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Adiponectin level in Egyptian type 2 diabetic patients and its relation to glycemic control and lipid profile

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Abstract

Background: Lower level of plasma adiponectin is associated with a higher incidence of type 2 diabetes (T2DM). The aim of this study was to examine the relationship between serum adiponectin and the degree of glycemic control and lipid profile in patients with T2DM. **Methods**: This cross sectional case control study included 40 T2DM patients and 20 healthy control subjects. All patients underwent anthropometric measures and thorough clinical evaluation. Serum adponectin, fasting and post prandial blood glucose, glycosylated hemoglobin (HbA_{1C}), cholesterol, and triglycerides were measured. **Results:** Patients with T2DM had lower level of adiponectin (4.5±2.6ng/ml) compared to healthy controls (9.47±1.32ng/ml)using independent sample t test (p=0.000). Spearman correlation analysis showed significant correlation between adiponectin and HbA_{1C}(r=-0.523; p=0.001)and fasting blood glucose (r=-0.325; p=0.042)in diabetic patients but not in controls. There was no significant correlation between adiponectin and age(r=0.085; p=0.603) or BMI(r=-0.096, p=0.55) in diabetic patients. **Conclusion**: Serum adiponectin level was significantly correlated with glycemic indices but not with lipid profile in T2DM patients.

Keywords: T2DM; adiponectin; lipid; HbA_{1C}.

Introduction

Diabetes is one of the most common health problems all over the world. The clinical impact of diabetes control on diabetes complications is well known **(Stratton et al., 2000)**. Characterizing molecular markers of metabolic control in diabetic patients could have diagnostic and therapeutic implications.

Adiponectin is one of the most abundant proteins secreted from adipocytes (**Takemura et al., 2007).** It has a pivotal role in glucose and lipid metabolism **(Kadowaki and Yamuchi, 2005).**Lower levels of adiponectin are associated with insulin resistance and atherogenic lipid profile (**Zhu et al., 2008)**

Previous studies have shown that lower level of plasma adiponectin is associated with a higher incidence of T2DM**(Li et al., 2009; Tilg et al., 2006).**However, previous studies showed controversial results regarding the association between glycemic indices and lipid profile and serum adiponectin in type 2 diabetes (T2DM). Moreover, previous reports showed that there is racial and etheric variation of adiponectin level**(Hulver et al., 2004)**. Also, serum adiponectin concentration differ according to lifestyle and socioeconomic status **(Buchan et al., 2012; Khanolkar et al., 2012)**.The aim of the present study was to investigate the relationship between serum adiponectin and the degree of glycemic control and lipid profile in patients with T2DM.

Methods

This cross-section study was conducted from September 2013 till January 2015.The participants were recruited from Kasr El Aini University Hospital, diabetes and endocrine clinic after approval of the institutional ethical committee.All patients provided informed consent to participate in this study. The study protocol and procedures conform to the ethical guidelines of the 1975 declaration of Helsinki.

The study included 40 patients with T2DM and 20 age matched healthy subjects selected as controls. Exclusion criteria included patients with anemia (hemoglobin less than 13 gm/L in male or 12 gm/L in female), history of hemoglobenopathies, renal impairment (creatinine >2 mg/dl) or liver failure.

All patients were subjected to thorough medical evaluation including determination of cardiovascular risk factors, history of coronary heart disease, stroke, or atherosclerosis; physical examination including anthropometric measures [weight, height and body mass index(BMI)]; and biochemical tests including fasting and post prandial blood glucose , glycosylated hemoglobin (HbA1C), high density lipoprotein cholesterol (HDL), Low density lipoprotein cholesterol (LDL), triglycerides (TG), complete blood count ,Alanine transaminase **(**ALT),International normalized ratio **(**INR),bilirubin, serum albumin , serum creatinine and serum adiponectin measurement.

Adiponectinsample collection and assay principle

Samples were assembled in serum separator tubes and were allowed to clot for 30 minutes. Centrifugation was done for 15 minutes at approximately 1000 x g and grossly hemolyzed samples were excluded. Serum was separated and stored at -80°C. Human adiponectin ELISA kits(R&D Systems, China) was used to quantify serum adiponectin level in ng/ml that employs the quantitative sandwich enzyme immunoassay technique using monoclonal antibody specific for the human adiponectin globular domain. The test was performed according to manufacturers' instructions.

