

Age- and Gender-Specific Variations in Serum Albumin, Ferritin, and High-Sensitivity C-reactive protein among Ischemic Heart Disease Patients: Evidence from Northeast India

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ABSTRACT

Background: Ischemic heart disease (IHD) is the leading cause of morbidity and mortality worldwide, with a particularly high burden in India. Biomarkers such as serum albumin, serum ferritin, and high-sensitivity C-reactive protein (hs-CRP) have been implicated in cardiovascular risk, but their variation across age and gender remains underexplored, especially in Northeast India.

Objective: To evaluate age- and gender-specific differences in serum albumin, ferritin, and hs-CRP among patients with IHD, and to examine correlations between these biomarkers.

Methods: A cross-sectional study was conducted at Agartala Government Medical College and G.B.P. Hospital from January 2024 to June 2025. A total of 104 patients with confirmed IHD were enrolled. Demographic data, clinical history, and laboratory investigations were collected. Serum albumin was measured using the Bromocresol Green method, ferritin by ELISA, and hs-CRP by immunoturbidimetric assay. Patients were stratified into four age groups (40–50, 51–60, 61–70, and >70 years) and by gender. Statistical analysis included descriptive statistics, ANOVA, t-tests, and Pearson's correlation.

Results: The mean age was 60.6 ± 11.9 years, with males comprising 73.1% of the cohort. Serum albumin declined with age (4.1 ± 0.3 g/dL in 40–50 years vs. 3.7 ± 0.4 g/dL in >70 years). Ferritin was significantly higher in males (232.5 ± 65.7 ng/mL) than in females (176.4 ± 58.3 ng/mL; $p < 0.01$). hs-CRP increased with age and was significantly higher in females (5.2 ± 2.0 mg/L) compared to males (4.6 ± 2.1 mg/L; $p < 0.05$). Correlation analysis revealed an inverse relationship between albumin and hs-CRP ($r = -0.42$, $p < 0.01$) and a positive correlation between ferritin and hs-CRP ($r = 0.36$, $p < 0.05$).

Conclusion: Age and gender significantly influence biomarker profiles in IHD patients. Older age is associated with hypoalbuminemia and elevated hs-CRP; males exhibit higher ferritin levels, and females demonstrate a greater inflammatory burden. These findings underscore the importance of demographic stratification in biomarker interpretation and may inform personalised risk assessment and management strategies in Northeast India.

Keywords: Ischemic heart disease, serum albumin, serum ferritin, high-sensitivity C-reactive protein (hs-CRP), age stratification, gender differences

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INTRODUCTION

Ischemic heart disease (IHD) remains the leading cause of morbidity and mortality worldwide, accounting for nearly 17.9 million deaths annually, which represents approximately 32% of all global deaths.¹ The burden is particularly pronounced in low- and middle-income countries, including India, where IHD contributes to nearly 28% of adult mortality.² The epidemiology of IHD in Northeast India reflects a rising trend, with increasing prevalence of hypertension, diabetes, smoking, and dyslipidaemia.³ Understanding the role of biochemical markers in relation to demographic variables such as age and gender is crucial for improving risk stratification and clinical management.

Biomarkers in Ischemic Heart Disease

Among the biomarkers implicated in cardiovascular pathology, serum albumin, serum ferritin, and high-sensitivity C-reactive protein (hs-CRP) have received considerable attention. Serum albumin, synthesised in the liver, is a marker of nutritional status and systemic inflammation. Hypoalbuminemia has been consistently associated with poor cardiovascular outcomes, including increased mortality in patients with coronary artery disease.⁴ Serum ferritin, an iron-storage protein, reflects both iron metabolism and inflammatory status. Elevated ferritin levels have been linked to atherosclerosis and adverse prognosis in IHD, although findings remain inconsistent across populations.⁵ hs-CRP, a sensitive marker of systemic inflammation, is widely recognised as an independent predictor of cardiovascular events in both healthy individuals and patients with established IHD.⁶

Age and Gender Differences in Biomarker Profiles

Age and gender are fundamental determinants of cardiovascular risk. Advancing age is associated with cumulative exposure to risk factors, endothelial dysfunction, and heightened inflammatory activity, all of which contribute to IHD progression.^{7,8} Gender differences in cardiovascular disease are well

established: men typically present with IHD at younger ages, whereas women often exhibit atypical symptoms and experience worse outcomes post-myocardial infarction.⁹ Biomarker levels may also vary by sex; for instance, hs-CRP tends to be higher in women, reflecting differences in hormonal regulation and adiposity.¹⁰ Similarly, ferritin levels are generally higher in men due to differences in iron metabolism, while albumin concentrations may decline with age, reflecting nutritional and inflammatory changes.¹¹

Rationale for Age- and Gender-Specific Analysis

Despite extensive research on individual biomarkers, few studies have systematically examined their variation across age and gender strata in IHD patients. Stratified analysis can provide insights into whether biomarker levels reflect demographic vulnerabilities, thereby aiding in personalised risk assessment. For example, elevated hs-CRP in older women may indicate heightened inflammatory risk, whereas high ferritin in middle-aged men may suggest iron-related oxidative stress contributing to coronary pathology. Such findings could inform tailored preventive and therapeutic strategies.

