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Assessment Of Chemerin Levels and Some Biochemical Indicators In Patients with Cardiovascular Diseases In The City of Samarra.

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Abstract

Diseases of the heart and blood vessels (CVD) are the leading cause of death worldwide, remaining an important concern for researchers, doctors, and patients alike. CVD encompasses a wide range of diseases that affect the heart, blood vessels, and blood. The study collected 80 blood serum samples, including 55 samples from patients with coronary artery disease and 25 healthy samples serving as a control group, collected from outpatient clinics in Samarra city from april 2023 to November 2023, with ages ranging from 25 to 55 years. The purpose was to evaluate the levels of chemerin , Superoxide Dismutase (SOD), Total Cholesterol (TC), Low-density lipoprotein (LDL-c), High-density lipoprotein (HDL-c), and Triglycerides (TG) in the coronary artery disease group and the control group. The results showed a significant increase ($P \leq 0.05$) in chemerin, TC, LDL-c, and TG levels in the patient group compared to the control group, as well as a significant decrease ($P \leq 0.05$) in SOD and (HDL-c) levels in the patient group compared to the control group. The area under the curve for chemerin and other measurements showed excellent accuracy in diagnosing the disease, in addition to high sensitivity and specificity, indicating the precision of the measurements as a diagnostic marker for the disease.

Key words: Cardiovascular Disease, Chemerin , SOD, TC, HDL, LDL, TG.

Introduction

Cardiovascular diseases (CVDs) are the primary worldwide cause of mortality and impairment in humans, constituting almost two-thirds of all global fatalities.[(1)] There is extensive and reliable research that clearly demonstrates the strong correlation between cardiovascular illnesses and obesity. This demonstrates the association between the excessive buildup of fat in the abdomen and the occurrence of metabolic abnormalities, including dyslipidemia, type 2 diabetes, and hypertension, which eventually result in the development of cardiovascular illnesses. [(2)] Obesity is linked to various metabolic abnormalities that disturb the cardiovascular equilibrium by triggering inflammatory processes that attract immune cells to the site of damage, decreasing nitric oxide (NO) levels, resulting in elevated blood pressure, movement of endothelial cells, increased cell multiplication, and breakdown of proteins. [(3)] Adipose tissue serves as an endocrine gland, apart from its job of storing extra fat. It produces physiologically active peptides known as adipokines, which are related to cytokines. These adipokines may have autocrine, paracrine, and hormonal effects on the body. [(4)] Adipokines have a crucial role in controlling the metabolism, differentiation, and energy storage of adipose tissue. They are necessary for maintaining normal physiological processes.[(5)] Additionally, adipokines may impact immunological responses, lipid metabolism, insulin sensitivity, vascular homeostasis, and vascular angiogenesis, hence exerting direct or

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indirect effects on individuals with cardiovascular illnesses.[6,7] Cardiovascular diseases (CVD) are the primary cause of mortality and morbidity on a global scale, including a diverse array of conditions, such as myocardial illnesses and disorders affecting the vascular system that supplies blood to the heart, brain, and other essential organs. [8]

Chemerin

Chemerin, an 18 kilo dalton protein, plays a crucial role in regulating several biological processes including adipogenesis, glucose homeostasis, tumorigenesis, inflammation, angiogenesis, myogenesis, and immune cell chemotaxis. The gene responsible for producing chemerin is referred to as the retinoic acid receptor responder 2 (RARRES2) or the tazarotene-induced gene 2 (TIG2).[9]

Subsequently, it was shown that chemerin[10,11] expression mostly occurs in human liver and fat cells. However, RARRES2 gene expression was also detected in several other tissues including the kidneys, pancreas, adrenal glands, lungs, and skin. [12-14].

The variations in chemerin expression across various cell types and tissues are significant and have implications for a range of disease conditions, including obesity, cancer, inflammation, heart disease, and vascular diseases [15-17]. It has been proposed that the regulation of chemerin expression is specific to different tissues and is influenced by metabolic and inflammatory mediators,[18] such as glucose, fatty acids, insulin, immunoregulatory cytokines, and nuclear receptor activators like glucocorticoids, retinoids, and vitamin D.[19]

The chemerin-receptor contact plays a crucial role in several cellular and signaling processes within the cardiovascular, neurological, and reproductive systems.[20-22]

