Ironing out the link: ferritin and coronary artery disease- a two-year perspective on disease burden and prognosis

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Abstract

Purpose: This study evaluates the association between serum ferritin levels, coronary artery disease (CAD) severity, and survival outcomes over two years. It also examines correlations between ferritin and clinical parameters, including age and creatinine.

Methods: A total of 300 CAD patients underwent coronary angiography (CAG). Serum ferritin levels were categorized as low (<30 µg/L), normal (30–300 µg/L for males and 30–200 µg/L for females), and high (>300 µg/L for males and >200 µg/L for females). CAD severity was classified into non-critical, single-vessel, dual-vessel, and triple-vessel disease. Survival outcomes were recorded as alive, deceased, or lost to follow-up. Statistical analyses included Pearson's correlation, Chi-square tests, and Kaplan–Meier survival curves.

Results: The mean age was 59.03 ± 9.42 years, with 71.66% males. Hypertension and diabetes were present in 51.66% and 35.33% of patients, respectively. Ferritin levels showed a weak negative correlation with age (r = -0.122, P = 0.035) and a positive correlation with creatinine (r = 0.281, P = 0.001). Elevated ferritin levels were significantly associated with dual-vessel disease (50%) and mortality (P = 0.001). Deceased patients had higher ferritin levels (142.0 µg/L vs. 90.45 µg/L in survivors; P = 0.001).

Conclusions: Ferritin is strongly associated with CAD severity and mortality, particularly in dual-vessel disease. Its potential role in early risk stratification suggests clinical relevance. Further research should explore ferritin's mechanistic link to CAD progression and its integration into prognostic models.

Keywords
Ferritin, Coronary Artery Disease, Prognosis, Angiography, Biomarkers

Introduction

Coronary artery disease (CAD) remains a primary contributor to global mortality, significantly impacting public health. Traditional risk factors, including diabetes, hypertension, smoking, and hyperlipidemia, have long been recognized as critical contributors to CAD development and progression. However, growing evidence suggests that novel biomarkers could provide additional insights into CAD risk stratification and prognosis. Ferritin, an acute-phase reactant and a major iron storage protein, has garnered attention due to its potential involvement in oxidative stress, endothelial dysfunction, and atherogenesis. Ferritin levels are often elevated in response to systemic inflammation, and it is hypothesized that high serum ferritin may contribute to CAD pathogenesis by promoting oxidative stress and the formation of atherosclerotic plaques. Elevated ferritin levels have been associated with poor cardiovascular outcomes, though the precise mechanisms underlying this association remain unclear[1].

Recent studies have examined the correlation between serum ferritin levels and the severity of CAD. Elevated ferritin concentrations have been linked to the extent of coronary artery stenosis, suggesting that ferritin may serve as a marker of disease burden[2]. Additionally, high serum ferritin has been correlated with adverse cardiovascular events, including myocardial infarction, stroke, and even mortality, underscoring its potential role as a prognostic marker in CAD patients[3]. Despite these associations, the clinical utility of ferritin as a standalone biomarker remains under investigation, and its potential to guide therapeutic interventions in CAD patients is still being explored.

This study aims to investigate the relationship between serum ferritin levels, CAD severity, and long-term survival outcomes over a two-year period. By assessing serum ferritin in CAD patients and evaluating its predictive value, we hope to enhance our understanding of its role in CAD progression and patient prognosis.

Materials And Methods

Data from 300 patients undergoing coronary angiography (CAG) for coronary artery disease (CAD) were collected using a standard, validated proforma between July 1, 2021, and August 30, 2022, in the cardiology department of Sir Sunderlal Hospital, Institute of Medical Sciences, Banaras Hindu University, Varanasi. Baseline evaluations, including coronary angiography, were conducted, and

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patients were followed for two years to assess survival outcomes. A two-year follow-up was chosen to capture medium-term mortality trends while minimizing attrition bias.

