ASSESSMENT OF ASPROSIN, TROPONIN, AND OTHER VARIABLES IN CARDIOVASCULAR DISEASES

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Abstract

Background: Asprosin is a newly discovered hormone produced during fasting and promotes the liver to release glucose into the bloodstream. Aim of the study: Evaluating the Troponin, asprosin, lipid profile, and liver function test in the blood serum of cardiovascular patients to find predictive significance of diagnosis for this disease. Methods: In this study, 140 samples have been collected (70 patients with cardiovascular disease, and 70 control) and distributed among different ages (40-60years) and for both genders from patients in Cardiac Care Unite (CCU) in Kirkuk Teaching Hospital and Azadi Teaching Hospital in Kirkuk city, from (27/11/2023) to (28/2/2024). The control groups consist of 70 subjects. They were collected from medical staff and relatives who were free from signs and symptoms of cardiovascular disease. Results: The present study showed increased level of Asprosine, Troponin, cholesterol, Triglycerides, LDL, VLDL, AST and ALT in patients with CVD that were (3.36±1.50 ng/ml, 97.7±32.6 ng/ml, 225.1±25.2 mg/dl, 209.5±8.3 mg/dl, 140.7±17.9 mg/dl, 41.9±4.61 mg/dl, 54.32±22.1 U/L, 44.18±7.17 U/L) compared with the control group that were (1.68± 0.15 ng/ml, 69.37± 13.69 ng/ml, 196.3±27.2 mg/dl, 165±6.1 mg/dl, 113.67±15.2 mg/dl, 33.00±3.22 mg/dl, 29.54±6.57 U/L, 21.33±5.43 U/L)respectively. A significant decrease in HDL in CVD patients was(42.5±7.97 mg/dl) as compared with the control which was(49.33±6.38 mg/dl)respectively. Conclusion: This study concluded an increase in aspronin and troponin in patients with CVD. In addition dyslipidemia and an increase in both AST and ALT in CVD patients.

Introduction

Cardiovascular disease (CVD) is a prominent contributor to global mortality, illness, and hospitalization rates [1]. CVD encompasses a range of medical conditions that impact the heart and blood arteries. These conditions mostly arise from the obstruction of blood flow, leading to a lack of blood reaching the heart. Atherosclerosis, characterized by the accumulation of lipid deposits on the inner walls of the blood arteries, is the primary cause of obstruction [2]. Laboratory biomarkers are considered valuable as tools for prognostic stratification. Over 100 novel biomarkers have been assessed in this regard, with more than 4000 clinical investigations published [3,4]. Cardiac troponin concentration is the most favoured indicator of damage to the heart muscle. High levels of cardiac troponin are strongly linked to a negative outlook in patients with acute coronary syndromes. They are also used to identify patients who are likely to benefit from an early invasive management approach[5]. In the late 1980s, cTnI was suggested as a marker for cardiac cell death. It is currently widely used and recognized as the recommended marker according to guidelines. Its purpose is to aid in the diagnosis of myocardial injury in various clinical conditions, including post-surgery myocardium trauma, chemotherapy cardiotoxicity, and other diseases associated with cardiac muscle injury [6].

Asprosin, a recently found adipokine, is classed as a cardamon hormone protein and was first identified in 2016. It is released by the white adipose tissue in the body (7). Asprosin is produced by the Fibrillin1 gene, which is found in various cells throughout the body, such as human cutaneous fibroblasts, pancreatic B cells, and peripheral tissues and organs [7,8,9]. Asprosin has been demonstrated to be linked to metabolic illnesses such as cardiovascular disease, diabetes, polycystic ovarian syndrome, and obesity. It has also been suggested as a potential diagnostic biomarker for these conditions [10]. Increased concentrations of liver enzymes are strongly associated with the emergence of cardiovascular disease (CVD) risk. Their growth may result in an elevation in stenosis, thereby leading to the formation of blood clots[11].

