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Original Article

EXPLORING THE ASSOCIATION BETWEEN SYSTEMIC BIOMARKERS AND ACUTE CORONARY SYNDROME: A CASE CONTROL STUDY IN KURDISH IRAQI PATIENTS

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ABSTRACT

Acute coronary syndrome (ACS) continues to be a major reason for global death, with multiple systemic biomarkers implicated in its pathogenesis. This clinical study was conducted to compare biochemical, hematological, homocysteine (HCY), body mass index (BMI), age, and blood pressure (BP) biomarkers, along with detecting their correlation with HCY, between ACS and healthy persons. About 70 (38-80 years) ACS and 30 (21-75 years) healthy clients in both gender males and females were subjected to this study. The concentration of creatinine, urea, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP), creatine kinase (CK-MB), glucose, vitamin D, uric acid, and HCY parameters were measured. Correlation of HCY with some of the measured parameters was also detected. Significantly higher HCY, CK-MB, glucose, BP, BMI, creatinine, AST, MID, RBC, MPV, RDW-CV, RDW-SD, but significantly lower MCV, MCH, PLT and PCT were observed in ACS patients than control. The other measured parameters exhibited no significant changes between the examined groups. However, HCY level was remarkably correlated with CK-MB, but didn't show any significant correlation with age, AST, ALT, ALP, creatinine, urea, glucose, uric acid, and vitamin D parameters. These findings confirm that Hyperhomocysteinemia (HHCY) is highly related with ACS and correlates with disease severity, suggesting its potential utility as a prognostic biomarker in coronary artery disease management.

KEYWORDS: Acute coronary syndrome, Coronary artery disease, Homocysteine, Hyperhomocysteinemia, Risk factors.

1. INTRODUCTION

Acute coronary syndromes are cardiovascular diseases (CVDs) that have been determined to be the major cause of death in both industrialized and developing nations, accounting for nearly 30% of all fatalities globally (Malakar *et al.*, 2019). The ACS is a collection of situations characterized by diminished blood flow to the heart, including ST-elevation myocardial infarction (STEMI), non-STEMI, and unstable angina (Zègre-Hemsey *et al.*, 2019). Cardiovascular disease , which is associated with blockage of the arteries and veins that supply the heart with blood, develops slowly and, in most coronary artery diseases (CADs), has no symptoms until it reaches advanced stages or the patient suffers sudden death (Sanchis-Gomar *et al.*, 2016). Multiple risk factors have been identified for ACS, including hypertension, diabetes, renal and hepatic dysfunction, elevated plasma homocysteine, vitamin D deficiency, thrombosis, and chronic inflammation (Adhikary *et al.*, 2022). Homocysteine is a non-essential amino acid that is made from the food amino acid methionine. The irregular metabolism of HCY may cause oxidative stress and cytotoxicity (Kumar *et al.*, 2017). A high concentration of HCY in the serum, called HHCY, have been pointed out as a risk factor for CAD because of their effects on endothelial function and vascular flexibility (Ganguly & Alam, 2015). Vitamin B12 and folate deficiency or methylenetetrahydrofolate reductase enzyme defect that affects homocysteine metabolism may cause mild to moderate HHCY (Mohan *et al.*, 2023).

High BP is a significant risk determinant for CVD that has strong causal evidence and is the cause of issues in the body of 25% of adults (Fuchs & Whelton, 2020). Its negative effect on the circulatory system, is mostly through the mechanical stress on the heart and the vessels, where BP levels are more than 140/90 mmHg (Kou *et al.*, 2024). It has been found that blood factors and hormones may have a role in the progress of hypertension-related changes of the cardiovascular system, their exact functions are still not clear and are probably minor (Zhao & Pei, 2020).

Thrombosis is a major problem in heart disease that can result in situations such as heart attack, ischemic stroke, and venous thromboembolism. Thrombosis is produced by the development of a thrombus within blood arteries, which contains fibrin, RBCs, platelets, leukocytes, and neutrophil extracellular traps while also impeding blood flow (Alkarithi *et al.*, 2021). The RBCs have been shown to facilitate thrombin production via the meizothrombin pathway. Elevated hematocrit facilitates the aggregation of platelets at sites of vascular damage by displacing platelets from the middle of the blood vessel to the vascular wall.

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Two populations of platelets that alter during clot formation include aggregating platelets, which are crucial for the early stages of clot formation, and procoagulant platelets, which help generate thrombin.(Yu *et al.*, 2025). Leukocytes, especially neutrophils and monocytes, are also present in the clot together with platelets. They activate the coagulation enzymes and, by expressing tissue factor, they initiate the coagulation process (Iba & Levy, 2018).

