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Serum Resistin Levels in Type 1 Diabetic Children and Factors Affecting the Circulating Concentrations

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ABSTRACT

Resistin is a hormone involves in regulation of blood glucose. The study estimated serum resistin level in type 1 diabetic children and assessed its relation to glycemic control, adiponectin, lipid profile and body fat distribution. Patients and method: The study included 35 type 1 diabetic children and of 35 ages matched healthy children. Blood sampling for evaluation of serum resistin, adiponectin, glycosylated hemoglobin and lipid profile. Anthropometric evaluation and abdominal ultrasonography were done. Results: Resistin was significantly higher whereas adiponectin was lower in diabetic patients. Resistin had a significant negative correlation with adiponectin, HDL and HbA1 %. The predictors affecting resistin circulating level were HDL and duration of T1DM. **Conclusion**: A significant increase in serum resistin was detected in diabetic children. The most important predicting factor for increasing resistin was duration of type 1diabetes.Whereas higher level of HDL could lower its circulating level. A decrease in serum adiponectin is associated with increase in serum resistin.

Keywords: Resistin; adiponectin; lipid profile; Type1diabetes.

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INTRODUCTION

Type 1 diabetes, is one of major health problem in children. It is characterized by impaired of a number of biological processes responsible for controlling physiological blood glucose level. Exogenous insulin is not regulated naturally. This may add more risk of premature atherosclerosis in children and adolescents with type 1 diabetes [1].

Resistin is a hormone involves in regulation of blood glucose [2, 3]. Many Studies carried of animal models showed that resistin increases gluconeogenesis and glycogenolysis leading to increase in hepatic insulin resistance and raising blood glucose levels. Chronic higher levels of resistin in rats leads to a systemic insulin resistance and in skeletal muscles resulting in glucose intolerance and elevation of blood triglyceride level [4-6].

According to several studies, plasma concentration of adiponectin is reduced in obese individual, they found that adiponectin, visceral, and negatively correlated with insulin resistance [7]. Additionally, Adiponectin has antidiabetic and antiatherogenic effect, [8 & 9]. It also has anti-inflammatory function so it accumulates in damaged vascular walls and modulates the endothelial inflammatory response to vascular injury [10]. The serum concentrations of adiponectin are abnormal in type 1 diabetic children it depends on many factors such as insulin therapy and glycemic control [11]

Our aim was therefore to evaluate serum resistin levels in type 1 diabetic children. Also to correlate results with glycemic control, adiponectin, lipid profile and body fat distribution.

MATERIAL AND METHODS

A cross-sectional observational study, included 35 type 1 diabetic children, another group of 35 age matched healthy children. An approval from the ethical committee of the National Research Centre, Cairo, Egypt was taken. Written informed consent was obtained from all patients, their parents and controls after full discussion about the aim of the study. The study was done at Pediatric Endocrinology Out-patient Clinic, National Research Center, Cairo, Egypt, during the period between September 2014 and December 2015. Exclusion criteria included cases with acute diabetic complications, as diabetic ketoacidosis or hypoglycemia; our cases have other autoimmune diseases as thyroiditis, Bronchial asthma, Malignancy or receiving immunosuppressive drugs. All included cases and controls were subjected to full medical history taking, and clinical examination.

Assessment of anthropometric measures including weight in kilograms (kg), height in centimeters (cm) waist circumference (WC), and hip circumference (HC) and body mass index (BMI) was measured as kg/m^2. Each measurement was taken as the mean of three consecutive measurements, using standardized equipment. The landmarks, instruments used and techniques followed were those recommended by the international biological program [12, 13].

Blood pressure was measured three times for patients and controls after 5-min rest in sitting position with the use of mercury sphygmomanometer. The mean value of 2nd and 3^{rd} measurement was calculated.

Abdominal ultrasonography:

We measured the maximum pre-peritoneal visceral fat thickness (VFT) and the minimum subcutaneous fat thickness (SFT) by Ultrasonography (US) .The visceral fat thickness was measured by 3.5-5 MHz convex –array probe. The thickness of subcutaneous fat was measured by placement of a 7.5-MHz or 3.75-MHz probe perpendicular to the skin on the epigastrium. Techniques followed were those recommended by Ismail et al, 2014 [14].

Laboratory Investigation

Venous blood was sampled after a 12-h fast, all patients and controls underwent:

Lipid Profile was assayed by an automated system of OLYMPUS AU400.

HBA1C is measured using Stanbio Glycohemoglobin kit which implies the quantitative colorimetric determination of glycohemoglobin in whole blood.

