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Research Article

Chemerin, IL-18 and IL-1 Beta as Biomarkers of Metabolic Syndrome in Egyptian Obese Children

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Abstract

Background and Objectives: Metabolic syndrome (MetS), one of the most serious global health issues, is considered chronic inflammatory states. Chemerin, Il-18 and Il-1 beta adipocytokines, plays an important role in linking Met S and inflammation. Few studies are conducted in Egypt to disclose the role of chemerin, Il-18 and Il-1 beta as combined biomarkers to increase its diagnostic accuracy. So the aim of our study was to evaluate the role of serum chemerin Il-18 and Il-1 beta as combined biomarkers for early detection of metabolic syndrome due to different genetic and environmental backgrounds.

Methods: The study enrolled 171 participants divided into three groups, 57 children in each group. Group I:, 57 healthy control children group II obese children without metabolic syndrome and obese children with metabolic syndrome in Group 3 and. ranging in age from 5 to 17, were included in the study. Anthropometric and blood pressure measurements were taken of the participants. Fasting blood glucose, serum triglycerides (TG), total cholesterol, high-density lipoprotein cholesterol (HDL-c), and low-density lipoprotein cholesterol (LDL-c) were measured. ELISA was used to assess the amounts of circulating chemerin.

Results: Met S requirements were satisfied by 57 individuals. Abdominal obesity was the most common Met S predictor (84.2%), followed by impaired fasting blood sugar (73.7%), and then each of high triglyceride and low HDL (68.4%). Serum chemerin levels were significantly higher in Met S than in non-Met S obese and healthy subjects (1211.7 ± 1569 ng/ml VS 337.5 ± 34.8 ng/ml and 470.3 ± 475.8 ng/ml respectively, $p < 0.001$). Serum chemerin levels were shown to be substantially linked with impaired fasting blood sugar ($r = 0.398$, $p = 0.009$) and low HDL ($r = -0.386$, $p = 0.012$) by correlation and multiple linear regression analysis.

Conclusion: Circulating chemerin Il-18 and Il-1 beta , levels were associated with metabolic syndrome and could be independent markers for this disorder.

Keywords: Children; Metabolic Syndrome; Chemerin; Il-18; Il-1 Beta; Biomarker; Obesity

Introduction

Obesity is a multifactorial chronic condition defined by an excess buildup of adipose tissue, which occurs most usually as a result of excessive food consumption and/or insufficient energy expenditure. Genetic, psychological, behavioural, dietary, environmental, and hormonal variables can all contribute to obesity

[1]. Obesity in children is a complicated public health issue that affects the majority of industrialised countries across the world [2]. According to the World Health Organization, childhood obesity is "one of the most important public health concerns of the twenty-first century" [3]. The cornerstone of weight control in children is family-based lifestyle interventions, such as food changes and increased physical activity [4]. Childhood obesity is linked to the onset of comorbidities that were previously thought to be "adult" disorders, such as type 2 diabetes, hypertension, nonalcoholic fatty liver disease, obstructive sleep apnea, and dyslipidemia [4]. Due to the steady rise in the prevalence of obesity and sedentary lifestyles, metabolic syndrome is becoming more frequent in children and adolescents with obesity all over the world [5].

The metabolic syndrome (MetS) in obese children is a collection of characteristics that, when combined, raise the risk of cardiovascular disease and are linked to insulin resistance (IR) and type 2 diabetes. The most commonly used definition for pediatric MetS is based on the Adult Treatment Panel III of the National Cholesterol Education Program (NCEP), which requires at least three of the following criteria: raised waist circumference, hypertension, hyperglycemia, hypertriglcerdemia, and decreased Low-Density lipoprotein Cholesterol HDL-C [6]. Although the fundamental mechanisms of MetS pathogenesis are still unknown, mounting evidence suggests that adipokines play an important role. Chemerin, Il-18 and Il-1 beta is a newly discovered adipokines [7].