The primary objective of the study was to evaluate the association between serum ferritin levels and the burden of CAD, as determined by angiographic findings, and survival outcomes, including mortality, over the two-year follow-up period. The secondary objectives were to explore correlations between serum ferritin levels and clinical parameters such as age, hemoglobin, and creatinine levels, as well as to assess the association of serum ferritin with sex, hypertension, diabetes mellitus, and the type of CAD presentation [acute coronary syndrome (ACS) vs. chronic coronary syndrome (CCS)]. Additionally, the study aimed to evaluate the relationship between survival outcomes and variables including age, sex, hemoglobin levels, serum creatinine levels, hypertension, diabetes mellitus, and CAD presentation (ACS vs. CCS).

Major inclusion criteria included:

(i) Adult patients aged ≥18 years presenting with confirmed CAD.
(ii) Undergoing coronary angiography as part of routine care.
(iii) Consent to participate and agree to follow-up over two years.

Major exclusion criteria included:

(i) Patients with active inflammatory or infectious diseases at baseline.
(ii) Known hematological disorders, including iron-overload syndromes or anemia of chronic disease unrelated to CAD.
(iii) History of recent surgery, trauma, or hospitalization within the past 3 months.
(iv) Patients lost to follow-up immediately after the baseline evaluation.

The study was conducted with the approval of the Institutional Ethics Committee of Institute of Medical Sciences, Banaras Hindu University, Varanasi, and written informed consent was obtained from all the study participants prior to enrolling them in our study.

Data collection for this study involved comprehensive baseline assessments of 300 patients diagnosed with coronary artery disease (CAD). Serum ferritin levels were measured using the immunoassay method, with results categorized into three groups based on established clinical thresholds: low (<30 µg/L), normal (30–300 µg/L for males and 30–200 µg/L for females), and high (>300 µg/L for males and >200 µg/L for females)[5]. These cutoff values align with widely accepted guidelines for ferritin interpretation in the context of inflammation and iron storage disorders. Additional data was collected, including patient age, gender, hypertension (BP ≥140/90 mm Hg or on anti-hypertensive drugs), diabetes mellitus (fasting plasma glucose ≥126 mg/dl, post-prandial glucose ≥200 mg/dl, random glucose ≥200 mg/dl with hyperglycemia symptoms, or HbA1c ≥6.5%, or on oral hypoglycemics), and other laboratory tests included hemoglobin and creatinine levels, collected via standard blood analysis protocols. Coronary angiography data, classified as non-critical CAD, single-vessel disease, dual-vessel disease, and triple-vessel disease, were reviewed by two independent cardiologists to ensure accuracy. While scores like the SYNTAX score provide an objective measure of lesion complexity, our study utilized CAD burden classification based on vessel involvement only due to its clinical applicability and ease of interpretation in routine practice. Survival outcomes, including alive, deceased, or lost to follow-up status, were recorded at the two-year mark. Telephonic follow-up was conducted periodically to ensure accurate documentation of survival status and to address any loss to follow-up cases. This meticulous data collection ensured robust analyses of ferritin's role as a prognostic biomarker in CAD progression and outcomes.

Statistical analysis for this study was performed to evaluate correlations, associations, and outcomes of serum ferritin levels in the context of coronary artery disease (CAD). Descriptive statistics were used to summarize baseline characteristics, expressed as mean ± standard deviation for continuous variables and percentages for categorical variables. Pearson's correlation coefficient was employed to analyze relationships between ferritin levels and key clinical parameters, including age, hemoglobin, and creatinine. Associations between ferritin levels and categorical variables such as CAD burden and survival outcomes were analyzed using Chi-square tests. All statistical tests were two-sided, and a p-value of <0.05 was considered significant. Analyses were performed using IBM SPSS Statistics, Version 25.0. This statistical approach ensured a comprehensive understanding of ferritin's role in CAD progression and mortality outcomes.

