

Hematological and biochemical parameter with level of Chemerin in Sera of non-ST-elevation myocardial infarction (NSTEMI) Iraqi patients

By

Dr.Shurooq Hussein Al-Marsomi ^{*1};Dr.Lubna Noori Naif ^{*2}; Dr.Shaymaa Mohammed Ahmed^{*3}; prof .Dr.Nihad Khalawe Tektook^{*4}

^{1*} Senior chief family medicine specialist / Karkh Health Directorate , Al-Adel sector, Hateen family health center / Ministry of Health and Environment, Baghdad, Iraq;^{2*} Senior family medicine specialist / Karkh Health Directorate , Al-Adel sector, Hateen family health center / Ministry of Health and Environment, Baghdad, Iraq ; ^{3*} Family medicine specialist/ Karkh Health Directorate , Al-Adel sector, Hateen family health center / Ministry of Health and Environment, Baghdad, Iraq ;^{4*} Middle Technical University /College of Medical and Health Technology, Medical Laboratory Techniques Department, Baghdad city, Iraq

Abstract: A cross-sectional study was conducted in Baghdad city from the first of March 2022 to the end of February 2023 included 40 patients who were diagnosed with ACS (NSTEMI) were included in the analysis of this study, who were admitted to the coronary care unit of our department of cardiology in Al-Yarmuk Teaching Hospital , Baghdad city to evaluate the predictive value of the chemerin protein for left ventricular systolic dysfunction (LVSD) in patients with acute coronary syndrome-NSTEMI (Non ST elevation myocardial infarction) and the study were also included 40 healthy control blood donors. Patients with clinical evidence of comorbidities were excluded from this study. The study protocol was approved by the local ethics committee of hospital. Complete blood counts, biochemical and cardiac biomarker values were evaluated upon admission to the coronary care unit. Five ml of blood were collected from each patient enrolled in this study. biochemical tests and chemerin level by ELISA (in echocardiography unite. Left ventricular ejection fraction measured using M-mode in the parasternal long-axis view. There was no significant difference between studied groups regarding sex, heart rate, hypertension, DM and BMI ($P>0.05$). Patients with NSTEMI have high mean of age and low rate of smoking ($P\leq 0.05$). The study showed that chemerin level was elevated significantly in patients with NSTEMI (372.6 ± 58.4 ng/ml) as compared healthy persons (198.5 ± 35.7 ng/dl), ($P<0.001$). The study showed that the highest mean of chemerin level was recorded in patients with NSTEMI who have EF $<40\%$ (382.4 ± 44.2 ng/ml) followed by group who EF 40-50% (301.5 ± 34.4 ng/ml) and the lowest mean was in patients with EF $>50\%$ (288.4 ± 35.4 ng/ml) ($P<0.001$). The study showed positive correlation between chemerin level and platelets counts in patients with NSTEMI and negative correlation of between EF and age patients with NSTEMI. **Conclusions:** Chemerin has been investigated as a simple a feasible new prognostic inflammatory marker for adverse cardiovascular outcomes in many types of cardiovascular diseases and a high chemerin is a strong and independent predictor for LVSD in patients with NSTEMI.

Keywords: Coronary artery disease; chemerin; EF%; NSTEMI

Introduction

Acute coronary syndrome (ACS) is a syndrome occur due to decrease blood flow in the coronary arteries, when a plaque within one of these arteries ruptures and form a clot ⁽¹⁾. The most common symptom is chest pain, often radiating to the left shoulder or angle of the jaw, crushing, central and associated with nausea and sweating. Many people with acute coronary syndromes present with symptoms other than chest pain, such as dyspnea, epigastric discomfort, nausea, or weakness may occur instead of chest discomfort, they appear to be more frequent in women, the elderly, and patients with diabetes mellitus ⁽²⁾. Acute coronary syndrome is commonly associated with three clinical manifestations, named according to the appearance of the electrocardiogram (ECG): ST elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI), or unstable angina ⁽³⁾. Acute ST segment elevation myocardial infarction (STEMI) most commonly occurs when thrombus formation results in complete occlusion of a major epicardial coronary artery. Adipose tissue serves not only as a mass of fat for storing energy but also as an active endocrine organ that secretes various bioactive adipokines. Most adipokines, such as tumor necrosis factor (TNF)- α , interleukin (IL)- 6, visfatin and leptin are well-known pro-inflammatory cytokines that accelerate atherosclerosis in experimental model ^(4,5). Chemerin, also known as tazarotene-induced gene 2 protein (TIG2) or retinoic acid receptor responder 2 (RARRES2), is a recently discovered adipocytokine that is released from liver and white fat tissue. It has been shown to regulate adipocyte differentiation, maturation, and metabolism. Several studied have demonstrated for the first time that chemerin levels were higher in STEMI patients with greater thrombus burden and higher level of inflammation ^(6,7). The aim of this study was to evaluate the predictive value of the chemerin protein for left ventricular systolic dysfunction (LVSD) in patients with acute coronary syndrome-NSTEMI (Non ST elevation myocardial infarction).

