Journal of Teachers Association
https://tajrmc.com/taj
Vol. 38, No. 2, 2025

pISSN 1019-8555
eISSN 2408-8854

RESEARCH ARTICLE | OPEN ACCESS **DOI:** https://doi.org/10.70818/taj.v38i02.0187

Relationship between Serum Homocysteine Levels among Young Patients with Acute Myocardial Infarction

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Citation:
Parveen E, Sarker MAM, Rahman M, Yousuf A, Nasrin S, Haque ABMM, Zaman R, Uddin S; Relationship between Serum Homocysteine Levels among Young Patients with Acute Myocardial Infarction. Journal of Teachers Association. 2025;38(2):20-27

Article History:
Received: 03.02.2025
Accepted: 18.04.2025
Published: 01.06.2025

ABSTRACT: ***Background:*** Acute Myocardial Infarction (AMI) is a leading cause of morbidity and mortality, particularly in young adults. Homocysteine, an emerging biomarker, has been implicated in cardiovascular risk, yet its role in young AMI patients remains underexplored. ***Objective:*** This study aimed to evaluate the relationship between serum homocysteine levels among young patients with acute myocardial infarction. ***Methods:*** A longitudinal descriptive study was conducted from July 2021 to June 2022 among 64 patients presenting with a first episode of acute myocardial infarction (AMI) at a tertiary-care hospital. The study took place in the Department of Medicine in collaboration with the Department of Cardiology, RMCH. Using purposive sampling, detailed demographic and clinical data were obtained from all participants, through a semi-structured questionnaire. Blood samples were taken within 12 hours of admission to measure serum homocysteine and troponin I, alongside lipid profiles, creatinine, electrolytes, vitamin B12, and folate. In-hospital complications were monitored until discharge or the end of hospitalization. Statistical analyses using SPSS 25.0 examined the associations between homocysteine levels, comorbidities, complications, and myocardial injury. ***Results:*** The mean age of respondents was 33.17±5.17 years, with 75% being male and 64.1% residing in rural areas. Hypertension (78.1%) and dyslipidemia (57.8%) were the most prevalent comorbidities. Elevated homocysteine levels were significantly associated with dyslipidemia ($p<0.001$) and higher troponin I levels ($r=0.803$, $p<0.001$). In-hospital complications occurred in 52.2% of patients with elevated homocysteine levels, while no complications were observed in those with normal levels ($p<0.001$). ***Conclusion:*** Elevated homocysteine strongly correlates with dyslipidemia, myocardial injury, and increased in-hospital complications in young AMI. Routine screening may improve risk assessment and outcomes, warranting further exploration.

Keywords: Acute Myocardial Infarction, Cardiovascular Diseases.

Article at a glance:

Study Purpose*: To investigate the relationship between serum homocysteine levels and clinical outcomes in young acute myocardial infarction patients.*

Key findings: *Elevated homocysteine levels were associated with dyslipidemia, increased troponin I, and more in-hospital complications in AMI patients.*

Newer findings: *This study highlights homocysteine as a strong prognostic marker for complications in young AMI patients, supporting routine early screening.*

Abbreviations: *AMI – Acute Myocardial Infarction, ICU – Intensive Care Unit, B12 – Vitamin B12.*

INRODUCTION

Acute Myocardial Infarction (AMI) is defined as the acute necrosis of myocardial tissue resulting from prolonged ischemia, typically due to obstructed blood flow in the coronary arteries.[1] Globally, AMI is a leading cause of morbidity and mortality, accounting for significant healthcare burdens in both developed and developing nations.[2] In Bangladesh, cardiovascular diseases, including AMI, are increasingly prevalent, particularly among younger populations, where the incidence is rising alarmingly.[3] The mortality rates associated with AMI

