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The Role Of Chemerin In Iraqi Patients With Acute Coronary Syndrome

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Background: Coronary artery disease (CAD) is the principal aetiology underlying angina pectoris, myocardial infarction (MI) and cardiac failure secondary to ischaemia, and is a key factor associated with the position of cardiovascular disease (CVD) as the primary cause of fatality on a global scale ,novel marker chemerin has anti inflammation and cardiovascular protective role. Chemerin, which has the alternative nomenclature retinoic acid receptor responder 2 (RARRES2), tazarotene-induced gene 2 protein and RAR-responsive protein TIG2 is a proinflammatory adipokine expressed in abundance in white adipose tissue and hepatocytes. Encoded by the RARRES2 gene, it has been linked with the inflammatory process.

Objective: To estimate chemerin levels in acute coronarysyndrome and find the prospect of use chemerin in diagnosis in ACS.

Patients and Methods: The study conduct with 80 patients and 58 control. The patients divided into two groups: (n=40) acute coronary syndrome, and (n=40) chronic stable angina, number of control (n=58).

Result: In this present study, observed that the mean age of patients with ACS was (61.25 years)and (62.65 years) chronic unstable angina cohort; and control group,(59.87 years).The mean of Chemerin of ACS, chronic stable angina cohort; and control group, are 73.519, 51.20 and 3. 36.47 ng/mlrespectively, Chemerin titers was; elevated levels on admission were noted in individuals presenting with ACS compared to control subjects and reach their peak within few hours after ACS.

Conclusion: Acute coronary syndrome patients showed a significant elevation in serum chemerin compared with control group.Thus, it may be used in the appraisal of such patients., serum chemerin has cardiovascular protective role and can be used as adiagnostic biomarkers in patients with ACS.

Keywords: serum Chemerin, biomarker, acute coronary syndrome.

Introduction:

Coronary artery disease (CAD) is the principal aetiology underlying angina pectoris, myocardial infarction (MI) and cardiac failure secondary to ischaemia, and is a key factor associated with the position of

cardiovascular disease (CVD) as the primary cause of fatality on a global scale (Neumann, Sousa-Uva et al. 2019).Typically,CAD comprises the formation of mural atherosclerotic plaques within the coronary arterial vasculature; these give rise to coronary artery stenosis, thereby reducing perfusion pressure and generating myocardial ischemia. A complication of these plaques includes arterial occlusion, which is the main pathogenesis underlying acute MI (AMI) **(Doenst, Haverich et al. 2019).**

In plaque progression the inflammation plays significant role and the inflammatory factors have mainly role in contributor to plaque formation (Tayet al, 2016; Wuet al, 2017) Incidences of ACS are rise in spite of new therapeutic technology advances and primary prevention (Rothet al, 2017;Tabaset al, 2015) Chemerin has been categorised as an adipokine owing to its contribution to fat cell differentiation, as alluded to previously, and uptake of glucose. The modest degree of inflammatory activity associated with obesity has been previously described, together with its role as a risk factor in CVD and atherosclerotic pathogenesis (Kalligeros, Shehadeh et al. 2020). Serum monocyte and endothelial cell engagements in the context of concomitant vascular mural impairment and general inflammation are pathognomonic of the underlying mechanisms (Dimitriadis, Kaur et al. 2018).Active chemerin participates in a number of pathogenetic mechanisms underlying inflammatory and metabolic disorders in fat cells and in respiratory, integumentary, cardiovascular, reproductive, gastrointestinal, skeletal and rheumatological systems (Schumacher, Mattern et al. 2014, Tolusso, Gigante et al. 2018).When an inflammatory response arises, the initial stage is neutrophil conscription to the injury locus, where they liberate proteases, e.g. elastase and cathepsin G, which trigger the production of active chemerin (Shin and Pachynski 2018). Chemerin stimulates chemotaxis of young dendritic cells and macrophages, thus combining intrinsic and adaptive immune systems to generate the desired immune function.(Shin and Pachynski 2018). Chemerin stimulates chemotaxis of young dendritic cells and macrophages, thus combining intrinsic and adaptive immune systems to generate the desired immune function. Therapy with chemerin diminishes the migration of white cells to the lesion and proinflammatory cytokine expression (Zhang, Xu et al. 2018). Thus, chemerin can behave as both a pro- and anti-inflammatory agent according to the physiological context.In obese individuals and those with T2DM, changes in serum adipokine titres have been documented (Helfer and Wu 2018), with elevated titres observed in obese individuals and associations noted with a range of metabolic syndrome parameters (Dimitriadis, Kaur et al. 2018). These data suggest that chemerin plays a role in CVD.