Materials and methods

A cross-sectional study was conducted in Baghdad city from the first of March 2022 to the end of February 2023 included 40 patients who were diagnosed with ACS (NSTEMI) were included in the analysis of this study, who were admitted to the coronary care unit of department of cardiology in Al-Yarmuk Teaching Hospital, Baghdad city and the study were also included 40 healthy control blood donors. Patients with clinical evidence of comorbidities (cancer, active infection, hematological proliferative diseases, active or chronic inflammatory or autoimmune diseases, recent blood transfusion, severe hepatic diseases, and renal failure, history of ischemic heart disease, known heart failure) were excluded from this study. The study protocol was approved by the local ethics committee of our hospital. Complete blood counts, biochemical and cardiac biomarker values were evaluated upon admission to the coronary care unit. Transthoracic echocardiography was performed on each patient in the echocardiographic unit. Five ml of blood were collected from each patient enrolled in this study. biochemical tests and chemerin level by ELISA (Biokit CO. USA) All measurements were performed using a available machine (GE Vivid 3 PRO, GE Vivid E9) in echocardiography unite. Left ventricular ejection fraction measured using M-mode in the parasternal long-axis view.

Results

There was no significant difference between studied groups regarding sex, heart rate, hypertension, DM and BMI ($P>0.05$). Patients with NSTEMI have high mean of age and low rate of smoking ($P\leq 0.05$) (Table 3.1).

Table 1: Baseline characteristics of studied cases

Variables	Studied groups		P. value
	Patients with NSTEMI (n:40)	Control groups (n:40)	
Sex, male: n (%)	65%	63%	0.43
Age (Mean \pm SD)	62.34 \pm 5.39	66.06 \pm 7.28	0.004
HR (mean (beat/min))	78 (49-115)	80 (51-127)	0.39

Hypertension	25 (52.8%)	14 (51.58%)	0.52
Type 2 diabetes	31.1%	28.3%	0.28
Smoking	35.83%	17.03%	0.02
Body mass index, kg/m ²	28.5 (18.2-41.6)	28.1 (17.1-40.8)	0.71

The study showed no significant differences between studied groups regarding lipid profile and hemoglobin level Table 1

Table 2: Hematological and biochemical characteristics of studied cases

Variables	Studied groups		P. value
	Patients with NSTEMI (n:40)	Patients with NSTEMI (n:40)	
Total cholesterol	194 (98-445)	186 (109-370)	0.52
LDL	120 (110-186)	121 (46-312)	0.51
HDL	40 (30-98)	40 (21-88)	0.83
Triglyceride	110 (60-311)	102 (63-294)	0.08
Hemoglobin level (g/dl) (mean±SD)	12.8± 1.73	12.56±1.72	0.45

The study showed that chemerin level was elevated significantly in patients with NSTEMI (372.6 ± 58.4 ng/ml) as compared healthy persons (198.5 ± 35.7 ng/dl), ($P < 0.001$), Table 3.3.

Chemerin level (ng/ml)	Studied groups		p. value
	Patients with NSTEMI (n:40)	Patients with NSTEMI (n:40)	
Mean ± SD	372.6 ± 58.4	198.5 ± 35.7	<0.001

The study showed that the highest mean of chemerin level was recorded in patients with NSTEMI who have EF <40% (382.4 ± 44.2 ng/ml) followed by group who EF 40-50% (301.5 ± 34.4 ng/ml) and the lowest mean was in patients with EF >50% (288.4 ± 35.4 ng/ml) ($P < 0.001$), Table 4.

