Serum Chemerin Levels relation with Waist circumference, Impaired fasting blood sugar, and Dyslipidemia in Obese Children and Adolescents

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Abstract

Background: **Childhood obesity is a growing global health problem associated with metabolic complications such as impaired glucose metabolism and dyslipidemia. Chemerin, an adipokine secreted by adipose tissue, has been implicated in obesity- related metabolic dysfunction. However, its relationship with clinical and biochemical parameters remains under investigation.** ***Objectives:*** **To evaluate the association between serum chemerin levels and waist circumference, fasting blood glucose, and lipid profile among obese children and adolescents.** ***Methods:*** **this cross-sectional study included 42 obese children and adolescents, ranging in age from 5 to 17, recruited from outpatient clinics in SCU hospital. There was no statistically significant difference in age, gender, or place of residence between the obese and control groups. The subjects' anthropometric and blood pressure measures were obtained. Fasting blood samples were obtained to measure serum chemerin, fasting blood, and lipid profile (serum triglycerides (TG), total cholesterol, high-density lipoprotein cholesterol (HDL-c), and low-density lipoprotein cholesterol (LDL-c)). Correlation between serum chemerin levels and metabolic parameters were analyzed using Pearson's correlation coefficient and multivariate regression models.** ***Results:*** **Compared to the control group, more than half (54.8%) of obese patients have waist circumferences in the 90th percentile for age and gender, which is statistically significant. The obese group had a greater mean chemerin level than the control group, but the difference was not statistically significant. By using correlation and multiple linear regression analysis, serum chemerin levels were found to be significantly correlated to impaired fasting blood sugar (r= 0.398, p = 0.009) and HDL (r= -0.386, p = 0.012).** ***Conclusions:*** **Elevated serum chemerin levels are significantly associated with central obesity, impaired fasting glucose, and dyslipidemia in obese children and adolescents. These findings suggest that chemerin may serve as an early biomarker for metabolic risk assessment.**

KeyWords: Chemerin, obesity, Waist circumference, Dyslipidemia, Fasting blood sugar.

Introduction

Obesity is known to be linked to adipokine dysregulation. Recent studies have discovered that the new adipokine chemerin, which functions as an autocrine, paracrine, and endocrine signaling molecule, is involved in the control of inflammation, adipogenesis, and glucose metabolism [(1)]. Chemerin acts as a powerful chemo attractant when acting as a ligand on cells expressing Chemerin receptors, according to data from an experimental investigation on human inflammatory fluids. Chemerin has also been found as a powerful chemo

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attractant of immature dendritic cells and macrophages, according to reports [2]. Chemerin was first discovered as a new adipokine in 2007. The research found that both chemerin and its receptor CMKLR1 (chemokine-like receptor1) were highly expressed in human white adipose tissue, indicating that it is a key source of chemerin. Chemerin also induces lipolysis in mature white adipose cells by directly activating hormone-sensitive lipase [3,4]. Chemerin levels have been linked to obesity indices in a direct positive relationship.

Although there is consensus that chemerin regulates glucose homeostasis, its role in regulating glucose tolerance remains unclear owing to the contradictory results derived from various in vivo and in vitro studies. Both glucose-stimulated insulin secretion from the pancreas and insulin-stimulated glucose uptake in peripheral tissues contribute to the proper regulation of glucose tolerance[7]. Chemerin and its receptor CMKLR1 are also expressed in the β cells of the pancreas, implying their role in modulating insulin secretion. Moreover, Chemerin has been reported to regulate insulin sensitivity and glucose uptake. Under high-fat diet feeding, loss of CMKLR1 exacerbates glucose intolerance, increases insulin level, and enhances insulin resistance in mice[8]. Chemerin mRNA expression levels differed by gender and adipose tissue, with expression levels considerably greater in women than men and subcutaneous adipose tissue than visceral adipose tissue [9]. Chemerin is also changed in prediabetic conditions, suggesting that glucose dysregulation may be an early pathogenic event [10].

Previous research has explored the relationship between serum chemerin levels and conditions such as diabetes and glucose intolerance. However, several aspects of this association remain unclear. Given that chemerin levels are influenced by body fat we aimed to investigate this relationship in specific population of obese children and adolescents. The primary objective of this study was to compare serum chemerin levels between healthy and obese participants within this age group.

