International Journal of Tropical Medicine 11 (5): 165-169, 2016
ISSN: 1816-3319

Hypoadiponectinemia Associated in Obesity and Type 2 Diabetes and Hyperadiponectinemia Closed with Type I Diabetes

[1]Lida Haghnazari, [2]Hamid Nomani, [1]Hamed Nowroozi, [1]Osman Hesami,
[2]Mehrali Rahimi and [1]Sahar Foroughinia
[1]Department of Clinical Biochemistry, [2]Department of Internal Medicine,
Kermanshah University of Medical Sciences, Kermanshah, Iran
[2]Department of Clinical Biolchemistrym, Kermanshah University of
Medical Sciencesm, Kermanshah, Iran

Abstract: Adiponectin decreases in Type 2 diabetes mellitus, insulin resistance and obesity. However, increases in several chronic statuses such as Type I diabetes associated with nephropathy or cardiovascular diseases. In this study, we investigated whether serum level of adiponectin may be considered as a useful biochemical marker for differentiating T1DM and T2DM and correlation with lipid profiles, waist circumstance and body mass index in Kermanshah population, West of Iran. This cross-sectional study was conducted on 100 diabetic patients Type 2 and 89 diabetic Type I and 99 and 66 non diabetic as control group matched for age and sex with T2DM and T1DM, respectively. Levels of adiponectin, HbA1c, lipid profiles were measured by ELISA, glycated hemoglobin and enzyme assay, respectively. Our finding showed, levels of serum adiponectin significantly increased in T1DM patients and decreased in T2DM patients. In addition, serum adiponectin concentration in T1DM patients was significantly higher of T2DM . Serum adiponectin level was significantly positive correlation with HbA1c in T1DM and with HDL-C in T2DM. Lipid profiles except of HDL-C were significantly higher in T2DM patients compared with T1DM patients. There was a significantly negative correlation between serum levels of adiponectin and obesity in T1DM and T2DM. Hypoadiponectinemia associated with obesity and T2DM patients while closed with T1DM and decrease BMI and serum adiponectin concentration which may be considered as a useful biochemical marker for differentiating T1DM and T2DM.

Key words: Type 1 and 2 diabetes, adiponectin, Body Mass Index (BMI), lipid profiles, biochemical marker

INTRODUCTION

Today, the adipose tissue as an endocrine organ with multiple hormones secretion is considered too has very important effects on the body metabolism reactions (Combs *et al*., 2003; Meier and Gressner, 2004). Adiponectin is collagen-like protein which is composed of a 244 amino acids and is secreted by adipose tissue. Adiponectin acts as hormone with anti-inflammatory, anti-diabetic and anti-atherogenic properties which regulates the metabolism of glucose and lipid in insulin-sensitive tissues (natural regulation of insulin sensitivity). It has a wide range of multimer complexes and combines with its collagen domain to formation 3 major oligomeric forms: adiponectin with low trimer, medium molecular weight (hexamer) and high molecular weight (12-18-mer) (Kadowaki *et al*., 2006). Different studies have suggested that the different forms of this hormone have different activities (Kadowaki *et al*., 2006; Hara *et al*., 2006).

Plasma levels of adiponectin reduced in individuals with insulin resistance (T2DM), obesity, atherosclerosis, glucose intolerance (Hara *et al*., 2002) and increased in several chronic status such as T1DM with nephropathy and cardiovascular disease, chronic heart failure and the end stage renal diseases (Gokulakrishnan *et al*., 2013). Adiponectin concentration is approximately, 0.01% of total plasma protein (Weyer *et al*., 2001), Plasma level of adiponectin is lower in males than females (Cnop *et al*., 2003). There is a negative correlation with intra-abdominal fats, age, amount of blood glucose level, triglycerides, C-Reactive Protein (CRP) but a positive correlation with the level of HDL (Maahs *et al*., 2007). Low level of adiponectin in T2DM associated with increased the risk of cardiovascular disease and retinopathy (Frystyk *et al*., 2005), so it seems genetic and environmental factors affect on amount of adiponectin in plasma. Findings of animal studies (obese/diabetic mice) and T2DM in humans indicated that injection of the adiponectin (globular domain) improve insulin resistance, increased of fatty

