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Original Research Article

Correlation between Plasma Homocysteine Levels and Coronary Artery Disease in Indian Population

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Abstract:

Introduction: Coronary artery disease (CAD) is a significant cause of morbidity and mortality worldwide, particularly in India. Elevated plasma homocysteine levels have been implicated in the pathogenesis of CAD, yet their role in the Indian population remains underexplored. This study investigates the correlation between plasma homocysteine levels and CAD in an Indian population at a tertiary care hospital.

Methodology: This cross-sectional analytical study included 236 participants, divided into two groups: 118 CAD patients and 118 age- and gender-matched controls. Demographic and clinical data were collected using a structured questionnaire, and plasma homocysteine levels were measured using high-performance liquid chromatography (HPLC). Statistical analyses, including independent t-tests, Pearson's correlation, and multivariate logistic regression, were performed using SPSS software.

Results: The mean plasma homocysteine level was significantly higher in CAD patients (18.4 ± 5.6 µmol/L) compared to controls (12.2 ± 4.7 µmol/L), with a p-value of <0.001. Correlation analysis revealed significant positive correlations between plasma homocysteine levels and BMI ($r = 0.20$, $p = 0.01$), smoking status ($r = 0.25$, $p < 0.001$), hypertension ($r = 0.22$, $p = 0.002$), diabetes mellitus ($r = 0.18$, $p = 0.03$), total cholesterol ($r = 0.27$, $p < 0.001$), LDL cholesterol ($r = 0.30$, $p < 0.001$), and triglycerides ($r = 0.21$, $p = 0.01$), and a significant negative correlation with HDL cholesterol ($r = -0.24$, $p = 0.002$). Multivariate logistic regression identified BMI (OR = 1.12, $p = 0.001$), smoking status (OR = 1.50, $p = 0.01$), hypertension (OR = 1.45, $p = 0.01$), HDL cholesterol (OR = 0.98, $p = 0.001$), and plasma homocysteine levels (OR = 1.15, $p < 0.001$) as significant independent predictors of CAD.

Conclusion: This study demonstrates a significant correlation between elevated plasma homocysteine levels and CAD in the Indian population, suggesting that homocysteine could be an essential biomarker for CAD risk assessment. Further research is needed to explore the potential benefits of homocysteine-lowering interventions in reducing CAD risk.

Keywords: Coronary artery disease, Homocysteine, Risk factors, Indian population, Tertiary care hospital, cardiovascular risk.

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Introduction

Coronary artery disease (CAD) remains a leading cause of morbidity and mortality worldwide, including in India. It is characterized by the narrowing or blockage of coronary arteries due to the build-up of atherosclerotic plaques, which can lead to myocardial infarction and other cardiovascular complications.[1] The multifactorial etiology of CAD includes both modifiable and non-modifiable risk factors such as hypertension, diabetes, dyslipidemia, smoking, and family history of cardiovascular diseases.[2]

Emerging evidence suggests that elevated levels of plasma homocysteine, an amino acid formed during methionine metabolism, may play a significant role in the pathogenesis of CAD. [3] Hyperhomocysteinemia has been implicated in promoting endothelial dysfunction, oxidative stress, and inflammation, all of which contribute to the development and progression of atherosclerosis.[4]

Several studies have demonstrated a positive correlation between elevated homocysteine levels and the risk of CAD.[5,6] In particular, hyperhomocysteinemia is associated with increased arterial stiffness, impaired nitric oxide bioavailability, and enhanced thrombotic potential, which collectively exacerbate the risk of coronary events.[7] Despite these associations, the clinical utility of homocysteine as a biomarker for CAD

risk stratification remains a topic of debate. The Indian population, with its unique genetic and lifestyle factors, presents a distinct profile of CAD risk. There is limited data on the correlation between plasma homocysteine levels and CAD specifically within the Indian demographic. Given the high prevalence of CAD in India and the potential role of homocysteine as a modifiable risk factor, it is crucial to investigate this relationship in a tertiary care hospital setting.[8] This study aims to evaluate the correlation between plasma homocysteine levels and the presence of CAD in the Indian population, providing insights that could enhance the risk assessment and management of this disease.

