International Journal of Cardiology Sciences

ISSN Print: 2664-9020
ISSN Online: 2664-9039
Impact Factor: RJIF 5.42
IJCS 2024; 6(1): 86-94
www.cardiologyjournals.net
Received: 13-02-2024
Accepted: 18-03-2024

Ali H Hanoon
Southern Technical University, Health and Medical Technical College, Iraq

Alaa K Jassim
Southern Technical University, Health and Medical Technical College, Iraq

Nidhal A Hashim
Southern Technical University, Maysan Technical Institute, Iraq

Corresponding Author:
Ali H Hanoon
Southern Technical University, Health and Medical Technical College, Iraq

The effect of homocysteine and troponin levels on the development and diagnosis of cardiovascular diseases

Ali H Hanoon, Alaa K Jassim and Nidhal A Hashim

DOI: https://doi.org/10.33545/26649020.2024.v6.i1a.55

Abstract
Background: One third of all deaths globally are thought to result from cardiovascular disease, and its incidence is continually rising. Being one of the diseases with several contributing causes, CVD is challenging to identify a single culprit.
Aims of the study: Determine the relationship between homocysteine and troponin levels in the blood and the risk of cardiovascular disease.
Methodology: A case-control study conducted at Al-Sadr general hospital and Maysan heart center in Maysan Governorate, Iraq from August 2023 to March 2024, it included 3 groups: a control group of 60 healthy individuals (40 males and 20 females), a group of 80 people with arterial syndrome. Acute coronary heart disease (50 males and 30 females), and a group of 40 individuals with chronic stable angina (22 males and 18 females). Ages ranged between 28 and 67 years. Cases that had pre-existing diseases that might affect the study results were excluded. 5 ml of each participant's blood was collected and analyzed after freezing at -20°C to measure homocysteine and troponin levels via ELISA.
Result: The results did not show statistically significant differences in homocysteine and troponin levels between men and women in cases of acute and chronic myocardial infarction. There was a statistical significance in the levels of troponin and homocysteine in the infarction group compared to the control group, without any significant differences compared to the diabetes group. The results also revealed statistical significance in cardiac indicators for the high blood pressure group with acute versus chronic infarction, and for the non-hypertensive groups with acute versus chronic infarction.
Conclusion: The results indicate that high levels of homocysteine and troponin are not affected by gender in cases of myocardial infarction, but their effect is clear compared to healthy individuals, confirming the importance of these indicators in diagnosing myocardial infarction. The lack of significance with the diabetes group suggests that diabetes does not directly affect these levels during infarction. Differences between blood pressure groups also highlight the importance of examining the effects of pressure on the development of infarction, whether acute or chronic.

Keywords: Cardiovascular diseases, homocysteine, troponin, acute myocardial infarction, chronic myocardial infarction, hypertension, diabetes mellitus

Introduction
Diseases of the heart and blood systems are what cardiovascular diseases (CVD) are all about. One-third of all deaths in the world are thought to be caused by cardiovascular disease, and the number of people who have it is still rising [1]. Heart disease is one of the diseases where many things can cause it, so it's hard to find just one. For this study, homocysteine is the most important thing. Coronary artery disease is when the arteries and veins that bring oxygen and food to the heart get narrowed or blocked. The Gensini scoring method divides coronary artery disease into three levels based on how bad it is: single vessel, double vessels, and triple vessels disease. As early as the 1990s, homocysteine was seen as a risk factor for atherosclerotic arterial disease and states of hypercoagulability. In a study, subgroup analyses also showed that people with chronic renal dysfunction had a higher chance of coronary artery disease when their homocysteine levels were high [2, 3]. There has been a long debate among researchers about the extent to which homocysteine is a risk factor for cardiovascular disease. It is believed by some that traditional risk factors may explain about half of the cases of cardiovascular disease, while others assert that new risk factors increase the accuracy of predictions of these diseases. However, these assumptions have faced considerable criticism, with some researchers revealing that traditional risk factors can

explain up to two-thirds of cases of coronary artery disease. For a risk factor to be considered useful as a diagnostic tool, it should have a strong, causal association with the disease in question. However, doubts remain about the extent of this link between homocysteine and cardiovascular disease [4, 5]. The Framingham Risk Rating (FRS) is a valuable tool to estimate an individual's likelihood of developing coronary artery disease based on traditional risk factors such as high cholesterol, high blood pressure, diabetes, and smoking. However, it is clear that this classification may not provide the required accuracy for individuals with high plasma homocysteine concentrations [6]. Researchers have observed a link between a slight increase in homocysteine levels and an increased risk of cardiovascular disease, such as heart attacks, strokes, and peripheral arterial disease. A homozygous mutation in the C,S gene can lead to very high levels of homocysteine in the blood, as the level of homocysteine can reach up to 40 times the normal average. It is estimated that one in every 100,000 babies born alive will have this disease. About half of these people will have a vascular event (Stroke, myocardial infarction, or other thromboembolic complication) before they turn 30 if they are not treated [7]. A different reason for serious hyperhomocysteinemia that is caused by genes is homozygous mutations of MTHFR. People who have these genes have been seen to get heart disease early. A big study, however, found that there was no statistically significant link between MTHFR genes and coronary heart disease. The only places where it was statistically significant were in the Middle East and Japan [8]. When it comes to heart health, cardiac troponin is a special marker that is linked to both heart imaging and heart results [9]. Researchers have found a link between high amounts of hs-cTn and coronary calcium scores and the development of unrecognised myocardial infarctions found on magnetic resonance images in people over 70 years old who don't have CVD. Several studies have shown that high sensitivity hs-cTnI can be used as an extra clinical marker to add to present records. It also shows differences based on gender and age [10, 11]. There are three types of troponin, which are muscular proteins. They are called isoforms C (cTnC), I (cTnI), and T (cTnT), and their sizes are 18, 23, and 35 kD, respectively. They all play a part in how the heart contracts and relaxes. The cTnC subunit binds calcium, the cTnI subunit stops actin-myosin contraction and moves between binding actin and cTnC depending on the amount of calcium inside the cell, and the cTnT subunit connects troponin to tropomyosin [12]. Study have shown that troponin getting into the bloodstream can happen after reversible damage. It is linked to normal myocyte turnover, the release of proteolytic degradation, an increase in wall permeability, or membranous blebs. On the other hand, tissue death caused by hypoxia and apoptosis can be linked to damage that can't be fixed. Different enzymes break them down into smaller pieces that are between 12 and 23 kD once they get into the bloodstream. Proteases like calpains, caspases, cathepsin L, and gelatinase A are very important in this breakdown process. Another thing that breaks things down is transglutamination. Lastly, the body gets rid of these substances. This can happen through endocytosis in the reticuloendothelial system of the spleen, liver, and bone marrow, or it can happen through the kidney system [13]. All three types can be found in the heart, but only cTnI and cTnT are found in the heart. This feature is very important for troponin measurement, which is the best way to confirm or rule out acute coronary syndrome in the emergency room. It is also used to divide myocardial infarction into five levels, as explained in the Fourth Universal Infarction Consensus Document, which came out in 2018 [14]. The TROPIC study found that events at 30 days could be predicted by both peak levels of troponins, but cTnI may be more reliable than cTnT in this group of one million patients. It has been observed in studies that high levels of cTnT and cTnI are associated with the development of poor outcomes in patients with chronic kidney disease, whether they are receiving dialysis treatment or not, and even for those who do not suffer from acute coronary syndrome [15]. The main goal of this research is to explore the relationship between homocysteine and troponin concentrations in the blood, and how they affect the increased risk of cardiovascular disease. It is known that changes in the levels of these biomarkers may indicate an increased risk of heart disease, including myocardial infarction and other serious conditions.