Materials and Methods

Subjects: In this study, 140 samples have been collected (70 patients with cardiovascular disease, and 70 control) and distributed among different ages (40-60years) and for both genders from patients in Cardiac Care Unite (CCU) in Kirkuk Teaching Hospital and Azadi Teaching Hospital in Kirkuk city, from (27/11/2023) to (28/2/2024). The control groups consist of 70 subjects. They were collected from medical staff and relatives who were free from signs and symptoms of cardiovascular disease, 10 were males and 10 were male. The patient was diagnosed with CVD for both genders based on the World Health Organization (WHO) which required the following:
1-Chest pain, heaviness or discomfort. Which lasted more than 30 minutes, located in the retrosternal area radiated to the left arm, neck, and jaw.
2-Typical ECG changes involving ST-segment elevation or depression, T-wave inversion, Q-wave development.
3-Serum cardiac biochemical markers elevation (Troponin, CK, CK-MB, Glutamate oxaloacetate transaminase, GOT). The first two criteria are diagnosed by a consultant physician.

Samples collection: A volume of five millilitres of venous blood was extracted from each patient. To prevent hemolysis, the blood sample should be aspirated slowly using a syringe needle from the veins in the cubital fossa. Additionally, a tourniquet should be applied 15cm above the site. All the samples exhibited significant hemolysis, were disregarded, and a new sample was collected.
The specimens were placed into sterile disposable tubes and incubated at ambient temperature for 30 minutes to allow for coagulation, or incubated in a water bath. Subsequently, they were centrifuged at a speed of 3000 revolutions per minute for 10 minutes. The serum was maintained at a temperature of -20 degrees Celsius and subsequently utilized for the quantification of total troponin, Asprosin, ALT, and AST .

Determination of human asprosin and cardiac troponin by ELISA: Following manufacturer instructions, US-made Cloud-Clone Corp. kits are used for the test. The kits' microplates are pre-coated with an Asprosin antibody. Samples are then put into microplate wells with biotin-conjugated Asprosin antibodies. Avidin-HRP is next. The sulphuric acid solution stops the enzyme-substrate reaction, and the colour change is detected at 450nm.

Determination of Serum troponin, liver function test and lipid profile: Serum troponin, was analyzed for all patients by Cobas e411 device. AST, ALT, cholesterol, triglyceride, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and very low-density lipoprotein (VLDL) were assessed by using Biolabo kits in a spectrophotometer device.
Statistical analysis: Data analysis was done using SPSS 24 and Graph Pad Prism 7. The significance level was $P < 0.05$. Each parameter has mean, SD, and SE descriptive statistics.

Results

Serum level of asprosine was significantly higher in patients with CVD compared with the control group (3.36±1.50 versus 1.68± 0.15 ng/ml, p<0.001). The mean serum level of troponin was significantly higher in patients with CVD compared with the control group (97.7±32.65versus 69.37± 13.69, p<0.001) ng/ml.
The serum level lipid profile concentrations in patients with CVD patients compared with the control group which was significantly different (p<0.05). The result of serum cholesterol, triglycerides, LDL, and VLDL levels increased in CVD patients that were (225.1±25.2, 209.5±8.3, 140.7±17.9, 41.9±4.61) mg/dl as compared with control that were(196.3±27.2, 165±6.1, 113.67±15.2, 33.00±3.22) mg/dl respectively. A significant decrease in HDL in CVD patients was(42.5±7.97) mg/dl as compared with the control which was(49.33±6.38) mg/dl. The serum level AST and ALT levels in patients with CVD patients compared with the control group which was significantly different (p<0.001). The result of serum AST level between the patient and control group was Mean ± SD which was (54.32±22.1 versus 29.54±6.57) U/L respectively. The result of Serum AST level between the patient and control group was Mean ± SD which was (44.18±7.17 versus 21.33±5.43) U/L, respectively (Table 1).

Table 1. Comparison between Patients and Control Group for measured parameters.