Vitamin D insufficiency affects around one billion individuals globally and is identified for its importance in calcium absorption and bone health. Emerging research shows that it also plays a role in heart health, with vitamin D receptors found in heart and blood vessel cells, indicating its contribution to cardiovascular function by influencing vascular tone and displaying antifibrotic and antihypertrophic properties in the heart (de la Guía-Galipienso *et al.*, 2021). Moreover, the endothelium, which is responsible for maintaining vascular integrity, protective functions severely weaken in chronic kidney disease (CKD), thereby increase cardiovascular risks. Patients with CKD are likely to develop subclinical atherosclerosis, which is a condition leading to myocardial infarction (Baaten *et al.*, 2023).

Heart and liver functions interact in a complex manner, and various diseases are the result of this interaction. Cardiac hepatopathy may become the cause of cardiac cirrhosis and cardiogenic hypoxic hepatitis, which are the symptoms of heart failure (Roca-Fernandez *et al.*, 2023). The aim of the heart therapy is to control heart disease for maintaining organ perfusion. Furthermore, severe cirrhosis may lead to the decrease of cardiac performance and the development of cirrhotic cardiomyopathy, which is accompanied by the impairment of systolic and diastolic function (Kaur & Premkumar, 2022).Diabetes-related CVD is the major reason for death and incapacity among diabetics, who manifest a greater occurrence of CVD than healthy individuals (Dal Canto *et al.*, 2019). The chance of CVD going up step by step with each higher fasting plasma glucose (FPG) level, even before the diagnosis of diabetes (Siam *et al.*, 2024). High levels of FPG are strongly linked to an increased risk of CVD. Diabetes mellitus (DM) is recognized for impairing endothelial nitric oxide synthase activity and increasing reactive oxygen species generation, thereby reducing nitric oxide bioavailability and leading to pro-atherogenic changes (Almourani *et al.*, 2019).

The aim of this study was to clarify the possible role of HCY in the pathogenesis and severity of ACS in Kurdish Iraqi patients. Additionally, assessing the condition of specific hematological parameters and the correlation between HCY and various biochemical metrics.

2. MATERIALS AND METHODS

Experimental Design:

The research was performed at the Cardiac Unit of Ashty Hospital, Soran, Iraq, between October 2024 and April 2025. Patients (males and females) included seventy individuals (38-80 years) confirmed to suffer from ACS, as shown through coronary angiography. When at least one of the principal coronary arteries showed a luminal stricture of 75% or higher, the patient suffered from ACS. Additionally, the patient population was divided into CAD severity groups, from mild to severe, based on their coronary angiographic results. For the control (males and females) population, thirty subjects (21-75 years) of the same gender as the patient populace) were chosen from persons who had previously attended the cardiac unit. Patients underwent coronary angiography that showed no luminal stricture within the coronary arteries of these subjects, which were found to be normal.

In addition, patients with malignancies, viral infections, the inability to give a valid blood sample for analysis, and a history of strokes were also not included in the study. Additionally, a substantial imbalance in the number of patients with ACS when compared to those in the control study group may be ascribed to the high number of patients with ACS who sought medical attention in comparison to the lower number of patients who did not have ACS but underwent angiography during the diagnosis of chest pain and showed results of normal angiographic findings. Carrying out the angiographic analysis among patients who do not have symptoms of ACS not only faces notable difficulties, but it is also accompanied by pain and substantial economic costs. moreover, it is crucial acknowledge that most individuals in the patient cohort were receiving pharmacological treatment to for CAD, BP, and dyslipidemia, as suitable for their circumstances.

Sample Collection:

To obtain clinical information about the participants, a structured questionnaire was used. This questionnaire inquired about risk factors of atherosclerosis, medical history both personal and familial, present use of medications, demographics, and anthropometrics. Clients were particularly asked to report any medications presently used, including the use of the oral contraceptive pill, as well as any medical procedures undergone. Prior to catheterization, approximately 10 mL of blood was obtained from each participant. This blood was placed into vials containing both plain and Ethylenediamine Tetra Acetic Acid (EDTA). The serum was subsequently obtained by centrifuging the blood for a period of 15 minutes at a force of 3000 g. Finally, taking into consideration the participants' identification numbers, each supernatant or serum was carefully placed in a separate Eppendorf tube and stored at a temperature of -85 °C until further processed. Moreover, a specific formula was used to calculate the BMI in kg/m², where an individual's height is denoted in square meters and their weight is indicated in kilograms (kg): BMI = Weight (kg) / Height (m)2.