Subjects and Methods

Subjects

Study design: The study was a comparative cross-sectional study done on obese children and adolescents at the Suez Canal University Hospitals' pediatric clinic in Ismailia city to investigate the link between serum chemerin and obesity, insulin resistance, and other measures.

Study population: After a full history, extensive clinical examination, including auxological evaluation, and exhaustive investigations, the research subjects were divided into the following groups: Healthy non-obese children and adolescents bringing their siblings to Suez Canal University's pediatric outpatient clinic (age and sex-matched). Group 1: Obese children (n=42); Group 2: Non-obese children and adolescents following their siblings to Suez Canal University's pediatric outpatient clinic (age and sex-matched).

Inclusion criteria of the obese group: Children and adolescents of both sexes with a BMI (Body Mass Index) of more than 95th percentile, aged 2 to 18 years, were included in the obese group. BMI was calculated based on the following formula BMI = weight (kg) / [height (m)]^2 then plotted against child gender and age in years on the CDC percentiles. The

control group consisted of children and adolescents of both sexes, aged 2 to 18, with a BMI between the 15th and 85th percentile. Patients with endocrine disorders or syndromic obesity, infections or acute illness, chronic diseases, and those on lipid-lowering, antihypertensive, or antihyperglycemic drugs were all excluded from the research.

Methods

Sample size: The power of the study was estimated using openEpi as follows: the mean chemerin level in the control group is 196.761.3 and in the obese group is 228.941.4. As a result, the power of the study is 80 percent and the confidence interval is 95 percent. The sample size was determined to be 84 in total, with 42 in each group [26]. Range, mean, standard deviation (SD), frequencies (number of instances), and relative frequencies were used to characterize the data (percentages). Unless otherwise noted, results are presented as mean + SD.

Ethical considerations: Each patient's parent, whether a child or a teenager, gave their informed permission. Furthermore, the ethics council of Suez Canal University has accepted this study procedure.

Study procedures: All participants underwent the following procedures: (1) a complete medical history; (2) a general and systemic examination; (3) measurements: weight, height, BMI, and waist circumference (WC); (4) laboratory investigations: Using conventional laboratory procedures and commercially accessible test kits, all individuals' fasting plasma glucose (FPG, mg/dl), total cholesterol (TC, mg/dl), high-density lipoprotein cholesterol (HDL, mg/dl), and triglyceride (TG, mg/dl) levels were measured (Roche Diagnostics GmbH, Mannheim, Germany). Friedewald formula was used to calculate cholesterol levels in low-density lipoprotein (LDL, mmol/L). Chemerin levels in serum were determined using a sandwich enzyme-linked immunosorbent assay (ELISA) kit (Human Chemerin Duo Set ELISA Kit, catalog No. DY2324, R&D Systems, Inc, Minneapolis, MN, USA) as directed by the manufacturer.

Statistical Analysis: In this research, the Student t-test was used to compare continuous data that were normally distributed and the Mann Whitney U test was used to compare data that were not normally distributed. The Chi-square (x2) test was used to compare categorical data. When the frequency is fewer than ten, Yates correction was employed instead. It was considered significant if the probability value (P-value) was less than 0.05 and highly significant if it was less than 0.01. A rock curve was used to determine the blood Chemerin cutoff level that distinguishes metabolic syndrome patients from obese people who do not have metabolic syndrome. A clinical test's sensitivity refers to its capacity to appropriately identify people who have the condition. All statistical analyses were carried out using the SPSS statistical software suite (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA).

Results

The study uses a comparative cross-sectional design to evaluate serum chemerin as a marker for early detection of metabolic syndrome. The following groupings of subjects were formed: Group 1: Obese with metabolic syndrome (n=19); Group 2: Obese without metabolic syndrome (n=23); Group 3: Healthy non-

obese children and adolescents accompanying their siblings to the pediatric outpatient clinic of Suez Canal University (n=42) (age and sex matched).

