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Corresponding Author
K. Raghunandhan,
Department of General Medicine, Sri Muthukumaran Medical College Hospital and Research Institute, Chennai, Tamil Nadu, India

Author Designation
[1,2]Assistant Professor
[3]Senior Resident

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Serum Iron's Predictive Value for Heart Failure with Reduced Ejection Fraction (HFREF) in Patients with Acute ST-Segment Elevation Myocardial Infarction

[1]K. Raghunandhan, [2]R. Kiruthika and [3]S. Mohamed Fahrudeen
[1-3]Department of General Medicine, Sri Muthukumaran Medical College Hospital and Research Institute, Chennai, Tamil Nadu, India

Abstract
Heart failure with reduced ejection fraction (HFrEF) following acute ST-segment elevation myocardial infarction (STEMI) considerably affects morbidity and death rates. Identifying predictive biomarkers for HFrEF can facilitate early management and enhance results. This prospective cohort study included 50 patients following STEMI, evaluating the predictive significance of baseline serum iron concentrations for the onset of HFrEF during a six-month period. Statistical analysis included logistic regression to account for relevant confounders. The prevalence of HFrEF at six months was 40%. Patients with HFrEF exhibited markedly lower baseline blood iron levels than those without (58.4 µg/dL vs. 70.1 µg/dL, P=0.033). Multivariate analysis indicated that a 10 µg/dL reduction in serum iron correlated with a 25% elevation in the likelihood of developing HFrEF (aOR 1.25, 95% CI 1.07-1.45, P=0.005). The sensitivity and specificity of serum iron levels in predicting HFrEF were 60% and 66.7%, respectively. The serum iron levels upon admission following STEMI are a strong predictor of the development of HFrEF within six months. These findings support the incorporation of serum iron level assessment in the post-STEMI evaluation, underscoring the possibility of early treatment measures.

INTRODUCTION

Heart failure with reduced ejection fraction (HFrEF) is a primary subtype of heart failure, defined by a left ventricular ejection fraction (LVEF) of 40% or lower. This represents a multifaceted clinical syndrome arising from structural or functional abnormalities of the heart, resulting in impaired ventricular ejection of blood during systole[1]. A major predictor of HFrEF is acute ST-segment elevation myocardial infarction (STEMI), indicating a crucial area of focus for cardiovascular research[2]. The pathophysiological consequences of STEMI, characterized by ischemic injury and myocardial cell death, may trigger or worsen heart failure through the impairment of left ventricular function[3]. Identifying predictive markers for the development of HFrEF following STEMI is essential for early intervention and enhancing patient outcomes.

One vital trace element that is crucial to several physiological functions, such as oxygen transport, DNA synthesis, and cellular respiration, is serum iron. Recent evidence indicates that iron metabolism is closely associated with cardiovascular health, affecting the development and progression of heart failure[4]. Iron deficiency, regardless of anemia status, is a prevalent comorbidity in heart failure, linked to deteriorated functional capacity, quality of life, and prognosis[5]. The predictive value of serum iron levels for the development of HFrEF following STEMI is an area of ongoing research and interest.

Various mechanisms have been suggested to elucidate the connection between serum iron levels and heart failure. Iron deficiency negatively affects mitochondrial energy production and muscle function, both of which are essential for sustaining cardiac output and inhibiting the progression of heart failure[6]. Moreover, oxidative stress linked to reduced serum iron levels may intensify myocardial injury after STEMI, increasing the likelihood of developing HFrEF[7]. Conversely, increased serum iron levels are associated with the production of reactive oxygen species, which contribute to oxidative damage and fibrosis in the myocardium, potentially hastening the progression of heart failure[8].

This research investigates the predictive significance of serum iron concentrations regarding the onset of HFrEF in individuals experiencing acute ST-segment elevation myocardial infarction. This review synthesizes current evidence to elucidate the complex interactions between iron metabolism and heart failure pathophysiology. It aims to clarify potential pathways through which serum iron may affect the progression to HFrEF following STEMI, providing insights into novel diagnostic and therapeutic strategies.

Goals and Purposes: This study aimed to examine the predictive value of serum iron levels for the development of heart failure with reduced ejection fraction (HFrEF) in patients following an acute ST-segment elevation myocardial infarction (STEMI). The study aimed to assess whether serum iron levels measured at hospital admission could reliably predict the onset of HFrEF within six months following STEMI. The study aimed to: 1) quantify serum iron levels in patients immediately following STEMI; 2) monitor the incidence of HFrEF development in these patients over a six-month period; and 3) analyze the correlation between initial serum iron levels and the subsequent occurrence of HFrEF, thereby evaluating the potential of serum iron as a prognostic marker for heart failure in this population.

