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Article

Clinical Significance of D-dimer and Lipid Profile Alterations in Patients with Heart Disease

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Abstract: D-dimer serves as a biomarker indicating the activation of the coagulation and fibrinolytic systems in reaction to the body's hypercoagulable condition. This study aimed to evaluate the role of D-dimer in diagnosing patients with dilated cardiomyopathy (DCM) and assessing their risk of developing intracardiac thrombosis, as well as examining its relationship with lipid disorders. DCM patients were compared with a healthy group in terms of D-dimer levels and lipid profiles, which included total cholesterol, triglycerides, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and very-low-density lipoprotein (VLDL). The results showed a significant increase in D-dimer levels in DCM patients compared to the control group, reflecting increased coagulation activity and fibrinolysis, and indicating a higher risk of cardiovascular complications. DCM patients also showed significantly higher levels of total cholesterol, triglycerides, and VLDL, while no significant differences were observed in LDL and HDL levels between the two groups. This suggests that D-dimer may be more closely associated with total cholesterol, triglycerides, and VLDL specifically. These results underscore the importance of D-dimer not only as an indicator of thrombotic activity but also as a factor associated with lipid abnormalities that contribute to the development of cardiovascular disease. Incorporating D-dimer testing into routine cardiac screening may enhance the chances of early detection and support effective therapeutic intervention. To further confirm its diagnostic and prognostic value, the study recommends conducting more comprehensive, multicenter studies with long-term follow-up in patients with heart, liver, and kidney disease.

Keywords: D-dimer, Lipid Profile, Heart Disease, Fibrinolysis

Introduction

The heart is a remarkable organ that incessantly circulates oxygenated blood throughout the body to support the vitality of numerous organs. The heart circulates 7,500 liters of blood daily. The heart operates autonomously, pulsating around 70 times each minute, which totals over 100,000 beats daily [1,2]. Cardiovascular disorders are the predominant noncommunicable conditions globally, responsible for almost one third of all fatalities worldwide [3,4]. Modifiable risk factors, including body mass index, systolic blood pressure, low-density lipoprotein cholesterol levels, tobacco use, and diabetes, contribute to the prevalence and incidence of cardiovascular disease; however, the extent of this contribution varies based on the populations examined and the methodologies employed [5.6].

These risk variables are utilised to calculate modern risk scores for estimating the 10-year risk of cardiovascular disease, but with varying weights assigned [7,8,9]. These cardiovascular risk variables have distinct correlations with both cardiovascular and non-cardiovascular outcomes. Tobacco consumption is significantly linked to early mortality, although increased blood pressure and non–high-density lipoprotein (HDL) cholesterol levels are more directly connected with cardiovascular disease [9,10,11].