Chemerin and Cardiovascular Diseases

There is enough evidence indicating that chemerin has several crucial functions in controlling the circulatory system and the development of cardiovascular disorders. It acts as an adipokine, a chemotactic factor, and a growth factor. Chemerin, an adipokine, regulates glucose and lipid levels, hence impacting the accumulation of lipids in the inner layer of blood vessels [23,24] and the advancement of atherosclerosis [23]. Chemerin plays a significant role in chemotactic attraction, facilitating the interaction between adipocytes, lymphoid cluster cells, and macrophages, and guiding them towards areas of injury. [11,25,26]are enclosed in parentheses. Chemerin increases the movement of calcium and the migration of mature adipocytes and macrophages in the vascular system. It also affects the levels of intercellular adhesion[27] and promotes the creation of multilayer blood vessels.[28,29] Chemerin acts as a growth factor by stimulating the development of small blood arteries to support the clustering of fat cells and controlling the creation of precursor cells produced from bone marrow.[30] Chemerin plays a crucial role in the development of hypertension by influencing vascular tone and smooth muscle contraction.[31,32] It also decreases vascular relaxation caused by nitric oxide and the production of cyclic guanosine monophosphate (cGMP).[33, 34]

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Super Oxide Dismutase

Superoxide dismutase (SOD) enzymes are metalloproteins that may facilitate the conversion of superoxide ion ($.O_2^-$) to hydrogen peroxide (H_2O_2) by catalysis. They are the most efficient antioxidant enzymes in humans. SOD enzymes function by scavenging superoxide ions, therefore inhibiting their interaction with nitric oxide (NO) and the subsequent generation of peroxynitrite (ONOO-). There are three distinct forms of SOD enzymes that vary in their subcellular location in order to be in close proximity to the site of active oxygen generation. These include cytosolic SOD1, mitochondrial SOD2, and extracellular SOD3. These kinds of enzymes have distinct metal cofactors necessary for their function. Both SOD1 and SOD3 rely on copper (Cu) and zinc (Zn) for their activity, and are hence referred to as Cu-ZnSOD. On the other hand, SOD2, commonly known as MnSOD, utilizes manganese (Mn) as its cofactor. [35]

The role of superoxide dismutase (SOD) enzymes in cardiovascular disorders has been elucidated. For instance, when the expression of SOD2 was suppressed, it resulted in heightened mitochondrial oxidative stress and enlargement of cardiac myocytes.[36]

Dyslipidemia

Dyslipidemia is characterized by atypical concentrations of lipids and lipoproteins in the bloodstream. This is indicated by increased levels of total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C), as well as triglycerides (TG), and decreasing levels of high-density lipoprotein cholesterol (HDL-C). On a global scale, dyslipidemia has been shown to be a significant predictor of various cardiac and cerebral events. This has prompted current efforts to emphasize the prevention and management of dyslipidemia as a major risk factor. Recognizing its predictive significance may help reduce the occurrence of stroke and myocardial infarction (MI) and alleviate associated suffering. [37, 38]

Chest discomfort is the predominant manifestation of coronary heart disease (CHD) resulting from arterial obstruction. It is the primary cause of mortality, with an annual mortality rate over 15%, mostly impacting men across all age brackets more than females. In 2015, Coronary Heart Disease (CHD) resulted in around 7.4 million fatalities, and it is projected that the number of deaths due by this ailment would reach 23.6 million by the year 2030. The incidence of chest discomfort varies from 0.06% in males below the age of 45 to 2.46% in those aged 75 and beyond.

The physiologic mechanism behind elevated blood lipid levels is a process called arterial calcification, which involves both inflammatory and immunological reactions. Initial phases of the condition entail the impairment of the endothelium, which is caused by oxidative stress resulting from elevated levels of blood lipids, smoking, diabetes, or hypertension. This is followed by the oxidation of low-density lipoprotein inside the blood vessels, leading to its buildup.[39]

Materials and Methods

Samples under study

A total of 80 blood samples were obtained from male patients diagnosed with coronary artery disease, with ages ranging from (25-55) years. A total of 55 blood

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samples were collected from patients with the condition, whereas 25 samples were obtained from healthy persons, who served as the control group. The specimens were obtained from ambulatory healthcare facilities in the urban area of Samarra over the period of april 2023 to November 2023. The samples were obtained using venous blood extraction, and the serum was isolated from the blood for further testing.

The research quantified the concentration of Chemerin using Enzyme-Linked Immunosorbent Assay (ELISA) assays supplied by the Chinese business(BT LAB). The blood serum's SOD (Superoxide Dismutase) level was determined by ELISA assays supplied by the Chinese business (BT LAB). Furthermore, the levels of total cholesterol (TC), low-density lipoprotein (LDL-c), high-density lipoprotein (HDL-c), and triglycerides (TG) were determined using the methodology offered by the French business (BIOLABO).