Patients and Methods:

Was a case control study performed in individuals with IHD between October 2020 and March 2021 at Al-Nafes Hospital andMedical City / Baghdad teaching hospital /CCU. 80 patients were recruited to the study, following their attendance with symptoms characteristic of IHD. The patients were clinically assessed, and a diagnosis of either ACS or chronic stable angina was made with the use of serial ECGs and cardiac enzymes.

Inclusion criteria: The inclusion criteria for the study were patients within the age-range 50-80 years (n = 80), with either troponin-positive ACS (n = 40) and troponin-negative chronic stable angina (n = 40). The diagnosis was established by a doctor.

Exclusion criteria: Patients were excluded from the study if theymet any of the following criteria: critically ill; advanced liver or kidney pathology; malignancy; established mental illness, such as schizophrenia; cerebrovascular accident; pregnancy; autoimmune condition; or previous intra-abdominal operation.

Sample collection:

2.5.3- Serum sample collection

7 mL blood was venesected in a sterile manner from all study subjects, and then subjected to 15 minutes centrifugation (3000) in order to extract the serum. It was then divided into three aliquots for the following:

(i) lipid profile and glucose, placed in a 1.5 mL Eppendorf tube;

(ii) CK-MB, high-sensitive troponin, also placed in a 1.5 mL Eppendorf tube and stored in a temperature of -20 °C prior to assay; and

(iii) chemerin; the tube was refrigerated and frozen only once at a temperature of -20 °C prior to the assays.

Method:The protein assays in this study, i.e.chemerin, were performed according to the vendor's guidelines using a human enzyme-linked immunoassay (ELISA) analyser. This could be preset to run each assay autonomously. Serum lipid profile test (Total cholesterol TC, triglyceride TG, High Density Lipoprotein (HDL), Low Density Lipoprotein LDL, Very LowDensity Lipoprotein (LDL) Fasting blood sugar FBSby calorimetry spectrophotometry.The statistical analysis: case control.

Result:A eighty patients and fiftyeight control in this study, the numbers of females and males in the ACS, chronic unstable angina and control cohorts were 16 (40%) and 24 (60%), 16 (40%) and 24 (60%),

and 25 (43%) and 33 (57%), respectively.The observedmales were more prevalent than femalesand there is statistically no a significant difference between the frequency of the patients in male and female groups compared to control group (p = 0.866)(Figure 1).

