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ORIGINAL ARTICLE

Variation of Adiponectin Levels in Normal and Obese subjects: Possible Correlation with Lipid Profiles

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Data available suggests that Adiponectin, an adipocyte–derived peptide, is associated with adiposity and could effect the regulation of glucose and lipid metabolism in humans. The aim of this study was to evaluate the association between serum adiponectin concentrations and anthropometric indices and lipid profiles among Iranian women with different grades of obesity. Materials and Methods: In this analytical descriptive study of 157 non-diabetic women (33 normal weight, BMI< 25 kg/m2 and 124 overweight and obese, BMI≥ 25kg/m2), serum adiponectin and leptin levels were measured using an enzyme-linked immunoassay. Fasting glucose and lipid profile levels determined by the glucose oxidize and enzymatic methods, respectively. Results: Mean serum adiponectin concentrationsignificantly decreased with obesity (p<0.05). Although adiponectin showed a significant negative correlation with BMI (r=-0.321), it was correlated with serum leptin (r=-0.139), glucose (r=0.259), LDL-C (r=-0.125), TGs (r=-0.210) levels, TSF (r=-0.145), WHR (r=-0.159), and positively with serum HDL-C concentration (r=0.218) in all subjects (p<0.05). Results of multiple regression analyses showed that adiponectin as a dependent variable had a significant correlation with BMI (ß=-0.605, P=0.017), waist circumference (ß=0.624,p=0.029),WHR(ß=-0.251, p=0.048), frame (ß=0.260, p=0.018), TC/HDL-C ratio (ß=-0.1.309, p=0.040) and LDL/HDL ratio (ß=-1.343, p=0.007) and changes in waist size had a significant effect on serum adiponectin levels. Conclusion: Our results suggested that adiponectin had an inverse correlation with adiposity indices and unfavorable lipid profiles, and that variation of waist circumference mostly affected Iranian women.

Key Words: Adiponectin, BMI, Obese, Lipid profile, Anthropometric indices

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Introduction

Obesity, defined as increase in the size of fat mass, is a major health problem in western and developing countries,[1] with many complications and is associated with the development of many diseases such as type 2 diabetes mellitus, hypertension and cardiovascular diseases.[2] Adipose tissue products many bioactive peptides 'adipocytokines' such as leptin and adiponectin. Adiponectin also called ARCP30, AdipoQ, and apM1, is a 247–amino acid peptide hormone, discovered in 1995, [3, 4] and is predominately expressed by differentiated adipocytes and other cell types that may express low levels of adiponectin.[5]Adiponectin is an anti-hyperglycemic,

anti-atherogenic and anti-inflammatory peptide, [6,7] abundant in human plasma with concentrations ranging from 5 to 30mg/mL, accounting for about 0.01% of total plasma protein, three times higher than concentrations of most other adipose tissue-derived hormones.[8] In a study of normal and obese subjects, plasma adiponectin was negatively correlated not only with body mass index (BMI), but also with serum leptin concentration.[9] Plasma adiponectin levels are lower in individuals with central obesity than those with peripheral or general obesity. Evidence suggests that high serum adiponectin concentrations are associated with high HDL-C concentration. In contrast, data on the relationship of adiponectin and unfavorable lipid levels has been inconsistent.[10-13]

Most previous studies focused on comparing serum adiponectin and leptin levels of normal individuals and patients, e.g. as in diabetic and non-diabetic subjects). In addition, there are few studies which assess these relationships in different grades of obesity. The inverse relationship of adiponectin serum level has been shown in diseases such as type 2 diabetes and cardiovascular diseases. Thus, its reduction could be considered as a contributing risk factor for development of the diseases mentioned.[14] Considering the aforementioned, this current study aimed at evaluating correlations between serum levels of adiponectin and the anthropometric indices and lipid profiles in Iranian women with normal weight and different grades of obesity.

Materials and methods

Study Subjects: In an analytical-descriptive study, conducted between April 2008 and September 2009, 159 non diabetic women, from the northwest of Iran, aged 17-45 years, were randomly selected. Informed consent was obtained from all subjects and the protocol was reviewed and approved by the institutional ethics committee of the Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Individuals were asked to complete questionnaires on anthropometric characteristics, smoking, alcohol consumption, personal history of disease and use of medications.

