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Chemerin as a Biomarker of Acute Coronary Syndrome

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Abstract

Intense coronary disorder (ACS) is a condition (set of signs and indications) because of diminished blood stream in the coronary courses with the end goal that piece of the heart muscle can't work appropriately or kicks the bucket. The point of study is to assess chemerin levels in patients with intense coronary disorder. The investigation included 100 subjects who were ordered into two gatherings; control bunch which included 20 subjects with typical coronary discoveries, and cases bunch which included 80 cases with ACS (counting STEMI, NSTEMI, and UA). All cases and controls were exposed to finish history taking, careful actual assessment, and routine lab examinations. Likewise, serum chemerin were estimated for all cases and controls. The mean age of the included subjects was 55.99 and 56.2 years for ACS and control bunches individually. Guys spoke to 55 and 52.5% of cases in the two gatherings individually, with no measurably huge distinction between the two gatherings (p=0.448). Serum chemerin level was fundamentally higher in the ACS gathering (268.8 ng/ml versus 115 ng/ml in controls – $p < 0.001$). On separating ACS cases into 3 subtypes, there was mellow huge distinction between STEMI, NSTEMI, and UA ($p = 0.086$). The best cutoff purpose of Chemerin to foresee the event of ACS was >249.5 ng/ml with 74.6% affectability, 82% particularity, 78% PPV, 72% NPV and precision of 72%. Chemerin was more touchy than troponin in distinguishing cases with ACS.

Keywords: Chemerin, Coronary Syndrome, ACS, Troponin.

1. Introduction

Cardiovascular sickness is one of the main sources of dreariness and mortality in the World, and atherosclerosis is the significant normal hidden infection [1].

Intense coronary condition (ACS) is a disorder (set of signs and side effects) because of diminished blood stream in the coronary corridors with the end goal that piece of the heart muscle can't work appropriately or kicks the bucket. The most well-known manifestation is chest torment, frequently transmitting to one side shoulder or point of the jaw, smashing, focal and related with sickness and perspiring. Numerous individuals with intense coronary conditions present with manifestations other than chest torment, especially, ladies, more established patients, and patients with diabetes mellitus [2].

The exact instrument fundamental the improvement of atherosclerotic vascular illness has not been completely clarified. Fat tissue has been appeared to discharge an assortment of solvent proteins, named adipokines, for example, leptin, adiponectin, and TNF. These components demonstration locally or potentially in different tissues to direct adipocyte science and foundational measures including insulin affectability, atherosclerosis, etc [3].

The quantity of known adipokines discharged from fat tissue is expanding, and the recognizable proof and portrayal of these emitted proteins is significant in arrangement how they may contribute toward the advancement of the metabolic disorder and atherosclerosis [4].

Chemerin, otherwise called tazarotene-incited quality 2 protein (TIG2) or retinoic corrosive receptor responder 2 (RARRES2), is an as of late found adipocytokine that is delivered from liver and white fat tissue. It has been appeared to control adipocyte separation, development, and digestion, and it balances the statement of adipocyte qualities, for example, glucose carrier 4, adiponectin, and leptin. These qualities are engaged with lipid homeostasis [5].

A few investigations have announced that chemerin levels are likewise connected with aggravation, adipogenesis, segments of metabolic conditions, lipid homeostasis, atherosclerosis, and fringe blood vessel firmness. Circling chemerin levels are discovered to be raised in different metabolic and fiery illnesses, for example, type 2 diabetes, metabolic disorder, psoriasis, and cardiovascular infections [6].

The job of chemerin in pathogenesis and improvement of cardiovascular illness and atherosclerosis has been explored in certain preliminaries, and a positive connection between's chemerin emission and coronary atherosclerosis has been appeared by certain reports. Nonetheless, negative investigations are likewise present [7].

We endeavored to decide if serum chemerin levels are related with the presence and degree of coronary corridor stenosis in patients with CAD.

The point of study is to assess chemerin levels in patients with intense coronary condition.

2. Patients and methods

This investigation is an imminent case control study that was directed over a time of one year, from December 2018 to December 2019, on patients analyzed as intense coronary disorder at Benha University Hospitals. Formal assent was gotten from all individual and the investigation convention was affirmed by the Banha clinical examination moral board.

The examination included 100 subjects who were isolated into two gatherings:

- Group A (Control gathering): This included 20 instances of suspected IHD with typical coronary angiography.

- Group B (Patient gathering): This included 80 cases with ACS (counting STEMI, NSTEMI, and insecure angina cases).