Methodology

This case-control study conducted at Al-Sadr general hospital and Maysan heart center in Maysan Governorate, Iraq from August 2023 to March 2024, included three groups: a group of 60 healthy individuals (40 males and 20 females), a group of 80 individuals with acute coronary syndrome (50 males and 30 females), and a group of 40 individuals with chronic stable angina (22 males and 18 feminine). Participants were aged between 28 and 67 years and were receiving a comprehensive diagnosis from specialist physicians. Subjects with known medical conditions such as cancer, autoimmune diseases, infections, immunosuppression, or use of statins were excluded, to avoid influencing the study results. 5 milliliters of human blood was collected from each individual, whether they were patients or controls. These samples were then transferred to sterile test tubes and left to clot at room temperature for 30 minutes. Next, the samples were centrifuged at 3000 rpm for 15 minutes. The resulting serum was then extracted and stored at a temperature of -20°C until it was ready for analysis. Homocysteine and troponin levels were measured by enzyme-linked immunosorbent assay using an ELISA device.

Ethical approval

Before the samples were taken, all of the patients who were going to be part of this study were properly informed and gave their verbal permission. The Committee on Publication Ethics at the Al-Sadr general Hospital in Maysan Governorate, gave its approval to the study.

Statistical analysis

Statistical analysis is often used to analyze quantitative data, and provides methods for data description, simple inference for continuous and categorical data. The procedure involves the collection of data leading to test of the relationship between two statistical data sets. In this study all data are presented as mean ± standard deviation. The statistical analyses were performed using SPSS (Version 26) and using using dependent t-test (Two-tailed) and independent t-test (two-tailed) for normally distribution variables, whereas the Mann-Whitney *U* and Wilcoxon test used for those variables that were not normally distributed. $p < 0.05$ was considered statistically significant.

Results

Comparison between Troponin and Homocystin levels in acute myocardial infraction patients according to sex

Results from the table regarding troponin and homocysteine levels in patients with acute heart attacks according to sex show that the average troponin levels in males were 25.34 with a standard deviation of 14.94, while the average homocysteine levels were 9.25 with a standard deviation of 2.34. In contrast, females recorded average troponin levels of 24.36 with a standard deviation of 14.58, and average homocysteine levels of 9.21 with a similar standard deviation of 2.34. The statistical value (*P* value) for both variables, troponin and homocysteine, was 0.816 and 0.99, respectively, which suggests that there are no significant statistical differences between males and females in terms of troponin and homocysteine levels in patients suffering from acute heart attacks.

Table 1: Mean± SD of Troponin and Homocystin levels in acute myocardial infraction patients according to sex

Parameters/patients	Troponin	Homocystin
Male	25.34±14.94	9.25±2.34
female	24.36±14.58	9.21±2.34
P Value	0.816	0.99

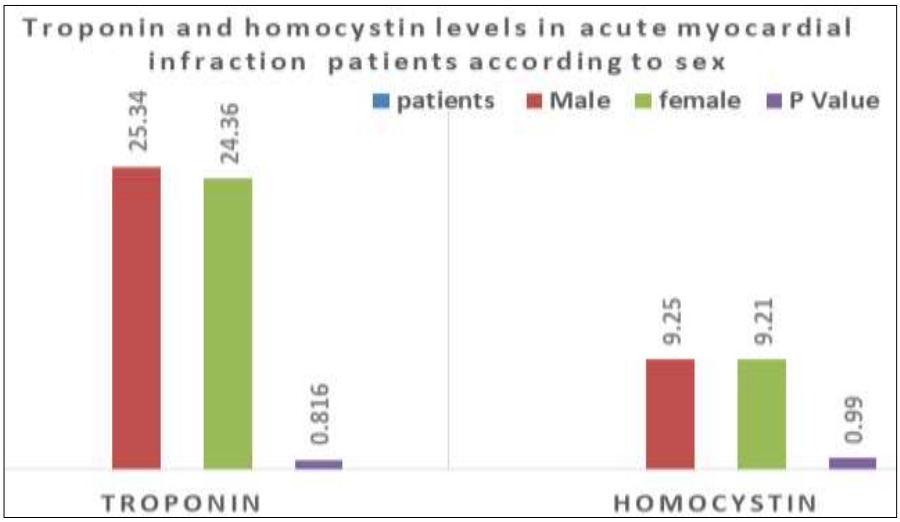

Fig 1: Troponin and Homocystin levels in AMI patients according to sex

Comparison between Troponin and Homocystin levels in chronic myocardial infraction patients according to sex