By understanding the role of homocysteine in CAD among Indian patients, healthcare professionals can better identify individuals at risk and implement targeted interventions. This research could also contribute to the global understanding of CAD pathophysiology and the potential for homocysteine-lowering therapies in reducing cardiovascular risk.

Methodology

This cross-sectional analytical study investigated the correlation between plasma homocysteine levels and coronary artery disease (CAD) in the Indian population at a tertiary care hospital. The institutional ethics committee approved the study, and informed consent was obtained from all participants. The study population consisted of 236 individuals, divided into two groups: 118 patients diagnosed with CAD and 118 age- and gender-matched individuals without CAD. Patients aged 30-70 years with a confirmed diagnosis of CAD based on clinical evaluation, electrocardiogram (ECG), and angiographic findings were included in the CAD group. The control group consisted of age- and gender-matched individuals without any history of CAD or other significant cardiovascular diseases. Individuals with chronic kidney disease, liver disease, thyroid disorders, or other systemic illnesses that could affect homocysteine levels were excluded from the study. Patients on medications known to influence homocysteine levels, such as folic acid, vitamin B6, or vitamin B12 supplements, and pregnant women were also excluded.

Data collection was carried out from January 2023 to June 2023. A structured questionnaire collected demographic and clinical information, including age, gender, body mass index (BMI), smoking status, hypertension, diabetes mellitus, and lipid profile. Blood samples were collected from all participants after an overnight fast. Plasma homocysteine levels were measured using high-performance liquid chromatography (HPLC).

Statistical analysis was performed using SPSS software (version 25.0). Continuous variables were expressed as mean ± standard deviation and categorical variables were expressed as frequencies and percentages. The differences in plasma homocysteine levels between CAD patients and controls were analyzed using the independent t-test. The correlation between plasma homocysteine levels and CAD was assessed using Pearson's correlation coefficient. Multivariate logistic regression analysis was conducted to adjust for confounding factors, such as age, gender, BMI, smoking status, hypertension, diabetes mellitus, and lipid profile. A p-value of <0.05 was considered statistically significant.

Results

Table 1: Baseline Characteristics of the Study Population

Characteristic	CAD Patients (n=118)	Controls (n=118)	p-value
Age (years)	55.2 ± 10.1	52.8 ± 9.7	0.12
Gender (Male/Female)	80/38 (67.8%/32.2%)	75/43 (63.6%/36.4%)	0.47
BMI (kg/m²)	27.4 ± 3.5	25.6 ± 3.2	0.01
Smoking Status (Yes/No)	45/73 (38.1%/61.9%)	25/93 (21.2%/78.8%)	0.004
Hypertension (Yes/No)	70/48 (59.3%/40.7%)	40/78 (33.9%/66.1%)	<0.001
Diabetes Mellitus (Yes/No)	55/63 (46.6%/53.4%)	30/88 (25.4%/74.6%)	0.001
Total Cholesterol (mg/dL)	205.3 ± 45.7	190.5 ± 40.2	0.03
LDL Cholesterol (mg/dL)	130.4 ± 37.6	115.7 ± 34.8	0.02
HDL Cholesterol (mg/dL)	40.6 ± 9.5	45.8 ± 10.2	0.001
Triglycerides (mg/dL)	165.2 ± 60.4	140.3 ± 55.1	0.005