Anthropometric Measurements: Anthropometric measurements were taken before breakfast, with subjects wearing light clothing without shoes. All subjects were classified into 5 groups based on BMI (WHO, Rep 2000), [15] which was calculated as weight (kg) divided by square of height (m^2). Subjects included 33 women as normal weight (BMI: 18.9-24.9 kg/m^2) and 126 women with different grades of obesity; 34 overweight, BMI 24.9–29.9 kg/m^2, 35 obese grade I, BMI: 29.9–34.9 kg/m^2, and 30 obese grade II, BMI: 34.9–39.9 kg/m^2 and 27 obese grade III women as BMI≥40 kg/m^2. Height was measured with a wall-mounted stadiometer (Kaveh.Co, Tehran, Iran) with an accuracy of 0.5 cm, and weight, on a digital glass scale (GES, 07-USA), with an accuracy of 0.1 kg. Waist and hip circumferences were taken with a soft tape in the standing position following normal expiration, waist being defined as the narrowest circumference between the costal margin and the iliac crest and hip as the widest circumference between the waist and the thigh. Waist to hip ratio (WHR) was calculated as waist circumference divided by hip circumference. Frame was measured by height (cm) divided to right hand wrist circumference (cm). Triceps skin fold thickness (TSF) was measured with an accuracy of 0.1mm using the Saehan skin fold caliper (SH5020, Korea).

Blood Collection: Blood for venous blood samples (10mL), collected from all individuals, after an overnight 12 hour fast, was drawn from the antecubital vein between 8:30 and 9:30 am. Sera, separated immediately after centrifugation with 3000 x g for 10 min, were stored at -70 C until biochemical analyses were performed.

Biochemical Analysis: Fasting blood glucose concentration was measured by glucose oxidize method (glucose kit, Pars Azmun, Cat. no. 1500017, Tehran, Iran). The intra- and inter-assay coefficients of variation were 1.74 and 1.19%, respectively. Serum lipid profiles including total cholesterol (TC; Cat. no. 1500010), triglycerides (TGs; Cat. no; 1500032), and high density lipoprotein-cholesterol (HDL-C; Cat. no. 1500034), using commercially available kits (Pars Azmun Co. Tehran, Iran) were measured by the Automatic analyzer (Abbott Alyson 300, USA). Low-density lipoprotein-cholesterol (LDL-C) was estimated indirectly using Friedewald's formula for subjects with a serum TG concentration<400mg/dL; LDL-C= total cholesterol (TC) – (HDL-C) - [triglycerides (TG) ÷ 5].

Serum adiponectin concentration was measured by the immunoassay method using a commercially human adiponectin ELISA kit (BioVendor GmbH, Heidelberg, Germany; Cat. no. RD191023100). The lowest detectable level of serum adiponectin was 0.5 µg/mL and intra- and inter-assay coefficients of variation were 4.2% and 9.5%, respectively. Serum leptin levels were measured by the immunoassay method using the BioVendor human leptin ELISA kit (BioVendor GmbH, Heidelberg,Germany;Cat no;RD191001100). The lowest detectable level of serum leptin was 0.2 ng/mL and intra- and inter -assay coefficients of variation were 4.2 and 6.7%, respectively.

Statistical analysis

Data, expressed as Mean ± SD statistics, were analyzed using SPSS 14.0. We used the analysis of variance (ANOVA) test to determine the overall differences between anthropometric and biochemical measures among groups. Correlations of adiponectin with other parameters were evaluated by the bivariate Pearson correlation coefficient test. Multiple Linear regression analysis was used to assess the effects of other parameters on adiponectin. $P<0.05$ was considered statistically significant.