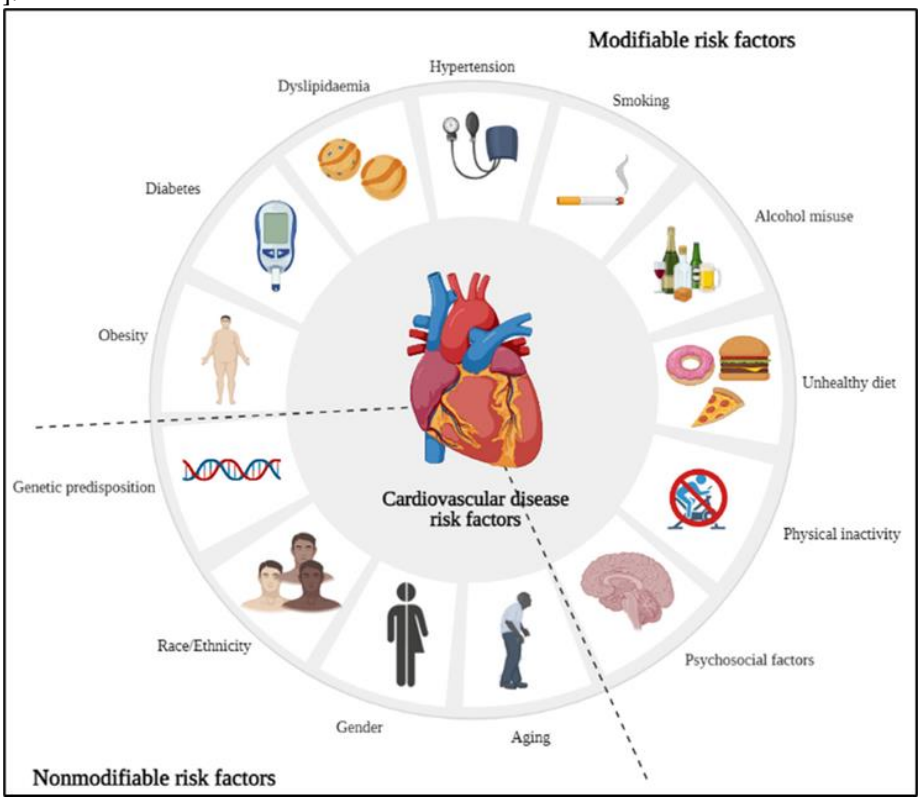

Figure 1. Risk factors for cardiovascular disease [4].

A customised alleviation of cardiovascular disease and mortality from all causes for individuals and populations may be attained by an enhanced comprehension of the region- and sex-specific correlations of these cardiovascular risk variables with the onset of cardiovascular illness [12,13,14]. The Global Cardiovascular Risk Consortium examined a globally standardised individual-level dataset from population-based cohorts to address the constraints of summary data and methodological variability [15,16,17].

Cardiovascular disease is attributed to both genetic and environmental factors. Genetic variables encompass type 2 diabetes, obesity, dyslipidemia, hypertension, elevated levels of low-density lipoprotein cholesterol (LDL-C), and diminished levels of high-density lipoprotein cholesterol (HDL-C). Non-genetic risks encompass tobacco use, insufficient physical exercise, and a diet rich in fats [18,19]. An important biomarker is D-dimer, a protein produced by the breakdown of fibrin during the clotting process and used as an indicator of the presence of clots in the body. Studies indicate that high levels of D-dimer are associated with heart disease including stroke, hypertension and high blood lipids [20,21]. This study aimed to measure D-dimer levels and their relationship with blood lipids (cholesterol, triglycerides, HDL, LDL, and VLDL) in patients with heart disease to demonstrate the importance of this index in predicting cardiovascular risk. The goal is to improve early diagnosis, predict cardiac risks, and accurately direct therapeutic interventions, thereby reducing the health and economic burden associated with this disease.

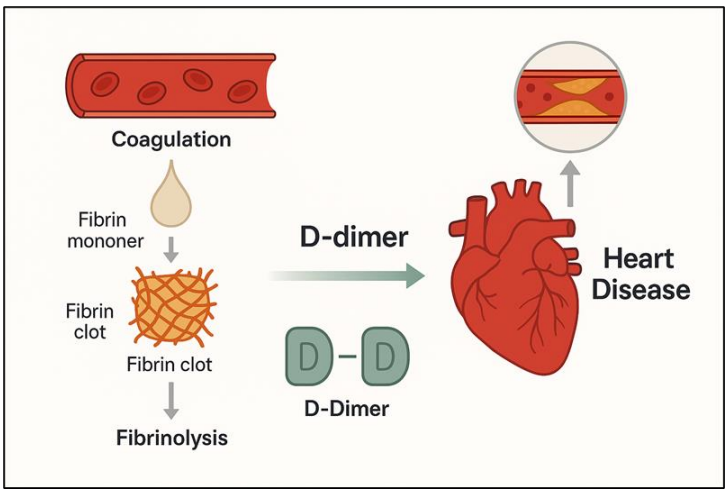

Figure 2. Shows the biomarkers of fibrinolysis, fibrin synthesis, and D-dimer release in relation to cardiovascular disease.

Materials and Methods

Study Population

A total of 30 serum samples were analysed, including 20 samples from patients with various cardiovascular diseases and 10 samples from apparently healthy individuals who served as controls.

Sample Collection and Preparation

Eight mL of venous blood was aseptically drawn using single-use syringes. 5 ml of this sample was placed in sealed gel tubes and centrifuged at 3000 rpm for 10 minutes. Serum was then collected using micropipettes. Serum samples were transferred to Eppendorf tubes and stored at −20 °C until lipid analysis was performed. The remaining 2.7 ml was placed in blue-capped tubes containing sodium citrate for the D-dimer assay.

Materials and Equipment

Commercial kits from Biolaboo (France) were used to determine levels of D-dimers, cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and very low-density lipoprotein cholesterol (VLDL-C). Laboratory equipment included a Kenza 240 Tx automated biochemical analyser (France), a Hettich centrifuge (Germany), a Genesys spectrophotometer (USA), a LapTech incubator (Korea), micropipettes (Japan), and test racks and tubes (China).

