Iraqi Journal of Science, 2026, Vol. 67, No. 4, pp: 2256-2266
DOI: 10.24996/ijs.2026.67.4.28

ISSN: 0067-2904

Evaluation of Ceruloplasmin and Some Biochemical Parameters in Iraqi Patients With Coronary Artery Disease

Mohanad S. AL-Fayyadh
Department of Biotechnology, College of Science, University of Baghdad. Baghdad, Iraq.

Received:12/9/2024 Accepted: 28/5/2025 Published: 30/4/2026

Abstract

The current work aimed to clarify the various biochemical parameters in individuals with coronary artery disease (CAD) that impact the ceruloplasmin activity. Thus, patients with CAD (n=38 CAD participants) and a healthy control group (n=38) were included. Their ages ranged from 42 to 67 years old. Ceruloplasmin activity (Cp), triglycerides (TG), total cholesterol (TC), high-density lipoprotein (HDL-c) , total protein (TP), albumin, creatinine, urea, malondialdehyde (MDA), and calcium were measured in the study in serum samples from each group. The findings of the comparison of measured parameters between CAD and control groups were as follows: Results revealed that the levels of TG, TC, VLDL-c, LDL-c, globulin, TP, creatinine, urea, MDA, and ceruloplasmin activity were significantly higher in CAD group compared with controls, whereas albumin, HDL-c, and calcium levels have been significantly lower.

Keywords: Cardio artery disease, Ceruloplasmin, Lipid profile, Total protein, Kidney function, Oxidative stress.

تقييم السيرولوبلازمين وبعض المؤشرات الكيموحيوية في المرضى العراقيين المصابين بأمراض الاوعية التاجية

مهند سلام مجيد الفياض

قسم التقنيات الاحيائية، كلية العلوم، جامعة بغداد.، بغداد، العراق

الخلاصة:

تهدف الدراسة الحالية لبيان تأثير فعالية السيرولوبلازمين مع بعض المؤشرات الكيمو حيوية في مرضى الشريان التاجي. لتحقيق ذلك تضمنت الدراسة مجموعتين ضمن أعمار (42–67 سنة)و مجموعة المرضى الشريان التاجي (38 شخص) ومجموعة الاصحاء (38 شخص). الدراسة تضمنت قياس بعض المؤشرات الكيمو حيوية في مصل نماذج كل مجموعة فعالية السيرولوبلازمين., الدهون الثلاثية, , الكوليستيرول الكلي, البروتينات الدهنية عالية الكثافة, البروتينات الكلية, الالبومين, اليوريا, الكرياتينين, مالوندای الديهايد و الكالسيوم. بناءا على مقارنة قياس المؤشرات بين مجاميع السيطرة ومرضى الشريان التاجي, كانت النتائج كالتالي: هنالك زيادة معنوية في الكوليستيرول الكلي, الدهون الثلاثية, البروتينات الدهنية واطئة الكثافة, البروتينات الدهنية واطئة الكثافة جدا, البروتينات الكلية, الكلوبيولين, اليوريا, الكرياتينين, مالون داي الديهايد و

Email: mohanad.majeed@sc.uobaghdad.edu.iq

فعالية السيرولوبلازمين, بينما كانت هنالك أنخفاض معنوي في البروتينات الدهنية عالية الكثافة, الالبومين و الكالسيوم في مجموعة مرضى الشريان التاجي مقارنة بمجموعة الاصحاء.

Introduction

Stroke, heart failure, hypertension (HTN), congenital heart disease, and peripheral artery disease are all included in the category of illnesses known as cardiovascular diseases (CVDs) [1]. Coronary artery disease (CAD) can be identified by developing atherosclerosis in coronary arteries that may be asymptomatic in some cases. Coronary heart disease (CHD), which is referred to as ischemic heart disease (IHD) as well, encompasses some of the conditions like stable angina, acute coronary syndrome (ACS), and silent myocardial ischemia. Mortality associated with CHD is mainly a result of CAD [2]. Reactive oxygen species (ROS) are viewed as one of the major factors in the disease's pathogenesis. In oxidative stress, ROS amount in the body increases gradually as a result of an increase in the production, lowered anti-oxidant defenses, or a combination of both, which leads to impairing the redox signaling and compromising molecular damage regulation [3]. Lipid peroxidation's primary aldehyde byproduct is the 3-carbon dialdehyde species malondialdehyde (MDA) that can be processed by enzymes or react with the proteins and tissues in order to generate adducts (MDA-modified macro-molecules), causing bio-molecular damages [3]. MDA, which is a reactive aldehyde, is one of many reactive electrophile species inducing toxic stress in the cells [3].