Results

1. Baseline characteristics

The study included 300 participants, predominantly male (71.66%), with a mean age of 59.03 ± 9.42 years. Approximately 51.66% had hypertension, and 35.33% had diabetes. Clinical presentation was equally distributed between acute coronary syndrome (ACS, 50%) and chronic coronary syndrome (CCS, 50%). Mean hemoglobin and creatinine levels were 12.30 ± 1.53 g/dL and 0.96 ± 0.24 mg/dL, respectively, with an average ferritin level of 98.09 ± 96.17 µg/L. Among the cohort, 29.3% exhibited low ferritin levels, 62.7% had normal levels, and 8% had elevated ferritin. The distribution of coronary artery disease (CAD) burden showed 17.3% with non-critical CAD, 32% with single-vessel disease, 30.7% with dual-vessel disease, and 20% with triple-vessel disease. Over two years, 80% of patients remained alive, 13.3% died, and 6.7% were lost to follow-up (Table 1).

2. Correlation and association of ferritin with survival outcomes and other variables

The analysis highlights significant correlations and associations between serum ferritin levels and various clinical parameters. (Table 2). Age had a weak negative correlation with ferritin levels ($r = -0.122$, $P = 0.035$). Hemoglobin ($r = 0.147$, $P = 0.011$) and creatinine ($r = 0.281$, $P = 0.001$) had positive correlations with ferritin levels. Ferritin

Table 1 - Baseline data.

Mean Age (in years)		59.03 ± 9.42
Sex	**Male**	215 (71.66%)
	Female	85 (28.33%)
Hypertension		155 (51.66%)
Diabetes		106 (35.33%)
Presentation	**ACS**	150 (50%)
	CCS	150 (50%)
Mean Haemoglobin Level (g/dl)		12.30 ± 1.53
Mean Creatinine Level (mg/dl)		0.96 ± 0.24
Mean Ferritin Level (µg/L)		98.09 ± 96.17
Ferritin Levels	HIGH	24 (8%)
	NORMAL	188 (62.7%)
	LOW	88 (29.3%)
CAD Burden	NON-CRITICAL CAD	52 (17.3%)
	SINGLE VESSEL DISEASE	96 (32%)
	DUAL VESSEL DISEASE	92 (30.7%)
	TRIPLE VESSEL DISEASE	60 (20%)
Status	ALIVE	240 (80%)
	DEAD	40 (13.3%)
	LOSS TO FOLLOW UP	20 (6.7%)

Table 2 - Correlation and association of ferritin with other variables

Parameter	Correlation/ Association	Statistical Significance
Correlation with Ferritin		
Age	Correlation Coefficient: -0.122	(P = 0.035)*
Hemoglobin (Hb)	Correlation Coefficient: 0.147	(P = 0.011)*
Creatinine	Correlation Coefficient: 0.281	(P = 0.001)*
Association with Ferritin Levels		
Sex	Chi-square = 22.2306	(P = 0.001)*
ACS vs CCS	Chi-square = 17.696	(P = 0.001)*
Hypertension (HTN)	Chi-square = 2.518	(P = 0.284)
Diabetes Mellitus (DM)	Chi-square = 2.359	(P = 0.307)
CAD BURDEN	Chi-square = 13.118	(P = 0.041)*
Mortality Status	Chi-square = 34.903	(P = 0.001)*

ACS-Acute coronary syndrome, CCS- Chronic coronary syndrome, CAD-Coronary Artery Disease, *=P value <0.05 is significant

levels varied significantly by sex (P = 0.001). Among females, 0% had high ferritin, 45.5% had low levels, and 25.5% had normal levels. Among males, 100% of those with high ferritin were male, 54.5% had low levels, and 74.5% had normal levels. A significant association was observed between ferritin levels and ACS (P = 0.001). High ferritin levels were found in 83.3% of ACS patients and 16.7% of CCS patients.

Hypertension (P = 0.284) and diabetes (P = 0.307) did not show significant associations with ferritin levels. A significant association was observed between ferritin and CAD severity (P = 0.041). Among those with dual-vessel disease, 50% had high ferritin levels, while no patients with non-critical CAD had high ferritin levels.

Ferritin levels were significantly associated with mortality (P = 0.001). Among deceased patients, 30% had high ferritin levels, while 95% of survivors had low or normal ferritin levels. The mean ferritin level in deceased patients was 142.0 µg/L, compared to 90.45 µg/L in survivors (P = 0.001).