D-dimer Measurement

The concentration of dimers was determined using the sandwich immunoassay (antibody-antigen-antibody complex) based on electroluminescence immunoassay (ECLIA). Specific antibodies immobilised on magnetic microparticles were incubated with patient plasma and labelled detector antibodies. After washing, electroluminescence was stimulated and quantified spectrophotometrically. Concentrations were determined by comparison with calibration standards and plotted on a standard curve.

Lipid Profile Determination

Total cholesterol and triglycerides were measured using enzymatic colourimetric methods on a Kenza 240 Tx analyser.

High-density lipoprotein (HDL-C) was determined after precipitation of low-density lipoprotein (LDL-C) and very-low-density lipoprotein (VLDL) cholesterol using phosphotungstic acid in the presence of magnesium ions, followed by enzymatic assay.

Low-density lipoprotein (LDL-C) was calculated using the Friedewald equation:

- LDL-C (mg/dL) = Total Cholesterol - (HDL + VLDL)

- Very-low-density lipoprotein (VLDL-C) was calculated using the following formula:
- Very-low-density lipoprotein (mg/dL) = Triglycerides (5)

Statistical Analysis

SPSS was used to process the data. Mean ± standard deviation (SD) was used to present the results. Student's t-test was used for group comparisons, and Duncan's multiple-range test was employed to identify group differences. P-values less than 0.05 were regarded as statistically significant.

Results and Discussion

Samples under study

The study was conducted on 30 blood serum samples, comprising 20 samples from patients with heart disease and 10 samples from healthy individuals serving as the control group, as shown in Figure 3.

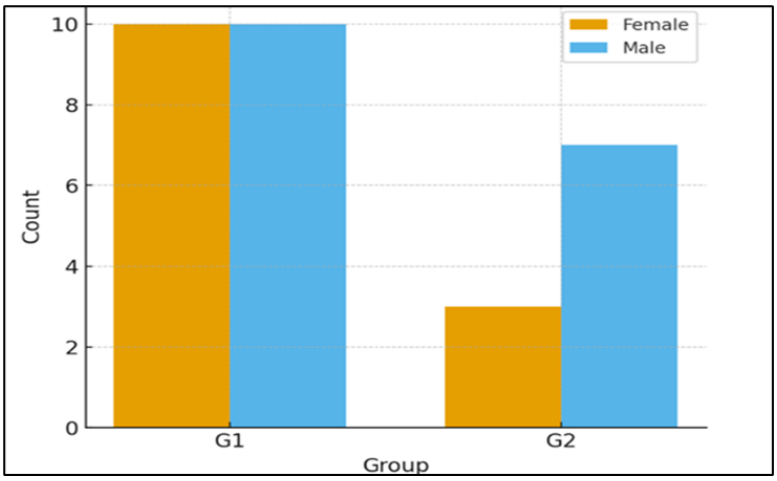

Figure 3. Distribution of patients and control by gender.

Levels of serum D-dimer

The level of D-dimer protein was measured in the blood serum of heart patients compared to healthy control samples, and the results were as shown in Figure 4. The results showed that the mean ± standard deviation (Mean ± S.D) of D-dimer levels was (1140 ± 835 ng FEU / ml) in the blood serum of patients with heart failure, while it was (117.7 ± 61.2 ng FEU / ml) nanograms / ml in the blood serum of healthy subjects. The results show a significant increase ($p \leq 0.05$) in the blood serum of heart patients compared to the healthy control sample.

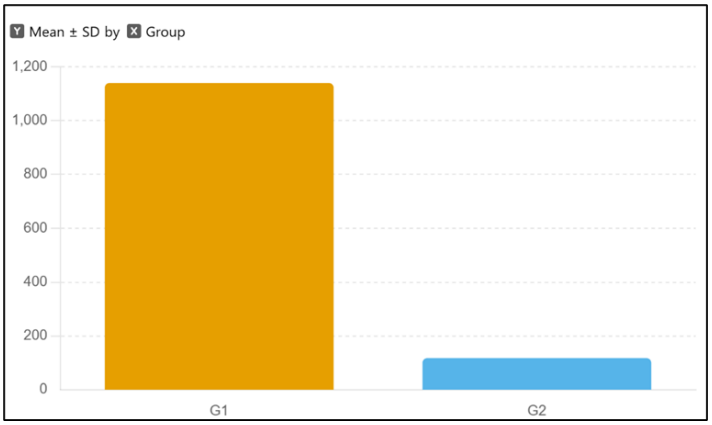

Figure 4. Average level of D-dimer in the blood serum of the samples under study.