Regional Context

In Northeast India, unique cultural, dietary, and socioeconomic factors may influence biomarker profiles. High prevalence of smoking, betel nut consumption, and dietary patterns rich in carbohydrates and low in protein may contribute to altered albumin and ferritin levels.¹² Moreover, limited access to healthcare and late presentation of IHD cases underscore the need for biomarker-based stratification to improve early detection and prognosis in this region.

Aim of the Study

The present study aims to evaluate age- and gender-specific variations in serum albumin, serum ferritin, and hs-CRP among patients with ischemic heart disease in Northeast India. By analysing biomarker levels across defined age

groups (40–50, 51–60, 61–70, >70 years) and between males and females, this study seeks to provide novel insights into demographic influences on biomarker expression. Such evidence may enhance the understanding of pathophysiological mechanisms and support the development of personalised management strategies for IHD.

MATERIALS AND METHODS

Study Design and Setting

This investigation was conducted as an observational cross-sectional study in the Department of General Medicine at Agartala Government Medical College and G.B.P. Hospital, Tripura, India. The study period extended from January 2024 to June 2025, encompassing one year of patient recruitment and six months of data management and analysis.

Study Population

Patients admitted with a clinical diagnosis of IHD were considered eligible. Diagnosis was established based on clinical presentation, electrocardiographic changes, and biochemical evidence of myocardial injury. Both male and female patients aged 18 years and above were included.

Inclusion criteria comprised:

- Adults (>18 years) with confirmed IHD (stable angina, unstable angina, NSTEMI, or STEMI).
- Availability of complete clinical and laboratory data.

Exclusion criteria were:

- Patients younger than 18 years.
- Individuals with hypoalbuminemia due to chronic liver disease, nephrotic syndrome, or malnutrition (serum albumin <3.5 g/dL).
- Patients with iron deficiency anaemia or other haematological disorders affecting ferritin levels.
- Patients unwilling to provide informed consent.

Sample Size Determination

Sample size was calculated using the Kish and Leslie formula (1965) for cross-sectional studies, considering a prevalence of IHD of 7.3% as reported by Ridker et al.¹³ With a 5% margin of error and a 95% confidence interval, the minimum required sample size was estimated at 104 participants, a target achieved during the study period.

Data Collection

Data were collected using a structured proforma that documented demographic details (age, sex), clinical history, cardiovascular risk factors (hypertension, diabetes, smoking, obesity), and laboratory findings.

Clinical evaluation included:

- Detailed history of chest pain and associated symptoms.
- Physical examination with emphasis on the cardiovascular system.
- Electrocardiography (12-lead ECG) to identify ischemic changes such as ST-segment elevation, depression, T-wave inversion, and pathological Q-waves.
- Cardiac troponin I assay for confirmation of myocardial injury.

Laboratory Investigations

Venous blood samples (5 mL) were collected under aseptic precautions within 24 hours of admission. Serum was separated and analysed for the following biomarkers:

- **Serum Albumin:** Estimated using the Bromocresol Green (BCG) dye-binding method.
- **Serum Ferritin:** Measured by enzyme-linked immunosorbent assay (ELISA).
- **High-sensitivity C-reactive protein (hs-CRP):** Quantified using an immunoturbidimetric assay.

All assays were performed in the central laboratory of AGMC & G.B.P. Hospital, adhering to standard operating procedures and manufacturer guidelines.

Age and Gender Stratification

Participants were categorised into four age groups: 40–50 years, 51–60 years, 61–70 years, and >70 years. Gender distribution was recorded as male or female. Biomarker levels were compared across these strata to identify age- and sex-specific variations.

Statistical Analysis

Data were entered into Microsoft Excel and analysed using SPSS, version 25. Descriptive statistics (mean, standard deviation, frequencies, percentages) were used to summarise demographic and clinical characteristics.

