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ESTIMATION OF CARBAMYLATED-LDL IN PATIENTS WITH CORONARY ARTERY DISEASE

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Abstract

Back ground: This study examined the associations between emerging lipid biomarkers, Carbamylated-LDL (C-LDL), and coronary artery disease (CAD). Globally, cardiovascular disease (CVD) continues to be the leading cause of death, with CAD playing a major role. Elevated carbamylated low-density lipoprotein (C-LDL) levels are one of the major risk factors for CAD. The development of atherosclerosis, a disorder marked by the buildup of lipid-laden plaques within artery walls, is linked to C-LDL and is known to cause decreased blood flow and possibly even heart attacks. High C-LDL levels have been strongly correlated with an increased incidence of CAD, as numerous investigations have shown. A number of therapeutic approaches have demonstrated effectiveness in lowering C-LDL levels and the risk of CAD, including lipid-lowering medications, statins, and lifestyle changes. This presentation highlights the continuous need for efficient therapeutic interventions by emphasizing the significance of C-LDL control in the prevention and treatment of CAD.

Objective: This study set out to determine whether there is a link between serum C-LDL levels and the likelihood and severity of CAD, to assess the inflammatory response following acute presentation with CAD .

Materials and Methods: A case-control study involving 138 subjects; 88 CAD patients, and 50 healthy individuals as a control who aged 40-75 years, was carried out. Serum C-LDL levels were made use of an ELISA technique

Results: The study revealed a significant increase in serum C-LDL levels when comparing patients to healthy control groups (19.0892 ±7.09962 pg/ml Vs 0.8136±0.11488 pg/ml, P =0.0000) respectively. The analysis of the receiver operating curve (ROC) for C-LDL showed that C-LDL is high AUC,

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which was 1.00 [95% CI (confidence interval) =1.00-1.00], sensitivity % =1, specificity % =1, cut-off points =1.677.
Conclusion: Patients who suffer from coronary artery disease and coronary arteries had higher level of C-LDL.
Key Words: Carbamylated-LDL, CAD, Inflammation, cytokine ,plaque

INTRODUCTION

Coronary artery disease (CAD), also known as coronary heart disease, is a prevalent type of heart illness characterized by the narrowing of coronary arteries due to plaque buildup, leading to reduced blood flow to the heart muscle [1]. This condition, primarily caused by atherosclerosis, can take years to manifest and often presents symptoms like breathlessness and chest discomfort, potentially culminating in a heart attack due to a complete blockage of blood supply. Treatment options for CAD include surgery and medication, while preventive measures such as maintaining a balanced diet, regular exercise, and smoking cessation can help mitigate the risk factors associated with the disease [1].

Globally, the burden of heart disease, including CAD, has been increasing over the past decades, emphasizing the importance of targeted prevention and control strategies to address this growing health concern [2].While low-density lipoprotein (LDL) is altered to become carbamylated-LDL (C-LDL) when isocyanic acid is added non-enzymatically to the lysine residues of apolipoprotein B-100, a crucial protein component of LDL. This process, called carbamylation, can take place in individuals with chronic kidney disease (CKD) or other disorders where urea levels are high [3-7]. Carbamylated low-density lipoprotein (C-LDL) plays a significant role in the pathogenesis of coronary artery disease (CAD) by promoting foam cell formation in the artery wall. Additionally, C-LDL contributes to endothelial dysfunction by reducing nitric oxide synthesis, leading to impaired vascular health and atherosclerosis progression.

The pro-inflammatory nature of C-LDL compared to native LDL enhances inflammatory reactions, increasing the likelihood of acute coronary events and unstable plaque development. Moreover, C-LDL exacerbates oxidative stress within the vascular system, further accelerating atherosclerosis and causing damage to endothelial cells [8]. Patients with chronic kidney disease (CKD) are at a higher risk of CAD due to elevated levels of carbamylated proteins, including C-LDL, associated with increased urea levels in this population [9].