Statistical analysis

The data collecting method for the study samples was conducted and statistically analyzed using the (SPSS 27) system to determine the mean, standard deviation, and t-Test for assessing differences between the main and secondary groups. The groups were considered significantly different at a probability threshold of ($P < 0.05$). The diagnostic accuracy was determined using the Receiver Operating Characteristic (ROC) curve test.

Results and Discussion

Table (1) presents the(mean ± standard deviation) values for Chemerin and Superoxide dismutase (SOD), as well as the measurements of Total Cholesterol (TC), Low-density lipoprotein (LDL), High-density lipoprotein (HDL), and Triglycerides (TG). It also includes the P-Value for comparing the control group with the patients.

Table (1) shows the levels of both Chemerin, (SOD), (TC), (LDL), (HDL), and (TG).

Groups / Parameters	Mean ± SD		p-value
	Control (n = 25)	Patients (n = 55)	
Chemerin(ng⁄ml)	36.23±5.90	49.30±10.46	<0.0001*
SOD(U⁄L)	93.857±19.190	87.829±9.534	<0.0001*
TC(mg/dl)	174.626±24.433	214.111±40.354	<0.0001*
LDL-c(mg/dl)	80.2±21	102.4±18.2	<0.0001*
HDL-c(mg/dl)	60.0±9	52.33±10.7	<0.0001*
TG (ng/ml)	113.6±24.9	142.5±12.3	<0.0001*

The table(1) displays the(mean ± standard deviation) of the Chemerin level in the serum of infected people, which was (49.30±10.46) ng/mL. In comparison, the serum of healthy

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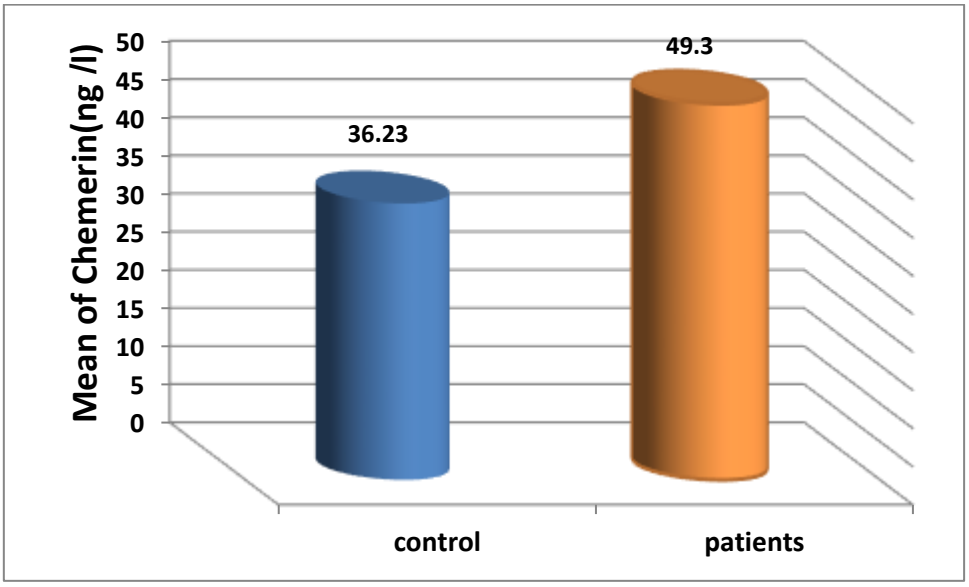
persons in the control group had a level of Chemerin (36.23±5.90) ng/mL. The data above demonstrate a statistically significant rise in the amount of Chemerin in the infected individuals compared to the control group, with a probability level of (P ≤0.05), as

seen in figure.(1)



Figure(1) The average level of Chemerin in the blood serum samples under study

The results we obtained align with the discoveries made by (Szpakowicz) et al [(40)] and (Dawood) et al [(41),] since they showed increased levels of chemerin in individuals with coronary artery disease.
Research indicates that chemerin plays a pivotal role in the development and advancement of cardiovascular illnesses. Chemerin, a hormone associated with obesity, regulates glucose and cholesterol levels, which in turn impacts the accumulation of fat in the inner lining of blood vessels and contributes to the development of atherosclerosis. Chemerin acts as a chemical substance that attracts phagocytic cells, stem cells, and natural killer cells in the vascular system. It promotes their mobility and interaction, as well as encourages the development of capillary blood vessels. The established function of chemerin in vascular inflammation, angiogenesis, and blood pressure control presents promising opportunities for the creation of therapeutic drugs that specifically target chemerin to treat heart and vascular disorders [(42).]

