Adiponectin Serum Levels in AdolescentBoys with Type 1 Diabetesin Relationships to Pubertal Growth,Development and Glycemic control

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Abstract

Introduction: Adiponectin is a protein hormone secreted exclusively by adipocytes that regulate the metabolism of lipids and glucose. It has antidiabetic, antiatherogenic and anti- inflammatory properties.

Objective: To asses adiponectin serum levels in adolescent boys with type 1 diabetes mellitus (T1DM) and to assessits relationships with pubertal development, body mass index (BMI) , glycemic control and insulin dosage.

Research design and methods: A case- control study was carried out on 45 adolescent boys with T1DM aged (12- 18) years and 37 healthy control boys of similar age. Each of the cases and control groups were divided into four subgroups according to their Tanner stage .Theywere subjected to full history, reviewing medical records, auxology andpubertal stage assessment. Serum total adiponectinlevelwas determined by ELISA technique in addition to glycatedhaemoglobin (HbA1c) and fasting blood glucose.

Results: Mean adiponectin serum level (±SD) was significantly higher in T1DM boys compared to healthy control group (12.93± 5.24µg/mlversus 8.91± 3.21µg/ ml) (P<0.001) . Such higher serum levels of adiponectin were detected mainly at Tanner stage 2 (16.57± 4.60 µg/ mlvs 11.88± 3.39 µg/ ml) (P= 0.025) and Tanner stage 3 (12.77± 3.71 µg/ ml vs.6.59± 1.54 µg/ ml) (P= 0.002). Adiponectin level decreased significantly during pubertal development in control groupand T1DM group. Adiponectin level was significantly higher in diabetic-poorcontrolled group than diabetic good- controlled group. Adiponectin was negativelycorrelated with pubertal stage, age, intermediate/ long acting insulin dose and positively correlated to HbA1c in diabetic group. Incontrol group adiponectin levels were negatively correlated with pubertal stage and BMI.

Conclusion: Adiponectin serum levels in adolescent boys with type 1diabetes were significantly higher than control mainly at early puberty. It decreased significantly during pubertal development and was strongly positively related to glycemic control.

مستويات هرمون الأديبونكتين بالذكور المراهقين المصابين بداء السكرى من النوع الأول وعلاقته بتطور البلوغ وإنضباط مستوى السكر بالدم.

المقدمه: الأديبونكتين هو احد الهرمونات التى تفرز فقط بواسطه الخلايا الدهنيه للجسم وينظم عمليات الأيض للدهون والسكريات. والأديبونكتين له خصائص مضاده لداء السكرى ولتصلب الشرايين وللالتهاب.

الهدف: هو تقييم مستويات هرمون الأديبونكتين فى الذكور المراهقين المصابين بداء السكرى من النوع الأول ودراسة علاقة تلك المستويات مع تطور البلوغ، معامل كتلة الجسم، انضباط مستوى السكر بالدموجرعة الإنسولين.

الأساليب: الدراسه الحاليه تم تنفيذها على ٤٥ من الذكور المراهقين المصابين بداء السكرى من النوع الأول بالمرحله السنيه من (١٢- ١٨) ومجموعه اخرى ضابطه تشمل ٣٧ مراهقا من الأصحاء بنفس المرحله السنيه. وقد تم تقسيم كلا من المرضى والأصحاء طبقا لتطور مرحلة البلوغ الى أربعة مجموعات من مرحله البلوغ الثانيه وحتى الخامسه حيث تم أخذ التاريخ المرضى ومراجعة السجلات المرضيه مع القياسلت الأنثربومتريه وتقدير مرحلة البلوغ وتم قياس مستويات الأديبونكتين الكلى بتقنية إليزا بالاضافة لقياس نسبة الهيموجلوبين السكرى والسكر الصائم بالدم.