This study has been undertaken for the purpose of framing out lipid and lipoprotein profiles in patients who have coronary heart disease, Dyslipidemia is a fundamental CAD cause. Increased levels of total cholesterol (TC), triglycerides (TG), low-density lipoprotein-cholesterol (LDL-c), and reduced high-density lipoprotein-cholesterol (HDL-c) are conventional factors of risk in myocardial infarction patients [4]. Cardiovascular diseases encompass a range of issues related to heart and blood vessels, including ischemic heart disease, rheumatic heart disease, and cerebrovascular disease, commonly referred to as strokes [5]. Coronary artery disease (CAD), a form of cardiovascular disease, is seen as one of the primary causes of illness and mortality, creating a significant socioeconomic burden globally [5]. Chronic kidney disease (CKD), which affects 10% - 15% of global adult populations, poses a significant challenge to the public health [6]. CKD can be identified by long-term, progressive damage to kidneys, which leads to gradual renal function loss with time. With the progression of CKD, the ability of the kidneys in the efficient filtering of the blood is weakened. Such renal function deterioration results in accumulating toxins and metabolic dysfunction, which leads to uremia ultimately. There is considerable evidences that CKD leads to a significant increase in risks of adverse cardio-vascular outcomes, which include myocardial infarction (MI), heart failure (HF), stroke, and cardiovascular mortality [6]. Critically, there is a bi-directional causality in this correlation. Conditions inducing the circulatory strain, notably hypertension, are referred to to as exacerbated renal damage because of a reduction in renal perfusion and ischemia, thereby reciprocally affecting the risks and progression of CVD and CKD [6].

It is undeniable that hypercholesterolemia, one of several cardiovascular risk factors, could be recognized from an early age as a predictor of future cardiovascular risks [7]. Ceruloplasmin (CP) is a member of the plasma protein class known as α2-glycoproteins. It is responsible for 95% of total circulatory copper in healthy adult individuals and is generated in the liver using copper, primarily from food. In addition to contributing to the metabolism of iron and copper, CP represents an acute-phase reactant that could operate as an anti-oxidant but produces free radicals, which might cause several diseases [8]. Interestingly, most dietary copper found in plasma that would ultimately contribute to the development of CP

was not consumed recently but several weeks or months prior. As a result, it will take time for the CP to reflect changes in the availability of copper in the diet.
Although oxidative stress might be a significant factor in the beginning of CVD, whether CP is a causal mediator or a passive marker of inflammation is still unknown. Reviewing scientific literature reveals that it is challenging to understand how CP affects CHD. To have a better understanding of the CP's impact on CHD risks, we have conducted the first study that presents information from observational studies that involve the CP's effects over the past thirty years. Anti-oxidants can compete with other oxidizable substrates at low concentration levels, significantly inhibiting or delaying the oxidation of substrates. Anti-oxidants' physiological function is to stop chemical processes, in particular, the ones that result from free radicals, from harming cellular components [9].

Blood urea nitrogen (BUN), which is a metabolic waste product of the protein that is created by the liver and excreted by the kidneys, is routinely employed as a bio-marker for evaluating the renal functions [10]. The research found a connection between the renal function indices like the glomerular filtration rate, BUN, and creatinine and CVD mortality [11]. The present study aims to evaluate some biochemical parameters such as lipid profile, kidney function tests, blood proteins, and lipid peroxidation represented by malondialdehyde (MDA) and first-time Cp, an antioxidant secreted from macrophages in patients with CAD.

Material and methods

Design of the study

This study has been conducted in the Department of Biotechnology at the College of Science at the University of Baghdad. Thirty-eight patients with heart disease either visited the cardiac clinic or were admitted to the hospital from December 2023 to March 2024, with 38 healthy subjects as a control group. This work performed specific tests on creatinine, urea, total protein, calcium, globulin, albumin, MDA, and lipid profile, including.TC, TG, VLDL-c, HDL-c, LDL-c, and ceruloplasmin activity. The samples were analyzed in the University of Baghdad's Chemical Lab by the Department of Biotechnology of the College of Science. A 5 mL blood sample was obtained from each patient using of a syringe and needle.

Serum Creatinine Determination:

Creatinine level in the serum have been colorimetrically determined by utilizing BIOLABO commercially available kits. Kidneys eliminate creatinine released throughout creatine phosphate metabolism. The colored creatinine picrate complex, carrying ionic limits, is created in the case where creatinine is combined (in a 1:1 ratio) with alkaline picrate. The colored complex production rate is correlated inversely with the creatinine content.

Serum Urea Determination:

Using a Randox kit, serum urea was colorimetrically quantified per Fawcett and Scott's [12].

Determining the serum total protein (TP):

Tietz [13] said that the colorimetric technique was used for measuring serum TP through Randox commercially available kits. This kit the uses Biuret approach to detect the amount of protein in the serum. The cupric ion interacts with the protein peptide bond in an alkaline medium, forming a colored complex.

Determining serum albumin concentration:

Albumin in the serum has been measured using a colorimetric method using a commercially available kit (CliniChem). In order to create a complex green color, this method relies on specific bromo-cresol green (BCG) binding, an anionic dye, and protein in acid pH. The sample's albumin concentration directly correlates with the color intensity that results.

Globulin Concentration Determination:

The total globulin level has been calculated by albumin subtraction from total protein [14].
Globulin concentration (g/dl) = TP (g/dl) – Albumin (g/dl).

Determining serum calcium

Serum calcium has been colorimetrically measured depending on Tietz [13] using a Biolabo kit.

Measurement of ceruloplasmin

, Ceruloplasmin activity has been evaluated according to Nomoto and Sunderman's approach [15].