The table (1) displays the (mean ± standard deviation) of the SOD level in the serum of the afflicted persons, which was measured at (87.829±9.534) U/L. In comparison, the serum of the healthy individuals in the control group had (mean ± standard deviation) of(93.857±19.190) U/L. The aforementioned findings demonstrate a substantial reduction in the amount of SOD in the afflicted people compared to the control group, with a

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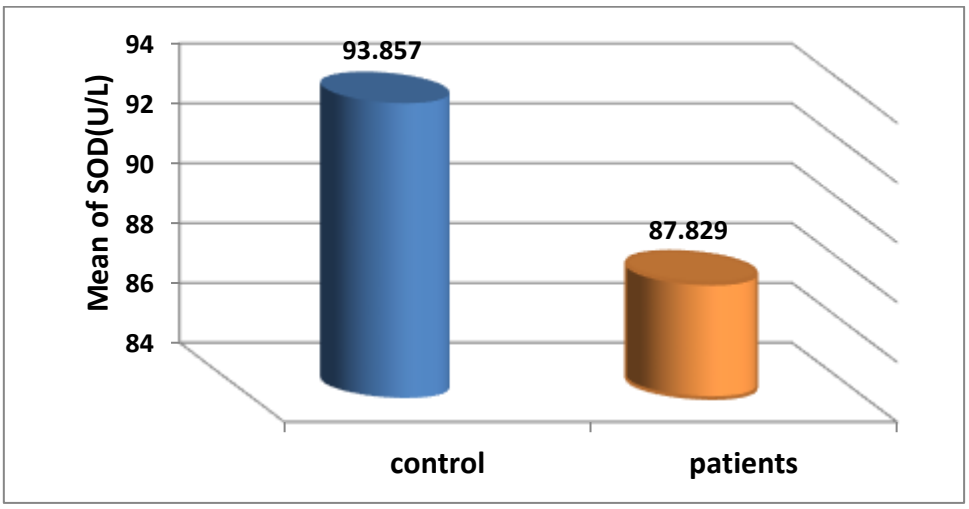
probability threshold of($P < 0.05$) as seen in figure (2).



Figure(2) The average level of SOD in the serum samples under study

The findings of the present investigation align with the results reported by(Xiuwen) et al [(43)] and(Gómez-Marcos) et al [(44)], who observed a reduction in the levels of Superoxide Dismutase (SOD) in individuals with cardiovascular conditions.

Oxygen Reactive Species (ROS) and Nitrogen Reactive Species (RNS) have a crucial role in controlling the function of the inner layer of blood vessels and vascular tone under the normal circumstances of the vascular system. Nevertheless, oxidative stress has detrimental consequences on human well-being, and several investigations have substantiated that elevated generation of reactive oxygen species/reactive nitrogen species (ROS/RNS) plays a role in the initiation and advancement of cardiovascular ailments. Antioxidant defense elements are essential for maintaining the balance and proper functioning of the vascular endothelium. The internal antioxidant defense system comprises a range of chemicals and enzymes, including superoxide dismutase, which plays a crucial role in protecting against the detrimental characteristics of reactive oxygen species (ROS). ROS are mostly produced by reactive oxidative species participating in the mitochondrial respiratory chain. Hence, the strategy of specifically focusing on antioxidant enzymes and maintaining a state of equilibrium in oxidative stress within the mitochondria has great potential for both the prevention and management of vascular disorders [(45).]

Extensive research has established the detrimental impact of oxidation on human health. These studies have demonstrated that the excessive generation of free radicals plays a significant role in the development and advancement of cardiovascular illnesses[(46-48)]. Hence, the antioxidant defense system is essential for maintaining the proper functioning of the vascular endothelium. Antioxidant enzymes serve as the primary defensive mechanism against oxidative harm. [(49-50).] Multiple studies have shown a link between reduced expression and activity of antioxidant enzymes and the onset of cardiovascular illnesses.[(51-53)] Therefore, more investigation is required to explore the use of free radicals in the cardiovascular system and their influence on the control of antioxidant enzymes. This study aims to generate novel diagnostic biomarkers and treatment techniques.