2.1 Inclusion criteria

- Acute myocardial infarction (AMI): including STEMI & NSTEMI myocardial infarction that was confirmed by a significant increase of troponin I, Creatine Kinase MB levels clinical finding & ECG.
- Unstable angina (UA): including cases with chest pain at rest with definite ischemic electrocardiographic changes: ST-segment changes and/or T-wave inversions.
- Control group: This consists of subjects with no significant lesions at coronary artery.

2.2 Exclusion criteria

- Valvular heart disease.
- Collagen disease.
- Advanced liver disease.
- Renal failure.
- Malignant disease.
- Septicemia.
- Other inflammatory disease or current steroid therapy.

An informed consent was obtained from all patients before participating in the study. All patients were assessed by the same cardiac team with standard evaluation approach. written informed consent was obtained from all patients before participating in the study.

All patient were subjected to full history taking, complete clinical examination, and investigations as troponin, CK-MB,CBC ,creatinine and lipid profile and Chemerin levels: Fasting blood samples (3 ml) were obtained the morning after admission for the rest of the study groups. The samples were collected in sodium heparin Vacutainers (Becton-Dickinson). Blood was centrifuged for 15 min at 3,000 g and the plasma were stored at -80°C until further use. The levels of plasma chemerin were measured by an enzyme-linked immunosorbent assay (ELISA), following the manufacturer's instructions. The ELISA intra-assay and inter-assay coefficients of variation were <5% and <10%, respectively.

2.3 Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA) Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test ($\chi 2$) and Fisher exact was used to calculate difference between qualitative variables as indicated. Quantitative data were expressed as mean ± SD (Standard deviation). Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data) while Mann Whitney U test was used for non-normally distributed Data (non-parametric data). Spearman's correlation was used to test the correlation between two variables with non-parametric quantitative data.

3. Results

The study included 100 subjects who were classified into two groups: Group A: control group (20 healthy subjects), Group B: cases with ACS (80 cases). The group of cases with ACS was furtherly subdivided into 3 subgroups; 39 cases with unstable angina (UA), 22 cases with STEMI and 19 cases with NSTEMI.

The age of the cases in the control group was 56.20± 10.88 years and in the ACS group was 55.99± 9.71 years with no statistically significant difference between the two groups (p= 0.932). Males represented 55 and 52.5% of cases in both groups respectively, with no statistically significant difference between the two groups (p=0.448). BMI was significantly higher in cases compared to controls (p = 0.005). The prevalence of HTN, DM and smoking were slightly higher in the cases with ACS as compared to the controls (p= 0.764, 0.189 and 0.188 respectively). Lipid profile showed significantly higher levels of cholesterol, LDL, and TG in cases compared to controls, while HDL did not differ significantly between the two groups, Table (1).

Table (1) Analysis of demographic data, chronic diseases, and lipid profile of the subjects in the two study groups.

		Groups		Test of significance
		Control group(A) (N=20)	ACS group(B) (N=80)	
	Age (years)	56.20± 10.88	55.99± 9.71	t= 0.085 p= 0.932
Sex	**Males**	11 55%	42 52.5%	$\chi 2$= 1.017
	Females	9 45%	58 47.5%	P=0.448
BMI		27.88± 2.47	32.38± 3.23	t= -4.621 p= 0.005
HTN	**Hypertensive**	10 50%	43 53.8%	$\chi 2$= 0.092
	Non-hypertensive	10 50%	37 46.2%	P= 0.764

Table (1) Continue

DM	**Diabetic**	6	30%	37	46.2%	χ2= ١.724
	Non diabetic	14	70%	43	53.8%	P= 0.189
Smoking	**Smoker**	9	45%	49	61.2%	χ2= ١.734
	Non-smoker	11	55%	31	38.8%	P= 0.188
Total cholesterol (mg/dl)		195.45±39.59		244.43±62.24		t= -7.246 p <0.001
TGs (mg/dl)		118.15 ± 37.90		187.85± 33.17		t= -10.421 p < 0.001
HDL (mg/dl)		45.60± 8.14		43.36± 11.50		t= 1.315 p= 0.372
LDL (mg/dl)		105.55±32.81		156.64±48.52		t= -7.845 p < 0.001
Creatinine (mg/dl)		0.98 ± 0.25		0.96 ± 0.24		t= 0.394 p= 0.694

P: probability. Categorical data expressed as Number (%) Quantitative data are expressed as mean ± SD
χ2= Chi-square test T: independent samples t-test.

