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Plasma Omentin-1 Levels Are Similar in Nondiabetic Metabolic Syndrome Patients and Healthy Subjects

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Abstract

Background: Omentin-1 which is mainly produced by omental adipose tissue and associated with insulin dependent glucose uptake is less in obese patients than lean subjects. The aims of this study were; first, to compare plasma omentin-1 levels between nondiabetic metabolic syndrome patients and healthy controls and second, to investigate the association of plasma omentin-1 with metabolic parameters.

Methods: According to International Diabetes Federation (IDF) criteria, 50 nondiabetic metabolic syndrome patients (23 male, 27 female) and 30 healthy control subjects (9 male, 21 female) were recruited in this study. After 12 hour-fasting, plasma omentin-1 levels were measured by enzyme-linked immunosorbent assay (ELISA) in venous blood samples.

Results: There was no difference in plasma omentin-1 levels between metabolic syndrome patients and control subjects (90.53 ± 23.14 ng/mL, 87.83 ± 17.10 ng/mL respectively; p = 0.55). In all subjects, plasma omentin-1 was positively correlated with triglyceride and negatively correlated with HDL-C (r = 0.24, p = 0.029; r = -0.62, p = 0.019, respectively).

Conclusions: The results of this study showed that although the plasma omentin-1 levels were correlated with high triglyceride and low HDL-C levels which are two of five metabolic syndrome's parameters, the plasma omentin-1 levels are similar in metabolic syndrome patients and healthy controls. To investigate the tissue omentin-1 levels in the same groups may enlighten the topic.

Introduction

Metabolic syndrome (MetS) is a cluster of cardiometabolic risk factors characterized by abdominal obesity, insulin resistance and chronic inflammation[1]. Environmental and genetic factors are forming the base of the metabolic syndrome. Sedentary life style, physical inactivity, imbalanced and over feeding result in metabolic syndrome in subjects with genetically vulnerable to insulin resistance [2, 3]. Even being clinically obese is not mandatory in the subjects with insulin resistance, there is generally abnormal fat distribution located at abdominal area. Many researchers claim that excessive visceral fat is more likely to be related with insulin resistance rather the other adipose tissue areas[4]. Visceral adipose tissue is especially more interesting than the subcutaneous adipose tissue, because recent researches showed that visceral fat is acting like an endocrine organ and it secretes varied adipokines which affect some steps in glucose and lipid metabolisms.

After the discovery of leptin and adiponectine, many other active substances secreted from visceral adipose tissue were detected [5-8]. Omentin (Intelectine)-1, which was firstly identified from the intestinal Paneth cells by Komiya, et al in 1998 and then from omental adipose tissue in 2004, is one of those adipokines [9, 10]. Omentin could be lately detected in plasma. Omentin is a protein made of 313 monoacids. It is mostly produced in stromal cells of adipose tissue and less in intestines, lungs, heart, kidneys and muscle tissue. *In vitro* recombinant omentin therapy increases insulin dependent glucose uptake in subcutaneous and visceral adipose tissue. Omentin-1 levels of obese subjects were found to be less than those of lean subjects [11]. In addition, omentin gene is established in 1q22-q23 loci. These loci were found to be related with type 2 diabetes in varied populations. That

Table 1. Demographic characteristics of the groups

	Group 1	Group 2	Group 3	p
Age (years)	45.96 ± 4.85	43.36 ± 7.18	43.27 ± 5.36	0.178
Weight (kg)	85.34 ± 14.9	84.8 ± 10.98	69.39 ± 14.5	<0.0001
BMI (kg/m^2)	31.29 ± 4.06	30.27 ± 4.08	26.01 ± 4.79	<0.0001
Waist circumference (cm)	105.08 ± 11.51	102.2 ± 9	84.83 ± 13.72	<0.0001
Hip cicumference (cm)	113.6 ± 7.07	110.32 ± 9.7	104.4 ± 10.97	0.002
Waist/Hip ratio	0.92 ± 0.07	0.93 ± 0.07	0.81 ± 0.07	<0.0001
Systolic blood pressure (mmHg)	132.4 ± 16.90	122.8 ± 15.68	116.67 ± 13.98	0.0027
Diastolic blood pressure (mmHg)	80 ± 9.13	76.2 ± 10.54	73.5 ± 11.68	0.085

