

Relationship between serum chemerin levels and insulin resistance index and cardio-respiratory function in non-active obese and lean men

Abstract

The aim of this study was to investigate the relationship between serum Chemerin levels and insulin resistance index and cardio-respiratory function in non-active obese and lean men. In a semi-experimental study, 50 non-active men were divided into two groups of 25 people (obese and lean). After nocturnal fasting, blood samples were taken from the brachial vein in the laboratory. From each person, 5 cc of serum was taken to determine the concentration of Chemerin, glucose, insulin in the resting state. The cardio-respiratory function of the subjects was also measured by VO_2 max assessment. For data analysis, Pearson correlation coefficient was used at the significance level of 5% by SPSS software version 22 assist. The results showed that there was a significant difference in serum Chemerin, insulin, HOMA-TR and maximum oxygen consumption between two groups (lean and obese) ($P < 0.05$). Serum Chemerin level of non-active obese males were more than non-active lean males ($P = 0.001$). In both groups, the Chemerin levels were directly correlated with body mass index, body fat percentage, insulin and insulin resistance and inversely correlated with cardio-respiratory function. These findings can be of importance in identifying the Adipokine role of Chemerin in metabolic and cardiovascular diseases in non-active obese and lean males.

Keywords: chemerin, cardio-respiratory, insulin resistance, obese

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Introduction

White adipose tissue in addition to playing a major metabolic role is an active endocrine organ and generates a number of signaling peptides with various biochemical functions called Adipokines.¹ Adipokines play important Autocrine/Paracrine roles in regulating the differentiation and metabolism of fat cells and local inflammatory responses.² Adipokines also plays important roles in regulating systemic lipid and glucose metabolism through endocrine/systemic administration in the brain, liver and muscles. Secretion and/or serum level of some Adipokines are strongly influenced by the degree of adipocytes (fat).³ Identifying and describing new adipocytes will increase our knowledge of the function of endocrine white fat tissue and help provide new molecular targets for developing therapeutic strategies for obesity and depended diseases.

Chemerin (RARRES2 or TIG2) is a recently discovered chemical absorbent protein and works as a ligand for mating receptor with protein ChemR23, (CMKLR1) G or DEZ, and participate in the adaptive and innate immunity.^{2,4} It is a new Adipokine that regulate development of adipocytes and metabolic function and glucose metabolism in the liver and skeletal muscles. Serum Chemerin levels increased in patients with obesity and is associated with various aspects of metabolic syndrome. So, Chemerin dual role in inflammation and metabolism may be provide a link between chronic inflammation and obesity and obesity-related disorders such as diabetes and cardiovascular disease.⁵ Huh et al.,⁶ by studying of patients with coronary artery disorder, explain that serum Chemerin levels is related to several risk factors for cardiovascular and coronary artery stenosis. However, they explained that Chemerin is not an independent risk factor for vascular diseases and there is necessity for further studies to identify multiple Chemerin role in cardiovascular disease.

Chemerin play a regulatory role in Adipocytes metabolism and Adipogenesis and this gives the potential importance of this pathway in biology of fat tissue. More identifying of Chemerin signaling and CMKLR1 is a potential factor in fat cells that can cause new therapeutic approaches for the treatment of obesity, type 2 diabetes and cardiovascular diseases.⁴

Landgraf et al.,⁷ found that in children, serum Chemerin levels correlated with body mass index and skin thicknes. Nevertheless, in the study of Huh et al.,⁶ lack of association between body mass index and waist with Chemerin levels of blood circulation has been reported. Lin et al.,⁸ found that Chemerin levels of serum had a positive correlation with body mass index, systolic blood pressure, insulin resistance index and triglyceride in diabetic patients. Findings of correlation between insulin resistance index and Chemerin levels of blood circulation are also contradictory, because on the one hand, Ouwens et al.,⁹ achieved a negative correlation between insulin sensitivity and Chemerin levels of blood circulation, while Huh et al.,⁶ showed no correlation between these two indicators. However, El-Mesallamy et al.,¹⁰ found that serum Chemerin levels in patients with type 2 diabetes (with or without ischemic heart disease) were higher than healthy subjects, and concluded that Chemerin in obesity and its related disorders like diabetes it plays an important role, but its role in cardiovascular disease is still unknown.