Corresponding Author: Hamid Nomani, Department of Clinical Biolchemistrym, Kermanshah University of Medical Sciencesm, Kermanshah, Iran

acid β oxidation in muscles, decrease of hepatic gluconeogenesis mediated by cAMP-activated protein kinase (Menzaghi *et al*., 2007). In this study, we investigated association between adiponectin levels and lipid profiles with susceptibility to T2DM, T1DM and obesity which may be considered as a useful biochemical marker for differentiating between T1DM and T2DM in this population.

MATERIALS AND METHODS

This is a case-control study with convenience sampling in Diabetics center of Kermanshah University of Medical Sciences in the period between Februarys to June 2015. Personal and family history was unremarkable. The procedures of the study were approved by the Helsinki research ethics committee of the Iranian authority ministry of health according to the World Medical Association Declaration of Helsinki and a written consent form was obtained from each patient.

Seven ml peripheral blood in Ethylene Diamine Tetra Acetic acid (EDTA) (0.5 mM) was obtained from 100 patients with T2DM unrelated (57 female and 43 male with a mean age 56.18+8.9 and BMI ≥27.4) and 89 patients with T1DM unrelated (44 female and 45 male with a mean age 19.65+7.33 and BMI = 21.5) all of the diabetics individuals that contain at least 3 years of experience in diabetes and 165 unrelated healthy individuals consisted of 99 and 66 non diabetic control subjects matched for age and sex with T2DM and T1DM, respectively.

Measurement of serum adiponectin level: Concentration of adiponectin in serum was measured by quantitative sandwich enzyme immunoassay technique (Kit Build Mediagnost company in Germany with sensitivity 0.6 ng mL^{-1}) according to the manufacturer's instructions.

Serum lipids: Serum lipid profiles included Low-Density Lipoprotein Cholesterol (LDL-C), High-Density Lipoprotein Cholesterol (HDL-C), Total Cholesterol (TC) and Tri Glyceride (TG) were measured by the standard enzymatic method (Pars Azmon kit, Iran), using an automated Erba XL-600 (Mannheim, Germany).

Determination of circumstance and body max index: The size of the round belly by using tape measure non-elastic was performed with an accuracy of 1 cm. At first, the weight of the people with at least clothes and without shoes by the Taiwanese digital scale with precision of 0.1 kg for size. We measured height subjects using a wall stadiometer 44440 making Kaveh carefully 0.1 cm in the posture of standing next to the wall without shoes. Body Mass Index (BMI) of dividing the weight (kg) on the square of height (m^2) was calculated.

Statistical analyses: Data were analyzed first for normality of distribution by using the Kolmogorov Smirnov test. Results were expressed as mean±SD for normally distributed data, median and Interquartile Range (IQR) for non-normally distributed data and percentages for categorical data. Comparison of groups was carried out with Student's t test, Mann Whitney U test and one-way ANOVA as appropriate. The correlation values of adiponectin concentration with lipids profiles, FBS, HbA1c%, BMI, waist circumstance and onset age of diabetes, age of T1DM and T1DM groups were calculated using Pearson correlation. Statistical significance was assumed at the $p<0.05$. The SPSS statistical software package version 19 was used for the statistical analysis.