Serum resistin levels were assayed using Biovender ELISA Kit Cat No RD191016100 according to manufacture's protocol which implies an interaction between microplate well precoated with polyclonal antihuman resistin antibody and sera containing resistin. A biotin labelled secondary polyclonal anti human resistin antibody is added followed by a Streptavidin-HRP conjugate. The absorbance of the developed color is proportional to resistin concentration. Serum adiponectin levels were assessed using an ELISA technique supplied by Orgenuim Cat No ADIPO25 which employs a solid phase ELISA assay designed for the quantitative measurement of human serum adiponectin according to manufacture's protocol.

Statistical analysis:

The standard computer program Statistical Package for the Social Sciences (SPSS) for Windows, release 12.0 (SPSS Inc., USA) was used for data entry and analysis. All numeric variables were expressed as mean ± standard deviation (SD). Comparison of different variables in various groups was done using Student t test for normal variable. Pearson correlation was also done. A linear multiple regression analysis was obtained to detect the predictors of serum resistin. P values < 0.05 were considered as statistically significant.

RESULTS

Our results showed that among the T1 diabetic children, 24 (68.5 %) were females and 11 (31.5 %) were males. Among controls 23 (65.7%) were females and12 (34.3%) were males. The mean age of T1DM cases was14.60± 2.63 year, while controls was14.03±3.52 years. There were no significant differences between diabetic children and controls in terms of age or gender (P > 0.05). All diabetic children were on insulin therapy regimen. The mean duration of T1DM was 5.36±3.32 years (1-15 years), mean insulin dose was 1.4 ± 0.5 U/kg/day and HbA1 % mean was 8.35±2.079 (4-13). Fatty liver was positive in12 cases (37.9%) while the percentage was in controls was (9.4%). A comparative study of demographic and fat distribution of children with diabetes and healthy controls is presented in Table I. A statistically significant difference was only presented by the parameter liver span (P = 0.005).

Table 1: Comparison between demographic and ultrasonography data of T1DM cases and controls

	T1DM cases(35)	Mean	Std. Deviation	Sig. (2-tailed)
	CONTROL(35)			
AGE	T1DM cases	14.60	2.63	NS
Year	CONTROLS	14.03	3.52	
BMI	T1DM cases	23.51	4.14	NS
	CONTROLS	23.14	3.98	
WHTR	T1DM cases	0.50	0.10	NS
	CONTROLS	0.51	0.10	
WHR	T1DM cases	0.85	0.06	NS
	CONTROLS	0.84	0.08	
Percentage	T1DM cases	25.52	6.52	NS
Body Fat	CONTROLS	26.21	6.70	
SBP	T1DM cases	105.38	12.74	NS
Mm Hg	CONTROLS	103.55	12.13	
DBP	T1DM cases	68.08	9.77	NS
mm Hg	CONTROLS	66.58	6.99	
Liver Span	T1DM cases	14.32	1.52	0.005
cm	CONTROLS	13.22	1.75	
SFT	T1DM cases	1.54	.58	NS
cm	CONTROLS	1.43	.84	
VFT	T1DM cases	3.73	1.22	NS
cm	CONTROLS	3.64	1.74	

BMI: Body mass index, SBP: systolic blood pressure, DBP: Diastolic blood pressure,
SFT: Subcutaneous fat thickness, VFT: visceral fat thickness.

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Results of comparative study between laboratory data of T1DM cases and controls are shown in Table 2. This revealed that there was significant difference between them as regards resistin (P= .033). While for serum adiponectin no statistical significance was achieved (p = .129) in spite of the observed tendency for slightly lower values in diabetes. Statistical analysis demonstrated a significant difference in serum cholesterol and LDL between the patients and controls (P = .018 and .034 respectively). Children with diabetes had higher serum level of triglyceride but no statistical significance was achieved. HDL showed no significant difference.

Table 2: Comparison between laboratory data of T1DM cases and controls

	1=T1DM 2=CONTROLS	Mean	Std. Deviation	Sig. (2-tailed)
RESISTIN ng/mL	T1DM cases	2.21	1.23	.033
	CONTROLS	1.72	0.71	
ADIPONECTIN µg/mL	T1DM cases	17.64	8.47	.129
	CONTROLS	20.52	7.00	
CHOLESTEROL (mg/dl)	T1DM cases	189.16	60.51	.018
	CONTROLS	162.97	28.06	
TRIGLYCERIDE (mg/dl)	T1DM cases	104.73	50.38	.113
	CONTROLS	89.13	31.91	
HDL (mg/dl)	T1DM cases	47.95	11.06	.178
	CONTROLS	43.26	10.36	
LDL (mg/dl)	T1DM cases	117.12	57.99	. 034
	CONTROLS	92.76	26.84	

LDL: low density lipoprotein. HDL: high density lipoprotein

Table 3 shows the percentile distribution of serum resistin and adiponectin in cases and controls. It was obvious that circulating resistin was increasing inT1DM while circulating adiponectin was decreasing.