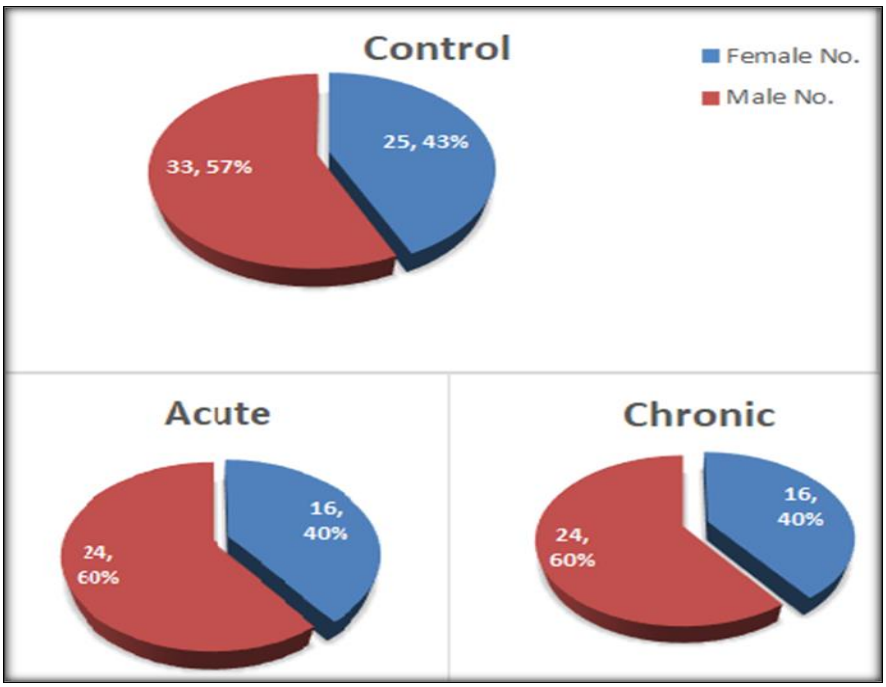

Figure (1): Pie-chart showing gender distribution amongst the three groups.

Biochemical variables among the three studies groupstable (1), and serum lipid profilesfigure (2) , were appearing to be significantly increase altogether in the ACS group andchronic unstable angina, there was more clearly lipid disorder, apart from the serum HDL-C which found to be decrease significantly in comparison with control group, look at table (1),Serum FBS in group ACS did not show any significant correlation with other parameter see table (1). Table (1)revealed a highly significant increase in Chemerin levels in (ACS and chronic stable angina) group of patients in compare with group control (p=0.001).

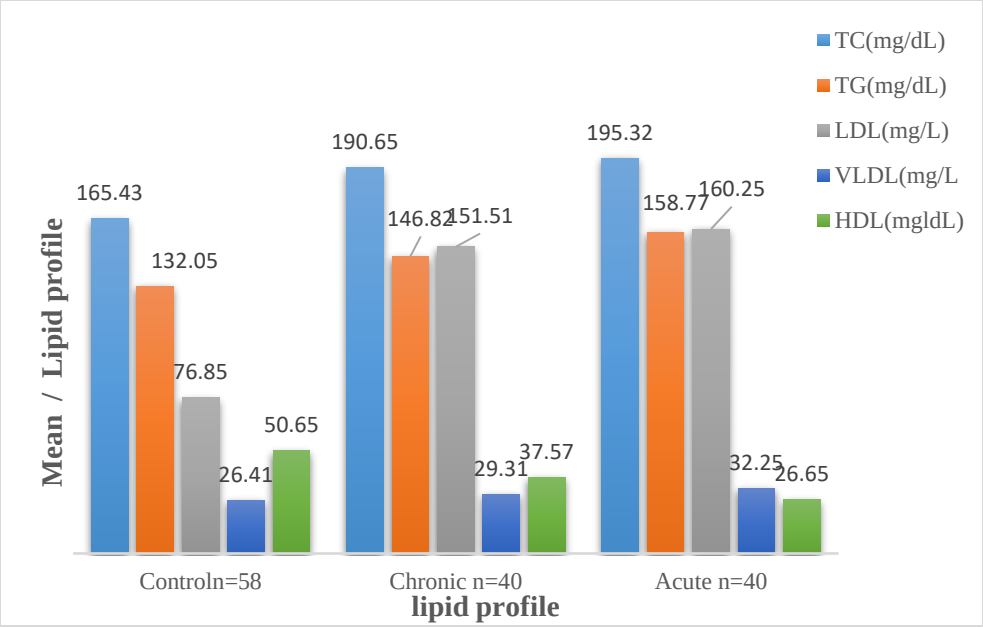

Figure (2): Average serum lipid profiles for the three cohorts.

