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The Role of IL-6 in Patients with Coronary Artery Disease

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ABSTRACT

Background: *One of the main causes of morbidity and death in the globe is coronary artery disease (CAD). The development and progression of atherosclerosis, which is typified by lipid buildup and plaque formation inside the artery walls, are significantly influenced by inflammation. One significant pro-inflammatory cytokine that has been linked to metabolic and cardiovascular conditions is interleukin-6 (IL-6). Atherosclerotic plaque development, lipid abnormalities, and endothelial dysfunction may all be exacerbated by elevated IL-6 levels. As a result, IL-6 has been proposed as a possible biomarker for CAD risk assessment and early identification.* ***Objective:*** *This study aimed to evaluate the association between serum IL-6 levels and coronary artery disease and to investigate the relationship between IL-6 and lipid profile parameters in patients compared with healthy individuals.* ***Materials and Methods:*** *A case–control study was conducted on 172 participants, including 86 CAD patients and 86 apparently healthy individuals as a control group. The participants were adults with comparable age ranges. Serum IL-6 levels were measured and several biochemical parameters were evaluated, including body mass index (BMI) and lipid profile markers such as triglycerides (TG), total cholesterol, HDL, LDL, and VLDL. Statistical analysis was performed to determine differences between groups, correlations among variables, and the diagnostic value of IL-6 using receiver operating characteristic (ROC) curve analysis.* ***Results:*** *The results showed a significant increase in serum IL-6 levels in CAD patients compared with the control group (0.6289 ± 0.448 vs 0.0935 ± 0.06254, P = 0.000). Significant differences were also observed in lipid profile parameters, where TG, total cholesterol, and VLDL levels were higher in patients, while HDL levels were significantly lower compared with controls. Correlation analysis indicated associations between IL-6 and several lipid parameters. ROC curve analysis demonstrated that IL-6 had good diagnostic performance for distinguishing CAD patients from controls, with an area under the curve (AUC) of 0.772 and a 95% confidence interval ranging from 0.697 to 0.846.* ***Conclusion:*** *The findings of this study indicate that IL-6 levels are significantly elevated in patients with coronary artery disease and may be associated with lipid metabolism disturbances and inflammatory processes. These results suggest that IL-6 may serve as a useful biomarker for the detection and evaluation of CAD risk.*

Keywords: Interleukin-6, Coronary artery disease, Inflammation, Lipid profile, Atherosclerosis.

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INTRODUCTION

A common kind of heart disease, coronary artery disease (CAD), sometimes called coronary heart disease, is defined by the narrowing of coronary arteries as a result of plaque accumulation, which lowers blood flow to the heart muscle. This disease, which

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is mostly brought on by atherosclerosis, can take years to show symptoms, such as dyspnea and chest pain, and may eventually result in a heart attack because of a total blockage of blood flow. While preventive actions including eating a balanced diet, exercising frequently, and quitting smoking can help reduce the risk factors linked to the condition, treatment options for CAD include surgery and medication[1-2].

The burden of heart disease, including CAD, has been rising globally over the past few decades, underscoring the significance of focused prevention and control measures to address this expanding health issue [3]. The pro-inflammatory cytokine interleukin-6 (IL-6) is essential to the inflammatory mechanisms that underlie coronary artery disease and atherosclerosis. Macrophages, endothelial cells, and vascular smooth muscle cells are among the cell types that release IL-6, especially in reaction to inflammatory stimuli within the arterial wall.[4-6].

By decreasing nitric oxide bioavailability and increasing vascular inflammation, elevated IL-6 levels have been linked to endothelial dysfunction and the advancement of atherosclerosis. Additionally, IL-6 increases the hepatic synthesis of acute-phase reactants such C-reactive protein (CRP), which intensifies systemic inflammation and is closely linked to cardiovascular risk[7-8].
IL-6's pro-inflammatory properties intensify inflammatory cascades in atherosclerotic plaques, raising the risk of acute coronary events and plaque instability. Additionally, IL-6 accelerates the development of plaque and vascular damage by causing oxidative stress and encouraging the recruitment of inflammatory cells to the vascular endothelium [8]. Increased circulating levels of inflammatory cytokines, such as IL-6, which are linked to higher cardiovascular morbidity and mortality in this population, contribute to the increased risk of CAD in patients with chronic kidney disease (CKD) [9-10].

