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RESEARCH ARTICLE

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Investigation of the correlation between Endocan, Interleukin-10, and biochemical parameters in Iraqi patients with cardiovascular diseases

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Abstract

The correlation between biomarkers endocan and interleukin-10 (IL-10) in patients with various cardiovascular diseases—angina pectoris, ischemic heart disease, and myocardial infarction—is examined in this work. There were 200 participants overall, 50 in each of the three disease groups and a control group of fifty healthy people. Along with other factors including renal function, glucose metabolism, and lipid profile, the study gauged serum levels of endocan and IL-10. With myocardial infarction patients showing the highest levels, results revealed that all patient groups had notably greater levels of endocan and IL-10 than healthy controls. With greater blood urea and serum creatinine levels than those with ischemic heart disease and angina pectoris, the study revealed that patients with myocardial infarction demonstrated notably impaired renal function. Along with a poorer lipid profile comprising increased total cholesterol, triglycerides, and low-density lipoprotein (LDL) levels, individuals with myocardial infarction also had higher fasting glucose and hemoglobin A1c levels. By comparison, the healthy control group had the lowest levels of these biomarkers and indicators. The results imply that levels of endocan and IL-10 could be markers of the degree and progression of cardiovascular disease. Particularly those with myocardial infarction showed more marked metabolic and renal abnormalities than those with ischemic heart disease or angina pectoris, so highlighting the possible use of these biomarkers in tracking disease severity and supporting clinical management of cardiovascular diseases.

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Keywords: Angina pectoris; ischemic heart disease; myocardial infarction; endocan and Interleukin-10.

1. Introduction

CVD refers to a range of disorders affecting the heart and blood vessels, and leads to serious conditions such as angina pectoris, ischemic heart disease, myocardial infarction, and death. According to the World Health Organization, CVD remains the leading cause of death globally. The process of atherosclerosis development starts during childhood and is one of the factors contributing to determining CVD events such as coronary artery disease or stroke later in life [1], [2]. As the disease progresses, it manifests through a combination of metabolic derangements, oxidative status imbalance, and endothelial dysfunction, and these events are avenues to a more complex spectrum of CVD. Since CVD is one of the most common diseases leading to morbidity and mortality worldwide, prevention of its occurrence, as well as timely detection, are important for healthcare [3], [4]. Classification of CVDs is diverse, but in general the clinical presentation is always subtle and insidious with few exceptions. Point of CVD presentation may start early with mild dyspnea, chest discomfort, fatigue in addition to mental health concerns [5], [6]. Other than chest pain or sudden death, these could include, an uneven pulse rate, low blood pressure and peripheral atherosclerosis. The modern model of reconstructive bilitative system includes clinical methods along with diagnostic modalities like echocardiography and coronary imaging, of course clinical examination is still of great importance [7], [8].

Cardio vascular disease contributes to the number of deaths around the world. Cardiovascular conditions account for nearly 31 percent of deaths on an annual basis. Apart from obesity and diabetes, it is also correlated with obesity and other diseases associated with one's way of living [9]. Such conditions affect both men and women across the globe and more than 17 million people were considered to have been affected in 2004 alone. Additionally, more than 23 million are expected to be affected by the year 2030 [10], [11]. Chest pain, fatigue, shortness of breath, and dizziness are just a few symptoms that might appear as the condition progresses. This illness, along with many others, is often asymptomatic for a long-time making diagnosis very difficult. To improve such a situation, the need for early diagnosis cannot be overstated as it can help minimize the risk of further complications. Adopting a range of diagnostic tests such as ultrasound, electrocardiograms, computed tomography, and magnetic resonance would allow medical practitioners to identify the diseases [12], [13]. When it comes down to Prevention, one must take into consideration controlling diabetes, high blood pressure, smoking, and sedentary lifestyles in conjunction with a proper and healthy diet as well as exercise. People suffering from these diseases, on the other hand, will have to modify their ways of living alongside routine medical checkups in order to reduce the chance for further invocations [14], [15]. Your heart disease risk is significantly reduced by simply altering your way of life, adopting a healthier diet, maintaining minimal intake of saturated fats, performing mild exercises like walking on a daily basis, using the mindfulness technique in its lifestyle [16], [17].

2. Materials and Methods

2.1.1 Equipment and analytical devices

The equipment and analytical devices utilized within the study are listed in (Table 1).

Table 1. Equipment and analytical devices utilized throughout the study.

Equipments and analytical devices	Company-Origin
Biochemistry analyzer	Mindray-China
Centrifuge device	Hettich-Germany

ELISA system	Mindray-China
Immunofluorescence analyzer	Boditech-South Korea
Incubator	ESCO-Lithuania
Multichannel pipette	Thermo Scientific- Germany
Pipette	Thermo Scientific- Germany
Printer	Canon-Taiwan
Refrigerator	LG- South Korea
Tips	IMC-China
Water path	Memmert-Germany

2.1.2 Kits

The study used specific kits, including those for measuring Endocan and Interleukin-10 (from Mybiosource, USA), as well as kits for evaluating HbA1c, blood glucose, serum creatinine, blood urea, and other lipid markers (from Mindray, China).

2.2 Methods

2.2.1 Participants

The kits utilized within the study are listed in (Table 2.).

Table 2. Kits utilized in the study.