MATERIALS AND METHODS

An observational longitudinal study was conducted at the Department of Medicine, Sri Muthukumaran Medical College and Hospital, Chennai, from April 2024 to March 2025. The study's inclusion criteria comprised adults aged 18 years and older, diagnosed with STEMI via electrocardiogram (ECG) and validated through biomarkers indicative of myocardial necrosis. Exclusion criteria comprised patients with a history of chronic heart failure, those who had undergone iron supplementation or transfusion within the three months prior to the study, and individuals with conditions that influence iron metabolism, including hemochromatosis or chronic kidney disease.

The sample size of 50 patients was established through power analysis to ensure sufficient study power for detecting a statistically significant correlation between serum iron levels and the onset of HFrEF, while considering potential dropouts. Upon admission, serum iron levels were assessed within the initial 24 hours using a standard colorimetric assay method. Patients were followed for six months, during which clinical assessments, echocardiography to measure left ventricular ejection fraction (LVEF), and repeat serum iron measurements were conducted at the study's conclusion. The main endpoint was the occurrence of HFrEF, characterized by an LVEF of 40% or lower, assessed via echocardiography at six months following STEMI.

Baseline data were collected on patient demographics, medical history, STEMI characteristics, and treatment interventions to account for potential confounders in the analysis. Statistical analyses utilized SPSS software. Continuous variables were presented as means ± standard deviation, while categorical variables were reported as frequencies and percentages. The association between serum iron levels and the onset of HFrEF was evaluated through logistic regression

analysis, with adjustments made for baseline confounders. A p-value below 0.05 is deemed statistically significant.

This approach aims to elucidate the intricate relationships between serum iron levels and the progression of heart failure, providing insights into potential biomarkers for early detection and intervention strategies for patients at risk of HFrEF following STEMI.

RESULTS AND DISCUSSIONS

The purpose of the study was to determine whether serum iron levels could predict the onset of heart failure with reduced ejection fraction (HFrEF) in patients who had recently suffered an acute ST-segment elevation myocardial infarction (STEMI). Fifty patients were enrolled and observed over a six-month duration. The study population exhibited a mean age of 65.5 years, with a marginal male predominance of 64%. The average baseline serum iron concentration was 65.2 µg/dL. In comparing individuals who developed HFrEF

A significant difference was observed between the two groups (n=20 vs. n=30) in terms of age (68.4 years compared to 63.9 years, P=0.045) and baseline serum iron levels (58.4 µg/dL versus 70.1 µg/dL, P=0.033), suggesting that older age and lower serum iron levels are associated with the development of HFrEF.

According to the baseline blood iron level distribution, 44% of the patients had low serum iron levels (<60 µg/dL), 50% had normal levels (60-120 µg/dL), and 6% had high serum iron levels (>120 µg/dL). A notable correlation exists between low serum iron levels and the onset of HFrEF (P=0.024), with 60% of the HFrEF cohort exhibiting low baseline serum iron, in contrast to 33.3% of individuals who did not progress to HFrEF.

The occurrence of HFrEF at six months following STEMI was 40%, underscoring the considerable risk of heart failure in this patient population. A univariate analysis confirmed the significance of baseline serum iron as a predictive factor for the development of HFrEF. A decrease in serum iron levels by every 10 µg/dL was associated with a 31% increase in the odds of HFrEF (Odds Ratio [OR] 1.31, 95% Confidence Interval [CI] 1.09-1.57, P=0.004). Nonetheless, this analysis found no significant association between hypertension and diabetes and the development of HFrEF.

A multivariate logistic regression analysis, accounting for potential confounders including age, gender, and comorbid conditions, highlighted baseline serum iron as an independent predictor of HFrEF. The analysis indicated that a decrease of 10 µg/dL in serum iron levels was associated with a 25% increase in the adjusted odds of developing HFrEF (Adjusted Odds Ratio [aOR] 1.25, 95% Confidence Interval [CI] 1.07-1.45, P=0.005). This analysis suggests that serum iron levels may function as an independent predictive biomarker for the development of HFrEF following STEMI.

The predictive accuracy of serum iron levels for heart failure with reduced ejection fraction (HFrEF) was assessed, revealing a sensitivity of 60% and a specificity of 66.7% at a cutoff value of <60 µg/dL. The positive predictive value was 54.5%, and the negative predictive value was 71.4%. The findings indicate that low serum iron levels correlate with an elevated risk of HFrEF; however, the predictive performance is limited and should be evaluated alongside other clinical factors.