In a study of troponin and homocysteine levels in patients with chronic myocardial infarction based on sex, data indicate that the mean troponin levels in males were 0.17, with a standard deviation of 0.06, while the mean homocysteine levels were 3.58, with a standard deviation of 1.28. On the other hand, the average troponin levels in females were 0.20 with a standard deviation of 0.07, and the average homocysteine levels were 3.16 with a standard deviation of 1.05. Statistical values (*P* value) did not show statistically significant differences between the sexes, as troponin recorded a value of 0.141 and homocysteine a value of 0.47, which indicates the convergence of the levels of these two indicators between males and females in patients with chronic myocardial infarction.

Table 2: Mean ± SD Troponin and Homocystin levels in chronic myocardial infraction patients according to sex

Parameters/ patients	Troponin	Homocystin
Male	0.17±0.06	3.58±1.28
female	0.20±0.07	3.16±1.05
P Value	0.141	0.47

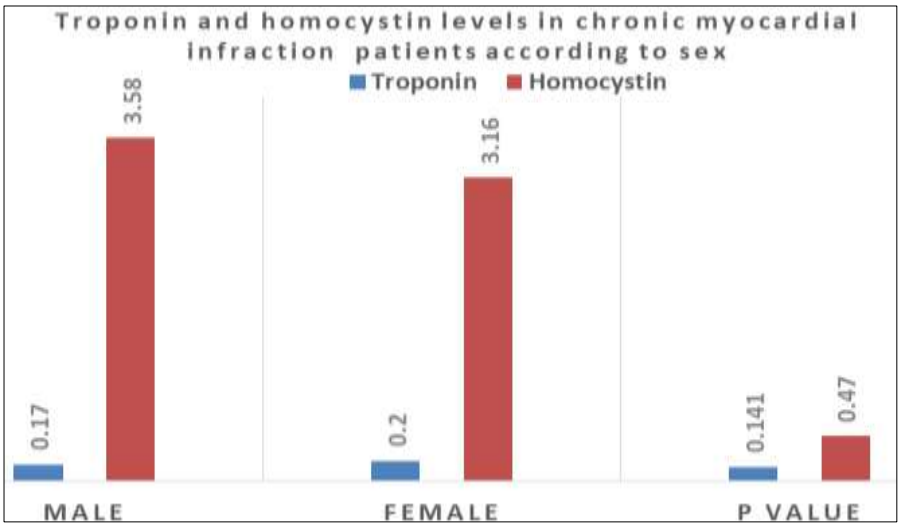

Fig 2: Troponin and Homocystin levels in CMI patients according to sex

Comparison between Troponin and Homocystin levels in acute, chronic myocardial infraction patients and control group.

A comparative study of troponin and homocysteine levels between acute and chronic myocardial infarction patients and controls shows that acute infarction patients have relatively high mean troponin levels of 25.14 with a standard deviation of 14.71 and homocysteine levels of 9.27 with a standard deviation of 2.33. In contrast, in patients with chronic infarction, the mean troponin levels were 0.18 with a standard deviation of 0.071 and homocysteine 3.39 with a standard deviation of 1.19. As for the control group, the average levels of troponin were recorded at 0.40, with a standard deviation of 0.23, and homocysteine at 2.66, with a standard deviation of 0.86, which reflects the clear disparity in the levels of these two indicators between acute and chronic infarction patients compared to healthy people.

Table 3: Mean± SD of Troponin and Homocystin levels in acute, chronic myocardial infraction patients and control group

Parameters/patients	Troponin	Homocystin
Acute	25.14±14.71	9.27±2.33
Chronic	0.18±0.071	3.39±1.19
control	0.40±0.23	2.66±0.86
P value	0.000**	0.000**

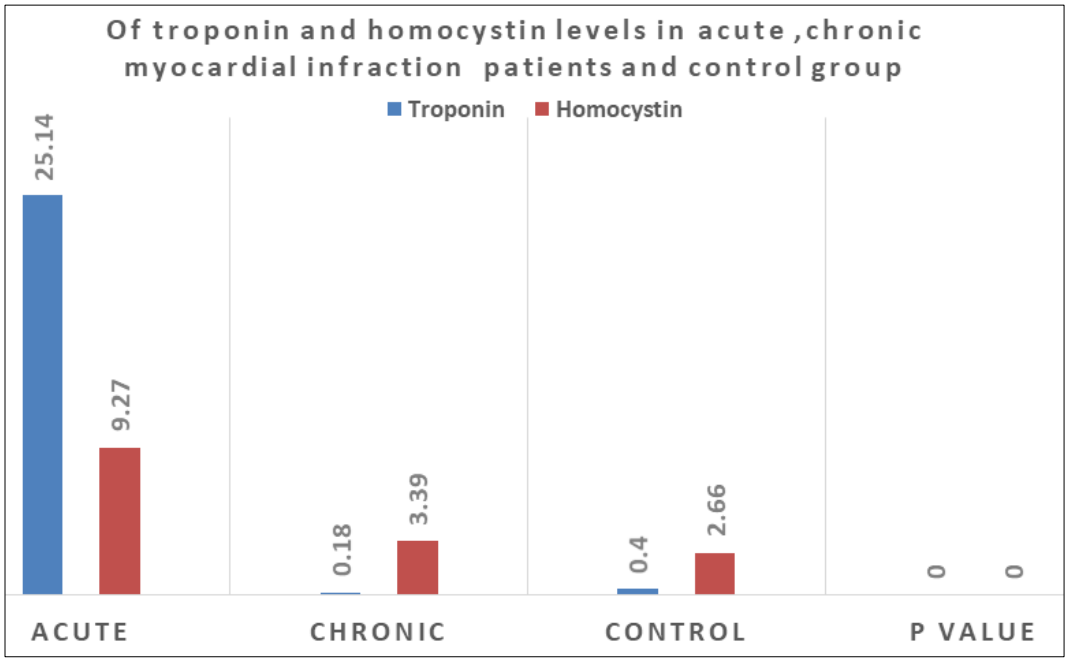

Fig 3: Troponin and Homocystin levels in acute, chronic myocardial infraction patients and control group