Statistical analyses

Data was coded and entered using the statistical package SPSS version 15. The data was summarized using descriptive statistics: mean, standard deviation, minimal and maximum values for quantitative variables and number and percentage for qualitative values. Statistical differences between groups were tested using Chi Square test for qualitative variables, independent sample t test for quantitative normally distributed variables while Nonparametric Mann Whitney test was used for quantitative variables which aren't normally distributed. Spearman correlation was done to test for linear relations between variables. *P*-Values less than or equal to 0.05 were considered statistically significant

Results

Patient characteristics

The mean age of the studied patients was (55.83$\pm$10.9) years and 57.5% of them were female. About half of them were using insulin and 55% were hypertensive (table 1).

Table 1. Characteristics of diabetic patients

T2DM patients characteristics	Results
Age (Mean±SD) (years)	55.83±10.9
Sex n(%) Male female	 17(42.5%) 23 (57.5%)
Smokers n (%)	14(35%)
History of hypertension n(%)	22(55%)
History of high cholesterol n (%)	6(15%)
Use of insulin n (%)	22(55%)
History of cerebrovascular disease n (%)	12((30%)

Clinical and Laboratory data of diabetic patients compared to control group.

There was no statistically significant difference between diabetics and control group regarding age and BMI .LDL level was significantly higher in diabetics (206.25±51.89mg/dl) compared to control (98.85±17.14mg/dl)(*P*= 0.000)**,**while HDL was significantly lower in diabetics (31.5±14.08 mg/dl) than the controls (40.7±6.4 mg/dl)(*P*=0.001) (table 2).

Table 2. Comparison of clinical and laboratory measurements of diabetics and control

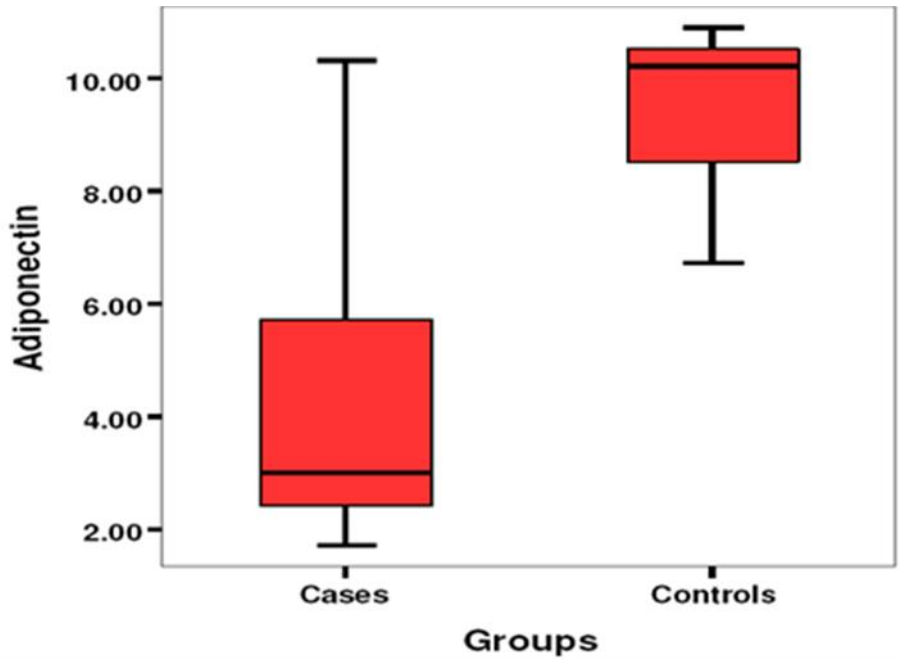
Variable	Diabetics	control	P-value
	Mean ± SD	Mean ± SD	
Age (years)	**53.82± 7.72**	**52.20±9**	**0.40**
[1]BMI(Kg/m^2)	**27.7±4.43**	**27.13±4.69**	**0. 632**
Hemoglobin (gm/dl)	**13.14±3.1**	**13.57±1.2**	**0.219**
Creatinine(mg/dl)	**0.87±0.24**	**0.8±0.3**	**0.527**
Albumin(gm/dl)	**4.19±0.27**	**4.17±0.30**	**0.780**
Bilirubin(mg/dl)	**1.09+0.39**	**1.13+0.36**	**0.654**
[2]INR	**1.21±0.19**	**1.17±0.185**	**0.447**
[3]ALT (IU/ml)	**27.05±10.08**	**25.75±9.02**	**0.616**
[4]FBG(mg/dl)	**218.45±59.8**	**89.23±10.07**	**0.000**
[5]2 hour PG (mg/dl)	**291.3±65.8**	**147.9±14.99**	**0.000**
[6]HbA1C (%)	**7.74±1.63**	**4.22±0.71**	**0.000**
Cholestrol(mg/dl)	**265.95±56.38**	**165.95±22.86**	**0.000**
[7]LDL(mg/dl)	**206.25±51.89**	**98.85±17.14**	**0.000**
[8]HDL(mg/dl)	**31.5±14.08**	**40.7±6.4**	**0.001**
Triglyceride(mg/dl)	**218.38±54.24**	**74.6±16.79**	**0.000**
adiponectin(ng/mL)	**4.5±2.6**	**9.47±1.32**	**0.000**