As shown in table 1, the mean age of the control group was 11.2 years while that of the obese group was 12.2 years. Regarding gender, obese females constitute 54.8 % of the obese group and 52.4% of the control group. It also shows that subjects from urban areas constitute 61.9% of the obese group and 59.5% of the control group. There was no statistically significant difference between the control and obese group regarding age, gender, or residence

Table 1. Demographic data of the studied groups:

Demographic data	Group		P value
	Control (n=42)	Obese (n=42)	
Age (years) mean±SD	11.2±3.8	12.2±3.7	0.194§NS
Gender Males N (%) Females N (%)	 20(47.6%) 22(52.4%)	 19(45.2%) 23(54.8%)	 0.827¶ NS
Residence Urban N (%) Rural N (%)	 25(59.5%) 17(40.5%)	 26(61.9%) 16(38.1%)	 0.823¶ NS

¶Chi-square test §Independent t test NS: Non-significant (P>0.05)

There was a statistically significant increase in weight, BMI, waist circumference among the obese group compared to the control group. Also, more than half (54.8 %) of obese group subjects have a waist circumference of ≥ 90th percentile for age and gender with a statistically significant increase compared to the control group (Table 2). No difference was found between the obese and control group regarding height.

Table 2. Anthropometric data of the studied groups:

Anthropometric data	Group		P value
	Control (n=42)	Obese (n=42)	
Weight (kg) mean±SD	38.3±13.9	66.0±25.3	<0.001**^
Height (cm) mean±SD	149.2±22.8	155.7±21.4	0.224 NS§
BMI (kg/m²) mean±SD	16.5±1.6	25.7±4.0	<0.001**§
Waist circumference (cm) mean±SD	64.2±6.7	81.4±11.4	<0.001**§
Waist circumference 90th percentile: Normal N (%) ≥ 90th percentile N (%)	 42(100.0%) 0(0.0%)	 19(45.2%) 23(54.8%)	 <0.001**¶

¶Chi-square test ^: Mann Whitney test §Independent t test
*NS: Non-significant (P>0.05) **: Highly significant (p <0.001)*

As shown in table 3, there was a statistically significant increase in mean SBP, DBP, and frequency of abnormal blood pressure among obese groups

compared to the control group. Also, there was a statistically significant increase in mean FBS and frequency of impaired fasting blood sugar among obese groups compared to the control group. Regarding lipid profile, there was a statistically significant increase in mean TG (TG ≥ 110 mg/dl) among the obese group compared to the control group. In addition, there was a statistically significant decrease in mean HDL and increase frequency of HDL < 40 mg/dl among obese group compared to control group. about 45% of the obese children matched the criteria for metabolic syndrome compared to 0% within control group which is statistically significant.

The Mean chemerin level was found to be higher in the obese group compared to the control group (Table 4). Without statistically significant difference p value nearly 0.7.

Table 3. Clinical and laboratory data of the studied groups:

Clinical data	Group		P value
	Control (n=42)	Obese (n=42)	
Blood pressure (mmHg)			
Systolic Mean±SD	93.7±8.5	104.1±11.2	<0.001**§
Diastolic Mean±SD	60.5±5.4	64.9±7.9	0.011*§
Blood pressure 90th percentile			
Normal N(%)	42(100.0%)	36(85.7%)	0.026*¶
≥ 90th percentile N(%)	0(0.0%)	6(14.3%)	
Fasting blood sugar (mg/dl) Mean±SD	71.5±14.1	91.9±19.2	<0.001**§
Normal N(%)	41(97.6%)	27(64.3%)	<0.001**¶
Impaired fasting blood sugar N(%)	1(2.4%)	15(35.7%)	
Triglycerides (mg/dl) Mean±SD	92.7±15.0	154.3±122.2	0.003*^
Normal N(%)	39(92.9%)	22(52.4%)	<0.001**¶
≥ 110, Significant for MetSN(%)	3(7.1%)	20(47.6%)	
HDL (mg/dl) Mean±SD	50.5±6.3	41.6±12.1	<0.001**§
Normal N(%)	40(95.2%)	22(52.4%)	<0.001**¶
< 40, Significant for MetSN(%)	2(4.8%)	20(47.6%)	
Metabolic syndrome			
No metabolic syndrome	42(100.0%)	23(54.8%)	<0.001**¶
Metabolic syndrome	0(0.0%)	19(45.2%)	

¶Chi-square test §Independent t test ^: Mann Whitney test
*NS: Non-significant (P>0.05) *: Significant (P<0.05) **: Highly significant (p <0.001)*

Table 4. Serum chemerin levels of the studied groups:

Serum chemerin	Group		P value
	Control (n=42)	Obese (n=42)	
Chemerin (ng/ml) Mean±SD	470.3±475.8	733.0±1129.3	0.778 NS^

^: Mann Whitney test

Moreover, as presented in table 5, We found that serum chemerin levels were significantly correlated with FBS and HDL. The serum chemerin levels have also a significant positive correlation with FBS;

while having a significant negative correlation with HDL (Figure 1,2).