Table 4: Relation of chemerin level with NSTEMI and percentage of EF

Chemerin level (ng/ml)	Patients with NSTEMI (n:40)			ANOVA	P. value
	EF: <40%	EF: 40-50	EF: >50%		
No.	20	10	10		
Mean	382.4 ± 44.2	301.5±34.4	288.4±35.4	23.5	<0.001

The study showed positive correlation between chemerin level and platelets counts in patients with NSTEMI (Figure 1).

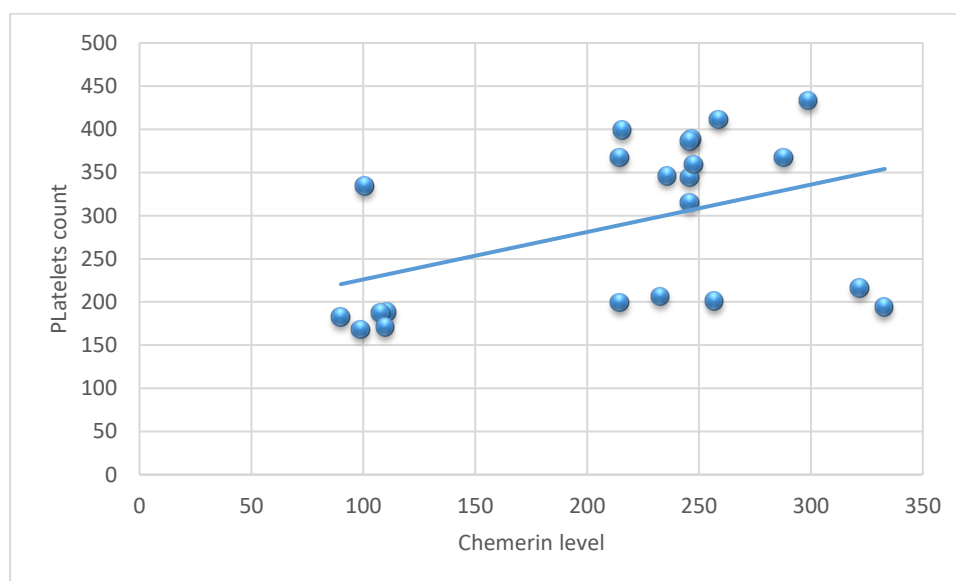


Figure 2: Correlation of platelets counts in patients with NSTEMI and chemerin level

The study showed negative correlation of between EF and age patients with NSTEMI (r : -0.426) (Figure 2).