Parameters	Control (n=30)	CVD patients (n=60)	p-value
Asprosine (ng/ml)	1.68±0.15	3.36±1.50	0.001
Troponin (ng/ml)	69.37±13.69	97.7±32.65	0.001
TC (mg/dl)	196.3±27.2	225.1±25.2	0.015 **
TG (mg/dl)	165±6.1	209.5±8.3	0.036 *
HDL (mg/dl)	49.33±6.38	42.5±7.97	0.042*
LDL(mg/dl)	113.67±15.2	140.7±17.9	0.028 *
VLDL (mg/dl)	33.00±3.22	41.9±4.61	0.041 *
AST (U/L)	29.54±6.57	54.32±22.1	0.01
ALT (U/L)	21.33±5.43	44.18±7.17	0.01

This study also shows the correlation between Asprosin (Troponin, TG, TC, VLDL, LDL, HDL, AST and ALT) in CVD patients. As shown in Figure (1), there is a weak correlation between asprosine and troponin (r=0.255), while no correlation between asprosine and (TG, TC, VLDL, LDL, HDL, AST and ALT), where r=0.163, 0.175,0. 0.163,115, 0.165, 0.053, 0.012

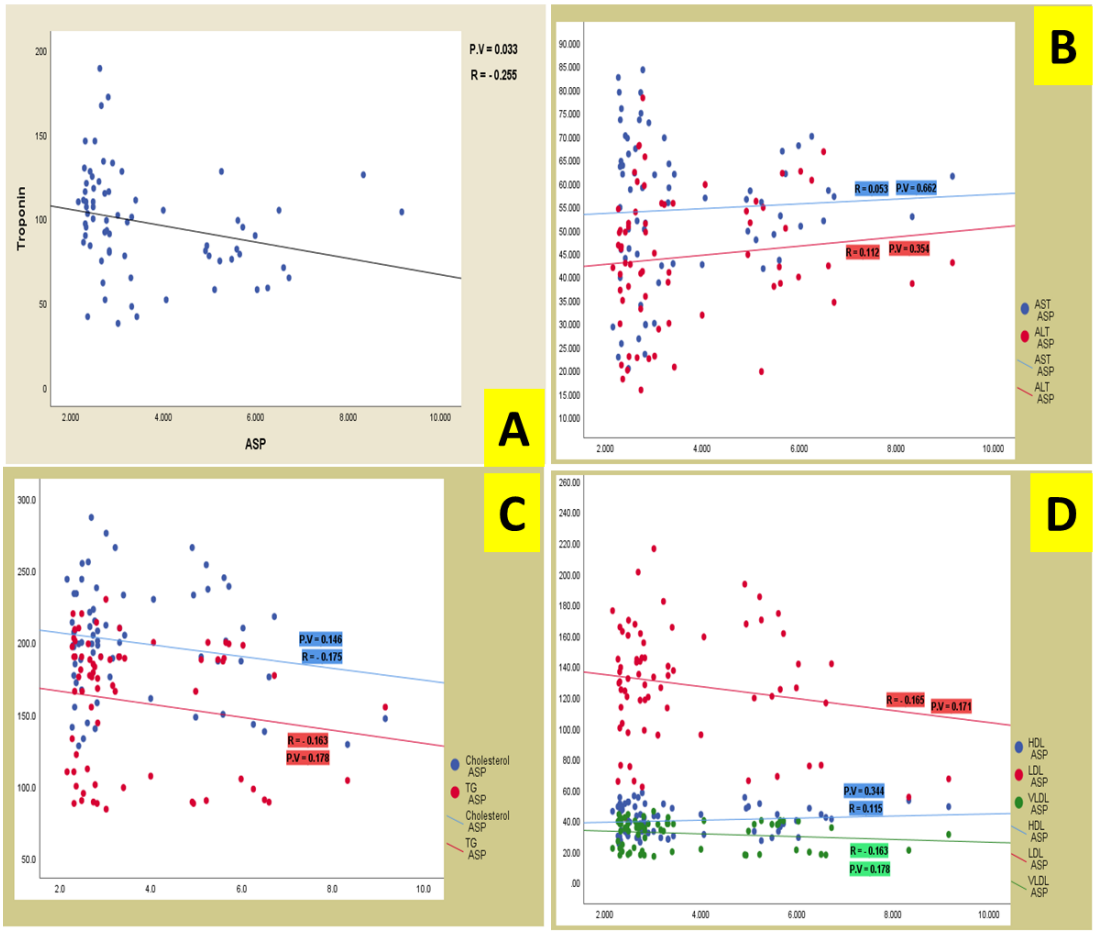

Figure 1. (A) The correlation between asprosine and troponin in CVD patients (B) The correlation between asprosine with AST and ALT in CVD patients (C) The correlation between asprosine with TG and TC in CVD patients (D) The correlation between asprosine with VLDL, HDL, and LDL in CVD patients.

Discussion

The present study showed that levels of asprosin in the bloodstream are notably higher in patients with coronary artery disease (CAD) compared to individuals without the condition. This finding aligns with the research conducted by AL-HADIDI and AL-OBAIDI, who also observed raised levels of asprosin in patients with atherosclerosis and myocardial infarction when compared to controls[12]. Asprosin is greatly increased in patients with cardiovascular disease, namely those with cardiomyopathy [13]. The research conducted by our team This statement confirms the findings of a prior study conducted by Moradi et al., which observed a notable rise in asprosin levels among individuals diagnosed with atherosclerosis[14]. While the precise function of asprosin remains uncertain, studies have indicated that increased amounts of this hormone may improve the process of mitochondrial respiration in cardiac muscle cells, therefore safeguarding the heart against hypoxia[13]. Acara et al. discovered a strong correlation between asprosin levels and illness severity in individuals with unstable angina pectoris [15]. Conversely, in a cohort research that followed patients for five years, Wen et al. discovered that elevated levels of asprosin protected against negative cardiac events in individuals with dilated cardiomyopathy [16]. Reduced levels of asprosin were associated with an increased likelihood of experiencing more severe clinical consequences. According to scientists, asprosin has a direct protective effect on cardiomyocytes by enhancing mitochondrial respiration in response to low oxygen levels (hypoxia) [16]. GÜVEN, Cengiz; KAFADAR demonstrated a positive correlation between elevated levels of Asprosin in the bloodstream and