The enzymatic breakdown of cross-linked fibrin, a process that occurs through a series of steps, produces D-dimer, a degradation product of fibrinogen. The D-dimer test is increasingly used in clinical

settings as a screening tool to rule out disseminated intravascular coagulation and venous thromboembolism, as it facilitates the identification of endogenous fibrinolysis and thrombin production. D-dimer has also been evaluated for its potential use in initiating anticoagulant therapy in individuals with certain cardiovascular diseases [22]. These results are consistent with previous studies [23,24,25], which demonstrated the potential of using D-dimer as a risk indicator for cardiovascular disease. This study identified a strong correlation between elevated D-dimer levels in the bloodstream and an augmented risk of myocardial infarction, cardiac tissue pathology, and hypertension.

In patients with end-stage heart failure brought on by idiopathic dilated cardiomyopathy, elevated D-dimer levels have been independently linked to poor long-term outcomes, showing better predictive value than traditional prognostic markers [26]. Plaque thrombosis, endothelial injury, or the presence of prothrombotic factors, such as high levels of von Willebrand factor or coagulation factor VIII, can all cause this [27]. Since fibrin is the final component to be broken down by fibrinolysis and the main result of the coagulation cascade, it is crucial for haemorrhage management. The effectiveness of fibrinolysis is greatly influenced by the architecture of the clot, the many kinds and forms of fibrinogen, the pace at which thrombin is produced, the reaction of the clot-forming cells, including platelets, and the general biochemical environment.The fibrinolytic system is controlled by a large number of cofactors, receptors, and inhibitors, just as the coagulation cascade. The fibrin-rich clot's surface or cells that express profibrinolytic receptors may exhibit fibrinolytic activity [28]. Dihydrotestosterone (DHT) levels can rise and the clotting system can be activated by inflammatory cytokines such as interleukin-6 (IL-6). DHT levels may rise in tandem with high C-reactive protein (CRP) levels [29]. The risk of heart disease rises as a result. Decreased intima function is also a factor that can contribute to elevated levels. D-dimer in heart patients disrupts the vital pathways responsible for preventing or dissolving clots, which leads to activation of the coagulation system and increased levels of D-dimer. The decrease in the function of the inner layer of blood vessels can be caused by several factors such as high blood pressure, high cholesterol, diabetes, smoking, and obesity [30,31]

Levels of serum lipids

The level of lipids (total cholesterol, triglycerides, high-density lipoproteins, low-density lipoproteins, and very low-density lipoproteins) was measured in the blood serum of patients with heart failure. The mean ± standard deviation of the lipids under study was as shown in table 1.

Table 1. Mean ± S.D. of lipid levels in the blood serum of the samples under study

Parameters	Mean ± SD	
	G1 n = 20	**G2 n = 10**
T.Cholesterol(mg/dl)	**201.1 ± 47.9 b**	**163.9± 9.42 A**
HDL-C (mg/dl)	**33.2 ± 18.6**	**41.36± 6.48**
Triglycerides(mg/dl)	**180.6 ± 77.0 b**	**84.0± 394. A**
LDL-C(mg/dl)	**107.6 ± 27.5**	**94.4± 18.4**
VLDL (mg/dl)	**36.1 ± 15.4**	**16.90± 6.61**

Level of Total cholesterol

The results revealed that the mean ± standard deviation (Mean±S.D) of total cholesterol levels was (201.1 ± 47.9 mg/100 cm3) in the blood serum of persons with heart disease, compared to (163.9 ± 24.9 mg/100 cm3) in the blood serum of healthy people. As shown in Figure 5, the results further demonstrate that the blood serum of patients with heart disease had a substantially higher total cholesterol level ($p < 0.05$) compared to the control sample.