Chemerin, Il-18 and Il-1 beta are implicated in a variety of physiological and pathological processes, including adipogenesis, insulin sensitivity, and immunological response, suggesting that it plays an important role in metabolic health [8]. In overweight pediatric patients, serum chemerin, Il-18 and Il-1 beta have been found to be positively linked with body weight and the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) in recent research [9]. Considering the variables that influence the metabolic syndrome in obese children [10]. Chemerin, Il-18 and Il-1 beta may possibly have a role in the development of cardiovascular illnesses in children and adolescents, according to previous research [11]. These findings show that chemerin, Il-18 and Il-1 beta may play key roles in the regulation of obesity and metabolic syndrome. However, few investigations on chemerin, Il-18 and Il-1 beta in obese children and adolescents have been conducted in Egypt in addition to different ethnic, genetic and environmental background [12].

To our knowledge, no previous research in Egypt have looked at serum chemerin, Il-18 and Il-1 beta concentrations in obese children and adolescents, or their relationships with BMI and lipid levels. The goal of this study is to investigate the link between serum chemerin, Il-18 and Il-1 beta and metabolic syndrome in obese children and adolescents, as well as to identify high-risk groups in the obese pediatric population that require therapy.

Subjects and Methods

Subjects

- **Study design:** The study was a comparative cross-sectional study conducted for patients at the Suez Canal University Hospitals' pediatric clinic in Ismailia city to assess the relationship between serum chemerin, Il-18 and Il-1 beta and metabolic syndrome in obese children and adolescents.
- **Study population:** The study participants were selected from the pediatric clinics of the Suez Canal University Hospitals in Ismailia and placed into the following groups after a detailed history, comprehensive clinical examination, including auxological assessment, and detailed investigations: Group 1: Healthy non-obese children and adolescents No 57, Group 2: Obese without metabolic syndrome (n = 57); Group 3:Obese witht metabolic syndrome (n = 57); accompanying their siblings to the pediatric outpatient clinic of Suez Canal University (age and sex matched) (n: 57).

Inclusion criteria of the obese group: The obese group was comprised of children and adolescents of both sexes with a BMI (Body Mass Index) of less than 95th percentile, aged 2 to 18 years. Children and adolescents of both sexes aged 2-18 years, with a BMI between the 15th and 85th percentile were included in the control group. Those with endocrine problems or syndromic obesity, infections or acute sickness, chronic illnesses, and patients on lipid-lowering, antihypertensive, or antihyperglycemic medicines were excluded from the study.

Methods

Sample size: The power of the study was estimated using open Epi [31] 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 171 in total, with 57 in each group [27]. 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 Consideration

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.

All participants underwent the following procedures: a complete medical history; a general and systemic examination; measurements: weight, height, BMI, and waist circumference (WC); 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). The Friedewald formula was used to calculate cholesterol levels in low-density lipoprotein (LDL, mmol/L). Chemerin, Il-18 and Il-1 beta levels in serum were determined using a sandwich enzyme-linked immunosorbent assay (ELISA) kit (Human Chemerin Duo Set ELISA Kit, catalogue No. DY2324, R&D Systems, Inc, Minneapolis, MN, USA) as directed by the manufacturer.

Diagnosis of metabolic syndrome patients

For diagnosis, we used Cook., *et al*. criteria. Three of the following must be present: waist circumference 90th centile, blood pressure 90th centile, triglyceride 110 mg/dl, HDL 40 mg/dl, and impaired blood glucose (100-125 mg/dl) [30].

Statistical analysis

Sample size calculation

This study included three groups; group I (normal weight healthy children), group II (obese children) and group III (obese children with metabolic syndrome). The sample size was calculated using the G*Power software (version 3.1.9.4) based the previous study conducted by Tan., *et al*. (2016)* that estimated the levels of chemerin, Il-18 and Il-1 beta in normal weight children, obese children and obese children with metabolic syndrome. Estimation of the sample size was performed considering a 5% false positive rate (type 1 error) and 95% power. A minimum of 57 individuals was required in each group.

Statistical analysis

The obtained data were tabulated and analyzed using the SPSS statistical software version 22 (IBM Corp., Armonk, NY, USA). Numerical data were presented as mean, SD, median and range, while non-numerical data were presented as frequency and percentage. After testing normality, Kruskal-Wallis test was used to compare the numerical data of the three groups and Chi square test was used to assess difference in the categorical data. Post hoc correction Tukey test was used for pairwise comparison. Spearman correlation test was used for correlation among numerical data. ROC analysis was conducted to assess the potential usefulness of plasma chemerin levels as marker for metabolic syndrome. P values less than 0.05 were considered statistically significant.