individuals diagnosed with heart failure. Furthermore, there was a separate and direct correlation between asprosin and the occurrence of heart failure. These data indicate that Asprosin may be a contributing factor in the development of heart failure[17].

The present investigation shows an increase in cardiac troponin levels in individuals with cardiovascular disease compared to the control group. A comprehensive retrospective cohort study observed a positive correlation between elevated cTn levels and a range of cardiovascular risk factors, as well as both cardiovascular and noncardiovascular diseases. However, it is worth noting that only patients with atherosclerosis showed a substantial increase in cardiac troponin levels. This suggests that cardiac troponin can be regarded as a biomarker for identifying individuals who are at risk of developing atherosclerosis[12].

Troponin, a cardiac enzyme, plays a crucial role in the contraction of both cardiac and skeletal muscles. Elevated concentrations of troponin T in the bloodstream have been linked to damage to the heart muscle, and these levels have been utilized to assess the extent of a heart attack (18). Cardiac indicators are involved in the diagnosis of ischemic heart disease (IHD) (19). The cTn marker is more sensitive and specific than the creatine kinase myocardial band (CK-MB) in diagnosing myocardial infarction (MI) when the cTn level is elevated. However, in unstable angina (UA), there is no increase in cTn levels. The cTn marker results in this investigation are consistent with the findings of other studies, including studies (19), (21), and (22).

This study contradicts the findings of [23] conducted in Iraq, which demonstrated that there were no significant changes in troponin levels between individuals with cardiovascular disease (CVD) and the control group. Missov et al. found that troponin T levels were significantly higher in 33 heart failure patients (mean, 0.14 0.439 ng/mL) compared to 47 healthy control subjects (mean, 0.0002 0.001 ng/mL; $P < 0.0001$) using the second-generation test. The researchers also discovered a negative association between troponin T and ejection fraction, with a correlation coefficient of -0.41 and a significance level of 0.01. The data presented indicate an elevation in cardiac troponin T levels in patients with heart failure, and this increase is directly proportional to the severity of the disease[24].