[1] BMI , body mass index; [2] INR, International normalized ratio; [3]ALT, Alanine transaminase; [4]FBG,fasting blood glucose; [5]2 hour PG,2 hour post prandial blood glucose; [6]HbA1C, glycosylated hemoglobin ; [7]LDL: low density lipoprotein; [8]HDL :high density lipoprotein

Adiponectin levels in diabetic patients compared to control group

Adiponectin ranged from 1.7 to 10.3 ng/mL with mean 4.5±2.6ng/mLin diabetics , while in control group adiponectin ranged from 6.7 to 10.9 ng/mL with mean 9.47±1.32 ng/mL, the difference between the 2 groups was statistically significant (*P*=0.000) (fig. 1).

Fig.1



Correlations between adiponectin and different parameters in diabetic patients

In patients with diabetes, Spearman correlation analysis showed no significant correlation between adiponectin and age (r=0.085; *p*=0.603),BMI (r=-0.096; *p*=0.55),cholesterol (r=-.079;*P*=0.630).The only significant correlation was between adiponectin and fasting blood glucose (r=-0.325; *p*=0.042) (fig. 2) and HbA1c (r=-0.523, *p*=0.001) (fig. 3).Table 3 shows adiponectin correlations with different parameters in diabetic patients.

Table 3. Correlation between adiponectin level and different variables in diabetics.

Variable	Correlation coefficient	P value
age	0.085	0.603
[1]BMI	-0.096	0.55
[2]FBG	-0.325	**0.042**
[3]2 hour PG	-0.191	0.237
[4]HbA1C	-0.523	**0.001**
Total cholesterol	-.079	0.630
[5]LDL	0.065	0.691
[6]HDL	0.038	0.814
Triglycerides	-0.169	0.297
Haemoglobin	-.204	0.207
Creatinine	0.172	0.289
[7]ALT	-0.051	0.754
S.albumin	-0.055	0.0737
bilirubin	0.148	0.361
[8]INR	0.033	0.838

[1] BMI , body mass index; [2]FBG,fasting blood glucose; [3]2 hour PG,2 hour post prandial blood glucose; [4]HbA1c; glycosylated hemoglobin; [5]LDL: low density lipoprotein; [6]HDL :high density lipoprotein;[7]ALT, Alanine transaminase;[8] INR, International normalized ratio

