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Serum Adiponectin Concentrations in Relation to Lipid Profile, Anthropometric Variables and Insulin Resistance in Patients with Metabolic Syndrome

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ABSTRACT

Introduction: Associations between serum adiponectin concentrations and anthropometric and metabolic parameters in obesity and diabetes have been elucidated; however, the relationship between serum adiponectin and cardiovascular risks in patients with metabolic syndrome are less studied. **Methods:** One hundred and sixty patients with metabolic syndrome (107 men and 54 women) were recruited for this study. Anthropometric indices of weight, height, waist circumference and hip circumference were measured. Serum adiponectin, lipid profile and fasting blood glucose (FBG) were measured by enzyme- linked immunosorbent assay method (ELISA). The homeostasis model assessment (HOMA) was used for determination of insulin resistance. **Results:** BMI was significantly higher and waist-to-hip ratio (WHR) was lower in women compared to men ($P < 0.001$ and < 0.05 respectively). Serum high density lipoprotein cholesterol (HDL-C) in women was significantly higher than in men (45.98 ± 11.15 versus 39.11 ± 8.43 mg/dl; $P < 0.001$). Serum adiponectin concentrations were negatively associated with serum triglyceride concentration and waist circumference in men and women respectively. There was also a positive relationship between serum adiponectin and HDL-C concentrations and age in men and women respectively ($P < 0.05$). Adjusting for the confounding effects of age and BMI using linear regression model, serum TG, LDL-C and WC were significant negative predictors of serum adiponectin concentrations ($P < 0.05$). **Conclusion:** Our findings showed that serum adiponectin concentration is related to anthropometric and metabolic parameters in patients with metabolic syndrome. Further studies are warranted to better clarify these associations and underlying mechanisms.

Key words: Adiponectin, BMI, insulin resistance, metabolic syndrome, WHR

INTRODUCTION

As metabolic syndrome is a cluster of disturbed glucose and insulin metabolism, abdominal adiposity, dyslipidemia and hypertension are associated with development of type 2 diabetes mellitus and cardiovascular diseases (CVD) (Lakka *et al.*, 2002). According to the National Cholesterol Education Programme (NCEP) report, metabolic syndrome is associated

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with 1.7 fold increase in CVD risk (Ford, 2005). The Third National Health and Nutrition Examination Survey (NHANES III) reported an alarming 30% prevalence of metabolic syndrome in middle aged men (Ford, Giles & Dietz, 2002). The prevalence of metabolic syndrome in different parts of Iran has been reported previously. In the Tehran Lipid and Glucose Study (TLGS), according to the Adult Treatment Panel (ATP) III criteria, 33.7% of adults aged ≥ 20 years old were suffering from metabolic syndrome (Zabetian, Hadaegh & Azizi, 2007). Other studies have reported 55% and 30.1% for the prevalence of metabolic syndrome in Iranian adult women and men respectively (Azimi-Nezhad *et al.*, 2012).

Adiponectin, an adipose tissue derived 244 amino acid polypeptide is a product of the most abundant gene transcript-1 (ap M1) of adipose (Haluzic, Parizkova & Haluzik, 2004). Adiponectin gene is exclusively expressed in white adipose tissue and to some extent in brown adipose tissue and has a high structural homology to collagens VIII and X; it also complements C1q 11-14 as well as TNF-*a* (Kazumi *et al.*, 2004). In fact, adiponectin inhibits the production of TNF-*a* in human aortic endothelial cells in a dose dependent manner (Matsubara, Maruoka & Katayose, 2002a,b). This peptide has insulin-sensitising and anti-diabetic properties and is inversely associated with adiposity (Meilleur *et al.*, 2010). Additionally, adiponectin exerts its anti-inflammatory effects via inhibiting the migration of monocytes and their transformation into foam cells (Tian *et al.*, 2009). Due to the close relationship of adiponectin with insulin resistance and components of type 2 diabetes mellitus, it has been proposed as a useful diagnostic criterion for diabetes or metabolic syndrome (Mojiminiyi *et al.*, 2007). Previous reports suggest that low serum adiponectin concentrations is associated with development of obesity, type 2 diabetes mellitus, dyslipidemia and coronary artery disease (Matsubara *et al.*, 2002a,b; Yang, Lee & Funahashi, 2002). However, data about the association of serum adiponectin with metabolic parameters and anthropometric indices in metabolic syndrome are scarce; therefore we examined the relationship between serum adiponectin concentrations, lipid profile, liver enzymes and insulin resistance as well as anthropometric parameters in patients with metabolic syndrome.