Comparison between Troponin and Homocystin levels in acute, chronic myocardial infraction patients and control group according to sex

Data on troponin and homocysteine levels in patients with acute and chronic myocardial infarction and controls, taking into account gender differences, show that there are subtle differences between males and females in each group. For acute and chronic myocardial infarction patients, troponin and homocysteine levels varied slightly between genders, as did the control group. Statistical values (*P* value) confirm that these differences are statistically significant, reflecting a significant influence of gender in addition to cardiac status on these two important indicators.

Table 4: Mean± SD of Troponin and Homocystin levels in acute, Chronic myocardial infraction patients and control group according to sex

Parameters/ patients	Troponin		Homocystin	
patients	M	F	**M**	**F**
Acute	25.34±14.94	24.36±14.58	9.25±2.34	9.21±2.34
chronic	0.17±0.06	0.20±0.07	3.58±1.28	3.16±1.05
control	0.39±0.23	0.39±0.23	2.79±0.90	2.49±0.80
P value	0.000	0.000	0.000	0.000

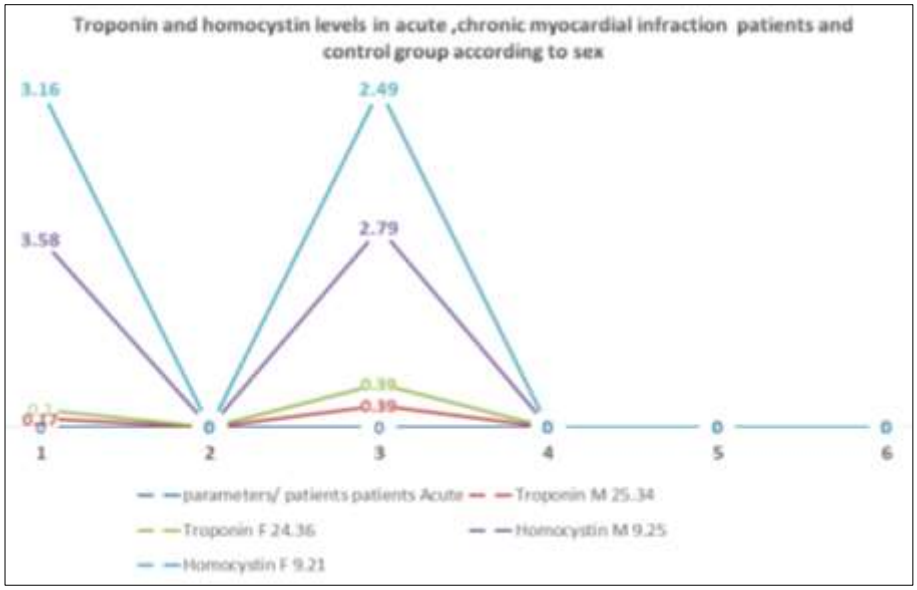

Fig 4: Troponin and Homocystin levels in acute, chronic myocardial infraction patients and control group according to sex

Comparison between Troponin and Homocystin levels in acute myocardial infraction patients with diabetes mellitus: The result shows the mean troponin and homocysteine levels with standard deviation In patients with acute myocardial infarction who had diabetes, troponin was 24.33±14.57, and homocysteine was 9.62±2.37. In comparison, in non-diabetic patients, the mean troponin level was 25.94 ± 14.98, and homocysteine level was 8.91±2.27. The results showed that the *P* values were 0.693 for troponin and 0.863 for homocysteine, indicating that there were no statistically significant differences between the two groups.

Table 5: Mean± SD of Troponin and Homocystin levels in acute myocardial infraction patients with diabetes mellitus

Parameters/ patients	Troponin	Homocystin
Diabetes mellitus	24.33±14.57	9.62±2.37
Non diabetes M.	25.94±14.98	8.91±2.27
P value	0.693	0.863

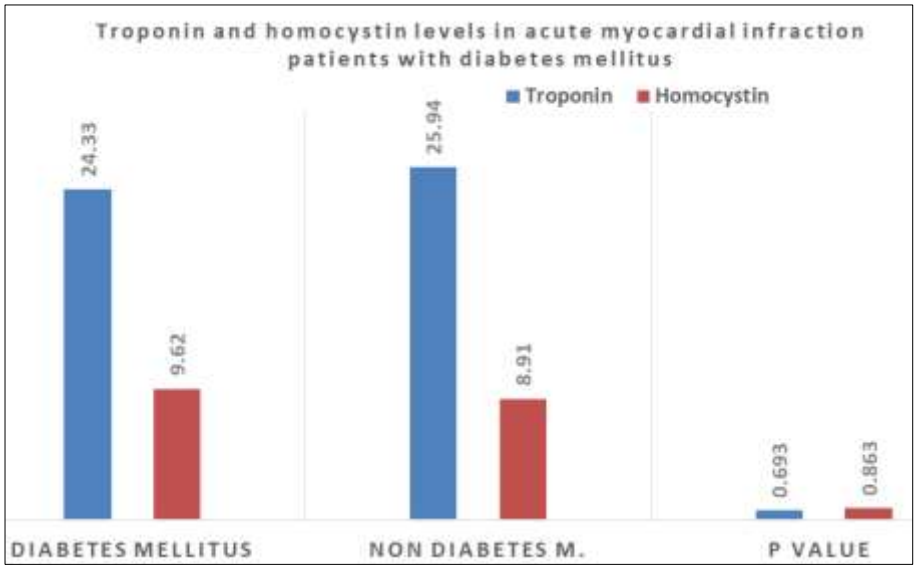

Fig 5: Troponin and Homocystin levels in acute myocardial infraction patients with diabetes mellitus