Serological Study:

This study examined various physiological biomarkers, encompassing hematological indicators, renal and hepatic function tests, blood glucose concentrations, vitamin D levels, uric acid, and HCY. A complete blood count (CBC) study was conducted using a Beckman Coulter DxH Series automated hematology analyzer (Beckman Coulter, Inc., Brea, CA, USA), which delivers extensive hematological profiles. A comprehensive assessment of biochemical parameters was performed to analyze numerous health markers, including creatinine, urea, CK-MB, ALT, AST, ALP, glucose, vitamin D, and uric acid. The tests were done using a fully automated biochemical analyzer (Cobas c111, Roche's Instrument Centre, Germany).

Additionally, serum levels of HCY were determined using a commercial sandwich enzyme-linked immunosorbent assay (ELISA) kit Catalogue Number: SL2047Hu, SunLong Biotech Co., LTD, China) following the manufacturer's protocols.

Statistical Analysis:

The data was analyzed using GraphPad Prism version 9. The normality of continuous variables was assessed before to doing the study. If the data followed a normal distribution, it was represented as mean ± standard deviation (SD), and the intergroup differences were assessed using the unpaired two-tailed t-test. For non-normal distributions, the data were presented as median (interquartile range) and examined with the Mann Whitney U test. Furthermore, Spearman's correlation coefficient was used to analyze the relationship between continuous variables. The Receiver Operating Characteristic curve analysis was used to ascertain the optimal cut-off points of the HCY biomarker for ACS risk variables and severity, focusing

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on the highest sensitivity index. A difference was deemed statistically significant when $P < 0.05$ in all cases.

3. RESULTS

Study Subject Demography:

The demographic information of the investigation is summarized in (Table 1). Thirty controls and seventy ACS patients made up the 100 participants in this study. Compared to controls (39.5 ± 12.97 years), the ACS group was significantly ($P < 0.0001$) older (60.41 ± 11.03 years). The sex distribution showed that there were more females in the control group (63.3%) than in the ACS group (44.3%), with males making up 55.7% of ACS patients and 36.7% of controls. However, this difference in the sex distribution was not statistically significant. ACS patients had a significantly ($P<0.0128$) higher BMI (29.71 ± 4.438 kg/m2) than controls (27.37 ± 4.821 kg/m2). ACS patients had higher mean arterial pressure (104.4 ± 14.92 vs. 94.90 ± 5.921 mmHg, $P<0.0011$) and systolic blood pressure (142.0 ± 23.74 vs. 124.1 ± 11.30 mmHg, $P<0.0001$). The ACS group's diastolic blood pressure tended to rise, but this was not statistically significant (85.54 ± 12.85 vs. 80.30 ± 4.276 mmHg). These baseline features reveal notable clinical and demographic differences between ACS patients and healthy controls, particularly in systolic BP, age, and BMI.

Table 1: Demonstrates the distribution of study participants by age, gender, body mass index, and Blood pressure.

Parameters		Groups (Means ± SD)		*P* value
		Control (n=30)	ACS (n=70)	<
Age (Years)		39.5 ± 12.97	60.41 ± 11.03	0.0001
Sex, n (%)	Female	19 (63.3%	31 (44.3%)	0.081
	Male	11 (36.7%)	39 (55.7%)	
BMI (kg/m²)		27.37±4.821	29.71±4.438	0.0128
Blood pressure	Systolic BP (mmHg)	124.1±11.30	142.0±23.74	0.0001
	Diastolic BP (mmHg)	80.30±4.276	85.54±12.85	0.0813
	Mean Arterial Pressure (mmHg)	94.90±5.921	104.4±14.92	0.0011

BMI, body mass index. Results are expressed as numbers or means ± SD.

Hematological Parameter Analysis:

Comparisons of hematological parameters between the ACS and control groups are shown in Table 2. The means of MID ($P<0.0007$), RBC ($P<.0028$), RWD-CV ($P<0.0008$), RDW-SD ($P<0.0213$), and MPV ($P<0.0347$), were significantly higher, but the means of MCV ($P<0.0202$), MCH ($P<0.0001$), PLT ($P<0.0001$), and PCT ($P<0.0017$) were significantly lower in ACS than those of control individuals. Conversely, the means for WBC, LYM, GRA, HGB, HCT, HCV, PDW, and P-LCR were only numerically different between the groups examined.