METHODS

The study comprised 160 patients with metabolic syndrome according to the National Cholesterol Education Program's Adult Treatment Panel III (NCEP-ATP III) criteria (Zabetian *et al.*, 2007). Exclusion criteria were a history of cardiovascular diseases, type 2 diabetes mellitus, cancer, renal diseases, being pregnant, and taking medications for hypertension or dislipidemia. At the beginning of the study, the subjects underwent a physical examination in which information about weight, height, waist circumference (WC), hip circumference, waist to hip ratio (WHR) and waist to height ratio (WHtR) and several biochemical assessments including serum lipids and insulin resistance was obtained (Jahangiri *et al.*, 2014). Homeostasis model assessment of insulin resistance (HOMA-IR) was used for assessment of insulin sensitivity based on the following formula: HOMA-IR: (glucose [mmol/l] × insulin [mU/l]) / 405 (Matthews *et al.*, 1985). High HOMA-IR scores denote low insulin sensitivity. The Quantitative Insulin Check Index (QUICKI index) QUICKI was calculated as: 1 / [log fasting insulin (U/l) + log fasting glucose (mg/dl); higher QUICKI values indicate greater insulin sensitivity (Viner *et al.*, 2005).

Serum aspartate aminotransferase (AST), alanin amino transferase (ALT), total cholesterol (TC), fating blood glucose (FBG), triglyceride (TG), high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL) were analysed by enzymatic colorimetric method (Pars – Azmoon, Tehran – Iran). Serum insulin was also analysed with enzyme linked immunosorbent assay method (ELISA-Monobind Insulin AccuBind, CA 92630, USA) with a sensitivity of 0.75 μIU/ml and mean inter- and intra-assay coefficient of variations (CV) of < 9.8% and < 8% respectively. Serum adiponectin was also analysed by ELISA method (AviBion, Fin-01720 Vantaa, Finland) with a sensitivity of < 0.185 ng/ml and mean inter- and intra-assay CV of ≤ 12% and ≤ 10% respectively.

Data are expressed as mean ± SD. The statistical tests including Kolmogrov-Smirnof test, independent sample *t*-test and correlation analysis by Pearson's correlation coefficient were performed by SPSS software (version 18, SPSS Inc., Chicago, IL, USA). Multiple linear regression models were used to examine the relationships between serum adiponectin, lipids, anthropometric variables and insulin resistance while adjusting for covariates. P values less than 0.05 were defined as the significance threshold.

RESULTS

The study sample comprised 160 individuals, 33.54% of whom were women. The females were approximately 6 years older and 2 kg/m^2 more obese than men (P < 0.05, Table 1). Waist circumference (WC) and WHR in men were higher than in women (P < 0.01). Among biochemical variables, only HDL-C was higher in women than in men (45.98 ± 11.15 vs 39.11± 8.43 mg/dl, P < 0.001). Serum adiponectin showed a negative association with TG in men (r = - 0.35, P = 0.004) and WC in women (r= -0.46, P = 0.03); accordingly it was positively associated with HDL-C (r = 0.27, P = 0.04) and age (r = 0.42, P = 0.04) in men and women respectively (P < 0.05, Figure 1). In the multiple regression model,

Table 1. Basic characteristics of patients by gender

Variable	*Men (n=107)*	*Female (n=54)*	*P*
Age (Years)	41.96 ± 10.41	48.13 ± 7.8	< 0.001
BMI (kg/m2)	29.70 ± 3.8	31.36 ± 5.9	0.034
Waist (cm)	105.51 ± 7.81	102.16 ± 0.06	0.008
WHR	0.94 ± 0.07	0.90 ± 0.06	< 0.001
WHtR	0.60 ± 0.04	0.63 ± 0.06	< 0.001
SBP (mmHg)	132.12 ± 12.49	131.13 ± 7.50	0.59
DBP (mmHg)	88.11 ± 7.11	88.56 ± 5.12	0.68
TC (mg/dl)	194.32 ± 36.89	196.39 ± 44.89	0.75
TG (mg/dl)	198.57 ± 11.65	176.49 ± 12.49	0.25
HDL(mg/dl)	39.11 ± 8.43	45.98 ± 11.15	<0.001
LDL (mg/dl)	128.33 ± 28.65	129.26 ± 38.81	0.59
FBG (mg/dl)	88.53 ± 13.10	92.64 ± 14.77	0.076
Insulin (µIU/ml)	17.26 ± 24.46	16.87 ± 16.86	0.94
HOMA-IR	3.66 ± 5.09	3.99 ± 4.49	0.80
QUICKI	0.34 ± 0.05	0.34 ± 0.04	0.61
AST(IU/l)	30.04 ± 10.22	28.65 ±10.56	0.62
ALT (IU/l)	27.02 ± 7.79	27.45 ± 9.50	0.85
Adiponectin (ng/ml)	13.46 ± 4.80	14.42 ± 4.63	0.40