are notably high, with studies indicating in-hospital mortality rates ranging from 33% to 55% in cases complicated by cardiogenic shock.[4] This underscores the critical role of AMI in public health, necessitating urgent attention to its risk factors and management strategies. Common risk factors for AMI include hypertension, diabetes, hyperlipidemia, smoking, and a sedentary lifestyle.[5] Additionally, genetic predispositions and psychosocial factors such as stress and depression have been implicated in increasing the risk of AMI .[6] The interplay of these factors contributes to the overall burden of cardiovascular diseases, which are exacerbated by lifestyle changes and urbanization in countries like Bangladesh.[3] Homocysteine is a sulfur-containing amino acid that is produced during the metabolism of methionine. Elevated serum homocysteine levels have been linked to cardiovascular diseases, including AMI, as they can induce endothelial damage, promote thrombosis, and facilitate atherosclerosis.[7] Specifically, hyperhomocysteinemia has been identified as a significant risk factor for the development of cardiovascular diseases, as it contributes to vascular injury and the progression of atherosclerotic plaques.[7] The association between high homocysteine levels and cardiovascular events highlights the need for monitoring this biomarker in at-risk populations.

Investigating homocysteine levels in young AMI patients is particularly important, as this demographic is often perceived to be at lower risk for cardiovascular events. However, emerging evidence suggests that younger individuals can experience significant morbidity and mortality from AMI, often due to unrecognized risk factors.[6] This underexplored group may benefit from early identification of biomarkers such as homocysteine, which could facilitate timely interventions and improve outcomes. In the context of Bangladesh; the burden of cardiovascular diseases is substantial, with a notable increase in cases among younger populations. Research focusing on the relationship between homocysteine levels and AMI in this demographic is limited, creating a critical gap in knowledge that needs to be addressed.[3] This investigation into the association of serum homocysteine levels in young patients with AMI serves to clarify the role of hyperhomocysteinemia as an independent risk factor and encourages clinicians to adopt targeted preventive measures. By emphasizing the significance of homocysteine testing in younger patients, healthcare providers can augment conventional risk assessment and tailor more effective, personalized interventions for long-term cardiovascular health.

METHODOLOGY

This longitudinal descriptive study, conducted from July 2021 to June 2022 at Rajshahi Medical College & Hospital in Bangladesh, involved the Departments of Medicine and Cardiology. The study protocol received approval from the Institutional Review Board of Rajshahi Medical College. Using purposive sampling, researchers gathered data from 64 patients aged 18-40, all experiencing their first acute myocardial infarction (MI). Each patient underwent a thorough history review and physical examination, including measurements of height, weight, body mass index, systolic and diastolic blood pressure, and assessments for anemia and signs of hypothyroidism. The study also involved investigations into lipid profiles, Troponin-I levels, and serum homocysteine levels. Acute MI diagnosis was confirmed by detecting a rise or fall in cardiac biomarkers, specifically troponin I, with at least one value exceeding the 99th percentile of the upper reference limit, alongside evidence of myocardial ischemia indicated by symptoms, ECG changes, or the development of pathological Q waves. Patients were monitored daily until discharge or death, and data was recorded on a structured collection sheet. Within the first 12 hours of the myocardial infraction, at least 5 ml of blood were collected to measure serum homocysteine levels, requiring a 10-12 hour fasting period before sample collection. Blood samples were centrifuged, and the separated serum was stored at -20C until analysis. Additional biochemical parameters, including lipid profile tests and random blood glucose levels, were measured using enzymatic colorimetric methods with a Roche Cobas system. Strict confidentiality and ethical standards were maintained throughout data storage and analysis. The data were analyzed using SPSS Version 25.0, with qualitative factors summarized by percentage and quantitative variables by mean and standard deviation. Pearson's correlation analysis, Chi-square test or fisher's exact tests were employed to determine relationships between variables.

