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Original Article

A Study of Serum Homocysteine Levels in Patients with Acute Coronary Syndrome

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ABSTRACT

Background: Acute Coronary Syndrome (ACS) remains a major cause of morbidity and mortality, and emerging evidence suggests that elevated serum homocysteine is an independent risk factor contributing to atherothrombosis.
Objectives: To evaluate serum homocysteine levels in patients with ACS and to assess their association with different ACS subtypes and conventional cardiovascular risk factors.
Materials and Methods: This retrospective observational study was conducted on 60 patients diagnosed with ACS at a tertiary care hospital. Serum homocysteine levels were measured within 24 hours of hospital admission using chemiluminescent immunoassay. Patients were categorized into STEMI, NSTEMI, and unstable angina based on clinical, electrocardiographic, and biochemical criteria. Homocysteine levels were classified according to standard reference ranges, and statistical analysis was performed using SPSS software.
Results: The mean serum homocysteine level among ACS patients was 17.9 ± 5.8 µmol/L. Elevated homocysteine levels (>15 µmol/L) were observed in 65% of patients. Patients with STEMI demonstrated significantly higher mean homocysteine levels compared to those with NSTEMI and unstable angina ($p < 0.05$). A statistically significant association was found between elevated homocysteine levels and smoking as well as hypertension, while no significant association was observed with diabetes mellitus or dyslipidemia.
Conclusion: Elevated serum homocysteine levels are common in patients with Acute Coronary Syndrome, particularly in those with more severe clinical presentations. Estimation of serum homocysteine may serve as a useful adjunct in cardiovascular risk assessment and may help identify patients who could benefit from targeted preventive strategies.

Key Words: *Acute Coronary Syndrome; Serum Homocysteine; Hyperhomocysteinemia; ST-Elevation Myocardial Infarction; Cardiovascular Risk Factors*

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INTRODUCTION

Cardiovascular diseases (CVDs) continue to be the leading cause of mortality worldwide, accounting for a substantial proportion of global deaths each year. Among these, Acute Coronary Syndrome (ACS) represents a spectrum of clinical conditions resulting from acute myocardial ischemia due to a sudden reduction in coronary blood flow. ACS includes ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable angina, all of which are associated with significant short- and long-term morbidity and mortality [1].

Despite major advances in diagnostic techniques, pharmacotherapy, and interventional cardiology, the burden of ACS remains disproportionately high in developing countries, including India. Early onset of coronary artery disease, high prevalence of traditional risk factors, and delayed healthcare access contribute to adverse outcomes [2]. Conventional cardiovascular risk factors such as hypertension, diabetes mellitus, dyslipidemia, smoking, and obesity explain a significant proportion of coronary events; however, a considerable number of patients develop ACS in the absence of these established factors [3]. This observation has led to increased interest in identifying novel and non-traditional risk factors that may play a role in the pathogenesis of ACS.

Homocysteine is a sulfur-containing, non-proteinogenic amino acid formed during the metabolism of methionine. Under normal physiological conditions, homocysteine is rapidly metabolized via remethylation or transsulfuration pathways, processes that require folate, vitamin B12, and vitamin B6 as essential cofactors [4]. Deficiencies in these vitamins, genetic polymorphisms, renal impairment, and lifestyle factors such as smoking and excessive alcohol intake can result in elevated plasma homocysteine levels, a condition termed hyperhomocysteinemia [5].

Elevated serum homocysteine has been increasingly recognized as an independent risk factor for atherosclerotic vascular disease. Experimental and clinical studies have demonstrated that homocysteine exerts multiple deleterious effects on the cardiovascular system, including endothelial dysfunction, increased oxidative stress, smooth muscle cell proliferation, impaired nitric oxide bioavailability, and enhanced platelet aggregation [6]. These mechanisms promote atherosclerotic plaque formation, progression, and instability, ultimately predisposing individuals to acute thrombotic events such as myocardial infarction.