MATERIALS AND METHODS

The study used a case control research approach, data was collected from 172 subjects obtained from AL-Najef Heart Center (AL-Sadder Hospital) in Najef , Iraq. Directorates between Feb, 2025 and Nov., 2025. The subjects, aged ranged between 30 to 70 years, were divided into two groups: 86 patients with CAD and 86 apparently healthy as a control group. The Sandwich-ELISA method was used to measure the levels of serum IL-6 (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 weight Kg to the square height m^2 [11].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. Continuous variables were provided as mean ± SD or as median and interquartile range in order to assess if the distribution was normal. The variables with a normal distribution that were examined included. Spearman's correlations were used to examine the relationship between the variables. at p = 0.00, the significance level was established. Serum concentration of IL-6 and determined using commercially available ELISA kits (sunlongbiotceh,china) . all the

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tests were performed according to the manufacturer's instructions.

RESULTS

Table 1 shows the comparison of several biomarkers between patients and control groups. The mean level of INL-6 in patients (0.6289 ± 0.448) was significantly higher than in controls (0.0935 ± 0.06254) with a P-value of 0.000. The mean age of patients was 46.7093 ± 7.01572 years compared with 44.2381 ± 9.86312 years in the control group, showing no significant difference (P = 0.091). BMI was significantly higher in patients (27.0654 ± 4.79224) than in controls (24.8882 ± 2.47938) with a P-value of 0.000. The level of triglycerides (TG) was also significantly increased in patients (71.3171 ± 19.666) compared to controls (44.3738 ± 16.422) (P = 0.000). Similarly, total cholesterol (CHLOST) was higher in patients (234.5057 ± 121.33) than in controls (173.4931 ± 7.996) with a significant difference (P = 0.000). In contrast, HDL levels were significantly lower in patients (29.4575 ± 10.439) compared with controls (62.9360 ± 49.353) (P = 0.000). LDL showed a statistically significant difference between patients (114.4748 ± 58.273) and controls (129.2695 ± 26.295) with a P-value of 0.033. Finally, VLDL levels were significantly higher in patients (20.3732 ± 5.6943) compared to controls (4.5321 ± 2.77600) (P = 0.000). Overall, most biomarkers showed significant differences between the patient and control groups except age.

Table 1. Comparison of IL-6 level in patients and healthy groups with p =0.000.

Biomarkers	Case	N	Mean± St. Deviation	P-value
INL-6	Patients	86	0.6289± .448	0.000
	Control	86	0.0935 ± 0.06254	
Age	Patients	86	46.7093±7.01572	0.091
	Control	86	44.2381±9.86312	
BMI	Patients	86	27.0654±4.79224	0.000
	Control	86	24.8882±2.47938	
TG	Patients	86	71.3171±19.666	0.000
	Control	86	44.3738±16.422	
CHLOST	Patients	86	234.5057±121.33	0.000
	Control	86	173.4931±7.996	
HDL	Patients	86	29.4575±10.439	0.000
	Control	86	62.9360±49.353	
LDL	Patients	86	114.4748±58.273	0.033
	Control	86	129.2695±26.295	
VLDL	Patients	86	20.3732±5.6943	0.000
	Control	86	4.5321±2.77600	