The table (1) displays the (mean ± standard deviation) of the TC level in the serum of afflicted persons was (214.111±40.354) mg/dl. In comparison, the TC level in the serum of healthy individuals in the control group was (174.626±24.433) mg/dl. The findings above demonstrate a

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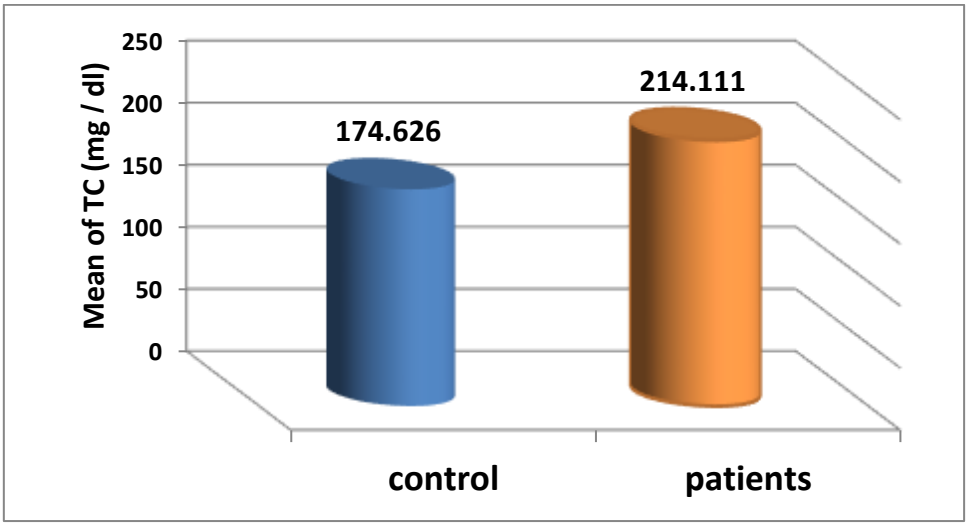
substantial increase in the amount of TC in the afflicted people compared to the control group, with a probability level of ($P < 0.05$), as seen in figure (3).



Figure(3) The average level of TC in the serum samples under study

The findings of the present investigation align with the findings of (Su-Min) et al [54] and (Sinya) et al [55], who reported elevated levels of total cholesterol in individuals with cardiovascular disease.

Elevated levels of blood cholesterol (TC) are often regarded as the primary factor contributing to coronary heart disease. It has been shown that high TC is directly linked to a heightened risk of cardiovascular disease [56]. Lipoprotein A is a complex structure that primarily carries lipid molecules in aqueous environments, such as blood plasma or other extracellular fluids. It consists of high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and very low-density lipoprotein cholesterol (VLDL-C)[57]. Multiple epidemiological and interventional investigations have established LDL-C as a significant risk factor for cardiovascular disease due to its prominent involvement in atherosclerotic disease [58, 59]. TC has largely supplanted LDL-C as the major lipid test for predicting cardiovascular disease risk in recent times. On the contrary, there is enough data indicating that HDL-C is negatively correlated with the likelihood of vascular problems, and lipoprotein is regarded as having anti-atherosclerotic properties .[60]

Both total cholesterol and LDL-C are crucial indicators of the effect of heart disease risks [61] since they are recognized as risk factors for heart disease. This finding aligns with earlier research that highlights the significance of maintaining appropriate cholesterol levels to lower the risk of mortality from heart disease.[62]

Table (1) presents the(mean ± standard deviation) for the concentration of low-density lipoprotein (LDL) in the serum of infected individuals, which was measured at(102.4±18.2) mg/dL. In comparison, the serum of healthy individuals in the control group had an LDL level of (80.2±21) mg/dL. The foregoing data clearly indicate that the amount of LDL has significantly increased ($P \leq 0.05$) in infected individuals compared to the control group, as shown in Figure.(4)

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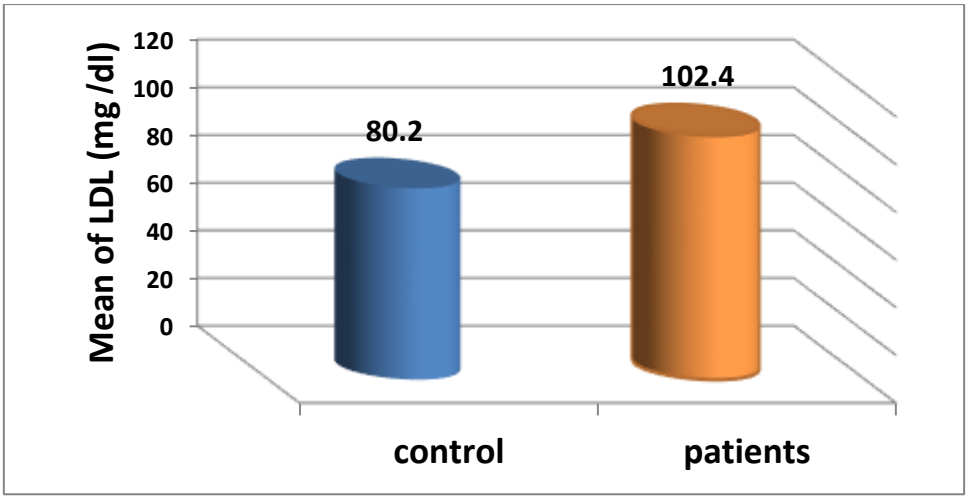

Figure (4) The average level of LDL in the blood serums of the samples under study

The results we obtained align with the research conducted by (Shabana) et al[(63),] which suggests that dyslipidemia or high levels of LDL cholesterol are significant contributors in the development of obesity and cardiac illnesses.