RESULTS AND DISCUSSION

Comparison levels of serum adiponectin, lipid profiles, biochemical variables and other demographic characteristics between T1DM patients and their control group and T2DM patients and their control group are summarized in Table 1 and 2, respectively. Serum concentration of adiponectin (19.4 (14-30.3) vs. 16.2 (9.2-21.7) μg mL^{-1}, $p = 0.001$) and HDL-C (49 (43-54) vs. 42.5 (38.8-48) mg dL^{-1}, $p<0.001$) were significantly higher in T1DM compared with their control subjects, however LDL-C (86 (78-94.5) vs. 100 (90-115) mg dL^{-1}, $p<0.001$) was significantly lower (Table 1). We observed in T2DM patients serum levels of adiponectin (9.1 (6.3-12.4) vs. 14.5 (8.2-21.5) μg mL^{-1}, $p<0.001$) and HDL-C (40 (34.3-45) vs. 44 (37-50) μg mL^{-1}, $p<0.001$) were significantly lower and serum level of TG 140 (111192) vs. 111(77.8-160), $p = 0.001$) was significantly higher compared with their control groups (Table 2 and 3).

Furthermore, correlations between adiponectin concentration with BMI duration of diabetes, onset age of diabetes, waist circumstance, HbA1C, FBS, cholesterol, LDL-C, HDL-C and TG in T1DM and T2DM patients are shown in Table 4. There were significant positive correlation between adiponectin concentration and HbA1C and FBS ($r = 0.255$, $p = 0.016$ and $r = 0.21$, $p = 0.045$), respectively however a negative correlation with duration of diabetes ($r = -0.22$, $p = 0.038$), BMI ($r = -0.196$, $p = 0.066$) and age ($r = -0.196$, $p = 0.065$) in T1DM patients. Interestingly a significant positive correlation between adiponectin concentration with HDL-C levels ($r = 0.31$, $p = 0.001$), onset age of diabetes ($r = 0.21$, $p = 0.033$) and age ($r = 0.194$, $p = 0.053$) and negative correlation with BMI in T2DM patients.

Table 1: Comparison levels of serum adiponectin, lipid profiles, biochemical variables and other demographic characteristics between Type 1 Diabetes Mellitus (T1DM) patients and their control group

Variables	T1DM	Control type 1	p-values
Sex (female/male)	44 (49.4%)/45 (50.8%)	34 (51.5%)/32 (48.5%)	0.994
Age (year)	19.7±7.3	18.1±8.3	0.23
BMI (kg/m^2)	21.9±4.1	22±3.1	0.45
Waist circumstance (cm)	76±11.8	76.7±11.3	0.72
Cholesterol (mg dL^{-1})	166.4±29.6	174.2±30.5	0.11
Triglyceride (mg dL^{-1})	112±51.6	127.7±55.6	0.07
LDL-C (mg dL^{-1})	86 (78-94.5)	100 (90-115)	*<0.001
HDL-C (mg dL^{-1})	49 (43-54)	42.5 (38.8-48)	*<0.001
Adiponectin (μg mL^{-1})	19.4 (14-30.3)	16.2 (9.2-21.7)	*0.004

Table 2: Comparison levels of serum adiponectin, lipid profiles, biochemical variables and other demographic characteristics between Type 2 Diabetes Mellitus (T2DM) patients and their control group

Variables	T2DM	Control type 2	p-values
Sex (female/male)	57 (57%)/43 (43%)	51 (53.7%)/44 (46.3%)	0.967
Age (year)	56.28.9	53.89.1	0.07
BMI (kg/m^2)	27.53.9	26.82.2	0.15
Waist circumstance	101.4511.35	102.168.30	0.62
Cholesterol (mg dL^{-1})	191 (168-210)	171 (140-$_{208}$)	*0.002
Triglyceride (mg dL^{-1})	140 (111192)	111 (77.8-160)	*0.001
LDL-C (mgd L^{-1})	109 (97-119)	101 (87.3-118)	*0.081
HDL-C (mgd L^{-1})	40 (34.3-45)	44 (37-50)	*0.002
Adiponectin (μg mL^{-1})	9.1 (6.3-12.4)	14.5 (8.2-21.5)	*<0.001

Table 3: Comparison levels of serum adiponectin, lipid profiles, biochemical variables and other demographic characteristics between T1DM patients and T2DM patients