Table 2: A Comparative Analysis of Hematological Parameters Between Acute Coronary Syndrome Patients and Controls.

Parameters	Groups (Means ± SD)		*P* value
	Control (n=30)	ACS (n=70)	<
WBC (10^9/l)	7.049 ± 1.377	7.385 ± 2.108	0.636
LYM% (%)	31.18 ± 6.425	29.11 ± 8.898	0.2413
MID% (%)	6.27 ± 2.176	8.926 ± 4.019	0.0007
GRA% (%)	62.55 ± 6.682	62.06 ± 10.31	0.7863
RBC (10^{12}/l)	4.548 ± 0.6435	4.834 ± 0.4307	0.0028
HGB (g/dl)	13.86 ± 2.012	13.84 ± 1.332	0.3981
HCT (%)	43.11 ± 5.953	44.08 ± 4.855	0.162
MCV (fl)	94.93 ± 4.84	91.25 ± 7.439	0.0202
MCH (pg)	30.49 ± 1.829	28.66 ± 2.032	0.0001
MCHC (g/dl)	32.09 ± 1.169	31.53 ± 2.395	0.0902
RDW-CV (%)	11.82 ± 0.7014	12.2 ± 0.716	0.0008
RDW-SD (fl)	42.82 ± 8.121	42.91 ± 5.658	0.0213
PLT (10^9/l)	268.1 ± 62.09	215.6 ± 57.53	0.0001
MPV (fl)	7.647 ± 0.8114	8.15 ± 1.076	0.0347
PDW (fl)	12.58 ± 1.597	12.55 ± 1.95	0.3695
PCT (%)	0.2009 ± 0.04233	0.1712 ± 0.04432	0.0017
P-LCR (%)	17.11 ± 6.327	17.87 ± 8.164	0.8914

WBC, white blood cell; LYM, Lymphocyte; GRA, granulocyte; MID, Middle-sized cells; RBC, red blood cell; HGB, hemoglobin; HCT, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, Mean Corpuscular Hemoglobin Concentration; RDW%, red cell distribution width; RDW-SD, red cell distribution-standard deviation; PLT, platelet; PCT, Plateletcrit; MPV, mean platelet volume; PDWs, Platelet Distribution Width; PLCR, Platelet larger cell ratio. Results are expressed as numbers or means ± SD.

Biochemical Parameter Analysis:

The biochemical measurements of the study are summarized in (Table 3). Statistical analysis revealed that urea, ALP, uric acid, and vitamin D exhibited no significant variations between the ACS and healthy groups. Whereas, each of CK-MB ($P < 0.0001$), glucose ($P < 0.0001$) and creatinine ($P<0.0008$) concentrations showed highly significant values in ACS patients versus to control individuals, also AST value significantly ($P = 0.0428$) greater in ACS patients over control group.

Table 3: Biochemical assessments of the examined population.

Parameters	Groups (Means ± SD)		*P* value
	Control (n=30)	ACS (n=70)	
CK-MB (ng/ml)	1.668± 0.9045	4.559± 3.384	<0.0001
Glucose (mg/dL)	107.5± 29.68	151.7± 58.73	<0.0001
Creatinine (mg/dL)	0.67± 0.2395	0.8674± 0.2712	0.0008
Urea (mg/dL)	26.59± 7.74	33.15± 20.62	0.0736
Uric acid (mg/dL)	4.214± 0.8459	4.44± 1.116	0.3694
ALT (U/L)	21.32± 13.08	27.71± 21.53	0.1532
AST (U/L)	20.41± 6.297	35.67± 54.01	0.0428
ALP (U/L)	84.03±31	89.18±47.01	0.8152
Vitamin D (ng/ml)	11.73± 4.488	11.19± 3.145	0.8414

AST, Aspartate aminotransferase; ALT, Alanine aminotransferase; ALP, Alkaline phosphatase, CK-MB, creatine kinase-MB, Results are expressed as numbers or means ± SD.

Determination of Serum Homocysteine in Acute Coronary Syndrome Patients and Healthy Persons:

Serum HCY concentration was significantly (P<0.0001) higher in ACS patients (16.87 ± 11.19 µmol/L) compared with control group (9.82 ± 2.77 µmol/L), representing a 72% elevation (Fig. 1). To investigate the link between HCY levels and illness severity, ACS patients were divided into three groups: mild, moderate, and severe. Homocysteine levels differed significantly across groups ($p < 0.0001$), suggesting that they rise with coronary artery involvement. This pattern is consistent with prior studies associating greater HCY levels to an increased burden of CVD (Schaffer *et al.*, 2014).