Comparison between Troponin and Homocystin levels in chronic myocardial infraction patients with diabetes mellitus

In the analysis of mean troponin and homocysteine levels with standard deviation of chronic myocardial infarction patients with diabetes, troponin levels with a mean of 0.18 and standard deviation of 0.07, and homocysteine levels with a mean of 3.30 and standard deviation of 1.22 were reported. While in non-diabetic patients, troponin levels with a mean of 0.18 and a standard deviation of 0.06 were observed, and homocysteine levels with a mean of 3.91 and a standard deviation of 1.38. The statistical values (*P* value) indicated 0.279 for troponin and 0.892 for homocysteine, indicating that there is no significant statistical difference between the two groups in these measurements.

Table 6: Mean± SD of Troponin and Homocystin levels in chronic myocardial infraction patients with diabetes mellitus

Parameters/ patients	Troponin	Homocystin
Diabetes mellitus	0.18±0.07	3.30±1.22
Non diabetes M.	0.18±0.06	3.91±1.38
P value	0. 279	0.892

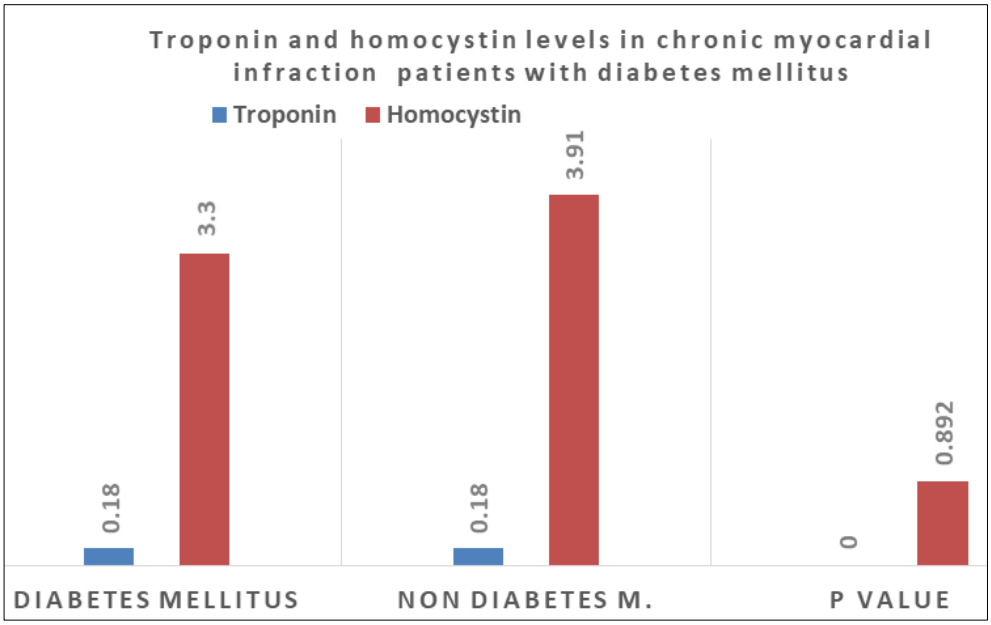

Fig 6: Troponin and Homocystin levels in chronic myocardial infraction patients with diabetes mellitus

Comparison between Troponin and homocystein levels in Acute and chronic myocardial infraction patients with diabetes mellitus and Non-diabetes

Analysis of the standard deviations and mean levels of troponin and homocysteine in acute and chronic heart attack patients reveals the following results: in acute heart attack patients with diabetes mellitus (Acute/DM), troponin levels were 24.33 with a standard deviation of 14.57, and homocysteine levels were 9.62 with a standard deviation of 2.37. For chronic heart attack patients with diabetes (Chronic/DM), troponin levels were 0.18 with a standard deviation of 0.07, and homocysteine 3.30 with a standard deviation of 1.22. The probability values (P value) showed statistically significant differences in both groups (acute/DM and chronic/DM), where the values were 0.000 and 0.004, respectively. Likewise, in acute heart attack patients without diabetes (Acute/Non-DM), troponin levels were 25.94 with a standard deviation of 14.98, and homocysteine 8.91 with a standard deviation of 2.27. For non-diabetic chronic heart attack patients (Chronic/Non-DM), troponin levels were 0.18 with a standard deviation of 0.06, and homocysteine 3.91 with a standard deviation of 1.38. The probability values for these groups indicated significant statistical significance in the acute/Non-DM group (*P* value 0.001), while there was no clear statistical significance in the chronic/Non-DM group (*P* value 0.084). These results indicate that there is a discrepancy in troponin and homocysteine levels between acute and chronic infarction cases in both diabetics and non-diabetics.