Determining serum total cholesterol (TC):

Using the commercially available kit (bio-Merieux), total cholesterol (T.chol) concentration was assessed useing of an enzymatic approach [16]. At 500nm, T. chol value has been spectro-photometrically specified.

Determination of serum HDL-c:

The (bio-merieux) kit has been utilized in order to measure HDLc levels by using an enzymatic approach [17]. The key concept of this approach is precipitating VLDL-c and LDL-c chylomicrons and lipoproteins by adding phosphotungstic acid in the presence of magnesium iones. HDL containing cholesterol and phospholipids has been included in the supernatant that was created after the centrifugation. At 500nm, HDL had been spectro-photometrically determined.

Determination of serum triglycerides (TG):

Using Bio-Merieux kit and the enzymatic approach that has been proposed by Prencipel and Fossati [18], the total serum TG concentration has been specified. The 500.0nm value has been designated as TG total serum concentration.

Determining the serum VLDLc:

VLDL-c has been specified depending on the classical equation of Friedewald *etal*. [19].
VLDL-c (mg/dl) = 0.20**x** TG (mg/dl).

Serum LDL-c Determination:

Serum LDL has been specified based on Friedewald's equation. LDLc =
TC – (VLDLc + HDLc).

Determination of Malondialdehyde (MDA):

The conclusion on the concentration of MDA in the serum has been based on the Aust and Buege technique [20]. The breakdown of poly-unsaturated fatty acids produces MDA, which is used as an easy way to measure peroxidation processes. Additionally, the thiobarbituric acid (TBA) used to estimate MDA produces a pink color when reacting with TBA, which may be read at λ max 535 nm [20].

Statistical analyses:

The Statistical Package for the Social Sciences (SPSS)- 22 software has been used for data analysis. Mean ± SD has been used to represent data. The research parameters have been checked in order to see whether they adhered to Gaussian distribution utilizing the Shapiro-Wilk test of normality. The Bonferroni Post Hoc test was used for multiple comparisons following ANOVA tests. Using Pearson's correlation analysis, the levels of the link were examined. A $p<0.05$ value had been indicated as significant [21].

Results and discussion

Level of lipid profile in coronary artery disease

Compared to the controls, patients with CAD have significantly different lipid profile levels. Compared to the control group, Table 1 shows a significant increase $p \leq 0.05$ in TC, TG, VLDL-c, and LDL-c in CAD participants. Compared to control subjects, HDL-C has a lower significance ($P \leq 0.05$).

Table1: Level of lipid profile in patients with CAD

Parameters	Control subjects Mean ±SD (N=38)	CAD subjects Mean ±SD (N=38)	P- values
T.ch (mg/dL)	133 ± 2.4	198 ± 5.5	≤ 0.05
TG (mg/dL)	88 ± 3.4	143 ± 4.4	≤ 0.05
HDL-C(mg/dL)	43 ± 3.1	35 ± 4.2	≤ 0.05
VLDL-C (mg/dL)	17.60 ± 1.6	28.6 ± 4.1	≤ 0.05
LDL-C (mg/dL)	72.4 ± 3,2	134.4 ± 6.1	≤ 0.05

According to the degree of coronary artery narrowing,myocardial responses can be classified as chronic ischemic heart disease, acute myocardial infarction, chest discomfort, and sudden cardiac death. The most prevalent risk factors for CHD include smoking, hypertension, diabetes, obesity, gender, stress, age, and dyslipidemia [22-24]. In addition, high TG levels, TC, LDL-c, VLDL-c, and low HDL-C levels are among the most frequently modifiable risk factors for CHD [25]. The widely recognized cholesterol-diet-CHD hypothesis results from cholesterol's crucial role in CHD. This theory states that elevated plasma cholesterol concentrations raise CHD risk. With declining concentrations of serum TC, this risk is declining.

Epidemiologic research findings revealed a significant risk factor for CHD is the co-occurrence of low HDL-c and increased TG levels [26]. Patients who have low HDL-c and higher TG have maximum rates of major coronary events, according to post hoc analyses of many trials [27]. Although there is some debate about whether elevated small, dense LDL-c particles constitute an independent risk factor, it is undeniably related to a higher CHD risk [27]. This is in agreement with the study conducted by Muntaha *et al*., [28], patients with CAD had lower HDL-c levels and higher TC, LDL-c, TG, and VLDLc than the healthy group..

. Vitamin D lack leads to impairing pancreatic beta cells' activity, which is a cause of insulin resistance, abnormalities in lipoprotein metabolism, and eventually higher levels of TG and lower levels of HDL-c. Managing dyslipidemia risks in T2DM represents a critical CAD prevention component. Those results have shown that low 25-OH D levels predict elevated atherogenic lipoproteins and vitamin D administration could help avoid the cardiovascular disease [29].

Effect of total protein in coronary artery disease

In this study, patients with CAD significantly increased $p \leq 0.05$ in serum TP and globulin levels, as seen in Table 2. Although there is a reduction in Albumin in CAD participants compared to the controls, significant $P \leq 0.05$.