Low-density lipoprotein (LDL) is responsible for transporting around 60-70% of the cholesterol present in the blood.[(64)] Its primary function is to carry cholesterol from the liver to peripheral tissues. High levels of LDL cholesterol are detrimental because they may collect and initiate the formation of atherosclerotic plaques on the walls of arteries [(65)]. Extensive randomized studies have shown that the reduction of low-density lipoprotein cholesterol by the use of HMG-CoA reductase inhibitors, often known as "statins," effectively decreases the occurrence of coronary events and morbidity in some individuals at high risk [(66).]

The table (1) displays the (mean ±standard deviation) of high-density lipoprotein (HDL-c) cholesterol level in the blood of patients, which was(52.33±10.7) mg/dl. In comparison, the serum of healthy persons in the control group had a level of(60.0±9) mg/dl. The data above demonstrate a significant drop in the HDL level in the patients compared to the control group, with a probability threshold of($P < 0.05$), as seen in Figure(5).

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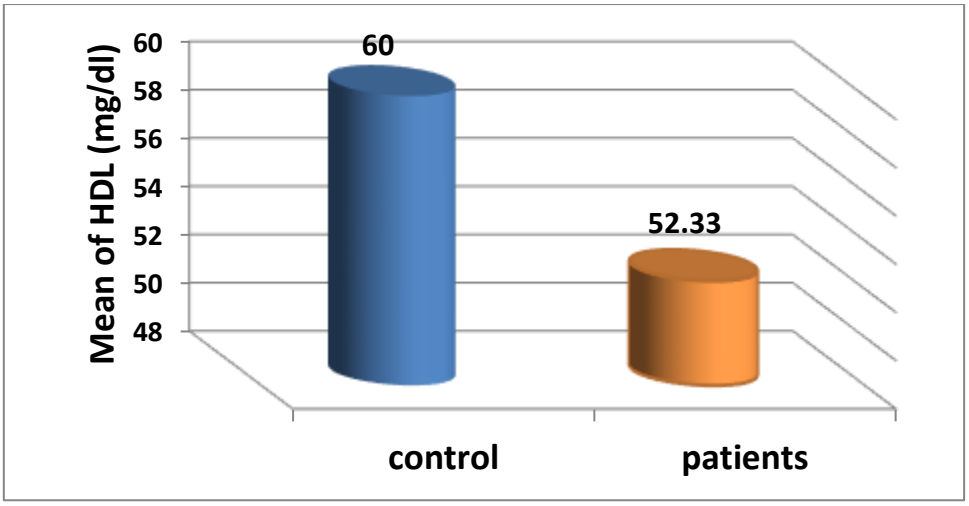

Figure (5) The average level of (HDL-c) in the blood serums of the samples under study

The results we obtained align with the findings of (Hedayatnia) et al [67], which suggest that the amount of (HDL-c) is reduced in individuals with cardiovascular illnesses. Epidemiological evidence confirms the negative correlation between levels of high-density lipoprotein cholesterol (HDL-c) and cardiovascular diseases [68]. Dyslipidemia, characterized by elevated triglyceride levels and reduced HDL-C levels, has been established as a significant risk factor for various diseases, such as obesity, diabetes, and cardiovascular diseases. Research suggests that there is a 2 to 3% reduction in the likelihood of developing cardiovascular illnesses for every 1 mg/dL rise in HDL-c levels [69]. Regardless of any disagreement, increased levels of triglycerides, whether during periods of fasting or non-fasting, also seem to constitute a separate risk factor for coronary artery disease [70,71]. Epidemiological studies provide evidence indicating that the presence of both decreased HDL-c and elevated triglyceride levels significantly increases the risk of developing coronary artery disease [72,73]. Furthermore, post-event analyses conducted in multiple studies have demonstrated that individuals with low HDL-c and high triglycerides experience a higher incidence of major coronary events.[74]

The table (1) displays the (mean ± standard deviation) of triglyceride (TG) levels in the serum of affected persons and healthy individuals (control group). The TG level was (142.5±12.3) ng/ml in the afflicted individuals, whereas it was (113.6±24.9) ng/ml in the healthy ones. The data above demonstrate a statistically significant rise in TG levels in the afflicted people compared to the control group, with a probability level ($P \leq 0.05$), as shown in figure(6).