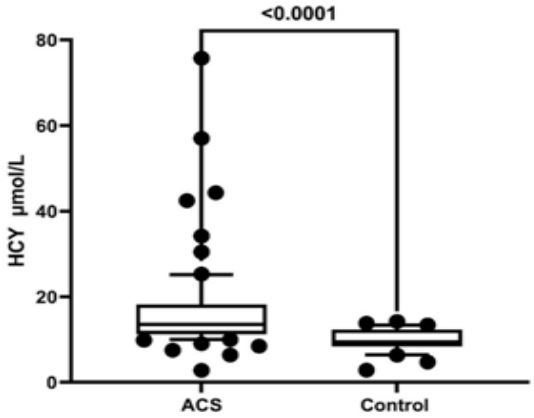

Figure 1: A c:ase-control study showing noticeably elevated homocysteine levels in acute coronary syndrome patients

Serum Homocysteine Concentrations Correlate with Age and Some Biochemical Variables in Acute Coronary Syndrome:

A Spearman correlation analysis found a significant positive association ($r = 0.3111$, $P < 0.0088$) between serum HCY levels and CK-MB in individuals with ACS. This study shows that as levels of CK-MB levels increase, HCY levels of HCY also increase in patients with ACS. However, there were no statistical correlations between blood levels of HCY and age, liver function parameters (AST, ALT, and ALP), renal parameters (creatinine and urea), glucose levels, vitamin D levels, and uric acid levels (Table 4). Findings such as this help shed light on the association between levels of HCY and various clinical parameters that exist within the context of an ACS event, and identify various factors that could affect HCY levels.

Table 4: Correlation between serum HCY levels and some parameters

Serum HCY level	Spearman correlation (r)	95% confidence interval	*P* value <	*P* value summary
Age	0.1162	-0.1291 to 0.3480	0.3383	Ns
Creatinine	0.05873	-0.1856 to 0.2962	0.6291	Ns
Urea	0.08884	-0.1562 to 0.3235	0.4646	Ns
ALT	-0.1955	-0.4174 to 0.04849	0.1049	Ns
AST	-0.1949	-0.4170 to 0.04902	0.1058	Ns
ALP	-0.06213	-0.2993 to 0.1823	0.6094	Ns
CK-MB	0.3111	0.07509 to 0.5141	0.0088	**
Glucose	0.06604	-0.1785 to 0.3029	0.587	Ns
Uric acid	0.0385	-0.2051 to 0.2776	0.7517	Ns
Vitamin D	-0.1481	-0.3763 to 0.09700	0.221	Ns

*Statistical significance.

Furthermore, this research endeavored to evaluate the predictive significance of serum HCY levels as a biomarker in the diagnosis of ACS, as demonstrated in (Fig. 2). The results obtained showed that HCY had a moderate predictive significance, with a cut-off of ≤ 11.13 µmol/L, AUC of 0.7540, sensitivity of 71.43%, and specificity of 73.33% ($p < 0.0001$, DOR = 6.7500). The ROC curve analysis exhibited that the levels

of HCY in the sera of patients could successfully distinguish patients from healthy persons. The most appropriate cut-off for the clinical prediction of the disease was the one that provided the best compromise between sensitivity and specificity. The obtained data show that measurements of HCY concentrations in the sera of patients could become a valuable contribution in the estimation of the risk and severity of CAD in hospitals.

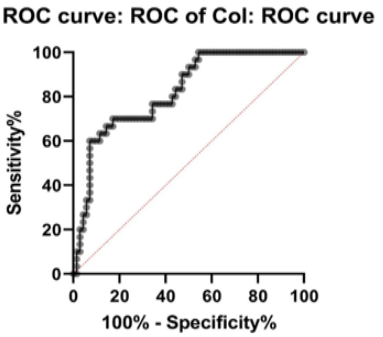

Figure 2: Shows a ROC curve study that uses blood homocysteine levels to predict acute coronary syndrome.

4. DISCUSSION

This study indicates a multi-parameters insight into the relationship between systemic biochemical and hematological markers and ACS within Kurdish Iraqi patients, underlining its clinical relevance to HCY. The findings from this research demonstrate that there are significant alterations within multiple physiological systems in ACS patients when compared to healthy participants, underlining the multifactorial nature of CAD.