Correlation between biomarkers was assessed using Pearson’s correlation coefficient and statistical significance was determined using the corresponding p-values. A p-value <0.05 was considered statistically significant.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee of Agartala Government Medical College (Ref. No. F.4 (6-13)/AGMC/Medical Education/IEC Approval/2022/24338). Written informed consent was obtained from all participants prior to enrolment. Confidentiality of patient data was strictly maintained, and all procedures adhered to the principles of the Declaration of Helsinki.

RESULTS

Study Population Characteristics

A total of 104 patients diagnosed with IHD were included in the analysis. The mean age of the cohort was 60.6 ± 11.9 years, ranging from 41 to 79 years. Table 1 shows that the majority of patients were in the 61–70-year age group (35.6%), followed by those aged 70 years and above (25.0%). The 40–50 year group accounted for 22.1% of cases, while the 51–60

year group represented the smallest proportion (17.3%).

Table 1: Age group-wise distribution of the cases (N=104)

Age group	Frequency	Percent
40-50 years	23	22.1
51-60 years	18	17.3
61-70 years	37	35.6
Above 70 years	26	25.0

Table 2 shows that the gender distribution was predominantly male (73.1%, n=76) over female (26.9%, n=28). Age-stratified analysis showed that male patients were more frequently represented across all age groups, particularly in the 61–70-year category (Table 3).

Table 2: Gender-wise distribution of the cases (N=104)

Gender	Frequency	Percent
Male	76	73.1
Female	28	26.9

Table 3. Gender-wise Distribution Across Age Groups (N=104)

Age Group (years)	Male (n, %)	Female (n, %)	Total (n,%)
40–50	19 (82.6%)	4 (17.4%)	23 (22.1%)
51–60	16 (88.9%)	2 (11.1%)	18 (17.3%)
61–70	24 (64.9%)	13 (35.1%)	37 (35.6%)
>70	17 (65.4%)	9 (34.6%)	26 (25.0%)
Total	76 (73.1%)	28 (26.9%)	104 (100%)

Serum Albumin Levels

The overall mean serum albumin concentration among IHD patients was 3.9 ± 0.4 g/dL. When stratified by age, albumin levels declined with advancing age. Patients aged 40–50 years had the highest mean albumin level (4.1 ± 0.3

g/dL), whereas those aged >70 years had the lowest (3.7 ± 0.4 g/dL).

Gender-specific analysis revealed that male patients had slightly higher albumin levels (mean 4.0 ± 0.3 g/dL) than female patients (3.8 ± 0.4 g/dL), although the difference did not reach statistical significance ($p > 0.05$).

Serum Ferritin Levels

The mean serum ferritin concentration in the study population was 215.6 ± 72.4 ng/mL. Age-wise comparison indicated that ferritin levels were highest in the 61–70-year group (mean 228.3 ± 68.9 ng/mL) and lowest in the 40–50-year group (mean 198.7 ± 70.2 ng/mL).

Gender analysis showed a marked difference: males had significantly higher ferritin levels (mean 232.5 ± 65.7 ng/mL) than females (mean 176.4 ± 58.3 ng/mL; $p < 0.01$). This finding is consistent with known physiological differences in iron metabolism between sexes.

hs-CRP Levels

High-sensitivity C-reactive protein (hs-CRP) levels were elevated across the cohort, with a mean value of 4.8 ± 2.1 mg/L. Age stratification demonstrated a progressive increase in hs-CRP with advancing age. Patients aged 70 years or older had the highest mean hs-CRP (5.6 ± 2.3 mg/L), while those aged 40–50 years had the lowest (3.9 ± 1.8 mg/L).

Gender-specific analysis revealed that female patients had higher hs-CRP levels (mean 5.2 ± 2.0 mg/L) than male patients (mean 4.6 ± 2.1 mg/L), a difference that was statistically significant ($p < 0.05$) [Tables 4 and 5].

Table 4. Mean Biomarker Levels by Age Group

Age Group (years)	Albumin (g/dL, Mean \pm SD)	Ferritin (ng/mL, Mean \pm SD)	hs-CRP (mg/L, Mean \pm SD)
40–50	4.1 ± 0.3	198.7 ± 70.2	3.9 ± 1.8
51–60	3.9 ± 0.4	210.5 ± 65.4	4.4 ± 1.9
61–70	3.8 ± 0.3	228.3 ± 68.9	5.1 ± 2.0
>70	3.7 ± 0.4	220.6 ± 72.1	5.6 ± 2.3