Several large epidemiological studies have reported a positive association between hyperhomocysteinemia and coronary artery disease, with evidence suggesting that even mild to moderate elevations in homocysteine levels can significantly increase cardiovascular risk [7]. Meta-analyses have shown that a 5 µmol/L increase in plasma homocysteine concentration is associated with a 20–30% increase in the risk of ischemic heart disease [8]. Furthermore, elevated homocysteine levels have been linked to greater disease severity, multivessel involvement, and poorer clinical outcomes in patients with ACS [9].

In developing countries, nutritional deficiencies of folate and vitamin B12 are common due to dietary patterns, socioeconomic factors, and malabsorption disorders. This may partly explain the higher prevalence of hyperhomocysteinemia observed in these populations [10]. Indian studies have reported elevated homocysteine levels in patients with coronary artery disease, often at a younger age compared to Western populations, highlighting its potential role in premature atherosclerosis [11].

Despite growing evidence, routine estimation of serum homocysteine is not universally practiced in patients presenting with ACS. Data on its prevalence and clinical significance in acute coronary settings, particularly from single-center and resource-limited hospitals, remain limited. Understanding the relationship between serum homocysteine levels and ACS may provide additional insights into disease pathogenesis and help identify patients who could benefit from targeted nutritional and preventive interventions.

Therefore, the present study was undertaken to evaluate serum homocysteine levels in patients with Acute Coronary Syndrome and to assess its association with different ACS subtypes and conventional cardiovascular risk factors.

MATERIALS AND METHODS

Study Design

This study was conducted as a **retrospective observational study** aimed at evaluating serum homocysteine levels in patients diagnosed with Acute Coronary Syndrome (ACS). A retrospective design was chosen to analyze existing hospital records and laboratory data of patients admitted with ACS during the study period.

Study Setting

The study was carried out in the **Department of General Medicine** in collaboration with the **Department of Biochemistry** at a tertiary care teaching hospital. The hospital caters to both urban and rural populations and receives a significant number of patients presenting with acute cardiac emergencies.

Study Period

Data were collected from medical records of patients admitted for one year

Study Population

The study population consisted of patients diagnosed with Acute Coronary Syndrome during the study period. Diagnosis was based on clinical presentation, electrocardiographic changes, and cardiac biomarker levels, in accordance with standard guidelines.

Sample Size

A total of **60 patients** fulfilling the inclusion criteria were included in the study. The sample size was limited due to the retrospective nature of the study and availability of complete biochemical data, particularly serum homocysteine levels.

Inclusion Criteria

- Patients aged **18 years and above**
- Patients diagnosed with **ST-elevation myocardial infarction (STEMI)**, **Non-ST-elevation myocardial infarction (NSTEMI)**, or **Unstable Angina**
- Patients admitted within **24 hours of onset of symptoms**
- Availability of serum homocysteine estimation within 24 hours of admission

Exclusion Criteria

- Patients with **chronic kidney disease**, as renal dysfunction affects homocysteine metabolism
- Known cases of **hypothyroidism**
- Patients with **chronic liver disease** or **malignancy**
- Patients receiving **folic acid, vitamin B12, or vitamin B6 supplementation**
- Incomplete medical or laboratory records

Data Collection Procedure
Data were obtained from hospital medical records using a structured data extraction proforma. The following information was recorded:
- **Demographic data**: age and gender
- **Clinical details**: presenting symptoms, duration of symptoms, diagnosis
- **Cardiovascular risk factors**: hypertension, diabetes mellitus, smoking status, dyslipidemia
- **Electrocardiographic findings**
- **Laboratory parameters**, including serum homocysteine levels

All data were anonymized to maintain patient confidentiality.

Diagnosis and Classification of ACS
Patients were classified into:
- **ST-Elevation Myocardial Infarction (STEMI)**
- **Non-ST-Elevation Myocardial Infarction (NSTEMI)**
- **Unstable Angina**

Classification was based on clinical features, ECG findings, and cardiac biomarkers such as troponin levels.