Results

The findings of demographic and anthropometric data are shown in table 1 no significant difference in age among rhree study groups as well as height.

		Group I (n = 57)	Group II (n = 57)	Group III (n = 57)	p- value
		Mean ± SD, Median (range)			
Age (years)		11.4 ± 3.67, 12 (4-17.5)	11.9 ± 3.66, 11.3 (6-17.8)	12.8 ± 3.7, 13.3 (5-17.3)	0.08[a]
Height (cm)		150.3 ± 22, 153 (103-183)	152 ± 21.6, 152 (118-183)	159.1 ± 21.2, 165 (112-187)	0.11 [a]
Weight (kg)	Post hoc Tukey test	38.9 ± 13.5, 38 (16.4-64.1)	62.5 ± 26.1, 62.1 (27.1-105.7)	68.7 ± 24.5, 76.5 (24.9-105.9)	< 0.001[a*]
		Group I vs. II p < 0.001*	Group II vs. III p = 0.29	Group I vs. III p < 0.001*	

BMI (kg/m^2)	Post hoc Tukey test	16.6 ± 1.6, 16.5 (16-20.1)	25.3 ± 4, 24.6 (19.2-32)	25.9 ± 4.1, 26.7 (16.5-32.1)	< 0.001[a]*
		Group I vs. II p < 0.001*	Group II vs. III p < 0.001*	Group I vs. III p < 0.001*	
WC (cm)	Post hoc Tukey test	64.5 ± 6.3, 64 (50-75)	76.2 ± 7.7, 76 (63-101)	88.7 ± 12.3, 94 (58-109)	< 0.001[a]*
		Group I vs. II p < 0.001*	Group II vs. III p = 0.63	Group I vs. III p < 0.001*	
		Count (%)			
Gender	Female	30(51)	32(68)	30(34)	0.91[b]
	Male	27(49)	25(32)	27(66)	
Residence	Urban	34(19)	34(38)	39(0)	0.54[b]
	Rural	21 (6)	21(10)	18(2)	

Table 1: Demographic and anthropometric data of the study participants.

BMI: Body Mass Index, WC: Waist Circumference, a: Kruskal-Wallis test, b: Chi Square Test, *: Statistically Significant.

		Group I (n = 57)	**Group II (n = 57)**	**Group III (n = 57)**	**p- value**
	Mean ± SD, Median (range)				
SBP (mm Hg)	Post hoc Tukey test	94.7 ± 8.28, 95 (78-109)	103.2 ± 7.58, 102 (92-127)	103.9 ± 14, 102 (80-130)	<0.001[a*]
		Group I vs. II p < 0.001*	Group II vs. III p = 0.93	Group I vs. III p < 0.001*	
DBP (mm Hg)	Post hoc Tukey test	60.8 ± 5.45, 60 (50-72)	63.6 ± 6.24, 62 (54-80)	65.7 ± 9.9, 64 (50-86)	0.022 [a*]
		Group I vs. II p = 0.11	Group II vs. III p = 0.31	Group I vs. III p = 0.002*	
FBG (mg/dL)	Post hoc Tukey test	72 ± 13.03, 70 (49-104)	82.4 ± 11.84, 79 (65-117)	108.2 ± 19.35, 114 (63-141)	<0.001 [a*]
		Group I vs. II p = 0.001*	Group II vs. III p < 0.001*	Group I vs. III p < 0.001*	
Triglycerides (mg/dL)	Post hoc Tukey test	92.3 ± 14.8, 91 (64-141)	125.6 ± 80.9, 100 (58-502)	187.5 ± 132.3, 161 (60-712)	<0.001 [a*]
		Group I vs. II p = 0.12	Group II vs. III p = 0.001*	Group I vs. III p < 0.001*	
HDL (mg/dL)	Post hoc Tukey test	50.5 ± 6, 51 (36-64)	46.8 ± 10.9, 47 (26-67)	35.5 ± 9.8, 32 (18-57)	<0.001 [a*]
		Group I vs. II p = 0.108	Group II vs. III p < 0.001*	Group I vs. III p < 0.001*	
IL-18 (pg/mL)	Post hoc Tukey test	93.4 ± 22.2, 94 (17-143)	126.9 ± 26.8, 121 (82-195)	165.4 ± 35.1, 165 (102-288)	<0.001 [a*]
		Group I vs. II p < 0.001*	Group II vs. III p < 0.001*	Group I vs. III p < 0.001*	

