ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Omentin-1: Novel Target in Childhood Obesity.

Dina Abu Zeid[1]*, Hanaa H Ahmed[2], Enas Mokhtar[3], Enas R Abdel Hamid[1], Wael H El Batal[1], and Amal Elshafie[4]

[1] Child Health Department, National Research Centre, Giza, Egypt.
[2] Hormones Department, National Research Centre, Giza, Egypt.
[3] Pediatrics Department, National Research Centre, Giza, Egypt.
[4]Department of Health Radiation Research, National Center of Radiation Research and Technology, Atomic Energy Authority, Cairo, Egypt.

ABSTRACT

The prevalence and magnitude of childhood obesity are increasing so rapidly nowadays. It is resulted in many health complications in adulthood. Fat tissue releases numerous bioactive molecules, called adipokines, which affect whole body homeostasis. Omentin-1 is a novel adipokine that is abundantly expressed in visceral fat tissue. The focus of our interest was to assess omentin-1 level in obese Egyptian children and its relation to anthropometric and metabolic parameters. Thirty obese children were compared with 30 matched healthy controls. All children were subjected to full clinical examination, anthropometric parameters were measured and fasting serum glucose, lipids, HOMA-IR and omentin-1 levels were determined. There was significant difference between obese and controls as regards HbA1c, total cholesterol and LDL while a highly significant difference as regard to HOMA-IR, triglycerides and HDL with higher values in obese group. In contrast omentin-1 serum level recorded highly significant reduction among obese subjects versus control counter parts but there was no significant correlation of serum omentin-1 level with anthropometric and metabolic findings. The present data indicate that omentin-1 serum level is low in obese children while no correlation with neither anthropometric nor metabolic syndrome parameters. Further studies needed to be done in our community on larger population with narrow age range that may reveal omentin-1 as a possible target in the treatment of childhood obesity.

Keywords: Obesity; Omentin-1; Adipokines; Metabolic Syndrome; Children

Corresponding author

ISSN: 0975-8585

INTRODUCTION

Obesity is a common childhood disease, it's now known as being a global epidemic [1]. In the twentieth century especially its last quarter, obesity prevalence in children and adolescents in developed countries had been increased by two to five times. This increase occurs in developing countries as well. In Egypt, nowadays there is an overwhelming problem which is obesity of children and adolescents leads to urgent need for implementation of plans with main goal for eradication of this problem [2]. During the last decades, obesity had been considered a public health problem mainly because of its complications as atherosclerosis, chronic kidney disease and increased cardiovascular morbidity and mortality [3]. It's also associated with many metabolic disorders including elevated blood pressure, insulin resistance and dyslipidemia, which are components of metabolic syndrome [4]. Generally, obesity is the abnormal or excessive accumulation of fat in adipose tissue to the extent that health may be impaired [5]. Adipose tissue is considered as an active endocrine organ which secretes a variety of bioactive molecules known as adipokines [6] which in recent years, believed to have fundamental role in obesity related metabolic disturbances [7]. These adipokines are resistin, visfatin, apelin, adiponectin, retinol binding protein-4, serum amyloid A, plasminogen activator inhibitor-1, angiotensinogen, vaspin, omentin, chemerin and zinc-alpha2-glycoprotein [8].

Omentin is a novel fat depot-specific adipokine with insulin-sensitizing effects identified from a cDNA library from visceral omental adipose tissue by Yang et al. in 2003 [9].Omentin mRNA is detected with major concentration in the stromal vascular fraction of visceral adipose tissue and while minor one in subcutaneous fat depots and mature adipocytes. Omentin had two homolgus isoforms omentin-1 and omentin-2; omentin-1 is the major circulating form [10].

As omentin-1 is considered to play a role in the pathogenesis of obesity and insulin resistance, so there is a need to measure its level. But, unfortunately, its circulating levels in obesity have not been adequately studied especially in children and its correlation with anthropometric and metabolic parameters in obese children is still controversial. Therefore, based on the presence of omentin-1 in the circulation and its potential role as insulin sensitizer the current study was conducted to measure its serum level in obese children and to explore its relation with the anthropometric and metabolic parameters.

MATERIALS AND METHODS

Study Population

This case control study included 30 obese children recruited from Nutrition Clinic, Medical Research Centre of Excellence, National Research Centre (NRC). They were 16 males and 14 females, their ages ranged from 4 to 15 years old.

Inclusion criteria were: Obese children with BMI above 95th percentile and Prepubescent (not more than Tanner stage 1).