Acute Myocardial Infarction (AMI)

AMI is diagnosed by elevated cardiac biomarkers (troponin I) above the 99th percentile, along with ischemic symptoms, ECG changes (ST-T shifts/LBBB), or pathological Q waves.[8]

Serum Homocysteine Levels

Normal: ≤ 15 µmol/L, Mild: 16-30 µmol/L, Moderate: 31-100 µmol/L, Severe: >100 µmol/L.[9]

Obesity Classification (WHO)

Underweight: BMI < 18.5, Normal: 18.5 - 24.9, Overweight: 25.0 - 29.9, Obese: ≥ 30.0.[10]

Lipid Profile (ATP III Classification)[11]

LDL Cholesterol (Primary Target) <100: Optimal, 100-129: Near optimal/above optimal, 130-159: Borderline high, 160-189: High, 190: Very high. Total Cholesterol <200: Desirable, 200-239: Borderline high, ≥240: High. Triglycerides <150: Normal, 150-199: Borderline high, ≥200: High. HDL Cholesterol <40: Low ≥60: High.

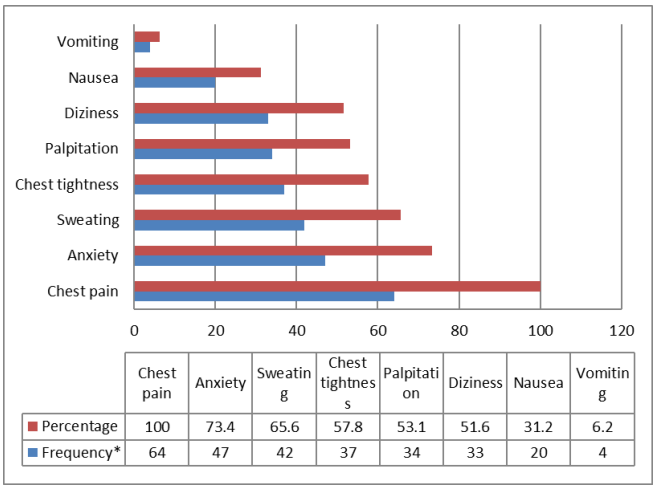
RESULTS

Results and observations of this study are given below in tables and figures. Among the participants majority were aged between 36 to 40 years (40.0%), mean age ±SD was (33.17±5.17) years. Males made up 75% of respondents, with 64.1% living in rural areas. SSC was the highest qualification for 34.4%, while 17.2% had no formal education. Occupation-wise, 26.6% worked in non-government jobs, 18.8% in government service, and 14.1% were housewives. Socio-economically, 40.6% had low income, while 7.8% were in the high-income group (Table 1).

Table 1: Demographic characteristics of the respondents (n=64)

Characteristics	Frequency	Percentage
Age groups (year)		
<25	8	12.5%
26-30	12	18.8%
31-35	18	28.1%
36-40	26	40.6%
Mean±SD	33.17±5.17	
Sex		
Male	48	75%
Female	16	25%
Residence		
Rural	41	64.1%
Urban	23	35.9%
Educational qualification		
No formal education	11	17.2%
Primary	13	20.3%
SSC	22	34.4%
HSC	10	15.6%
Graduate and above	8	12.5%
Occupation		
Govt service	12	18.8%
Non-Govt service	17	26.6%
Business	3	4.7%
Housewife	9	14.1%
Others	23	35.9%
Socio-economic status		
Low income	26	40.6%
Lower middle class	20	31.3%
Upper middle class	13	20.3%
High income	5	7.8%

The clinical characteristics showed chest pain (100%) was the most common symptom, followed by anxiety (73.4%) and sweating (65.6%), while nausea (31.2%) and vomiting (6.2%) were the least reported (Figure 1).



	Chest pain	Anxiety	Sweating	Chest tightness	Palpitation	Diziness	Nausea	Vomiting
Percentage	100	73.4	65.6	57.8	53.1	51.6	31.2	6.2
Frequency*	64	47	42	37	34	33	20	4

Figure 1: Distribution of Clinical Presentation of Respondents (n=64)

*Multiple responses

The distribution of comorbidities among respondents showed that hypertension was the most prevalent, affecting 50 individuals (78.1%), followed by dyslipidemia with 37 cases (57.8%). Diabetes mellitus was reported in 23 respondents (35.9%), while obesity had the lowest prevalence at 19 cases (29.7%) (Figure 2).