النتائج: مستوى هرمون الأديبونكتين كان بصورة ملحوظه أعلى بالذكور المراهقين المصابين بداء السكرى من النوع الأول مقارنة بالأصحاء .تلك المستويات الأعلى وجدت بصفه أساسيه بالمرحلة الثانيه والثالثه للبلوغ. كما ينخفض مستوى الأديبونكتين بمرضى السكرى من النوع الاول وكذلك الاصحاء بصوره ملحوظه أثناء تطور البلوغ. ومستوى هرمون الأديبونكتين كان أعلى بمجموعة مرضى السكرى ذات التحكم الردئ بانضباط السكر بالدم عن المجموعه ذات التحكم الجيد بانضباط مستوى السكر. وقد وجدت علاقه عكسيه بالمصابين بداء السكرى من النوع الأول بين مستوى هرمون الأديبونكتين ومرحلة البلوغ والسن وجرعة الإنسولين متوسط وطويل المفعول وبصوره طرديه مع مستوى الهيموجلوبين السكري. وبالمجموعه الضابطه توجد علاقه عكسيه بين مستوى الأديبونكتين ومرحلة البلوغ ومعامل كتلة الجسم.

الخلاصه: مستويات هرمون الأديبونكتين فى الذكور المراهقين المصابين بداء السكرى من النوع الأول أعلى بصوره ملحوظه عن الأصحاء وخاصة بالمراحل الأولى لتطور البلوغ وينخفض مستواه بصوره ملحوظه أثناء تطور البلوغ كما ترتبط بصوره ملحوظه بإنضباط مستوى السكر بالدم.

Introduction:

Type 1 diabetes is generally thought to be precipitated by an immune-associated, if not directly immune- mediated, destruction of insulin- producing pancreatic β cells (Todd, 2010). The global incidence of type 1diabetes is increasing worldwide, at an annual rate of (3- 5)%, particularly in children under the age of 5 years, and this trend leads to a significant health burden (Patterson et.al., 2009).

Adiponectin is a protein hormone secreted exclusively by adipocytes that regulate the metabolism of lipids and glucose (Savino et.al., 2008). Among adipokines, adiponectin has gained considerable attention because of its antidiabetic, antiatherogenic and anti- inflammatory properties. Circulating adiponectin levels are determined by various genetic, anthropometric, hormonal, inflammatory, dietary, and pharmacological factors (Dalamaga et.al., 2012).

The data concerning adiponectin in children and adolescents with type 1 diabetes are sparse and controversial. While some studies have showed that serum adiponectin levels were higher in T1DM Children and adolescents (Abd El- Maksoud et.al., 2009; Barnes et.al., 2008), other studies did not report any difference (Habeeb et.al., 2012; Morales et.al., 2004).

The relationship of adiponectin to glycemic control is controversial with some studies showing strong relationship (Barnes et.al., 2008) and others failed to demonstrate such relationship (Galler et.al., 2007). In addition, the effect of insulin therapy in modifying adiponctin serum level in T1DM adolescents is controversial.

Pubertal development is characterized by many physiological changes, involving both hormonal and metabolic processes, and these factors together with psychological issues are frequently responsible for poor glycaemic control. Treatment may be complicated by poor compliance, difficulties in targeting insulin therapy and concerns about weight gain (Dunger, 1992). Studies in adolescents have documented that pubertal development has an effect on adiponectin serum levels and that gender difference in adiponectin develop during pubertal development (Böttner et.al., 2004).

Aim Of The Study:

To assessadiponectin serum levels in adolescent boys with type 1 diabetes mellitusand to explore the relationships between adiponectinand pubertal development, body mass index, glycemic controland insulin treatment.

Subjects And Methods:

The present study was a case- control study conducted on 45 diabetic adolescents boys aged (12- 18) years previously diagnosed as type 1 diabetes, recruited from diabetes clinic at the National Institute of Diabetes and Endocrinology, Cairo, Egypt and 37 healthy controls boys. Written informed consent was obtained from the parents, and the study was approved by the Ethics Committee of the Institute of Postgraduate Childhood Studies and by that of the National Organization forTeaching Hospitals and Institutes.

Each ofthe cases and control groups were further divided into four subgroups according to their Tanner stage (Tanner stage 2- 5) each containing a number ranging from (11- 12) boys for casesand (8- 10) boys for the control. The cases and control groups were cross matched by age, Tanner stage and BMI. Within each Tanner stage the cases and control were matched by age and BMI.

Inclusion criteria for cases were: males, (12- 18) years old, Tanner stage 2: 5, diagnosis of type 1 diabetes according to criteria of American Diabetes Association (Ada, 2014), no diabetic complicationsand disease duration not less than 1 year. All patients were on insulin therapy only (two daily or multiple daily injections) with no other concomitant medications.