The **table 2** show the comparison of biomarkers between male and female participants in both patient and control groups. The mean level of INL-6 was significantly higher in male patients (0.7018 ± 0.46535) compared with male controls (0.1201 ± 0.05482) (P = 0.001), and it was also higher in female patients (0.3097 ± 0.11138) than in female controls (0.0285 ± 0.01209) (P = 0.000). For triglycerides (TG), male patients showed a mean value of 51.1237 ± 21.69618 compared with 55.5911 ± 7.31473 in controls, while female patients had higher values (84.2744 ± 19.33779) compared with female controls (61.3652 ± 9.42782), with significant differences (P = 0.000 and P

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= 0.009). Total cholesterol (CHLOST) was markedly elevated in male patients (161.4040 ± 42.39683) compared with male controls (59.2039 ± 13.35929), and in female patients (230.8331 ± 36.73218) compared with female controls (72.0422 ± 19.38046), showing highly significant differences (P = 0.000 and P = 0.001). For HDL, male patients had a mean value of 28.7301 ± 11.36843 compared with 171.9279 ± 6.99313 in controls, while female patients showed 32.6401 ± 3.13273 compared with 177.3124 ± 9.09766 in controls, with statistical significance between sexes (P = 0.178 and P = 0.012). LDL levels were 98.6492 ± 49.85183 in male patients and 123.9552 ± 22.61249 in male controls, while female patients had higher levels (183.7116 ± 39.10428) compared with female controls (142.2363 ± 30.39082), with significant differences (P = 0.000 and P = 0.001). Finally, VLDL levels were higher in male patients (20.774 ± 6.20368) than in controls (15.4256 ± 4.74823), whereas female patients showed 18.6164 ± 1.61542 compared with 18.8597 ± 6.67194 in controls, with significant differences (P = 0.000 and P = 0.025). Overall, several biomarkers showed significant variations between patients and controls as well as between males and females.

Table 2. Correlations between IL-6 and parameters in patients and healthy groups.

Biomarker	Sexual	Patient Mean±Std. Deviation	Control Mean±Std. Deviation	P-value
INL6patient	Males	0.7018±0.46535	0.1201±0.05482	0.001[a]
	Females	0.3097±0.11138	0.0285±0.01209	0.000[b]
TGpatient	Males	51.1237±21.69618	55.5911±7.31473	0.000[a]
	Femaless	84.2744±19.33779	61.36529.42782	0.009
CHLOSTpatient	Males	161.4040±42.39683	59.2039±13.35929	*0.000[a]*
	Females	230.8331±36.73218	72.0422±19.38046	0.001 [b]
HDLpatient	Males	28.7301±11.36843	171.9279±6.99313	0.178 [a]
	Females	32.6401±3.13273	177.3124±9.09766	0.012
LDLpatient	Males	98.6492±49.85183	123.9552±22.61249	0.000[a]
	Females	183.7116±39.10428	142.2363±30.39082	0.001 [b]
VLDLpatient	Males	20.774±6.20368	15.4256±4.74823	0.000[a]
	Females	18.6164±1.61542	18.8597±6.67194	0.000[a] 0.025 [b]

a. between males and females of patients same group.
b between males and females of controls same group.

Table 3 presents the Pearson correlation analysis between biomarkers in patients and control groups. In patients, HDL showed a significant positive correlation (r = 0.463, P = 0.000), whereas in the control group it showed a weak negative correlation (r = −0.227, P = 0.036). Total cholesterol (CHLOST) showed no significant correlation in patients (r = −0.011, P = 0.923), while in controls it showed a weak negative correlation that was statistically significant (r = −0.217, P = 0.044). Triglycerides (TG) demonstrated a weak negative correlation in patients (r = −0.104, P = 0.343) and also a weak negative correlation in controls (r = −0.211, P = 0.051), but these were not statistically significant. Similarly, LDL showed a very weak negative correlation in

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patients (r = −0.020, P = 0.854) and in controls (r = −0.204, P = 0.060), with no significant association. In contrast, VLDL presented a weak negative correlation in patients (r = −0.126, P = 0.249), which was not significant, while in the control group it showed a strong negative correlation that was highly significant (r = −0.438, P = 0.000). Overall, the results indicate that HDL in patients and VLDL in controls showed the most significant correlations compared with the other biomarkers.