The results consistently demonstrate a strong link between dyslipidemia (abnormal lipid profiles) and the occurrence of cardiovascular disease. For instance, TAWFIQ et al. demonstrated elevated levels of total cholesterol and LDL, which increased the likelihood of developing ischemic heart disease[25]. LDL-C is well recognized as a significant contributor to the occurrence of revascularizations, ischemic strokes, atherothrombotic processes, and cardiovascular mortality [26]. Both US and European cardiovascular guidelines acknowledge LDL-C as a crucial modifiable risk factor [27,28]. These trials have demonstrated a significant reduction in the risk of cardiovascular disease (CVD) in individuals with a high risk of atherosclerotic cardiovascular disease (ASCVD) who were undergoing statin therapy [29,30]. Wallace et al. and Wilson et al. have established a clear correlation between serum LDL-C levels and the occurrence of cardiovascular disease (CVD) [31,32]. Studies have demonstrated that elevated levels of total cholesterol (hypercholesterolemia), specifically LDL cholesterol, contribute to the development of atherosclerosis. This condition involves the buildup of cholesterol and fatty acids in the walls of arteries. On the other hand, HDL cholesterol is generally regarded as protective and helps transport cholesterol back to the liver [33-36]. Aminotransferase, which includes AST (aspartate aminotransferase) and ALT (alanine aminotransferase), is a widely recognized indicator of liver damage. Aminotransferase (AST) is present in both liver and cardiac tissue, while alanine aminotransferase (ALT) is only found in the liver [37]. This study concurs with the findings of [38], which demonstrate elevated levels of AST and ALT in CAD. The correlation between increased ALT levels and the risk of cardiovascular disease (CVD) can be attributed to the association of this condition with a variety of CVD risk factors. Muscular disorders and trauma result in increased levels of aminotransferases and can contribute to a negative prognosis. Nevertheless, the primary mechanism elucidating the cardiovascular disease (CVD) risk linked to elevated alanine aminotransferase (ALT) levels is the presence of clinical or subclinical liver illness, namely hepatic disease. ALT is positively associated with liver fat as assessed by magnetic resonance spectroscopy in both men and women [39,40].

Simultaneously, the association between cardiovascular disease (CVD) and elevated aspartate aminotransferase (AST) levels can be explained by four pathways. The primary factor leading to increased AST levels in the bloodstream is liver disease[41]. Furthermore, an elevated AST level is associated with many cardiovascular risk factors such as insulin resistance, metabolic syndrome, and obesity; as indicated by reference [42]. Furthermore, an elevated AST level can be indicative of chronic alcoholism[43,44]. In addition, an elevated AST level can be indicative of structural cardiovascular disease. This occurs when AST is released from the myocardium during periods of increased stress or acute coronary artery syndromes[45]. Several trials have been conducted to repair the damaged tissue, such as, using CoQ10[46,47], or prophylaxis by using hypolipidemic plant (hypericum perforatum)[48], or using stem cells[49].

Conclusion

The outcomes of this study was the noted increase in aspronin and troponin levels among patients with CVD. Elevated troponin, in particular, is well-documented as an indicator of myocardial injury, reflecting its critical role in diagnosing acute coronary syndromes. The rise in aspronin, although less commonly discussed than troponin, may point to emerging facets of cardiac pathology that warrant further exploration. Additionally, dyslipidemia—a lipid disorder marked by abnormal cholesterol levels—was prevalent among these patients, aligning with established risk factors for CVD and contributing to atherosclerotic processes. Crucially, the study also reported heightened levels of AST and ALT, liver enzymes that typically signify hepatic stress or damage when elevated. This could indicate a systemic interaction where cardiovascular pathology induces secondary hepatic effects or reflect overlapping comorbidities such as non-alcoholic fatty liver disease often observed in CVD populations. Collectively, these biomarkers not only assist in diagnosing and monitoring CVD but also enrich our understanding of its multifaceted impact on patient health.