All cases were subjected to following:

1. Full medical history and reviewing the medical records: To collect data concerningchronological age, age of onset of diabetes, diabetic duration, insulin regimen, insulin type, daily insulin dose.
2. Clinical examinations included: Auxology (weight, height assessment and BMI calculation). Auxological data were evaluated according to Egyptian percentile Charts (Ghalli et.al., 2002). Pubertal assessmentwas done according to Tanner criteria (Tanner, 1962).
3. Laboratory Investigations: After an overnight fast venous blood samples were obtained in the morning and dividedinto two parts. The first partwas used for fasting plasma glucose by the enzyme glucose oxidase methodand Glycated hemoglobin using HPLC fully automated system (Bio- Rad D-10 Haemoglobin testing system). The second part was immediately centrifuged at 4000 revolution for 5 minutes. Aftercentrifugation, serum was separated, stored at –20◦C until hormone determination. Serum adiponectin in samples was determined using an ELISA KITS (Assay Max Human Adiponectin ELLISA Kit) provided by Assaypro LLC company (USA). Intra- assay and inter- assay coefficients of variation were 4.3% and 7.2% respectively.

Statistical Analysis:

All statistical calculations were done using computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows. Comparison of numerical variables was done using Student ttest for comparing 2 groups when data was normally distributed and Mann Whitney Utest when not normally distributed. P values less than 0.05 was considered statistically significant.

Results:

Table (1) Comparison between control and diabetic groups as regards number of cases at various pubertal stages

Variables			Group		X^2	P Value
			Control	Diabetic		
Pubertal Stage	T2	Number	10	12	0.124	0.989
		% Within Group	27.0%	26.7%		
	T3	Number	8	11		
		% Within Group	21.6%	24.4%		
	T4	Number	10	11		
		% Within Group	27.0%	24.4%		
	T5	Number	9	11		
		% Within Group	24.3%	24.4%		
Total		Number	37	45		
		% Within Group	100.0%	100.0%		

Table (1) shows that there was statistically no significant difference between control and diabetic groups as regards number of cases at various pubertal stages (P= 0.989).

Table (2) Comparison between control and diabetic groups as regards descriptive and clinical parameters

Variables	Control (n= 37)	Diabetic (n= 45)	T- Test	
	Mean± SD	Mean± SD	t	P Value
Age (Years)	14.67± 1.61	14.69± 1.54	- 0.061	0.951
Weight (Kg)	44.43± 10.42	46.41± 10.55	- 0.849	0.398
Height (Cm)	153.56± 11.55	157.19± 10.05	- 1.523	0.132
Body Mass Index	18.56± 2.00	18.56± 2.56	0.016	0.987
<5th Bmi Percentile	16.02±0.69 (N=	15.61±1.05 (N=	0.824	0.426

Variables	Control (n= 37)	Diabetic (n= 45)	T- Test	
	Mean± SD	Mean± SD	t	P Value
	6)	8)		
5- 85 Bmi Percentile	19.06±1.79 (N= 31)	19.19± 2.33 (N= 37)	- 0.266	0.791
Systolic BP (mm/Hg)	110.22± 6.28	110.56± 7.63	- 0.213	0.832
Diastolic BP (mm/Hg)	64.37± 3.52	71.78± 8.34	- 5.408	0.0001**
Fasting glucose (mg/dl)	80.66± 8.35	176.80± 52.31	- 12.143	<0.0001**
HbA1C	5.60±0.47	9.39± 1.29	- 18.349	<0.0001**
HbA1C in diabetic good controlled (n= 12)		7.66±0.78		
HbA1C in diabetic poor controlled (n= 33)		10.02±0.73		
Age of onset of diabetes (years)	-	9.18± 3.20	-	-
Duration of diabetes (years)	-	5.51±3.33	-	-
Insulin dose per day (units)	-	50.24± 20.36	-	-
Insulin dose per kg (units/kg)	-	1.09±0.37	-	-
Dose of regular insulin (units)	-	27.07± 10.68	-	-
Dose of intermediate/ long acting insulin (units)	-	22.73±1 2.97	-	-

Table (2) shows descriptive and clinical parameters of control and diabetic groups.