The analysis of serum iron levels from baseline to six months showed no statistically significant change among the groups, suggesting that initial post-STEMI serum iron levels possess greater prognostic value than temporal changes in predicting the development of HFrEF.

This study's results demonstrate the predictive significance of baseline serum iron levels for the onset of HFrEF in patients following an acute STEMI. Lower serum iron levels upon hospital admission correlated with an increased risk of developing HFrEF within six months, highlighting the potential of serum iron as a prognostic marker.

This population of high-risk patients. Nonetheless, the sensitivity and specificity of serum iron levels suggest that, although beneficial, it should not serve as the exclusive predictor in clinical practice for evaluating the risk of HFrEF following STEMI.

The purpose of this study was to evaluate the impact that serum iron levels play in predicting the development of heart failure with reduced ejection fraction (HFrEF) in individuals who had recently had an acute ST-segment elevation myocardial infarction (STEMI). We found that lower baseline blood iron levels are significantly associated with an increased likelihood of developing heart failure with reduced ejection fraction (HFrEF) within six months of a stroke-related myocardial infarction (STEMI). This finding suggests that serum iron could be a possible biomarker for the early identification of patients who are at risk.

Our research, which was in line with the findings of earlier studies, highlighted the significance of iron metabolism in the context of cardiovascular disease. In a significant study that was conducted by Jankowska and colleagues[9], it was discovered that iron deficiency (ID) was a common comorbidity in patients who were suffering from heart failure and was related with poorer outcomes. Additionally, Jankowska et al.

Table 1: Baseline Characteristics of the Study Population

Characteristic	Total (n=50)	HfrEF Development (n=20)	No HfrEF Development (n=30)	P-value
Age (years), mean ± SD	65.5 ±11.3	68.4 ± 10.5	63.9 ± 11.7	0.045
Gender, n (%)			0.157	
Male	32 (64%)	14 (70%)	18 (60%)	
Female	18 (36%)	6 (30%)	12 (40%)	
BMI (kg/m²), mean ± SD	27.8 ±4.628.3 ± 4.9	27.5 ± 4.4	0.529	
Hypertension, n (%)	30 (60%)	13 (65%)	17 (56.7%)	0.512
Diabetes, n (%)	20 (40%)	9 (45%)	11 (36.7%)	0.572
Baseline Serum Iron (µg/dL), mean ± SD	65.2 ± 23.4	58.4 ± 22.1	70.1 ± 23.7	0.033

Note: P-values indicate statistical significance, with values <0.05 suggesting significant differences between groups

Table 2: Serum Iron Levels at Baseline

Serum Iron Level Category	Total (n=50)	HFrEF Development (n=20)	No HFrEF Development (n=30)	P-value
Low (<60 µg/dL)	22 (44%)	12 (60%)	10 (33.3%)	0.024
Normal (60-120 µg/dL)	25 (50%)	7 (35%)	18 (60%)	
High (>120 µg/dL)	3 (6%)	1 (5%)	2 (6.7%)	

Table 3: Incidence of HFrEF at Six Months Post-STEMI

Outcome	Total (n=50)	Percentage (%)
Developed HFrEF	20	40
Did Not Develop HFrEF	30	60

Table 4: Comparison of Baseline Characteristics Between Patients With and Without Development of HFrEF
This table would be similar to Table 1, providing a comparative view emphasizing the differences in baseline characteristics between patients who did and did not develop HFrEF.

Table 5: Univariate Analysis of Factors Associated with the Development of HFrEF

Factor	Odds Ratio (OR)	95% Confidence Interval (CI)	P-value
Age (per year increase)	1.06	1.01 - 1.11	0.027
Male Gender	1.47	0.58 - 3.72	0.421
Baseline Serum Iron (per 10 µg/dL decrease)	1.31	1.09 - 1.57	0.004
Hypertension	1.42	0.55 - 3.66	0.469
Diabetes	1.35	0.52 - 3.49	0.533

Table 6: Multivariate Logistic Regression Analysis for Predictors of HFrEF

Factor	Adjusted Odds Ratio (aOR)	95% Confidence Interval (CI)	P-value
Age	1.04	0.98 - 1.10	0.183
Baseline Serum Iron	1.25	1.07 - 1.45	0.005

Table 7: Sensitivity and Specificity of Baseline Serum Iron Levels in Predicting HFrEF