No	Kit	Company-Origin
1	Endocan	Mybiosource-USA
2	Interleukin-10	Mybiosource-USA
3	HbA1c, Blood glucose, Blood urea, Serum creatinine, TC, TG, and HDL	Mindray-China

2.2.2 Samples collection

Blood samples were collected from each participant. Five millilitres were divided into two tubes: 3 mL in a gel tube for serum separation (processed by centrifugation), and 2 mL in an EDTA tube for HbA1c evaluation. The serum was stored at -20°C for further analysis.

2.2.3 Human endocan

The Human Endocan levels were measured using a sandwich ELISA method. Anti-Human Endocan antibodies were pre-coated onto a 96-well plate, and biotin-labeled detection antibodies were used. After adding the specimen and performing a series of wash steps, HRP-Streptavidin was added, followed by a substrate solution to generate a color change. The concentration of Human Endocan was determined by measuring the optical density at 450 nm (Figure 1).

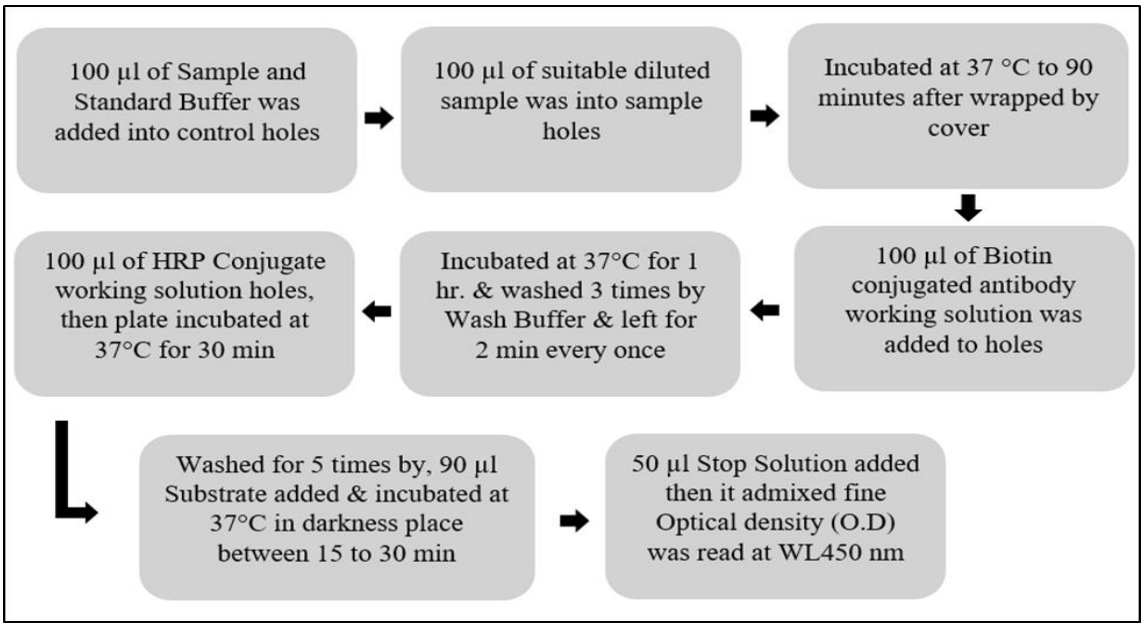

Fig.1. Diagram of endocan assay.

2.2.4 Human interleukin-10

The concentration of Human Interleukin-10 was measured using a sandwich ELISA method. Anti-Human Interleukin-10 antibodies were pre-coated onto a 96-well plate, and biotin-labeled detection antibodies were used. After incubation and washing, HRP-Streptavidin was added to initiate a color change, which was measured at 450

nm. The optical density of the yellow color produced was proportional to the concentration of Interleukin-10 in the sample (Figure 2).

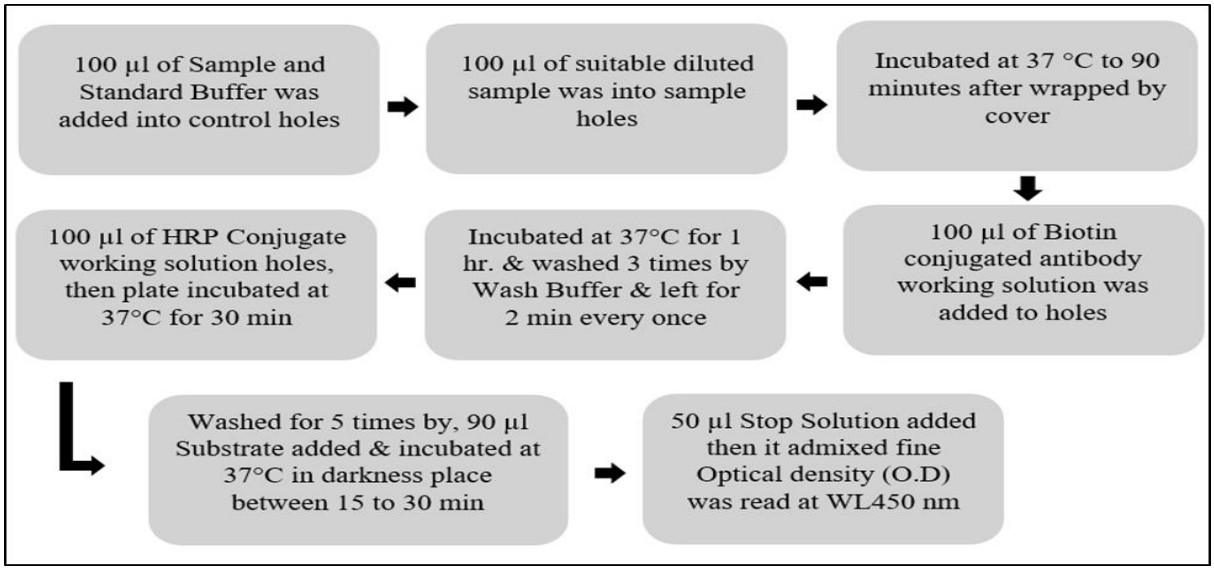

Fig. 2. Diagram of Interleukin-10.