Table (3) Comparison between control and diabetic groups regardingadiponectin serum levels

Variable	Control (N= 37)	Diabetic (N= 45)	t	P Value
	Mean± SD	Mean± SD		
Adiponectin (µg/ml)	8.91± 3.21	12.93± 5.24	- 4.266	0.0001**

Table (3) shows thatAdiponectin serum level (±SD) was significantly higher in T1DM boys compared to healthy control group (12.93± 5.24 µg/ml versus 8.91± 3.21 µg/ ml) (P<0.001)

Table (4) Comparison of adiponectin serum levels between control and diabetic groups at various pubertal stages

	Pubertal Stage	Control	Diabetic	Mann- Whitney Test	
		Mean±SD	Mean±SD	Z	P
Adiponectin (µg/ml)	T2	11.88± 3.39	16.57± 4.60	- 2.242	0.025*
	T3	6.59± 1.54	12.77± 3.71	- 3.139	0.002**
	T4	8.90± 2.80	11.21± 5.93	- 0.704	0.481
	T5	7.70± 2.11	10.84±0. 94	- 1.861	0.063

Table (4) showsthatthe higher levels of adiponectin in T1DM adolescent boys were detected mainly at Tanner stage 2 (16.57± 4.60 µg/ ml vs 11.88± 3.39µg/ml) (P= 0.025) and Tanner stage 3 (12.77± 3.71 µg/ml vs. 6.59± 1.54 µg/ml) (P= 0.002). The difference was not significant at T4 (P= 0.481) and T5 (P= 0.063).

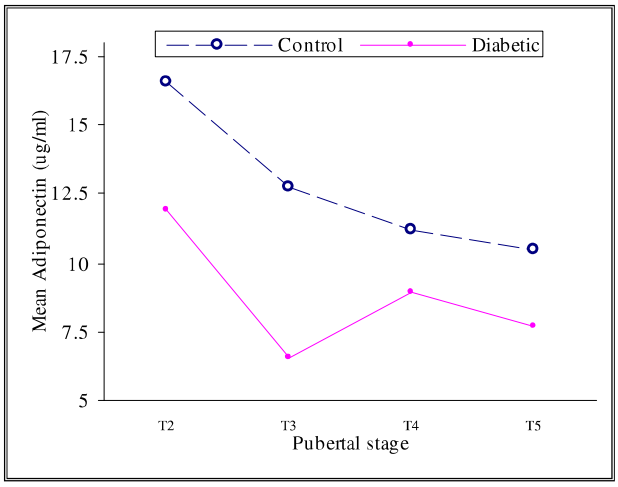

Figure (1) Variation in adiponectin serum level during pubertal development in control and diabetic groups

Figure (1) shows thatadiponectin serum levels decreased significantly during pubertal development in control group and T1DM group so that level at Tanner stage 5 was significantly lower than level at Tanner stage 2 (7.70± 2.11 versus 11.88± 3.3 µg/ml, P= 0.009) in control group and (16.57± 4.60µg/ml versus 10.84± 4.94 µg/ ml, p< 0.043) in T1DM group. Also there was significant decrease of adiponectin level between Tanner stage 2 and Tanner stage 3 in control group (11.88± 3.39 versus 6.59± 1.54 µg/ ml, P= 0.001). The rate of decline in adiponectin serum level in T1DM boys was more smooth and regular in diabetic than control group.

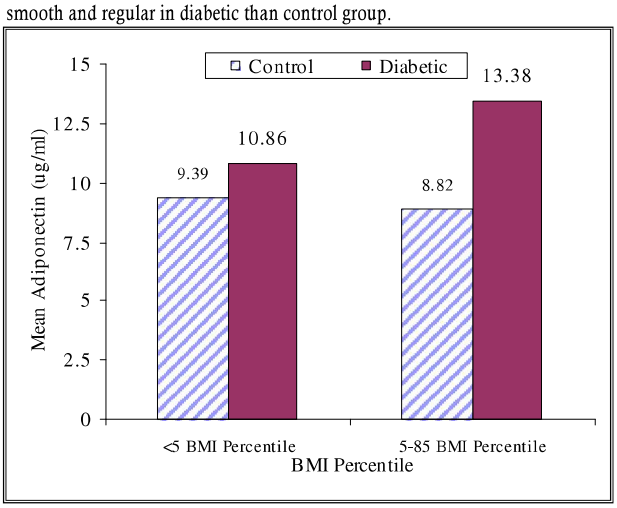

Figure (2) Comparison between control and diabetic groups as regards serum adiponectin level according to BMI percentile

Figure (2) shows thatthere was no difference between control and diabetic as regards adiponectin serum levels in underweight groups (P= 0.334) while the difference was significant between control and diabetic in normal weight groups (P≤ 0.0001).