Exclusion criteria were: Obese children with chronic illness or prolonged use of medications and obese children with major congenital anomalies.

Thirty healthy children with BMI below 85th percentile of matched age and sex were included as control group.

Ethical Considerations

The study had been approved by the Medical Research Ethical Committee of NRC. An oral consent was obtained from each subject in the study and written informed consent from their parents after explanation of the aim of the study.

Each child (patients& controls) was subjected to:

- Full medical history laying stress on family history of obesity

- Physical examination and anthropometric evaluation: Weight was measured using SECA balance scale with a sensitivity of 0.1 kg and height was measured using a Harpenden stadiometer with a sensitivity of 0.1 cm. waist circumference and hip circumference were measured in centimeters
- Biochemical analysis:

All serum samples were obtained between 8:00 and 9:00 am under fasting conditions. Fasting serum glucose, lipids, insulin resistance (IR) was calculated by homeostasis model assessment (HOMA). HOMAIR was calculated according to HOMAIR equation= [Fasting Plasma Glucose (mmol/L) × Fasting Plasma Insulin (mIU/L)] /22.5 [11].

Serum omentin-1 was measured by a detection set for ELISA application (Glory Science Co., Ltd, Del Rio, USA) according to manufacturer's instruction.

Statistical Analysis

The collected data were coded, tabulated, and statistically analyzed using IBM SPSS statistics (Statistical Package for Social Sciences) software version 22.0, IBM Corp., Chicago, USA, 2013.Descriptive statistics were done for quantitative data as minimum& maximum of the range as well as mean±SD (standard deviation) for quantitative parametric data, while it was done for qualitative data as number and percentage. Inferential analyses were done for quantitative variables using independent t-test in cases of two independent groups with parametric data. In qualitative data, inferential analyses for independent variables were done using Chi square test for differences between proportions. While correlations were done using Pearson's correlation for numerical parametric data. Linear regression model was used to find out independent factors affecting Omentin-1 level, but nothing significant was yielded. The level of significance was taken at P value < 0.050 is significant, otherwise is non-significant.

RESULTS

A total of 30 obese children (16 males 53.3% and 14 females 46.7%) mean age, 8.2±2.9 years and 30 healthy children (14 males 46.7% and 16 females 53.7%) mean age, 7.9±2.9 years were included in this study. As shown in table (1).There was highly significant difference between obese and controls as regards weight, BMI, waist circumference, hip circumference and waist- hip ratio.

Table (1): Comparison between study groups regarding anthropometric measures

Variable	Obese n= 30	Controls n= 30	P Value
Weight (kg)	48.8±16.1	32.2±7.7	<0.001*
Height (cm)	129.0±16.0	128.8±15.0	0.950
BMI (kg/m^2)	28.3±3.4	19.2±0.6	<0.001*
Waist circumference (cm)	84.4±7.5	61.4±9.3	<0.001*
Hip circumference(cm)	92.8±9.2	80.8±10.0	<0.001*
Waist- Hipratio	0.9±0.0	0.8±0.0	<0.001*

Data are expressed as mean ± SD, *P value < 0.05 was considered significant.
BMI: Body Mass Index.

There was significant difference between obese and controls as regards HbA1c, total cholesterol and LDL while the difference was highly significant as regards HOMA-IR, triglycerides and HDL with higher values in obese group (Table 2).

Table (2): Comparison between study groups regarding fasting blood glucose, insulin, glycated hemoglobin

Variable	Obese n= 30	Controls n= 30	P Value
Fasting glucose (mg/dL)	94.6±9.5	95.6±5.9	0.627
Fasting insulin (mIU/L)	14.3±7.0	13.5±4.1	0.598

ISSN: 0975-8585

HOMA-IR	3.4±1.7	0.9±0.4	<0.001*
HbA1c%	5.8±0.6	5.4±0.6	0.006*
Total cholesterol (mg/dL)	141.5±23.7	127.9±18.2	0.016*
Triglycerides (mg/dL)	87.8±38.3	59.4±10.4	<0.001*
HDL (mg/dL)	37.7±9.4	54.3±6.8	<0.001*
LDL (mg/dL)	85.9±24.0	69.2±13.5	0.002*

Data are expressed as mean ± SD, *P value < 0.05 was considered significant.
HOMA: homeostasis model assessment- insulin resistance, HbA1c: hemoglobin A1c, HDL: high density lipoprotein, LDL: low density lipoprotein.