2.2.5 Serum creatinine

Serum creatinine was measured using a colorimetric reaction with alkaline picrate. The creatinine in the sample reacts with picrate, and the color change is measured kinetically at a wavelength of 490 nm. The analysis was performed automatically using a biochemistry analyzer.

2.2.6 Blood urea

Blood urea levels were measured using an enzymatic and colorimetric method where urease breaks down urea into ammonium ions, which then form a blue-green complex with chloride and salicylate. The results were automatically obtained using a biochemistry analyzer.

2.2.7 Blood glucose

Blood glucose was measured using the Trinder method, where glucose is oxidized to gluconic acid and hydrogen peroxide by glucose oxidase. The peroxide reacts with 4-amino-antipyrine and chloro-4-phenol to produce a red-colored compound, which is measured at 500 nm using a biochemistry analyzer.

2.2.8 HbA1c

The HbA1c test uses a sandwich method to detect immune complexes formed between the antigen in the reagent and the sample. The intensity of fluorescence generated by these complexes is proportional to the percentage of glycated hemoglobin in the blood, and results were obtained automatically using a biochemistry analyzer.

2.2.9 Total Cholesterol

Total cholesterol levels were measured through an enzyme-catalyzed hydrolysis and oxidation process. The product, quinone-imine, is synthesized by peroxidase from 4-amino-antipyrine and phenol, and the concentration is determined using a biochemistry analyzer.

2.2.10 Triglycerides

Triglycerides were measured by breaking down lipoproteins using lipolysis enzymes. The resulting compound, quinone imine, was formed by peroxidase and hydrogen peroxide reacting with 4-amino antipyrine and 4-chlorophenol. Results were obtained automatically using a biochemistry analyzer.

2.2.11 High-density lipoprotein

High-Density Lipoprotein (HDL) was measured using a homogeneous method without centrifugation. Specific antibodies bound to HDL cholesterol, allowing selective measurement of HDL-cholesterol through an enzymatic test, and the results were obtained automatically using a biochemistry analyzer.

2.2.12 Low-density lipoprotein and very low-density lipoprotein

Low-Density Lipoprotein (LDL) and Very Low-Density Lipoprotein (VLDL) were calculated using the formulas: LDL = TC - HDL - VLDL and VLDL = TG/5.

2.3 Statistical analysis

The statistical analysis was performed using SPSS 21.0 and Microsoft Excel 2013. Numerical data were presented as mean and standard deviation, and the independent sample t-test was used for group comparisons. Categorical data were analyzed using the chi-square test, with statistical significance set at $p \leq 0.05$.

3. Results and Discussion

3.1 Demographic characteristics of the study groups

3.1.1 Age of study population

This study included 200 participants divided into four groups with a mean age of 49.88±6.14 for the healthy control, 55.32±6.39 for angina pectoris patients, 52.30±6.32 for ischemic heart disease patients, and 53.28±6.37 for myocardial infarction patients. Statistically significant age differences ($p < 0.001$) were found across the groups. Cardiovascular diseases like ischemic heart disease, myocardial infarction, and angina pectoris predominantly affect individuals over 50, especially in Iraq, and are often associated with factors such as atherosclerosis, hypertension, diabetes, and smoking. Age-related endothelial dysfunction, chronic inflammation, and oxidative stress also contribute to increased cardiovascular risk, underscoring the importance of managing these risk factors to prevent disease progression in older adults (Figure 3).

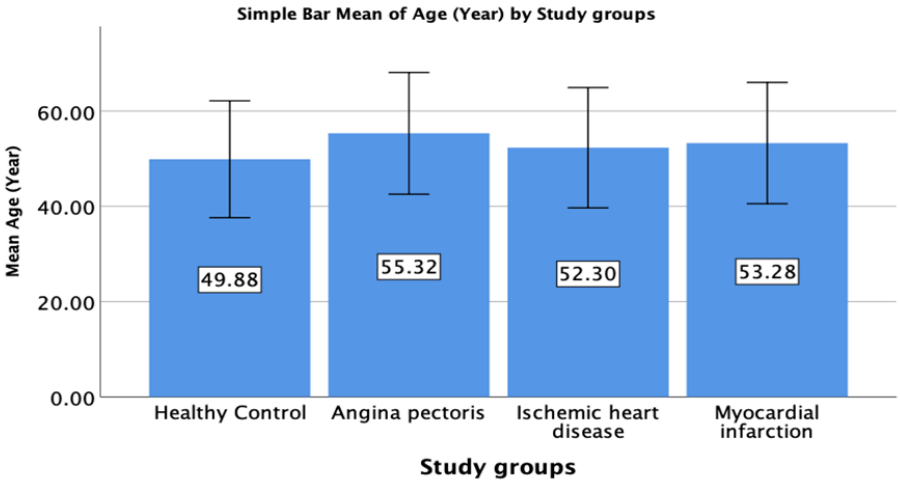

Fig. 3. Age distribution across all study groups' population.