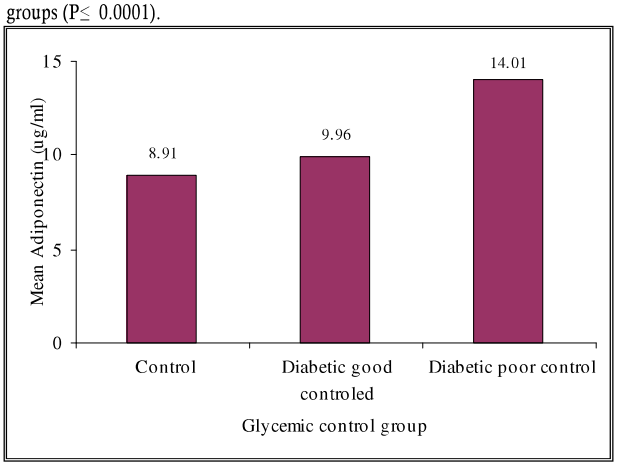

Figure (3) Adiponectin serum levels in control, diabetic good- glycemic control and diabetic poor- glycemic control groups groups
*Higher in diabetic (poor- controlled) than diabetic (good- controlled) P= 0.018
≠ Higher in diabetic (poor- controlled) than control group P<0001

Figure (3) shows thatAdiponectin serum levels were significantly higher in T1DM poor- controlled group (HbA1c ≥ 8.5%) than in good- controlled group (HbA1c<8.5%) (14.01± 5.22 µg /ml versus 9.96± 4.15ug/ ml P< 0.001) and higher than control group (14.01± 5.22µg /ml versus 8.91± 3.21µg/ ml P= 0.018), however, there was no significant difference between good controlled diabetic group and control group (P= 1.00). Figure (4) Correlation of adiponectin to glycatedhaemoglobin in the diabetic group

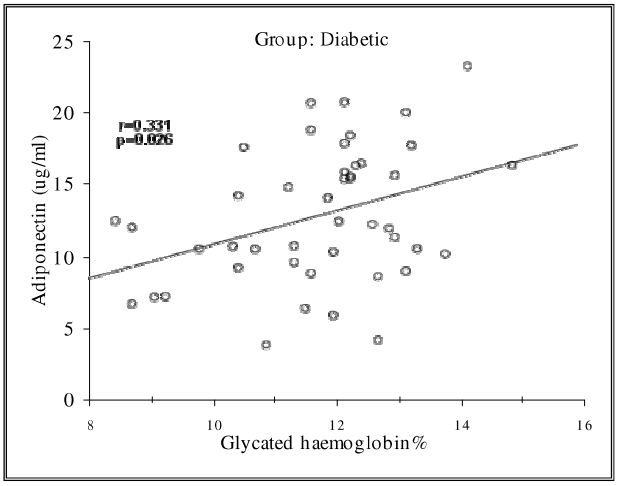

Figure (4) shows a significantpositive correlation of adiponectin to glycatedhaemoglobin in the diabetic groupFigure (5) Correlation of adiponectin to dose of intermediate/ long acting insulin in the diabetic group

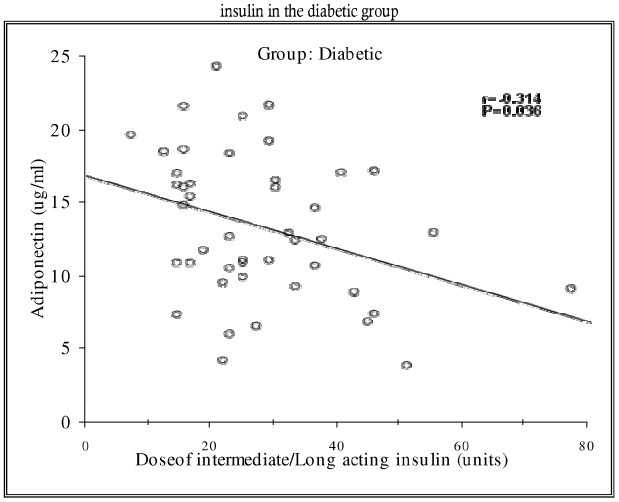

Figure (5) shows a significant negativecorrelation of adiponectin to dose of intermediate/ long acting insulinin the diabetic groupFigure (6) Correlation of adiponectin to body mass index in control group