Table 7: Mean± SD of Troponin and homocystein levels in Acute and chronic myocardial infraction patients with diabetes mellitus and Non-diabetes

Patient	Troponin	Homocystin
Acute/DM	24.33±14.57	9.62±2.37
Chronic/DM	0.18±0.07	3.30±1.22
P. Value	0.000**	0.004**
Acute /Non-DM	25.94±14.98	8.91±2.27
Chronic /Non-DM	0.18±0.06	3.91±1.38
P value	0.001	0.084

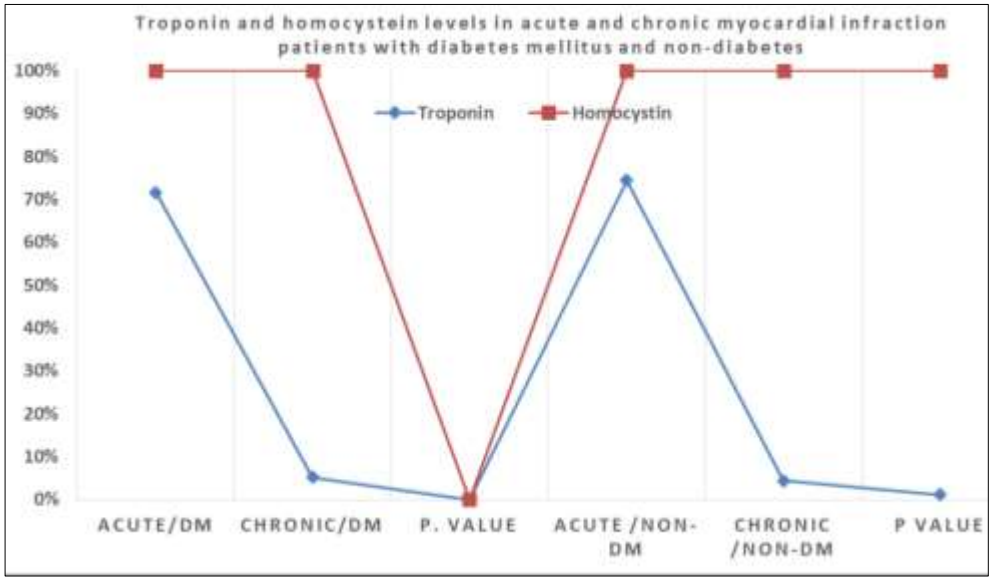

Fig 7: Troponin and homocystein levels in Acute and chronic myocardial infraction patients with diabetes mellitus and Non-diabetes

Comparison between Troponin and homocystein levels in Acute and chronic myocardial infraction patients with Hypertension and Non-hypertension

The study found that the average levels of troponin and homocysteine differ between acute and chronic myocardial infarction patients with high blood pressure and patients without it. In cases of acute myocardial infarction with high blood pressure, the mean troponin was 25.29 and homocysteine 8.95, with a standard deviation of 14.25 and 2.59, respectively. As for chronic cases with high blood pressure, the average troponin was 0.19 and homocysteine 3.37 with a standard deviation of 0.07 and 1.10, respectively, with a *P* value indicating statistical significance (*P* value 0.000). In contrast, for cases of acute myocardial infarction without hypertension, the mean troponin was 24.95 and homocysteine 9.65, with a standard deviation of 15.45 and 1.93. In chronic cases without high blood pressure, values of 0.16 were recorded for troponin and 3.42 for homocysteine, with a standard deviation of 0.06 and 1.37. The statistical value was significant for acute cases (*P* value 0.000) while it did not show statistical significance in chronic cases (*P* value 0.186).

Table 8: Mean± SD of Troponin and homocystein levels in Acute and chronic myocardial infraction patients with Hypertension and Non-hypertension

Patient	Troponin	Homocystin
Acute/Hyper.	25.29±14.25	8.95±2.59
Chronic/Hyper.	0.19±0.07	3.37±1.10
P. Value	0.000	0.000
Acute /Non-Hyper.	24.95±15.45	9.65±1.93
Chronic /Non-Hyper.	0.16±0.06	3.42±1.37
P value	0.000	0.186

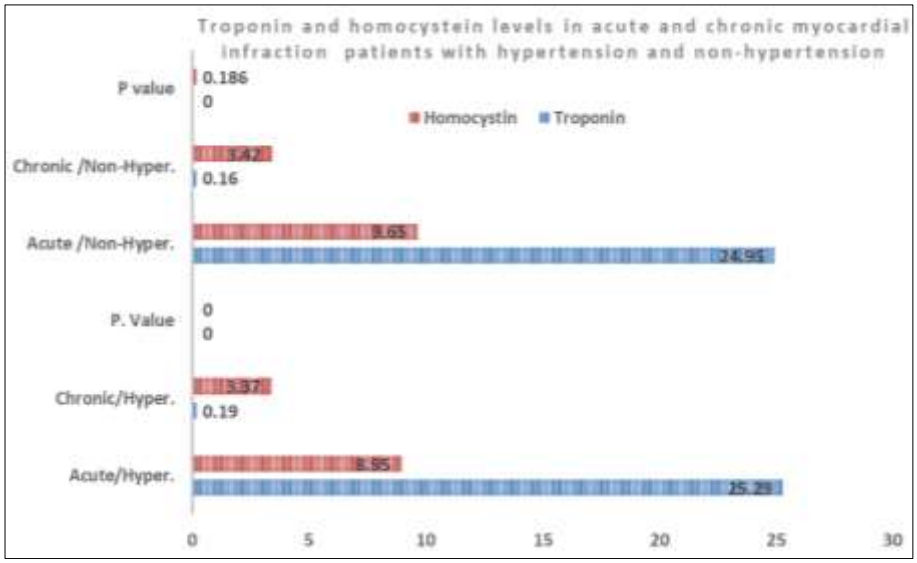

Fig 8: Troponin and homocystein levels in Acute and chronic myocardial infraction patients with Hypertension and Non-hypertension