Variables	T1DM	T2DM	p-values
Sex (female/male)	44 (49.4%)/45 (50.6)	57 (57%)/43 (43%)	0.29
Age (year)	19.77.3	56.28.9	<0.001
BMI (kg/m^2)	21 (18.6-24.6)	27.3 (25.2-29.7)	*<0.001
Waist circumstance (cm)	75 (68-80.5)	100 (96-110)	*<0.001
Cholesterol (mg dL^{-1})	168 (146.5.182)	191 (168-210)	*<0.001
Triglyceride (mg dL^{-1})	105 (75-132)	140 (111192)	*0.019
LDL-C (mg dL^{-1})	86 (78-94.5)	109 (97-119)	*<0.001
HDL-C (mg dL^{-1})	49 (43-54)	40 (34.3-45)	*<0.001
Adiponectin (μg mL^{-1})	19.4 (14-30.3)	9.1 (6.3-12.4)	*<0.001
Duration of diabetes	3 (2-6)	4 (6-12)	*<0.001
HbA1C (%)	8.51.4	8.21.41	0.09
Fasting blood sugar (mg dL^{-1})	180.279	192.466.6	0.24

Statistical analyses were done using t-test and by *non-parametric 2 independent samples test Mann-Whitney

Table 4: Correlation between adiponectin concentrations with BMI, duration of diabetes, onset age of diabetes, waist circumstance, HbA1C, FBS, cholesterol, LDL-C, HDL-C and TG have been compared in T1DM and T2DM patients

Variables	Adiponectin level inT1DM patients	Adiponectin level in T2DM patients
Onset age of diabetes	r = -0.074, p = 0.49	r = 0.21, p = 0.033
Age (year)	r = -0.196, p = 0.065	r = 0.194, p = 0.053
BMI (kg/m^2)	r = -0.2, p = 0.046	r = -0.02, p = 0.8
Waist circumstance (cm)	r = -0.179, p = 0.093	r = 0.12, p = 0.23
Cholesterol (mg dL^{-1})	r = -0.141, p = 0.19	r = 0.12, p = 0.22
Triglyceride (mg dL^{-1})	r = -0.02, p = 0.85	r = 0.01, p = 0.9
LDL-C (mg dL^{-1})	r = -0.05, p = 0.64	r = 0.085, p = 0.39
HDL-C (mg dL^{-1})	r = -0.096, p = 0.38	r = 0.31, p = 0.001
Duration of diabetes	r = -0.22, p = 0.038	r = -0.05, p = 0.6
HbA1C (%)	r = 0.255, p = 0.016	r = 0.03, p = 0.8
Fasting blood sugar (mg dL^{-1})	r = 0.21, p = 0.045	r = 0.1, p = 0.32

CONCLUSION

Obesity and metabolic syndrome have a widespread prevalence and is one of the very important health problems (Ranjbar *et al*., 2012). Adiponectin is secreted from adipose tissue and may be associated with various metabolic diseases such as diabetes mellitus (Gokulakrishnan *et al*., 2013). Previous studies indicated that adiponectin affects on insulin synthesis and consequence play a role in glucose and lipid metabolism (Gokulakrishnan *et al*., 2013; Kadowaki *et al*., 2006). This case control study demonstrated there was negative correlation between decreased level of adiponectin with obesity and increased risk of T2DM. So, we suggest adiponectin may have a protective role against T2DM. Moreover, results of this study indicated a

hyperadiponectinemia may be associated with T1DM. These findings were consistent with results obtained by Gokulakrishnan *et al.* (2013) that reported adiponectin concentrations were higher in T1DM and lower in T2DM compared with the control group. Our results indicated patients with T1DM have higher serum levels of adiponectin and HDL-C compared with T2DM subjects. Although in T2DM patients BMI, waist circumstance, cholesterol, TG and LDL-c serum concentration were significantly higher than in compared with T1DM group. Urbanavieius *et al.* (2000) assessed adiponectin plasma concentration in individuals with pre-diabetes and to compare it with the plasma concentration in newly diagnosed T2DM and control group. They reported that serum adiponectin level was lower in obese subjects in compare with non-obese control groups but the difference was not considerable. Adiponectin level was same in pre-diabetes and T2DM groups and was significantly lower than in control group (Urbanavicius *et al.*, 2008).

