Serum chemerin correlated to the SYNTAX score in obese Egyptian patients with coronary artery disease

Noha Hassanin, Yasser Sharaf, Mervat Al-Anany, Essam Faisal

Cardiology Department, Cairo University, Cairo, Egypt

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SOUHRN

Kontext: Chemerin je nově objevený adipokin, u něhož byla prokázána těsná korelace s obezitou, metabolickým syndromem a zánětlivým stavem. Stále však není jasné, zda lze jeho hodnot využít u pacientů s kardiovaskulárním onemocněním.

Cíl: Cílem studie bylo zjistit, zda hodnoty chemerinu v séru korelují se závažností ischemické choroby srdeční (ICHS) u obézních Egyptanů.

Materiál a metody: Do studie bylo zařazeno 100 pacientů, u nichž bylo provedeno koronarografické vyšetření z klinicky indikovaných důvodů a byli rozděleni podle indexu tělesné hmotnosti (body mass index, BMI) do dvou skupin: 50 pacientů (skupina A) s BMI (≥ 30 kg/m²) a 50 pacientů (skupina B) s hodnotou BMI ≤ 25 kg/m². Závažnost ICHS se stanovovala podle skóre SYNTAX a hodnoty chemerinu v séru se měřily metodou ELISA.

Výsledky: Hodnoty chemerinu v séru byly vyšší u obézních pacientů ($p = 0,019$) a korelovaly se skóre SYNTAX ($r = 0,533$; $p < 0,001$), BMI, obvodem pasu, FPG, indexem hmoty levé komory (left ventricular mass index, LVMI) a hodnotou C-reaktivního proteinu měřenou vysoce senzitivní metodou (high-sensitivity C-reactive protein, hs-CRP) ($p < 0,005$ pro všechny). Hodnoty chemerinu v séru se zvyšovaly s přibývajícím počtem postižených tepen ($p = 0,013$). Vícečetná lineární regresní analýza prokázala, že hodnoty chemerinu v séru jsou nezávislým prediktorem skóre SYNTAX ($\beta = 0,432$; $p < 0,001$) a jsou spojeny i s mírou hypertrofie levé komory (left ventricular hypertrophy, LVH) ($p = 0,004$).

Závěr: Hodnoty chemerinu v séru byly u obézních pacientů vyšší a souvisely s LVH a zánětem. Byla nalezena i významná korelace se závažností ICHS u egyptských pacientů s ICHS.

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ABSTRACT

Background: Chemerin is a newly discovered adipokine which has been found closely associated with obesity, metabolic syndrome, and inflammatory status. However, it remains unclear whether chemerin is involved in patients with cardiovascular disease.

Objective: The aim of the study was to examine whether serum chemerin levels are associated with the severity of coronary artery disease (CAD) in obese Egyptian patients.

Material and methods: The study enrolled 100 patients who underwent coronary angiography for clinically indicated reasons classified according to body mass index (BMI) into two groups, 50 patients (group A) with BMI (≥ 30 kg/m²) and 50 patients (group B) with BMI ≤ 25 kg/m². Severity of CAD was estimated with SYNTAX score and serum chemerin level was measured using ELISA method.

Results: Serum chemerin level was higher in obese patients ($p = 0.019$), and it was positively correlated with SYNTAX score ($r = 0.533$, $p < 0.001$), BMI, waist circumference, FPG, left ventricle mass index (LVMI) and high sensitivity C-reactive protein (hs-CRP) (p value < 0.005 for all). Serum chemerin levels were significantly increased with an increasing number of diseased vessels ($p = 0.013$). At multiple linear regression analysis serum chemerin level was found to be an independent predictor of SYNTAX score ($\beta = 0.432$, $p < 0.001$). Serum chemerin also was associated with LVH ($p = 0.004$).

Conclusion: Serum chemerin levels were higher in obese patients and were associated with LVH and inflammation. Also it has a significant correlation with severity of coronary artery disease in Egyptian patients with coronary artery disease.