IL-1β (pg/mL)	Post hoc Tukey test	0.57 ± 0.28, 0.52 (0.1-1.3)	0.86 ± 0.4, 0.79 (0.2-1.9)	1.5 ± 0.54, 1.47 (0.59-2.6)	<0.001 a*
		Group I vs. II p = 0.001*	Group II vs. III p < 0.001*	Group I vs. III p < 0.001*	
Chemerin (ng/mL)	Post hoc Tukey test	84.2 ± 12.9, 85.6 (52.9-109.2)	109.6 ± 11.7, 110.6 (85.5-32)	143.3 ± 25.1, 138.5 (99.5-22.1)	<0.001 a*
		Group I vs. II p < 0.001*	Group II vs. III p < 0.001*	Group I vs. III p < 0.001*	

Table 2: Clinical and biochemical data of the study participants.

SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, FBG: Fasting Blood Glucose, HDL: High Density-lipoprotein, IL: Interleukin, a: Kruskal-Wallis test, *: Statistically Significant.

This study revealed statistically significant difference of chemerin levels in particular in group II and group III as depicted in figure 1.

Figure 1: Chemerin levels in the three study groups.

Statistically significant Elevated levels of interleukin 18 were found in study groups compared to healthy control children as shown in figure 2, 3.

Figure 2: IL-18 levels in the three study groups.

Figure 3: IL-1β levels in the three study groups.

Elvated serum chemerin were significantly positively correlated with systolic blood pressure, fasting blood glucose and HDL-C as shown in table 3 and diagrammatic presentation in figures 4, 5 and 6 respectively.

Figure 4: Significant positive correlation between Chemerin levels and SBP in the metabolic syndrome group.

Figure 5: Significant positive correlation between Chemerin levels and FBGin the metabolic syndrome group.

Figure 6: Significant negative correlation between Chemerin levels and HDL in the metabolic syndrome group.

	Chemerin (ng/mL)							
	All patients (n = 171)		Group I (n = 57)		Group II (n = 57)		Group III (n = 57)	
	ρ	p-value	ρ	p-value	ρ	p-value	ρ	p-value
Age (years)	0.13	0.08	0.081-	0.55	0.11	0.44	-0.12	0.4
Height (cm)	0.14	0.07	0.08-	0.55	0.18	0.18	-0.02	0.9
Weight (kg)	0.42	<0.001*	0.079-	0.55	0.18	0.17	0.07	0.63
BMI (kg/m^2)	0.61	<0.001*	-0.12	0.38	0.14	0.29	0.13	0.34
WC (cm)	0.63	<0.001*	0.009	0.95	0.13	0.33	0.17	0.22
SBP (mm Hg)	0.36	<0.001*	-0.15	0.28	0.17	0.22	0.39	0.003*
DBP (mm Hg)	0.28	<0.001*	-0.15	0.28	0.17	0.21	0.17	0.22
FBG (mg/dL)	0.62	<0.001*	-0.02	0.87	-0.05	0.7	0.4	0.002*
Triglycerides (mg/dL)	0.43	<0.001*	-0.16	0.24	0.32	0.01*	0.19	0.16
HDL (mg/dL)	-0.55	<0.001*	-0.26	0.051	0.05	0.71	-0.48	<0.001*
IL-18 (pg/mL)	0.69	<0.001*	0.14	0.31	0.05	0.69	0.08	0.53
IL-1β (pg/mL)	0.55	<0.001*	-0.12	0.36	-0.06	0.67	-0.01	0.93

Table 3: Correlation of the plasma chemerin levels with the patients' data.

ρ: Rho; correlation coefficient of Spearman correlation test.