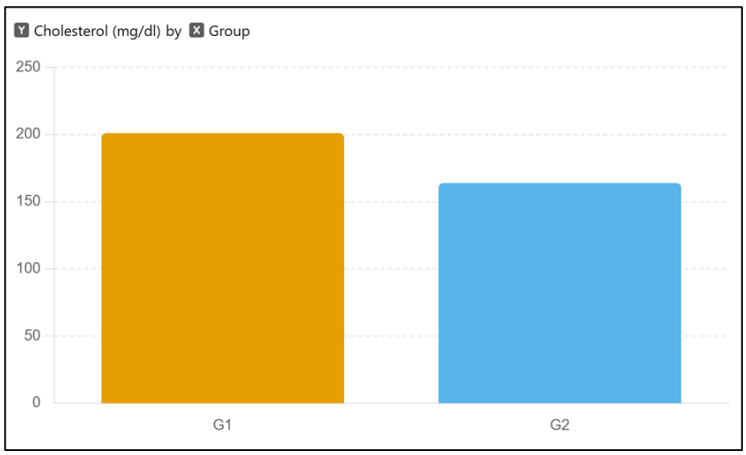

Figure 5. Average level of cholesterol in the blood serum of the samples under study.

Heart patients elevated total cholesterol levels are caused by oxidative stress and fat peroxidation, which inhibits the excretion (secretion) of bile salts and steroid substances. This is because active oxygen species alter the activity of the enzyme cholesterol acyl transferase, which is in charge of absorbing total cholesterol in the intestine, raising its level [32, 33].

The cause for the high level of total cholesterol may be due to nutrition, as it is considered one of the factors that cause high concentrations of fats in the plasma, as they rise due to eating foods containing a high percentage of saturated fats [34]. Similarly, the balance between the quantity of fat that enters the body and the mechanism that removes it determines the concentration of fats in the body. A stable state has a steady metabolism. The process of balancing reduces this rise in concentration when the rates of building and demolition are equal, but there is a slight increase in fat intake [35]. In contrast, a very high intake of cholesterol results in a minor adaptation process, meaning that dietary cholesterol cannot significantly alter the liver's natural ability to produce cholesterol. As a result, the cholesterol consumed causes cholesterol esters to be deposited in the blood vessel lining, narrowing the blood vessels and reducing the amount of blood that flows through them [36,37].

High-Density Lipoprotein Cholesterol (HDL-C)

The results indicated a non-significant reduction in the serum levels of HDLC in patients relative to healthy individuals. The findings indicated that the mean ± standard deviation (Mean±S.D) of the HDLC level for patients was (33.2 ± 18.6) mg/100 cm3, whereas for healthy individuals it was (41.36 ± 6.48) mg/100 cm3, as seen in Figure 6.

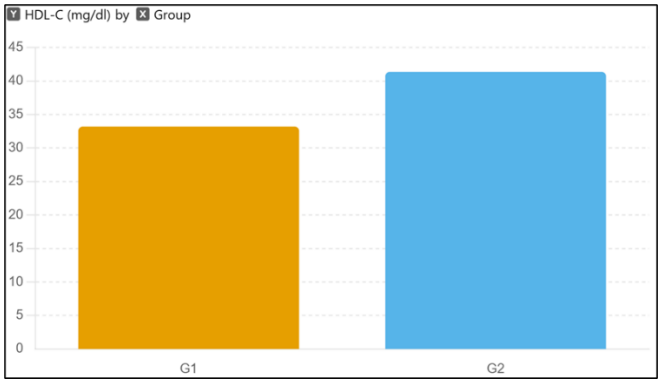

Figure 6. Average level of HDL-C in the blood serum of the samples under study.

A decreased concentration of high-density lipoprotein cholesterol (HDL-C) significantly increases the risk of cardiovascular disease. Foam cells packed with cholesterol esters are identified as the hallmark of atherosclerotic plaques. A plethora of data supports the notion that enhancing cholesterol efflux from foam cells through high-density lipoprotein (HDL) particles, the initial stage of

reverse cholesterol transport (RCT), is a feasible antiatherogenic strategy. However, enthusiasm for the therapeutic potential of modulating reverse cholesterol transport (RCT) in treating cardiovascular disease (CVD) has waned due to the lack of correlation between CVD risk and standard measurements in intervention trials, particularly HDL cholesterol (HDL-C), which demonstrates an inconsistent relationship with HDL function and RCT [38].

Level of Triglycerides (TG)

The findings indicated that the mean ± standard deviation (Mean ± SD) of triglyceride levels was 180.6 ± 77.0 mg/100 cm^3 in the blood serum of patients with cardiac disease, in contrast to 84.0 ± 32.4 mg/100 cm^3 in the blood serum of healthy controls. Triglyceride levels in the blood serum of patients with heart disease considerably increased at a probability threshold of $p < 0.05$ compared to healthy persons in the control group, as seen in Figure 7.