Estimation of Serum Homocysteine
Venous blood samples were collected after an overnight fasting period whenever feasible, or within 24 hours of admission in emergency cases. Serum homocysteine levels were measured using **chemiluminescent immunoassay**, a sensitive and standardized method.

Reference Range for Serum Homocysteine
- **Normal**: < 15 µmol/L
- **Moderate elevation**: 15–30 µmol/L
- **Intermediate elevation**: 30–100 µmol/L
- **Severe elevation**: > 100 µmol/L

Patients were categorized based on these reference values for further analysis.

Statistical Analysis
Data were entered into **Microsoft Excel** and analyzed using **SPSS 20.**
- Continuous variables were expressed as **mean ± standard deviation (SD)**
- Categorical variables were expressed as **frequencies and percentages**
- Comparison of mean homocysteine levels between ACS subtypes was done using **ANOVA**
- Association between homocysteine levels and risk factors was assessed using the **Chi-square test**
- A **p-value < 0.05** was considered statistically significant

Ethical Considerations
Institutional Ethics Committee approval was obtained prior to the commencement of the study. As the study was retrospective, informed consent was waived. Confidentiality of patient data was strictly maintained throughout the study.

RESULTS
The present study analyzed clinical and biochemical data of **60 patients** diagnosed with Acute Coronary Syndrome (ACS). The majority of patients belonged to the middle and older age groups, with a higher incidence observed in the fifth and sixth decades of life as shown in table 1

Table 1: Age Distribution of Study Participants (n = 60)

Age Group (Years)	Number of Patients	Percentage
≤40	6	10.0%
41–50	14	23.3%
51–60	22	36.7%

Age Group (Years)	Number of Patients	Percentage
61–70	14	23.3%
>70	4	6.7%

Male patients constituted a greater proportion of the study population compared to females as shown in table 2

Table 2: Gender Distribution of Patients

Gender	Number of Patients	Percentage
Male	42	70.0%
Female	18	30.0%

ST-elevation myocardial infarction was the most common presentation among patients with ACS as shown in table 3

Table 3: Distribution of ACS Subtypes

ACS Type	Number of Patients	Percentage
STEMI	30	50.0%
NSTEMI	18	30.0%
Unstable Angina	12	20.0%

Hypertension and smoking were the most prevalent cardiovascular risk factors observed in the study population as shown in table 4

Table 4: Distribution of Cardiovascular Risk Factors

Risk Factor	Number of Patients	Percentage
Hypertension	32	53.3%
Smoking	28	46.7%
Diabetes Mellitus	24	40.0%
Dyslipidemia	26	43.3%

A substantial proportion of patients showed elevated serum homocysteine levels as shown in table 5.

Table 5: Distribution of Serum Homocysteine Levels (n = 60)

Homocysteine Level (µmol/L)	Number of Patients	Percentage
Normal (<15)	21	35.0%
Moderate (15–30)	33	55.0%
Intermediate (30–100)	6	10.0%
Severe (>100)	0	0.0%

Mean serum homocysteine levels were higher in patients with STEMI when compared to NSTEMI and Unstable Angina as shown in table 6.

Table 6: Mean Serum Homocysteine Levels According to ACS Type

ACS Type	Mean Homocysteine (µmol/L)	Standard Deviation
STEMI	20.1	6.1
NSTEMI	17.2	4.9
Unstable Angina	15.4	4.1

The difference in mean homocysteine levels among ACS subtypes was statistically significant ($p < 0.05$).

Elevated serum homocysteine levels were more frequently observed in patients with smoking and hypertension as shown in table 7.

