Assessment of Serum Concentrations of Omentin-1 in Children with Type 1 Diabetes as Indicator of Insulin Resistance

Mahmoud Mohamed El-Adly*[1], Mohamed Nagiub Abu-Elfotoh[1],
Hesham Samy Abd-Elhamed[2], Ahmed Mohamed Gaballah[1]
Departments of [1]Pediatrics and [2]Clinical Pathology, Faculty of Medicine – Zagazig University
*Corresponding Author: Mahmoud Mohamed El-Adly, **Mobile:** (+20)01024683929**, Email:** mosad8rashed@gmail.com

ABSTRACT
Background: Omentin-1, a protein produced mainly in visceral adipose tissue. Its function is most likely to increase insulin sensitivity and stimulate glucose metabolism. This effect can be both local and systemic.
Objective: To evaluate the concentrations of selected gastric peptide omentin-1 in serum of children with type 1 diabetes, relevant to the disease duration.
Patients and Methods: This case control prospective study was conducted during the period from 2018 to 2020. This study was carried out in Endocrinology Unit and Outpatient Clinic at Pediatric Department, Zagazig University Hospital. The sample size was 85 (17 in every group). Serum omentin-1 level was measured.
Results: Cases were significantly higher than control regarding FBS, PPBS and HA1c. Cases were significantly higher than control as it was distributed as 426.04 ± 137.6 and 103.21 ± 32.5 respectively. Significant AUC with cutoff > 191.7 and 100.0% sensitivity and specificity. Regarding FBS & PPBS, control group were significantly lower than other groups but group 4 was significantly higher than other groups regarding PPBS. Regarding HA1c, control group was significantly lower than other groups but groups 1 & 4 were significantly higher than other groups. Concerning omentin, control group was significantly lower than other groups and group 4 was significantly higher than other groups also groups 2 & 3 were significantly higher than group 1.
Conclusion: T1DM is a common health problem in the pediatric age group. Omentin-1 level was significantly high in T1DM and its level is strongly correlated to duration and insulin resistance.
Keywords: Type 1 Diabetes, Omentin-1, Insulin Resistance.

INTRODUCTION

Type 1 diabetes is autoimmune disease with multiple factors that may accelerate the start and the course on the disease. It has also strong genetic predisposition [1]. The disease can start in any age, but usually it starts more in childhood with the maximum incidence at the time of puberty, so it was called juvenile diabetes [2].

The incidence of type 1 diabetes mellitus is increasing rapidly worldwide with the incidence rate in children below 5 years in Europe is increasing to the double in the last 20 years. Type 1 diabetes makes up an estimated 5–10% of all diabetes cases. The number of people affected globally is unknown, although it is estimated that about 80,000 children develop the disease each year. Rates of disease vary widely with approximately 1 new case per 100,000 per year in East Asia and Latin America and around 30 new cases per 100,000 per year in Scandinavia and Kuwait [3].

Despite the usage of insulin in the treatment of type 1 diabetes mellitus. This disease is still associated with increased morbidity due to the disease complications affecting the cardiovascular, renal and nervous systems, which is affecting the quality of life and life expectancy of the children suffering from it. Arise of insulin resistance incidence makes it important to search for resistance reliable markers that gives idea on insulin resistance [1].

The increasing knowledge on the functions of intestinal peptides and adipokines in the body allows the assumption of their major role linking the process of food intake, nutritional status and body growth, largely through the regulation of glucose metabolism and insulin resistance. The alimentary tract and human adipose tissue constitute an important part of the endocrine system producing the greatest amounts of regulatory peptides.

Food intake control is substantially regulated by the hypothalamic neurons that receive various signals from the so-called circuit-adipose tissue, stomach, intestines, thyroid or pancreas [4].

One of the adipokines is omentin-1, a protein produced mainly in visceral adipose tissue. Its function is most likely to increase insulin sensitivity and stimulate glucose metabolism and this effect can be both local and systemic. In vitro studies have demonstrated that omentin-1 increases insulin sensitivity by stimulating insulin-dependent glucose uptake in both subcutaneous and visceral adipocytes so levels of these adipokines can reflect the tissue resistance to insulin therapy [5].

The study aimed to evaluate the concentrations of selected gastric peptides omentin-1 in serum of children with type 1 diabetes relevant to the disease duration.

PATIENTS AND METHODS

I. Technical design:

A) Site of the study:

This study was carried out in Endocrinology Unit and Outpatient Clinic at Pediatric Department, Zagazig University Hospital.

B) Type of study:

Case control study.