Table 1. Anthropometric indices in normal weight and different grades of obesity

Variants	Normal n=33	Overweight n=34	Obese I n=35	Obese II n=30	Obese III n=27
Age (yrs)†	24.60±7.2	29.58±10.5	35.94±8.7	35.60±9.0	36.30±8.7
Height (cm)†	160.64±5.9	159.51±6.2	158.60±4.0	156±6.4	154.46±4.4
Weight (kg) †	57.04±7.5	70.55±6.3	82.10±7.0	90.10±8.9	101.50±5.5
BMI (Kg/m^2)†	21.99±2.3	27.68±1.3	32.37±1.3	36.77±1.2	42.58±2.5
WC (cm)†	73.63±8.0	89.82±8.8	101.43±9.6	106.35±10.1	122.30±7.2
HC (cm) †	90.63±10.6	102.94±4.8	111.82±6.4	118.52±7.3	129.50±5.8
WHR †	0.82±0.1	0.87±0.8	0.90±0.1	0.92 ±0.1	0.94±0.1
MAC (cm) †	25.84±2.6	29.86±1.7	31.42±2.1	32.95±3.0	36.00±2.5
Chest (cm) †	84.25±2.6	95.76±5.6	105.27±5.0	110.10±5.8	122.40±5.0
TSF (mm) †	15.81±4.5	22.22±4.9	27.21±4.2	28.36±5.1	33.80±3.7
Frame†	10.53±0.4	10.47±0.5	9.74±0.6	9.42±0.7	9.20±0.5

BMI (body mass index); WC (waist circumference) and HC (hip circumference); Waist-to-hip, ratio (WHR); Mid arm circumference (MAC); Triceps skin fold thickness (TSF); Data are presented as (mean ± SD),
† $P<0.05$: significant

Results

Anthropometric indices in normal weight and different grades of obesity are presented in Table 1. There were statistically significant differences in height, weight, waist circumference, hip circumference, WHR, wrist circumference and TSF among groups ($p<0.05$), whereas mean age showed no increase between groups. Mean biochemical parameters in normal weight and different grades of obese women are shown in Table 2. Serum levels of adiponectin, leptin, glucose, TC, TGs, HDL-C and LDL-C were significantly different among groups ($p<0.05$).

Table 2. Biochemical parameters in normal weight and different grades of obesity

Groups Variants	Normal n = 33	Overweight n=34	Obese I n=35	Obese II n=30	Obese III n=27
Adiponectin(µg/mL)†	25.55±6.1	23.28 ±5.6	22.09± 5.1	21.22± 6.0	19.55± 4.9
Leptin(ng/mL) †	21.47±16.9	32.80±17.8	43.38±15.7	45.15±13.2	55.28±21.5
Glucose(mg/dL) †	72.84±13.2	76.70±7.8	86.31±13.4	88.66±10.3	92.11±23.1
TC (mg/dL) †	168.69±31.5	202.64±33.2	212.94±33.4	217.46±34.3	223.33±31.5
TG (mg/dL) †	85.69±45.4	130.11±45.8	145.68±42.9	155.40±44.8	184.96±60.9
HDL-C(mg/dL) †	53.42±9.6	46.41±9.6	42.27±9.6	39.24±5.3	34.77±7.2
LDL-C(mg/dL) †	99.86± 30.9	129.95±30.4	141.5±33.5	144.42±35.4	148.34±30.7
HDL-C/LDL-C Ratio†	0.38±0.1	0.33±0.2	0.32±0.1	0.31±0.1	0.27 ± 0.1

Triglycerides (TGs); Total cholesterol (TC); High density lipoprotein-cholesterol (HDL-C); Low-density lipoprotein-cholesterol (LDL-C); Data are presented as mean ± SD, † $P< 0.05$: significant

Table 3. Bivariate Pearson correlation of serum adiponectin with lipid parameters and anthropometric indices in subjects

Variables	Correlation with Adiponectin	
	R	p value
TC (mg/dL)	-0.188	0.001
TG (mg/dL)	-0.210	0.003
HDL (mg/dL)	0.218	0.008
LDL (mg/dL)	-0.125	0.050
LDL/HDL Ratio	-0.159	0.050
Glucose(mg/dL)	-0.292	0.001
Leptin (ng/mL)	-0.136	0.050
Height(cm)	0.186	NS
Weight (kg)	-0.139	0.045
TSF (mm)	-0.145	0.040
BMI (kg/m2)	-0.321	0.001
Frame	-0.297	NS
Chest (cm)	-0.153	0.048
Waist (cm)	-0.148	0.040
hip (cm)	-0.066	0.039
WHR	-0.159	0.041
MAC (cm)	-0.136	0.044