Group 1: Prediabetic metabolic syndrome patients; Group 2: Normoglycemic metabolic syndrome patients; Group 3: Control subjects

relationship gives rise to thought that Omentin-1 may play a role in the development of type 2 diabetes. In our study, we aimed to investigate the changes in plasma Omentin-1 levels in nondiabetic subjects with metabolic syndrome and healthy controls who were categorized according to their glucose levels and waist circumferences.

Materials and Methods

Patients

The study was conducted between April 2010 and May 2010 in Internal Medicine Outpatient Clinic of Goztepe Training and Research Hospital with 80 nondiabetic participants (50 metabolic syndrome patients and 30 healthy controls; 42 fe-

male, 38 male; mean age 44.14 ± 5.9 years) who were more than 18 years old. Subjects with severe liver or kidney diseases, acute infection, type 1 or 2 diabetes, and subjects having diseases or using drugs that affect plasma glucose levels were excluded. Patients with metabolic syndrome were consecutively randomized according to their fasting plasma glucose (FPG) levels. All participants were categorized as Group 1 (Prediabetic patients with metabolic syndrome [FPG between 100 and 125 mg/dL, n = 25]), Group 2 (Normoglycemic patients with metabolic syndrome [FPG < 100 mg/dL, n = 25]) and Group 3 (Healthy controls who were age and gender equivalents of the other groups with FPG < 100 mg/dL, n = 30).

Local Ethics Committee approval was obtained for the research (Date: 06.04.2010, Decision No: 1/C). Written informed consents were taken from all participants according

Table 2. Basal biochemical parameters of the groups

	Group 1	Group 2	Group 3	p
Fasting plasma glucose (mg/dl)	108.92 ± 7.2	90.04 ± 7.76	91.67 ± 9.6	< 0.0001
Total cholesterol (mg/dl)	217.72 ± 52.42	209.72 ± 33.12	205.77 ± 36.48	0.79
Triglyceride (mg/dl)	213.64 ± 114.32	215.88 ± 87.3	94.07 ± 38.26	< 0.0001
HDL-C (mg/dl)	47.04 ± 10.46	41.76 ± 7.95	61 ± 14.18	< 0.0001
LDL-C (mg/dl)	150.04 ± 41.7	145.92 ± 26.88	134.07 ± 29.37	0.18
HbA1C (%)	5.85 ± 0.43	5.65 ± 0.29	5.44 ± 0.31	0.0001

Group 1: Prediabetic metabolic syndrome patients; Group 2: Normoglycemic metabolic syndrome patients; Group 3: Control subjects

Table 3. Plasma Omentin-1 levels of the groups

	Group 1	Group 2	Group 3
Plasma Omentin-1 (ng/mL)	95.98 ± 25.85	85.08 ± 19.05	87.83 ± 17.10

Group 1: Prediabetic metabolic syndrome patients; Group 2: Normoglycemic metabolic syndrome patients; Group 3: Control subjects

to 1964 Helsinki Declaration.

Flow of the study

Information on demographic characteristics and comorbid diseases of the patients were obtained. Blood pressure, height, weight, waist and hip circumferences of the patients were measured on physical examination by the same person. Body mass indexes (BMI) of the patients were calculated by using height and weight values. Clinical data and fasting biochemical parameters (fasting plasma glucose, total cholesterol, triglyceride, HDL-C, LDL-C, AST, ALT, creatinine, TSH and free T4) performed in the last week before the onset of the study were collected from the files of the subjects.