Table 5. Correlation between Chemerin and different parameters among obese children:		
Variable	Chemerin (n=42)	
	r	P value
Age (years)	0.032	0.839 NS
Weight (Kg)	0.035	0.828 NS
Height (cm)	0.113	0.478 NS
BMI (Kg/m^2)	0.012	0.940 NS
Waist circumference (cm)	0.249	0.112 NS
Systolic Bp (mmHg)	0.036	0.822 NS
Diastolic Bp (mmHg)	-0.008	0.959 NS
FBS (mg/dl)	0.398	0.009*
Triglycerides (mg/dl)	-0.068	0.667 NS
HDL (mg/dl)	-0.386	0.012*
*r: Spearman's correlation coefficient NS: Non-significant (P>0.05) *: significant (p<0.05)*		

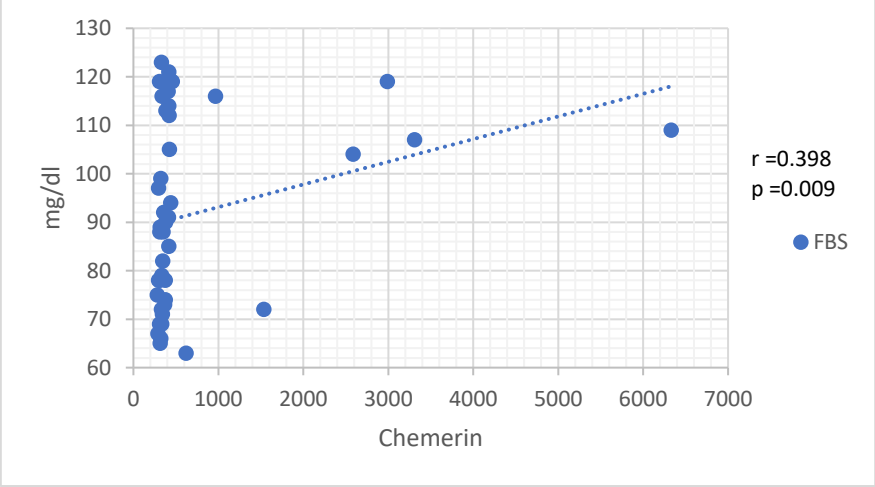

Figure 1. Correlation between Chemerin and FBS among obese children.

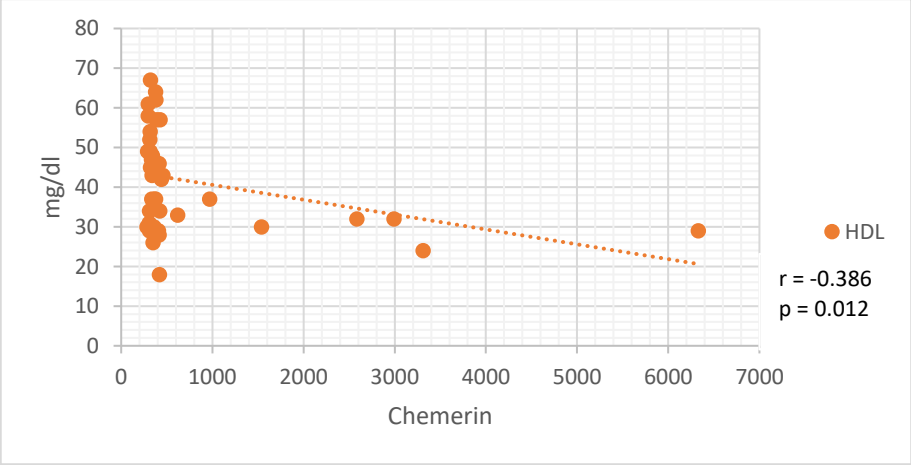

Figure 2. Correlation between Chemerin and HDL among obese children.

Discussion

Obesity is a global public health problem and predisposes individuals to diabetes and cardiovascular disease [15]. The prevalence rates of metabolic syndrome have markedly increased not only in adults but also in children and adolescents throughout the world over the past 30 years [16]. Although the underlying mechanisms remain to be elucidated, accumulating evidence has uncovered a critical role of adipokines. Chemerin, encoded by the gene Rarres2, is a newly discovered adipokine involved in inflammation, adipogenesis, angiogenesis, and energy metabolism [15].