Table 3. Pearson correlation between IL-6 and parameters in patients and healthy groups.

Biomarker		Patient	Control
HDL patient	Pearson Correlation	.463**	-.227*
	Sig. (2-tailed)	.000	.036
	N	86	86
CHLOST patient	Pearson Correlation	-.011	-.217*
	Sig. (2-tailed)	.923	.044
	N	86	86
TG patient	Pearson Correlation	-.104	-.211
	Sig. (2-tailed)	.343	.051
	N	86	86
LDL patient	Pearson Correlation	-.020	-.204
	Sig. (2-tailed)	.854	.060
	N	86	86
VLDL patient	Pearson Correlation	-.126	-.438**
	Sig. (2-tailed)	.249	.000
	N	86	86

The Receiver Operating Characteristic (ROC) curve analysis demonstrated that the biomarker had a good diagnostic performance in distinguishing patients from controls. The area under the curve (AUC) was 0.772, indicating a moderate to good level of accuracy. The standard error was 0.038, and the result was statistically significant with a P-value of 0.0001, rejecting the null hypothesis that the true area equals 0.5. Furthermore, the 95% confidence interval ranged from 0.697 to 0.846, suggesting reliable discriminatory ability. Overall, the ROC curve shows that the tested marker possesses acceptable sensitivity and specificity for differentiating between patient and control groups. Shows **Table 4 and Figure 1.**

Table 4. Receiver Operating Characteristic (ROC) Analysis.

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.772	.038	.000	.697	.846
a. Under the nonparametric assumption				
b. Null hypothesis: true area = 0.5				

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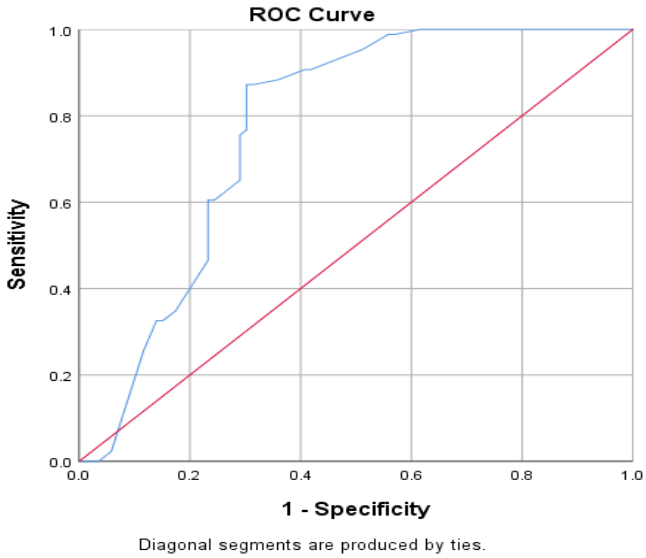

Figure 1: Receiver operating characteristic (ROC) curve of IL-6.

DISSCUSION

The present study aimed to evaluate the relationship between inflammatory biomarkers and lipid profile parameters in patients compared with healthy control subjects. The results of the current study demonstrated significant differences in several biochemical parameters between the two groups, indicating a possible interaction between inflammation and lipid metabolism in the pathogenesis of the disease.

Interleukin-6 (IL-6) levels were substantially greater in patients than in the control group, according to the results shown in Table 1. An essential pro-inflammatory cytokine, IL-6 is crucial for immunological control and inflammatory processes. Numerous inflammatory and cardiovascular disorders have been linked to elevated IL-6 levels, which may indicate that patients have systemic inflammation. These findings are in line with earlier research showing a link between elevated IL-6 levels and both increased cardiovascular risk and disease progression (12).