3.1.2. Distribution of study population groups according to sex

The study observed a higher prevalence of males in the groups with ischemic heart disease, myocardial infarction, and the control group, while an equal distribution of sexes was seen in the angina pectoris group. However, there were no statistically significant sex differences across the groups (p-value 0.287). Cardiovascular disease characteristics vary notably between men and women due to biological, hormonal, and lifestyle differences. Men are generally more susceptible to these conditions, partly due to the protective effects of estrogen in premenopausal women, which helps maintain vascular health and reduces atherosclerosis risk. Testosterone, linked to risk factors like smoking and obesity, may also play a role. Additional factors influencing sex-based differences in cardiovascular disease include anatomical variations, lifestyle choices, and responses to stress, with men often at higher risk due to lifestyle patterns, larger heart size, and higher smoking rates (Table 3)

Table 3. Study population groups stratified according to sex distribution.

		Study groups			
		Healthy Control	Angina pectoris	Ischemic heart disease	Myocardial infarction
Sex	Female	20	25	23	16
		40.00%	50.00%	46.00%	32.00%
	Male	30	25	27	34
		60.00%	50.00%	54.00%	68.00%
Total		50	50	50	50
p-value				0.287	

3.2 Endocan serum levels of study groups

The study revealed that endocan serum levels were significantly elevated in all patient groups compared to the healthy control group, with the highest levels observed in myocardial infarction patients (2.14±0.19 ng/ml), followed by ischemic heart disease (1.72±0.19 ng/ml) and angina pectoris patients (1.2±0.15 ng/ml), and the lowest in the control group (0.76±0.17 ng/ml), with high statistical significance (p-value <0.001). Endocan, a vascular endothelial proteoglycan, has become a critical biomarker in cardiovascular disorders due to its involvement in inflammation, endothelial dysfunction, and plaque development. Elevated endocan levels indicate systemic inflammation, which accelerates atherosclerosis and myocardial infarction risks. Endocan's influence on endothelial function—such as impaired vasodilation and increased vascular permeability supports its role in advancing ischemic heart disease. Furthermore, high endocan levels correlate with plaque instability, linked to myocardial infarction and unstable angina. This study aligns with prior research, reinforcing endocan as a marker for cardiovascular disease diagnosis, prognosis, and as a potential therapeutic target. Further research is essential to clarify its therapeutic applicability and mechanisms in cardiovascular disease management (Figure 4).

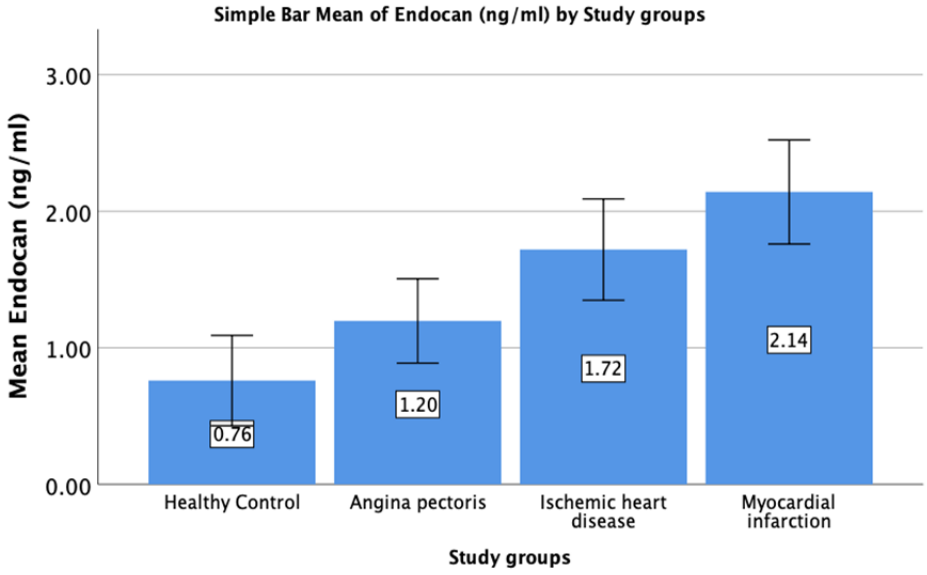

Fig. 4. Endocan serum levels between study populations.

3.3 Interleukin-10 (IL-10) serum levels of study groups

This study revealed that IL-10 serum levels were significantly higher in all patient groups compared to the healthy control group (Figure 5). Myocardial infarction patients showed the highest IL-10 levels (57.01±8.15 pg/ml), followed by ischemic heart disease patients (46.19±7.61 pg/ml) and angina pectoris patients (40.69±6.93 pg/ml), with the lowest levels found in the healthy control group (1.96±0.4 pg/ml). These results were statistically significant (p-value <0.001). IL-10 is an acid-labile anti-inflammatory cytokine that plays a crucial role in regulating and suppressing inflammation, especially following cardiac events. Its timing in the re-perfused myocardium after post ischemia owing to modified macrophage activity greatly reduces the influence plastic changes exert on the matrix and aids in tissue repair. In athero-sclerosis, for instance, greater IL-10 levels occur in cardiovascular patients owing to tissue damage

and inflammation and IL-10 is secreted for mitigating the inflammation. The present findings support other findings in the course of this research in which it was demonstrated that CAD was associated with an increase in serum IL-10 and it was shown that IL-10 decreased T-cell and macrophage responses and angiogenesis. The study of the function of IL-10 in these patients may provide the basis for development of novel strategies to treat IL-10 mediated cardiovascular diseases associated with inflammation.