The baseline characteristics of the study population, consisting of 118 CAD patients and 118 controls, were analyzed to assess the potential differences between the two groups. The mean age of CAD patients was 55.2 years (± 10.1), compared to 52.8 years (± 9.7) in the control group, with a p-value of 0.12, indicating no significant difference in age. The gender distribution was relatively similar between the groups, with 67.8% males and 32.2% females in the CAD group and 63.6% males and 36.4% females in the control group (p = 0.47). Notably, the mean BMI was significantly higher in CAD patients (27.4 ± 3.5 kg/m²) compared to controls (25.6 ± 3.2 kg/m²), with a p-value of 0.01. Smoking status showed a significant difference, with 38.1% of CAD patients being smokers com-

pared to 21.2% of controls (p = 0.004). Hypertension was present in 59.3% of CAD patients, significantly higher than the 33.9% observed in controls (p < 0.001). Similarly, diabetes mellitus was more prevalent among CAD patients (46.6%) compared to controls (25.4%), with a p-value of 0.001. Lipid profile parameters also showed significant differences between the groups. The mean total cholesterol level was higher in CAD patients (205.3 ± 45.7 mg/dL) compared to controls (190.5 ± 40.2 mg/dL) (p = 0.03). LDL cholesterol levels were significantly elevated in CAD patients (130.4 ± 37.6 mg/dL) compared to controls (115.7 ± 34.8 mg/dL) (p = 0.02). Conversely, HDL cholesterol levels were significantly lower in CAD patients (40.6 ± 9.5 mg/dL) compared to controls (45.8 ± 10.2 mg/dL) (p = 0.001). Triglycerides levels were also significantly higher in CAD patients (165.2 ± 60.4 mg/dL) compared to controls (140.3 ± 55.1 mg/dL) (p = 0.005).

Table 2: Plasma Homocysteine Levels in CAD Patients and Controls

Group	Plasma Homocysteine Level (µmol/L)	p-value
CAD Patients	18.4 ± 5.6	<0.001
Controls	12.2 ± 4.7	

Plasma homocysteine levels were measured in both CAD patients and controls to determine their association with coronary artery disease.

The results indicated that the mean plasma homocysteine level in CAD patients was significantly higher, at 18.4 µmol/L (± 5.6), compared to 12.2 µmol/L (± 4.7) in the control group. This difference was statistically significant, with a p-value of less than 0.001.

These findings suggest a strong association between elevated plasma homocysteine levels and the presence of coronary artery disease, highlighting the potential role of homocysteine as a risk factor in the development and progression of CAD.

Table 3: Correlation between Plasma Homocysteine Levels and CAD Risk Factors

Variable	Correlation Coefficient (r)	p-value
Age	0.15	0.04
BMI	0.20	0.01
Smoking Status	0.25	<0.001
Hypertension	0.22	0.002
Diabetes Mellitus	0.18	0.03
Total Cholesterol	0.27	<0.001
LDL Cholesterol	0.30	<0.001
HDL Cholesterol	-0.24	0.002
Triglycerides	0.21	0.01

The correlation between plasma homocysteine levels and various CAD risk factors was analyzed to understand the relationships among these variables. The analysis revealed several significant correlations. Age showed a weak positive correlation with plasma homocysteine levels (r = 0.15, p = 0.04). Body mass index (BMI) had a slightly stronger positive correlation (r = 0.20, p = 0.01), indicating that higher BMI is associated with higher homocysteine levels.

Smoking status was found to have a moderate positive correlation with plasma homocysteine levels (r = 0.25, p < 0.001), suggesting that smokers tend to have elevated homocysteine levels. Similarly, hypertension was positively correlated with homocysteine levels (r = 0.22, p = 0.002), as was diabetes mellitus (r = 0.18, p = 0.03), indicating that these conditions are associated with higher homocysteine levels.

Lipid profile parameters also showed significant correlations. Total cholesterol (r = 0.27, p < 0.001) and LDL cholesterol (r = 0.30, p < 0.001) both had positive correlations with plasma homocysteine levels, suggesting that higher cholesterol levels are associated with elevated homocysteine. Conversely, HDL cholesterol negatively correlated with homocysteine levels (r = -0.24, p = 0.002), indicating that higher HDL levels are associated with lower homocysteine levels. Triglycerides also positively correlated (r = 0.21, p = 0.01), reinforcing the association between lipid abnormalities and elevated homocysteine levels.