Results of this study indicated that there is a straight correlation between adiponectin levels and HbA1C and FBS serum concentration in T1DM patients and also between adiponectin concentration with HDL-C levels, onset age of diabetes and age in T2DM patients. Li's meta-analysis study about correlation between Adiponectin level with risk of T2DM showed higher adiponectin levels has protective effect on risk of T2DM among various populations including East Asians, Asian Indians, African Americans and Native Americans accordance with a dose-response ratio (Li *et al.*, 2009). Forsblom *et al.* (2011) indicated adiponectin had positive associated with all-cause mortality during a median of 11 years and the highest adiponectin concentrations in T1DM patients was associated with the shortest survival. Moreover, their results showed the mortality risk adjusted with adiponectin was not correlation with glycaemic and lipid control. Barne *et al.* (2008) in their research mentioned mean adiponectin levels, adjusted for age, sex and Tanner stage were higher in persons with T1DM than in control subjects, also a positive relationship between adiponectin and HbA1c in youth with T1DM, even after adjustment for age, sex and race/ethnicity. Heilman *et al.* (2009) reported children with diabetes had significantly elevated blood pressure, plasma, high sensitive C-Reactive Protein (hsCRP), Intercellular Adhesion Molecule-1 (ICAM-1), adiponectin levels and decreased homocysteine, Asymmetric Dimethylarginine (ADMA), concentrations than their control group. Uttra *et al.* (2011) studied the distribution and pattern of hyperlipidemia in patients who suffer from diabetes mellitus. They reported diabetic patients have a increased risk of develop hyperlipidemia and the pattern of lipid abnormalities was high triglyceride in 22 (31%) patients, high LDL in 14 (19%), low HDL in 08 (11%), high cholesterol in 10 (14%) and combined hyperlipidemia in 18 (25%) diabetic patients. T1DM children and adolescents were more susceptible to dyslipidemia in compared with healthy control and in compared with normoalbuminuric children had a higher mean waist circumference (Mona *et al.*, 2015). Our findings showed, hypoadiponectinemia associated with obesity and T2DM patients while hyperadiponectinemia closed with T1DM and decrease BMI. These results indicated that serum adiponectin concentration which may be considered as a useful biochemical marker for differentiating T1DM and T2DM in this population. Further studies with larger sample sizes and different ethnicities are necessary to verify our findings.

REFERENCES

Barne, M.M., D. Curran-Everett, R.F. Hamman, D. Maahs and E.J. Mayer-Davis *et al.*, 2008. Determinants of adiponectin levels in young people with type 1 diabetes. Diabetes Med., 25: 365-369.

Cnop, M., P.J. Havel, K.M. Utzschneider, D.B. Carr and M.K. Sinha *et al.*, 2003. Relationship of adiponectin to body fat distribution, insulin sensitivity and plasma lipoproteins: Evidence for independent roles of age and sex. Diabetologia, 46: 459-469.

Combs, T.P., A.H. Berg, M.W. Rajala, S. Klebanov and P. Iyengar *et al.*, 2003. Sexual differentiation, pregnancy, calorie restriction, and aging affect the adipocyte-specific secretory protein adiponectin. Diabetes, 52: 268-276.

Forsblom, C., M.C. Thomas, J. Moran, M. Saraheimo and L. Thorn *et al.*, 2011. Serum adiponectin concentration is a positive predictor of all cause and cardiovascular mortality in type 1 diabetes. J. Internal Med., 270: 346-355.

Frystyk, J., L. Tarnow, T.K. Hansen, H.H. Parving and A. Flyvbjerg, 2005. Increased serum adiponectin levels in type 1 diabetic patients with microvascular complications. Diabetologia, 48: 1911-1918.