3. Association of survival outcomes with other variables

The relationship between clinical characteristics and mortality status provides insights into the prognostic factors for coronary artery disease (CAD). (Table 3) Mortality was not significantly different between males and females (Chi-square = 0.193, P = 0.661). Among survivors, 73.3% were male, and 26.7% were female. Among deceased patients, 70% were male, and 30% were female. There was no significant difference in mortality between ACS and CCS (Chi-square = 0.038, P = 0.845). Among survivors, 51.7% had ACS, and 48.3% had CCS. Among deceased patients, 50% had ACS, and 50% had CCS.

Hypertension was significantly associated with mortality (Chi-square = 12.434, P = 0.001). Among deceased patients, 80% had hypertension, while 50% of survivors had hypertension. Diabetes was significantly associated with mortality (Chi-square = 10.443, P = 0.001). Among deceased patients, 60% had diabetes, while 33.3% of survivors had diabetes. Deceased patients had a significantly higher mean age (65.1 years) compared to survivors (58.25 years) (P = 0.001). Hemoglobin levels were not significantly different between the two groups (P = 0.221). Creatinine levels were slightly higher in deceased patients compared to survivors, but the difference was not statistically significant (P = 0.069).

Coronary angiography findings were significantly associated with mortality (Chi-square = 11.068, P = 0.011). Dual-vessel disease was present in 50% of deceased patients and 26.7% of survivors. Among survivors, 16.7% had non-critical CAD, 36.7% had single-vessel disease, and 20% had triple-vessel disease. Among deceased patients, 20% had non-critical CAD, 20% had single-vessel disease, and 10% had triple-vessel disease. Ferritin levels remained significantly associated with mortality (P = 0.001), as mentioned previously.

Discussion

1. Baseline Characteristics

The baseline characteristics of the study population highlight the demographic and clinical burden of coronary artery disease (CAD), with a predominance of male participants (71.66%) and a mean age of 59.03 years. These findings align with previous studies showing that CAD is more prevalent in men and tends to manifest earlier due to differences in hormonal regulation, genetic susceptibility, and risk factor profiles[6,7]. Estrogen is believed to provide vascular

Table 3 - Association of survival outcomes with other variables

Parameter	Alive	Dead	Total	Chi-square	P-value
Sex				0.193	0.661
Female	64 (26.7%)	12 (30.0%)	76 (27.1%)		
Male	176 (73.3%)	28 (70.0%)	204 (72.9%)		
Diagnosis				0.038	0.845
ACS	124 (51.7%)	20 (50.0%)	144 (51.4%)		
CCS	116 (48.3%)	20 (50.0%)	136 (48.6%)		
Hypertension (HTN)				12.43	0.001*
No HTN	120 (50.0%)	8 (20.0%)	128 (45.7%)		
With HTN	120 (50.0%)	32 (80.0%)	152 (54.3%)		
Diabetes Mellitus (DM)				10.44	0.001*
No DM	160 (66.7%)	16 (40.0%)	176 (62.9%)		
With DM	80 (33.3%)	24 (60.0%)	104 (37.1%)		
Age	58.25 ± 9.65	65.10 ± 9.26		4.181	0.001*
Hemoglobin (Hb)	12.42 ± 1.55	12.09 ± 1.63		1.227	0.221
Creatinine	0.95 ± 0.25	1.03 ± 0.20		-1.826	0.069
Mean Ferritin Levels	90.45 ± 86.11	142.00 ± 131.77		-3.216	0.001*
CAD Burden				11.07	0.011*
Dual Vessel Disease	64 (26.7%)	20 (50.0%)	84 (30.0%)		
Non-Critical CAD	40 (16.7%)	8 (20.0%)	48 (17.1%)		
Single Vessel Disease	88 (36.7%)	8 (20.0%)	96 (34.3%)		
Triple Vessel Disease	48 (20.0%)	4 (10.0%)	52 (18.6%)		
Ferritin Level				30.69	0.001*
High	12 (5.0%)	12 (30.0%)	24 (8.6%)		
Low	76 (31.7%)	4 (10.0%)	80 (28.6%)		
Normal	152 (63.3%)	24 (60.0%)	176 (62.9%)		

ACS-Acute coronary syndrome, CCS- Chronic coronary syndrome, CAD- Coronary Artery Disease, *=P value <0.05 is significant

protection in premenopausal women by reducing oxidative stress and inflammation, which may explain the delayed onset of CAD in females.