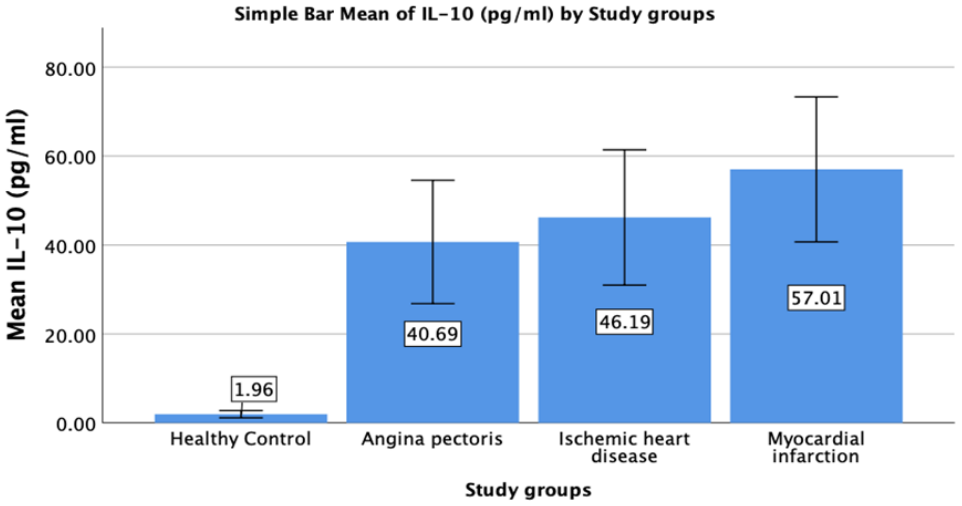

Fig. 5. IL-10 serum levels between study populations.

3. 4 Renal functions

3.4.1 Blood urea concentration of study groups

In contrast to the control group, whose blood urea mean levels averaged 22.72±2.09 mg/dL, those suffering from myocardial infarction, ischemic heart disease, and angina pectoris had significantly higher levels: 33.02±5.59 mg/dL, 30.42±3.83 mg/dL, and 27.28±2.63 mg/dL respectively. Blood urea concentration differences across the mentioned study groups are also very statistically significant (p-value <0.001), as is shown in figure 6.

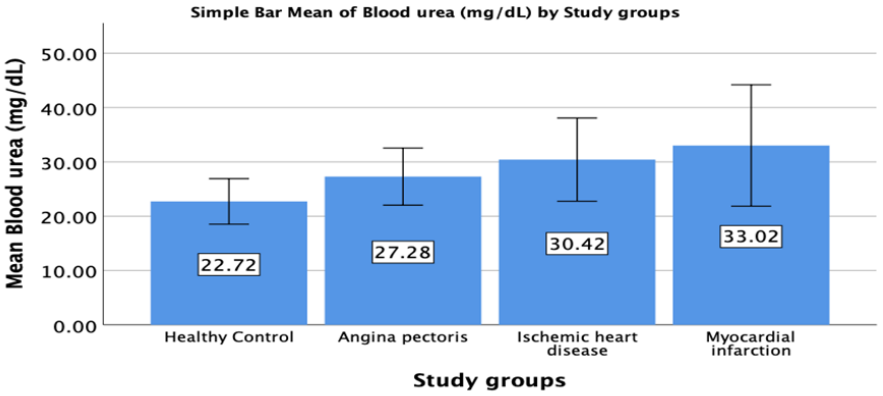

Fig. 6. Comparisons of blood urea concentration between study groups.

3.4.2 Creatinine serum concentration of study groups

This study showed that serum creatinine levels were significantly higher in patients with myocardial infarction (0.9±0.12 mg/dL), ischemic heart disease (0.88±0.09 mg/dL), and angina pectoris (0.79±0.09 mg/dL) than in the healthy control group (0.71±0.1 mg/dL), with a highly significant difference (p-value <0.001). Elevated blood urea and creatinine levels in cardiovascular patients suggest potential renal impairment, which may result from factors like acute kidney injury, reduced renal perfusion, infections, atherosclerosis, and hypertension. These renal function indicators highlight the importance of monitoring kidney health in patients with cardiovascular diseases to prevent further deterioration (Figure 7).

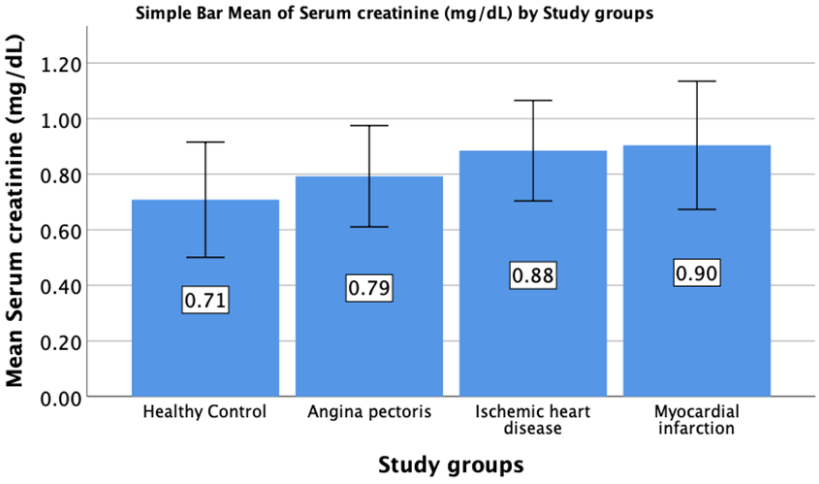

Fig. 7. Comparisons of creatinine serum concentration between study groups.