Discussion

The current study found a high significant increase in the levels of serum troponin among ACS patients compared to control. This agree with the results of Muhammad U Ashraf *et al*, who revealed a an elevation in levels of troponin in Myocardial Infarction (MI) patients [16]. Elevated troponin indicates cardiac muscle injury, which is central to the pathophysiology of these conditions [17]. Troponin, a protein complex involved in muscle contraction, is released into the bloodstream when myocardial cells are damaged, providing a sensitive and specific marker for cardiac events [18]. Troponin assays have improved the early detection and risk stratification of patients with ACS, leading to better clinical outcomes [19]. Hence, monitoring troponin levels is essential for the effective management of MI and ACS. It suggested this elevation in troponin level may due to a necrosis of the cardiac cell which prevents troponin from attaching tropomyosin and do not lies within the groove between actin filaments in muscle tissue, so it releases in the blood stream [19]. Troponin is a highly specific marker for myocardial injury and is used extensively in the diagnosis of acute coronary syndromes (ACS). However, its levels in patients with chronic CAD do not always show significant differences when compared to a healthy control group. For instance, a study by analyzed troponin levels in patients with chronic CAD and found no significant elevation compared to the control group. The study suggested that while troponin is a sensitive marker for myocardial damage, its levels remain relatively unchanged in chronic CAD due to the lack of ongoing myocardial necrosis typically seen in more acute conditions like MI [20]. This lack of significant difference can be attributed to the nature of chronic CAD, where the myocardial ischemia is transient and typically resolves with rest or medication, thereby not causing sufficient myocardial injury to release troponin into the bloodstream [21]. Therefore, troponin, which is excellent for detecting myocardial injury in ACS, might not be a reliable biomarker for assessing stable angina where the ischemic episodes are less severe and reversible. The current results showed a significant elevation in each of acute and chronic group compared to the healthy control group. These results agree with who demonstrated that patients presenting with acute MI had significantly elevated homocysteine levels compared to age-matched healthy controls [22]. The results of current study also are in agreement with the results of [23]. On the other hand our study disagrees with the results of, which showed a significant decrease ($p< 0.001$) in the homocysteine levels of the patients with MI [24]. Numerous clinical studies have demonstrated a positive association between elevated serum homocysteine levels and the risk of ACS and MI. For instance, a meta-analysis by Zhou *et al.* analyzed data from multiple cohort studies and found that

individuals with higher homocysteine levels had a significantly increased risk of developing coronary artery disease, including ACS and MI. This association clearly shows how homocysteine can mainly indicate the risk of cardiovascular disease [25]. When heart arteries become blocked or acute coronary syndromes occur, understanding several mechanisms can explain how high homocysteine levels lead to increased cardiovascular events. Through studies, it has been shown that homocysteine negatively affects the inner lining layer of blood vessels by reducing nitric oxide production and increasing oxidative stress, which ultimately contributes to atherosclerosis and disruption of the fatty layers within blood vessels [26]. In addition, homocysteine may directly damage vascular endothelial cells, increasing the expression of adhesion molecules, leading to enhanced inflammatory processes within the arterial wall [27]. In addition to direct effects on blood vessel function, high homocysteine levels are a contributing factor in the occurrence of clots. This increases the risk of clots forming inside blood vessels, which may lead to serious complications such as strokes or heart attacks. Homocysteine interferes with the normal clotting mechanisms by promoting platelet activation and aggregation, thus enhancing the prothrombotic state associated with ACS and chronic CAD [28]. Furthermore, homocysteine can induce adverse remodeling of the myocardium following ischemic injury, exacerbating myocardial damage and impairing recovery post-MI [29]. However, it is essential to acknowledge that while there is a clear association between serum homocysteine levels and cardiovascular risk, the causal relationship remains complex and multifactorial. Other factors such as genetic predisposition, lifestyle factors (e.g., diet, smoking), and comorbidities (e.g., hypertension, diabetes) also contribute significantly to the development of ACS and CCAD.

Conclusion

The results show that there are no statistically significant differences in homocysteine and troponin levels between men and women in cases of heart attack, whether acute or chronic. However, there was a statistically significant difference in the levels of these indicators between the heart attack group compared to the control group, without any statistically significant differences between diabetics and the control group. In addition, the results showed statistical significance in the levels of cardiac indicators among groups of patients with high blood pressure when comparing acute and chronic heart attacks, as well as among groups without high blood pressure when comparing acute and chronic cases of heart attacks. These results may be explained by the fact that homocysteine and troponin levels, as indicators of cardiac damage, are more influenced by the occurrence of a heart attack itself than by gender differences or the presence of diabetes. This suggests that the biological mechanisms that cause and develop heart attacks may be largely shared between the sexes and independent of the effect of diabetes. While the presence of statistical significance in the levels of cardiac indicators among groups of patients with high blood pressure reflects the role of high blood pressure as an influential factor that is significantly linked to an increase in the risk and severity of heart attacks, whether acute or chronic.