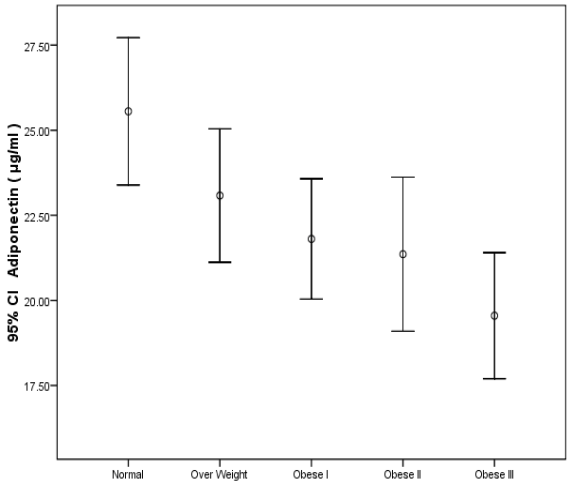

Figure 1. Mean serum adiponectin concentrations in women with normal weight and in different grades of obesity

In normal weight subjects, mean serum adiponectin was significantly (1.2-fold) higher than in obese ones (Fig. 1). In contrast, there was a 2-fold increase of serum leptin concentrations in obese compared to normal

subjects. Mean concentrations of LDL-C, TC and TGs were about 3, 1.3 and 1.8-fold higher in obese than normal weight subjects, respectively. In contrast, mean serum HDL-C level was 1.2-fold higher in normal weight than in obese women.

The Pearson correlation coefficient test was used to determine correlations between serum adiponectin levels and anthropometric characteristics and biochemical variables among groups (Table 3). Results indicated an inverse correlation between adiponectin and BMI (r = -0.321, P = 0.001); there were correlations between adiponectin levels and serum leptin (r = -0.136, P = 0.050), glucose (r = -0.292, P = 0.001), LDL-C (r = -0.125, P = 0.050), TG (r = -0.210, P = 0.003) levels, TSF (r = -0.145, P = 0.040), WHR (r = -0.159, P = 0.041) (Table 3); a significant positive correlation was found between serum adiponectin and HDL-C levels (r = 0.218, P = 0.008) (Fig. 2.a), and inverse correlations were observed with total cholesterol (r = -0.188, P = 0.001) (Fig. 2.b) and triglycerides (r = -0.210, P = 0.003) (Fig. 2.c).

Results of multiple linear regression analyses between adiponectin and the other parameters studied, indicated that adiponectin, as a dependent variable, had a significant correlation with BMI (ß = -0.605, P = 0.017), waist circumference (ß=0.624, P = 0.029), WHR (ß =-0.251, P=0.048), frame (ß=0.260, P=0.018), TC/HDL-C ratio (ß = -0.1.309, P=0.040) and LDL/HDL ratio (ß = -1.343, P=0.007) in all subjects (P<0.05). Waist circumference as an independent variable was seen to have the most effect on adiponectin levels (ß=0.624).