Keywords:

Coronary artery disease

Serum chemerin

SYNTAX score

Address: Noha Hassanin, M.D., Cardiology Department, Cairo University, Cairo, Egypt, e-mail: Noha.Ali@kasralainy.edu.eg

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Introduction

Obesity promotes cardiovascular disease via many mechanisms including ectopic lipid deposition, hyperglycemia, and the development of a procoagulant state.¹

Accumulating evidence from animal models indicates that the pathogenesis of obesity-related metabolic dysfunction involves the development of a systemic, low-grade inflammatory state.²

One study covering fifty-two countries from eight geographical regions worldwide showed that adult men and women in the Middle East have the highest mean BMI after the USA. Additionally, the women in this region have the highest waist-to-hip ratio compared with all other regions.³ Similar results were reported by the Chronic Disease Collaborating Group in a study covering 199 countries.⁴

Obesity in Africa and Egypt

The prevalence of overweight and obesity among women increased in all the 24 countries. Trends were statistically significant in 17 of the 24 countries in the case of obesity and 13 of the 24 for overweight. In Ghana, overweight almost doubled ($p = 0.001$) while obesity tripled ($p = 0.001$) between 1993 and 2014. Egypt has the highest levels of overweight and obesity at 44% (95% CI 42–46.5%) and 39% (95% CI 36.6–41.8%), respectively, in 2014 and the trend showed significant increase ($p = 0.005$) from 1995 levels. Also, obesity doubled in Kenya, Benin, Niger, Rwanda, Ivory Coast and Uganda, while tripled in Zambia, Burkina Faso, Mali, Malawi and Tanzania. Ethiopia

and Madagascar had the lowest prevalence of both obesity and overweight, with overweight ranging from 7% to 12% and obesity from 1% to 4%.⁵

WHO and the categorization of BMIs

Four categories were established: underweight, normal, overweight, and obese. An individual would be considered to be underweight if his/her BMI was in the range of 15 to 19.9, normal weight if the BMI was 20 to 24.9, overweight if the BMI was 25 to 29.9, and obese if it was 30 to 35 or greater. Using linear regression, a BMI of 16.9 in men and 13.7 in women represents a complete absence of body fat stores.^{6,7}

Abdominal obesity

Imaging cardiometabolic studies recently conducted in large cohort studies (Framingham Heart Study and the Jackson Heart Study) have shown that excess visceral adiposity accompanied by excess ectopic fat deposition such as excess heart, liver, and intrathoracic fat was significantly associated with cardiac and metabolic abnormalities, and that such relationship was independent from the amount of total or subcutaneous adipose tissue.⁸

Depending on their location, fat depots present distinct metabolic properties, different states of inflammation or adipo(cyto)kines excretion, leading to major individual differences regarding the impact of obesity on cardiometabolic risk (from protective to neutral to increased risk) (Fig. 1).⁹

A important distinction should therefore be made between the various adipose depots; the non-ectopic

Fig. 1 – Distribution of ectopic fat.¹¹

Fig. 2 – Adipocytokine influences on the cardiovascular system, inflammation, and insulin resistance.¹⁸ CAD – coronary artery disease; CHD – coronary heart disease; CRP – C-reactive protein; CVD – cardiovascular disease; EC – endothelial cell; HUVECS – human umbilical vein endothelial cells; MABP – mean arterial blood pressure; NF- κ B – nuclear factor kappa-light-chain-enhancer of activated B cell; TNF α – tumor necrosis factor alpha; VSMC – vascular smooth muscle cell.

fat (or subcutaneous fat) appears to be less metabolically deleterious, its primary role being energy storage, whereas excess ectopic fat defined as an excess lipid accumulation in the visceral adipose depots and in normally lean tissues (intrahepatic, intramuscular, renal sinus, pericardial, myocardial and perivascular fat) is clearly a health hazard.¹⁰

Obesity and coronary heart disease (CHD)

The INTERHEART (an international case-control analysis of the risk factors for a first myocardial infarction conducted in more than 15,000 patients presenting with myocardial infarction in 52 countries) study gathered data to determine the 9 most important risk factors which contributed over 90% of the risk of having heart attack in 16,000 patients studied. This study confirmed that central fat accumulation or abdominal obesity presents as much risk to developing heart attack as smoking.¹²

In obesity, chronic caloric excess induces the accumulation of dietary fatty acids in the adipose tissue until its storage capacity becomes saturated, leading to a spillover of lipids which are then stored in normally lean tissues such as the liver, muscles and in the intra-abdominal or visceral adipose depots.