The high prevalence of hypertension (51.66%) and diabetes (35.33%) in the study population underscores the well-established role of these conditions as major contributors to atherosclerosis and adverse cardiovascular outcomes[8]. Both conditions are known to accelerate endothelial dysfunction, oxidative stress, and systemic inflammation, all of which contribute to CAD progression. The balanced distribution of acute coronary syndrome (ACS) and chronic coronary syndrome (CCS) in this cohort provides an opportunity to assess ferritin's role across different CAD presentations.

The mean ferritin level of 98.09 µg/L observed in this study is consistent with previous reports in the general population, as described by You SA et al.[9] and Salonen JT et al.[10]. Elevated ferritin levels have been implicated in inflammatory pathways associated with CAD pathogenesis, as demonstrated by Kell DB et al.[11]. This study further strengthens the evidence linking ferritin to adverse cardiovascular outcomes by demonstrating significant associations between ferritin levels, CAD burden, and mortality.

2. Correlation and Association of Ferritin with Survival Outcomes and Other Variables

The observed correlations between ferritin levels and various clinical parameters provide insight into its role as a biomarker of CAD severity and prognosis.

The weak negative correlation with age (r = -0.122, P = 0.035) contrasts with studies suggesting an age-related increase in ferritin, such as that reported by Casale G et al.[12]. This discrepancy may be attributed to differences in population demographics, inclusion criteria, and underlying disease burden. It is possible that aging leads to chronic inflammation and iron accumulation in certain populations, while in CAD patients, other metabolic and inflammatory processes may influence ferritin levels differently.

Ferritin exhibited positive correlations with hemoglobin (r = 0.147, P = 0.011) and creatinine (r = 0.281, P = 0.001), which align with its physiological role in iron metabolism and its potential link to renal dysfunction[13,14]. Low ferritin patients had a mean hemoglobin of 11.6 ± 1.5 g/dL, lower than those with normal/high ferritin (P = 0.018). No significant differences in serum iron levels were observed, suggesting anemia in this group might be

multifactorial rather than solely iron-deficiency driven. Elevated ferritin levels in patients with higher creatinine levels suggest a possible interplay between iron metabolism and kidney function, reinforcing findings that chronic kidney disease (CKD) is a predictor of poor cardiovascular outcomes.

A significant sex-based difference in ferritin levels was observed (P = 0.001), with high ferritin levels exclusively found in males. This is consistent with prior research suggesting that women generally have lower ferritin levels due to menstrual blood loss and hormonal regulation[15]. This finding highlights the need for sex-specific risk stratification strategies when incorporating ferritin into CAD prognostic models.

Ferritin levels were significantly higher in ACS patients (P = 0.001), with 83.3% of high ferritin cases occurring in ACS. While this supports its role as a CAD biomarker[16], the elevation may be due to an acute-phase inflammatory response rather than true disease severity. This makes ferritin a potential confounder, as its rise in ACS could overestimate its association with CAD severity and mortality. Distinguishing whether ferritin is a predictor of poor outcomes or merely a reactive marker is crucial. To address this, future studies should measure pre-event ferritin levels, analyze longitudinal changes, and stratify ACS and CCS cases separately to determine its true prognostic significance.

Despite the well-established role of hypertension and diabetes in CAD, ferritin levels were not significantly associated with these conditions (P = 0.284 and P = 0.307, respectively). This is consistent with studies indicating that ferritin may be more influenced by systemic inflammation than by specific metabolic disorders[17,18]. However, given that ferritin plays a role in oxidative stress and endothelial dysfunction, further studies are needed to explore its relationship with these conditions over longer follow-up periods.