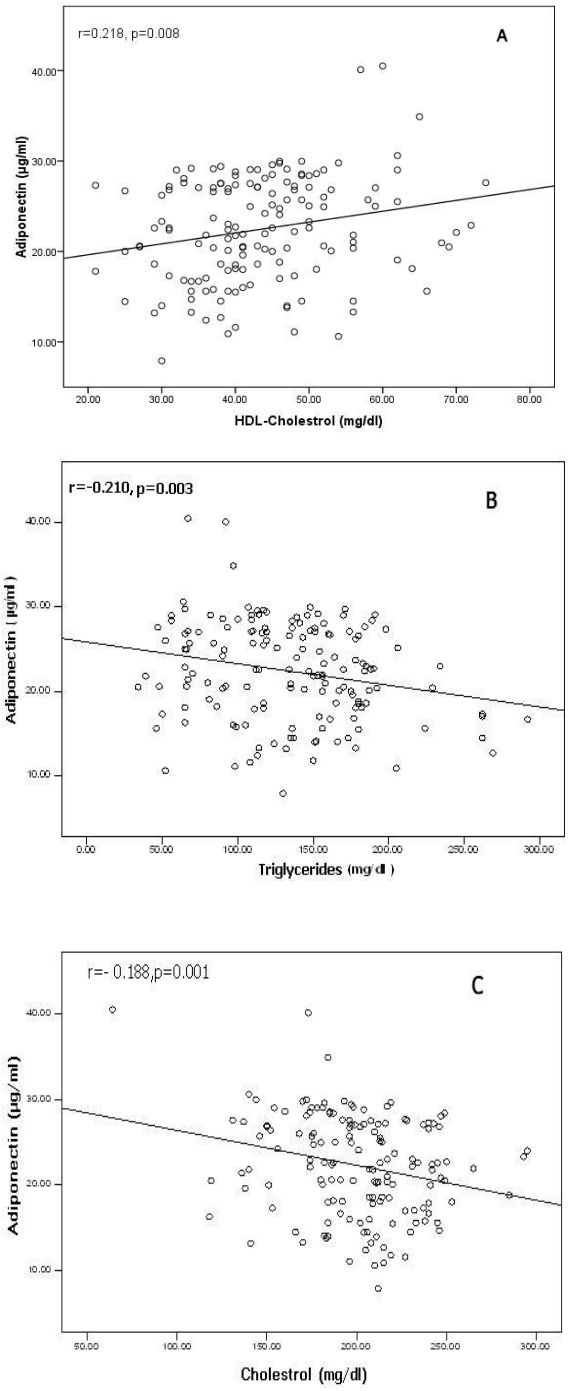

Figure2.Relationship between serum adiponectin and HDL-C levels (A), serum adiponectin and cholesterol levels (B) and, serum adiponectin and triglycerides (C) in women with normal weight and different grades of obesity

Discussion

The current research was different in that it studied the correlation of serum adiponectin level with anthropometric indices and lipid profiles in non-diabetic women with different grades of obesity. In contrast, many studies have investigated these relationships in healthy and unhealthy individuals, but there are relatively few studies on the different

grades of obesity. Reduction in adiponectin levels in obese subjects may be correlated with onset of many common diseases such as diabetes type 2, cardiovascular diseases and other obesity related complications.[14] Our results demonstrate that serum adiponectin levels, contrary to leptin, decreased with decreases in obesity and adiposity indices. A cross-sectional study in Italy of non-diabetic subjects, indicated plasma adiponectin was significantly higher in non-obese than in obese individuals. However, adiponectin contrary to leptin, had a negative correlation with BMI, waist circumference; waist-to-hip ratio (WHR).[16] A study in Taiwan of overweight and obese subjects reported hypoadiponectinemia in obese subjects; also, adiponectin levels were negatively correlated with BMI and WHR.[17] Another study of healthy non-diabetic adolescents indicated that plasma adiponectin was negatively related to BMI, fat mass, waist circumference and WHR.[18] Additionally, previous studies in Japanese individuals demonstrated plasma adiponectin concentration was negatively correlated with BMI and hence lower in obese, than in lean subjects;[19-21] our results, in agreement with this finding, demonstrated that plasma adiponectin concentrations are inversely related to fat distribution indices (waist, hip circumferences and WHR) as the measures of adiposity. Therefore, our results also confirm that adiponectin is the only adipose-specific protein known to date, that, despite its exclusive production in white adipose tissue, is negatively correlated with obesity, findings similar to those in rodents where the murine homologue of adiponectin-adipoQ is also down-regulated in obesity.[22] The adiponectin gene is predominantly expressed in adipose tissue and its expression decreases in obese diabetic(db/db)murrain models.[23] Results of across-sectional study on the Indian-Caucasian women and men showed that there was an inverse correlation between adiponectin and BMI and body fat mass.[24] Results of other studies supported an inverse correlation between serum adiponectin and serum leptin levels,[16,25,26] results similar to ours. The molecular basis of down-regulation of adiponectin gene expression and its secretion from adipose tissue in non-diabetic obese individuals has not been completely understood. However, some researchers suggest that there is inhibition feedback process in increasing of body fat mass and increasing of other cytokines.[27] Others indicate the decrease in half-time of adiponectin molecules in blood circulation of obese subjects and increase in molecule degradation.[28] In obese subjects, with increase of BMI and body fat mass, adiponectin mRNA expression in adipose tissue is decreased, and low serum adiponectin levels are related to a higher risk of diabetes.[29] Although adiponectin is secreted mainly from adipose tissue, its levels are paradoxically lower in obese than in lean humans which is in contrast to most other adipocytokines, whose levels are increased in obesity in proportion to increasing total body fat mass. It is possible that although adiponectin expression is activated during adipogenesis, a feedback inhibition in its production may occur during development of fat mass due to increase in the production of other adipocytokines. In addition, adipocytokines such as TNF-α may decrease adipocyte expression and secretion of adiponectin.[30] It has been suggested that with increasing grades of obesity, there may be a decrease in the metabolic functioning of adipocytes, along with hypertrophy and/or aging of these cells.[31]