MATERIALS AND METHODS

In the study used a case-control research approach, data was collected from 138 subjects obtained from AL-Najef Heart Center (AL-Sadder Hospital) in Najef , Iraq. Directorates between Feb, 2023 and Nov., 2023. The subjects, aged ranged between 40 to 75 years, were divided into two groups: 88 patients with CAD and 50 apparently healthy as a control group. The Sandwich-ELISA method was used to measure the levels of serum C-LDL (sunlong biotech , China), and a SMART-120 chemistry analyzer was used to measure the levels of lipid profiles and other compounds in human serum. (colorimetric enzymatic method). The BMI is expressed as kg/mˆ2, which is the result of dividing the

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weight (in kg) by the square of the height (in m) [10].The questionnaire gathered demographic data such as sex, age, smoking status, sedentary lifestyle, and family history of CAD for both patients and healthy controls. Exclusion criteria included subjects with chronic diseases like diabetes, cirrhosis, end-stage renal disease (ESRD), acute heart failure, stroke, skeletal muscle injury, malignancy, endocrine dysfunction, and other inflammatory conditions .

STATISTICAL ANALYSIS

Using SPSS software, version 17.0 (SPSS Inc., Chicago, IL, USA), statistical analysis was carried out. To determine if the distribution of continuous variables was normal, Continuous variables were presented as median and interquartile range or as mean ± SD. The examination of variables with a normal distribution comprised... Spearman's correlations were used to examine the relationship between the variables. at $p = 0.00$, the significance level was established. Serum concentration of C-LDL and were determined using commercially available ELISA kits (sunlongbiotceh,china) . all the tests were performed according to the manufacturer's instructions.

RESULT

The clinical characteristics and metabolic parameters of the study participants are summarized in Table 1-1,1-2,1-3. The table 1-1 study compared various lipid parameters between patients and control groups, revealing significant differences. The mean C-LDL levels were markedly higher in patients (19.0892 ± 7.09962 pg/ml) compared to controls (0.8136 ± 0.11488 pg/ml, $p = 0.000$). Total cholesterol (TC) was also significantly elevated in patients (227.4476 ± 76.71572 mg/ml) versus controls (160.8959 ± 68.59730 mg/ml, $p = 0.000$). Triglyceride (TG) levels were substantially higher in the patient group (160.8959 ± 68.59730 mg/ml) than in controls (51.5274 ± 36.49274 mg/ml, $p = 0.000$). Conversely, HDL-C levels were significantly lower in patients (24.0731 ± 7.774 mg/ml) compared to the control group (48.1409 ± 7.62331 mg/ml, $p = 0.000$). Additionally, LDL-C levels were elevated in patients (178.6470 ± 75.088 mg/ml) versus controls (136.8607 ± 68.175 mg/ml, $p = 0.001$), and VLDL-C levels were also higher in patients (10.4487 ± 7.23854 mg/ml) compared to controls (8.1845 ± 4.54163 mg/ml, $p = 0.025$). These findings indicate significant lipid profile differences between patients and healthy controls, suggesting a strong association between altered lipid metabolism and the studied condition.

The table 2-1 show the relationships between circulating(carbamylated) levels of low-density lipoprotein (C-LDL) and a number of indicators in both healthy controls and patients with coronary artery disease (CAD). C-LDL levels were not significantly correlated with age, BMI, cholesterol, triglycerides, iron, low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), high-density lipoprotein (HDL), alkaline phosphatase (ALP), calcium, sodium, potassium, or zinc in patients with CAD.

The Receiver Operating Characteristic (ROC) curve for C-LDL in individuals with Coronary Artery Disease (CAD) is shown in Figure 3-1. A graphical representation known as the ROC curve illustrates the C-LDL testing system's diagnostic capacity as a function of the discrimination threshold. Plotting the real positive rate (sensitivity) versus the false positive rate (specificity) at different threshold values is how it is created. A single indicator of overall accuracy is the area under the ROC curve (AUC);

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a value of 1 denotes perfect accuracy, while a value of 0.5 denotes no discriminative power. This curve is essential for evaluating CLDL's efficacy and dependability as a biomarker for CAD diagnosis. In the patient group, the level of were C-LDL plotted using ROC curves. The cut-off values and AUC were derived based on the specificity and sensitivity of the test. In the patient group, C-LDL is high AUC, which was 1.00 [95% CI (confidence interval) =1.00-1.00], sensitivity % =1, specificity % =1, cut-off points =1.677 (Table3, Figure2).

Table1.1. Comparison of C-LDL level in patients and healthy groups with p =0.000.