Table 4: Multivariate Logistic Regression Analysis for CAD

Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Age	1.02	1.00 - 1.04	0.07
Gender	1.10	0.80 - 1.51	0.56
BMI	1.12	1.05 - 1.19	0.001
Smoking Status	1.50	1.10 - 2.04	0.01
Hypertension	1.45	1.10 - 1.90	0.01
Diabetes Mellitus	1.30	1.00 - 1.70	0.05
Total Cholesterol	1.01	0.99 - 1.02	0.10
LDL Cholesterol	1.01	0.99 - 1.02	0.08
HDL Cholesterol	0.98	0.97 - 0.99	0.001
Triglycerides	1.01	1.00 - 1.02	0.10
Plasma Homocysteine Level	1.15	1.08 - 1.23	<0.001

The multivariate logistic regression analysis was conducted to identify independent coronary artery disease (CAD) predictors among the study participants. The analysis revealed several significant predictors. Age showed a trend towards significance with an odds ratio (OR) of 1.02 (95% CI: 1.00 - 1.04, p = 0.07), suggesting a slight increase in CAD risk with increasing age, although this did not reach statistical significance.

Gender did not emerge as a significant predictor of CAD, with an OR of 1.10 (95% CI: 0.80 - 1.51, p = 0.56). Body mass index (BMI) was a significant predictor, with an OR of 1.12 (95% CI: 1.05 - 1.19, p = 0.001), indicating that higher BMI is associated with increased risk of CAD. Smoking status also significantly predicted CAD, with smokers having an OR of 1.50 (95% CI: 1.10 - 2.04, p = 0.01).

Hypertension was another significant predictor, with an OR of 1.45 (95% CI: 1.10 - 1.90, p = 0.01), highlighting the increased risk of CAD in individuals with hypertension. Diabetes mellitus showed a borderline significance, with an OR of 1.30 (95% CI: 1.00 - 1.70, p = 0.05), suggesting a higher risk of CAD among diabetic individuals.

Regarding lipid profile, total cholesterol (OR: 1.01, 95% CI: 0.99 - 1.02, p = 0.10) and LDL cholesterol (OR: 1.01, 95% CI: 0.99 - 1.02, p = 0.08) were not significant predictors. However, HDL cholesterol was significantly inversely associated with CAD risk, with an OR of 0.98 (95% CI: 0.97 - 0.99, p = 0.001), indicating that higher HDL levels are protective against CAD. Triglycerides did not significantly correlate with CAD (OR: 1.01, 95% CI: 1.00 - 1.02, p = 0.10).

Notably, plasma homocysteine levels were a strong and independent predictor of CAD, with an OR of 1.15 (95% CI: 1.08 - 1.23, p < 0.001). This finding underscores the significant role of elevated homocysteine levels in increasing the risk of coronary artery disease.

Table 5: Distribution of Plasma Homocysteine Levels

Quartile	Plasma Homocysteine Level Range (µmol/L)	CAD Patients (n=118)	Controls (n=118)	p-value
Q1 (Lowest)	<10	5 (4.2%)	28 (23.7%)	<0.001
Q2	10-14.9	18 (15.3%)	40 (33.9%)	
Q3	15-19.9	40 (33.9%)	30 (25.4%)	
Q4 (Highest)	≥20	55 (46.6%)	20 (16.9%)	

The distribution of plasma homocysteine levels among CAD patients and controls was analyzed by dividing the levels into quartiles. The analysis revealed significant differences between the two groups across the quartiles. In the lowest quartile (Q1), with plasma homocysteine levels less than 10 µmol/L, only 5 CAD patients (4.2%) were present, compared to 28 controls (23.7%).

This difference was statistically significant, with a p-value of less than 0.001, indicating that lower homocysteine levels are much more common in the control group.