Other our results showed that adiponectin was inversely correlated with leptin, and unfavorable lipid profiles. Baratta R et al [32] indicated that adiponectin, contrary to leptin, was negatively correlated with fasting plasma glucose, TC/HDL-C ratio and triglycerides, whereas it was positively correlated with HDL-C.[16] Yang WS et al[17], in a study in Korea, showed that obese subjects had elevated fasting plasma glucose and triglyceride levels, but low levels of high-density lipoprotein-cholesterol. Other studies report that serum adiponectin correlates negatively with serum triglycerides and LDL-C, and positive-

ly with HDL-C levels in obese subjects.[33-34] Our results, in agreement with these findings, showed that low adiponectin concentrations were associated with unfavorable lipid profiles and low concentrations of HDL-C. Regarding the relationship between adiponectin and HDL-C, it has been suggested that the possible mechanisms may partially be explained with the proxisome proliferate–activated receptor-a (PPAR-α), which affects the genes, associated with HDL-C metabolism. Adiponectin stimulated PPR-α ligand activates in liver and skeletal muscles, which results in the increased synthesis of HDL-C.[35] Additionally, a recent study showed that adiponectin had a significant negative correlation with fasting glucose levels in all subjects. Results of two studies on the non-diabetic men and women by Mohlig M et al[36] and Brame LA et al[37] indicated that adiponectin levels were inversely associated with fasting glucose. It is speculated that adiponectin facilitates glucose uptake by increasing glucose transporter-4 expression and its translocation also stimulates glucose utilization and fatty acid oxidation in skeletal muscles and in the liver which suppresses gluconeogenesis in the liver.[38, 39]

Results of multiple regression analyses show that waist size had the most effects on serum adiponectin As previous studies indicate, waist circumference is an indicator of body fat distribution, and with increasing degrees of obesity or fat mass, levels of adiponectin tend to decrease.[18] Therefore, decrease in waist size, and increased adiponectin concentration may help lower the prevalence of obesity and its complications.

To conclude, the results of this study show that serum adiponectin levels decreased with obesity and were accompanied by increases in anthropometric indices, serum leptin and glucose levels and unfavorable lipid parameters. It is recommended that adiponectin levels be measured routinely in medical laboratories and abnormal levels be considered as risk factors for obesity-related diseases. However, further experimental studies on the in vitro and in vivo effects of lipid profiles and other clinical parameters on adiponectin are needed to clarify the role of adiponectin on the parameters of obesity parameters and related complications.

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References

1. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW Jr. Body mass index and mortality in a prospective cohort of U.S. adults. N Engl J Med 1999; 341: 1097-105.
2. Yang W, Kelly T, He J. Genetic epidemiology of obesity. Epidemiol Rev 2007; 29: 49-61.
3. Trujillo ME, Scherer PE. Adiponectin-journey from an adipocyte secretory protein to biomarker of the metabolic syndrome. J Intern Med 2005; 257:167-75.
4. Hu E, Liang P, Spiegelman BM. AdipoQ is a novel adipose-specific gene dysregulated in obesity. J Biol Chem 1996; 271: 10697-703.
5. Nakano Y, Tobe T, Choi-Miura NH, Mazda T, Tomita M. Isolation and characterization of GBP28, a novel gelatin-binding protein purified from human plasma. J Biochem 1996; 1 20 : 803-12.
6. Otero M, Lago R, Gomez R, Lago F, Dieguez C, Gómez-Reino JJ, et al. Changes in plasma levels of fat-derived hormones adiponectin, leptin, resistin and visfatin in patients with rheumatoid arthritis. Ann Rheum Dis 2006: 65: 1198-201.
7. Senolt L, Pavelka K, Housa D, Haluzík M. Increased adiponectin is negatively linked to the local inflammatory process in patients with