Biochemical parameters

Subjects accepted to participate in the study were invited to the clinic in the next morning after 12 hour fasting duration at 8:00 am. For measuring Omentin-1, venous blood samples were collected into plain tubes. Samples were centrifuged with 4000 cycle/min for 15 minutes and serum was separated and then stored at -70°C until analysis for a week. Omentin-1 was studied on human Omentin 1 enzyme-linked immunosorbent assay (ELISA) kit with Pasteur ELISA device (APO-TECH Corporation, Switzerland).

Statistics

All statistical analyses were made by using the software SPSS for Windows V15.0. Normality of distribution of variables was tested by Shapiro-Wilk and Kolmogorov-Smirnov tests. Subjects were compared for differences in anthropometric and biochemical data by two tailed Mann-Whitney U or Student's t test. Kruskal-Wallis test or Oneway ANOVA was performed for comparison of two or more independent

samples. Correlations between variables were determined by Pearson correlation test or Spearman's Rho. Data are expressed as means ± SD. A p value below 0.05 (two tailed) was considered to be statistically significant.

Results

Eighty subjects (42 female, 38 male) were categorized as Group 1 (Prediabetic patients with metabolic syndrome, n = 25), Group 2 (Normoglycemic patients with metabolic syndrome, n = 25) and Group 3 (Healthy controls who were age and gender equivalents of the other groups, n = 30). There were no differences in age and gender of three groups (p = 0.257, p = 0.101, respectively). The demographic and biochemical parameters of the groups can be seen in Tables 1 and 2.

Omentin-1 levels were similar between patients with metabolic syndrome and control subjects (90.53 ± 23.14 ng/mL, 87.83 ± 17.10 ng/mL, respectively; p = 0.55). There was also no difference in plasma Omentin-1 level among three groups (p = 0.16; Table 3).

Even the patients were categorized according to their BMI, plasma Omentin-1 levels were similar among three groups (p = 0.80; Table 4). There was no significant difference in plasma Omentin-1 levels of patients with FPG < 100 mg/dL and ≥ 100 mg/dL (p = 0.073; Fig. 1).

Plasma Omentin-1 level was positively correlated with triglyceride and negatively correlated with HDL-C (r = 0.24, p = 0.029; r = -0.62, p = 0.019, respectively; Fig. 2). In female subjects, plasma Omentin-1 was positively correlated with systolic blood pressure, FPG and HbA1c (r = 0.29, p = 0.046; r = 0.33, p = 0.023; r = 0.31, p = 0.032, respectively). However, there was only a negative correlation between plasma Omentin-1 and HDL-C in male subjects (r = 0.39, p = 0.027).

Table 4. Plasma Omentin-1 levels according to BMI groups

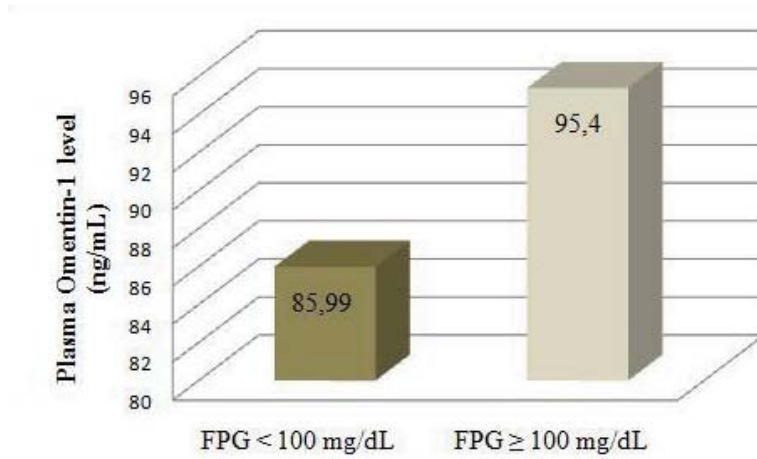|	BMI groups		
	< 25 kg/m^2	25-29.9 kg/m^2	≥ 30 kg/m^2
Plasma Omentin-1 (ng/mL)	86.18 ± 14.67	90.60 ± 23.62	89.82 ± 20.82