Table 2: Serum TP, albumin, and globulin in patients with CAD

Parameters	Control subjects Mean ±SD (N=38)	CAD Subjects Mean ±SD (N=38)	P- value
TP (g/dl)	6.90±0.62	7.8±0.72	≤0.050
Albumin (g/dl)	4.6±0.41	3.31±0.51	≤0.050
Globulin (g/dl)	2.3±0.51	4.49±0.73	≤0.050

Studies have shown that patients with atherosclerosis and type 2 diabetes have higher TP levels when compared to healthy people because these conditions alter not just the metabolism of glucose and lipids but also of protein [30]. The fact that protein intake significantly influences serum TP levels could cause a discrepancy in findings between such works [31]. Compared with the healthy group (Table 2), the albumin levels in the CAD group declined, however, there was a significant difference between CAD and the controls, and the results for globulin were quite the opposite. As insulin regulates albumin expression in the liver, findings from various works [32] demonstrated that albumin level was reduced in atherosclerosis [32]. Insulin specifically inhibits albumin production by acting directly on the liver [33]. Because of the cross-sectional nature of the study indicating more significant mortality with hypoalbuminemia, lower albumin levels could increase the risk of atherosclerosis [34]. Albumin's capacity to transport bilirubin gives it an indirect anti-oxidant function [35]. People with CAD showed a decrease in serum albumin's anti-oxidant capacity, which might exacerbate oxidative stress (OS) and lead to vascular and metabolic morbidities [36]. Proteins have been chosen for the evaluation in the present study based on their roles in the mechanisms underlying atherosclerosis, atherogenesis, and plaque instability, which includes vascular inflammations, aberrant lipid regulation, thrombosis, metabolism hormones, and vascular smooth muscle and extracellular matrix (ECM) re-modeling [37]. Serum albumin represents one of the essential nutritional indicators, the main oncotic pressure factor, and body fluid modulator [38]. In clinical settings, as critical and simple nutritional indicators. It is used in general for the evaluation of clinical courses of different illnesses, which include burns, shock status, trauma, hemorrhage, bleeding events, terminal renal dysfunctions, acute respiratory distress syndrome, post-resuscitation, and nutritional therapy [39,40]. A serum albumin level reduction is typical in critically ill patients and is generally a result of increased wasting, bleeding because of inflammations, and Albumin leakage from the gastrointestinal tract [38]. Albumin levels may decrease as well because of the re-distribution from the intra-vascular space to the interstitial space, which results from increased capillary permeability or poor nutritional status and liver function reflection [41]. Albumin's action and pathophysiology are thought to be essentially correlated with cardiac dynamics and inflammation and share numerous features with CVD's aggravating factor [42].

Kidney function related to coronary artery disease.

Patients with CAD significantly differed in their creatinine, urea, and calcium levels, as seen in Table 3. Compared to the controls, the creatinine and urea levels in the CAD group are much higher ($p \leq 0.05$). Compared with the healthy participants, patients with CAD had lower serum calcium levels with a significance level of $p \leq 0.05$.

Table 3: Creatinine, urea, and calcium levels in patients who have CAD

Parameters	Controls subjects Mean ±SD (N=38)	CAD subjects Mean ±SD (N=38)	P-value
Urea (mg/dl)	14.90±2.9	47.8±6.8	≤0.05
Creatinine (mg/dl)	0.60±0.2	2.6±0.6	≤0.05
Calcium (mmol/L)	1.87±0.3	1.1±0.32	≤0.05

As a result of increased exposure to and accumulation of several cardiovascular risk factors, the mortality and morbidity of CVD were steadily rising globally [43]. According to prior research, risk factor-based control and prevention methods could significantly lower cardiovascular risk . Additionally, a few clinical studies have discovered that the increase in serum creatinine levels that frequently signifies a decline in the glomerular filtration rate could be utilized as a predictive CVD marker [44].. Increased creatinine levels were reported

to play a role in the increase of the risks of various CVDs. Understanding how creatinine interacts with different cardiovascular risk factors and patient cardiovascular risk is necessary. Serum creatinine levels were closely related to cardiovascular risk variables in our investigation. When assessing risks for the development of CVD, serum creatinine must be considered in addition to conventional CVD risk variables as it is a reasonably convenient biochemical measure [44].

In the case where most of the human kidney is affected by pathological damages, and the glomerular filtration rate (GFR) percentage is reduced (over 50%), the case of an elevated serum creatinine level could be clinically evident. Its concentration is dependent upon various factors, including the rate at which creatinine is produced, the volume of distribution, extrarenal metabolism, and renal injury [45]. High serum creatinine frequently reduces the glomerular filtration rate, is prone to water-sodium retention, and raises the burden on heart and cardio-vascular risk [46]. Serum creatinine behaves as a pro-inflammatory state marker, and inflammation-mediated endothelial dysfunction was shown to be related to the occurrence of cardiovascular events in adult females who have a reduction in renal function. Uncertainty exists regarding underlying mechanisms causing the correlation between baseline serum calcium levels and CAD. Reduced serum Ca has the potential to interfere with electrophysiological activity. Low serum Ca levels for cardiomyocytes can prolong the plateau phase of ventricular action potential and delay Ca channel closure, which is considered one of the independent high-risk factors for mortality [47]. Vascular smooth muscle cells could be damaged by calcium insufficiency, which might worsen cardiovascular conditions and worsen the prognosis for CAD patients. Blood pressure could also rise and disturb lipid metabolism [48]. Wang *etal*., [49] have observed that higher levels of serum calcium have been related to lower rates of mortality amongst CAD patients, which suggests that there are possible protective effects [49]. On the other hand, Zhang *et al*., [50] have reported a positive correlation between higher levels of serum calcium and coronary atherosclerosis severity in patients who are undergoing cardiac CT, which is an indication of the fact that increased levels of calcium might be a contributing factor to the vascular calcification [50].