The current clinical analysis has confirmed previous research proving that people with ACS are generally much older than those in the control group. The current study aligns with previous research confirming its assertion about the importance of the age factor in diagnosing ACS, thus affirming a known insight about the leading role of senior age in risk factors in the development of CAD (Anh *et al.*, 2021). There is scientifically based support for this relationship because vascular aging encompasses endothelial dysfunction, arterial stiffness, and chronic exposure to metabolic and lifestyle stressors (Rodgers *et al.*, 2019).

Although not statistically significant, more men were found to be present in the ACS group in comparison with the healthy group, consistent with previous data indicating a higher burden of CAD in the former group. Sex-related variations in the pathophysiology of blood vessels and the protective effect of the female hormone in premenopausal women may be the reasons for this finding (Johnston *et al.*, 2015; Pelletier *et al.*, 2016). Furthermore, an earlier beginning and a more severe form of coronary atherosclerosis have been consistently recorded in men, whereas women often develop the illness at a later age and exhibit a variety of clinical manifestations (Regitz-Zagrosek & Gebhard, 2023).

In the current study BMI significantly elevated in ACS patients versus the controls. This finding parallel with extensive evidence founding obesity as an independent risk factor for CAD (Manoharan *et al.*, 2022; Pham *et al.*, 2024). Obesity promotes atherogenesis through adipocytokine-mediated inflammation, endothelial dysfunction, insulin resistance, all of which cluster to enhance ACS (Kirichenko *et al.*, 2022).

Statistical analysis revealed that BP significantly elevated in ACS patients compared to healthy group, confirming BP as a significant changeable risk factor for ACS. The mechanical stress imposed by elevated BP on the heart and blood vessels contributes directly to vascular remodeling, left ventricular hypertrophy, and accelerated atherosclerosis (Masenga & Kirabo, 2023; Wu *et al.*, 2025). Although diastolic BP is the biggest determinant of CAD in younger and middle-aged adults, this association becomes reversed, and pulse pressure has the largest direct link with CAD in those over 60 years of age (Weber *et al.*, 2016). The pathophysiological processes of BP as a risk factor for CVD are complicated, including the impact of BP as a physical force on the formation of atherosclerotic plaque, as well as the link among pulsatile hemodynamics/arterial stiffness and coronary perfusion (Poznyak *et al.*, 2022). These findings underscore the vital role of BP regulation in ACS preventive and treatment regimens.

One of the central findings of this study is the high amount of serum HCY in the ACS group in comparison with the normal group. This is constant with previous studies that associate HHCY with an increase in heart disease risk (Miñana *et al.*, 2021; Unadkat *et al.*, 2024). Homocysteine, a nonessential amino acid metabolized from methionine, was reported by various researchers as an autonomous risk factor for ACS. The credible mechanisms would be endothelial dysfunction, production of oxidative stress, promotion of proliferation of vascular smooth muscle cells, and thrombosis (Zhu *et al.*, 2019). The present findings agree and confirm the relevance of the levels of HCY as a modifiable risk factor for the progress of ACS, whereas it is possibly the case that the elevated levels of HCY can be the consequence of a deficiency of folic acid and/or vitamin B12, renal disorders, or genetic defects pertaining to the regulation of HCY (Bosevski *et al.*, 2020; Unadkat *et al.*, 2024).

There was a considerable increase in the levels of CK-MB in the ACS group, which was expected considering its established role as a marker of myocardial infarction. Creatine kinase-MB has a longstanding reputation as the gold standard for diagnosing myocardial infarction. The CK-MB is an isoenzyme of creatine kinase, mostly located in the myocardium. Elevation starts 4–6 hours after the initiation of myocardial necrosis and persists for 24–48 hours. Serial testing may enhance the sensitivity and specificity of CK-MB in identifying myocardial injury (Thygesen *et al.*, 2018; Motamed *et al.*, 2023). The demonstration of high levels of CK-MB in the present study group suggests that the myocardium is still being exposed to unfavorable circumstances within the group suffering from ACS, since CK-MB suggests myocardial injury. Cardiac troponins have largely replaced the role of CK-MB at present, although the latter is employed in the diagnosis of reinfarction of the myocardium (Lyngbakken *et al.*, 2019).

The glucose values in the ACS patients demonstrated a marked increase relative to the control group, reinforcing the well-proven connection that exists between hyperglycemia and CVD. The results obtained from the current study are well supported by other studies that demonstrated the clear linkage that exists between the fasting plasma glucose values and the risk that clients face concerning CVD, even if they are not diabetic (Patsouras *et al.*, 2019). The DM is linked to endothelial dysfunction. Consequently, it is essential to understand the causes of endothelial failure induced by DM and to identify therapies that enhance or restore endothelial function to avoid diabetic vascular problems (Maruhashi & Higashi, 2021). The progressive rise in the risk for CVD for every rise in the fasting plasma glucose values reinforces the importance of glycemic control and its relevance in the management and prevention of CAD.