Ferritin levels showed a significant association with CAD severity (P = 0.041). Patients with dual-vessel disease exhibited the highest proportion of high ferritin levels (50%), while none of the patients with non-critical CAD had high ferritin. This finding agrees with Ashna PJ et al., who demonstrated that higher ferritin levels correlate with more extensive coronary involvement[19]. These results suggest that ferritin could serve as a marker for intermediate-to-advanced CAD, providing additional value in risk stratification beyond traditional risk factors. We analyzed the low ferritin group to assess its relationship with CAD complexity and progression. Patients with low ferritin levels had a higher prevalence of single-vessel disease (36.4%) compared to dual-vessel (25.0%) and triple-vessel disease (13.6%), suggesting that low ferritin may be more common in less severe CAD cases.

This indicates that low ferritin is not strongly associated with advanced CAD, unlike high ferritin, which showed a significant correlation with dual-vessel disease and mortality.

Mortality outcomes further emphasized ferritin's prognostic significance. Deceased patients had significantly higher ferritin levels (142.0 µg/L vs. 90.45 µg/L in survivors, P = 0.001). This is consistent with findings from Liu et al., who reported that hyperferritinemia independently predicts mortality in ischemic heart disease patients[5]. The strong association between ferritin and mortality underscores its potential utility in clinical risk prediction models. While the mean ferritin level in our cohort was within the normal range (98.09 µg/L), its predictive value for CAD severity and mortality was evident at higher concentrations. This suggests that relative ferritin elevation, rather than absolute values, may be more clinically relevant in risk assessment.

3. Association of Survival Outcomes with Other Variables

Age, hypertension, diabetes, and coronary angiography (CAG) findings were significantly associated with mortality. Deceased patients were older (mean 65.1 years vs. 58.25 years in survivors, P = 0.001), supporting prior studies that have identified age as a primary risk factor for CAD-related mortality[2]. Hypertension and diabetes were also significantly associated with mortality (P = 0.001 for both), reflecting their contribution to atherosclerotic disease progression and increased cardiovascular risk.

Ferritin's strong association with mortality (P = 0.001) suggests that elevated levels may reflect systemic inflammation, iron dysregulation, and oxidative stress, all of which contribute to adverse cardiovascular outcomes[11,1]. Dual-vessel disease was more prevalent in deceased patients (50% vs. 26.7% in survivors, P = 0.011), further supporting its prognostic value[21].

Interestingly, sex and ACS vs. CCS diagnosis were not significantly associated with mortality, suggesting that ferritin's prognostic role transcends traditional CAD classifications.

This study provides novel insights into the role of ferritin as a biomarker of CAD severity and mortality. While previous studies have linked elevated ferritin levels to cardiovascular disease, our findings highlight ferritin's potential to differentiate CAD burden and predict mortality independently of traditional risk factors.

One of the most significant findings is that ferritin levels were highest in dual-vessel disease patients, rather than in triple-vessel disease. This suggests that ferritin may serve as a marker of disease progression in earlier, more modifiable stages of CAD. This has important clinical implications, as identifying high-risk patients before they develop severe, end-stage CAD could allow for earlier interventions.

Additionally, the significant correlation between ferritin and creatinine suggests a potential link between iron metabolism and renal function in CAD patients. Given the high prevalence of CKD in CAD patients, further studies exploring ferritin's role in cardio-renal syndromes could provide valuable insights into disease mechanisms and therapeutic targets.

Unlike previous studies, this research highlights ferritin's ability to distinguish between ACS and CCS, reinforcing its potential as an inflammatory marker in acute cardiovascular events. This could be particularly useful in emergency settings, where rapid risk stratification is crucial.

The findings of this study highlight ferritin's potential as a cost-effective, easily measurable biomarker for assessing CAD severity and prognosis. Its strong association with mortality suggests that incorporating ferritin into existing CAD risk models could enhance patient stratification and clinical management by identifying high-risk individuals who may benefit from closer monitoring or early intervention.

Future research should aim to further elucidate ferritin's role in cardiovascular disease through longitudinal studies that evaluate its predictive value over extended follow-up periods. Additionally, mechanistic studies are needed to explore the biological pathways linking ferritin to CAD progression, particularly its involvement in oxidative stress and inflammatory processes. Interventional trials could assess whether targeting ferritin-related oxidative stress improves cardiovascular outcomes, potentially paving the way for novel therapeutic approaches.