BMI, body mass index; WHR, waist to hip ratio; WHtR, waist to height ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; HDL, high density lipoprotein; LDL, low density lipoprotein; FBG, fasting blood glucose; HOMA-IR, homeostatic model assessment for insulin Resistance; AST, aspartate aminotransferase; ALT, alanin aminotransferase.

Table 2. Stepwise multiple regression analysis on all patients for serum adiponectin concen-trations as dependent variable

Variable	*β (P)*	*SE*	*P value*
FBG (mg/dl)	0.064	0.047	0.58
TG (mg/dl)	-0.37	0.006	0.004
LDL (mg/dl)	-0.36	0.024	0.047
TC (mg/dl)	0.32	0.02	0.076
HDL(mg/dl)	0.74	0.061	0.54
Waist circumference (cm)	-0.22	0.11	0.048

Adjusted for the effects of age and BMI; FBG, fasting blood glucose; TG, triglyceride; LDL, low density lipoprotein; TC, total cholesterol; HDL, high density lipoprotein cholesterol.

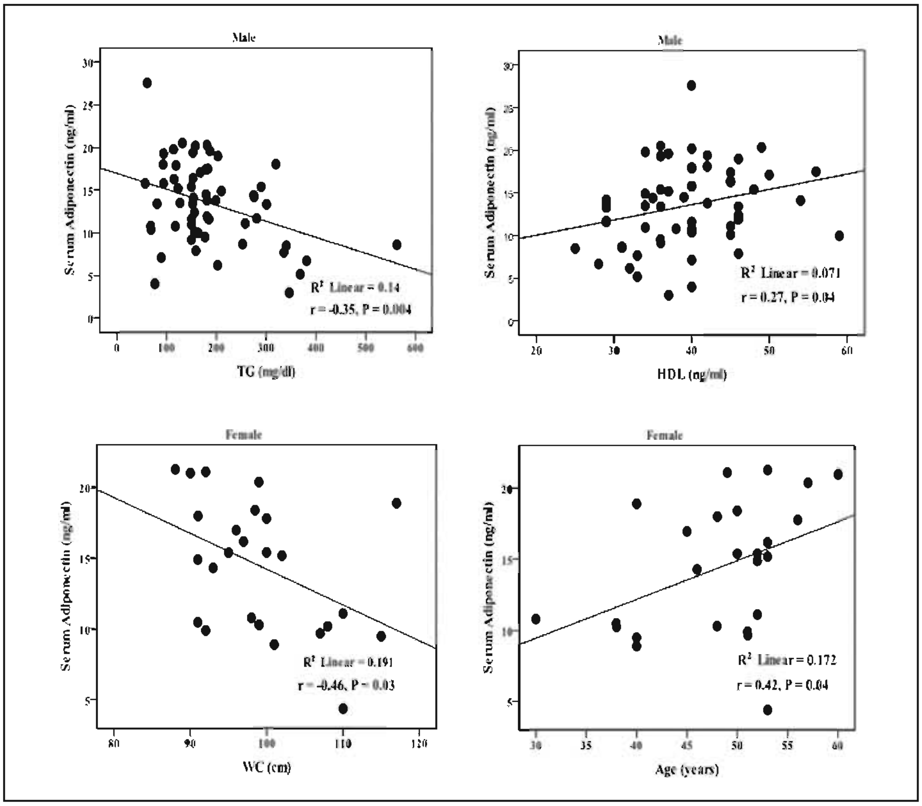

Figure 1. Significant correlation between serum adiponectin and TG, HDL, WC and age in male and female patients

with adiponectin as an dependent variable, after adjusting for the confounding effect of age and BMI, serum TG, LDL-C and WC were potent negative predictors of serum adiponectin concentrations of all the participants (P < 0.05)(Table2).