References

1. Alaour B, Liew F, Kaier TE. Cardiac Troponin-diagnostic problems and impact on cardiovascular disease. Annals of medicine. 2018 Nov 17;50(8):655-65.
2. Alnajjar MK, Abu-Naser SS. Heart sound analysis and classification for cardiovascular disease diagnosis using deep learning. Int. J. Aca. Eng. Res. 2022; 6(1):7-23.
3. Collins DR, Tompson AC, Onakpoya IJ, Roberts N, Ward AM, Heneghan CJ. Global cardiovascular risk assessment in the primary prevention of cardiovascular disease in adults: systematic review of systematic reviews. BMJ open. 2017 Mar 1;7(3):e013650.
4. Emdin M, Vittorini S, Passino C, Clerico A. Old and new biomarkers of heart failure. European Journal of Heart Failure. 2009 Apr;11(4):331-5.
5. Everett BM, Brooks MM, Vlachos HE, Chaitman BR, Frye RL, Bhatt DL. Troponin and cardiac events in stable ischemic heart disease and diabetes. New England Journal of Medicine. 2015 Aug 13;373(7):610-20.
6. Garg P, Morris P, Fazlanie AL, Vijayan S, Dancso B, Dastidar AG, Plein S, Mueller C, Haaf P. Cardiac biomarkers of acute coronary syndrome: from history to high-sensitivity cardiac troponin. Internal and emergency medicine. 2017 Mar;12:147-55.
7. Ugur K, Aydin S. Saliva and blood asprosin hormone concentration associated with obesity. International journal of endocrinology. 2019;2019(1):2521096.
8. You M, Liu Y, Wang B, Li L, Zhang H, He H, Zhou Q, Cao T, Wang L, Zhao Z, Zhu Z. Asprosin induces vascular endothelial-to-mesenchymal transition in diabetic lower extremity peripheral artery disease. Cardiovascular Diabetology. 2022 Feb 15;21(1):25.
9. Shabir K, Brown JE, Afzal I, Gharanei S, Weickert MO, Barber TM, Kyrou I, Randeva HS. Asprosin, a novel pleiotropic adipokine implicated in fasting and obesity-related cardio-metabolic disease: Comprehensive review of preclinical and clinical evidence. Cytokine & Growth Factor Reviews. 2021 Aug 1;60:120-32.
10. Yuan M, Li W, Zhu Y, Yu B, Wu J. Asprosin: a novel player in metabolic diseases. Frontiers in endocrinology. 2020 Feb 19;11:64.