Parameter	Patients Mean±SD	Control Mean±SD	P-value
C-LDL pg/ml	19.0892 ±7.09962	0.8136±0.11488	0.000
TC mg/ml	227.4476±76.71572	160.8959±68.59730	0.000
TG mg/ml	160.8959±68.59730	51.5274±36.49274	0.000
HDL-C mg/ml	24.0731±7.774	48.1409±7.62331	0.000
LDL-C mg/ml	178.6470±75.088	136.8607±68.175	0.001
VLDL-C mg/ml	10.4487±7.23854	8.1845±4.54163	0.025

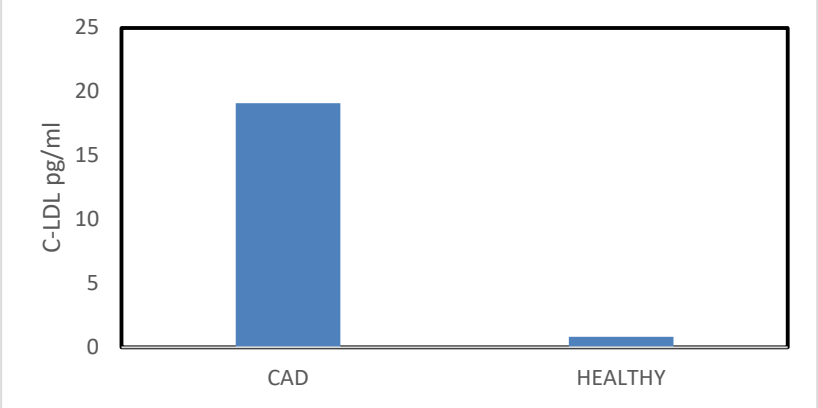

Figure 1: The difference in the mean levels of C-LDL between CAD and the control group (T-test was used significantly at p =0.00).

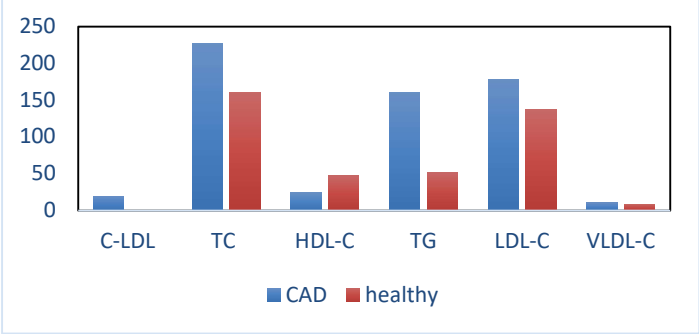

Figure 2: The difference in mean levels of C-LDL and the lipid profile between CAD and control group

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(T-test was used significantly at p =0.00)

Table2. 1: Correlations between C-LDL and parameters in patients and healthy groups

Variables	Groups			
	CAD Patients		Controls	
	r	p	r	p
Age	-.019	0.859	-.004	.977
BMI(kg/m^2)	-0.062	0.559	0.071	0.626
Cholesterol mg/ml	-0.089	0.40	0.106	0.515
TG mg/ml	-0.089	0.403	0.004	0.978
HDL mg/ml	0.115	0.282	0.147	0.372
LDL mg/ml	-0.109	0.305	-0.152	0.350
VLDL mg/ml	0.075	0.485	0.106	0.515
Iron µg/dl	-0.131	0.220	-0.041	0.800
ALP U/L	-0.034	0.751	0.007	0.965
Ca mg/dl	-0.048	0.653	-0.021	0.897
Na mmol/l	-0.036	0.736	0.159	0.326
K mmol/l	0.017	0.872	0.046	0.776
Zn µg/dl	-.032	0.766	.099	.544

T-test was *: significant at p ≤ 0.05 SD: standard deviation; S: significant; TC: Total cholesterol; LDL-C: Low-density lipoprotein cholesterol; TG: Triglycerides; HDL-C: High-density lipoprotein cholesterol; VLDL-C: Very low-density lipoprotein cholesterol BMI: Body mass index.

DISSCUSION

Prior to now, protein carbamylation has only been quantitatively significant across the spectrum of renal diseases because uremia creates an environment that is conducive to this posttranslational modification.[11,12] Numerous investigations have indicated that carbamylation—and specifically C-

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LDL—may have a significant role in the increased incidence of cardiovascular disease (CVD) in individuals with chronic kidney disease (CKD)[13-16]. Elevated levels of low-density lipoprotein cholesterol (LDL-C) have been strongly linked to a higher risk of coronary heart disease (CAD) in observational studies [17] [18]. Clinical trials have demonstrated that reducing LDL-C levels significantly decreases the incidence of CAD events, with statins and other lipid-lowering medications being effective in this regard [19] [20]. Specifically, statin therapy has been shown to lower LDL-C levels in high-risk patients, leading to a reduction in heart attacks and strokes, highlighting the importance of managing LDL-C levels in preventing cardiovascular events [19]. This evidence underscores the critical role of LDL-C in CAD development and the effectiveness of interventions targeting LDL-C reduction in mitigating CAD risk.