Creatinine values were found to be higher in subjects with ACS than those without, when considering renal function. The finding is also consistent with literature evidence, suggesting that the risk of post-contrast acute kidney injury is twice as high in people who have diabetes mellitus and atrial fibrillation, especially when baseline creatinine is high (Sarnak *et al.*, 2003; Kuźma *et al.*, 2020). This finding supports the well-established

bidirectional link between CKD and CVD. Patients with impaired kidney function are known to have reduced endothelial protective effects, increased cardiovascular risks, and increased chances of acquiring subclinical CAD, which may progress into myocardial infarction (Jankowski *et al.*, 2021). The kidney and heart connection is an important factor in managing ACS patients because techniques that promote improved kidney functions are also beneficial in improving heart functions.

Statistical analysis of liver function indices showed a substantial elevation of AST in patients with ACS relative to controls. This finding is supported by (Zhang *et al.*, 2016; Ndrepepa *et al.*, 2018), Evidence exists that liver function indices can be useful non-specific markers for estimating the degree of atherosclerosis (Doganer *et al.*, 2015). Many studies have shown a strong correlation between cardiac and hepatic function. Heart failure can be associated with cardiac hepatopathy, hypoxic hepatitis due to cardiac causes, and cardiac cirrhosis. In turn, late-stage cirrhosis can cause cardiac dysfunction, known as cirrhotic cardiomyopathy (El Hadi *et al.*, 2020). These findings improve understanding of the systemic nature of ACS and underscore the importance of evaluating overall organ function in patients with ACS.

Conversely, urea, ALP, uric acid, and vitamin D levels showed no significant differences between the study groups. Vitamin D deficiency has been identified as correlated significantly with higher cardiovascular risk among individuals of diverse ethnicity (Kheiri *et al.*, 2018; Zittermann & Pilz, 2019), Lack of any significant difference among the Kurdish Iraqi subjects recommends that vitamin D levels may not be a point of prominent differentiation in the current study. However, since vitamin D receptors are found in cardiovascular tissues and vitamin D possesses antifibrotic and antihypertrophic effects, (Latic & Erben, 2020), its putative role in the pathophysiology of ACS warrants further studies.

This study demonstrated significant changes in the levels several hematological parameters reflecting the complex pathophysiology of ACS. Patients with ACS exhibited significantly higher count of RBCs compared to the control subjects. This may indicate compensatory erythropoietic responses to the chronic tissue hypoxia or may pose a risk for the potential viscosity and thrombotic events (Gotoh *et al.*, 2015). Nitric oxide (NO) produced by the activity of endothelial NO synthase (eNOS) is crucial for the regulation of vascular homeostasis and has been observed to lose activity with ACSs. Recent studies have reported the interaction of RBCs and the endothelium for the regulation of blood flow (Zhuge *et al.*, 2023). Indices of PLT also showed considerable variation, MPV readings were substantially greater than in controls, while the number and PCT were substantially lower in ACS patients. This is particularly significant, given the evidence that all these parameters demonstrate deviations in PLT function among ACS patients. Larger PLTs are known to have enhanced levels of metabolism and enzymes, an enhanced tendency of thrombus formation, and contribute towards the high thrombosis event rates that occur in CVD (Chang *et al.*, 2019). The negative correlation between MPV and PLT count in the present ACS population could imply an increased consumption of PLTs in the regions of arterial injury or thrombus development. The present findings are consistent with the accepted role of PLTs during the thrombosis phenomenon, where PLTs undergo morphological or functional alterations, resulting in the development of various PLT subsets, such as pro-coagulant PLTs involved in thrombin synthesis, or aggregating PLTs involved in primary clot development (Zarmehri *et al.*, 2020). Exposure to the drug represents a vital element of the context in the evaluation of these findings. To be more specific, in the current study, 72.9% of the ACS patients were aspirin users prior to blood sample. Moreover, aspirin is definitely understood to have irreversible inhibition of cyclooxygenase-1 (COX-1), thereby leading to decreased thromboxane A_2 generation and consequently PLT activation and aggregation (Patrono *et al.*, 2017). Perhaps one of the reasons for decreased PLT values and PLT indices is linked to the aforementioned pharmacologic effect of aspirin.

