

Assessment of serum Chemerin level and it's association with obesity indices and hs-CRP in a group of Egyptian obese children

Ahmed Sayed Ismail Aly Assistant researcher, National Research Center

Prof.Howida Hosny El Gebaly: Professor of Pediatrics, Dean of Faculty of Postgraduate Childhood Studies, Ain Shams University.

Prof.Salwa Reda El Batroy: Professor of Biological Anthropology, National Research Centre.

Prof.Mona Mamdouh Hassan: Professor of Pediatrics, Diabetes, Endocrine and Metabolism Pediatric Unit, Cairo University.

Prof.Moushira Erfan Zaki: Professor of Biological Anthropology, National Research Centre.

Abstract

Background: Childhood obesity is now forming a global problem with subsequent health problems. It is now claimed that adipokines secreted by adipose tissue are responsible for such consequences. Chemerin, a recently discovered adipokine, may be linked to obesity and obesity-associated metabolic complications and may form a link between immune system, adipose tissue and inflammation.

Aim: This study aims to assess serum Chemerin among obese children compared to non obese children and assess its relation to the inflammation and obesity indices.

Methods: This comparative cross- sectional study was conducted in collaboration of Faculty of Postgraduate Studies, Ain Shams University, National Research Centre and Cairo University on 45 obese subjects (BMI \geq 95th percentile) aged from 6 to 11 years recruited from Obesity Clinic of the Diabetes, Endocrine and Metabolism Pediatric Unit (DEMPU), Pediatric Hospital, Cairo University and Obesity Clinic at Medical and Scientific Centre of Excellence, National Research Center compared to 45 healthy children age and sex matched. Serum Chemerin, high- sensitive C- reactive protein (hs- CRP), waist circumference (WC), hip circumference (HC) were measured; BMI, waist- to- hip ratio (WHR) and waist- height ratio (WHtR) were calculated.

Results: Serum Chemerin was significantly higher in obese than in non- obese children (143.49 ± 16.598 , 87.7 ± 8 ng /L, respectively, $P < 0.001$). Among obese children Chemerin concentration had a significant positive correlation with hs- CRP level even after adjusting for BMI, age and sex while no correlation was present with obesity indices (BMI z score, WC Z score, HC, WHR and WHtR).

Conclusion: Chemerin concentration was higher in obese children and hs- CRP was in positive relation with Chemerin level.

Recommendations: Our findings show that Chemerin is linked to inflammation in obese children and thus can be considered as an early marker of the inflammatory process in obesity.

Key words: Chemerin- Obesity- Inflammation- Obesity indices- hs- CRP- children.

تقييم مستوى الكيميرين وإرتباطه بمؤشرات السمنة والبروتين المتفاعل C عالي الحساسية

في مجموعة من الأطفال المصريين الذين يعانون من السمنة

الخلفية: تشكل السمنة لدى الأطفال حالياً مشكلة عالمية بما يترتب عليها من مشاكل صحية ويعتقد حالياً ان الاديوكونات التي تفرزها الأنسجة الدهنية هي المسؤولة عن مثل هذه المشاكل. الكيميرين وهو من الاديوكونات المكتشفة حديثاً قد يكون ذو علاقة بالسمنة والمضاعفات الأيضية المرتبطة بالسمنة وقد يشكل صلة بين الجهاز المناعي والأنسجة الدهنية والالتهابات.

الهدف: يهدف البحث الى تقييم مستوى الكيميرين في الأطفال الذين يعانون من السمنة بالمقارنة مع الأطفال الأصحاء وتقييم علاقته بمؤشرات الالتهاب والسمنة.