C) Sample size:

The sample size was calculated by Community Medicine Department, Faculty of Medicine, Zagazig University according to the following: Assuming that level of omentin-1 in diabetic patients is 124.8 ± 40 and in control group is 157 ± 50, at confidence level 95% and power 80%, so total sample size is 85 (17 in every group) .

- **Group 1:** Children with newly diagnosed type 1 diabetes after D.K.A. attack (17 child).
- **Group 2:** Children with type 1 diabetes for less than five years (17 child).
- **Group 3:** Children with type 1 diabetes for a period of five to ten years (17 child).
- **Group 4:** Children with type 1 diabetes for more than 10 years (17 child) [4].

D) Target population:

Children with Type 1 DM visiting the Outpatient Clinic and Endocrinology Unit in Zagazig University Hospitals

Inclusion criteria:

- **Cases:** Male and female children with T1DM aging from 1 to 18 years old (n: 68) divided into four groups.
- **Healthy control:** age and sex matched healthy children (n: 17)

Exclusion criteria:

1- Cases with acute or chronic systemic disorders
2- Cases with adipose tissue diseases
3- Cases with autoimmune diseases
4- Patient or caretakers or guardian did not consent to participate in the study.

II. Operational design

Methods:

Full history:

- Age and characteristics of onset of diabetes (e.g., DKA, asymptomatic laboratory finding).

Clinical examination:

- All children were thoroughly examined as following
- Height, weight and BMI

Laboratory Investigations:

1. HbA1c:

Done by Direct Enzymatic HbA1c Assay, which is an enzymatic assay that use lysed whole blood samples and subject them to extensive protease digestion with Bacillus species protease. This process releases amino acids including glycated valines from the hemoglobin beta chains.

2. Fasting Blood Sugar (FBS) · Share and 2h Postprandial Blood Sugar (PPBS): -

Acquired from patients own home follow up charts used by them to follow up their disease.

3. Serum omentin-1 level by ELISA (Sandwich technique): -

Done under supervision of Prof. Dr. Ahmed Mohammed Gaballa in Central Laboratories of Zagazig University Hospitals by using SunRed Biotechnology Company Omentin-1 ELISA kits.

Ethical and patient approval:

Approvals obtained for performing the study from Institutional review board (IRB) of Zagazig University. Informed consent was obtained from written informed consent was taken from parents for participation in the study. After being informed about the aims and process of the study as well as applicable objectives.

Statistical analysis

Data were imported into Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis. According to the type of data, qualitative data were represented as number and percentage, quantitative data were represented as mean ± SD. The following tests were used to test differences for significance: difference and association of qualitative variable by Chi square test (X^2). Differences between quantitative independent groups by t test. P value was set at ≤ 0.05 for significant results.

RESULTS

There was no significant difference between cases and control regarding age or anthropometric measures (Table 1).

Cases were significantly higher than control regarding FBS, PPBS and HA1c (Table 2).

Cases were significantly higher than control as it was distributed as 426.04 ± 137.6 and 103.21 ± 32.5 respectively (Table 3).

Significant AUC with cutoff >191.7 and 100.0% sensitivity and specificity (Table 4).

Regarding FBS & PPBS, control group was significantly lower than other groups but group 4 was significantly higher than other groups regard PPBS. Regarding HA1c, control group was significantly lower than other groups but groups 1 & 4 were significantly higher than other groups (Table 5).

Regarding omentin-1, control group was significantly lower than other groups and group 4 was significantly higher than other groups. In addition, groups 2 & 3 were significantly higher than group1 (Table 6).

Table (1): Age and anthropometric measures distribution between cases and control

	Cases (N=68)	Control (N=17)	t	P
Age	10.35 ± 3.42	9.17 ± 2.95	0.996	0.322
Weight	32.89 ± 10.58	28.0 ± 8.91	1.491	0.140
BMI	25.61 ± 2.71	24.71 ± 1.07	1.321	0.190

Table (2): FBS, PPBS (a) and HA1c (b) distribution between cases and control

	Case (N=68)	Control (N=17)	t	P
FBS(mg/dl)	108.66 ± 18.15	89.64 ± 6.49	4.235	<0.001**
PPBS (mg/dl)	192.6 ± 7.71	139.17 ± 17.51	5.670	<0.001**
HA1C	7.83 ± 1.87	4.69 ± 0.47	6.805	<0.001**

Table (3): Omentin-1 distribution between cases and control

	Case (N=68)	Control (N=17)	t	P
Omentin	426.04 ± 137.6	103.21 ± 32.5	5.977	<0.001**