Table 5: Mean Biomarker Levels by Gender

Gender	Albumin (g/dL, Mean \pm SD)	Ferritin (ng/mL, Mean \pm SD)	hs-CRP (mg/L, Mean \pm SD)
Male	4.0 ± 0.3	232.5 ± 65.7	4.6 ± 2.1
Female	3.8 ± 0.4	176.4 ± 58.3	5.2 ± 2.0

Correlation Between Biomarkers

Correlation analysis, as shown in Table 6, demonstrated a significant inverse relationship between serum albumin and hs-CRP ($r = -0.42$, $p < 0.01$), indicating that lower albumin levels were associated with higher inflammatory activity. Serum ferritin showed a positive correlation with hs-CRP ($r = 0.36$, $p < 0.05$), suggesting that elevated ferritin may reflect an inflammatory state in addition to iron storage. No significant correlation was observed between serum albumin and ferritin ($r = -0.12$, $p > 0.05$).

Table 6: Correlation Between Biomarkers

Biomarker Pair	Correlation Coefficient (r)	p-value
Albumin vs hs-CRP	-0.42	<0.01
Ferritin vs hs-CRP	+0.36	<0.05
Albumin vs Ferritin	-0.12	>0.05

Summary of Age- and Gender-Specific Findings

- Age: Advancing age was associated with lower albumin, higher ferritin, and higher hs-CRP levels.

- Gender: Males exhibited higher ferritin concentrations, while females demonstrated higher hs-CRP levels. Albumin levels were marginally higher in males, but not statistically significant.

- Overall: The combined biomarker profile suggests that older patients and female patients may exhibit a heightened inflammatory burden, whereas males demonstrate greater iron storage status.

DISCUSSION

This study investigated the age- and gender-specific variations in serum albumin, serum ferritin, and high-sensitivity C-reactive protein (hs-CRP) among patients with IHD in Northeast India. The results demonstrated three key findings: (i) serum albumin levels declined progressively with advancing age, (ii) serum ferritin concentrations were significantly higher in males compared to females, and (iii) hs-CRP levels were elevated in older patients and significantly higher in females than males. Furthermore, correlation analysis revealed an inverse relationship between albumin and hs-CRP, and a positive association between ferritin and hs-CRP. These findings highlight the interplay between nutritional status, iron metabolism, and systemic inflammation in the pathophysiology of IHD, while also underscoring demographic influences.

Serum Albumin and Cardiovascular Risk

Serum albumin is a multifunctional protein synthesised in the liver, responsible for maintaining oncotic pressure, transporting hormones, and exerting antioxidant effects. Hypoalbuminemia has been consistently associated with adverse cardiovascular outcomes. In the present study, albumin levels declined with age, which may reflect age-related changes in nutritional status, hepatic function, and chronic inflammation. Similar findings have been reported by Yilmaz et al., who identified low albumin as an

independent predictor of long-term cardiovascular mortality in stable coronary artery disease.^{4,14}

The inverse correlation between albumin and hs-CRP observed in this study supports the hypothesis that inflammation contributes to hypoalbuminemia. Elevated hs-CRP may suppress albumin synthesis through cytokine-mediated hepatic effects, while low albumin may exacerbate oxidative stress and vascular injury.^{15,16} Thus, albumin may serve as both a marker and mediator of cardiovascular risk, particularly in elderly patients where nutritional deficiencies and chronic inflammation coexist.

Serum Ferritin and Iron Metabolism

Ferritin is an intracellular iron-storage protein, and serum ferritin levels reflect both iron stores and inflammatory activity. In this study, ferritin concentrations were significantly higher in males compared to females, consistent with physiological differences in iron metabolism. Men generally have greater iron stores due to the absence of menstrual blood loss, while women often exhibit lower ferritin levels, particularly in premenopausal years.¹⁷

Elevated ferritin in IHD patients may contribute to atherosclerosis through iron-mediated oxidative stress. Sullivan's "iron hypothesis" proposed that excess iron catalyses free radical formation, promoting lipid peroxidation and endothelial injury.¹⁸ Subsequent studies have provided mixed evidence: some report positive associations between ferritin and cardiovascular risk,⁵ while others find no significant relationship.¹⁹ In the present study, ferritin correlated positively with hs-CRP, suggesting that elevated ferritin may partly reflect inflammatory activation rather than iron overload alone. This dual role complicates interpretation but underscores ferritin's relevance in cardiovascular pathology.

hs-CRP as an Inflammatory Marker

hs-CRP is a highly sensitive marker of systemic inflammation and has been extensively

validated as a predictor of cardiovascular events. Ridker et al. demonstrated that hs-CRP independently predicts first cardiovascular events from traditional risk factors.²⁰ In the current study, hs-CRP levels increased with age and were significantly higher in females.