Plasma Il-18 levels were positively correlated with almost all components of metabolic syndrome including BMI, waist circumference, systolic and diastolic blood pressure , fasting blood glucose, triglycerides and HDL as shown in table 4, figures 7 and 8 respectively.

	IL-18 (pg/mL)							
	All patients (n = 171)		Group I (n = 57)		Group II (n = 57)		Group III (n = 57)	
	ρ	p-value	ρ	p-value	ρ	p-value	ρ	p-value
Age (years)	0.24	0.001*	0.15-	0.27	0.41	0.002*	0.25	0.06

Height (cm)	0.23	0.002*	0.17	0.2	0.18	0.18	0.24	0.08
Weight (kg)	0.5	<0.001*	0.14	0.3	0.46	<0.001*	0.32	0.01*
BMI (kg/m^2)	0.68	<0.001*	-0.03	0.8	0.49	<0.001*	0.34	0.01*
WC (cm)	0.63	<0.001*	0.12	0.4	0.26	0.05	0.24	0.07
SBP (mm Hg)	0.27	<0.001*	0.25	0.6	0.27	0.045*	0.04	0.79
DBP (mm Hg)	0.22	0.003*	0.21	0.12	0.24	0.07	0.17	0.22
FBG (mg/dL)	0.53	<0.001*	0.03	0.8	0.34	0.009*	0.24	0.07
Triglycerides (mg/dL)	0.46	<0.001*	0.02	0.9	0.34	0.01*	0.16	0.23
HDL (mg/dL)	-0.38	<0.001*	-0.3	0.02*	0.17	0.2	0.16	0.23

Table 4: Correlation of the plasma IL-18 levels with the patients' data.

ρ: Rho; correlation coefficient of Spearman correlation test.

Figure 7: Significant positive correlation between IL-18 levels and weight in the metabolic syndrome group.

Figure 8: Significant positive correlation between IL-18 levels and BMI in the metabolic syndrome group.

Both plasma chemerin and IL-1β levels were highly significantly correlated with all metabolic syndrome components as depicted in table 5 and figure 9.

	IL-1β (pg/mL)							
	All patients (n = 171)		**Group I (n = 57)**		**Group II (n = 57)**		**Group III (n = 57)**	
	r	**p-value**	**r**	**p-value**	**r**	**p-value**	**r**	**p-value**
Age (years)	0.29	<0.001*	0.0-	0.49	0.41	0.002*	0.23	0.09
Height (cm)	0.3	<0.001*	0.13	0.3	0.18	0.18	0.28	0.04*
Weight (kg)	0.48	<0.001*	0.1	0.45	0.46	<0.001*	0.21	0.11
BMI (kg/m^2)	0.56	<0.001*	0.07	0.6	0.45	0.001*	0.19	0.16
WC (cm)	0.53	<0.001*	0.06	0.7	0.13	0.16	0.23	0.53
SBP (mm Hg)	0.33	<0.001*	0.01	0.9	0.36	0.006*	0.18	0.18
DBP (mm Hg)	0.17	0.02*	0.07	0.6	0.33	0.01*	0.17	0.22

FBG (mg/dL)	0.44	<0.001*	0.02	0.87	0.11	0.34	0.04	0.8
Triglycerides (mg/dL)	0.33	<0.001*	0.28	0.03*	0.01	0.95	0.1	0.46
HDL (mg/dL)	-0.35	<0.001*	-0.14	0.3	0.05	0.14	0.3	0.89

Table 5: Correlation of the plasma chemerin IL-1β levels with the patients' data.

ρ: Rho; correlation coefficient of Spearman correlation test.

Figure 9: Significant positive correlation between IL-1β levels and height in the metabolic syndrome group.

The receiver operating analysis revealed high sensitivity of chemerin 86% and specificity 93% in differentiating metabolic syndrome cases among all participants. The sensitivity of Il-18 was 84.2% and specificity 80.8% and IL-1β had 82.5% sensitivity and 72.8% specificity in all participants. While the sensitivity of chemerin, Il-18 and IL-1β reached 86%,84.2% and 78.9% respectively in obese children and adolescents. In addition the specificity of chemerin, Il-18 and IL-1β was 86%,64.9% and 70.2% in differentiating metabolic syndrome table 6 and figures 10, 11, 12, and 13.