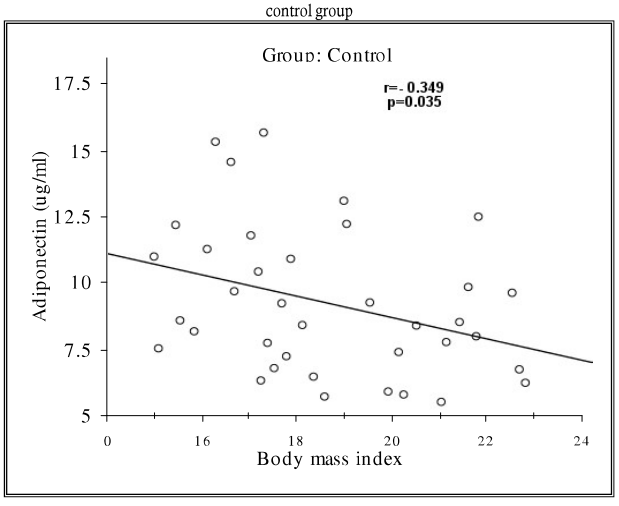

Figure (6) shows a significant negative correlation of adiponectin to BMI incontrol group

Table (4) Stepwise multiple regression analysis of T1DM group with adiponectin as dependent variable

Predictors	Standardized Beta Coefficient β	Std. Error SEβ	P	R2	ANOVA P
Pubertal Stage	- 0.293	0.616	0.035	0.325	0.001
Dose Intermediate/Kg	- 0.277	3.091	0.043		
Hba1c%	0.269	0.428	0.047		

Stepwise Regression analysis model in T1DM boys with adiponectin as dependent variable showed that Tanner stage (β=- 0.293, p= 0.035), dose of intermediate /long insulin (β=- 0.277, p= 0.043) and Glycatedhaemoglobin% (β= 0.296, p= 0.047) to be most significant predictors of adiponectinlevel in T1DM boys explaining 32.5% of variation in adiponectin serum levels 1n T1DM boys (R square= 0.325, P= 0.001)

Discussion:

The results of the present study revealed that mean adiponectin serum level (±SD) was significantly higher in T1DM group compared to healthy control group. Most studies in children and adolescents with T1DM revealed similar results to our study regarding elevated adiponectin serum levels inT1DM adolescents (Jaleel et.al., 2013; Abd El- Maksoud et.al., 2009; Barnes et.al., 2008).

In diabetic patients with constant hyperglycemia, the glycosylation process is probably altered, and this could lead to an altered adiponectin function. Consequently, a modified adiponectin molecule could lead to adiminished negative feedback, a mechanism that is an essential part of hormonal systems, and thus to increased adiponectin concentrations in diabetes (Saraheimo et.al., 2005).In accordance with this theory we detected significant positive relationship between adiponectin andHbA1c and serum adiponectin levels was significantly higher in diabetic poor- glycemic control group than diabetic-good glycemic control group.

Low levels of insulinin T1DM patients cause future expression of adiponectin gene and more adiponectin secretion (Faraj et.al., 2008). In accordancewith this theory Celi et.al. (2006) postulated that lack of insulinization in T1DM leads to an elevation of adipoectin concentrations. However, a possible role of insulin therapy in modifying adiponectin serum levels was postulated by Celi et.al. (2006) andHabeeb et.al. (2012).

A third hypothesis was postulated by Schalkwijk et.al. (2006) who postulated that adiponectin may be enhanced in type 1 diabetic patients as a physiologic counter regulatory response to mitigate endothelial damage and vascular damage. However, in present study elevated adiponectin levels could not be related to this theory as our patients did not have known complications of T1DM as detected by reviewing medical records and clinical examinations.

In contrast to results of elevated serum adiponectin level in adolescents with T1DM, Celi et.al. (2006) and Morales et.al. (2004) reported that adiponectin levels adolescents with type 1 diabetes did not differ from those in healthy subjects. These authors may have analyzed male and female patients at different pubertal stages together whereas adiponectin is affected by gender and pubertal development.