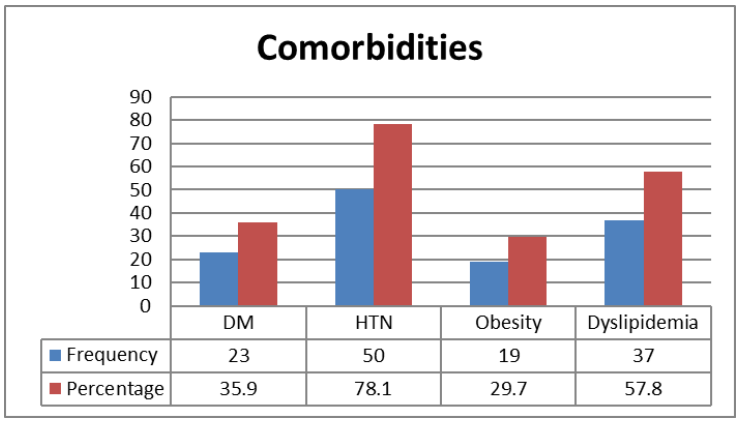


Figure 2: Distribution of Comorbidities Among the Respondents (n=64)

The distribution of serum homocysteine levels among respondents showed that nearly half (46.9%) had moderate hyperhomocysteinemia, 28.1% had normal levels, 17.2% had mild, and 7.8% had severe. The mean homocysteine level was 41.61±32.41 µmol/L (Table 2).

Table 2: Distribution of Serum Homocysteine Level by the Respondents (n=64)

S. Homocysteine level (µmol/L)	Frequency	Percentage
Normal	18	28.1%
Mild hyperhomocysteinemia	11	17.2%
Moderate hyperhomocysteinemia	30	46.9%
Severe hyperhomocysteinemia	5	7.8%
Mean±SD	41.61±32.41	

Among AMI respondents, dyslipidemia showed a significant association with increased homocysteine levels (100%, p<0.001). Hypertension (72.0%), diabetes (69.6%), and obesity (78.9%) were more common in those with elevated levels but were not statistically significant (Table 3).

Table 3: Relation between homocysteine level and the comorbidities among the AMI respondents (n=64)

Comorbidities	Homocysteine level among AMI		p-value
	Increased (n=46)	Normal (n=18)	
DM	16 (69.6%)	7 (30.4%)	c0.758ns
HTN	36 (72.0%)	14 (28.0%)	c0.966ns
Obesity	15 (78.9%)	4 (21.1%)	c0.414ns
Dyslipidemia	37 (100.0%)	0 (0.0%)	**c<0.001s**

c= Chi square test
s= Statistically significant if p value (<0.05)

Among young AMI patients, 62.5% had no in-hospital complications. Ventricular fibrillation occurred in 18.8%, heart failure in 15.6%, and mortality was 3.1% (Table 4).

Table 4: Distribution of the respondents according to their in-hospital complications of young AMI patients (n=64)

In-hospital complications	Frequency	Percentage
Ventricular fibrillation	12	18.8%
Heart failure	10	15.6%
Death	2	3.1%
No complications	40	62.5%

In-hospital complications were significantly higher in AMI respondents with elevated homocysteine levels (52.2%), while none occurred in those with normal levels (p<0.001). Conversely, all respondents with normal homocysteine levels remained complication-free (Table 6)

Table 5: Relation between homocysteine level and in-hospital complications among the AMI respondents (n=64)

In hospital complications	Homocysteine level among the young AMI respondents		p-value
	Increased (n=46)	Normal (n=18)	
Present	24 (52.2%)	0 (0.0%)	**f<0.001s**
Absent	22 (47.8%)	18 (100.0%)	

f= Fisher's Exact test
s= statistically significant if p value (<0.05)

The mean levels of Vitamin B12, folate, and serum creatinine were 463.67±71.27 pg/ml, 4.73±0.81 ng/ml, and 0.96±0.34 mg/dl, respectively. Serum sodium and potassium averaged 130.31±5.68 mmol/L and 3.56±0.657 mmol/L, while random blood glucose and troponin I were 9.43±5.42 mmol/L and 14.78±5.02 ng/ml. HDL, LDL, total cholesterol, and triglycerides had mean values of 42.08±6.79 mg/dl, 154.22±17.50 mg/dl, 158.41±17.30 mg/dl, and 186.23±17.60 mg/dl (Table 6).