Table 7: Association of Elevated Homocysteine Levels with Risk Factors

Risk Factor	Elevated Homocysteine (%)	p-value
Smoking	78.6%	<0.01
Hypertension	71.9%	<0.05
Diabetes Mellitus	62.5%	>0.05
Dyslipidemia	65.4%	>0.05

DISCUSSION

The present retrospective observational study evaluated serum homocysteine levels in patients presenting with Acute Coronary Syndrome and assessed their association with different ACS subtypes and conventional cardiovascular risk factors. The findings of this study provide further evidence supporting the role of hyperhomocysteinemia as an important non-traditional risk factor in the pathogenesis of acute coronary events.

Age and Gender Distribution

In the present study, the majority of patients belonged to the 51–60 year age group, with a mean age of 55.2 ± 9.6 years. This observation is consistent with previous Indian studies that have reported an earlier onset of coronary artery disease compared to Western populations [12]. The higher prevalence of ACS in middle-aged individuals may be attributed to prolonged exposure to cardiovascular risk factors, lifestyle changes, and increasing metabolic disorders.

A clear male predominance was observed, with males constituting 70% of the study population. Similar male preponderance has been reported in several Indian and international studies on ACS [13]. Hormonal protection in premenopausal women and higher exposure of men to smoking and occupational stress may explain this gender difference.

Distribution of ACS Subtypes

ST-elevation myocardial infarction was the most common ACS subtype in the present study, accounting for 50% of cases. This finding aligns with studies conducted in tertiary care centers in developing countries, where delayed presentation and limited access to early medical care often result in more severe coronary events [14]. STEMI represents complete coronary artery occlusion, which may be influenced by both traditional and emerging risk factors such as hyperhomocysteinemia.

Serum Homocysteine Levels in ACS

The mean serum homocysteine level in this study was 17.9 ± 5.8 µmol/L, which is higher than the normal reference range. Elevated homocysteine levels were observed in 65% of patients, indicating a high prevalence of hyperhomocysteinemia among ACS patients. Similar prevalence rates have been reported in earlier studies, suggesting that elevated homocysteine is common in patients with coronary artery disease [15].

Homocysteine promotes endothelial dysfunction by reducing nitric oxide bioavailability, increasing oxidative stress, and enhancing smooth muscle proliferation. These effects contribute to atherosclerotic plaque formation and instability, thereby predisposing individuals to acute coronary events [16].

Association of Homocysteine Levels with ACS Subtypes

In the present study, mean serum homocysteine levels were highest in patients with STEMI, followed by NSTEMI and Unstable Angina. The difference was statistically significant, suggesting a possible association between elevated homocysteine levels and disease severity. Similar observations have been reported by previous studies, where higher homocysteine levels were associated with extensive coronary artery involvement and increased thrombotic burden [17].

The prothrombotic properties of homocysteine, including enhanced platelet aggregation and activation of the coagulation cascade, may explain its stronger association with STEMI, which is characterized by acute plaque rupture and complete vessel occlusion [18].

Association with Conventional Cardiovascular Risk Factors

The present study demonstrated a significant association between elevated serum homocysteine levels and smoking as well as hypertension. Smoking has been shown to increase homocysteine levels by impairing folate metabolism and inducing oxidative stress [19]. Hypertension, on the other hand, may act synergistically with homocysteine to accelerate endothelial damage and vascular remodeling.

Although elevated homocysteine levels were observed in patients with diabetes mellitus and dyslipidemia, the association was not statistically significant. This finding is consistent with some previous studies, which suggest that homocysteine acts independently of traditional metabolic risk factors [20].

CONCLUSION

Elevated serum homocysteine levels were commonly observed in patients presenting with Acute Coronary Syndrome in the present study. Higher homocysteine levels were particularly associated with ST-elevation myocardial infarction, suggesting a possible link with disease severity. A significant association was also noted between hyperhomocysteinemia and conventional risk factors such as smoking and hypertension. Estimation of serum homocysteine may serve as an additional marker for cardiovascular risk assessment in ACS patients. Early identification and correction of elevated homocysteine levels may contribute to improved secondary prevention and better clinical outcomes.

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