Fig.2

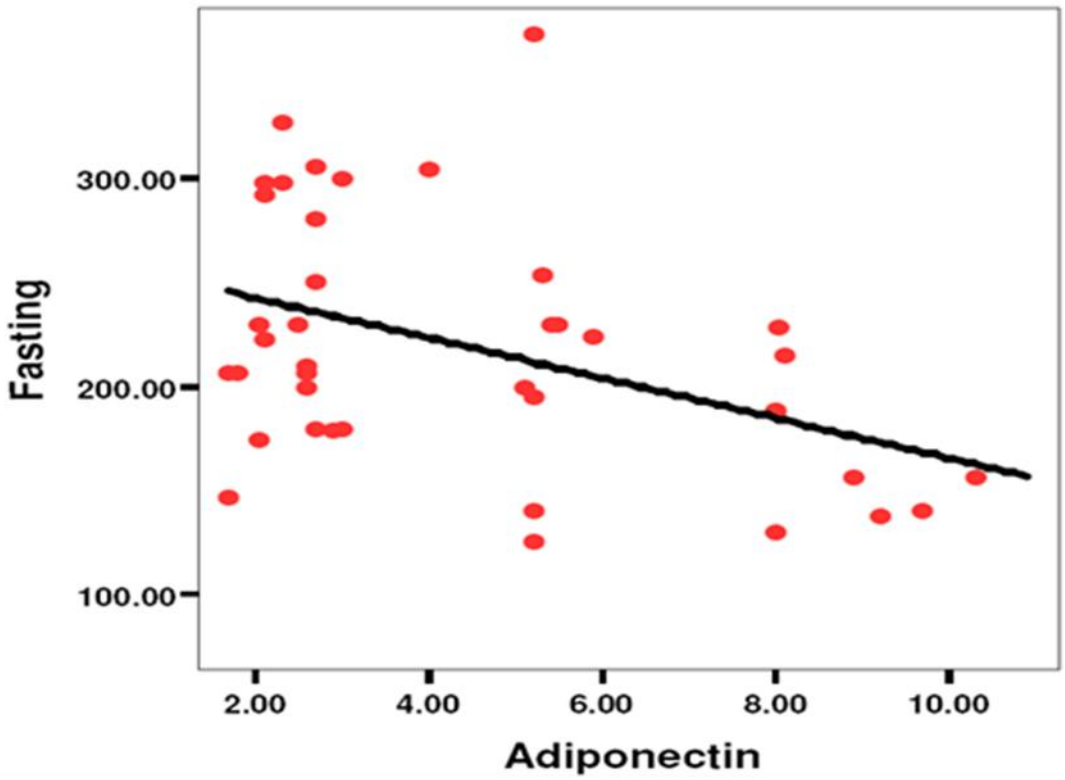
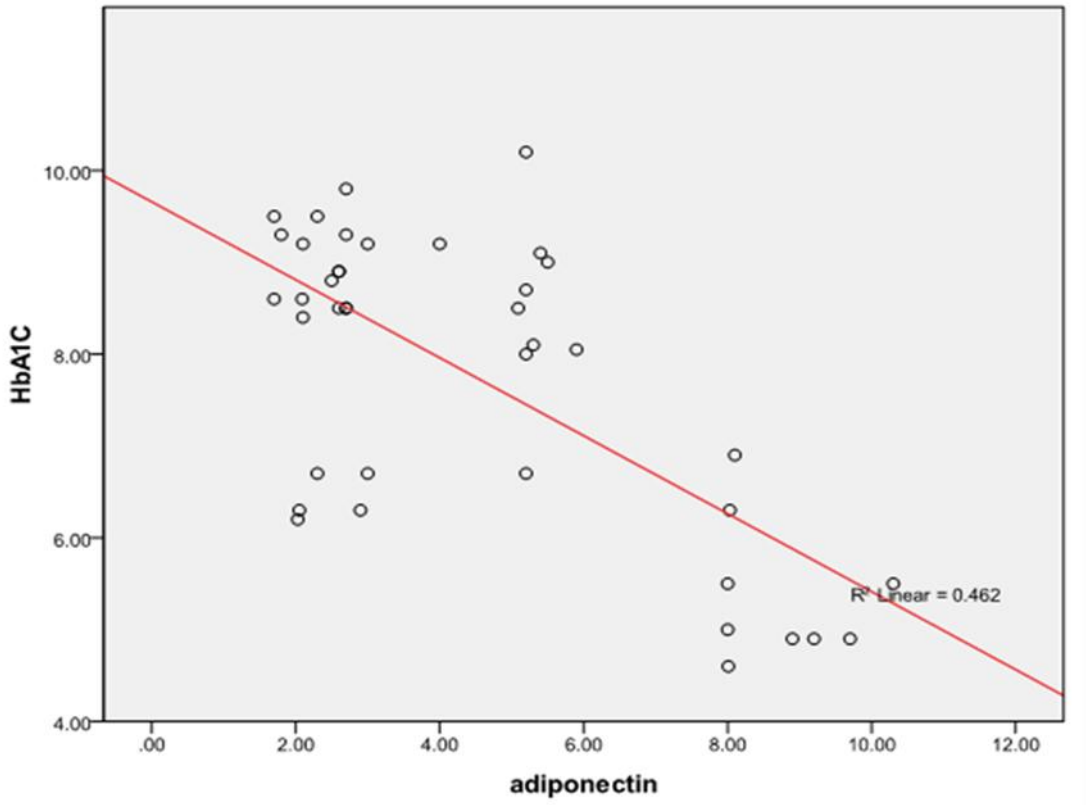

Fasting
300.00
200.00
100.00
2.00
4.00
6.00
8.00
10.00
Adiponectin

Fig.3


HbA1C
10.00
8.00
6.00
4.00
.00
2.00
4.00
6.00
8.00
10.00
12.00
adiponectin
R² Linear = 0.462

Discussion

The current study showed that adiponectin level was lower in diabetic patients compared to controls. Many previous studies reported negative association between serum adiponectin level and insulin resistance and T2DM **(Li et al., 2012; Yamamoto et al., 2014)**.