Table 4: Area under curve with cutoff and vlidity of Omentin

Area	Cutoff	P	95% Confidence Interval		Sensitivity	Specificity
			Lower Bound	Upper Bound		
1.000	>191.7	0.00**	1.000	1.000	100.0%	100.0%

Table (5): FBS, PPBS and HA1c distribution measures among studied groups

	Control	Group1	Group2	Group3	Group4	F	P
FBS (mg/dl)	89.64±6.49*	118.29±5.84	116.94±16.94	118.52±14.5	117.88±23.09	11.210	<0.001**
PPBS (mg/dl)	139.17±17.51!	182.41±11.99#	180.29±39.62#	180.58±27.2#	220.11±48.7*	13.850	<0.001**
HA1C	4.69±0.47*	9.29±1.5#	6.9±0.76!	6.55±1.24!	8.57±2.21#	29.216	<0.001**

Similar group   * significant different groups

Table (6): Omentine-1 distribution among studied groups

	Control	Group1	Group2	Group3	Group4	F	P
Omentin-1	103.21±31.8	248.09±27.3!	332.27±24.9#	390.23±24.4#	733.59±235.9*	76.55	<0.001**

Similar group   * significant different groups

DISCUSSION

As regards Age, weight and BMI distribution between cases and control, there was no significant difference between cases and control regarding age or anthropometric measures.

Regarding weight, height and BMI, there was a great difference between cases and matched control of same age. Cases tend to be either underweight or obese unlike healthy control of same age and sex. On the other hand, concerning height, cases were shorter than control of same age and sex that is due to the nature of the disease, which impact normal growth of children. In the study of **Baltadjiev et al.** [6] Weight and height were significantly affected by diabetes in cases unlike healthy control, which come to agree with our results

Regarding FBS, PPBS and HA1c distribution between cases and control, they were significantly higher than control. Group 4 was significantly higher than other groups regarding PPBS. Regarding HA1c,

control group was significantly lower than other groups, but groups 1 & 4 were significantly higher than other groups.

Regarding Omentin-1 distribution between cases and control, there was a statistically significant difference between cases and control groups. Cases were significantly higher than control. The median Omentin-1level was 426.04 ± 137.6 and 103.21 ± 32.5 respectively. Regarding ROC Curve analysis for Omentin-1; regarding cases, significant AUC with cutoff was >191.7 and 100.0% sensitivity and specificity. In the study of **Tichá et al.** [7] omentin-1 levels were found to be high in cases and significantly high with longer duration this agrees with our results. In another study by **As´habi et al.** [8], also omentin-1 levels were found to be higher in cases than control, which indeed agrees with our results. On the other hand, **Abd El Dayem et al.** [9] reported that omentin-1 in cases of T1DM was significantly lower than in control, which

disagrees with our results. Our results were consistent with **Nurten** *et al.* [10] where they reported that omentin-1 levels were elevated (p < 0.001) in type 1 diabetic children than in controls. Omentin-1 were elevated in longstanding patients compared to healthy controls (p < 0.001). They concluded that omentin-1 in pediatric type 1 diabetes patients indicate the presence of metabolic changes caused by adipose tissue dysregulation, which do not normalize during insulin therapy.

In the study of **Habi** *et al.* [11], they made a systematic review and meta-analysis of observational studies on the association between omentin and diabetes. Their analysis failed to show any significant association between omentin-1 and T1DM. The results of previous studies in this issue are inconsistent. In other words, some evidence proved lower level of omentin in T1DM subjects but **Nurten** *et al.* [10] revealed higher levels of this adipokine in these populations. Another sub-group of our study included T2DM patients, the analysis proved lower levels of omentin in these populations, which is consistent with previous report but was not confirmed by some.

Another systematic review and meta-analysis was done by **Pan** *et al.* [12] to assess omentin-1 in diabetes mellitus. They conclude that forty-two eligible studies were included in the final meta-analysis. There was no significant difference in omentin-1 concentration between patients with type 1 diabetes mellitus and the controls. On the other hand, lower concentration levels of omentin-1 were observed in patients with gestational diabetes mellitus (standardized mean difference:-0.44, 95% confidence interval:-0.76; -0.12, p = 0.007), or type 2 diabetes mellitus (standardized mean difference: -1.74, 95% confidence interval: -2.31; -1.16, p< 0.001) than in the controls. Which is also come in disagreement with our results.

CONCLUSION

T1DM is a common health problem in the pediatric age group. Omentin-1 level was significantly high in T1DM and its level was strongly correlated to duration and insulin resistance. Although in literature there is diversity in analysis of Omentin-1 level in T1DM patients, which varies between high and low,

further work up should be done especially on ethnicity of the studied population to figure out if it has a role in this variation.

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