Discussion

The purpose of this study is to examine the relationship between serum chemerin, Il-18 and Il-1 beta and metabolic syndrome in

Differentiation	Marker	Cutoff value	AUC	p-value	Sensitivity	Specificity
Metabolic syndrome in all participants	Chemerin	119.6	95.8%	<0.001*	86%	93%
	IL-18	131.5	89.6%	<0.001*	84.2%	80.8%
	IL-1β	0.91	87.9%	<0.001*	82.5%	72.8%
Metabolic syndrome in obese patients	Chemerin	120	91.9%	<0.001*	86%	86%
	IL-18	132.5	81.5%	<0.001*	84.2%	64.9%
	IL-1β	0.99	81.8%	<0.001*	78.9%	70.2%

Table 6: ROC analysis for the chemerin, IL-18, and IL-1β diagnostic value in differentiation of the metabolic syndrome cases.

AUC: Area Under Curve.

Figure 10: ROC of chemerin for differentiation of metabolic syndrome cases in all the study participants.

Figure 11: ROC of chemerin for differentiation of metabolic syndrome cases in obese patients.

Figure 12: ROC of IL-18 and IL-1B for differentiation of metabolic syndrome cases in all the study participants.

Figure 13: ROC of IL-18 and IL-1B for differentiation of metabolic syndrome cases in obese patients.

obese children and adolescents who attend the pediatric clinic of Suez Canal University Hospitals in Ismailia city located 150 Km eastern to Cairo, Egypt.

In our study, 57 obese children and adolescents with metabolic syndrome, 57 children and adolescents without metabolic syndrome and 57 normal healthy control children and adolescents are compared. This study enrolled 57obese and adolescents out of 114 obese children who satisfied the Cook., *et al*. 2003 criteria for metabolic syndrome diagnosis,. Our study's MetS prevalence was somewhat higher than that of Imunovi., *et al*. 2016, who discovered that MetS prevalence among obese youngsters was 37.4 percent [14]. According to research conducted by Zaki., *et al*. in 2012, MetS prevalence among obese Egyptian children was 25% [15]. According to the IDF, the prevalence of metabolic syndrome was 32 percent in recent research [16].

According to De Ferranti., *et al*. 2007, the World Health Organization, the National Cholesterol Education Program, and the International Diabetes Federation, the prevalence of MetS in five European countries (France, Greece, Italy, Poland, and Hungary) was 35.7 percent, 31.4 percent, 20.3 percent, and 16.4 percent, respectively [17]. The prevalence statistics reported from epidemiological surveys vary substantially even within the same nation due to the adoption of diverse criteria for identifying the metabolic syndrome. As a result of the various diagnostic criteria, it is difficult to compare the reported prevalence rates of metabolic syndrome throughout the world, as well as data between research.

In the present study, increased waist circumference (54.8%) was shown to be the most common predictor of metabolic syndrome in obese people, followed by low HDL and high triglyceride (47.6%), impaired fasting blood sugar (35.7%), and finally raised blood pressure (14.3%). According to Dejavitte., *et al*. 2020, increased waist circumference was the most common factor (77.4%), followed by low HDL (49.4%), although impaired fasting glucose was third (15%), followed by high triglyceride (5.6%), and raised blood pressure (1.1%). Increased waist circumference was also the most common determinant (85%), followed by low HDL (20%), high triglyceride (13.3%), impaired fasting glucose, and elevated blood pressure with the same frequency (8.3%) in another study conducted by Zaki., *et al*. 2012 among Egyptian obese children [15,18].

In young individuals, waist circumference, which is independent of insulin resistance, plasma lipid levels, and blood pressure, is a significant predictor of metabolic syndrome [19]. Even when children and adolescents are fat and have similar BMIs, individuals with substantial volumes of visceral adipose tissues have worse insulin sensitivity than those with little amounts [20].