Such saturation in the storage capacity of lipids in subcutaneous adipose tissue and the resulting ectopic fat deposition induce a combined state of inflammation and insulin resistance. In addition, adipo(cyto)kines secreted by adipose tissue are also involved in modulating processes promoting atherosclerosis such as endothelial vasomotor dysfunction, hypercoagulability, and dyslipidemia.¹³

Levels of many inflammatory mediators are altered in obesity. First, circulating C reactive protein (CRP) and tumor necrosis factor (TNF) (production by adipose tissue) levels are increased, but other mediators (such as IL-6 and IL-1 β , and monocyte chemo-attractant protein 1) and hormones (such as adiponectin and leptin) are also known to potentially contribute to the inflammatory profile observed in obesity, particularly of abdominal obesity.¹⁴

Adipokines

Adipose tissue is now known to express and secrete a variety of bioactive peptides, known as adipokines which act at both the local (autocrine/paracrine) and systemic (endocrine) level.¹⁵

Adipokines act centrally to regulate appetite and energy expenditure, and peripherally affect insulin sensitivity, oxidative capacity, and lipid uptake. Nevertheless,

as a dynamic organ, the adipokine profile changes in response to the amount and condition of adipose tissue.¹⁶

Most of adipokines including tumor necrosis factor- α (TNF- α) and interleukin (IL)-6 display pro-inflammatory properties and are harmful in the setting of obesity-linked diseases. Imbalanced production of adipokines caused by obesity could contribute to the development of obesity-linked metabolic and cardiovascular complications.¹⁷ Figure 2 illustrates the various aspects of adipokines effects on cardiovascular system.

Chemerin

Chemerin is a secreted protein with a complex but well-established role in immune function. Parallel lines of investigation also support the notion that chemerin is a novel adipokine that regulates adipocyte development and metabolic function as well as glucose metabolism in liver and skeletal muscle tissues. A growing body of human experimental data indicates that serum chemerin levels are elevated in patients with obesity and that they exhibit a positive correlation with various aspects of the metabolic syndrome.¹⁹

The chemerin gene, also known as tazarotene-induced gene 2 (*TIG2*) or retinoic acid receptor responder 2 (*RARRES2*), was originally identified as a novel retinoid-responsive gene in psoriatic skin lesions.²⁰

Chemerin and lipid homeostasis

Hyperlipidemia is considered an important risk factor in the development of cardiovascular diseases. Positive correlations were found between chemerin and triglycerides, low-density lipoprotein cholesterol and blood pressure levels.²¹

Chemerin and atherosclerosis

Atherosclerosis is among different conditions that have associations with chemerin on various epidemiologic levels. This is because of receptors on macrophages and the role of chemerin in the inflammatory cascade probably increasing the strength of macrophage activity in damaged tissues and helping immune-cell migration towards the damaged region.²² Chemo-attraction is one of the most important roles of chemerin, and by this way, macrophages interact with dendritic cells and natural killer cells and are targeted towards areas of damage. Similarly, intercellular adhesion molecule-1 (ICAM-1) and E-selectin interacting with the endothelium are induced by chemerin.^{22,23}

In two studies on Chinese patient populations, serum chemerin levels were significantly higher in the group with CAD, in comparison with those who did not have CAD and it was correlated to the extent of coronary artery disease.²⁴ Although significantly high serum chemerin levels were found in CAD, it is not clearly known if this increased level represents a predictor for CAD or is a result of atherosclerotic plaque morphology.²⁵

Aim of work

The aim of this study is to examine whether serum levels of chemerin are associated with metabolic parameters and the severity of coronary artery disease in obese Egyptian patients and to determine whether serum chemerin can be considered as an independent predictor of coronary artery stenosis score (SYNTAX score).

tian patients and to determine whether serum chemerin can be considered as an independent predictor of coronary artery stenosis score (SYNTAX score).

Patients and methods

This was a prospective observational study that was conducted on 100 patients presented to the heart catheterization unit at the Cardiology Department in Cairo University Hospital. Patients were divided into two groups, group A included 50 obese patients (BMI ≥ 30 kg/m²) with CAD and group B included 50 non-obese patients (BMI = 18–25 kg/m²) with CAD.