11. Monami M, Bardini G, Lamanna C, Pala L, Cresci B, Francesconi P, Buiatti E, Rotella CM, Mannucci E. Liver enzymes and risk of diabetes and cardiovascular disease: results of the Firenze Bagno a Ripoli (FIBAR) study. Metabolism. 2008 Mar 1;57(3):387-92.
12. Al-Hadidi EE, Al-Obaidi WM. Assessment of asprosin level and some physiological variables in patients with cardiovascular diseases in Kirkuk city, Iraq. Biomedicine. 2022 Nov 14;42(5):973-7.
13. Zhang L, Chen C, Zhou N, Fu Y, Cheng X. Circulating asprosin concentrations are increased in type 2 diabetes mellitus and independently associated with fasting glucose and triglyceride. Clinica chimica acta. 2019 Feb 1;489:183-8.
14. Moradi N, Fouani FZ, Vatannejad A, Bakhti Arani A, Shahrzad S, Fadaei R. Serum levels of Asprosin in patients diagnosed with coronary artery disease (CAD): a case-control study. Lipids in health and disease. 2021 Aug 21;20(1):88.
15. Acara AÇ, Bolatkale M, Kızıloğlu İ, İbişoğlu E, Can Ç. A novel biochemical marker for predicting the severity of ACS with unstable angina pectoris: Asprosin. American Journal of Emergency Medicine. 2018.
16. Wen MS, Wang CY, Yeh JK, Chen CC, Tsai ML, Ho MY, Hung KC, Hsieh IC. The role of Asprosin in patients with dilated cardiomyopathy. BMC Cardiovascular Disorders. 2020 Sep 7;20(1):402.
17. Wang G, Fan C, Chai Y, Yu X, Xing M, Lv Z, Yuan S, Dai H. Association of serum Asprosin concentrations with heart failure. BMC Cardiovascular Disorders. 2023 Dec 14;23(1):617.
18. De Lemos JA, Drazner MH, Omland T, Ayers CR, Khera A, Rohatgi A, Hashim I, Berry JD, Das SR, Morrow DA, McGuire DK. Association of troponin T detected with a highly sensitive assay and cardiac structure and mortality risk in the general population. Jama. 2010 Dec 8;304(22):2503-12.
19. Chacko S, Haseeb S, Glover BM, Wallbridge D, Harper A. The role of biomarkers in the diagnosis and risk stratification of acute coronary syndrome. Future science OA. 2018 Jan 1;4(1): FSO251.
20. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, White HD. Fourth universal definition of myocardial infarction (2018). European Heart Journal. 2019 Jan 14;40(3):237-69.
21. Sandoval Y, Apple FS, Smith SW. High-sensitivity cardiac troponin assays and unstable angina. European Heart Journal: Acute Cardiovascular Care. 2018 Mar 1;7(2):120-8.
22. Park KC, Gaze DC, Collinson PO, Marber MS. Cardiac troponins: from myocardial infarction to chronic disease. Cardiovascular research. 2017 Dec 1;113(14):1708-18.
23. Al-Obaidi AZ, Al-Saffar JM. Serum Level of Interleukin-33, C-Reactive Protein, and Troponin in Iraqi Coronary Artery Disease Patients. Iraqi Journal of Science. 2020 Feb 27:314-21.
24. Missov E, Mair J. A novel biochemical approach to congestive heart failure: cardiac troponin T. American Heart Journal. 1999 Jul 1;138(1):95-9.
25. Tawfiq OA, Hilal NN, Jumaa AM. Relationship between Lipid Profile and Thyroid Disturbance and Ischemic Heart Disease in Iraqi Patients. South Asian Res J Pharm Sci. 2023;5(5):192-5.
26. Berman AN, Blankstein R. Optimizing dyslipidemia management for the prevention of cardiovascular disease: a focus on risk assessment and therapeutic options. Current cardiology reports. 2019 Sep;21:1-0.
27. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, Braun LT, De Ferranti S, Faiella-Tommasino J, Forman DE, Goldberg R. 2018.AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019 Jun 18;139(25):e1082-143.
28. Catapano AL, Graham I, De Backer G, Wiklund O, Chapman MJ, Drexel H, Hoes AW, Jennings CS, Landmesser U, Pedersen TR, Reiner Ž. 2016 ESC/EAS guidelines for the