المنهجية: هذه الدراسة هي دراسة مقطعية مقارنة، أجريت بالتعاون في كلية الدراسات العليا، جامعة عين شمس والمركز القومي للبحوث وجامعة القاهرة واشتملت هذه الدراسة على عدد 45 طفلاً يعانون من السمنة مع مؤشر كتلة الجسم فوق 95، أعمارهم بين 6 إلى 11 سنة تم جمعهم من عيادة السمنة، وحدة الغدد الصماء والسكر مستشفى الأطفال، جامعة القاهرة وعيادة السمنة بمركز التميز العلمي، المركز القومي للبحوث وتم مقارنتهم بـ 45 طفلاً من الأصحاء ذوي عمر وجنس مطابقين. وقد تم اجراء القياسات الأنتروبومترية: الوزن، الطول، محيط الخصر، محيط الأرداف مع حساب مؤشر كتلة الجسم ونسبة الخصر للطول ونسبة الخصر للأرداف، بالإضافة الى القياس المعمل لمستوى الكيميرين والبروتين المتفاعل-C عالي الحساسية.

النتائج: أظهرت الدراسة ارتفاع مستوى الكيميرين في الأطفال المصابين بالسمنة مقارنة بالمجموعة الضابطة (143.49 ± 16.598 مقابل 87.7 ± 8 ng/L) على التوالي $P < 0.001$ (وفي مجموعة الأطفال البدناء وجد علاقة أيجابية بين الكيميرين والبروتين المتفاعل - C عالي الحساسية حتى بعد ضبط مؤشر كتلة الجسم والسن والجنس بينما لم توجد علاقة بينه وبين مؤشرات السمنة (محيط الخصر، محيط الأرداف، مؤشر كتلة الجسم، نسبة الخصر للطول ونسبة الخصر للأرداف).

الخلاصة: ارتفاع مستوى الكيميرين بشكل ملحوظ عند الأطفال البدناء مع وجود علاقة أيجابية بين الكيميرين والبروتين المتفاعل-C عالي الحساسية مما يشير على وجود علاقة بين الكيميرين والالتهاب في الأطفال البدناء ومن ثم يمكن اعتباره علامة مبكرة لعملية الالتهاب في السمنة.

الكلمات المفتاحية: كيميرين- السمنة- الالتهاب- مؤشرات السمنة- البروتين المتفاعل-C عالي الحساسية.

Introduction:

Obesity is an uprising medical health problem with associated medical consequences making it a global pandemic both in developed and developing countries (Ebbeling et.al., 2002). With an estimated number of 340 million children affected globally (WHO, 2018), childhood obesity is now considered one of the major public health problems affecting the youth. In Egypt, obesity has a high prevalence and became a problem in Egyptian youth (Salazar et.al., 2006).

The impact of childhood obesity on public health is profound being a major risk factor for many health complications as cardiovascular diseases and metabolic complications with consequent decrease in life expectancy (Lee et.al., 2010).

Obesity can be subdivided into central or abdominal obesity and peripheral obesity with central obesity constituting the most dangerous type of obesity as it has been linked to metabolic dis- regulation as metabolic syndrome, cardiovascular disorders, T2D and certain cancers (Wildman et.al., 2008, Supriya et.al., 2018).

The golden standard for measuring central obesity is imaging but due to being expensive making them not applicable in clinical setting more simple measures as waist circumference, waist to hip ratio and waist to height ratio are being used in clinical practice (Owolabi et.al., 2017).

The key element of obesity is white adipose tissue, which acts as an endocrine tissue secreting so- called adipokines which are involved in the regulation of a variety of systemic processes such as food intake, nutrient metabolism, insulin sensitivity and inflammation (Katsareli and Dedoussis; 2014) and considered one of the mechanisms that connect obesity with such comorbidities.

Central obesity was found to be associated with high level of adipokine secretion (Supriya et.al., 2018).

One of the newly identified adipokines, Chemerin, is a chemoattractant protein that plays a role in the differentiation of adipocytes and glucose metabolism and is associated with obesity, inflammation, and atherosclerosis (Fontes et.al., 2018).

Chemerin has been reported to act as a pro- inflammatory adipokine causing chemotaxis of immature dendritic cells and macrophages thus initiating the immune response at the sites of inflammation or tissue injury (Parolini et.al., 2007, Hart and Greaves; 2010) and was found to be associated with systemic markers of inflammation, such as high sensitivity C- reactive protein (hsCRP), interleukin- 6, and tumor necrosis factor- α (Chakaroun et.al., 2012). Also it was found that Chemerin involved in adipogenesis, angiogenesis and energy metabolism (Helfer and Wu; 2018). Furthermore, adult obese patients with metabolic syndrome had elevated Chemerin levels associated with cardiovascular risk factors such as hyperglycemia, dyslipidemia, and hypertension (Stejska et.al., 2008).