Effect of oxidative stress on CAD patients

Ceruloplasmin (Cp) activity and Malondialdehyde (MDA) in the group with CAD is significantly increased ($p \leq 0.05$) in comparison with the controls, as listed in Table 4.

Table 4: Ceruloplasmin activity and MDA levels in CAD and healthy patients.

Parameters	Control subjects Mean ±SD (N=38)	CAD subjects Mean ±SD (N=38)	P-value
Cp activity (U/L)	789±121.3	1150±278.4	≤0.05
MDA (mg/L)	0.62±0.13	1.4±0.32	≤0.05

Table 4 shows that patients with CAD had higher MDA levels than the healthy group. This characteristic is one of the cells' final poly-unsaturated fatty acid peroxidation products in cells. Since MDA is a well-known indicator of anti-oxidant status and oxidative stress [51], an increase in MDA levels denotes the existence of OS, as adipose tissue secretes adipokines, which trigger the formation of ROS and result in the process known as oxidative stress (OS). . According to Pizzino *et al*., [52], the OS is typically brought on by either genetics or environmental factors such as smoking, poor dietary habits, and exposure to toxins. Increased lipid peroxidation impairs the function of the membrane by decreasing its fluidity and altering the actions of receptors and enzymes linked to the membrane. MDA is a persistent end product of the lipid peroxidation. It may be described as a three-carbon aldehyde in various forms in aqueous solutions. MDA has been used as a lipid peroxidation biomarker

and an indicator for damages caused by free radicals [53]. Obesity is thought to be a condition of chronic inflammation that creates OS. According to Pizzino *et al*., [54], lipid peroxidation caused by OS and these ROS can aid in the development of atherosclerosis if the generation of these ROS surpasses the cell's antioxidant. The levels of MDA significantly increased in an Indian study of obese males. Increased accumulation of fats, obesity, and the consumption of high-calorie, high-fat meals are all directly related to changes in OS [54].
A study has been carried out to ascertain the association between potential OS markers and accelerated development of carotid atherosclerosis in patients with CKD. Discovered that CVD, particularly atherosclerosis, could be indirectly identified by assessing OS markers like MDA [55]. Serum ferroxidase, the enzyme under study (CP), is a positive acute-phase reactant because it rises in concentration in response to inflammation and cell damage. It helps to bind iron to transferrin by oxidizing it from ferrous (2+) to ferric iron (3+). It might play a role in regulating the oxidation of membrane lipids [56]. High levels of CP could result in vascular injury by producing free radicals (FRs) and oxidizing LDL to make it more atherogenic. Because freed copper could contribute to oxidative disease, the ROS interferes with copper's ability to attach to CP, limiting its usual protective function [57]. This study presents strong evidence that supports serum MDA utility as one of the reliable biomarkers for the evaluation of CAD and its potential in predicting adverse cardiovascular outcomes. Such oxidative stress gradient, as the levels of MDA have indicated, aligns with the theory that oxidative mechanisms play a crucial part in atherosclerosis and subsequent cardiovascular events' progression [58]. The observed gradient suggested a direct relationship between oxidative stress intensity and CAD advancement. Oxidative stress plays a role in endothelial dysfunctions, plaque instability, and inflammation, all vital in CAD progression [59]. The increasing MDA levels with the severity of CAD underscore its potential as a reliable marker for assessing this disease's progression and prognosis.

Conclusion

The present work, concluded that CAD patients had significantly higher TC, TG, LDL levels, urea, creatinine, TP, globulin, MDA, and CP activity. These results might be helpful for CHD treatment and similar future research.

Ethical clearance

The Research Ethical Committee promotes scientific study by ethically appraising Iraq's environmental, higher education, health, and scientific research ministries.

REFERENCES

[1] G. Wang, S. D. Grosse, and M. W. Schooley, "Conducting research on the economics of hypertension to improve cardiovascular health," *American Journal of Preventive Medicine*, vol. 53, no. 3, pp. S115–S117, 2017.

[2] P. Lancellotti and B. Cosyns, "Highlights of acta cardiologica," *Acta Cardiologica*, vol. 77, no. 6, pp. 469–470, 2022.

[3] A. N. Ghada, E. S. Ghada, M. E. Dalia, and A. K. Marwa, " Serum malondialdehyde as a marker of oxidative stress in rheumatoid arthritis," *Egyptian Rheumatology and Rehabilitation*, vol. 51, no. 43, pp. 1-6, 2024.

[4] C. Sridevi, M. Susheel, H. Prakash, D. N. Digvijay, and S. Ankit, " Evaluation of Lipid Profile Management in Coronary Artery Disease Patients on Statin Therapy: A Single-Centre, Retrospective, Observational Study," *Cureus*, vol,16, no.10, pp. e71942, 2024.