There were no positive cases of troponin in the control group while there were 56.25% of the cases in the ACS positive for troponin with statistically significant difference between the two groups (p < 0.001). The mean level of CKMB in the control group was 14.10 ± 4.34 while the level was 43.35 ± 31.07 in the ACS group with high statistically significant difference (p < 0.001). The median level of chemerin in the control group was 115 ng/ml with range between 111 and 292.1 ng/ml while in the ACS group the level was 268.8 ng/ml with range between 127 and 798.3 ng/ml in the ACS group with statistically significant difference between the two groups (p < 0.001), Table (2).

Table (2) Analysis of cardiac examination of the cases in the two study groups.

	Groups		**Test of significance**
	Control group (N=20)	**ACS group (N=80)**	
Positive troponin	0 (0%)	45 (56.25%)	χ2= 8.256 P < 0.001
CKMB (IU/L)	14.10± 4.34	43.35± 31.07	t= -4.185 p < 0.001*
Chemerin (ng/ml)	115 (111-292.1)	268.8 (127-798.3)	z= - 16.586 p <0.001

P: probability. Categorical data expressed as Number (%) Quantitative data are expressed as median (range) or mean ± SD χ2= Chi-square test T: independent samples t-test Z: Mann Whitney U test statistically significant when (p<0.05)

There was a significant positive correlation between Chemerin level and multiple parameters including BMI, cholesterol, TG, and LDL (p < 0.001). There was no significant correlation between the Chemerin level and other parameters included in the study. table 3

Table (3) Correlation between chemerin and other parameters in the study.

	Chemerin	
	r	**p**
Age	0.013	0.898
BMI	0.542	<0.001*
EF	-0.009	0.929
CKMB	-0.041	0.689
Cholesterol	0.478	0.001*
TGs	0.336	0.009*
HDL	0.110	0.270
LDL	0.411	0.001*
Creatinine	-0.024	0.811

r: spearman's correlation p: probability statistically significant (p< 0.05)

The best cutoff point of Chemerin to predict the occurrence of ACS was >249.5 ng/ml with 58% sensitivity, 82% specificity, 78% PPV, 72% NPV and accuracy of 72%, AUC=0.688, Fig (1).

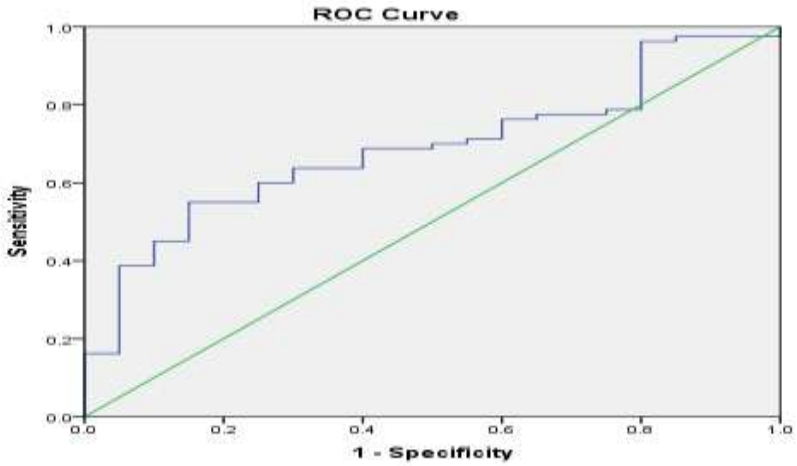

Fig (1) ROC curve for differentiation between control group and cases with ACS according to chemerin levels.

Chemerin has more sensitivity compared to troponin in detecting cases with ACS. Nevertheless, specificity was higher for troponin, Table (4).

Table (4) Chemerin versus troponin in detecting ACS cases.

	Sensitivity	Specificity	PPV	NPV	Accuracy
Chemerin	74.6%	82%	78%	72%	72%
Troponin	85.5%	93%	100%	36.4%	80.3%

4. Discussion

In this investigation, the middle degree of chemerin in the benchmark group was 115 with range somewhere in the range of 111 and 292.1 while in the ACS bunch the level was 268.8 with range somewhere in the range of 127 and 798.3 in the ACS bunch with genuinely huge distinction between the two gatherings ($p < 0.001$).

This came in concurrence with Hamdy et al. who indicated that chemerin levels were altogether higher in diabetic patients than in solid subjects (57.65 versus 28.8 ng/l – $P < 0.0001$). Additionally, the creators announced that chemerin levels were altogether higher in cardio-diabetic patients than in sound subjects and diabetic patients (93.97 versus 57.65 – $P < 0.0001$) [8].

This additionally came as per Wang and Zhang who found that serum chemerin levels of coronary course sickness (CAD) patients were altogether higher than that of control subjects [9].