Also, although few studies have investigated the effect of exercise on Chemerin levels of blood circulation,^{11,12} but as far as our knowledge is concerned, there has not been a finding for relationship between Chemerin levels and physical readiness indices such as cardio-respiratory function (ie, VO_2 max) in obese and lean men. Saremi et al.,¹¹ by studying on overweight and obese individuals, found that a 12 week of aerobic exercise decreased Chemerin levels of serum. In a

cross-sectional study on obese people, Chakaroun et al.,¹² found that weight loss programs (such as 12 weeks of exercise, a 6 month diet with a caloric restriction, or 12 months after an overweight surgery) decreased the Chemerin levels of serum.

Less than a decade has passed since the discovery of Chemerin,^{5,13} and little information is available on the role of this adipokine in humans. Findings related to the relationship between Chemerin levels and insulin resistance is contradictory.^{6,9,10,14} Even the findings regarding the relationship between the levels of Chemerin and the blood indicators are not compatible. However, the association of adipokine of Chemerin with body fat¹⁵ and higher serum levels of that in obese subjects has been reported in comparison with lean subjects.^{7,16} However, there are few findings on the physiological linkages between Chemerin in lean subjects.¹⁶ Therefore, the study of the physiological relationships of Chemerin in abnormal body fat (obesity and leanness) can help explain the role of Chemerin in these patient states with problems and complications.¹⁷ Also, although the relationship between non-active lifestyle and high risk of diseases such as diabetes and cardiovascular disease has been accepted,¹⁸ and findings have been made regarding the effect of exercise on the levels of circulated Chemerin,^{11,12} but the relationship between physical fitness (with an emphasis on cardio-respiratory readiness) and Chemerin levels has been less studied. The aim of this study was to investigate the relationship between Chemerin levels of serum and some of the iconology indicators such as blood pressure, fat profile, insulin resistance index and cardio-respiratory function in obese and lean men.

Materials and methods

The research method was descriptive correlational and was performed as a semi-experimental study. The statistical population included obese and lean men in the city of Maku. The sampling of the research was purposeful, so that the subjects were selected through recall and in several stages and selected based on the research objectives. Initially volunteering was conducted among higher education institutions and universities, medical centers, adult education centers and community associations and sports teams in the city of Maku. After visiting volunteers, according to BMI of volunteers, people with a BMI of more than 30 (obese volunteers) or less than 18/5 (lean volunteers) were selected and the rest were excluded from the study. According to the health history questionnaire, volunteers were admitted who were habitually less activated in terms of their previous training status (in the 6 months prior to the commencement of the study, have not regular physical activity). After obtaining the written consent of the volunteers, they completed the Physical Activity Preparedness Form (PAR-Q) and received a medical examination in order to confirm their health. Another treatment was removed from the research. Those with a history of cardiovascular disease, diabetes, thyroid disease, and any condition (besides obesity and weight loss), or taking any medication (with or without prescribing physician) or under any type of diet or other treatment were excluded from the research. Eventually, 25 obese volunteers were randomly selected from the remaining and 25 lean volunteers were randomly assigned to the lean group.