management of dyslipidaemias. Polish Heart Journal (Kardiologia Polska). 2016;74(11):1234-318.
29. Sabatine MS, Giugliano RP, Keech AC, Honarpour N, Wiviott SD, Murphy SA, Kuder JF, Wang H, Liu T, Wasserman SM, Sever PS. Evolocumab and clinical outcomes in patients with cardiovascular disease. New England journal of medicine. 2017 May 4;376(18):1713-22.
30. Schwartz GG, Steg PG, Szarek M, Bhatt DL, Bittner VA, Diaz R, Edelberg JM, Goodman SG, Hanotin C, Harrington RA, Jukema JW. Alirocumab and cardiovascular outcomes after acute coronary syndrome. New England Journal of Medicine. 2018 Nov 29;379(22):2097-107.
31. Wallace C, Newhouse SJ, Braund P, Zhang F, Tobin M, Falchi M, Ahmadi K, Dobson RJ, Marçano AC, Hajat C, Burton P. Genome-wide association study identifies genes for biomarkers of cardiovascular disease: serum urate and dyslipidemia. The American Journal of Human Genetics. 2008 Jan 10;82(1):139-49.
32. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. Circulation. 1998 May 12;97(18):1837-47.
33. Klop B, Elte JW, Castro Cabezas M. Dyslipidemia in obesity: mechanisms and potential targets. Nutrients. 2013 Apr 12;5(4):1218-40.
34. Niroumand S, Khajedaluee M, Khadem-Rezaiyan M, Abrishami M, Juya M, Khodaee G, Dadgarmoghaddam M. Atherogenic Index of Plasma (AIP): A marker of cardiovascular disease. Medical journal of the Islamic Republic of Iran. 2015;29:240.
35. Proctor SD, Vine DF, Mamo JC. Arterial permeability and efflux of apolipoprotein B–containing lipoproteins assessed by in situ perfusion and three-dimensional quantitative confocal microscopy. Arteriosclerosis, Thrombosis, and Vascular Biology. 2004 Nov 1;24(11):2162-7.
36. Glasser SP, Mosher A, Howard G, Banach M. What is the association of lipid levels and incident stroke? International journal of cardiology. 2016 Oct 1;220:890-4.
37. Yokoyama M, Watanabe T, Otaki Y, Takahashi H, Arimoto T, Shishido T, Miyamoto T, Konta T, Shibata Y, Daimon M, Ueno Y. Association of the aspartate aminotransferase to alanine aminotransferase ratio with BNP level and cardiovascular mortality in the general population: the Yamagata study 10-year follow-up. Disease markers. 2016;2016(1):4857917.
38. Mahmud MS, Ashoor LS. Nesfatin-1 is a biomarker that plays a role in the inflammatory process of coronary artery diseases in Iraqi patients with non-alcoholic fatty liver disease. Bionatura, 2013; 3(8):1-8.
39. Kotronen A, Yki-Järvinen H, Sevastianova K, Bergholm R, Hakkarainen A, Pietiläinen KH, Juurinen L, Lundbom N, Sørensen TI. Comparison of the relative contributions of intra-abdominal and liver fat to components of the metabolic syndrome. Obesity. 2011 Jan;19(1):23-8.
40. Ndrepepa G, Kastrati A. Alanine aminotransferase—a marker of cardiovascular risk at high and low activity levels. Journal of Laboratory and Precision Medicine. 2019 Sep 9;4.
41. Adams LA, Anstee QM, Tilg H, Targher G. Non-alcoholic fatty liver disease and its relationship with cardiovascular disease and other extrahepatic diseases. Gut. 2017 Jun 1;66(6):1138-53.
42. Porter SA, Pedley A, Massaro JM, Vasan RS, Hoffmann U, Fox CS. Aminotransferase levels are associated with cardiometabolic risk above and beyond visceral fat and insulin resistance: the Framingham Heart Study. Arteriosclerosis, thrombosis, and vascular biology. 2013 Jan;33(1):139-46.
43. Piano MR. Alcohol's effects on the cardiovascular system. Alcohol research: current reviews. 2017;38(2):219.
44. Chiva-Blanch G, Badimon L. Benefits and risks of moderate alcohol consumption on cardiovascular disease: current findings and controversies. Nutrients. 2019 Dec 30;12(1):108.

45. Ndrepepa G. Aspartate aminotransferase and cardiovascular disease—a narrative review. Journal of Laboratory and Precision Medicine. 2021 Jan 30;6.
46. Al-Thanoon ZA, Merkhan M. CoQ10 improved liver function and redox status in pollution-exposed workers. Pharmakeftiki. 2024 Jun 18;36(2).
47. Althanoon ZA, Merkhan MM. CoQ10 dampens the deleterious impact of doxorubicin-induced liver and spleen injury in white Albino rats. Pharmacology. 2023;27.
48. Hamed ZS, Abed RR, Almashhadany MS, Merkhan MM. Effects of Hypericum perforatum on serum lipid vascular systems in mice. Iraqi Journal of Veterinary Sciences. 2022 Apr 1;36(2):525-30.
49. Nasser MI, Qi X, Zhu S, He Y, Zhao M, Guo H, Zhu P. Current situation and future of stem cells in cardiovascular medicine. Biomedicine & Pharmacotherapy. 2020 Dec 1;132:110813.