In patients with ACS, the values of red cell distribution width (RDW-CV and RDW-SD) were considerably elevated. High values of RDW are reflective of a condition where the size of blood cells varies considerably, and it has been recognized as a new marker for the presence of heart disease (Salvagno *et al.*, 2015). The increase is thought to occur due to inflammation, low levels of iron, hemolysis, oxidative damage, and nephropathy, which are commonly observed with the pathophysiology of ACS. Several investigations have shown the correlation between elevated values of RDW and adverse cardiovascular events (Tonelli *et al.*, 2008; Talarico *et al.*, 2021), and the findings of the current study confirm the efficacy of RDW as a potential marker for the risk valuation of individuals with ACS.

The proportion of mid-sized cells (MID), comprising monocytes, eosinophils, and basophils, was markedly elevated in patients with ACS compared to healthy persons. The results already mentioned back up this finding. Eosinophils, basophils, and monocytes are inflammatory cells that play a noteworthy role in the pathogenesis of heart illnesses. Eosinophils can induce endothelial dysfunction by discharging toxic granules that compromise blood vessels (Memioğlu *et al.*, 2025). Monocytes are crucial in the development of atherosclerosis and plaque formation, resulting in elevated MID values (Moore & Tabas, 2011). Monocytes can turn into macrophages inside the arterial wall. These macrophages help make foam cells, release pro-inflammatory cytokines, and make plaques that are more likely to break (Yang *et al.*, 2024). The increase in MID in this study of ACS patients suggests the presence of chronic systemic inflammation and immunological activation, aligning with the inflammatory traits of atherosclerosis.

Correlation analysis revealed a significant positive association between serum levels of HCY and CK-MB ($r = 0.3111$, $p = 0.0088$). This finding supports the previous study, which demonstrated that high HCY levels induce cardiac injury due to oxidative stress and result in increased levels of CK-MB from damaged cardiac cells (L. Wang *et al.*, 2020). El Oudi et al., 2011. revealed similar positive associations between HCY and cardiac biomarkers in patients with ACS. More so, HHCY has been recognized as an independent predictor of myocardial injury, with high levels of CK-MB indicating the degree of myocardial injury (X. Wang *et al.*, 2012). On this basis, HCY has shown potential as an additional biological marker in estimating vulnerability and risks associated with the cardiovascular system (Esse *et al.*, 2019).

There were no significant findings of association of age, creatinine, urea, glucose, uric acid, and vitamin D levels with the levels of HCY. The association of blood glucose and HCY is only one of the several factors that might have been exposed to be related with HCY in prior studies (Deng *et al.*, 2020),Also between HCY and creatinine (Pan *et al.*, 2021), The lack of significant association observed in this cohort analysis may suggest population-specific traits, limited sample size, or the confounding effects of drugs often administered to ACS patients, like as statins (Zeng *et al.*, 2025), antiplatelet Representatives (Eikelboom *et al.*, 2012), and antihypertensive medications (Ettehad *et al.*, 2016).

Previous studies, which categorized patients with ACS based on mild, moderate, and severe classifications based on their angio-graphic severity, found significant variations in HCY levels among the groups, indicating a potential association between HCY and disease severity, rather than a mere association with ACS. The dose-response relationship demonstrated above supports the hypothesis that HCY is a potential underlying mechanism for ACS, validating its utility for measuring disease severity (Calim *et al.*, 2020).

CONCLUSION

The study's results indicated an important correlation between higher blood levels of HCY and ACS in Kurdish Iraqi patients; specifically, the results strongly correlated with CK-MB. In patients with coronary artery syndrome, there were highly significant elevations in CK-MB, glucose, blood pressure, creatinine, AST, MID, RBC, RWD-CV, RDW-SD, and MPV; however, MCV, MCH, PLT, and PCT were significantly lower comparison to healthy clients. It can be noted from the findings of the study that HCY in blood plasma may be used as a clinical marker to determine the disease; however, consideration and qualification should still be exercised in view of its relation to unknown confounding factors. Additional studies with longer-term observations and larger samples testing multiple factors affecting blood HCY level are warranted to determine its application in the care of individuals with ACS.

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Ethical Statement:

The authorization to perform this investigation was provided by the Ethical Committee of the University of Soran, Soran, Iraq (No.: 1, 25th September 2025).

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Z.A.S., Data Collection, Laboratory Analysis and Writing. S.A.M., Supervision, Project, Administration, Validation, Review & Editing. M.S.S., Design of the Project and Data Analysis.

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