One of the confounder in the association between adiponectin and diabetes is obesity **(Nigro et al., 2014)**. The results of the current study demonstrated that although, no significant difference of BMI between diabetics and controls, adiponcetin level was lower in diabetic patients compared to controls. This agrees what was found by other researchers that the association between adiponectin levels and diabetes risk remains unchanged after adjustment for BMI **(Yamamoto et al., 2014, Li et al, 2012)**.

The explanation of the association between diabetes and adiponectin could be related to the anti-inflammatory effects of adiponectin by suppressing Interleukin 6 (IL-6) and Monocyte chemoattractant protein-1(MCP-1) production and by increasing peroxisome proliferator-activated receptors (PPAR) gamma expression**(Lira et al.,2012)**.Also, adiponectin increases insulin sensitivity directly by stimulating hepatic insulin signaling by enhancing Insulin receptor substrate 2 (IRS-2) expression**(Awazawa et al.,2011),**and increasing glucose uptake by stimulating the translocation of the glucose transporter 4 (GLUT4) to the cell surface **(Ceddia et al.,2005).**

However, a more recent Mendelian study found no consistent evidence that genetically determined reduced adiponectin levels promote the development of T2DM**(Lira et al.,2012)**, which suggests that the changes in adiopenctin levels could be a result of the alteration in insulin sensitivity and blood glucose level.

The results of this study demonstrated negative correlations between serum adiponectin and glycemic indices in diabetic patients. This coincides with the findings of previous studies. **Goodarzi et al. (2007)** found significant negative correlation between adiponectin and HbA1c in a cohort of T2DM patients. **Durrani et al. (2015)** reported that hypoadiponectinemia is associated with worse glycemic control in T2DM patients with coronary heart disease.

However, increased adiponectin level was reported to be associated with higher levels of blood glucose in established T1DM **(Maahs et al., 2007)**.Also**, Pilacinski et al.(2016)**found significant association between HbA1c and elevated adiponectin level independent from other variables. This difference between adiponectin level in type 1 and type 2 diabetes may be related to weight loss and hypercatabolic state associated with Type 1 diabetes particularly at the time of presentation.

In the present study, there was no statistically significant difference of adiponectin level between patients using insulin and those treated with oral hypoglycemics. Generally, the effect of insulin on adiponectin levels is debatable. One study of insulin treatment in diabetic mice, suggested that there is no effect of insulin treatment on adiponectin levels **(Fujita et al., 2005)**.Another study in diabetic mice reported that both insulin and metformin treatment prevent the development of hypoadiponectinemia **(Schmid et al, 2013)**

T2DM is known to be associated with dyslipidemia characterized by low HDL and high triglyceride levels. The findings of the current study revealed no significant correlation between adiponectin and any of measured plasma lipids. Several studies have investigated the relationship between adiponectin and plasma lipids but, the results are controversial **(Makedou et al., 2011 and Durrani et al., 2015)**.

Most of previous studies showed that the level of adiponectin has an inverse relationship with LDL and TG, and a positive correlation with HDL**(Durrani et al., 2015;Kimm et al.,2010 and Matsubaraet al.,2002)**.However, another study showed no significant correlation between circulating adiponectin concentration, LDL cholesterol and total cholesterol in diabetic patients **(Mantzoros et al.,2005),** patients with familial hyperlipidemia**(van der Vleuten et al.,2005**) and overweight subjects **(Alitinova et al.,2007)**.Moreover, a positive relationship was found between adiponectin concentrations and LDL in pregnant females (**Makedou et al.,2011)** .

One of the possible mechanisms mediating adiponectin effect on TG is the activation of PPAR αin liver. It also affects HDL cholesterol by reducing the activity of the enzyme lipoprotein lipase **(Yamauchi et al., 2003)**. There is racial and Ethnic variation in the expression of PPAR α gene and in the activity of lipoprotein lipase **(Wang et al., 2014 ;Després et al., 2000).** This could partially explain the absence of significant association between adiponctin level and any of lipid measurements in the present study. In concordance with our results, an Egyptian study of

adiponctin level in HCV infected patients that revealed no significant correlation of serum adiponectin with TC, HDL, LDL, TG **(Ramzy et al., 2011)**

Potential limitations of our study should also be mentioned. First, the study included small number of cases. Second, it was a case control cross sectional study. The effect of adiponectin gene polymorphism on glycemic control and lipid profile in Egyptian T2DM patients needs further investigation.

Conclusions

Adiponectin showed significant negative correlation with glycemic indices in T2DM patients. However, there was no significant association between serum adiponectin and plasma lipids in the studied population.

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