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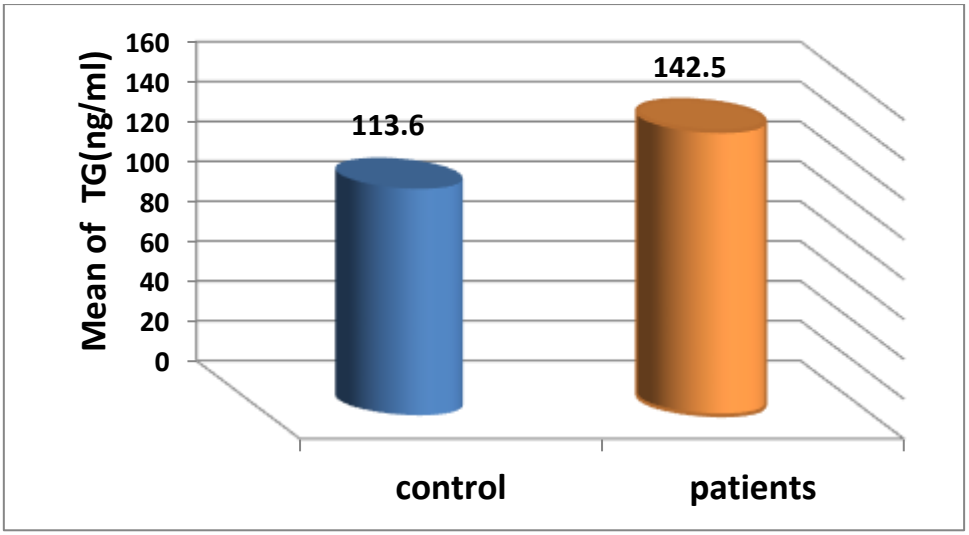

Figure (6) The average level of (TG) in the blood serums of the samples under study

Research conducted by (Tsion) et al [75] and (Hedayatnia)et al [67] has shown a clear correlation between elevated levels of triglycerides and an increased susceptibility to cardiovascular disease.

Consistently high levels of triglycerides (TG) are linked to lower concentrations of high-density lipoprotein (HDL), which are often associated with increased levels of glucose in the blood. This is because when there is a large amount of sugar in the blood (hyperglycemia), cholesterol esters are transferred from HDL to very low-density lipoprotein (VLDL) molecules.[76] This process, facilitated by hepatic lipase, further reduces the concentration of HDL by converting it into smaller molecules that are quickly removed from the blood.[77] The VLDL molecules that are formed as a consequence become tiny, dense LDL-C molecules that have a reduced amount of cholesterol esters. These molecules are then absorbed by macrophages in the arterial wall, leading to the development of arteriosclerosis.[78] Lipid disease may be described as an elevation in the levels of total cholesterol (TC), low-density cholesterol (LDL-C), and triglycerides (TG), or a decrease in the concentration of high-density cholesterol (HDL-C) in the bloodstream. Cardiovascular disease was deemed to be associated with lipid problem. [67]

The Receiver Operating Characteristic Curve (ROC)

The Receiver Operating Characteristic (ROC) analysis was used to assess the efficacy of chemical tests in the biochemical diagnosis of the illness in our research, as well as to establish the optimal threshold values for various variables. Calculations were performed to determine the sensitivity and specificity. The AUC, or area under the ROC curve, serves as a concise indicator of diagnostic accuracy.

Table(2) displays the diagnostic validity criteria, including sensitivity, specificity, and accuracy tests, for the infected group in comparison to the control group.

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Table (2) Predictive values for the infected

Parameters	Cut off	Sensitivity %	Specificity %	Accuracy	AUC	P-value
Chemerin	>62.1846	76.67	90.00	0.6667	0.874	<0.0001
SOD	>120.1793	83.33	85.33	0.6667	0.894	<0.0001
TC	≤0.722	100.00	76.67	0.7667	0.905	<0.0001
LDL-C	>2.7851	90.00	86.67	0.7667	0.915	<0.0001
HDL-C	>26.73	81.67	93.33	0.7500	0.942	<0.0001
TG	>12.017	76.67	80.00	0.5667	0.804	<0.0001

Through the multivariate statistical analysis, the sensitivity, specificity and cut-off values of each variable were found and shown in Table (2). We note that the sensitivity values of TC and LDL-c are high, which means that these variables can be used as a diagnostic function for cardiovascular disease,as in Figures (7), (8) ,(9) ,(10), (11),(12).