Procedure

During a briefing meeting at the test site (physical fitness club), the research objectives, the design and methodology of the research, the

test protocol for evaluation of VO₂max (cardio-respiratory function index), laboratory evaluations (eg. blood sampling), and the timing of the research was explained in detail to the volunteers. Also, the points that subjects were required to observe during the implementation of the research protocol, as well as the timetable for their referral to the club and laboratory, were reminded. Meanwhile, subjects were asked to participate in the fasting state for testing and sampling. After three days (to ensure that subjects do not exercise excessive physical activity on daily activities), subjects were asked to attend the fitness club at 8 am. General characteristics of the subjects (age, height, weight, BMI, body fat percentage) were recorded. Three days before blood sampling, the subjects were monitored for discontinuation of drug use, smoking, caffeine and excessive physical activity for daily living activities, as well as observing adequate sleep and consumption of iso-caloric diet. At 8 am in the morning, the rest blood samples were taken from the brachial vein at the site of the diagnostic laboratory. From each person, 5 cc of serum was taken to determine the concentration of Chemerin, glucose, insulin in the resting state. Serum samples were stored at -20°C until measurements were taken. The cardio-respiratory function of the subjects was also measured by VO₂max assessment.

Data collection tools

Anthropometric features

Participants' weight was measured by digital weighing scale with a minimum accuracy of 0.1 kg and with calibrated ability (ws 80 model, made in Switzerland) and height was measured by a 0.1 cm centimeter gauge with a brocade plate (Machinen AG model, made in Switzerland). BMI was calculated by dividing body weight (kg) by squared height (m²). Body density was estimated by measuring subcutaneous fat at three points of the body (chest, triceps and under scapular) with caliper (minimum 1 mm accuracy, Harpenden brand, made in UK) and calculating body density estimated by Jackson and Pollack formula.^{19,20}

Cardio-respiratory function

The subterranean test of the Astrand-Rayming bike on the wheel of the meter (Robibactx magnetic resonance wheel of the ROBIMAX 7750 model, made in Taiwan) was used to determine the VO₂max of the subjects.²¹

Insulin resistance

The insulin resistance index was also estimated by the HOMA-IR formula.²²

Biochemical indicators

Measurement of serum Chemerin concentration (Human Chemerin ELISA kit, CV in evaluation of 1.5%, CV of between evaluation 8.3%, minimum detection limit of 0.1 ng/ml, BioVendor made in Czech Republic) by ELISA method (Awernes stat fax 303 plus, made in USA) and serum insulin concentration measurements (Insulin CIATM Kit, Monobind Inc., made in USA, sensitivity of 25 IU/ml μ , Catalog Number 2475-300) by quantitative Luminescence (Berthold Device, made in Germany).

Data analysis

Descriptive statistics (mean \pm standard deviation) were used to describe the distribution of society in a normal way. The Kolmogorov-

Smirnov test was used to compare the mean of two groups with independent t-test and Pearson correlation coefficient were used at the significance level of 0.05 to examine the relationship between serum Chemerin levels and other physiological variables. All statistical analyzes were performed using SPSS software version 22.

Results

Table 1 describes the general characteristics of subjects including age, height, weight, body fat and BMI. According to Table 1, there is a significant difference in weight, body fat percentage and BMI between two groups (P<0.05).

According to Table 2, there is a significant difference between the two groups (lean and obese) in serum Chemerin level, serum insulin, HOMA-TR and maximum oxygen consumption (P<0.05). However, there is no significant change in fasting glucose between the two groups. According to Table 3, the results of Pearson correlation test showed that in both groups, Chemerin levels with body mass index (r=0.34, P=0.001, r=0.30, P=0.001 respectively), percentage of body fat (r=0.35, P=0.004, r=0.32, P=0.009 respectively), insulin (r=0.42, P=0.001, r=0.31, P=0.002 respectively), insulin resistance (r=0.40, P=0.001, P=0.001, r=0.003, P=0.003 respectively) was directly correlated with cardio-respiratory function (r=-0.38, P=0.001, r=-0.31, P=0.001 respectively). In addition, in non-active obese and lean males, Chemerin serum levels had no correlation with glucose levels (r=0/14 and r=0.09, respectively).