Table(*1*): Anthropometric and biochemical variables among the three studies groups

	Mean values ±SD(ANOVA)Test			
Parameter	Acute (N=40)	Chronic (N=40)	Control (N=58)	**P value**
Age (year)	61.25±8.29[a]	62.65±7.14[a]	59.87±7.04[a]	**0.238**
Gender				**0.866**
Male	24(60.00%)	24(60.00%)	33(57.00%)	
Female	16(40.00%)	16(40.00%)	16(40.00%)	
FPG (mg/dL)	97.32±11.26[a]	99.82±8.02[a]	99.37±7.97[a]	**0.411**
TC (mg/dL)	195.32±56.94[b]	190.65±50.07	165.43±25.74[a]	**0.001**

TG (mg/dL)	161.27±38.92[b]	146.56±23.08[b]	132.06±11.66[a]	**0.001**
HDL-C (mg/dL)	25.65±9.7[b]	37.43±4.51[b]	50.44±14.25[a]	**0.001**
VLDL-C (mg/dL)	32.75±7.78[b]	29.31±4.61[b]	26.41±2.33[a]	**0.002**
LDL-C (mg/dL)	160.52±36.15 [b]	151.51±63.04 [b]	76.86±13.28 [a]	**0.001**
S. Chem (ng/L)	73.519 ± 11.18 a	9.66 ±0.78 b	3.94 ±1.42 b	**0.001**

Sig. P < 0. 05; high Sig. P < 0. 01; no asterisk: P> 0. 05

"Similar small letters indicate unimportant differences while different lowercase letters indicate large differences"

DISCUSSION:

CAD arises from an ongoing inflammatory process which is linked with CAD risk factors, e.g. hypercholesterolaemia, T2DM and tobacco use (Spitzer, Hahn et al. 2019). The data from this study are in keeping with the perspective that the studied proteins could be implicated in the pathogenesis of atherosclerosis and its associated conditions.The number of male patient group is above female group in this study as illustrated and Table (1). however, Although males numerically outnumbered females in the patient groups, this failed to reach significance (p = 0.866) Table (1)). CAD therefore impacts both genders. These data concur with previous work which reported that the risk of CAD is greater in men than in women (Sanchis-Gomar et al., 2016),(Savonitto et al. 2016) also described the lower prevalence of coronary atherosclerosis in females compared with their age-matched male counterparts. The risk for females increases following the menopause, being responsible for significant morbidity and mortality during this life stage (Prasad, Harikrishnan et al. 2017).Which found that mean values of serum chemerin levels for the controls, patients with ACS and chronic stable angina were 36.47 ± 3.40, 73.519 ± 11.18 and 51.20 ± 7.41, respectively, reflecting a notable difference between patient and control levels (p = 0.01) (Table (1)). These figures are in alignment with earlier studies (Aronis, Sahin-Efe et al. 2014, Elnoamany, Dawood et al. 2020).Chemerin titres can be used to forecast the likelihood of acute

coronary insults; elevated levels on admission were noted in individuals presenting with ACS compared to control subjects (Aronis, Sahin-Efe et al. 2014, Recinella, Orlando et al. 2020). (Nankam, Blüher et al. 2021) reported that chemerin is a de novo adipokine linked with obesity and metabolic syndrome, and demonstrated its raised levels in patients diagnosed with ACS. BMI has also been associated with chemerin titres (Landgraf, Friebe et al. 2012, Jialal 2021). A further study noted elevated serum chemerin concentrations in patients with ACS compared to a monitored cohort; alterations in its level were observed as the ACS evolved. Thus, it may be used in the appraisal of such patients. The data from the current study are in keeping with findings previously published by (Salesi, Gani et al. 2018). (Mirmajidi, Izadi et al. 2019) showed a direct association between serum chemerin and FBS in individuals with CAD. Additional studies have reported similar data to the current study, and noted the relationship between serum chemerin and TC (Baig, Alghalayini et al. 2020).

Conclusion:

Chemerin, has an important role in defending effects on heart and quantity of Chemerin in patient cohorts with Acute coronary syndrome may aid in diagnosis and to avoid complication of patients with ACS.

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