Adiponectin in diabetic patients had a significant negative correlation with resistin and positive correlation with HDL (Table 4). While resistin had a significant negative correlation with adiponectin and HDL (r= -.541, P=.000 and r= -.613, P=.000 respectively) and a significant positive correlation with HbA1 %(r=.397, P=.033)

Table3: Resistin and adiponectin percentiles in cases and controls

	RESISTIN	Cases	Controls
Percentiles	5	1.00	.59
	25	1.50	1.10
	50	1.80	1.60
	75	2.60	2.20
	95	5.00	2.91
Adiponectin		Cases	Controls
Percentiles	5	10.100	10.57
	25	12.77	14.40
	50	15.20	20.10
	75	19.30	25.92
	95	43.50	32.00

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Table 4: Correlation between serum resistin and adiponectin and different parameters in T1DM cases

		RESISTIN	ADIPONECTEN
RESISTIN	Correlation Coefficient	1.000	-.541(**)
	Sig. (2-tailed)	.	.000
ADIPONECTEN	Correlation Coefficient	-.541(**)	1.000
	Sig. (2-tailed)	.000	.
CHOLESTEROL	Correlation Coefficient	.048	-.133
	Sig. (2-tailed)	.776	.431
TRIGLYCERIDE	Correlation Coefficient	-.082	-.057
	Sig. (2-tailed)	.628	.736
HDL	Correlation Coefficient	-.613(**)	.583(**)
	Sig. (2-tailed)	.000	.000
LDL	Correlation Coefficient	.268	-.070
	Sig. (2-tailed)	.139	.702
LIVER SIZE	Correlation Coefficient	.136	-.083
	Sig. (2-tailed)	.414	.619
Fatty liver	Correlation Coefficient	.242	-.244
	Sig. (2-tailed)	.144	.140
SFT	Correlation Coefficient	.286	.312
	Sig. (2-tailed)	.082	.057
VFT	Correlation Coefficient	.068	.220
	Sig. (2-tailed)	.698	.204
Duration of DM1	Correlation Coefficient	.256	-.041(*)
	Sig. (2-tailed)	.350	.672
HbA1 %	Correlation Coefficient	.397(*)	.064
	Sig. (2-tailed)	.033	.741

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).

Table5: shows the results of multiple regressions. The independent variables affecting resistin circulating level were HDL and duration of T1DM. Serum HDL level negatively affects resistin serum level, while duration of T1DM positively affects it.

Table 5: Results of Multiple Regression Analysis

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	4.748	.891		5.331	.000
	HDL	-.062	.016	-.504	-3.865	.000
	Duration of T1DM	.145	.048	395	3.030	.005

Dependent Variable: RESISTIN

DISCUSSION

The effect of type 1 diabetes mellitus on circulating resistin level remains unclear .Our results showed that circulating resistin was significant higher inT1DM cases than healthy controls. Similar result was shown by Katarzyna et al,[15].On the other hand, Martos-Moreno et al. showed that the resistin concentrations were similar inT1DM cases and controls [16]. Schäffler et al found that there was significantly higher serum resistin levels in control group [17]. Our data showed negative correlation between serum resistin and HbA1 %, so resistin was lower in better controlled cases. Therefore, insulin could help in regulation of resistin secretion although it is not the main regulator. Same observation reported by Liu et al. being reported that insulin could

superss resistin but it was not its major regulator [18].We reported strong negative correlation between serum resistin and circulating HDL. Same result recorded by Owecki et al, [19] and Malo et al, [20]. Low HDL level could directly affect glucose metabolism [21]. Furthermore, low HDL decreases its direct anti-inflammatory properties, and its ability to alter intracellular lipid environment and reduce micro inflammation [22]. This may lead to more inflammation and increase resistin level.

An important observation was the significant negative correlation between circulating resistin and adiponectin. This result suggests that adiponectin could play a protective role in T1D children through decreasing resistin. We found non-significant lower level of serum adiponectin inT1D children. This is in agreement with Blaslov et al, [23].On the other hand, Morales et al, [24] reported that diabetic patients had a significantly higher adiponectin than controls. In general, factors control levels of adiponectin in type 1 diabetes appear complex. Authors reported that a decrease in adiponectin in children and adolescents with type 1diabetes were strongly related to increasing weight, waist circumference, with aging and puberty progression. Our results add that duration of the disease and serum HDL concentration were the most important predictor of serum resistin level.

CONCLUSION

A significant increase in serum resistin was detected in diabetic children. The most important predicting factor for increasing resistin was duration of type 1diabetes.Whereas higher level of HDL could lower its circulating level. A decrease in serum adiponectin is associated with increase in serum resistin.

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