Concerning omentin-1 serum level, there was a highly significant difference between the studied groups being lower in obese(7.3±2.8) than control counterparts (17.3±3.3) as shown in Table (3)

Table (3): Comparison between study groups regarding Omentin-1 serum level

Variable	Obese n= 30	Controls n= 30	P Value
Omentin-1 (ng/mL)	7.3±2.8	17.3±3.3	<0.001*

Data are expressed as mean ± SD, *P value < 0.05 was considered significant.

Interestingly, there was no significant correlation ofomentin-1 serum level with anthropometric and other laboratory findings among the studied groups as indicated in Table (4)

Table (4): Correlation of omentin-1 serum level with anthropometric and laboratory findings

	Obese n= 30		Control n= 30	
	r	P Value	r	P Value
Weight	0.066	0.729	0.083	0.662
Height	0.008	0.965	0.023	0.904
BMI	0.188	0.321	0.350	0.058
Waist	-0.022	0.908	0.128	0.501
Hip	0.073	0.702	0.120	0.526
Waist- hip ratio	-0.178	0.347	0.007	0.970
Glucose	0.298	0.110	0.295	0.114
Insulin	-0.120	0.529	0.006	0.975
HOMA-IR	-0.072	0.707	-0.211	0.264
HbA1c	0.275	0.141	0.014	0.943
Cholesterol	-0.004	0.983	0.330	0.075
Triglycerides	-0.063	0.741	-0.069	0.718
HDL	-0.016	0.934	-0.079	0.678
LDL	0.024	0.900	-0.049	0.798

*P value < 0.05 was considered significant.
BMI: Body Mass Index, HOMA: homeostasis model assessment- insulin resistance, HbA1c: hemoglobin A1c, HDL: high density lipoprotein, LDL: low density lipoprotein.

DISCUSSION

Obesity is associated with an array of health problems in children. Visceral obesity is strongly associated with insulin resistance, hyperglycemia, dyslipidemia, and hypertension [12]. Adipose tissue derived many molecules, collectively called adipokines, omentin-1 is one of the recently discovered adipokines.

Omentin-1 had a key role in obesity abnormalities either clinical as cardio metabolic complications (dyslipidemia, type 2 diabetes mellitus and atherosclerosis) or subclinical as insulin resistance and low grade inflammation, which in turn result in cardiovascular disease in youth [13,14]

Omentin-1 is a 34 kDa protein which was first known in the Paneth cells of the small intestine. It's mainly produced by visceral adipose tissue, thymus, heart, small intestine and colon. It leads to enhancement of insulin stimulated glucose transport through improvement of insulin signal transduction [15].

In the last few years, despite there is increase in adipose tissue derived pro-inflammatory factors description but they are still not enough used in the clinical practice of childhood obesity. [14]

To our knowledge, this study had been conducted for the first time in Egypt on obese children to reveal the level of serum omentin-1 in them and its relation to the anthropometric and metabolic parameters. Our results had shown that obese children are prone to dyslipidemia in the form of elevated total cholesterol, triglycerides, low-density lipoprotein (LDL) and reduced high-density lipoprotein (HDL). These high levels indicate the importance of screening for dyslipidemia in obese children. These results were strongly fitted with the previuos studies of Klop et al. [16] and Korsten-Reck et al. [17]

The present study results showed that the HOMA-IR and HbA1c levels of the obese group were significantly higher than those of controls which make an alarm that even when obese children apparently had no symptoms of diabetes mellitus or insulin resistance but actually, they had the early indicators of metabolic complications. These results were matched with what had been found by Onalet al. [18] while to the opposite of Sngun et al. [19] findings which showed higher HOMA-IR levels in obese children than healthy children and normal HbA1c in both groups.

In the current study we found significantly lower serum levels of omentin-1 in obese group in comparison with the control while no significant correlation of its level with anthropometric nor other laboratory findings. In Prats-Puig et al. [20] study there was high levels of omentin-1 in obese patients with more severe insulin resistance, increased triglycerides and family history of diabetes as their work was conducted in a group of 161 healthy prepubertal children with very narrow age range (7± 1 year). Meanwhile, in Schipper et al. [21] study there wasn't any significant difference between normal weight and obese subjects as regards omentin-1 level

In accordance with our results, other studies which had been conducted on adults have indicated that omentin-1 level and omentin 1 gene expression in visceral adipose tissue are decreased in obesity [22, 23]. These were in agreement with Oswiecimska et al [24] conclusions, that serum omentin-1 concentration is low in obese subjects and increase with loss of body weight as in subjects with anorexia nervosa. All of these findings were explained by Ohashi et al. [25] as obesity is associated with low levels of chronic inflammation, were found to indirectly down regulate serum omentin level so in turn, weight loss and different inflammatory states could be modulators of omentin expression and function. Our findings go with those of Catliet al. [26] the only difference that they found a negative correlation of omentin-1 with BMI, WC, HOMA-IR and insulin levels. This may be due to their sample size which was larger than ours.