Figure 1. Plasma Omentin-1 levels according to fasting plasma glucose categories
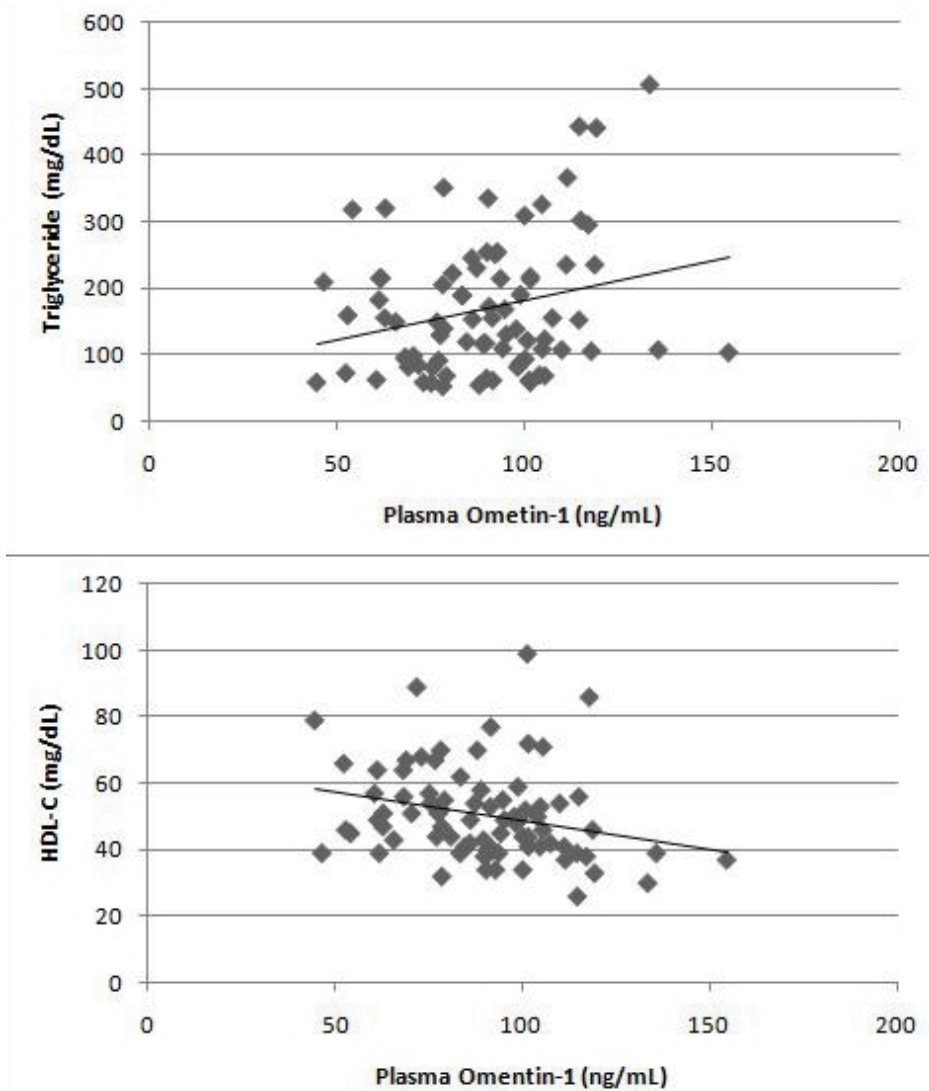

Figure 2. The correlation of plasma Omentin-1 with triglyceride and HDL-C in all patients

Discussion

Abdominal obesity is one of the dominant characteristics of metabolic syndrome. According to the results of the recent study, even there was a correlation between plasma Omentin-1 and triglyceride and HDL-C, plasma Omentin-1 levels were similar in patients with metabolic syndrome and healthy subjects regardless of their BMI.