Table 1 General characteristics of subjects

Variable	Subjects		P
	Obese (n=25)	Lean (n=25)	
Age (yr)	3/5±2/29	8/4±1/28	215/0
Height (cm)	4/8±179	2/8±184	325/0
Weight (kg)	1/9±3/97*	6/6±6/62	000/0
Body Fat (%)	2/3±9/31*	5/2±5/17	000/0
BMI (kg/m ²)	0/3±7/30*	9/1±3/18	000/0

*There was a significant difference in P <0.05 level (independent t test)

Table 2 Physiological and biochemical characteristics of the subjects

Variable	Subjects		P
	Obese	Lean	
Chemerin (ng/ml)	6/31±1/245*	8/25±5/178	001/0
Insulin (U/mlμ)	3/2±1/15*	7/1±2/11	005/0
Fasting glucose(mmol/Lit)	4/0±1/4	3/0±4/4	176/0
HOMA-IR	2/0±8/2*	2/0±2/2	003/0
VO ₂ max (ml.kg-1.min ⁻¹)	9/5±4/44*	8/5±3/39	001/0

*There was a significant difference in P <0.05 level (independent t test)

Table 3 The results of Pearson correlation test for investigating the relationship between serum Chemerin levels and selected physiological variables

Variable	Subjects			
	Obese		Lean	
	r	P	r	P
Chemerin (ng/ml)	-	-	-	-
BMI (kg/m ²)	34/0	001/0*	30/0	001/0*
Body fat (%)	35/0	004/0*	32/0	009/0*
Insulin (U/mlμ)	42/0	001/0*	31/0	002/0*
Fasting glucose(mmol/Lit)	14/0	165/0	09/0	291/0
HOMA-IR	40/0	001/0*	32/0	003/0*
VO ₂ max (ml.kg-1.min ⁻¹)	38/0-	001/0*	31/0-	001/0*

*Significant correlation in the level of P <0.05

Discussion

Non-active obese men have higher Chemerin serum levels compared with non-active lean men. Chemerin serum levels in non-active obese and lean men were not correlated with glucose levels. In both non-active obese and lean men, Chemerin levels have direct correlation with body mass index, body fat percentage, insulin levels and insulin resistance but it has inverse correlation with cardio-respiratory activity. The findings of this study showed that the levels of circulated Chemerin in non-active obese men are more than non-active lean men and in both groups, serum Chemerin levels have a direct correlation with body mass index and body fat percentage. This finding is in line with the findings of ^{7,15,23,24} but Opposed to the findings of Huh et al.⁶ For example, in the study of Alfadda et al.,¹⁵ that was performed on adult males and females with different degrees of obesity, serum Chemerin concentrations showed a positive correlation with body mass index, and they concluded that the levels of Chemerin is correlated with obesity indices. In the study of ^{23,24} on apparently healthy, overweight and obese adults, a positive correlation was found between Chemerin levels and body mass index, waist circumference and body fat percentage. Also, Landgraf et al.,⁷ found that Chemerin concentrations were significantly higher in obese children than lean children. In contrast, in the study of Huh et al.,⁶ patients with coronary artery disease had no significant correlation between Chemerin levels and body mass index and waist circumference.

It seems that the physiological mechanism of the relationship between Chemerin levels and body mass index and body fat is related to this important finding that fat tissue is the main source of Chemerin secretion in humans⁵ and therefore It is expected that with the increase of fat levels in humans, the production and release of this adipokine also increases. In fact, Chemerin plays a role in Adipogenicity and fat cell metabolism.⁴ According to the findings of the present study, Chemerin levels of serum have direct correlation with insulin levels and insulin resistance in non-active obese and lean men, but have no significant correlation with glucose levels.

The issue of the relationship between the circulated Chemerin levels with insulin and its possible role in insulin resistance is one of

the most important issues among former researchers. In the present study, which was conducted on non-active obese and lean men, the results of the study were compared with those studies whose characteristics of the subjects were similar to present study subjects. However, the findings of this study are consistent with the findings of some of these researchers^{9,16,23,24} and are contradictory with others.^{13,15} Fatima et al.,^{24,25} found that the levels of Chemerin is positively correlated with serum insulin level and HOMA-IR. Ouwens et al.,⁹ observing a negative correlation between insulin sensitivity and fasting Chemerin levels in normoglysemic obese males, stated that fasting Chemerin levels may be used as an indicator for determining insulin resistance in healthy men without the usual characteristics of metabolic disorders. In the study of Chu et al.,⁶ there was a positive correlation between the insulin resistance index and the Chemerin levels in apparently healthy and overweight adults.²³ In the study of Yoo et al.,¹⁶ which was performed on obese and non-obese subjects, there was a significant correlation between Chemerin levels and insulin resistance index.