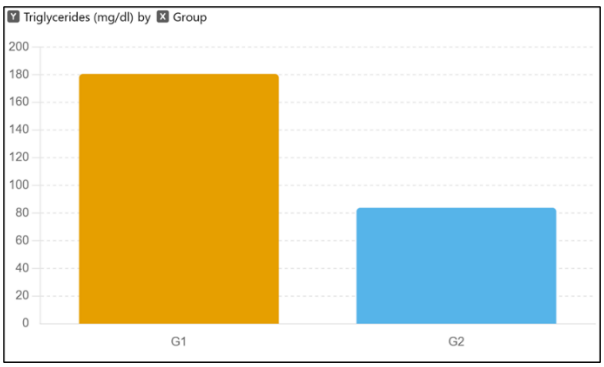

Figure 7. Average triglyceride level in the blood serum of the samples under study.

Hypertriglyceridemia is a common risk factor for cardiovascular disease (CVD) and is becoming increasingly significant in the context of the present epidemics of obesity and insulin resistance. Elevated triglyceride (TG) levels serve as indicators for several forms of atherogenic lipoproteins. Individuals with hypertriglyceridemia may face considerable risk for cardiovascular disease, even with low-density lipoprotein cholesterol levels within target ranges, necessitating interventions that enhance dietary habits, mitigate obesity, and encourage consistent physical activity. Patients at high risk with hypertriglyceridemia, including individuals with diabetes, cardiovascular disease, or metabolic syndrome, may require supplementary pharmacotherapy in addition to statins to manage other lipid irregularities [39,40,41].

Low-density lipoprotein cholesterol (LDL):

The findings indicated that the mean ± standard deviation (Mean ± S.D.) of LDL-C levels in blood was 107.6 ± 27.5 mg/dL for patients with heart failure, in contrast to 94.4 ± 18.4 mg/dL for the healthy control group. The results indicated that LDL-C levels were not substantially elevated at a probability threshold of $p < 0.05$ in patients with heart failure compared to healthy control participants, as seen in Figure 8.

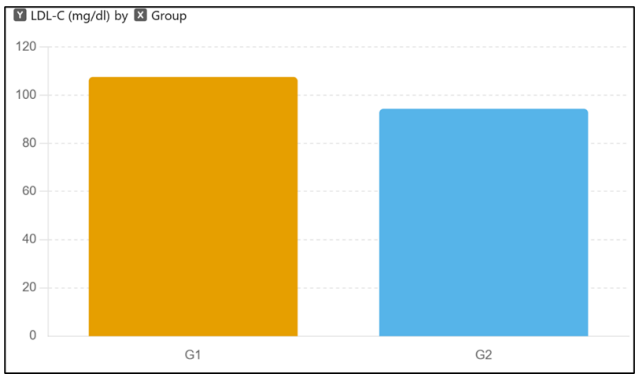

Figure 8. Average LDL-C level in the blood serum of the samples under study.

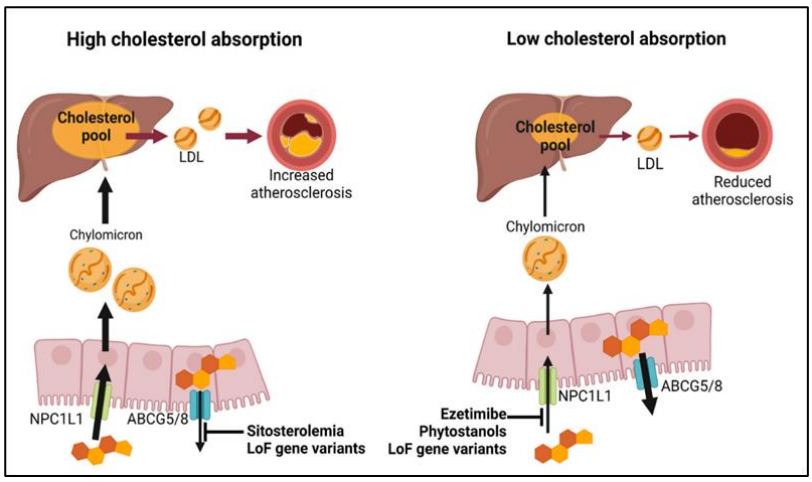

Figure 9. Cholesterol metabolism in high and low cholesterol absorption scenarios. Pharmacological, nutritional, and genetic modulation of cholesterol in enterocytes and the implications for the risk of atherosclerotic cardiovascular diseases [36].

