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Relationship of Serum Adiponectin With Blood Lipids, HbA_1c, and hs-CRP in Type II Diabetic Postmenopausal Women

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Adipose tissue has been considered an important endocrine organ. Adiponectin secretes from adipose tissue and plays an important role in the regulation of glycemia, β-oxidation in muscle, and decreased insulin resistance in the liver. The objectives of this study were to compare the levels of adiponectin, hs-C-reactive protein (CRP), HbA1c, and blood lipids among diabetic and healthy postmenopausal women, and to determine the relationship between circulating adiponectin and development of type II diabetes. This case-control study was performed on 28 diabetic and 42 age-matched healthy women. All participants were postmenopausal. Serum adiponectin concentrations, serum triglycerides (TG), cholesterol, low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) concentrations were determined. Blood HbA1c and serum hs-CRP were also measured. Adiponectin levels were significantly decreased ($P<0.01$) in the diabetic patients as compared to normal control subjects. Adiponectin levels were negatively associated with hs-CRP, LDL-C, HbA1c, TG, and total cholesterol (TC). A positive correlation was observed between adiponectin and HDL-C. The obtained data indicate that diabetic women have lower adiponectin levels compared to healthy women. HbA1c as an indicator of glycemic control has a negative correlation with serum adiponectin. Adiponectin may play an important role in the pathogenesis of diabetes, and may be an independent predictor of the development of diabetes in women. J. Clin. Lab. Anal. 21:197–200, 2007.

Key words: adiponectin; hs-CRP; glycated hemoglobin

INTRODUCTION

Adipose tissue, in addition to its function as the major storage depot for lipids, plays active roles in normal metabolic homeostasis.

Adiponectin is a hormone produced solely by adipocytes and is a regulator of glucose and energy homeostasis (1). Adiponectin (also known as $ACRP_{30}$, aPM_1, AdipoQ, and GBP28) is an adipocyte-derived protein present in circulating plasma with range of 5–30 μg/mL in healthy humans (2). Adiponectin plays an important role in regulating glycemia, lipidemia, endothelial dysfunction, and the proinflammatory mechanism in humans (3). A low plasma adiponectin concentration is associated with a decrease in whole-body insulin sensitivity in humans (4–6), and was shown to be predictive of future development of diabetes in few studies (7–9). A diabetes susceptibility locus has been mapped to human chromosome 3q27, where the adiponectin gene is located. Thus both genetic and functional data suggest that adiponectin could be involved in the pathogenesis of type II diabetes (9). Adiponectin levels are negatively associated with obesity, hyperlipidemia, and insulin resistance (3). In

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addition, adiponectin appeared to have substantial anti-inflammatory properties in in vitro and in vivo animal studies (10). Furthermore, the roles of adiponectin in stimulating β-oxidation in muscle and decreasing insulin resistance in the liver indicate its possible involvement in the development of type II diabetes (11). Previous studies have not fully evaluated the potential association between adiponectin levels and circulating inflammatory marker and lipoprotein abnormalities among diabetic women (3). Jaleel et al. (12) determined serum adiponectin concentrations in diabetic type II postmenopausal women with and without the complications of ischemic heart disease. They showed that blood lipid concentrations increased but HDL decreased with a decrease in adiponectin concentration. However, they indicated that the mechanism by which adiponectin affects HDL is unknown. In this study we examined the correlation of serum adiponectin concentration with HbA1c and blood lipid profiles in diabetic and healthy postmenopausal women. Also, the correlation of hs-CRP as an inflammatory marker with serum adiponectin was investigated.

MATERIALS AND METHODS

Study Groups

The study included 28 diabetic women and 42 age-matched healthy women. To avoid the effect of hormones, such as estrogen, progesterone, and androgens, on the plasma levels of adiponectin, all selected diabetic and healthy subjects were postmenopausal. The study protocol was approved by the ethics committee of the Hamadan University of Medical Sciences. Written informed consent was obtained from each participant.