In the present studyAdiponectin serum levels decreased significantly during pubertal developmentboth in control and diabetic groups. Several studies in healthy adolescent boys showed similar pattern of decline of adiponectin serum levels during pubertal development (Bottner et.al., 2004; Martos- Moreno et.al., 2006; Andersen et.al., 2007) and TSOU et.al. (2004) demonstrated thatadiponectin levels exhibited a V shape (transient drop) with a remarkable trough in boys aged (10- 12) years. Such remarkable dropin adiponectin levels coincideswith the occurrence of an increase in testosterone level associated with male puberty.

In T1DM children and adolescents the longitudinal study by Galler et.al. (2007) revealed that serum adiponectin levels decreased during puberty and were significantly lower at the end of puberty compared with pre- pubertal stage. Similarly, Karmifar et.al. (2013) demonstrated thatadiponectin level was

negatively associated with puberty state (prepuberty- puberty- post puberty) in T1DM adolescents.

In the present study higher serum levels of adiponectin in T1DM adolescent boys were detected, when compared with Tanner stage- matched control, only at Tanner stage 2 and Tanner stage 3 (early puberty). Gökşen et.al. (2013) found that there were no differences in adiponectin levels between T1DM (17.6± 4.0 years) adolescents and controls (16.43± 4.1) at such late pubertal stages. In T1DM pubertal girls Iniguez et.al. (2008) observed higher adiponectin levels at Tanner stage 2 and Tanner stage 3 only (early puberty) with similar levels at Tanner stage 4 and Tanner stage 5 (late puberty).

Glycemic control in diabetic subjects is known to deteriorate during puberty. In both the intensive and the conventional treatment groups, adolescents had 1% higher average long- term blood glucose levels (measured by HbA1c) compared with the adults (Diabetes Control and Complications Trial, 1994). In addition to endocrine changes associated with puberty, leading to greater insulin resistance many adolescents experience a deterioration in metabolic controloften attributable to erratic meal and exercise patterns, poor adherence to treatment regimens, hazardous and risk taking behaviours and eating disorders (Court et.al., 2009).

Adiponectin serum level in present study was significantly higher in T1DM poor- controlled group than in good- controlled group and higher than control group, however, there was no significant difference between good controlled diabetic group and control group. These results were similar to those of Karamifar et.al. (2013). Such variation in adiponectin serum levels between different glycemic control groups reflects the importance of metabolic control in determining serum adiponectn levels in T1DM and possibility of depending on adiponectin serum levels as sensitive biomarker of glycemic control in T1DM patients.

We detected a significant positive correlation between adiponectn and HbA1C levels in T1DM Group. In agreement with our study several studies in children and adolescents with T1DM have documented such relationship between adiponectin and HbA1c (Karamifar et.al., 2013; Habeeb et.al., 2012; Barnes et.al., 2008). Such correlation was explained by altered glycosylation process in diabetic patients as explained previously. On the other hand, other studies in children and adolescents with T1DM failed to show such relationship between adiponectin and glycemic control (Goksen et.al., 2013; Abd El- Maaksoud et.al., 2009; Galler et.al., 2007).

Strong negative correlation between adiponectin and dose of intermediate/ long acting insulin /kg was detected in the present study. Such correlation was present even after adjustment for HbA1C, insulin type and insulin regimen. Dose of intermediate/ long acting insulin/ kg in our study, though increased between Tanner stages in diabetic group, this difference didn't reach significance.

The relationship of adiponctin to insulin is controversial. In an older in vitro study by Fasshauer et.al. (2002) chronic exposure of insulin decreased adiponectin gene expression in the cultured 3T3- L1 adipocytes. In more recent study by Blümer et.al. (2008) insulin had a direct stimulatory effect on adiponectin gene expression in 3T3- L1 adipocytes.

In healthy adolescentsRiestra et.al. (2011);I niguez et.al. (2008); Tsou et.al. (2004) reported that adiponectin serum levels negatively correlated with serum insulin and insulin resistance. On the other hand Celi et.al. (2006); Kettaneh et.al. (2006); Snehalatha et.al. (2008) did not find correlation of adiponectin to fasting insulin and insulin sensitivity in healthy control subjects.

One of explanations of elevated adiponectin levels in T1DM is that absolute endogenous insulin deficiency may contribute to elevated serum adiponectin in type 1 diabetes (Imagawa et.al., 2002).

In adult studies for subjects with type T1DM and similar to our results Insulin dose was inversely related to adiponectin serum level in the studies byMaahs et.al. (2007) and Pereira et.al. (2012).

