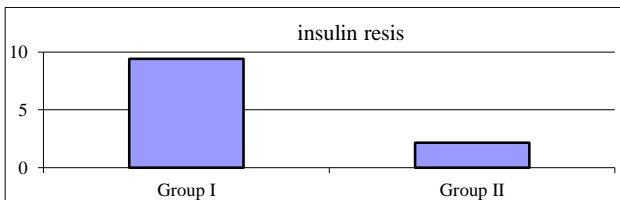
Figure 3: Comparison between MS Patients (Group 1) and Control (Group II) as regard to Insulin resistance.

There were highly significant increases in mean serum total cholesterol, mean serum triglyceride, mean serum LDL and mean serum uric acid and highly significant decrease in mean serum HDL in MS group compared with control group. Table 3.

Significant negative correlation was present between plasma adiponectin and age(r value -0.375), waist circumference(r value -0.757), body mass index (r value -0.521), systolic blood pressure(r value -0.518), diastolic blood pressure(r value -0.608), fasting blood sugar(r value -0.519), insulin resistance(r value -0.783), serum insulin(r value -0.906) and triglycerides(r value -0.764). Also there was significant positive correlation between plasma adiponectin and HDL (r value 0.681). Table 4.

Table 3: Comparison between group I (MS) and control as regard lipid profile and serum uric acid.

Parameters	group I	control	P value	Sig
L.D.L. (mg/dl)	129.16 ±27.3	97.18 ±14.99	0.000	HS
H.D.L. (mg/dl)	41.28±4.74	65.80±15.42	0.000	HS
S. cholesterol (mg/dl)	202.72 ±36.1	141.40±41.21	0.000	HS
TG. (mg/dl)	213.89±56.01	111.20±20.96	0.000	HS
S. uric acid(mg/dl)	6.02±1.11	4.77±1.21	0.000	HS

Table 4: Correlation between plasma Adiponectin and other parameters in patient group.

Parameters	Adiponectin R value	Significance
Age	-0.375	S
Body Weight	-0.211	NS
Height	-0.031	NS
Waist circumference)	-0.757	S
Body Mass Index	-0.521	S
S.B.P.	-0.518	S
D.B.P.	-0.608	S
Fasting blood sugar	-0.519	S
Post prandial blood sugar	-0.179	NS
Insulin resistance	-0.783	S
Serum insulin	-0.906	S
LDL	-0.007	NS
HDL	0.681	S
Cholesterol	-0.093	NS
Triglycerides	-0.764	S
Uric acid	0.002	NS

DISCUSSION

The number of patients with MS is expanding worldwide. The prevalence in developed and developing countries is comparable, ranging from 15.2% to 43.7%.[19,20]

Brooks et al., showed that a low level of circulating adiponectin may be used as a possible biomarker for MS.[21]

Reduced adiponectin levels seem to be not just a biomarker, but play a causal role in the development of IR, MS, T2DM, hypertension, dyslipidemia and atherosclerosis.[22,23] Hypoadiponectimia has already been associated with the risk of the MS in several

populations.[24-25] Therefore; measurement of adiponectin levels has been considered as being a useful biomarker or even a target for the management of the MS.

In our study, we measured plasma adiponectin levels in 40 subjects with MS and 20 subjects without MS served as control. The mean ± SD of plasma adiponectin was highly significant decreased in MS patients (5.40±1.09 µg/mL) in comparison to the control (9.26±1.09 µg/mL). (P value < 0.000).

In agreement with our results, Matsuzawa et al.[7] concluded that hypoadiponectinemia is observed with visceral fat accumulation, in cases of MS. Also hypoadiponectinemia together with the increase of TNF-α induced by the accumulation of visceral obesity might be a major background of vascular changes as well as metabolic disorders, including insulin resistance, which are the characteristics of metabolic syndrome.

Our results was also in agreement with Santaniemi et al.,[26] as they found that in both the sexes, the plasma adiponectin levels were lower in subjects with MS when compared with subjects with no diagnosis of MS (P<0.001), and Plasma adiponectin levels did not differ between subjects with National Cholesterol Education Program (ATPIII) and International Diabetes Federation-defined MS. They concluded that lower adiponectin levels were associated with different components of the MS and there was a trend towards decreasing adiponectin levels with an increasing number of components of MS in both the sexes. They also concluded that adiponectin levels correlate with most of the components of the MS.

Recently, Thanakun et al.,[27] in a study measured adiponectin level in both saliva and plasma among cases of MS, they found that Plasma adiponectin was decreased in patients with MS (p < .001). Interestingly they found significant correlation between salivary and plasma adiponectin (r = .211, p = .018).

Our study revealed that there was difference between the two studied groups as regard the other measured parameters, as it showed significant increase in body weight, body mass index, waist circumference, blood pressure (systolic and diastolic), fasting blood sugar, serum insulin and insulin resistance, serum cholesterol, triglycerides, LDL and serum uric acid in MS patients when they compared with control group, P<0.000. It also showed significant decrease in HDL level in MS patients in comparison to the control P<0.000.

Correlation of plasma adiponectin with the studied parameters in patient group revealed significant negative correlation between plasma adiponectin and waist circumference, body mass index, SBP, DBP, fasting blood sugar, insulin resistance, serum insulin, and triglycerides. Also significant positive correlation between plasma adiponectin and serum HDL was found.

This correlation results was in agreement with Santaniemi et al.,[26] as they found that adiponectin was correlated negatively with measures of body fat, fasting plasma glucose and triglycerides, and positively correlated with HDL-cholesterol.

The correlation results also was in agreement with Thanakun et al.,[27] as They concluded that increased triglyceride and waist circumference were associated with risk of having a low level of plasma adiponectin.

Taking into consideration the high world prevalence of obesity, MS, T2DM and CAD, the possibility of a defined and unique therapeutic target to simultaneously combat their development becomes increasingly important.[28] An interesting approach could be the development of adiponectin-targeted drugs chemically designed to induce the activation of its receptors and/or post receptor signaling pathways. Such a move may also be able to reverse "adiponectin resistance", which has been observed in both experimental and human research models.[29-30]

Correction of the patient's lifestyle helps to up regulate the plasma adiponectin levels. Low adiponectinemia in obese patients is raised via continued weight loss programs in both diabetic and nondiabetic individuals. Diet modifications, like intake of fish and omega-3 supplementation, also increase adiponectin levels. Some antidiabetic and cardiovascular drugs, like glitazones, glimepiride, and angiotensin converting enzyme inhibitors are also able to improve adiponectin concentration. Fibric acid derivatives, like fenofibrate, have been reported to enhance adiponectin levels.[31]

CONCLUSION

We conclude that plasma level of adiponectin was significantly low in patient with MS in comparison to the control, and adiponectin levels could help as a biomarker for cases of MS.

Recommendations

We recommend more similar researches to concentrate on the point related to the role of adiponectin not only as maker for diagnosis but also as a target for treatment of metabolic syndrome.

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