Aim:

The present study aims to measure serum chemerin level and assess it's association with obesity indices and hs- CRP in a group of Egyptian obese children.

(Assessment Of Serum Chemerin Level...)**Subjects and Methods:**

This study was a comparative cross- sectional study carried out in the Obesity Clinic of the Diabetes, Endocrine and Metabolism Pediatric Unit (DEMPU), Pediatric Hospital, Cairo University and Obesity Clinic at the "Medical Research Excellence Center (MERC)", National Research Centre (Egypt) from January 2016 to January 2017 to evaluate the status of Chemerin in obese children and its relation with central obesity and hs- CRP. The study included 45 obese children ($\geq 95^{\text{th}}$ BMI percentile for age and sex according to the 2002 standard growth curves for the Egyptian children and adolescents of both sexes (Ghalli et.al., 2008) their ages ranged between 6 and 11 years compared to 45 healthy children and adolescents age and sex matched included as controls (BMI < 85th percentile).

Exclusion criteria: Children with identified causes of obesity such as identified syndromes or chromosomal defects or endocrinal disorders and those who were treated with drugs that may affect body weight if used for long time as glucocorticoids.

Ethical approvals were obtained from the Ethical Committee of "Faculty of Postgraduate Childhood Studies". A verbal approval was taken from every child participated in the current study, in addition to a written informed consent from one of the parents after explanation of the aim of the study and it's possible benefits for identifying the effect of obesity on health.

For each child, complete clinical examination; including cardiac examination, chest examination and abdominal examination to exclude any chronic disease that may affect the growth of the child, has been done. Medical history of any present or past illness, such as renal, hepatic or endocrinal, and drug intake history, either steroids or anticonvulsant have been taken.

Anthropometric assessment: For every child in the study, body weights (Wt), height (Ht), waist circumference (WC), hip circumference (HC) were measured. Then BMI, Waist to Hip ratio (WHR) and Waist to Height ratio (WHtR) was calculated. The landmarks, instruments used and techniques followed were those recommended by the international biological program I. B. P (Hiernaux and Tanner; 1969).

For laboratory tests, early morning forearm venous blood samples (5 ml) were obtained from each participant; after overnight fasting (12 hours). Professional staff performed venipuncture. The blood samples were left to clot and sera were separated by centrifugation for 10 minutes at 3000 rpm then stored at -80 °C for batch assessments. Serum Chemerin and hs- CRP were measured using enzyme- linked immunosorbent assay (ELISA).

Statistical Analysis:

The clinical and laboratory data were recorded on an "Investigation report form". These data were tabulated, coded then analyzed using SPSS software version 17, SPSS Inc., Chicago, IL, USA to obtain the results.

Results:

The present work is a comparative cross- sectional study that included

45 obese children of both sexes ($\geq 95^{\text{th}}$ BMI percentile for age and sex). They were 22 males and 23 females, with a mean age of 9.443 ± 1.619 years. This study group was compared to 45 age and sex matched healthy children included as controls. The control group was 21 males and 24 females with mean age of 9.021 ± 1.66 years.

Comparisons between the 2 groups regarding anthropometric assessment, and laboratory findings were presented in table (1) and figures (1)-(3).

The comparison between both groups showed that all parameters showed a highly significant difference except for age.

Table (1) Comparison between the obese subjects and the control.

	Obese subjects (n: 45)		Control (n: 45)		P- Value	Sig
	Mean	$\pm Sd$	Mean	$\pm Sd$		
Age (Years)	9.443	1.619	9.021	1.66	>0.05	NS
Weight Z Score	3.377	1.07	-0.178	0.877	<0.001	HS
Height Z Score	0.757	1.08	-0.926	3.957	<0.001	HS
Bmi- Z Score	3.382	1.081	-0.068	1.174	<0.001	HS
Wc Z Score	2.0018	0.332	-0.272	0.978	<0.001	HS
WHR	0.907	0.0512	0.8504	0.0414	<0.001	HS
WHtR	0.622	0.572	0.452	0.04	<0.001	HS
Chemerin(ng/L)	143.49	16.598	87.70	8.007	<0.001	HS
hs- CRP(mg/L)	4.889	0.5436	3.068	0.4215	<0.001	HS

* Significant at (P<0.05) ** Highly significant at (<0.001)

hs- CRP= high sensitive C- reactive protein, WC=w aist circumference, WHR= Waist to Hip ratio, WHtR= Waist to Height ratio.