rheumatoid arthritis. Cytokine 2006: 35: 247-52.
8. Matsubara M, Maruoka S, Katayose S. Inverse relationship between plasma adiponectin and leptin concentrations in normal-weight and obese women. Eur J Endocrinol 2002; 147: 173-80.
9. Chan DC, Watts GF, Ng TW, Uchida Y, Sakai N, Yamashita S, et al. Adiponectin and other adipocytokines as predictors of markers of triglyceride-rich lipoprotein metabolism. Clin Chem 2005; 51: 578-85.
10. Tschritter O, Fritsche A, Thamer C, Haap M, Shirkavand F, Rahe S, et al. Plasma adiponectin concentrations predict insulin sensitivity of both glucose and lipid metabolism. Diabetes 2003; 52: 239-43.
11. Baratta R, Amato S, Degano C, Farina MG, Patanè G, Vigneri R, et al. Adiponectin relationship with lipid metabolism is independent of body fat mass: evidence from both cross-sectional and intervention studies. J Clin Endocrinol Metab 2004; 89: 2665-671.
12. Matsubara M, Maruoka S, Katayose S .Decreased plasma adiponectin concentrations in women with dyslipidemia. J Clin Endocrinol Metab 2002; 87: 2764-769.
13. Kazumi T, Kawaguchi A, Hirano T, Yoshino G. Serum adiponectin is associated with high-density lipoprotein cholesterol, triglycerides, and low-density lipoprotein particle size in young healthy men. Metab 2004; 53: 589-93.
14. Díez JJ, Iglesias P. The role of the novel adipocyte-derived hormone adiponectin in human disease. Eur J Endocrinol 2003; 148: 293-300.
15. World Health Organization. Obesity: preventing and managing the global epidemic. Report of a WHO Consultation. World Health Organ Tech Rep Ser 2000; 89: 1-253.
16. Baratta R, Amato S, Degano C, Farina MG, Patanè G, Vigneri R, et al. Adiponectin relationship with lipid metabolism is independent of body fat mass: evidence from both cross-sectional and intervention studies. J Clin Endocrinol Metab 2004; 89: 2665-71.
17. Yang WS, Lee WJ, Funahashi T, Tanaka S, Matsuzawa Y, Chao CL, et al. Plasma adiponectin levels in overweight and obese Asians. Obes Res 2002; 10: 1104-10.
18. Huang KC, Lue BH, Yen RF, Shen CG, Ho SR, Tai TY, Yang WS. Plasma adiponectin levels and metabolic factors in non-diabetic adolescents. Obes Res 2004; 12 (1):119-124.
19. Ouchi N, Kihara S, Arita Y, Maeda K, Kuriyama H, Okamoto Y, et al. Novel modulator for endothelial adhesion molecules: adipocyte-derived plasma protein adiponectin. Circulation 1999; 100: 2473-6.
20. Arita Y, Kihara S, Ouchi N, Takahashi M, Maeda K, Miyagawa J, et al. Paradoxical decrease of an adipose-specific protein, adiponectin, in obesity. Biochem Biophys Res Commun 1999; 257: 79-83.
21. Hotta K, Funahashi T, Arita Y, Takahashi M, Matsuda M, Okamoto Y, et al. Plasma concentrations of a novel, adipose-specific protein, adiponectin, in type 2 diabetic patients. Arterioscler Thromb Vasc Biol 2000; 20: 1595-9.
22. Hu E, Liang P, Spiegelman BM.AdipoQ is a novel adipose-specific gene dysregulated in obesity. J Biol Chem 1996; 271:10697-703.
23. Yatagai T, Nagasaka S, Taniguchi A, Fukushima M, Nakamura T, Kuroe A, et al. Hypoadiponectinemia is associated with visceral fat accumulation and insulin resistance in Japanese men with type 2 diabetes mellitus. Metabolism 2003; 52: 1274-8.
24. Smith J, Al-Amri M, Sniderman A, Cianflone K. Leptin and adiponectin in relation to body fat percentage,waisttohip ratio and the apoB/apoA1 ratio in Asian Indian and Caucasian men and women. Nutr Metab (Lond) 2006; 3: 18.
25. Weyer C, Funahashi T, Tanaka S, Hotta K, Matsuzawa Y, Pratley RE, et al. Hypoadiponectinemia in obesity and type 2 diabetes: close association with insulin resistance and hyperinsulinemia. J Clin Endocrinol Metab 2001; 86: 1930-5.
26. Pańkowska E, Szalecki M. Adiponectin as an adipose tissue hormone and its role in the metabolic syndrome and cardiovascular disease. Endokrynol Diabetol Chor Przemiany Materii Wieku Rozw 2005; 11:187-90 (Polish).
27. Mohammadzadeh G, Zarghami N, Bahrami M, Larijhani B. Serum levels of Adiponectin in non diabetic and diabetic obese individuals. Iranian Journal of Diabetes and Lipid Disorders 2007; 7: 177-87 (Persian).
28. Hoffstedt J, Arvidsson E, Sjölin E, Wåhlén K, Arner P. Adipose tissue adiponectin production and adiponectin serum concentration in human obesity and insulin resistance. J Clin Endocrinol Metab 2004; 89:1391-6.
29. Yang WS, Chen MH, Lee WJ, Lee KC, Chao CL, Huang KC, et al. Adiponectin mRNA levels in the abdominal adipose depots of non-diabetic women. Int J Obes Relat Metab Disorder 2003; 27: 896-900.
30. Wang B, Jenkins JR, Trayhurn P. Expression and secretion of inflammation-related adipokines by human adipocytes differentiated in culture: integrated response to TNF-alpha. Am J Physiol Endocrinol Metab 2005 ; 288: E731-740.