Patients who refused to participate in the study or those with significant renal impairment (serum creatinine ≥ 2 mg/dl or creatinine clearance ≤ 60 ml/min) were excluded from the study. The study protocol was approved by the local Ethics Committee. All patients were subjected to detailed medical history and clinical examination.

Diabetes mellitus was defined as fasting plasma glucose ≥ 126 mg/dl and/or random plasma glucose ≥ 200 mg/dl and/or self-reported diabetes.²⁶ Hypertension was defined according to the recently released American College of Cardiology (ACC)/American Heart Association (AHA) hypertension guidelines.²⁷

Anthropometric measurement

Body mass index (BMI) was calculated according to the following formula: BMI = body weight (kg) / height (m²). Waist circumference (WC) was measured at the level of mid-distance between the bottom of the rib cage and the top of the iliac crest after expiration. Hip circumference was measured at the level of the trochanter major. Waist-to-hip ratio (WHR) was calculated by dividing WC in centimeter (cm) by hip circumference in cm.

Obesity was defined as BMI ≥ 30 kg/m². Abnormal waist circumference was defined as WC ≥ 94 cm for male and ≥ 80 cm for women. Abnormal waist/hip ratio was defined as WHR ≥ 0.90 in men and ≥ 0.85 in women.²⁸

Laboratory work-up

Complete blood count, high sensitivity C-reactive protein (hs-CRP), serum creatinine, liver function tests, lipid profile and serum chemerin level.

Serum chemerin level

A 5 ml blood sample was drawn from patients who agree to participate in this study. The samples were separated and stored at -20 °C. An Enzyme-Linked Immunosorbent Assay (ELISA) kit was used to assay human chemerin in the sample according to the manufacturer's instructions (SinoGeneclon Co., Ltd, Product No.: SG-10352).

Coronary angiography results

Standard coronary angiography was done through trans-femoral and trans-radial approach using modified Seldinger technique. At least five angiographic views, including two orthogonal views, were obtained for the left coronary artery and at least two orthogonal views for the right coronary artery were taken. Angiographic results were interpreted by two angiographers who were

blinded to clinical or demographic data. Coronary angiography was utilized to identify lesions (50–99% lumen diameter reduction) indicating the presence of possible significant lesion.

Assessment of the severity of coronary artery disease

The SYNTAX score (SS) is an angiographic grading tool to determine the complexity of coronary artery disease (Fig. 3).

This angiographic grading tool was published in 2005.²⁹ The SYNTAX score is the sum of the points assigned to each individual lesion identified in the coronary tree with >50% diameter narrowing in vessels >1.5mm diameter. The coronary tree is divided into 16 segments according to the AHA classification (Fig. 4). Each segment is given a score of 1 or 2 based on the presence of disease and this score is then weighted based on a chart. SSs were classified as follows: high (≥ 33), intermediate (23–32), and low (≤ 22).

SYNTAX score (SS) definitions

1. Dominance:

- a) Right dominance: the posterior descending coronary artery is a branch of the right coronary artery.
- b) Left dominance: the posterior descending artery is a branch of the left coronary artery.
- c) Co-dominance does not exist as an option at the SYNTAX score (Fig 4).

2. Number of lesions: Each coronary lesion with a diameter stenosis $\geq 50\%$ in vessels ≥ 1.5 mm must be scored. Each lesion can involve ≥ 1 diseased segments.

3. Segments involved per lesion: If serial stenoses are less than 3 vessel reference diameters apart, they should be scored as one lesion. However, stenoses at a greater distance from each other (more than 3 vessel reference diameters), are considered as separate lesions.

SYNTAX score items

1. Dominance
2. Number of lesions
3. Segments involved per lesion, with lesion characteristics
4. Total occlusions with subtotal occlusions:
 - a) Number of segments
 - b) Age of total occlusions
 - c) Blunt stumps
 - d) Bridging collaterals
 - e) First segment beyond occlusion visible by antegrade or retrograde filling
 - f) Side branch involvement
5. Trifurcation, number of segments diseased
6. Bifurcation type and angulation
7. Aorto-ostial lesion
8. Severe tortuosity
9. Lesion length
10. Heavy calcification
11. Thrombus
12. Diffuse disease, with number of segments

Fig. 3 – SYNTAX score items.²⁹

Fig. 4 – Definition of the coronary arteries segments.²⁹

Lesion characteristics

4. Total occlusion:

- No intra-luminal antegrade flow (TIMI 0) beyond the point of occlusion.
- However, antegrade flow beyond the total occlusion might be maintained by bridging collaterals and/or ipsi collaterals.
- Bridging collaterals: Small channels running in parallel to the vessel and connecting proximal vessel to distal and being responsible for the ipsilateral collateralization.