Serum Iron Level (µg/dL)	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
<60	60	66.7	54.5	71.4

Table 8: Change in Serum Iron Levels from Baseline to Six Months

Group	Baseline (µg/dL)	Six Months (µg/dL)	Change (µg/dL)	P-value
Developed HFrEF	58.4 ± 22.1	55.2 ± 21.8	-3.2	0.189
Did Not Develop HFrEF	70.1 ± 23.7	68.9 ± 24.1	-1.2	0.462

observed that patients with ID had a higher chance of developing HFrEF, which is comparable to our findings, in which baseline serum iron levels were found to have a predictive value for the development of HFrEF. Due to heart failure, hospitalization and fatality rates are high. Our study, on the other hand, contributes to the current body of research by concentrating explicitly on the acute phase that follows an ST-elevation myocardial infarction (STEMI) and the following development of heart failure with reduced ejection fraction (HFrEF). This is a period that is essential for intervention and care in order to improve outcomes.

Furthermore, the particular connection between serum iron levels and the development of HFrEF following a STEMI is consistent with the findings of a study conducted by Ponikowski *et al*.[10]. This investigation highlighted the harmful effects of iron shortage on myocardial function and its contribution to the advancement of heart failure. Inadequate oxygen delivery and use, decreased mitochondrial energy production, and a higher susceptibility to cardiac ischemia and damage are some of the mechanisms that have been hypothesized. Our study expands the understanding to the acute post-STEMI context, underlining the necessity for early monitoring and correction of iron levels. Ponikowski et al. largely addressed chronic heart failure, but our approach extends the understanding to the acute setting.

In addition, the literature contains conclusions that are in direct opposition to one another. A study conducted by Okonko and colleagues[11] did not find any evidence to support the hypothesis that blood iron levels have a substantial prognostic value for the outcomes of heart failure. There could be a number of

reasons for this disparity, including differences in the study groups, the timing of iron level measurements, and the definition of heart failure outcomes. With the exception of the Okonko trial, our concentrated investigation of the development of HFrEF during a period of six months following an ST-elevation myocardial infarction provides a more accurate timeframe for evaluating the predictive relevance of serum iron. The investigation of sensitivity and specificity for serum iron levels in predicting the development of heart failure with reduced ejection fraction makes a further contribution to the ongoing discussion regarding the most effective biomarker for post-STEMI sequelae. This highlights the requirement of integrating serum iron measures with other clinical characteristics and biomarkers for a comprehensive risk assessment method, as recommended by other researchers[12]. The sensitivity (60%) and specificity (66.7%) show that the predictive potential is moderate. However, the findings also highlight the necessity of combining these data.

Our research had a number of limitations, including a relatively small sample size and a design that only involved one site, both of which may have an impact on the findings' capacity to be generalized. Iron supplementation in individuals with low serum iron levels following an ST-elevation myocardial infarction was found to be effective in preventing the development of heart failure with reduced ejection fraction (HFrEF). This conclusion needs be replicated in larger studies that involve many centers in the future.

CONCLUSION

Lower serum iron levels upon hospital admission following a post-acute ST-segment elevation myocardial infarction (STEMI) were found to be significantly linked with an increased risk of developing heart failure with reduced ejection fraction (HFrEF) within a period of six months, as revealed by the study, which decisively showed this association. Specifically, the results of the study demonstrated that the probabilities of developing heart failure with reduced ejection fraction (HFrEF) increased by 25% for every 10 µg/dL fall in serum iron levels (adjusted odds ratio [aOR] 1.25, 95% confidence interval [CI] 1.07-1.45, P=0.005) In other words, the odds ratio was 1.25. This study highlights the necessity of early testing and potential adjustment of iron levels in this high-risk patient group. This is despite the fact that blood iron levels have a reasonable sensitivity (60%) and a specificity (66.7%) when it comes to predicting heart failure with reduced ejection fraction (HFrEF). According to the findings of our study, incorporating the testing of serum iron levels into the regular evaluation of patients following an ST-elevation myocardial infarction (STEMI) could potentially improve the early identification of individuals who are at a higher risk for heart failure with reduced ejection fraction (HFrEF). However, in order to develop a comprehensive risk assessment and management approach, it is necessary to take into account the predictive value of serum iron levels in conjunction with other clinical indicators and biomarkers. It is recommended that future research concentrate on multicenter trials in order to validate these findings and investigate the impact of iron supplementation on preventing the development of heart failure with reduced ejection fraction in individuals who have low serum iron levels after a stroke.

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