This study is a comparative cross-sectional study, performed for attendants of the pediatric clinic of Suez Canal University Hospitals in Ismailia city to determine the association of serum chemerin and metabolic syndrome in obese children & adolescents.

Our results showed that there was a statistically significant increase in mean SBP, DBP among obese groups compared to the control group. Zaki *et al.*, 2012 came in agreement with us.

In the present study, there was a statistically significant increase in mean FBS among obese groups compared to the control group[17]. Ba *et al.*, 2019 reported significantly higher FBS in obese than in non-obese. Zaki *et al.*, 2012 reported the same[17,18].

Regarding lipid profile, our results showed a statistically significant increase in mean TG among the obese group compared to the control group and there was a statistically significant decrease in mean HDL among the obese group compared to the control group. Rizk and Yousef, 2012 reported the same results[19]. Zaki *et al.*, 2012 reported a significant difference in HDL only[18]. While Ba *et al.*, 2019 reported a significant difference in TG only[17].

This could be explained by the effect of chemerin on lipid and glucose metabolism and its role in modulating immune responses. Chemerin participates in the regulation of adipocyte metabolism and differentiation, increasing body mass, which may explain its higher concentrations in obese individuals and its association with features related to obesity [20]. Chemerin signaling is essential during the hyperplasia phase differentiation of pre-adipocytes into adipocytes. Increased concentrations of this adipokine in adipose tissue cause the recruitment of immune cells, consequently increasing the expression of inflammatory mediators such as CRP-US, interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) [9]. the mechanisms of action of chemerin on glucose metabolism have not been fully elucidated yet, this seems to be due to reduction of insulin-sensitive agents such as transport of glucose type 4 (GLUT-4), leptin, and adiponectin, or due to increase in levels of insulin-resistant agents such as IL-6.6 [21].

Our results revealed that the mean chemerin level was higher in the obese group compared to the control group but without statistical significance. Ba *et al.*, 2019 and Maghsoudi *et al.*, 2016 reported that serum chemerin was found to be significantly higher in obese children than in control group members. The difference may be due to the small sample size in this study[17,22].

Although there is consensus that chemerin regulates glucose homeostasis, its role in

regulating glucose tolerance remains unclear owing to the contradictory results derived from various in vivo and in vitro studies. Several studies provide some insight into the role of chemerin–CMKLR1 or chemerin–GPR1 axis in coordinating glucose-induced insulin secretion but the precise mechanisms are still not clear [7]. The study also reported a significant negative correlation between chemerin and HDL. Maghsoudi *et al.*, 2016 and Ouerghi *et al.*, 2020 reported the same result[23,24]. This came in disagreement with Ba *et al.*, 2019 who reported no significant correlation[17]. HDL has a protective effect on the endothelium due to its function of reverse cholesterol transport, preventing LDL oxidation and, thus, reducing its atherogenic potential [25]. One possible explanation for the association of chemerin with the levels of lipid profile components lies in its action on lipid metabolism in the liver, skeletal muscle, and adipose tissue, and the stimulation of lipolysis in adipocytes. Chemerin is suggested to play a role in the regulation of enzymes responsible for lipid metabolism by reducing the accumulation of adenosine cyclic monophosphate (cAMP) and stimulating calcium release in adipocytes [22].

Our results showed no significant correlation between chemerin and waist circumference. This came in agreement with Ba *et al.*, 2019. Several studies by Ouerghi *et al.*, 2020, Maghsoudi *et al.*, 2016 and Chu *et al.*, 2012 reported a significant correlation between chemerin and waist circumference or visceral adipose tissue[17-19,25]. This may be related to a difference in the fat distribution of children from Egypt compared with children from other countries.

Conclusion:

In our sample of Egyptian children and adolescents, chemerin levels were higher among the obese group than the control group but without statistical significance. Chemerin levels were correlated positively with impaired fasting blood sugar negatively with HDL. These findings suggest that chemerin might be an independent promising adipokine marker of required intervention among obese patients. Further research is necessary to confirm these findings and to evaluate serum chemerin levels as a predictor of accelerated atherosclerosis.

Limitations: Our relatively small sample size is considered as a limitation of our study. The cross-sectional nature of our study limited the determination of cause-effect relationships, and therefore, additional longitudinal studies with larger sample sizes are necessary to confirm our findings.

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