In conclusion, our data clearly indicate that omentin-1 serum level is low in obese children while no correlation with neither anthropometric nor metabolic syndrome parameters. We recommend further studies to be done in our community on larger population with narrow age range that may reveal omentin-1 as a possible target in the treatment of childhood obesity.

REFERENCES

[1] Stewart L. Medicine 2015; 43: 108- 111.
[2] Samy MA, Khairy SA, Ibrahim SA, Matter MK, Hassan H. Am Sci J 2012; 8: 595- 603.
[3] Reaven G, Abbasi F, McLaughlin T. Recent Prog Horm Res 2004; 59: 207- 223.
[4] Chen F, Wang Y, Shan X, Cheng H, Hou D, Zhao X, et al. Plos one 2012; 7: doi: 10.1371
[5] Lahti-Koski M.and Gill T. Pediatr Adolesc Med Basel Karger 2004; 9: 1–19
[6] Al-Suhaimi EA and Shehzad A. Eur J Med Res 2013; 18: doi: 10.1186/2047-783X-18-12.
[7] Harwood HJ Jr. Neuropharmacol 2012; 63: 57-75.

[8] De Oliveira Leal V and Mafra D. Clinica Chimica Acta. 2013; 419: 87–94
[9] Pan HY, Guo L, Li Q. Diabetes Res Clin Pract 2010; 88: 29- 33
[10] de Souza Batista CM,Yang RZ, Lee MJ, Glynn NM, Yu DZ, Pray J, et al. Diabetes 2007; 56: 1655- 1661.
[11] Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DA, Turner RC. Diabetologia 1985; 28: 412-419
[12] Klein S. Diabetes Care 2010; 33: 1693- 1694
[13] Kwon Hand Pessin JE. Front Endocrinol (Lausanne). 2013; 4: doi: 10.3389/fendo.2013.00071
[14] Barraco GM, Luciano R, Semeraro M, Prieto-Hontoria PL, Manco M. Int J Mol Sci 2014; 15: 19760-19776.
[15] Tsuji S, Uehori J, Matsumoto M, Suzuki Y, Matsuhisa A, Toyoshima K, et al. J Biol Chem 2001; 276, 23456- 23463.
[16] Klop B, Elte Jan Willem F, Cabezas MC. Nutrients 2013; 5: 1218-1240
[17] Korsten-Reck U, Kromeyer-Hauschild K, Korsten K, Baumstark MW, Dickhuth HH, Berg A. Vasc Health Risk Manag 2008; 4: 1089-94.
[18] Onal ZE, Atasayan V, Gürbüz T, Hepkaya E, Nuhoglu C. Afr Health Sci 2014; 14:533-538
[19] Sangun Ö, Dündar B, Köşker M, Pirgon O, Dundar N. J Clin Res Pediatr Endocrinol 2011; 3: 70-76
[20] Prats-Puig A, Bassols J, Bargallo E, Mas-Barareda M, Ribot R, Soriano-Rodriguez P et al. Obesity 2011; 19: 1905–1907.
[21] Schipper HS, Nuboer R, Prop S, Van Den Ham HJ, de Boer FK, Kesmir C, et al. Diabetologia 2012; 55: 2800–2810.
[22] Auguet T, Quintero Y, Riesco D, Morancho B, Terra X, Crescenti A, et al. BMC Med Genet 2011; 12. doi: 10.1186/1471-2350-12-60.
[23] El-Mesallamy HO, El-Derany MO, Hamdy NM. Diabet Med 2011;28 :1194-200.
[24] Oswiecimska J, Suwala A, Swietochwska E, Ostrowska Z, Gorcyzca P, Ziora-Jakutowicz K, et al. Physiol Res 2015; 64: 701- 709.
[25] Ohashi K, Shibata R, Murohara T, Ouchi N. Trends Endocrinol Metab 2014; 25: 348-355.
[26] Catli G, Anik A, Abaci A, Kume T, Bober E. Exp Clin Endocrinol Diabetes 2013; 121: 595–600.