3.5 Blood glucose indices

3.5.1 Fasting blood glucose of the study groups

The mean serum fasting glucose levels were significantly higher in patients with myocardial infarction (130.12±22.18 mg/dL) compared to those with ischemic heart disease (125.46±24.65 mg/dL) and angina pectoris (111.64±13.51 mg/dL) (Figure 8). All patient groups exhibited elevated serum fasting glucose levels compared to healthy controls (90.04±5.24 mg/dL). These disparities were statistically significant (p-value <0.001) across all groups.

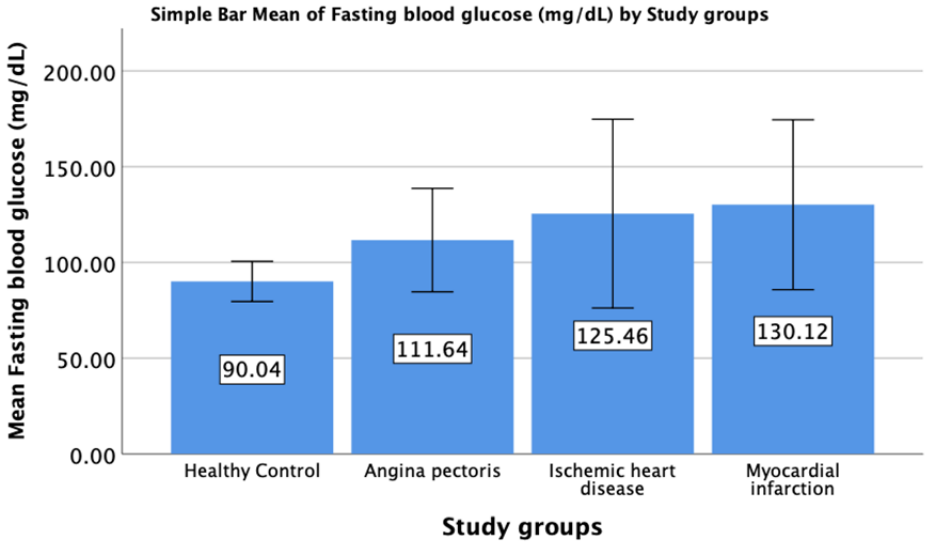

Fig. 8. Comparisons of fasting glucose serum levels between study groups.

3.5.2 Hemoglobin A1c (HbA1c) blood concentration of the study groups

The study found significantly higher HbA1c blood concentrations in patients with myocardial infarction (6.37±0.61%), ischemic heart disease (6.19±0.71%), and angina pectoris (6.05±0.53%) compared to the healthy control group (5.21±0.34%), with a statistically significant difference (p-value <0.001). These elevated HbA1c levels indicate impaired glucose metabolism, a known risk factor for cardiovascular diseases. Diabetes and cardiovascular diseases are closely linked, with diabetes increasing the prevalence of coronary heart disease and stroke. Elevated glucose levels contribute to endothelial damage, inflammation, and increased clotting, further exacerbating cardiovascular risk. Understanding the relationship between HbA1c and cardiovascular conditions can aid in better prevention and treatment strategies (Figure 9).

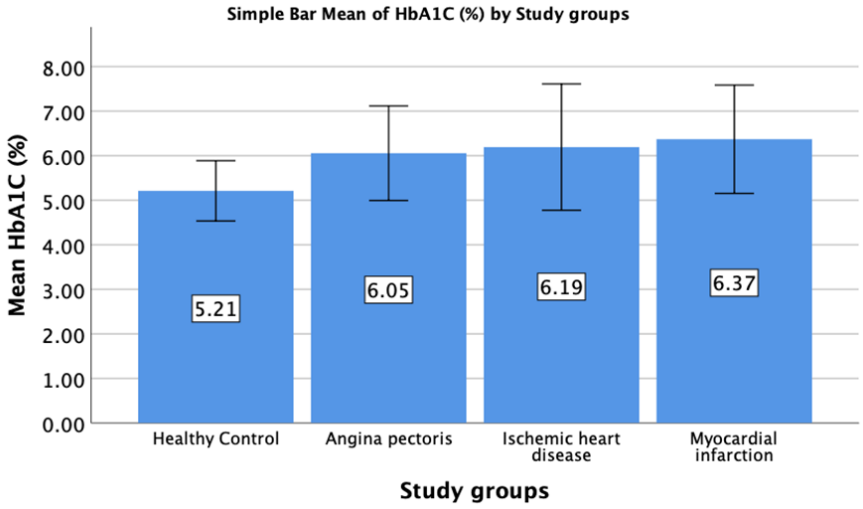

Fig. 9. Comparisons of HbA1c blood concentrations between study groups.

3.6 Lipid profile

3.6.1 Total cholesterol (TCL) of the study groups

All patient groups showed elevated TCL compared to the healthy control group (Figure 10). Additionally, the myocardial infarction patients exhibit higher TCL concentrations (172.60±22.13 mg/dL) than ischemic heart disease (132.7±18.56 mg/dL) and angina pectoris patients (111.08±16.97 mg/dL), while, the healthy control group showed lower TCL concentration (92.64±15.53 mg/dL).