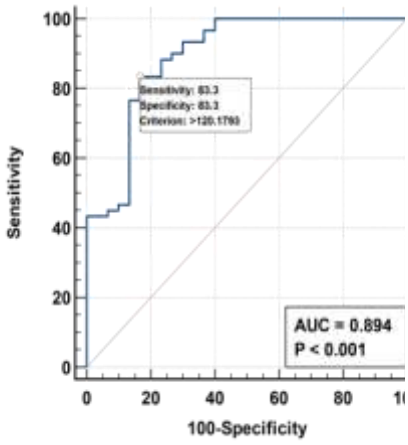

Figure (7) ROC curve for Chemerin

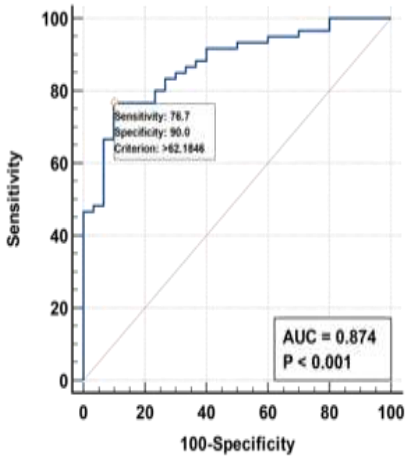

Figure (8) ROC curve for(SOD)

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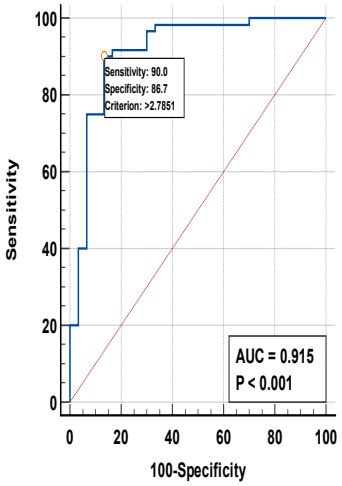

Figure (10) ROC curve for(LDL-c)

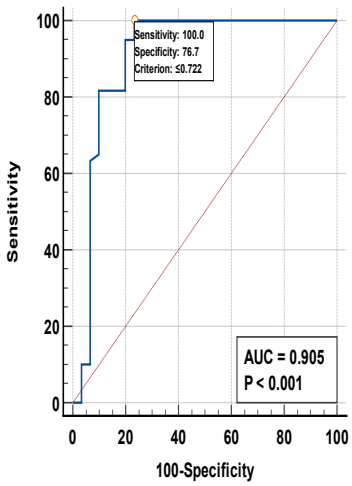

Figure (9) ROC curve for(TC)

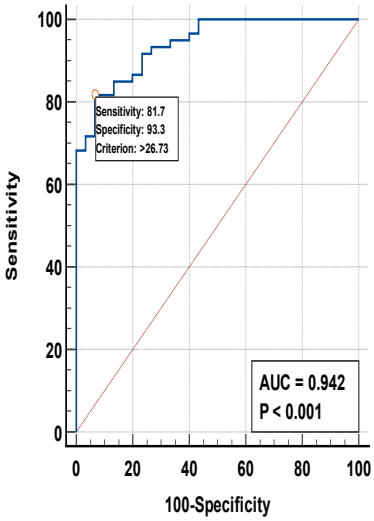

Figure (11) ROC curve for(HDL-c)

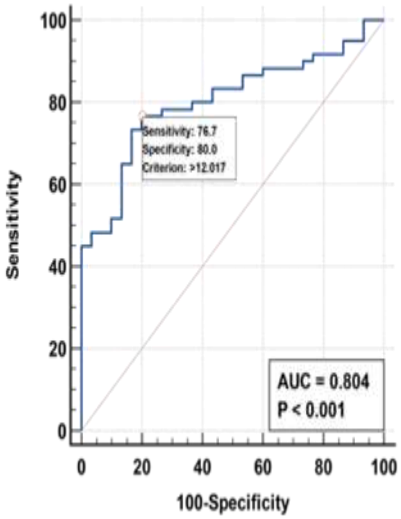

Figure (12) ROC curve for(TG)

It is clear from the above figures that the area under the curve of the above variables is close to 1, which indicates excellent accuracy in diagnosing the disease.

Conclusions

From our study, we conclude that there is an increase in the level of Chemerin and each of (TC), (LDL-c) and (TG) in the group of patients with cardiovascular diseases compared to the control group, while there is a noticeable decrease in the level of each of (SOD) and (HDL-c),as the Chemerin and the rest of the parameters are diagnostic signs of the disease as the area under the curve approaches 1, which indicates the accuracy of the measurement.

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