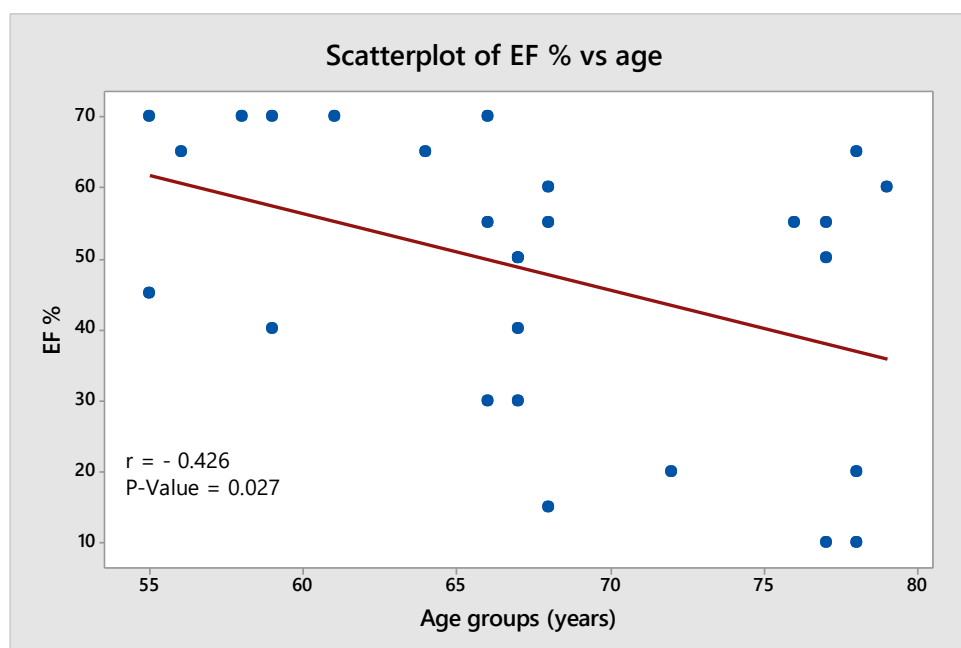


Figure 3.2: Correlation of EF with age patients with NSTEMI and high PLR

Discussion

Patient with elevated PLT have high mean of age and low rate of smoking ($P \leq 0.05$). Roman *et al* ⁽⁶⁾ in a similar recent study demonstrated that the patients in the high NSTEMI group were older in age ($p < 0.001$) and showed no significant relation with sex, heart rate, HT, DM, BMI. On a related level, Kutzleb *et al* ⁽⁷⁾ in another recent study indicated that patients with NSTEMI were belonged to high age group. In a recently published systematic comprehensive review and meta-analysis, which included 10 studies involving 8932 patients diagnosed with ACS, Goralski *et al* ⁽⁸⁾ concluded that an elevated chemerin level is a predictor of both in-hospital adverse outcomes and long-term adverse outcomes in patients with ACS. The adipokines which are released from the adipose tissue such as chemerin play different roles in the inflammatory process causing development and acceleration of atherosclerosis and contributing to the presence of acute coronary syndromes ⁽¹⁻³⁾. It has been also found that serum chemerin levels are correlated with both arterial stiffness and coronary arterial plaques ⁽⁴⁾. Lepira *et al.* found a weak relationship about the relation between chemerin and coronary plaque burden and the number of noncalcified plaques in subjects undergoing CT angiography ⁽⁹⁾.

However, in some studies, serum chemerin levels have not been demonstrated to be related with the atherosclerotic plaque burden ⁽¹⁰⁾. Cuspidi et al ⁽¹¹⁾ also found a significant relationship between the serum chemerin levels and extent of coronary artery disease; however, serum chemerin levels were significantly correlated with inflammatory markers and coronary thrombus burden. This finding may be a clue that chemerin is an important factor in the inflammatory process of acute STEMI. Increased chemerin levels as a marker of inflammation have been shown to be related with increased morbidity and mortality in STEMI patients ⁽¹²⁾. The relationship between high thrombus burden and chemerin levels which has been recently shown by Mattu et al ⁽¹³⁾ is one of the explanations of this relationship, they also found increased chemerin levels in patients with thrombus burden. Besides, serum chemerin levels were also increased in these patients, and after multivariate analysis, this finding still persisted. Bioactive adipokines are secreted by adipose tissue and the list of adipokines has reached hundreds of factors. Accumulating evidence established that obesity, characterized by a condition of excess adipose tissue, resulted in the imbalance of pro-inflammatory/anti-inflammatory adipokines, and therefore deeply involved in the development of atherosclerotic disease ⁽¹⁴⁻¹⁶⁾. The point that adipokine is the bridge between obesity and atherosclerosis is no longer controversial. In the present study, we found positive correlation between chemerin and platelets which was consistent with many previous studies ^(14,17). Correlation analyses also demonstrated that increased chemerin levels were positively correlated with EF% but negatively correlated with LVEF and that reduced adiponectin levels were positively correlated with LVEF but negatively correlated with LVEDD in ACS. This is concordant with other studies that showed a significant trend toward a chemerin and EF% ⁽¹⁸⁻²¹⁾.

Conclusions: Chemerin has been investigated as a simple a feasible new prognostic inflammatory marker for adverse cardiovascular outcomes in many

types of cardiovascular diseases and a high chemerin is a strong and independent predictor for LVSD in patients with NSTEMI.