Table 6: Mean value of laboratory parameter of the respondents (n=64)

Laboratory parameter	Mean±SD
Vitamin B12 (pg/ml)	463.67±71.27
Folate (ng/ml)	4.73±0.81
S. Creatinine (mg/dl)	0.96±0.34
S. Sodium (mmol/L)	130.31±5.68

S. Potassium (mmol/L)	3.56±0.657
Random blood glucose(mmol/L)	9.43±5.42
Troponin I (ng/mL)	14.78±5.02
HDL (mg/dl)	42.08±6.79
LDL (mg/dl)	154.22±17.50
Total cholesterol (mg/dl)	158.41±17.30
Triglyceride (mg/dl)	186.23±17.60

The Scatter plot diagram showed a strong linear correlation (Pearson) between serum homocysteine level and S. troponin I level of respondents, which indicates that serum troponin I increases along with the increase serum homocysteine (r=.803, p<0.001, <.05)

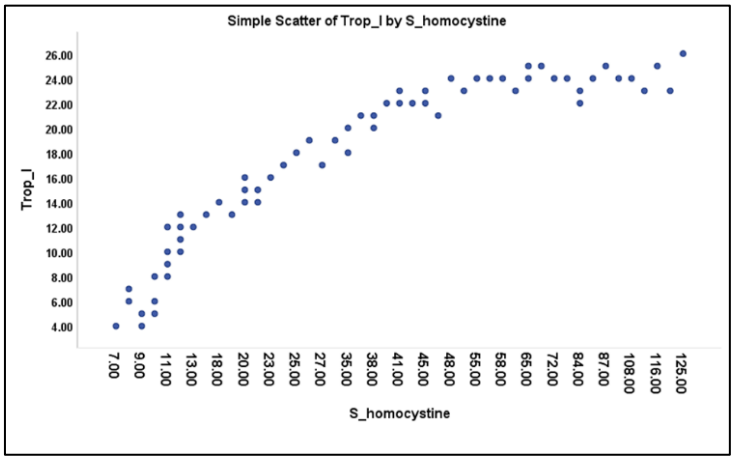


Figure 3: Scatter plot diagram showing the correlation between serum homocysteine level and S.troponin I level in respondents (n=64)

DISCUSSION

Acute myocardial infarction (AMI) is a manifestation of coronary heart disease that contributes to both illness and death.[12] Elevated levels of plasma homocysteine are recognized as an independent risk factor for coronary heart disease, as well as peripheral vascular and cerebrovascular diseases.[13] Although the precise mechanism is not fully understood, it is suggested that endothelial dysfunction, accelerated LDL oxidation, reduced arterial vasodilation, oxidative stress, and platelet activation resulting from increased homocysteine levels may contribute to hyperhomocysteinemia-induced atherosclerotic complications, such as coronary artery disease, in young individuals.[9] This descriptive longitudinal study included 64 patients, regardless of sex, race, or ethnic group, who were admitted with a first-time history of AMI. The primary goal was to evaluate serum homocysteine levels in young patients with acute MI.The demographic findings revealed that the majority of respondents were aged between 36 and 40 years, with a mean age of 33.17±5.17 years. Males constituted the majority 48(75%), and most participants resided in rural areas (64.1%). In the study by Sudam V. Khedkar *et al.*, the average age of participants was 36.7 years, with 48.9% of cases occurring between the ages of 31 and 40 years, and 33.3% in the 41–45-year range.[14] A study by Sun *et al.* indicated that the majority (96.01%) of young patients with acute coronary syndrome (ACS) were male.[15]

