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Serum Adiponectin Levels are Inversely Correlated with Insulin Resistance in Obese Men with Type 2 Diabetes

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ABSTRACT

Background: Obesity is associated with several chronic conditions such as atherosclerosis and hypertension. All of these are risk factors that contribute to metabolic syndrome, which in turn can lead to cardiovascular disease and type 2 diabetes.
Objectives: In this study, we aimed to show the relationship between insulin resistance and serum levels of adiponectin, an anti-inflammatory adipokine, in obese men with type 2 diabetes.
Patients and Methods: Serum concentrations of adiponectin, insulin, and glucose were measured in 48 obese men (BMI > 29) with type 2 diabetes, aged 37 to 53 years and having a body weight of 80 to 100 kg. Insulin resistance index values were calculated using measurements of fasting glucose and insulin levels. Using Pearson's correlation test, the relationship of serum adiponectin concentration with insulin resistance, serum glucose, and insulin levels, was determined.
Results: The results showed a significant inverse relationship between adiponectin concentration and insulin resistance in type 2 diabetic patients ($p = 0.000$, $r = -0.59$). In addition, a significant relationship was observed between fasting glucose and adiponectin levels ($p = 0.005$). The relationship between insulin and adiponectin levels was not significant ($p = 0.196$).
Conclusions: Our findings indicate that the concentration of adiponectin, an anti-inflammatory and antidiabetic marker, is a precise insulin resistance predictor in obese patients with type 2 diabetes.

▸ *Implication for health policy/practice/research/medical education:*
Although it has been shown that the decline in serum adiponectin involves in development of insulin resistance and diabetes, there is discrepancy in this field. This study focusing on type 2 obese diabetic men indicates that serum adiponectin can be a predictor for insulin resistance. The results might be useful for research in the field of lipid metabolism, obesity and diabetes.

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1. Background

Several different adipokines are involved in the etiology and occurrence of insulin resistance, systemic inflammation, and atherosclerosis (1, 2). Some of these adipokines directly or indirectly affect insulin sensitivity and insulin secretion, and others regulate fat and glucose metabolism (3). The adipokine adiponectin, through its anti-diabetic and anti-atherogenic effects, plays an im-

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portant role in type 2 diabetics and metabolic syndrome patients (4, 5). Conversely, a decline in plasma or serum levels of adiponectin due to genetic or environmental factors has been implicated in the development of diabetes and insulin resistance syndrome (6). Unlike other adipokines such as TNF-α and resistin, which cause insulin resistance in obesity or type 2 diabetes, adiponectin expression is reduced in obese people and insulin-resistant animal models (7). Thus, reduction in plasma adiponectin levels reduces insulin sensitivity and prompts the onset of diabetes in such animal models (8).

Some studies have also indicated a relationship between adiponectin levels and body fat content in diabetic patients. A recent report showed an inverse relationship of serum adiponectin levels with fasting insulin levels and insulin resistance, and when BMI and percentage of body fat were reduced to normal levels in the studied patients, this relationship became insignificant (9). However, other studies suggest an inverse relationship between adiponectin and insulin resistance that is independent of body fat content (10, 11). Insulin has been shown to reduce adiponectin levels in both humans and animals (12). Cross-sectional and longitudinal studies have shown that lower levels of adiponectin are associated with increased incidence of type 2 diabetes (13, 14). The reduction of levels of this hormone also has been observed in other diseases related to insulin resistance, including coronary heart disease (15, 16) and hypertension (15, 17).

Recent scientific evidences support serum adiponectin concentration as a predictive index for type 2 diabetes (18). However, unlike the above findings, in a recent study no difference in adiponectin levels was observed between type 2 diabetic patients and healthy subjects (19). It was found that the fasting plasma adiponectin level and adiponectin gene expression in diabetic and non-diabetic patients was similar, and adiponectin gene expression was independent of the degree of obesity and insulin sensitivity (19). Another recent study showed that the expression of adiponectin receptors is similar in skeletal muscle of diabetic and non-diabetic men (20). Some studies also failed to find a significant relationship between adiponectin and fasting glucose levels (21). Furthermore, a study by Stigler et al. found no effect of adiponectin on insulin secretion from pancreatic beta cells (22). In another study, despite the identification of a direct relationship between adiponectin and HDL levels, no relationship was observed between this peptide hormone and other parameters such as body weight; TG, TC, and LDL-C levels; lipid profiles; insulin resistance; and anthropometric characteristics (23). The findings of Patty et al. also suggested that adiponectin is not a suitable predictor of insulin resistance (24).