[5] K. Kainaat, U. Pothu, M. Tariq, and S. Alok, " Role of lipid Profile, circulating Malondialdehyde (MDA) and Oxidized LDL as a biochemical risk marker for coronary artery disease," *Frontiers in Health Informatics*, vol. 13, no. 7, pp. 1087-1100, 2024.

[6] Z. Xiaoqin, R. Weiqiang, and L. Ke, " Causal Links Between Renal Function and Cardiac Structure, Function, and Disease Risk," *Global Heart*, vol. 19, no. 1, pp. 1-14, 2024.

[7] M. Mirjam and M. V. Nataša, " Lipid Biomarkers and Atherosclerosis—Old and New in Cardiovascular Risk in Childhood, " *International journal of molecular science (IJMS)*, vol. 24, no. 3, pp. 1-17, 2023.

[8] J.J. Félix, A. Hortensia, G. Elena, A.M. Miguel, S. Paula, C. Alba, A. Margarita and A.G. Jose, "Copper, Ceruloplasmin, Zinc, and Manganese Levels in Brain and Biological Fluids from Parkinson's Disease Patients: Systematic Review and Meta-Analysis" *Cells*, vol. 15, no. 3, pp. 288, 2026.

[9] P.A. Antonio, L. Laura, F.A. Juan, A. Alvaro, L. Jose and D. Javier, " Ceruloplasmin and Coronary Heart Disease—A Systematic Review" *Nutrients,* vol, 12. No. 10, pp. 3219, 2020.

[10] M.S. Danie, H.K. Thai, M. Murlidhar, L. Ramesh, D.C.H.R. Derren, D. Pojsakorn and C.K.W. Richard, " Blood Urea Nitrogen-to-Creatinine Ratio to Differentiate Upper From Lower Gastrointestinal Bleeding: A Systematic Review and Meta-Analysis" *Journal of Gastroenterology and Hepatology,* vol. 0, no. 2, pp. 1-11.

[11] K. Bhatia, S. Mohanty, B. K. Tripathi, B. Gupta, and M. K. Mittal, "Predictors of Early Neurological Deterioration in Patients with Acute Ischaemic Stroke with Special Reference to Blood Urea Nitrogen (BUN)/Creatinine Ratio & Urine Specific Gravity, " *Indian Journal of Medical Research*, vol. 141, no. 3, pp. 299–307, 2015.

[12] J. K. Fawcett and J. E. Scott, "A rapid and precise method for the determination of urea," *Journal of Clinical Pathology*, vol. 13: no. 2, pp. 9-156, 1960.

[13] N. W. Tietz, "Clinical Guide to laboratory tests.3rd edition.WB saunders company" Philadelphia, pp 518-519, 1995.

[14] T. B. Janice, " In: Clinical Methods: The History, Physical, and Laboratory Examinations." 3rd edition. Boston: Butterworths, 1990. Chapter 101.

[15] F. W. Sunderman and S. Nomoto, "Measurement of human serum ceruloplasmin by its pphenylenediamine oxidase activity, "*Clinical Chemistry*,vol. 16, no. 3, pp. 903-910, 1970.

[16] W. Richmond, "Determination of cholesterol by enzymatic method, " *Clinical Chemistry*, vol. 19, pp. 1350-1356, 1973.

[17] M. Burstein, "Measurement of lipid profile, " *Journal of Lipid Research*, vol.11, pp.583, 1970.

[18] P. Fossatti, and Prencipel, "Determination of triglycerides by enzymatic method," *Clinical Chemistry*, vol. 28, no. 2077, 1982.

[19] W. T. Friedewalds, R. I. Levy, M. Wite, and D. S. Fredrickson, "Estimation of the concentration of low density lipoprotein Cholesterol in plasma without the use of preparative ultra Centrifuge," *Clinical Chemistry*, vol.18,pp. 499-502, 1972.

[20] A. Nur, J. B. Nusrat, and Rafiquzzaman. "Review on in vivo and in vitro methods evaluation of anti-oxidant activity," *Saudi Pharmaceutical Journal*, vol. 21, no. 2, pp. 143-152, 2017.

[21] T. Glover, and K. Mitchell, "An introduction to Biostatistics," 2nd ed. Waveland press.Inc. Third Edition, 2008.

[22] S. Mohammed, H. Lonnie, W. Zhixin, B. Jessica, O. Suzanne, L. Sonya, E. T. Heath, and M. Paul, "Hypertension and Cardiovascular Disease Risk Among Individuals With Versus Without HIV," *Hypertension*, vol. 80, no. 4, pp.852–860, 2023.

[23] N. Fekri, P. Khaloo, A. Ramezankhani, M. A. Mansournia, F. Azizi, and F. Hadaegh, "Association of body mass index with life expectancy with and without cardiovascular disease," *International Journal of Obesity*, vol. 44, no. 4.pp. 195–203, 2020.

[24] B. Vergès, "Cardiovascular disease in type 1 diabetes: a review of epidemiological data and underlying mechanisms," *Diabetes Metab*, vol. 46, no. 6, pp. 442–9, 2020.