Numerous studies have demonstrated that LDL-C is the primary transporter of cholesterol from the liver to peripheral tissues and comprises a significant proportion of cholesterol, wherein elevated LDL-C levels contribute to atherosclerosis [42,43,44]. The reason for the increased LDL-C concentration in the serum of males and females may be attributed to an increase in MDA levels resulting from oxidative stress or due to the oxidation of high-density lipoprotein receptors in the serum [43,45]. This rise is also ascribed to heightened fat consumption. An elevation in dietary cholesterol delivered to the liver results in diminished efficacy of LDL-C receptors, leading to the accumulation of LDL-C molecules at elevated quantities within the bloodstream, hence facilitating their infiltration through the arterial wall and contributing to atherosclerosis [46,47]. Moreover, an insufficient intake of fruits and vegetables results in the heightened oxidation of LDL-C molecules in the circulation, thereby diminishing their affinity for receptors [48]. The high concentration of LDL-C is attributed to a decrease in the effectiveness of the lipoprotein lipase enzyme, which leads to the failure to decompose T.G and the conversion of most of the VLDL-C to LDL-C, and thus an increase in its level in the blood serum, which is undesirable because it constitutes a risk factor for the development of heart disease [49].

Very Low-Density Lipoprotein Cholesterol(C-VLDL)

The findings indicated that the mean ± standard deviation (Mean±S.D) of serum VLDL-C levels was (36.1 ± 15.4) mg/100 cm^3 in patients with cardiac disease, in contrast to (16.90 ± 6.61 mg/100 cm^3 in the serum of the healthy control group .The findings indicated that VLDL-C levels were significantly elevated at a $p < 0.05$ level in patients with heart disease compared to the healthy control group, as shown in Figures 10.

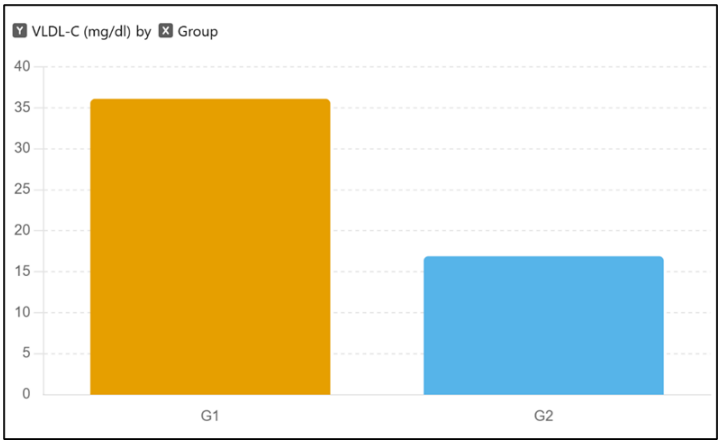

Figure 10. Average VLDL-C level in the serum of the samples under study.

Hypertriglyceridemia is a common risk factor for cardiovascular illness (CVD) and is becoming increasingly significant in the context of the present epidemics of obesity and insulin resistance. Elevated triglyceride (TG) levels serve as indicators for several forms of atherogenic lipoproteins. Individuals with hypertriglyceridemia may face considerable risk for cardiovascular disease, even with low-density lipoprotein cholesterol levels within target ranges, necessitating interventions that enhance dietary habits, mitigate obesity, and encourage consistent physical activity. Patients at high risk with hypertriglyceridemia, including individuals with diabetes, cardiovascular disease, or metabolic syndrome, may require supplementary pharmacotherapy in addition to statins to manage other lipid irregularities [50].

Conclusion

This study concluded that D-dimer levels were significantly elevated in patients with heart disease compared to healthy individuals, suggesting its potential use as a biomarker of cardiovascular function. Patients with heart disease had elevated levels of cholesterol, triglycerides, and VLDL, suggesting lipid changes that may facilitate disease progression. In contrast, HDL and LDL cholesterol levels remained unchanged in these individuals, suggesting that the most significant changes were explicitly related to total cholesterol, triglycerides, and VLDL. Further research is needed to clarify the relationship between D-dimer and lipid parameters, and D-dimer levels should be regularly monitored in patients with heart and liver disease to improve early diagnosis and clinical assessment. Additional research is needed to explore the relationship between D-dimer levels and kidney disease, considering their future diagnostic and prognostic significance.

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