5. Trifurcation: A junction of three branches, one main vessel and two side-branches. Trifurcations are only scored for the following segment junctions: 3/4/16/16a, 5/6/11/12, 11/12a/12b/13, 6/7/9/9a and 7/8/10/10a (Fig. 5A).

6. Bifurcation: Type A bifurcation is a division of a main, parent branch into two daughter branches of at least 1.5 mm. Bifurcation lesions may involve the proximal main vessel, the distal main vessel and the side branch according to the **Medina classification** (Figs 5B, 6).

7. Aorto-ostial lesion: A lesion is classified as aorto-ostial when it is located within 3 mm of the origin of the coronary vessels from the aorta.

8. Severe tortuosity: One or more bends of 90° or more, or three or more bends of 45° to 90° proximal of the diseased segment (Fig. 5C).

9. Length >20mm: Estimation of the length of that portion of the stenosis that has $\geq 50\%$ reduction in luminal diameter in the projection where the lesion appears to be the longest. (In case of a bifurcation lesion at least one of the branches has a lesion length of >20mm) (Fig. 5D).

10. Heavy calcification: Multiple persisting opacifications of the coronary wall visible in more than one projection surrounding the complete lumen of the coronary artery at the site of the lesion.

11. Thrombus: Spherical, ovoid or irregular intraluminal filling defect or lucency surrounded on three sides by contrast medium seen just distal or with-

Fig. 5 – (A) Trifurcation lesion; (B) bifurcation lesion; (C) severe tortuosity; (D) lesion length >20 mm; (E) thrombus; (F) diffuse disease lesion.

in the coronary stenosis in multiple projections or a visible embolization of intraluminal material downstream (Fig. 5E).

- 12. Diffuse disease/small vessels:** Present when at least 75% of the length of any segment(s) proximal to the lesion, at the site of the lesion, or distal to the lesion has a vessel diameter of <2 mm (Fig. 5F).

A bifurcation is a division of a main parent branch into two daughter branches of at least 1.5 mm. Bifurcation lesions may involve the proximal main vessel, the distal main vessel, and the side branch according to the Medina classification (Fig. 6).

Fig. 6 – Medina classification of bifurcation lesions³⁰ (MB: main branch; SB: side branch).

Statistical analysis

After data were collected, they were analyzed by Statistical Package of Social Science (SPSS) version 19. Unless denoted otherwise, categorical data are described as count and percentages and continuous data are described as means $\pm$ SD or median. Logarithmic transformation was used for chemerin due to the high degree of skewing. A student's *t* test (for data that was normally distributed) or a Mann-Whitney test (for data that was not normally distributed) and Pearson Chi-square test (for data that were categorical variables) were used to compare the obese and non-obese samples. Correlations between serum chemerin levels and continuous variables were determined using Pearson's correlation (for normally distributed data) or Spearman's correlation (for non-normally distributed data). Two-tailed *p*-value <0.05 will be considered significant.

Results

This observational cross-sectional study was carried out at Cardiology Department in Cairo University Hospital during the period extending from November 2016 to June 2017. The study enrolled 100 patients who underwent coronary angiography for clinically indicated reasons. Patients were classified according to BMI into two groups (group A) included 50 patients with BMI (≥ 30 kg/m²) and (group B) included 50 patients with BMI ≤ 25 kg/m².

However, when patients were classified according to waist circumference using the international diabetes federation cut points,³¹ we found that 61% of our study patients have abdominal obesity including 11 patients with normal BMI.

Fig. 7 – Serum chemerin levels correlated to number of affected vessels (A) to presence of one-vessel vs. multivessel disease (B).

Fig. 8 – Serum chemerin levels correlated to severity of SYNTAX score.

Male gender predominated in our sample and 70% of participants were older than 50 years. According to mode of presentation, 40 patients were presented with acute coronary syndrome and 60 patients were diagnosed with stable coronary artery disease (Table 1).