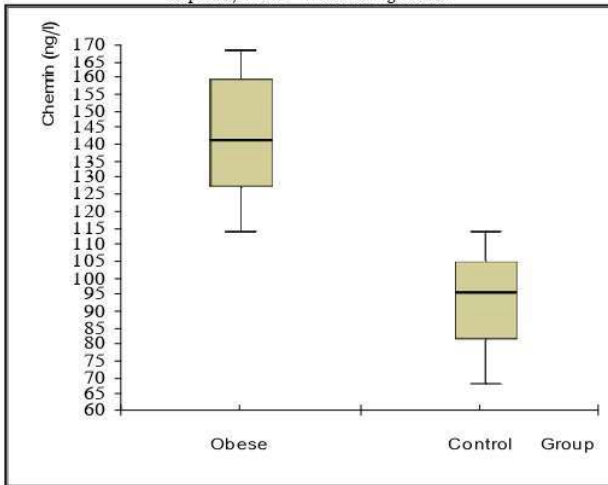


Figure (1) Chemerin level in obese and control.

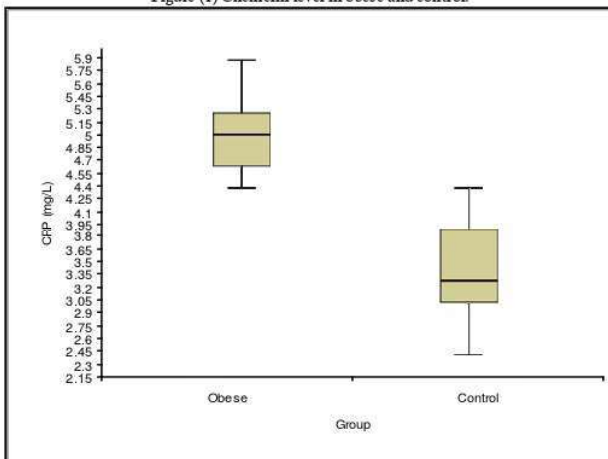


Figure (2) hs- CRP level in obese and control. Wt= weight, Ht= height, WC=w aist circumference, WHR= Waist to Hip ratio, WHtR= Waist to Height ratio.

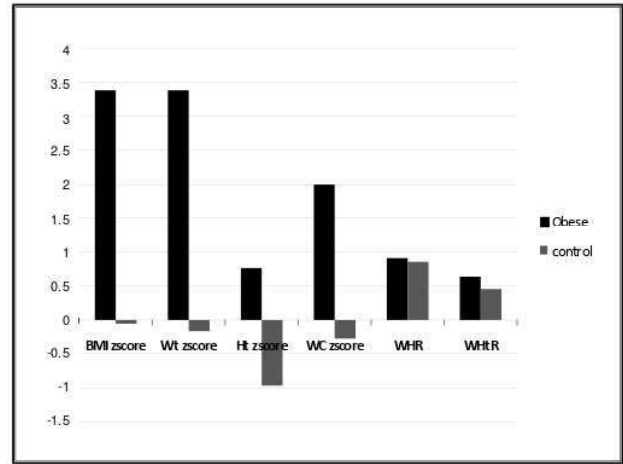


Figure (3) Comparison between the 2 groups regarding anthropometric assessment.

In the obese group, the correlation of Chemerin with anthropometric parameters and hs- CRP have been investigated to illustrate the relationship between them table (2). Chemerin showed significant positive association with hs- CRP only fig (4) which remained significant even after adjustment for anthropometric parameters and age.