Diabetes Confirmation

In accordance with the criteria of the National Diabetes Data Group (13), confirmation of diabetes required at least one of following: 1) an elevated plasma glucose concentration (fasting plasma glucose ≥ 140 mg/dL, random plasma glucose ≥ 200 mg/dL) plus at least one classic symptom (excessive thirst, polyuria, weight loss, or hunger); 2) no symptom, but at least two elevated plasma glucose concentrations (by the above criteria) on different occasions; or 3) treatment with hypoglycemic medication (insulin or oral hypoglycemic agent). The participants provided information on their age, weight, height, and menopausal status. We calculated the body mass index (BMI) as the ratio of weight (in kilograms) to the square of height (in meters). Participants with cardiovascular disease (angina pectoris, myocardial infarction, coronary bypass surgery, coronary angioplasty, or stroke), other systemic diseases, or smoking were excluded.

Laboratory Methods

Venous blood was drawn from all patients and control subjects after overnight fasting. Serum samples were kept at –70°C for subsequent assay. Serum adiponectin was measured by means of a competitive enzyme-linked immunosorbent assay (ELISA) kit obtained from Biovendor Laboratory Medicine Inc. (Brno, Czech Republic). Serum C-reactive protein (CRP) was measured using an hs-CRP ELISA kit (DRG Instrument GmbH, Marburg, Germany) and a microplate reader (Rosys Anthos 2010, Wals, Austria). HbA1c was determined using the chromatographic-ion exchange method (Biosystem kit, Spain). Total cholesterol (TC) was measured using cholesterol esterase/cholesterol oxidase/peroxidase reactions. High-density lipoprotein cholesterol (HDL-C) was determined using the phosphotungstic acid/magnesium chloride precipitation method. A triglyceride (TG) assay was performed using lipase/glycerol kinase/glycerol-phosphate oxidase/peroxidase reactions. All lipid assays were carried out using colorimetric methods (Pars Azmun kits, Iran). Low-density lipoprotein cholesterol (LDL-C) was calculated by means of the Friedewald formula (14) from TC, HDL-C, and TG values. All biomarker assays were carried out on a UV-visible spectrophotometer (Spectronic Genesys 2; Spectronic Instruments, USA).

Statistical Analysis

Data are given as the mean $\pm$ SD. An unpaired Student's *t*-test was used to compare the obtained data between the two groups. $P<0.05$ was considered significant. Spearman correlation coefficient was used to evaluate the bivariate relationship between serum levels of adiponectin and lipoproteins, CRP, and HbA1c. All statistical analyses were performed using the SPSS 13.0 for Windows statistical package (SPSS, Chicago, IL).

RESULTS

The baseline characteristics are shown in Table 1. Serum adiponectin levels were significantly lower in diabetic women compared to healthy women ($P<0.01$).

As shown in Table 2, in diabetic women the correlation coefficient revealed that the serum levels of adiponectin were positively and strongly associated with HDL-C ($P<0.01$) and negatively correlated with TG ($P<0.01$).

Significant and negative associations were also found between adiponectin and CRP ($P=0.022$), HbA1c ($P=0.032$), and LDL-C ($P=0.005$). There was no

TABLE 1. Baseline characteristics of the healthy and diabetic women

Parameter	Healthy women (n = 42)	Diabetic women (n = 28)	*P* value
Adiponectin (microgram/mL)	10.29±1.93	7.29±1.42	<0.001
CRP (mg/liter)	3.20±1.60	9.65±2.02	<0.001
HbA_{1c} (%)	5.00±0.65	7.98±0.813	<0.001
Total cholesterol (mg/dL)	180±18.0	223.2±16	<0.001
HDL-C (mg/dL)	50.7±5.7	42.82±7.10	<0.01
LDL-C (mg/dL)	106.4±21.3	136.6±18.0	<0.01
Triglyceride (mg/dL)	126.2±24.8	218.9±33.1	<0.001
BMI (kg/m^2)	26.8±2.1	26.5±1.9	0.137
Age (years)	56.14±5.5	59.5±5.67	0.072