Laboratory data of the study groups revealed that the obese patients had higher serum levels of FPG, HbA_{1c} and chemerin (Table 2). Positive correlation was found between WC and BMI ($r = 0.842$, $p < 0.001$), serum triglycerides level ($r = 0.208$, $p < 0.038$), HbA_{1c} ($r = 0.214$, $p < 0.033$) and serum chemerin level ($r = 0.279$, $p = 0.005$). This positive correlation also indicated that the more participant got older the more their WC ($r = 0.357$, $p < 0.001$).

Table 1 – Clinical characteristics of all patients

Variable	All study patients (%)
Male gender	73
Abdominal obesity according to WC	61
Abdominal obesity according to W/HR	62
Smoker	47
DM	50
HTN	55
Dyslipidemia	86
Mode of presentation	
STEMI	24
NSTEMI	7
UA	9
SCAD	60

CAD – coronary artery disease; DM – diabetes mellitus; HTN – systemic hypertension; NSTEMI – non-ST-segment elevation myocardial infarction; SCAD – stable coronary artery disease; STEMI – ST-segment elevation myocardial infarction; UA – unstable angina; WC – waist circumference; W/HR – waist to hip ratio.

Angiographic findings

Standard coronary angiography was carried out through trans-femoral and trans-radial approach using modified Seldinger technique revealed the following findings (Table 3).

Figures 7, 8 represent the significant differences in serum chemerin levels according to number of affected coronary vessels and also according to SYNTAX score class among study patients. It is obvious that serum chemerin levels were significantly higher in patients with multives-

Table 2 – Laboratory data of the study groups

Variables	All patients	Group A (n = 61)	Group B (n = 39)	p value
	Mean ± SD			
Cholesterol (mg/dL)	175.1 ± 42.6	173.2 ± 43.4	178.0 ± 41.8	0.5
TG (mg/dL)	145.7 ± 35.3	149.2 ± 40.8	140.4 ± 23.8	0.2
FPG (mg/dL)	116.4 ± 25.5	120.9 ± 28.7	109.4 ± 17.6	0.006
HbA _{1c}	7.1 ± 1.5	7.4 ± 1.5	6.6 ± 1.4	0.010
Chemerin (ng/L)	138.3 ± 36.8	146.8 ± 36.8	124.9 ± 33.1	0.013

FPG – fasting plasma glucose; HbA_{1c} – hemoglobin A_{1c}; TG – triglycerides.

Table 3 – SYNTAX score of the study groups

Variable	Abdominal obesity (n = 61)	No abdominal obesity (n = 39)	p value
SYNTAX score Low ^a	39 (63.9%)	29 (74.4%)	0.291
SYNTAX score Intermediate ^b	18 (9.5%)	8 (20.5%)	
SYNTAX score High ^c	4 (6.6%)	2 (5.1%)	
Mean ± SD			
Overall SYNTAX score	18.89 ± 9.01	16.88 ± 7.84	0.3

SYNTAX score ^a low = <22; ^b intermediate = 23–32; ^c high = >33.

sel disease than one-vessel disease and in patients with higher SYNTAX score class of severity.

Discussion

Obesity, particularly abdominal obesity increases the risk of hypertension, diabetes mellitus, dyslipidemia, insulin resistance, metabolic syndrome, obstructive sleep apnea, and kidney disease. All of which are risk factors for CAD.³² Chemerin has recently been added to the adipokine family as a novel chemo attractant protein.³³

There is growing evidence about the role of this protein in metabolic syndrome, obesity, diabetes, cardiovascular diseases, Crohn's disease, arthritis and cancer.³⁴

The current study investigated the relationship between circulating chemerin and severity of CAD in patients who underwent clinically indicated coronary angiography.

The study enrolled 100 patients who underwent coronary angiography for clinically indicated reasons. Patients were classified according to BMI into two groups: group A included 50 patients with BMI (≥30 kg/m²) and group B included 50 patients with BMI ≤25 kg/m².

However, when patients were classified according to waist circumference we found that 61% of our study patients have abdominal obesity including 11 patients with normal BMI.

Obese patients (group A) had a higher prevalence of DM, HTN and dyslipidemia ($p = 0.046$, $p = 0.045$, $p = 0.021$, respectively) along with significantly higher levels of FPS ($p = 0.001$) and HbA_{1c} ($p = 0.002$) as well as positive correlation with serum TG level ($r = 0.346$, $p = 0.000$). No statically significant difference in the mean SYNTAX score was identified between the two study groups.