When looking at the subgroups of ACS in this investigation, The middle Chemerin level in the cases with UA was 276.4 with range somewhere in the range of 133.2 and 588.3, in the cases with STEMI the middle degree of Chemerin was 231.32 with range somewhere in the range of 127 and 290.3 while the middle level in the cases with NSTEMI was 292.8 with range somewhere in the range of 141.8 and 798.3 with mellow critical level between the three gatherings ($p=0.086$).

Nonetheless, Liang et al.[10] who found that the degree of chemerin was altogether higher in the intense myocardial localized necrosis (AMI)and unsteady angina(UA) bunches than in the steady angina (SA) and control gatherings.

Ateş et al. [11] announced that the serum chemerin levels were altogether expanded in patients with STEMI when contrasted with cases with stable angina pectoris (521.0 ± 157.2 versus 268.3 ± 86.4 individually).

In our investigation, there was genuinely huge positive relationship between's Chemerin level and BMI, cholesterol, TG, LDL, and every cardiovascular score ($p < 0.05$). This demonstrates that chemerin levels correspond with the danger variables of ischemia in ACS cases.

This came in concurrence with Yan et al. in an investigation of 430 subjects that went through coronary angiography CAD was decidedly connected with expanding serum chemerin levels and this affiliation stayed critical subsequent to adapting to age, sex, and other set up danger factors for CAD. The chances proportions (95% CI) of CAD across expanding quartiles of serum chemerin were 1.04 (0.61–1.78), 1.08 (0.63–1.83), and 1.87 (1.07–3.24), ($P = 0.386$, 0.508, and 0.012, separately) [12].

Ateş and his partners Serum chemerin levels were discovered to be essentially corresponded with CRP levels ($r = 0.47$, $p < 0.001$) and top CK-MB levels ($r =$

0.376, p < 0.001). Nonetheless, there was no relationship between's the serum chemerin levels and Gensini score (r = 0.083, p = 0.355) [11].

Hamdy et al. who uncovered a critical positive relationship between's serum chemerin level and cholesterol, TG, CRP, FBG, andHbA1Cin type2 diabetes mellitus gathering, and cardio-diabetic patients [8].

Wang and Zhang found a critical positive relationship between serum chemerin and fatty substances, and high-affectability CRP in CAD patients [9].

Osman et al. discovered that serum chemerin level was emphatically associated with all out cholesterol, LDL-C and fatty oils in sort 2 diabetes mellitus bunch [13].

Moreover, Ji et al. exhibited that CRP, which is a set up marker of aggravation, was emphatically corresponded with chemerin in intense coronary disorder (ACS) patients. The creators likewise discovered critical yet powerless connections between's serum chemerin fixations and fasting glucose, fatty oil, complete cholesterol, LDL-cholesterol and hsCRP in CAD patients [14].

Gao et al. thought about chemerin mRNA articulation in epicardial fat tissue from patients with and without CAD, exhibiting that chemerin mRNA articulation in epicardial fat is emphatically connected with the presence and seriousness of CAD. These affiliations remained genuinely critical even after change for age, sex, BMI and midsection boundary [15].

In this examination, the best cutoff purpose of Chemerin to anticipate the event of ACS was >249.5 ng/ml with 74.6% affectability, 82% explicitness, 78% PPV, 72% NPV and precision of 72%. The region under the bend was 0.688.

Nonetheless, Hamdy et al. [8] announced lower an incentive for chemerin, that was75 ng/ml, Area under bend (AUC) for chemerin was 0.877. This outcome shows the great legitimacy of the above biochemical marker to separate diabetic patients than cardio-diabetic patients.

The distinction between the current investigation and this examination could be clarified by the way that the patient in the last investigation was all diabetic with higher weakness to create cardiovascular entanglements including ACS.

Sell et al. clarified these discoveries by the way that fat tissue communicates chemerin and chemokine-like receptor-1, and arrival of chemerin is identified with the volume of adipocyte. Besides, the arrival of the high centralization of chemerin is identified with insulin obstruction at the degree of lipogenesis by its reversible official to the extracellular space of insulin receptor-tyrosine kinase in fringe tissues and diminishing the pace of auto-phosphorylation and resulting downstream intracellular flagging falls [16].

5. Conclusion

In light of our examination results, chemerin can be utilized as a possible marker for ACS cases. Likewise, its levels fundamentally relate with the level of ischemia in ACS cases as per the gensini score, vessel score and seriousness score. Henceforth, it very well may be useful in controlling the administration methodology.

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