The clinical presentation of the study participants included chest pain (100%), chest tightness (57.8%), nausea (31.25%), and vomiting (16%). Co-morbidities observed in the respondents were hypertension (78.1%), diabetes mellitus (35.9%), obesity (29.7%), and dyslipidemia (57.8%). A significant association was found between elevated homocysteine levels and dyslipidemia (100%, p<0.001). Similarly, research by Coen D.A. Stehouwer *et al.*, indicated that elevated homocysteine levels at baseline correlated with a higher prevalence of stroke (OR, 4.61; 95% CI, 1.79 to 11.89; P for trend, 0.002) and an increased risk of cerebrovascular-related mortality

in subjects without hypertension (RR, 6.18; 95% CI, 2.28 to 16.76), but not in those with hypertension.[16] Alam N *et al.* observed that serum homocysteine levels were significantly higher in individuals with dyslipidemia (23.8 vs 18.3; p=0.010), while other cardiovascular risk factors did not show significant associations (p>0.05).[12] About 18 (28.1%) had normal homocysteine level and others had hyperhomocysteinemia followed by mild 11 (17.2%), moderate 30 (46.9%) and severe 5 (7.8%). The mean value of serum homocysteine level was 41.61±32.41µmol/L. Prevalence of hyperhmocysteinemia was observed as 64.4% in the study of Sudam V. Khedkar *et al.* ,The mean value of investigation profile of the respondents, followed by S. creatinine, S. Sodium, S. potassium, RBS and troponin I were 0.96±0.34 (SD) mg/dl, 130.31±5.68 (SD) mmol/L, 3.56±0.657 (SD) mmol/L, 9.43±5.42 (SD) mmol/L, 7.61±3.38 (SD) % and 14.78±5.02(SD) ng/mL.[14] The electrolytes such as Na+, K+ levels in AMI cases (132.51 ± 4.5, 3.88 ± 0.57) and Troponin I was significantly higher in AMI cases (10.369 ± 9.32, p<0.001) in comparison with healthy control group (0.256 ± 0.2) in Rakesh Mudaraddi *et al.*, The Scatter plot diagram showed a strong linear correlation between serum homocysteine level and S.troponin I level of respondents, which indicates that serum troponin I increases along with the increase serum homocysteine (r=.803, p=<0.001, <.05).[18] P-value was determined by the Pearson correlation test. Significant positive correlation was found between Serum Troponin-I level with homocysteine level and the values of Pearson's correlation coefficient was 0.273 which is significant (p<0.001) in Alam N *et al.*[12]

The in-hospital complication rates further emphasized the clinical significance of homocysteine. Patients with increased homocysteine levels had a significantly higher rate of complications (52.2%), while none of the patients with normal homocysteine levels experienced complications (p<0.001). Ventricular fibrillation (18.8%) and heart failure (15.6%) were the most common complications, with a mortality rate of 3.1%. This suggests that elevated homocysteine levels may serve as a predictor for adverse in-hospital outcomes in young AMI patients. In other studies, had showed plasma homocystine levels were significantly elevated in heart failure patients, ventricular fibrillation and recurrent AF patients.[11,19] This study, while insightful, has limitations. The relatively small sample size (n=64) restricts the generalizability of the findings to a larger population. As a single-center study in a specific region, the results might not reflect diverse populations with varying genetic and environmental risk factors. The observational design prevents establishing causation between homocysteine levels and AMI outcomes. Uncontrolled confounding factors, including dietary habits, smoking, and medication use, could have affected homocysteine levels. Finally, long-term cardiovascular outcome data were unavailable.

CONCLUSION

This study emphasizes the important role of homocysteine in young AMI patients, especially its strong link to dyslipidemia, myocardial injury, and complications during hospitalization. Regularly screening for and managing hyperhomocysteinemia could help lower cardiovascular risks and improve health outcomes. Additional research is needed to investigate possible treatments aimed at lowering homocysteine levels in this high-risk group.

Acknowledgement

The authors express their gratitude to all participating patients and the hospital authorities for their cooperation and support during this study.

Source of funding: Not applicable.

Conflict of Interest: The authors declare no conflict of interest.

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Journal of Teachers Association
Official Journal of Teachers Association
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