Table (2) Correlation of Chemerin with anthropometric indices and hs- CRP

Parameter	Chemerin			
	r	p	r ^a	p ^a
Age	0.015	0.923		
BMI Z Score	0.111	0.466		
Wc Z Score	0.162	0.287		
WHR	0.064	0.676		
WHtR	0.266	0.77		
Hs- CRP	0.408**	0.005	0.396*	0.010

* Significant at (P<0.05) ** Highly significant at (P<0.001)

hs- CRP= high sensitive C- reactive protein, WC=Waist Circumference, WHR= Waist to Hip ratio, WHtR= Waist to Height ratio.

p^a= Partial correlation analysis after adjustment for anthropometric parameters and age and sex.

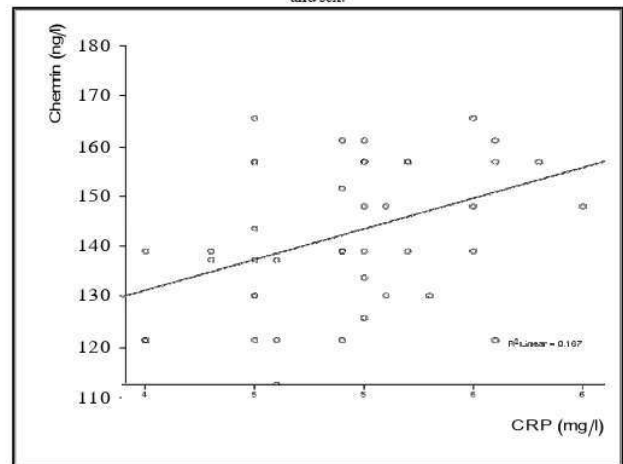


Figure (4) Correlation between Chemerin and hs- CRP in obese children

Discussion:

In the present study, anthropometric assessment and hs CRP were found to be significantly elevated in obese subjects in comparison to controls. These results are in agreement with previous studies conducted on obese children (Landgraf et.al., 2012, Ba et.al., 2014). Regarding Chemerin, obese subjects exhibited a significantly higher level which is accordant with other studies that have been done in adults (Bozaoglu et.al., 2007, Shin et.al., 2012) and children (Landgraf et.al., 2012, Hamza

et.al., 2016). This elevated level of Chemerin in obese children is due to the fact that visceral fat tissue is considered the primary source for circulating Chemerin as it is highly expressed in white adipose tissue (Goralski et.al., 2007) and it's mRNA expression in visceral adipose tissue is significantly increased in obese individuals (Chakaroun et.al., 2012).

In the current study, there was no association between chemerin serum level and anthropometric indices of central obesity in the obese group. In contrast to our results, previous studies have found positive correlations between Chemerin, WC, WHR and WHtR (Bozaoglu et.al., 2007, Corona- Meraz et.al., 2016, Hamza et.al., 2016, Niklowitz et.al., 2018). On the other hand, other studies reported no association between Chemerin and WC and WHR which is in agreement with our results (Stejskal et.al., 2008, Shehata et.al., 2015, Sh et.al., 2016).

Obesity is will recognized to be a status of low- grade chronic inflammation, and this process of inflammation is assumed to be the 1st step in the progression of obesity related morbidities (Szmítko et.al., 2003). hs- CRP is elevated with the occurrence of inflammation or tissue damage and is widely applicable in laboratory monitoring of inflammation and it is more sensitive and accurate than ordinary CRP (Kamath et.al., 2015). In the current study, Chemerin showed a significant positive association with hs- CRP in obese children which remained significant even after adjustment of BMI z score, sex and age in the partial correlation analysis. Those results were accordant with previous studies which showed that elevated Chemerin level was positively associated with increased level of hs- CRP (Wang et.al., 2015, Lachine et.al., 2016). Furthermore, Er et.al., 2019 implied that high Chemerin and CRP levels and their combination have a synergistic effect that is associated with the severity and poor prognosis of coronary artery disease as Chemerin is also a type of inflammatory factor that participates in the inflammatory reactions.

Conclusion:

The current study showed that obese children had a higher level of Chemerin in comparison to their normal counter- peers which had a positive association with hs- CRP indicating a potential pathophysiologic link between Chemerin and obesity associated inflammation.

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