[25] Z. Xiangmei, W. Dongying, and Q. Lijie, "Lipid profile and prognosis in patients with coronary heart disease: a meta-analysis of prospective cohort studies," *BMC Cardiovascular Disorders*, vol. 21. No. 69, pp. 1-15, 2021.

[26] J. Jeppesen, H.O. Hein, P. Suadicani, and F. Gyntelberg, "Relation of high TG–low HDL cholesterol and LDL cholesterol to the incidence of ischemic heart disease an 8-year follow-up in the Copenhagen male study," *Arteriosclerosis, Thrombosis, and Vascular Biology* . vol. 17, no. 6, pp. 1114–1120, 2018.

[27] C.M. Ballantyne, A.G. Olsson, T.J. Cook, M.F. Mercuri, T.R. Pedersen, and J. Kjekshus, "Influence of low high-density lipoprotein cholesterol and elevated triglyceride on coronary heart disease events and response to simvastatin therapy in 4S," *Circulation,* vol. 104, no. 25, pp. 3046–3051, 2017.

[28] A.A. Muntaha, K.R. Manal, and A.I. Ammar, "StudyofSome Biochemical Parameters in Patients with Coronary Artery Disease with and without Type 2 Diabetes," *Journal of the Faculty of Medicine Baghdad*, vol. 66, no. 1, pp. 12-19, 2024.

[29] A. Rezaul, U. Bashir, U. Mojib, R. Mahbubur, and M. Sougata, "Lipid Profile of Coronary Heart Disease Patients: A Prospective Observational Study" *World Journal of Cardiovascular Surgery* , vol.11 no.11, 2021.

[30] R. Gougeon, "Insulin resistance of protein metabolism in type 2 diabetes and impact on dietary needs: a review," *Canadian journal of diabetes*, vol. 37, no. 2, pp. 115-120, 2013.

[31] S. Riaz, M. Tariq, and S. Aslam, "Association of serum protein levels in the diabetic patients with risk of cardiovascular disease and nephropathy in Pakistani population," *Journal of Research in Diabetes & Metabolism*, vol. 4, no. 1, pp. 011-015, 2018.

[32] U. Adiga and P. Kathyayani, "Association of Insulin Resistance with Liver Biomarkers in Type 2 Diabetes Mellitus, " *International Journal of Pharmaceutical and Phytopharmacological Research*. Vol. 9, no. 1, pp. 88-91, 2019.

[33] Q. Chen, M. Lu, B.R. Monks, and M.J. Birnbaum, "Insulin is required to maintain albumin expression by inhibiting forkhead box O1 protein," *Journal of Biological Chemistry*, vol. 291, no. 5, pp. 2371-2378, 2016.

[34] S. Beddhu, G.A. Kaysen, G. Yan, M. Sarnak, L. Agodoa, D. Ornt, and A.K. Cheung, "Association of serum albumin and atherosclerosis in chronic hemodialysis patients," *American journal of kidney diseases*, vol. 40, no. 4, pp. 721-727, 2002.

[35] D.A. Belinskaia, P.A. Voronina, V.I. Shmurak, M.A. Vovk, AA Batalova, R.O. Jenkins, and N.V. Goncharov, "The universal soldier: Enzymatic and non-enzymatic anti-oxidant functions of serum albumin," *Anti-oxidants*, vol. 9, no. 10, pp. 1-28, 2020.

[36] R.S. Lindsay, J. Krakoff, R.L. Hanson, P.H. Bennett, and W.C. Knowler, "Gamma globulin levels predict type 2 diabetes in the Pima Indian population," *Diabetes,* vol. 50, no. 7. pp. 1598-1603, 2001.

[37] L. Jiqing, W. Jiate, F. Ping, and G. Jianhua, "Identification of novel proteins for coronary artery disease by integrating GWAS data and human plasma proteomes," *Heliyon*, vol. 10, no. 19, pp. e38036, 2024.

[38] Y. Goro, T. Atsushi, G. Yuhei, and N. Koichi, "The role of albumin level in cardiovascular disease: a review of recent research advances," *Journal of Laboratory and Precision (JLPM)*, vol. 8, no. 7, pp. 22-57,2023.

[39] H.C. Cheng E.H. Yang, and C.T. Wu, "Hypoalbuminemia is a predictor of mortality and rebleeding in peptic ulcer bleeding under proton pump inhibitor use," *Journal of the Formosan Medical Association*, vol. 117, no. 4, pp. 316-325, 2018.

[40] A.I. Quero, C.R. Fernández, and G.R. Fernández, "Study of serum albumin and BMI as nutritional markers in hemodialysis patients," *Nutricion hospitalaria: organo oficial de la Sociedad Espanola de Nutricion Parenteral y Entera*l, vol. 31, no. 3, pp. 1317-1322, 2014.

[41] S. Arques, "Human serum albumin in cardiovascular diseases," *The European Journal of Internal Medicine*, vol. 52, no. 3, pp. 8-12, 2018 a.

[42] S. Arques, "Serum albumin and cardiovascular diseases," A comprehensive review of the literature", *Annales de Cardiologie et d'Angéiologie* (Paris), vol. 67, no. 6, pp. 82-90, 2018 b.