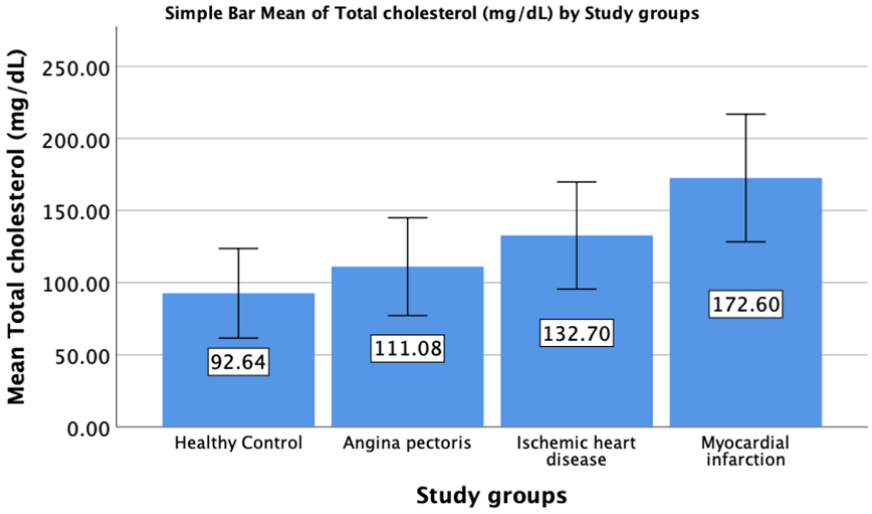

Fig. 10. Comparisons of total cholesterol concentrations between study groups.

3.6.2 Triglyceride (TG) of the study groups

All patient groups exhibited elevated TG levels compared to the healthy control group (Figure 11). Notably, myocardial infarction patients displayed the highest TG concentrations (239.46±40.94 mg/dL), surpassing those observed in ischemic heart disease (179.62±42.97 mg/dL) and angina pectoris patients (119.4±41.08 mg/dL). Conversely, the healthy control group exhibited significantly lower TG levels (39.28±24.21 mg/dL).

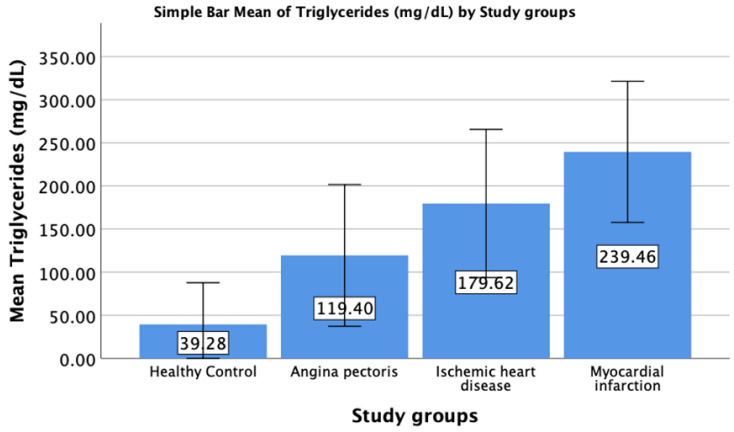

Fig. 11. Comparisons of triglyceride concentrations between study groups

3.6.3 High-density lipoprotein (HDL) of the study groups

The data presented in figure 12 revealed that patients with myocardial infraction exhibited lower HDL concentrations (27.96±5.7 mg/dL) than all study groups, followed by ischemic heart disease patients (29.48±5.8 mg/dL) and angina pectoris patients (30.92±5.78 mg/dL). In contrast, the healthy control individuals showed higher HDL concentrations (42±5.77 mg/dL) than all patient groups.

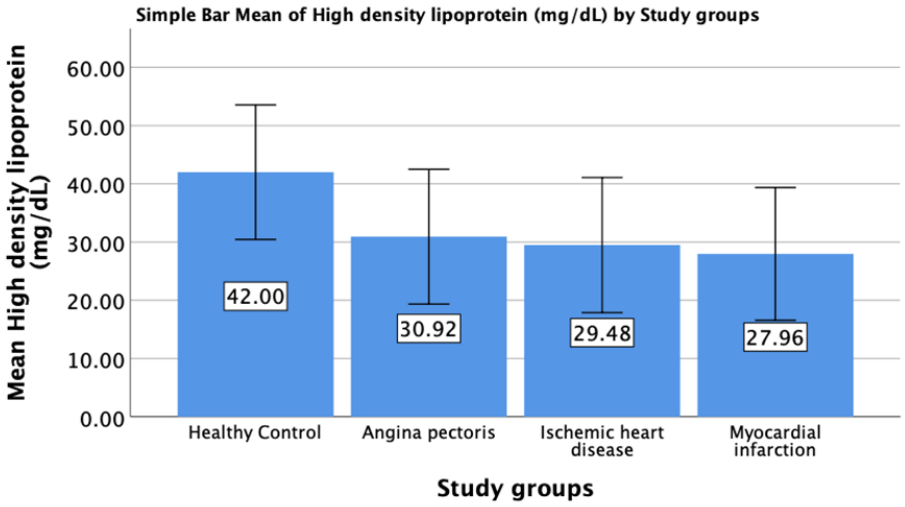

Fig. 12. Comparisons of high-density lipoprotein concentrations between study groups.