TABLE 2. Correlation between adiponectin and blood lipids, HbA1c, and CRP in healthy and diabetic women

	Correlation coefficient (r)	
Trait	Diabetic women (n = 28)	Healthy women (n = 42)
CRP	−0.431*	−0.83
HbA_{1c}	−0.407*	−0.451
Total cholesterol	−0.537*	−0.788
HDL-C	0.847*	0.813
LDL-C	−0.516*	−0.817
Triglyceride	−0.872*	−0.722
BMI	−0.792*	−0.650
Age	−0.26	−0.007

*$P<0.05$.

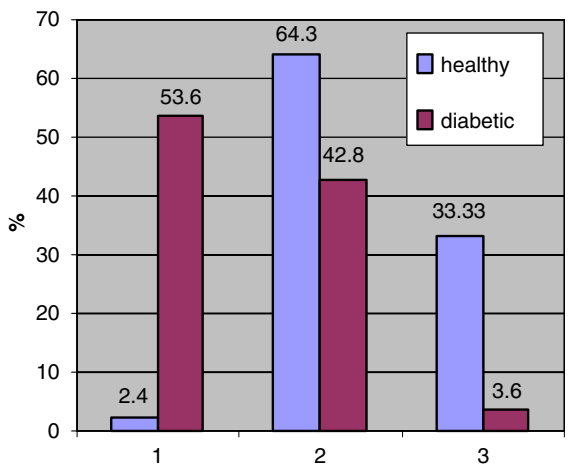

Fig. 1. Comparison of the distribution of subjects (%) in tertiles of adiponectin in diabetic and healthy women (tertile 1 = 3–6.9; tertile 2 = 7–10.9; tertile 3 = 11–14.9 μg/mL).

significant correlation between adiponectin and age ($P = 0.181$) in diabetic women, whereas the correlation was significant with BMI ($P<0.01$).

The percentage distribution of the diabetic and healthy women in tertiles of adiponectin is shown in Fig. 1. The tertile values of adiponectin were as follows: tertile 1 = 3–6.9; tertile 2 = 7–10.9; and tertile 3 = 11–14.9 μg/mL.

A higher percentage of diabetic women were in tertile 1 (53.6%) as compared to healthy women (2.4%).

DISCUSSION

This study shows that the serum adiponectin concentrations were lower in diabetic women as compared to healthy women. Similar reports were published by some investigators (15,16), whereas one study failed to observe this difference between diabetic and control subjects (17).

Daimon et al. (7) found a direct correlation between serum levels of adiponectin and age, whereas our data indicate that age does not influence serum adiponectin. Hotta et al. (18) reported the relationship between adiponectin and insulin resistance in rhesus monkeys. They showed that the plasma level of adiponectin began to decrease in the earlier stage of obesity, when insulin resistance and hyperinsulinemia were progressing (18). An accumulation of evidence from animal and human studies demonstrated that adiponectin plays an important role in the pathophysiology of diabetes and is a risk factor for cardiovascular disease (3). The modulation of insulin sensitivity or insulin resistance by adiponectin has been examined extensively (15,16,19). We found a significant and negative correlation between adiponectin and inflammatory marker and TG; however, Zurawska-Klis and Drzewoski (20) did not find any correlation between these factors. A genetic polymorphism in the adiponectin gene was identified as being associated with obesity and insulin resistance. The mechanism behind the influence of adiponectin on insulin sensitivity in humans is currently unclear (17). Adiponectin treatment reverses insulin resistance in animal models (21).

In summary, we found lower levels of adiponectin in diabetic women as compared to healthy women, and there was no correlation between adiponectin and age. HbA1c as an indicator of glycemic control showed a negative correlation with serum adiponectin. Low

adiponectin concentration may predict the development of diabetes and may have an important role in the pathogenesis of diabetes.

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