Conflict of Interest: Not available

Financial Support
Not available

References

1. Mangge H, Becker K, Fuchs D, Gostner JM. Antioxidants, inflammation and cardiovascular disease. World J Cardiol. 2014;6(6):462-77. DOI: 10.4330/wjc.v6.i6.462.
2. Shenov V, Mehendale V, Prabhu K, Shetty R, Rao P. Correlation of serum homocysteine levels with the severity of coronary artery disease. Ind. J Clin .Biochem. 2014;29(3):339-44. DOI: 10.1007/s12291-013-0373-5.
3. Veeranna V, Zalawadiya SK, Niraj A, Pradhan J, Ference B, Burack RC, *et al*. Homocysteine and reclassification of cardiovascular disease risk. J Am Coll Cardiol. 2011;58:1025-1033. DOI: 10.1016/j.jacc.2011.05.028.
4. Faeh D, Chiolero A, Paccaud F. *Homocysteine* as a risk factor for cardiovascular disease: Should we (still) worry about it? Swiss Med Wkly. 2006;136:745-56.
5. Pang X, Liu J, Zhao J, Mao J, Zhang X, Feng L, *et al*. *Homocysteine* induces the expression of C-reactive protein via NMDAr-ROS-MAPK-NF-κB signal pathway in rat vascular smooth muscle cells. Atherosclerosis. 2014;236:73-81. DOI: 10.1016/j.atherosclerosis.2014.06.021.
6. Werida RH, Omran A, El-Khodary NM. Sortilin and *homocysteine* as potential biomarkers for coronary artery diseases. Int J Gen Med. 2021;14:6167-6176.
7. Jin N, *et al*. Elevated *homocysteine* levels in patients with heart failure: A systematic review and meta-analysis. Medicine. 2021;100(33).
8. Cziraki A, *et al*. Morphological and functional remodeling of the ischemic heart correlates with *homocysteine* levels. J Cardiovasc Dev Dis. 2023;10(3):122.
9. Welsh P, Preiss D, Hayward C, Shah ASV, McAllister D, Briggs A, *et al*. Cardiac Troponin T and Troponin I in the General Population. Circulation. 2019;139:2754-64. DOI: 10.1161/CIRCULATIONAHA.118.038529.
10. Olson F, Engborg J, Grønhøj MH, Sand NP, Lambrechtsen J, Steffensen FH, *et al*. Association between high-sensitive troponin I and coronary artery calcification in a Danish general population. Atherosclerosis. 2016;245:88-93. DOI: 10.1016/j.atherosclerosis.2015.12.017.
11. Barbier CE, Themudo R, Bjerner T, Johansson L, Lindahl B, Venge P, *et al*. Cardiac troponin I associated with the development of unrecognized myocardial infarctions detected with MRI. Clin Chem. 2014;60:1327-35. DOI: 10.1373/clinchem.2014.222430.
12. Parmacek MS, Solaro RJ. Biology of the Troponin Complex in Cardiac Myocytes. Prog Cardiovasc Dis. 2004;47:159-76. DOI: 10.1016/j.pcad.2004.07.003.
13. Lippi G, Cervellin G. Degradation of troponin I in serum or plasma: mechanisms, and analytical and clinical implications. Semin Thromb Hemost. 2012;38:222-9. DOI: 10.1055/s-0032-1301419.
14. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, *et al*. Fourth Universal Definition of Myocardial Infarction 2018. Circulation. 2018;138-e651. DOI: 10.1161/CIR.0000000000000617.

15. Michos ED, Wilson LM, Yeh HC, Berger Z, Suarez-Cuervo C, Stacy SR, *et al*. Prognostic value of cardiac troponin in patients with chronic kidney disease without suspected acute coronary syndrome: A systematic review and meta-analysis. Ann Intern Med. 2014;161:491-501. DOI: 10.7326/M14-0743.
16. Ashraf MU, Aslam M, Ajmal MR, Habib A. Relationship of serum *homocysteine* levels with cardiac troponin and ejection fraction in patients admitted with acute coronary syndrome. Int J Adv Res. 2014;2(3):131-135.
17. Park KC, Gaze DC, Collinson PO, Marber MS. Cardiac troponins: From myocardial infarction to chronic disease. Cardiovasc Res. 2017;113(14):1708-1718.
18. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, *et al*. Fourth universal definition of myocardial infarction (2018). Eur Heart J. 2018;40(3):237-269.
19. Newby LK, Neumann JT, Sorensen NA, Chapman AR. Diagnosis and management of myocardial injury in the absence of obstructive coronary artery disease: A consensus document from the fourth universal definition of myocardial infarction global task force (2018). Eur Heart J. 2019;40(3):239-247.
20. Smith DE, Hornstra JM, Kok RM, Blom HJ, Smulders YM. *Homocysteine* levels and the risk of osteoporotic fracture. N Engl J Med. 2018;350(20):2033-41.
21. Peng YM, Liu C, Huang C, Luo J. Serum high concentrations of *homocysteine* and low levels of folic acid and vitamin B12 are significantly correlated with the categories of coronary artery diseases. BMC Cardiovasc Disord. 2017;17(1).
22. Page JH, Ma J, Chiuve SE, Stampfer MJ, Selhub J, Manson JE, *et al*. Plasma total cysteine and total *homocysteine* and risk of myocardial infarction in women: A prospective study. Am Heart J. 2010;159(4):599-604.
23. Zhou K, Zhao R, Geng Z, *et al*. Association between *homocysteine* and coronary artery disease: a meta-analysis. Clin Chim Acta. 2019;488:36-43.
24. Poddar R, Sivasubramanian N, DiBello PM, Robinson K, Jacobsen DW. *Homocysteine* induces expression and secretion of monocyte chemoattractant protein-1 and interleukin-8 in human aortic endothelial cells: implications for vascular disease. Circulation. 2017;103(22):2717-23.
25. Zhang Y, Vittinghoff E, Pletcher MJ, *et al*. Associations of blood pressure and cholesterol levels during young adulthood with later cardiovascular events. J Am Coll Cardiol. 2019;74:330-341.
26. Xu XY, Guo CY, Chen YL, *et al*. Role of *homocysteine* in arterial thrombosis and related diseases. Ann Transl Med. 2020;8(5):237.
27. Sasongko TH, Iskandar R, Siregar NC, *et al*. Hyperhomocysteinemia as a risk factor for chronic stable angina and myocardial infarction: a case control study. Int J Angiol. 2016;25(4):223-7.
28. Shih CC, Shih YL, Chen JY. The association between *homocysteine* levels and cardiovascular disease risk among middle-aged and elderly adults in Taiwan. BMC Cardiovasc Disord. 2021;21:1-8.
29. Zhang ZY, *et al*. *Homocysteine*, hypertension, and risks of cardiovascular events and all-cause death in the Chinese elderly population: A prospective study. J Geriatr Cardiol. 2021;18(10):796.

How to Cite This Article
Hanoon AH, Jassim AK, Hashim NA. The effect of homocysteine and troponin levels on the development and diagnosis of cardiovascular diseases. International Journal of Cardiology Sciences. 2024;6(1):86-94.