31. Hu E, Liang P, Spiegelman BM. AdipoQ is a novel adipose-specific gene dysregulated in obesity. J Biol Chem 1996 ; 271: 10697-703.
32. Baratta R, Amato S, Degano C, Farina MG, Patane G, Vigneri R, et al. Adiponectin relationship with lipid metabolism is independent of body fat mass: evidence from both cross-sectional and intervention studies. J Clin Endocrinol Metab 2004; 89: 2665-671.
33. Kantartzis K, Rittig R, Balletshofer B, Machann JR , Schick F, Porubska K, et al . Favorable lipid profile, decreased inflammation, and less ectopic fat accumulation depend on adiposity. Clin Chem 2006; 52: 1934-42.
34. Von Eynatten M , Schneider JG, Humpert PM, Rudofsky G, Schmidt N, Barosch P, et al. Decreased plasma lipoprotein lipase in hypoadiponectinemia. Diabetes Care 2004; 27: 2925-9.
35. Côté M, Mauriège P, Bergeron J, Alméras N, Tremblay A, Lemieux I, et al. Adiponectinemia in visceral obesity: impact on glucose tolerance and plasma lipoprotein and lipid levels in men. J Clin Endocrinol Metab 2005; 90: 1434-9.
36. Möhlig M, Wegewitz U, Osterhoff M, Isken F, Ristow M, Pfeiffer AF, et al. Insulin decreases human adiponectin plasma levels. Horm Metab Res 2002; 34:655-8.
37. Brame LA, Considine RV, Yamauchi M, Baron AD, Mather KJ. Insulin and Endothelin in the acute regulation of adiponectin in vivo in humans. Obesity Res 2005; 13: 582-8.
38. Ceddia RB, Somwar R, Maida A, Fang X, Bikopoulos G, Sweeney G. Globular adiponectin increases GLUT4 translocation and glucose uptake but reduces glycogen synthesis in rat skeletal muscle cells. Diabetologia 2005; 48: 132-9.
39. Fu Y, Luo N, Klein RL, Garvey WT. Adiponectin promotes adipocyte differentiation, insulin sensitivity, and lipid accumulation. J Lipid Res 2005; 46: 1369-79.