DISCUSSION

The present study demonstrates that serum adiponectin concentration is positively associated with HDL-C concentration and age in men and women with metabolic syndrome; it has also a negative relationship with serum TG and WC in male and female participants. HOMA-IR or liver enzymes were not potent predictors of serum adiponection concentrations ($P < 0.05$).

Adiponectin gene could be mapped to human chromosome 1q 21.4-1q23 a region close to familial combined hyperlipidemia (FCH) gene with the main features of elevated LDL and TG and decreased HDL concentrations (Kazumi *et al.*, 2004). These findings are the same as previous reports in obesity and this further confirms the close relationships between obesity and metabolic syndrome (Farhangi *et al.* (2013 a,b). The negative and positive relationships between serum adiponectin, TG and HDL-C concentrations further confirms this fact.

Our findings are in agreement of previous reports; in the study by Meillleur *et al.*(2010), serum adiponectin was in negative relationship with WC, BMI and fat mass and in positive relationship with HDL-C, TC and age in a large African cohort (Meilleur *et al.*, 2010). Huang *et al.* (2004) and Cnop *et al.* (2003) obtained similar results. Several previous reports found a sex-based difference between serum adiponectin concentrations with higher concentrations of this adipokine being reported in women (Arita, Kihara & Ouchi, 1999; Zoccali *et al.*, 2002; Cnop *et al.*, 2003). We also found a higher but non-significant amount of this adipokine in our female participants. It appears that the sex-based difference in body fat distribution (Cnop *et al.*, 2003) or possible inhibitory effects of androgens on adiponectin secretion from adipocytes (Nishizawa *et al.*, 2002) could be taken into account. This can also explain the sex-based difference in our results.

The possible underlying mechanism of the positive and negative relationships of serum adiponectin with serum HDL-C and TG could be partly mediated by the effect of this adipokine on hepatic lipase activity; Schneider *et al.* (2005) found that adiponectin is a potent predictor of hepatic lipase secretion rather than insulin even after adjusting for age, BMI, sex and other factors; lower serum adiponectin concentrations is a stimulator of hepatic lipase action (Despres *et al.*,1989).

In our study, in contrast to several previous reports of an inverse relationship between insulin resistance and serum adiponectin concentrations (Cnop *et al.*, 2003; Huang *et al.*, 2004; Mojiminiyi *et al.*, 2007), serum insulin concentrations or HOMA-IR were not in a relationship with adiponectin even after adjustment for confounders such as age or BMI. This difference in results may stem from the nature of the disease; none of them were in metabolic syndrome. The lack of association between adiponectin and HOMA-IR also has been reported by Kazumi *et al.* (2004) in young healthy men. We are of the opinion that the failure to demonstrate this association suggests that adiponectin may be associated primarily with adiposity and atherogenic lipid profile which is subsequently modified by IR.

CONCLUSION

In conclusion, circulating adiponectin is significantly associated with serum lipids and WC in adult men and women with metabolic syndrome. Further studies are needed to better clarify these associations.

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Conflict of interest

The authors declare that there is no conflict of interest.

REFERENCES

Arita Y, Kihara S & Ouchi N (1999). Paradoxical decrease of an adipose-specific protein, adiponectin, in obesity. *Biochem Biophys Res Commun* 257 (1): 79-83.

Azimi-Nezhad M, Herbeth B, Siest G, Dade S, Ndiaye NC, Esmaily H, Hosseini SJ, Ghayour-Mobarhan M & Visvikis-Siest S (2012). High prevalence of metabolic syndrome in Iran in comparison with France: what are the components that explain this? *Metab Syndr Relat Disord* 10 (3): 181-188.

Cnop M, Havel PJ, Utzschneider KM, Carr DB, Sinha MK, Boyko EJ, Retzlaff BM, Knopp RH & Brunzell JD (2003). Relationship of adiponectin to body fat distribution, insulin sensitivity and plasma lipoproteins: evidence for independent roles of age and sex. *Diabetologia* 46 (4): 459-469.

Despres J, Ferland M, Moorjani S, Nadeau A, Tremblay A, Lupien P J, Theriault G & Bouchard C (1989). Role of hepatic-triglyceride lipase activity in the association between intra-abdominal fat and plasma HDL cholesterol in obese women. *Arteriosclerosis* 9: 485-492.

Farhangi MA, Keshavarz SA, Eshraghian M, Ostadrahimi A, Saboor-Yaraghi AA (2013a). White blood cell count in women: Relation to inflammatory biomarkers, haematological profiles, visceral adiposity, and other cardiovascular risk factors. *J Health Popul Nutr* 31(1): 58-64.