The metabolic syndrome groupIII had considerably greater serum chemerin, Il-18 and Il-1 beta levels than the non-metabolic syndrome obese and control groups, according to the current

study. These findings are in line with the findings of numerous earlier investigations, which have found that people with metabolic syndrome had greater serum chemerin, Il-18 and Il-1 beta levels than people without it. Dahpy., *et al*. 2020 conducted case control research in Egypt with 100 patients with MetS and 68 healthy participants and found that serum chemerin levels were considerably higher in MetS subjects than in non-MetS subjects [21]. Ouerghi., *et al*. 2020, Tunisian research investigated the relationship between circulating chemerin and metabolic syndrome (MetS) and cardio-metabolic risk factors in adolescents, reported the same [22]. It was discovered that participants with MetS had greater serum chemerin concentrations. Maghsoudi., *et al*. 2016 did cross-sectional research with 225 obese children (101 with MetS and 124 without MetS) and 119 lean controls, they found that Chemerin levels were considerably higher in obese children, particularly in those with MetS [23].

Chemerin, Il-18 and Il-1 beta influence on lipid and glucose metabolism, as well as its function in immune response modulation, might explain this. Il-18 and Il-1 beta Chemerin signaling is required for pre-adipocyte differentiation into adipocytes during the hyperplasia phase. Increased levels of this adipokine in adipose tissue attract immune cells, which leads to increased production of inflammatory mediators such CRP-US, interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF-) [25]. The mechanisms of chemerin, Il-18 and Il-1 beta influence on glucose metabolism are yet unknown, however it appears to be attributable to a decrease in insulin-sensitive agents like glucose transporter 4 (GLUT-4), leptin, and adiponectin, or an increase in insulin-resistant agents like IL-6.6 [26].

According to the current study, the optimal cut off value for serum chemerin in distinguishing non-metabolic and metabolic syndrome participants was 382 ng/ml, with a sensitivity of 84.2% and a specificity of 80%. Dahpy., *et al*. 2020 found a lower chemerin cutoff value of 209 ng/ml with a sensitivity of 86% and a specificity of 35.3% [21]. Stejskal., *et al*. (2008) found that the chemerin cutoff of 240 ng/ml had 75% sensitivity and 67% specificity [27]. This can be explained by the development of ELISAs that target a wider range of chemerin isoforms. It has been discovered that obese individuals' adipose tissue undergoes greater C-terminal chemerin processing, resulting in the identification of larger levels of bioactive chemerin in the circulation system.

A multiple stepwise linear regression test was used to find the clinical factors most significantly related with serum chemerin, Il-18 and Il-1 beta levels in MetS patients. Our findings revealed a substantial positive connection between serum chemerin, Il-18 and Il-1 beta levels and FBS. This finding was supported by Dahpy., *et al*. 2020 and Ouerghi., *et al*. 2020, but Ba., *et al*. 2019 found no significant relationship [21,22,28].

Chemerin, Il-18 and Il-1 beta and HDL were also shown to have a strong negative connection in the research. The similar finding was reported by Maghsoudi., *et al*. 2016 and Ouerghi., *et al*. 2020 [22,23]. This was in contrast to Ba., *et al*. 2019, who claimed that there was no significant link. Because of its reverse cholesterol transport role, HDL protects the endothelium by limiting LDL oxidation and thereby lowering its atherogenic potential [28,29]. So it's suggested that chemerin, Il-18 and Il-1 beta were associated with almost all components of metabolic syndrome and may serve as helpful independent diagnostic biomarkers for early detection of metabolic syndrome.

Conclusion

Chemerin, Il-18 and Il-1 beta levels were substantially greater in the metabolic syndrome group than in the non-metabolic syndrome obese and control groups in our study of Egyptian children and adolescents. Chemerin, Il-18 and Il-1 beta levels were shown to have a positive correlation with impaired fasting blood sugar and a negative correlation with HDL. These data show that chemerin, Il-18 and Il-1 beta might be a potential metabolic syndrome adipokines markers on its own. To validate these findings and assess serum chemerin, Il-18 and Il-1 beta levels as a predictor of accelerated atherosclerosis or decreased glucose tolerance, more large studies are needed. Furthermore, future research directions that include but not limited to targeting chemerin, Il-18 and Il-11 beta for future therapeutic interventions for treatment and prenetion. of metabolic syndrome in children and adolescents.

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