3.6.4 Low-density lipoprotein (LDL)

All patient cohorts had increased LDL levels compared to the healthy control group (Figure 13). Furthermore, patients with myocardial infarction have elevated LDL levels (96.75±22.14 mg/dL) compared to those with ischemic heart disease (67.3±20.38 mg/dL) and angina pectoris (56.28±20.64 mg/dL). Meanwhile, the healthy control group has a reduced LDL concentration (42.78±18.31 mg/dL).

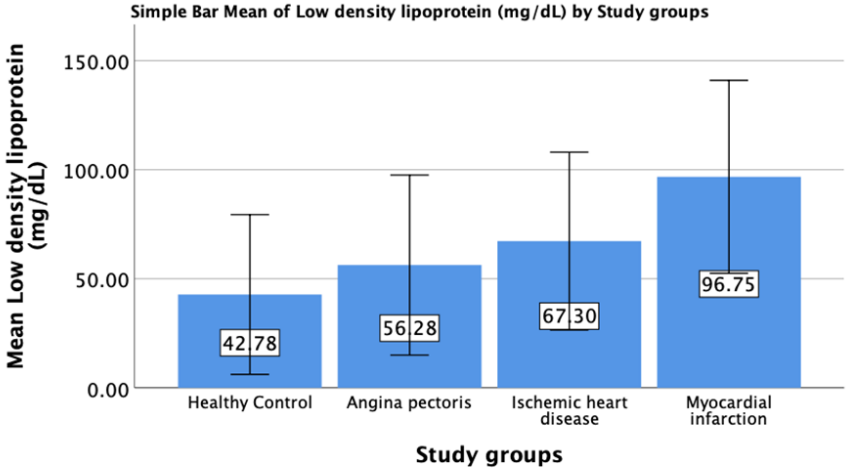

Fig. 13. Comparisons of low-density lipoprotein concentrations between study groups.

3.6.5 Very low-density lipoprotein (VLDL)

All patient groups exhibited elevated VLDL levels compared to the healthy control group. Notably, myocardial infarction patients displayed the highest VLDL concentrations (47.89±8.19 mg/dL), surpassing those observed in ischemic heart disease (35.92±8.59 mg/dL) and angina pectoris patients (23.88±8.22 mg/dL). Conversely, the healthy control group exhibited significantly lower VLDL levels (7.86±4.84 mg/dL) (Figure 14).

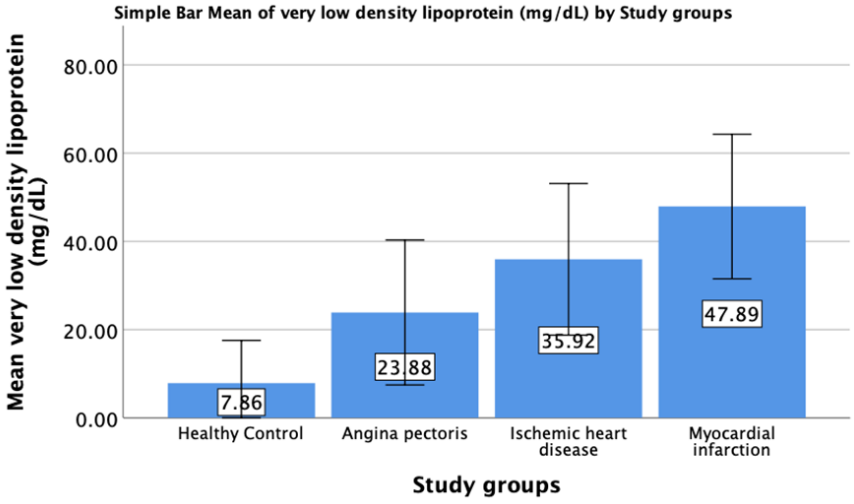

Fig. 14. Comparisons of very low-density lipoprotein concentrations between study groups.

Dyslipidemia, characterized by abnormal lipid levels such as increased total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG), along with decreased high-density lipoprotein cholesterol (HDL-C), is a major risk factor for cardiovascular and cerebrovascular diseases, including stroke and myocardial infarction. The study found elevated cholesterol levels and decreased HDL-C in patients, which aligns with the established link between high cholesterol, atherosclerosis, and cardiovascular disease. Elevated LDL-C and triglycerides contribute to plaque formation in arteries, promoting inflammation and narrowing blood vessels, increasing the risk of cardiovascular events.

4. Conclusions

Patients over 50 are more susceptible to cardiovascular diseases, with age-related factors like arterial stiffening and heart muscle weakening playing key roles. Older males have a higher incidence of ischemic heart disease and angina, likely due to hormonal, genetic, and lifestyle factors. Higher endocan levels in patients highlight its role as a proinflammatory biomarker in cardiovascular disease. Increased IL-10 levels reflect the body's anti-inflammatory response in cardiovascular conditions. Elevated blood urea, creatinine, glucose, HbA1c, and abnormal lipid profiles indicate kidney dysfunction, dysglycemia, and dyslipidemia, all contributing significantly to cardiovascular disease risk.

Author Contribution

Ghadah Azeez Khaleefah, Youssra Al-Hilaly, Rayane Mahious, Ebru Halvacı; wrote, edited, drew figures and developed the article. Fatih Sen; supervisor and responsible person.

Acknowledgments

The authors dedicated this publication to the 100th anniversary of the Republic of Türkiye. As scientists raised by Türkiye, they are proud to be citizens of this country.

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