References

1. Scherer P. E. Adipose tissue: from lipid storage compartment to endocrine organ. *Diabetes*. 2006;55(6):1537–1545.
2. Ahima R. S., Flier J. S. Adipose tissue as an endocrine organ. *Trends in Endocrinology and Metabolism*. 2000;11(8):327–332.
3. Trayhurn P., Wood I. S. Adipokines: inflammation and the pleiotropic role of white adipose tissue. *British Journal of Nutrition*. 2004;92(3):347–355.
4. Kahn B. B., Flier J. S. Obesity and insulin resistance. *Journal of Clinical Investigation*. 2000;106(4):473–481.
5. Nagpal S., Patel S., Jacobse H., et al. Tazarotene-induced gene 2 (TIG2), a novel retinoid-responsive gene in skin. *Journal of Investigative Dermatology*. 1997;109(1):91–95.
6. Roman A. A., Parlee S. D., Sinal C. J. Chemerin: a potential endocrine link between obesity and type 2 diabetes. *Endocrine*. 2012;42(2):243–251. doi: 10.1007/s12020-012-9698-8.
7. Kutzleb C., Busmann A., Wendland M., Maronde E. Discovery of novel regulatory peptides by reverse pharmacology; spotlight on chemerin and the RF-amide peptides metastin and QRFP. *Current Protein and Peptide Science*. 2005;6(3):265–278.
8. Goralski K. B., McCarthy T. C., Hanniman E. A., et al. Chemerin, a novel adipokine that regulates adipogenesis and adipocyte metabolism. *Journal of Biological Chemistry*. 2007;282(38):28175–28188.

9. Lepira FB, Kayembe PK, M'buyamba-Kabangu JR, Nseka MN. Clinical correlates of left ventricular hypertrophy in black patients with arterial hypertension. *Cardiovasc J S Afr* 2006;17:7-11.
10. Addo J, Smeeth L, Leon DA. Hypertensive target organ damage in Ghanaian civil servants with hypertension. *PLoS One* 2009;4:e6672.
11. Cuspidi C, Sala C, Negri F, Mancina G, Morganti A; Italian Society of Hypertension. *et al.* Prevalence of left-ventricular hypertrophy in hypertension: An updated review of echocardiographic studies. *J Hum Hypertens* 2012;26:343-9.
12. Musi N, Guardado-Mendoza R. Adipose tissue as an endocrine organ. In: Ulloa-Aguirre A, Michael Conn P, editors. *Cellular Endocrinology in Health and Disease*. Boston, MA: Academic Press; 2014. p. 229-37.
13. Mattu HS, Randeva HS. Role of adipokines in cardiovascular disease. *J Endocrinol* 2017;216:T17-36.
14. Leal Vde O, Mafra D. Adipokines in obesity. *Clin Chim Acta* 2013;419:87-94.
15. Roh SG, Song SH, Choi KC, Katoh K, Wittamer V, Parmentier M, *et al.* Chemerin – A new adipokine that modulates adipogenesis via its own receptor. *Biochem Biophys Res Commun* 2007;362:1013-8.
16. Bondue B, Wittamer V, Parmentier M. Chemerin and its receptors in leukocyte trafficking, inflammation and metabolism. *Cytokine Growth Factor Rev* 2011;22:331-8.
17. Davenport AP, Alexander SP, Sharman JL, Pawson AJ, Benson HE, Monaghan AE, *et al.* International union of basic and clinical pharmacology. LXXXVIII. G protein-coupled receptor list: Recommendations for new pairings with cognate ligands. *Pharmacol Rev* 2013;65:967-86.

18. Skrzeczyńska-Moncznik J, Stefńska A, Zabel BA, Kapińska-Mrowiecka M, Butcher EC, Cichy J, *et al.* Chemerin and the recruitment of NK cells to diseased skin. *Acta Biochim Pol* 2009;56:355-60.
19. Goralski KB, McCarthy TC, Hanniman EA, Zabel BA, Butcher EC, Parlee SD, *et al.* Chemerin, a novel adipokine that regulates adipogenesis and adipocyte metabolism. *J Biol Chem* 2007;282:28175-88.
20. Ernst MC, Issa M, Goralski KB, Sinal CJ. Chemerin exacerbates glucose intolerance in mouse models of obesity and diabetes. *Endocrinology* 2010;151:1998-2007.
21. Döcke S, Lock JF, Birkenfeld AL, Hoppe S, Lieske S, Rieger A, *et al.* Elevated hepatic chemerin mRNA expression in human non-alcoholic fatty liver disease. *Eur J Endocrinol* 2013;169:547-57.