Gokulakrishnan, K., V. Aravindhan, A. Amutha, S. Abhijit and H. Ranjani*et al.*, 2013. Serum adiponectin helps to differentiate type 1 and type 2 diabetes among young Asian Indians. Diabetes Technol. Ther., 15: 695-701.

Hara, K., M. Horikoshi, T. Yamauchi, H. Yago and O. Miyazaki *et al.*, 2006. Measurement of the High-Molecular weight form of adiponectin in plasma is useful for the prediction of insulin resistance and metabolic syndrome. Diabetes Care, 29: 1357-1362.

Hara, K., P. Boutin, Y. Mori, K. Tobe and C. Dina, *et al*., 2002. Genetic variation in the gene encoding adiponectin is associated with an increased risk of type 2 diabetes in the Japanese population. Diabetes, 51: 536-540.

Heilman, K., M. Zilmer, K. Zilmer, P. Kool and V. Tillmann, 2009. Elevated plasma adiponectin and decreased plasma homocysteine and asymmetric dimethylarginine in children with type 1 diabetes. Scand. J. Clin. Lab. Invest., 69: 85-91.

Kadowaki, T., T. Yamauchi, N. Kubota, K. Hara, K. Ueki and K. Tobe, 2006. Adiponectin and adiponectin receptors in insulin resistance, diabetes and the metabolic syndrome. J. Clin. Invest., 116: 1784-1792.

Li, S., H.J. Shin, E.L. Ding and R.M. van Dam, 2009. Adiponectin levels and risk of type 2 diabetes. A systematic review and meta-analysis. J. Am. Med. Assoc., 302: 179-188.

Maahs, D.M., L.G. Ogden, J.K.S. Bergeon, G.L. Kinney and R.P. Wadwa *et al*., 2007. Determinants of serum adiponectin in persons with and without type 1 diabetes. Am. J. Epidemiol., 166: 731-740.

Meier, U. and A.M. Gressner, 2004. Endocrine regulation of energy metabolism: Review of pathobiochemical and clinical chemical aspects of leptin, ghrelin, adiponectin and resistin. Clin. Chem., 15: 1511-1525.

Menzaghi, C., V. Trischitta and A. Doria, 2007. Genetic influences of adiponectin on insulin resistance, type 2 diabetes and cardiovascular disease. Diabetes, 56: 1198-1209.

Mona, H.M., S.A. Sahar, S.M. Hend and A.W.A. Nanees, 2015. Dyslipidemia in type 1 diabetes mellitus: Relation to diabetes duration, glycemic control, body habitus, dietary intake and other epidemiological risk factors. Egypt. Pediatr. Assoc. Gazette, 63: 63-68.

Ranjbar, S.H., M.M. Amoli, O.T. Malazy, Y. Rumi and J.T. Bazzaz *et al*., 2012. Effect of adiponectin gene polymorphisms on waist circumference in patients with diabetes. J. Diabetes Metab. Disord., 11: 1-14.

Urbanavicius, V., A. Abraitiene, D. Vitkus, R. Borovkiene and Z.A. Kucinskiene, 2008. Adiponectin and insulin resistance in pre-diabetes and early type 2 diabetes mellitus. Gerontologija, 9: 7-14.

Uttra, K.M., B.R. Devrajani, S.Z.A. Shah, T. Devrajani, T. Das, S. Raza and Naseem, 2011. Lipid profile of patients with diabetes mellitus (A multidisciplinary study). World Applied Sci. J., 12: 1382-1384.

Weyer, C., T. Funahashi, S. Tanaka, K. Hotta, Y. Matsuzawa, R.E. Pratley and P.A. Tataranni, 2001. Hypoadiponectinemia in obesity and type 2 diabetes: Close association with insulin resistance and hyperinsulinemia. J. Clin. Endocrine Metab., 86: 1930-1935.