These findings are concordant with **M. Ashutosh Niraj et al.** that enrolled 770 patients and study severity of coronary artery disease in obese patients undergoing coronary angiography where they emphasized that obese patients being referred for coronary angiography have a paradoxically lower CAD burden (Duke myocardial jeopardy scores) and prevalence of high-risk coronary anatomy (significant left main or triple vessel disease) compared to their nonobese comparators despite a higher prevalence of diabetes, hypertension and dyslipidemia, implying the presence of an apparent **obesity paradox**.

However, they found that after adjustment of other major cardiovascular risk factors, BMI was no longer an independent predictor of CAD burden or severity on multivariate stepwise linear regression analysis.³⁵ Other studies failed to detect an association of BMI with 1-year all-cause or cardiac-specific mortality after adjustment for potential confounding variables.³⁶

The current study found that obese patients (group A) have higher serum chemerin level than non-obese patients (group B) ($p = 0.019$). This finding is concordant with another study that found a positive correlation of BMI with serum chemerin level in patients with CAD and metabolic syndrome and lack of this correlation with normal people.³⁷

Obesity according to waist circumference (WC)

Abdominal obesity is assessed through measurement of WC. An increase in WC carries a greater risk of development of future cardiovascular events and diabetes than increased BMI. The prevalence of abdominal obesity in our study based upon the IDF guidelines was 50.7% for men and 88.9% for women. A positive correlation was found between WC and most of the cardiometabolic risk factors.

Despite the uncontrolled DM in patients with abdominal obesity, no statistically significant difference in the mean SYNTAX score and number of affected vessels was identified between the two study groups according to WC. Discordant with Yan et al.²⁴ but concordant with Lachine et al.,³⁸ we found a positive significant correlation of WC with serum chemerin levels ($r = 0.299$, $p = 0.003$).

We found high serum chemerin levels in females ($p = 0.012$) contrary to others who found similar chemerin levels in females and males.²⁴ This finding can be attributed to higher prevalence of obesity among female patients (only 7.7% are non-obese) with subsequent higher serum chemerin level and also the fact that our study is not sex matched.

Serum chemerin levels showed significant positive correlations with obesity parameters, FPG, hs-CRP, and SYNTAX score. This suggested that chemerin was elevated probably due to obesity and chronic inflammations that is reflected by significant positive correlation with BMI and hs-CRP as well as with severity of CAD that assessed by SYNTAX score. Serum chemerin level was significantly higher in patients with multivessel disease than patients with one-vessel disease ($p = 0.017$). Moreover, using SYNTAX score, serum chemerin was found to be higher in intermediate and high scores ($p < 0.001$).

A study assessed the relationship between serum chemerin level and the severity of CAD in Egyptian patients with type 2 diabetes concluded that there was a positive correlation between serum chemerin level and cardio-metabolic disease, with a significant association between serum chemerin concentration and severity of CAD using SYNTAX score.³⁸

Li Xiaotao et al. in their cross-sectional study that enrolled 188 Chinese participants concluded that serum chemerin levels were significantly increased with an increasing number of diseased vessels and Gensini score ($p = 0.024$).³⁹ It was demonstrated that in patients with metabolic syndrome, chemerin levels were higher in patients with CAD than patients without CAD and also showed a significant positive correlation with CAD severity.³⁷

Concordant with other studies^{25,38} we found that hs-CRP has a significant positive correlation with serum chemerin ($r = 0.365$, $p = 0.001$) and with SYNTAX score ($r = 0.244$, $p = 0.014$).

Conclusion

Serum chemerin level was higher in obese patients. Moreover, it was an independent predictor for severity and complexity of CAD (using SYNTAX score). The study found a significant correlation between serum chemerin and hs-CRP as a marker of inflammation. One of the limitations of the study was that we enrolled patients with CAD without enrolling healthy controls.

Thus, we could not determine the odds ratio of various cardiometabolic factors in coronary atherosclerosis. Moreover the sample size was relatively small. More longitudinal follow-up studies are needed to investigate the prognostic value of elevated serum chemerin in patients with CAD.

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Conflict of interest

None declared.

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