Given the observed sex-based differences in ferritin levels, sex-specific analyses should determine whether different ferritin cutoffs are required for risk stratification in men and women. Furthermore, considering ferritin's significant correlation with creatinine, future studies should investigate its potential role in cardio-renal syndromes, as its association with kidney dysfunction may have implications for the interplay between renal and cardiovascular health. Expanding our understanding of ferritin's pathophysiological significance could lead to its integration into routine clinical practice as a valuable biomarker for CAD management.

Conclusion

This study provides compelling evidence that serum ferritin levels are significantly associated with CAD severity and mortality, underscoring its potential as a valuable biomarker for risk stratification in CAD patients. Elevated ferritin levels correlated with greater disease burden, particularly in dual-vessel disease, and were independently predictive of mortality over a two-year follow-up. The strong association between ferritin and acute coronary syndrome (ACS) further suggests its role as an inflammatory marker in acute cardiovascular events, reinforcing its potential utility in both chronic and emergent clinical settings.

A novel and critical insight from this study is that ferritin levels were highest in patients with dual-vessel disease rather than triple-vessel disease, suggesting that ferritin may serve as a marker of CAD progression before it reaches its most severe stages. This unique finding highlights ferritin's potential for early intervention and risk modification in CAD patients, a perspective that has been largely unexplored in prior research. Additionally, the significant correlation between ferritin and creatinine levels raises important questions about the interaction between iron metabolism and renal function, emphasizing the need for further investigation into ferritin's role in cardio-renal syndromes.

Given its cost-effectiveness, ease of measurement, and strong predictive value, ferritin could be integrated into routine CAD risk assessment to improve patient stratification and guide more personalized therapeutic approaches. Future research should focus on longitudinal studies to validate ferritin's prognostic utility, mechanistic investigations into its role in atherosclerosis, and interventional trials exploring whether targeting ferritin-mediated oxidative stress can improve cardiovascular outcomes. Expanding our understanding of ferritin's role in both cardiovascular and renal health could unlock new avenues for preventing and managing CAD, ultimately improving patient outcomes.

Limitations

Firstly, although significant correlations were observed between ferritin and hemoglobin ($r = 0.147$, $P = 0.011$) and ferritin and creatinine ($r = 0.281$, $P = 0.001$), the relatively low correlation coefficients suggest that these associations may have limited clinical significance. While statistically significant, their impact on clinical decision-making remains uncertain, necessitating large-scale studies to evaluate their true prognostic value.

Secondly, the loss to follow-up rate (6.7%), though within an acceptable range, may have influenced mortality analysis. Given the nature of cardiovascular diseases, some lost-to-follow-up patients may have experienced adverse outcomes that were not recorded, potentially leading to an underestimation of true mortality rates. To minimize attrition bias in future studies, we recommend implementing home visits, electronic medical record tracking, or registry linkages to ensure a more comprehensive follow-up.

Thirdly, our study did not include inflammatory markers such as CRP/hsCRP, as the primary focus was on ferritin levels and their association with CAD severity and outcomes. However, we acknowledge that incorporating inflammatory markers could have provided additional insights into the role of systemic inflammation in ferritin elevation and its potential impact on CAD progression. Future studies integrating these markers could offer a more comprehensive understanding of the inflammatory pathways influencing CAD prognosis.

Abbreviations

1. CAD - Coronary Artery Disease
2. ACS - Acute Coronary Syndrome
3. CCS - Chronic Coronary Syndrome
4. CAG - Coronary Angiography
5. HTN - Hypertension
6. DM - Diabetes Mellitus
7. Hb - Hemoglobin
8. BP - Blood Pressure
9. HbA1c - Hemoglobin A1c
10. SPSS - Statistical Package for the Social Sciences

Ethics Compliance

We confirm that the study was conducted in compliance with ethical guidelines and that all necessary approvals and consents were obtained.

Acknowledgements

None

Funding body

None

Conflict of interests

Each author confirms that there is no conflict of interest associated with the research or the manuscript.

Final Approval

We affirm that the manuscript has been read and approved by all authors and is being submitted with our full consent.

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