2. Objectives

The above review demonstrates the contradiction in previous research results regarding the relationship between plasma adiponectin levels and insulin resistance. Hence, the present study was carried out to determine the relationship of adiponectin levels with insulin resistance, and glucose and insulin levels, in obese type 2 diabetic men.

3. Patients and Methods

The protocol of this study was approved by the Saveh Branch of Islamic Azad University, Iran. Forty-eight adult obese diabetic male patients (BMI ≥ 29) with an average age of 44 years and an average weight of 92 kg were selected at random to participate in this study. Written informed consent was obtained from all participants. The subjects were non-athletes and non-smokers. They did not have motion or orthopedic abnormalities. The minimum time since diagnosis with type 2 diabetes for these subjects was 5 years. Anthropometric parameters of studied subjects were initially measured and recorded at the Physiology Lab of Saveh Azad University, Iran. The height of participants was measured in the standing position without shoes, with shoulders against a wall. The weights of subjects were measured using a digital scale with a 100-g maximum error (Taiwan), with minimal clothing and without shoes. To calculate body mass index, the formula of body weight (kilograms) divided by height (meters) squared was used. The blood pressure of subjects was taken twice from their right arm after 10 minutes resting in a sitting position, according to standard procedures, and the average was recorded.

After these initial measurements, a blood sample was taken from each subject at 8–10 am. The subjects were asked to abstain from any sports or heavy physical activity for 2 days before blood sampling. To accurately measure metabolic variables, blood sampling was conducted after 12 to 14 hours overnight fasting. After 10 minutes complete rest in a sitting position, an 8-ml venous blood sample was taken from each individual's left hand vein. To measure fasting glucose levels, the standard enzymatic (glucose oxidase) method was used (Pars Azmoon, Iran). After centrifugation at 3000 rpm for 10 minutes, the separated serum was removed and maintained at -80°C until analysis. Adiponectin and insulin levels were measured using ELISA kits (Biovendor Company, Czech Republic, and Demeditec Diagnostics, Germany). The intra-assay and inter-assay coefficients of variation for the insulin ELISA were 2.60% and 2.88% respectively, and the sensitivity of the method was 1.76 μIU/ml. The intra-assay and inter-assay coefficients of variation for the adiponectin ELISA were 3.3% and 6.2% respectively, and the sensitivity of the method was 1–50 ng/ml. Insulin resistance for each individual was calculated by applying the fasting insulin and glucose concentrations to a standard insulin resistance assessment formula (25). After measuring and calculating the adiponectin, insulin, glucose, and insulin resistance variables for all subjects, the relationship

Table 1. Clinical and anthropometric profiles of the diabetic study subjects

	Mean ± SD	Range
Age, y	44 ± 9	37–53
Weight, kg	92 ± 12	80–100
Height, cm	173 ± 5	165–184
BMI, kg/m²	31 ± 3	29–35
Visceral fat, mm	13 ± 2.2	10–17
Systolic pressure, mmHg	130± 19	100–160
Diastolic pressure, mmHg	85 ± 9	70–100
Total cholesterol, mg/dl	211 ± 25	160–243
Triglycerides, mg/dl	180 ± 59	120–313
Low-density lipoprotein, mg/dl	125 ± 23	111–158
High-density lipoprotein, mg/dl	47 ± 5	40–51
Glucose, mg/dl	223 ± 46	165–296
HbA1c, %	9.06 ± 0.7	8.26–9.94
Insulin, μIU/ml	9.79 ± 3.01	6.40–16.50
Insulin resistance index value	5.11 ± 0.90	3.46–6.72
Adiponectin, μg/dl	5.3 ± 1.23	3.20–6.40

of each pair of variables was determined using Pearson's correlation test and SPSS statistical software (Version 13).

4. Results

The anthropometric, clinical, and biochemical profiles of the studied subjects are summarized in *Table 1*.

In the present study, fasting serum adiponectin levels and insulin resistance were determined in obese male patients with type 2 diabetes. The results of correlation analysis indicated a significant inverse relationship between adiponectin level and insulin resistance in these patients (r = -0.59, p = 0.000) *(Figure 1)*. Thus, a lower serum adiponectin level was associated with a higher level of insulin resistance. Although the results also showed that levels of adiponectin, an inflammatory marker, had a linear relationship with fasting insulin levels, this association was statistically insignificant (r = 0.45, p = 0.196). However, the correlation between serum adiponectin levels and fasting glucose levels was linear and significant (r = -0.67, p = 0.005).