In the second quartile (Q2), with plasma homocysteine levels ranging from 10 to 14.9 µmol/L, 18 CAD patients (15.3%) and 40 controls (33.9%) were observed. This quartile also showed a higher proportion of controls with intermediate homocysteine levels than CAD patients. The third quartile (Q3), with homocysteine levels ranging from 15 to 19.9 µmol/L, contained 40 CAD patients (33.9%) and 30 controls (25.4%), showing a reversal where higher levels were more common among CAD patients. In the highest quartile (Q4), with plasma homocysteine levels of 20 µmol/L or greater, a

substantial 55 CAD patients (46.6%) were observed, in contrast to only 20 controls (16.9%). This significant difference further underscores the association between elevated homocysteine levels and the presence of coronary artery disease.

Discussion

This study investigated the correlation between plasma homocysteine levels and coronary artery disease (CAD) in an Indian population at a tertiary care hospital. The findings revealed that plasma homocysteine levels were significantly higher in CAD patients than in controls, underscoring the potential role of homocysteine as a risk factor for CAD. Our study found that CAD patients had a mean plasma homocysteine level of 18.4 ± 5.6 μmol/L, significantly higher than the 12.2 ± 4.7 μmol/L observed in controls ($p < 0.001$). This is consistent with previous research, which has shown that elevated homocysteine levels are associated with an increased risk of CAD. For instance, the meta-analysis of Humphrey et al. (2008) [9] demonstrated that hyperhomocysteinemia is a strong and independent risk factor for coronary heart disease. Similarly, Nygård et al. (1997)[10] reported a significant association between elevated homocysteine levels and mortality in CAD patients.

The correlation analysis in our study revealed that plasma homocysteine levels were positively correlated with several established risk factors for CAD, including BMI, smoking status, hypertension, diabetes mellitus, total cholesterol, LDL cholesterol, and triglycerides while showing an inverse correlation with HDL cholesterol. These findings align with other studies documenting the relationship between homocysteine and cardiovascular risk factors. Bhatnagar et al. (2006)[11] reported that hyperhomocysteinemia is linked with endothelial dysfunction, oxidative stress, and inflammation, which are key mechanisms in the pathogenesis of atherosclerosis and CAD.

The multivariate logistic regression analysis identified BMI, smoking status, hypertension, HDL cholesterol, and plasma homocysteine levels as significant independent predictors of CAD. Notably, plasma homocysteine levels had an odds ratio of 1.15 (95% CI: 1.08 - 1.23, $p < 0.001$), indicating that each unit increase in homocysteine level significantly raises the risk of CAD. These results corroborate findings from the Homocysteine Studies Collaboration (2002)[12], highlighting the importance of homocysteine as an independent risk factor for ischemic heart disease and stroke.

The distribution analysis showed that higher plasma homocysteine levels were markedly more prevalent among CAD patients, with 46.6% of CAD patients in the highest quartile (≥20 μmol/L) compared to only 16.9% of controls. This significant difference underscores the role of elevated homocysteine levels in the pathophysiology of CAD. Clarke et al. (2011)[13] also reported similar findings, suggesting that homocysteine-lowering interventions could potentially reduce the incidence of CAD.

The results of this study have important clinical implications. Given the strong association between elevated plasma homocysteine levels and CAD, screening for homocysteine levels in high-risk individuals could aid in the early identification and management of CAD. Moreover, therapeutic strategies aimed at lowering homocysteine levels, such as supplementation with folic acid, vitamin B6, and vitamin B12, may be beneficial in reducing CAD risk. This is supported by intervention studies showing that homocysteine-lowering therapy can decrease the risk of cardiovascular events.

Conclusion

In conclusion, this study demonstrates a significant correlation between elevated plasma homocysteine levels and coronary artery disease in the Indian population. The findings highlight the importance of considering homocysteine as a potential biomarker for CAD risk assessment and the need for further research to explore homocysteine-lowering interventions as a preventive strategy for CAD.

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