In table 1-1 comparative study investigating C-LDL levels, it was found that patients had a significantly higher mean C-LDL level of compared to a healthy control group with a lower mean C-LDL level, indicating a substantial difference between the two groups. This disparity in C-LDL levels was statistically significant with a p-value of 0.000, highlighting the importance of C-LDL levels as a potential marker in distinguishing between patients and healthy individuals. The study underscores the relevance of monitoring C-LDL levels in clinical settings to assess cardiovascular risk and metabolic conditions, emphasizing the significance of lipid profiles in disease prevention and management [21,22]. C-LDL levels also did not significantly correspond with t parameters in the control group in table2-1 [23]. These findings demonstrate the independence of C-LDL levels from these measures in both CAD patients and healthy controls, implying that C-LDL levels do not significantly correlate with the parameters listed. The Receiver Operating Characteristic (ROC) curve for C-LDL in individuals with Coronary Artery Disease (CAD) is shown in Figure 3-1. This curve is essential for evaluating CLDL's efficacy and dependability as a biomarker for CAD diagnosis.

Through a variety of approaches, carbamylated low-density lipoprotein (C-LDL) has emerged as a critical biomarker of coronary artery disease (CAD), significantly impacting the progression of atherosclerosis. Increased recruitment of immune cells, lipid accumulation in macrophages, decreased endothelial repair, and endothelial dysfunction are associated with elevated C-LDL levels [24]. In addition, C-LDL interacts with LOX-1, the lectin-like receptor for oxidized LDL, to promote the development of atherosclerosis and vascular inflammation [25]. Altered high-density lipoprotein (HDL) C-LDL in diabetic patients promotes atherosclerosis by enhancing monocyte adhesion and stimulating pro-inflammatory pathways, which helps in the formation of CAD [26]. Moreover, decarbonylated LDL, a critical component of atherosclerosis, causes vascular damage and endothelial dysfunction, highlighting the role that LDL modifications play in the pathophysiology of CAD [27]. These results highlight the importance of C-LDL as a powerful biomarker for and relation to CAD in atherosclerosis by way of inflammation, oxidative stress, and endothelial dysfunction.

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Table3. 1: Receiver operating characteristic of C-LDL in patients with CAD

Parameter	UAC	Cut-off	Sensitivity	Specificity	CI 95%	P-value
C-LDL pg/ml	1.00	1.677	1.00	1.00	1.00-1.00	0.000

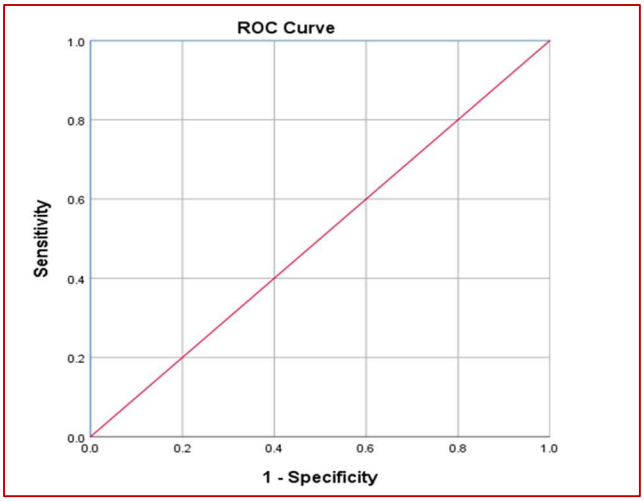

Figure 3: Receiver operating characteristic (ROC) curve of C-LDL in CAD patients

CONCLUSION

The serum concentration of C-LDL is elevated in patients with CAD. the onset and course of coronary artery disease are significantly influenced by the presence of C-LDL. By encouraging inflammation, foam cell production, endothelial dysfunction, and oxidative stress, C-LDL quickens the atherosclerotic process and raises the risk of cardiovascular outcomes. improved CAD preventive and treatment plans may result from a greater understanding of and focus on C-LDL.

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CONFLICT OF INTEREST

All parties involved certify that there is none. The donors had no input with the creation of the lesson, the gathering, analysing, or interpreting of data, the drafting of the manuscript, or the making of decisions.Release the findings.

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