The age-related rise in hs-CRP may reflect cumulative exposure to risk factors, endothelial dysfunction, and chronic low-grade inflammation associated with ageing.²¹ The higher hs-CRP levels in females are consistent with findings from the Multi-Ethnic Study of Atherosclerosis, which reported elevated CRP in women compared to men, potentially due to differences in adiposity, hormonal regulation, and immune response.¹⁰ Elevated hs-CRP in women may partly explain their worse outcomes following myocardial infarction, despite lower ferritin levels.

Interplay Between Biomarkers

The combined analysis of albumin, ferritin, and hs-CRP provides insights into the complex interplay between nutrition, iron metabolism, and inflammation in IHD. The inverse relationship between albumin and hs-CRP suggests that inflammation suppresses albumin synthesis, while the positive correlation between ferritin and hs-CRP indicates that ferritin may act as an acute-phase reactant. Together, these findings highlight the potential utility of a composite biomarker approach.

The CRP-to-albumin ratio (CAR) has recently emerged as a prognostic marker in cardiovascular disease, reflecting the balance between inflammation and nutritional status.²² Although CAR was not the primary focus of this analysis, the observed inverse correlation between albumin and hs-CRP supports its relevance. Similarly, ferritin's dual role as an iron-storage protein and inflammatory marker suggests that its interpretation should be contextualised alongside hs-CRP.

Age- and Gender-Specific Implications

The stratified analysis underscores the importance of demographic factors in biomarker interpretation. Older patients

exhibited lower albumin and higher hs-CRP, reflecting a state of malnutrition-inflammation complex syndrome, which has been linked to poor prognosis in cardiovascular disease.²³ Female patients had higher hs-CRP levels, suggesting heightened inflammatory risk, whereas males had higher ferritin levels, indicating greater iron-related oxidative stress. These differences may inform personalised risk assessment and management strategies.

For example, elderly patients with low albumin and high hs-CRP may benefit from nutritional interventions and anti-inflammatory therapies. Male patients with elevated ferritin may require monitoring of iron status and oxidative stress, while female patients with elevated hs-CRP may benefit from aggressive risk-factor modification to mitigate the inflammatory burden.

Regional Context and Public Health Relevance

The findings are particularly relevant in Northeast India, where unique cultural and dietary practices may influence biomarker profiles. High prevalence of smoking, betel nut consumption, and carbohydrate-rich diets may exacerbate inflammation and nutritional deficiencies.²⁴ Limited access to healthcare and late presentation of IHD cases further highlight the need for biomarker-based stratification to improve early detection and prognosis.

By identifying age- and gender-specific variations in albumin, ferritin, and hs-CRP, this study provides evidence that can inform regional public health strategies. For instance, nutritional supplementation programs targeting elderly populations, iron monitoring in men, and inflammatory risk assessment in women may enhance cardiovascular prevention efforts.

Strengths and Limitations

The strengths of this study include its focus on a Northeastern Indian cohort, stratified analysis by age and gender, and simultaneous evaluation of three key biomarkers. This approach provides novel insights into

demographic influences on biomarker expression in IHD.

However, several limitations must be acknowledged. First, the cross-sectional design precludes causal inference. Second, ferritin levels may be influenced by comorbid conditions such as liver disease or infection, which were not fully controlled. Third, although adequate for statistical analysis, the sample size may limit generalizability. Finally, the study did not include long-term follow-up to assess prognostic outcomes, which would strengthen the clinical relevance of biomarker variations.

Future Directions

Future research should focus on longitudinal studies to evaluate the prognostic significance of age- and gender-specific biomarker variations in IHD. Incorporating composite indices such as the CRP-to-albumin ratio and ferritin-to-CRP ratio may enhance predictive accuracy. Additionally, mechanistic studies exploring the pathways linking iron metabolism, inflammation, and nutritional status to cardiovascular outcomes are warranted. Expanding research to diverse populations across India would also improve generalizability and inform national cardiovascular prevention strategies.

CONCLUSION

This study demonstrates that serum albumin, ferritin, and hs-CRP exhibit significant age- and gender-specific variations among patients with ischemic heart disease. Older age is associated with lower albumin and higher hs-CRP, males exhibit higher ferritin, and females demonstrate higher hs-CRP. These findings highlight the interplay between nutrition, iron metabolism, and inflammation in IHD and underscore the importance of demographic stratification in biomarker interpretation. Incorporating age- and gender-specific biomarker profiles into clinical practice may enhance personalised risk assessment and management, ultimately improving cardiovascular outcomes in Northeast India and beyond.

Declaration by Authors

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