Omentin is an adipokine that regulates insulin activity [12]. It increases insulin stimulated uptake of glucose and Akt phosphorylation in adipocytes. We found no difference between subjects with metabolic syndrome and healthy controls. On the other hand, visceral Omentin-1 and plasma Omentin levels in obese subjects were less than the lean subjects in the study of Souza Batista, et al [13]. However, unlike our study, subjects were not evaluated according to the presence of metabolic syndrome in this study, so they ignored some of the parameters of the metabolic syndrome and they also found that plasma Omentin-1 was positively correlated with HDL-C. They have used a part of the participants of Amish Family Diabetes Study [14] who were relatives to each other. Different than that study, our sample was randomly selected from whole population. One of the differences between studies was the technique used to determine Omentin-1 levels. De Souza Batista, et al used western blot technique, but we studied Omentin-1 with ELISA kit. Even the western blot technique can determine tiny levels of protein, it is obviously more difficult and less sensitive than ELISA technique to perform and also open to do errors.

Plasma Omentin-1 levels were similar between genders in our study. In the study of de Souza Batista, et al, plasma Omentin-1 was higher in women, on the other hand Moreno-Navarrete, et al [15] who used ELISA technique, found that plasma levels of Omentin-1 is higher in men. It shows us that plasma Omentin levels can be affected from other factors rather than gender and we can see differences among studies. On the other hand, the design of the study of Moreno-Navarrete, et al is different than ours. It is a weight loss study with less subjects (n = 35) and they only took obese people. Even they found negative correlation between plasma Omentin-1 and weight, BMI and waist circumference, there wasn't a correlation neither in obese (n = 32) nor in abdominal obese subjects (n = 63) in our study.

In another study, plasma Omentin-1 levels were evaluated in women with polycystic ovary syndrome (n = 20) which includes obesity and insulin resistance as important components [16]. Plasma Omentin-1 levels were less in women with polycystic ovary syndrome and there was a negative correlation between plasma Omentin-1 and BMI. According to our findings, there was no such a correlation even in female subjects (n = 42).

In a recent study of Pan, et al, they investigated plasma Omentin-1 levels (with ELISA technique) in subjects with normal glucose tolerance, impaired glucose regulation and treatment-naive newly diagnosed type 2 diabetes [17]. In subjects with either impaired glucose regulation or type 2 diabetes, plasma omentin-1 levels were less than the control group. Differently, plasma Omentin-1 levels were similar in prediabetic subjects and control group in our findings. However, we did not perform oral glucose tolerance test (OGTT) to determine glucose regulation and we evaluated the situation only according to FPG, so there are 13 normoglycemic, healthy subjects who do not carry all metabolic syndrome criteria although they have high waist circumference and 25 normoglycemic metabolic syndrome patients in our study. We should keep in mind that the results might be different if we performed OGTT.

It is the first study which investigated the relationship of metabolic syndrome parameters with plasma Omentin-1 in metabolic syndrome patients and healthy subjects aged between 18-65 years old. The limitations were that we did not perform OGTT or measure insulin levels. On the other hand, to take nondiabetic metabolic syndrome patients and to exclude subjects who were taking drugs affecting glucose metabolism were the strong sides of the study.

As a result, plasma Omentin-1 levels are similar among prediabetic and normoglycemic metabolic syndrome subjects and healthy controls. Metabolic syndrome includes many cardiovascular risk factors other than the abdominal obesity, so many conflicting variables can affect the results. It puts forth the necessity of future studies for consideration to enlighten the association of metabolic syndrome with Omentin-1.

Conflict of Interest

The authors declare no conflict of interest.

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