In contrast, Bozaoglu et al.,¹³ found that the levels of plasma Chemerin did not differ significantly among subjects with type 2 diabetes and normal subjects. In a study by Alfadda et al.,¹⁵ there was no relationship between serum Chemerin concentrations, fasting glucose, insulin, and insulin resistance index. However, several studies have shown that the development of insulin resistance and type 2 diabetes in obesity begins with topical adipokine responses. In this model, the increased in release of adipokines (such as leptin, TNF α and CCL₂), as well as free fatty acids from triglyceride-rich fat cells, stimulates infiltration of macrophages and activates local inflammatory response. In a pre-existing system, activated macrophages release additional pro-inflammatory molecules that permanently inflame the response and affect the sensitivity of the adipocyte to insulin.¹⁻³

According to the findings of the present study, the Chemerin levels of serum were inversely correlated in with reversible cardiovascular function non-active obese and lean men. In other words, in both groups of non-active obese and lean men, the circulated levels of Chemerin were lower in those who had higher cardio-respiratory readiness, and vice versa. However, some studies have investigated the effect of aerobic training on blood circulation Chemerin levels,^{12,26-29} but the relationship between Chemerin levels of serum and cardio-respiratory index has not been studied in non-active men, especially lean subjects.

Chakaroun et al.,¹² showed that weight loss programs (including 12 weeks of exercise) can reduce the serum Chemerin concentration. They concluded that insulin resistance and inflammation independently from body mass index, predict a high concentration of serum Chemerin. Reduced expression and serum Chemerin concentration of can independently help to improve insulin sensitivity and subclinical inflammation. Venojärvi et al.,²⁷ found that implementation walking or strength training on middle aged obese men (40-65 years old) with glucose regulation deficiency had reduced levels of serum Chemerin. Poorvegar & Bahram²⁸ also found that three months of high-intensity jump training reduced the Chemerin levels in overweight men.

In contrast, Zolfaghary et al.,²⁶ found that after 12 weeks of aerobic training, the Chemerin levels of obese women did not change. Also, in their study, weight, BMI, body fat percentage, insulin, glucose and insulin resistance index remained unchanged. The researchers found that the lack of nutrition control and the motivation of the subjects

contributed to not changing the variables. Jafari et al.,²⁹ also concluded that 8 weeks' endurance training reduced the plasma Chemerin levels in overweight and obese girls, but resistance training did not have a significant effect.

The lack of coordination among the findings of studies on the exercise effect on the circulated Chemerin levels can be attributed to the differences in the research from various aspects such as the characteristics of subjects include species (human or animal), gender (female or male), the status of obesity (obese or lean), and physical fitness (active or non-active) as well as the characteristics of the exercise protocol used (type, duration, and severity). It seems that exercise and physical fitness can be independently from changes in weight and fat percentage, or related to it, associated with serum Chemerin levels.^{2,12,28} However, more studies are required on the relationship between the levels of circulated Chemerin and the level of cardio-respiratory readiness and other components of health-related fitness.

Conclusion

In the non-active obese men, the levels of circulated Chemerin were more than non-active lean men and directly correlated with body mass index, body fat percentage, insulin and insulin resistance and inversely correlated with performance of cardio-respiratory system in both groups. In addition, in non-active obese and lean males, serum Chemerin levels are not correlated with glucose levels. These findings can be important in identifying the role of Chemerin Adipokine in metabolic and cardiovascular diseases in non-active obese and lean people.

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Conflict of interest

The author declares there is no conflict of interest.

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