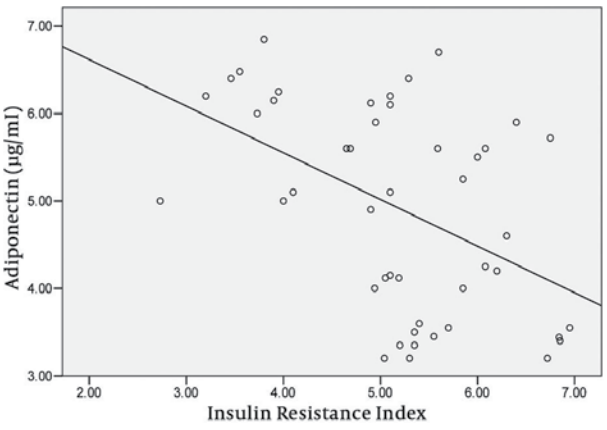

Figure 1. The Relationship between Serum Adiponectin Levels and Insulin Resistance in Obese Type 2 Diabetic Patients (r = -0.59, p = 0.000)

5. Discussion

Although various studies have demonstrated a significant relationship between serum adiponectin levels and insulin resistance in obese type 2 diabetic subjects and patients with other obesity-related diseases (7, 8, 16), other studies have failed to observe this relationship (19, 23, 24). This study, confirming some of the published findings, identified a significant inverse relationship between fasting serum adiponectin levels and insulin resistance in obese type 2 diabetic patients. Thus, consistent with the findings of previous reports, the findings of this study showed that adiponectin level can be used as a predictive index for insulin resistance in obese patients with type 2 diabetes.

The prevalence of obesity has increased dramatically in recent years and is associated with several chronic diseases, such as coronary artery disease, hypertension, metabolic syndrome, and, in particular, type 2 diabetes (26). Insulin resistance is one of the key features of these diseases (26). Adipose tissue, in addition to storing body fat reserves, secrets several cytokines and peptide hormones that play important roles in energy homeostasis and are implicated in some chronic diseases. Adiponectin, an anti-inflammatory adipokine, is abundantly secreted by adipose tissue and directly sensitizes body tissues to insulin. A decrease in levels of adiponectin due to genetic or hormonal factors has been strongly implicated in the development of insulin resistance, type 2 diabetes, meta-

bolic syndrome, and other chronic diseases that are associated with obesity (6). Surprisingly, although adipose tissue is the main source of adiponectin, research findings suggest that the blood level of adiponectin is reduced in obese or type 2 diabetics who have large reserves of fat tissue (7, 8). Reduction of adiponectin levels has been suggested to play a central role in the increased incidence of type 2 diabetes and insulin resistance syndrome (6). In this study, we showed that fasting adiponectin levels in type 2 diabetic patients has a significant inverse relationship with insulin resistance, indicating that reduced adiponectin in these patients is associated with increased insulin resistance. Therefore, based on the findings of this study along with other research findings, it can be stated that the serum adiponectin level is a precise predictive index of insulin resistance in patients with type 2 diabetes. Previous published findings have shown that a low adiponectin level is associated with greater insulin resistance and higher prevalence of type 2 diabetes (23). Adiponectin levels are reduced in obese animal models, which reduces insulin sensitivity and prompts type 2 diabetes onset (8). In addition, a significant inverse relationship between adiponectin and fasting glucose levels was observed in this study. This indicates that a decrease in adiponectin concentration is associated with an increase in fasting glucose levels, which is the main determinant of type 2 diabetes in obese patients. In this regard, Burg and colleagues showed that increasing plasma levels of adiponectin, by injection of recombinant adiponectin, resulted in a temporary reduction in plasma glucose levels due to inhibited expression of liver gluconeogenesis enzymes in diabetic mice (27). We have previously reported a lower level of serum adiponectin in diabetic women compared to healthy subjects (28). In addition, levels of HbA1c, an indicator of glycemic control, showed a negative correlation with serum adiponectin levels (28).

Research studies have shown that long-term treatment with adiponectin leads to improved insulin resistance in diabetic mice (27). Consistent with this, in the present study we observed a significant inverse relationship of adiponectin and its receptors with insulin resistance. These findings suggest that increasing levels of systemic adiponectin and its receptors could be used as a novel therapeutic treatment for insulin resistance, type 2 diabetes, and cardiovascular disorders that are associated with obesity (29).

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