Farhangi MA, Saboor-Yaraghi AA, Eshraghian M, Ostadrahimi A, Keshavarz SA (2013b). Serum transforming growth factor β (TGF-β) is associated with body mass index in healthy women. *Acta Endocrinologica (Buc)* 9(3): 361-368
.

Ford ES (2005). Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome: a summary of the evidence. *Diabetes Care* 28 (7): 1769-1778.

Ford ES, Giles WH & Dietz WH (2002). Prevalence of the metabolic syndrome among US adults. *JAMA* 287 (3): 356-359.

Haluzic M, Parizkova J & Haluzik MM (2004). Adiponectin and its role in the obesity-induced insulin resistance and related complications. *Physiol Res* 53: 123-129.

Huang K, Lue BH, Yen RF, Shen CG, Ho SR, Tai TY & Yang WS (2004). Plasma adiponectin levels and metabolic factors in non-diabetic adolescents. *Obes Res* 12 (1): 119-124.

Jahangiri L, Shojaeezadeh D, Najafi M, Mohammad K, Abbasalizad Farhangi M & Montazeri A (2014). "Red Ruby": an interactive web-based intervention for life style modification on metabolic syndrome: A study protocol for a randomised controlled trial. *BMC Public Health* 14: 748-756.

Kazumi K, Kawaguchi A, Hirano T & Yoshino G (2004).Serum adiponectin is associated with high-density lipoprotein cholesterol, triglycerides, and low-density lipoprotein particle size in young healthy men. *Metaboism* 53 (5): 589-593.

Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J & Salonen JT (2002). The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. *JAMA* 288 (21): 2709-2716.

Matsubara M, Maruoka S & Katayose S (2002a). Decreased plasma adiponectin concentrations in women with dyslipidemia. *J Clin Endocrinol Metab* 87 (6): 2764-2769.

Matsubara M, Maruoka S & Katayose S (2002b). Inverse relationship between plasma adiponectin and leptin concentrations in normal-weight and obese women. *Eur J Endocrinol* 147: 173-180.

Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF & Turner RC (1985). Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 28 (7): 412-419.

Meilleur K, Doumatey A, Huang H, Charles B, Chen G, Zhou J, Shriner D, Adeyemo A & Rotimi C (2010). Circulating adiponectin is associated with obesity and serum lipids in West Africans. *J Clin Endocrinol Metab* 95 (7): 3517-3521.

Mojiminiyi OA, Abdella NA, Arouj MA & Nakhi AB (2007). Adiponectin, insulin resistance and clinical expression of the metabolic syndrome in patients with Type 2 diabetes. *Int J Obes* 31: 213-220

Nishizawa H, Shimomura I, Kishida K, Nishizawa H, Shimomura L, Kishida K, Maeda N, Kuriyama H, Nagaretani H, Matsuda M, Kondo H, Furuyama N, Kihara S, Nakamura T, Tochino Y, Funahashi T & Matsuzawa Y (2002). Androgens decrease plasma adiponectin, an insulin-sensitizing adipocyte-derived protein. *Diabetes Care* 51 (9): 2734-2741.

Tian L, Luo N, Klein RL, Chung BH, Garvey WT & Fu Y (2009). Adiponectin reduces lipid accumulation in macrophage foam cells. *Atherosclerosis* 202 (1): 152-161.

Viner RM, Segal TY, Lichtarowicz-Krynska E & Hindmarsh P. (2005). Prevalence of the insulin resistance syndrome in obesity. *Arch Dis Child* 90: 10-14.

Yang WS, Lee WJ & Funahashi T (2002). Plasma adiponectin levels in overweight and obese Asians. *Obes Res* 10 (11): 1104-1110.

Zabetian A, Hadaegh F, Azizi F (2007). Prevalence of metabolic syndrome in Iranian adult population, concordance between the IDF with the ATP III and the WHO definitions. *Diabetes Res Clin Pract* 77 (2): 251-257.

Zoccali C, Mallamaci F, Tripepi G, BenedettoFA, CutrupiS, ParlongoS, MalatinoLS, Bonanno G, Seminara G, Rapisarda F, Fatuzzo P, Buemi M, Nicocia G, Tanaka S, Ouchi N, Kihara S, Funahashi T & Matsuzawa Y (2002). Adiponectin, metabolic risk factors, and cardiovascular events among patients with end-stage renal disease. *J Am Soc Nephrol* 13 (1): 134-141.