[43] C. Weiwei, G. Runlin, L. Lisheng, Z. Manlu, W. Wen, and W. Yongjun, "Outline of the report on cardiovascular diseases in China, 2014," *European Heart Journal Supplements*,vol. 18, no. 5, pp. 2–11, 2016.

[44] B. Bagheri, N. Radmard, A. Faghani-Makrani, and M. Rasouli, "Serum creatinine and occurrence and severity of coronary artery disease," *Medical Archives*, vol. 73, no. 3, pp. 154–6, 2019.

[45] J. L. Li, "What is the clinical significance of elevated creatinine?," *Health Life*, vol. 07, no. 27, pp. 1-9, 2022.

[46] K. R. Rye, and P. Barter, "Function and metabolism of pre-beta migrating, lipid-poor apolipoprotein," *Arteriosclerosis, Thrombosis, and Vascular Biology*,vol. 24, no. 3, pp. 421–8, 2014.

[47] T. Javanainen, S. Ishihara, E. Gayat, B. Charbit, R. Jurkko, and R. Cinotti, "Prolonged corrected QT interval is associated with short-term and long-term mortality in critically ill patients: Results from the FROG-ICU study," *Intensive Care Medicine*, vol. 45, no. 5, pp. 746–8, 2019.

[48] S. Behradmanesh and H. Nasri, "Association of serum calcium with level of blood pressure in type 2 diabetic patients," *Journal of Nephropathology*, vol. 2, no. 4, pp. 254-257, 2013.

[49] M. Patel, A. Agrawal, R. Sachin, Acharya, Sunil, " Serum Calcium Levels and its Association with Coronary Artery Disease," *Journal of the Scientific Society*, vol. 49, no, pp. 256-259, 2022.

[50] C. Zhang, C.A. Bangming, X. Huang, G.U. Jian, X.I. Ming, Y.A. Xiangjun, and L.I. Hongxia, "Associationbetween serum calcium and first incident acute myocardial infarction: a cross-sectional study," *Iran Journal of Public Health*, vol. 49, no. 7, pp. 1278, 2020.

[51] S. Gaweł, M. Wardas, E. Niedworok, and P. Wardas, "Malondialdehyde (MDA) as a lipid peroxidation marker, " *Wiadomosci lekarskie (Warsaw, Poland: 1960)*, vol. 57, no. pp. 453-455, 2004.

[52] G. Pizzino, N. Irrera, M. Cucinotta, G. Pallio, F. Mannino, V. Arcoraci, F. Squadrito, D. Altavilla, and A. Bitto, "Oxidative stress: harms and benefits for human health," *Oxidative medicine and cellular longevity*, vol. 121, no. 4, pp. 527-533, 2017.

[53] W.H.R. Aneeza, N. Hira, N. Atif, L. Sadia, L. Uswah, A. Tooba and R. Saira, " Relationship between the oxidative stress biomarkers and coronary heart disease: Pathogenesis to therapeutic aspects" *World J Cardiol, vol. 18, no. 2, pp. 113624.*

[54] P. Manna, and S.K. Jain, "Obesity, oxidative stress, adipose tissue dysfunction, and the associated health risks: causes and therapeutic strategies, " *Metabolic syndrome and related disorders*, vol. 13, no.10, pp. 423-444, 2015.

[55] L.A. Toualbi, M. Adnane, K. Abderrezak, W. Ballouti, M. Arab, C. Toualbi, H. Chader, R. Tahae, and A. Seba, "Oxidative stress accelerates the carotid atherosclerosis process in patients with chronic kidney disease," *Archives of Medical Sciences. Atherosclerotic Diseases*, vol. 5no. 4, pp. e245, 2020.

[56] P.A.D. Antonio, L. Laura, F.A. Juan, A. Alvaro, L. José, and D. Javier, " Ceruloplasmin and Coronary Heart Disease A Systematic Review, " *Nutrients*, vol. 12, no. 3219, pp. 1-15, 2020.

[57] G. Satyanarayana, N. Keisham, H.S. Batra, M. Khan, S. Gupta, and V. Mahindra, "Evaluation of Serum Ceruloplasmin Levels as a Biomarker for Oxidative Stress in Patients With Diabetic Retinopathy, "*Cureus*, vol. 13, no. 2, 2021.

[58] X. Li, D. Guo, H. Zhou, Y. Hu, X. Fang, Y. Chen, and F. Zhang, "Side effects of coronary stenting such as severe coronary stenosis and multiple coronary chronic total occlusions in elderly patients via induced pro-inflammatory and prooxidative stress," *Mediators Inflamm*,vol. 3, no. 1, pp. 7147652, 2019.

[59] Asfandiyar, H. Noorul, A.Z. Imran, K. Zeshan, Ashraf, U.K. Rezuan, Rumman, H.K. Mohammad, and O. Fatima, "Estimation of Serum Malondialdehyde (a Marker of Oxidative Stress) as a Predictive Biomarker for the Severity of Coronary Artery Disease (CAD) and Cardiovascular Outcomes," *Cureus*, vol. 16, no. 9, pp. e69756, 2024.