In T1DM Egyptian adolescents, Habeeb et.al. (2012) revealed normal adiponectin level in the studied uncomplicated T1DM adolescent patients and suggested that absolute insulin deficiency may contribute to elevated level of serum adiponectin in type I diabetes, but appropriate regular treatment with insulin returned these levels to normal. ThoughCeli et.al. (2006) found no correlation of adiponectin to insulin dosage, they assumed that the higher adiponectin levels detected in prepubertal T1DM children in comparison to control in their study may be attributable to inefficient insulin treatment, as demonstrated by positive association of adiponctin concentration with HbA1c in their study.

On the other hand, Abd El- Maksoud et.al. (2009) found no relationship between adiponectin and daily insulin dose. Similarly, Iniguez et.al. (2008) didn't detect relationship of adiponectin to insulin dose in a study of T1DM adolescents girls and explained this by the fact that other factors, such as number of insulin injection and type and proportion of prandial/ basal insulin concentrations, may be important for determining the insulin levels reaching the adipose tissue and thus affect the adiponectin secretion. And that self-report of insulin dose in pediatric group is not a reliable index of insulinization.

Such negative correlation of adiponectin to intermediate/ long insulin dose/ kg in our study may reflect low intermediate/ long acting insulin dosage (inefficient insulin treatment), as demonstrated by positive association between adiponectin and HbA1c in our study. In view of such negative correlation of adiponectin to insulin dosage in our study elevated adiponectin levels at early puberty, associated with poor metabolic control, may be related to inappropriate insulin dosage at this early stages where insulin requirements is the highest during male developmentas detected byWiegand et.al. (2008). The increase of insulin dose at late pubertal stages together with improved insulin sensitivity and glycemic control may have reduced adiponetin levels to normal.

There was an inverse relationship between adiponectin and BMI in control group. Several studies in healthy adolescents have documented that traditional inverse relationship between adiponectin and BMI (Anderson et.al., 2007; Bottner et.al., 2004). Jaleel et.al. (2013) and Panagopoulou et.al. (2008) reported such relationship in obese participants at adolescent age group compared with controls. On the other hand, other studies in healthy adolescents revealed a weak or no correlation of adiponctin to anthropometric measurements (Schoppen et.al., 2010; Snehalatha et.al., 2008; Mitsnefes et.al., 2007).

Such relationship was explained by heightened oxidative stress, chronic inflammation and macrophage infiltration of adipose tissues. Reactive- oxygen species (ROS) and pro- inflammatory cytokines are potent inhibitors of adiponectin gene expression in cultured adipocytes and could, therefore, contribute to lowering adiponectin release by "Obese" adipose tissue (Guerre-Millo, 2008).

InT1DM subjectsin the current studyno correlation was detected between adiponectin and BMI. Similar to our results Karamifar et.al. (2013); Abd El-Maksoud et.al. (2009) andHeliman et.al. (2009) foundno correlation of adiponectin with BMI in T1DM adolescents. As all of our patients were of normal or underweight group with no cases of overweight or obesity when plotted on Egyptian percentile for BMI (Ghalli et.al., 2002), such distribution of subjects may be a cause of non- correlation with serum adiponectin levels in T1DM group and weak correlation in control group as several studies had documented that the relationship of adiponectin to obesity parameters become evident only in overweight or obese subjects. Adiposity had a greater impact on adiponectin levels in girls than in boys as suggested by Woo et.al. (2005) and all of our patients were of male gender. In addition in adolescent boys increment in BMI may be mainly attributed to accumulation of fat- free tissue, it is expected that BMI may not correlate to adiponectin during pubertal development (Xu et.al., 2012). Several studies in adolescents showed that adiponectinis more closely related to waist circumference, a surrogate measure of central adiposity, than with total adiposity as assessed by BMI, (Wagner et.al., 2008, Huang et.al., 2004). However, In contrast to previous results other studies by Galler et.al. (2007); Gökşen et.al. (2013); Atwa and Shora et.al. (2011) detected the traditional inverse relationship between adiponectin and adiposity in T1DM children and adolescents.

Conclusion:

Adiponectin serum levels in adolescent boys with type 1diabetes were significantly higher than control mainly at early puberty. It decreased significantly during pubertal development and was strongly related to pubertal stage and glycemic control.

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