Furthermore, there was no discernible age difference between the patients and controls in this investigation, suggesting that the age distribution of the two groups was quite similar. Age is therefore unlikely to have an impact on the observed biochemical differences. However, when compared to controls, patients' body mass index (BMI) was noticeably greater. Obesity and metabolic disorders, which are known to increase inflammatory reactions and contribute to the development of metabolic and cardiovascular diseases, are frequently linked to elevated BMI (13).

Significant alterations in the parameters of the lipid profile were also shown by the results. In particular, patients had significantly higher levels of triglycerides (TG), total cholesterol (CHLOST), and very-low-density lipoprotein (VLDL) than controls. Atherosclerosis and metabolic problems are frequently linked to elevated levels of these lipids, which are thought to be significant risk factors for cardiovascular illnesses. Atherosclerotic plaque development and endothelial dysfunction have been linked to aberrant lipid metabolism, according to earlier research (14).

Conversely, the present study found that high-density lipoprotein (HDL) levels were significantly lower in patients compared with the control group. HDL is commonly referred to as the “good cholesterol” because it plays a protective role in cardiovascular health by

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facilitating reverse cholesterol transport and removing excess cholesterol from peripheral tissues. Reduced HDL levels may therefore increase the risk of cardiovascular complications (15). In addition, low-density lipoprotein (LDL) showed significant differences between patients and controls, further supporting the presence of lipid abnormalities in patients.

The impact of sex variations on biomarker levels was investigated in the results shown in Table 2. According to the study, both male and female patients had greater levels of IL-6 than the corresponding control groups, indicating that inflammation is prevalent in both sexes. Nonetheless, some differences in lipid profile parameters were noted between males and females. Certain lipids, especially LDL and total cholesterol, were more common in female individuals. These discrepancies could be explained by sex-specific hormonal and metabolic changes that affect inflammatory reactions and lipid metabolism (16).

Additionally, the correlation analysis shown in Table 3 assessed the connection between lipid profile characteristics and IL-6. The findings showed a strong positive association between IL-6 and HDL in patients, indicating that inflammatory activity may cause changes in HDL levels. On the other hand, although these relationships were typically weak and not statistically significant, negative correlations were found between IL-6 and other lipid markers such total cholesterol, triglycerides, LDL, and VLDL. These results imply that there may be several regulatory mechanisms involved in the intricate link between inflammation and lipid metabolism. According to earlier studies, inflammatory cytokines can affect hepatic lipid synthesis and lipoprotein formation, which in turn can affect lipid metabolism (17–18).

The diagnostic performance of IL-6 as a potential biomarker for differentiating patients from healthy persons was assessed using the Receiver Operating Characteristic (ROC) curve in addition to the biochemical analyses. According to the ROC analysis, the diagnostic accuracy was moderate to good, with an area under the curve (AUC) of 0.772. For diagnostic purposes, an AUC value between 0.7 and 0.8 is typically regarded as appropriate. The outcome was statistically significant (P = 0.000), indicating that IL-6 can significantly distinguish between patients and controls. Additionally, a dependable degree of diagnostic performance was shown by the confidence interval. These results provide credence to the possibility of using IL-6 as a biomarker for illness monitoring and identification (19–20).

Overall, the findings of the present study suggest that patients exhibit both increased inflammatory activity and significant disturbances in lipid metabolism. The elevation of IL-6 together with abnormal lipid profile parameters highlights the possible interaction between inflammatory processes and metabolic abnormalities. Such interactions may contribute to disease progression and increase the risk of cardiovascular complications.

CONCLUSION

According to the current study, IL-6 levels were significantly higher in patients than in healthy controls, suggesting that inflammation plays a substantial role in the illness. Significant abnormalities in lipid profile measures were also noted, such as elevated levels of TG, CHLOST, LDL, and VLDL and lower levels of HDL in the patients. These results imply that dyslipidemia is present and linked to the illness. A correlation between lipid characteristics and inflammatory indicators was revealed by correlation analysis.

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Furthermore, IL-6 has a moderate diagnostic value in differentiating patients from controls, according to ROC analysis.

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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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