Nigerian Medical Journal
NIGERIA MEDICAL ASSOCIATION
Print ISSN 0300-1652, E-ISSN 2229-774X

Original Article

Clinical Characteristics of Iron Deficiency in Patients with Chronic Heart Failure at a Major Referral Centre in Southern Nigeria

***Aisha O Ajala[1], Boma Oyan[2], Sotonye Dodiyi-Manuel[1], Edeogu Julius[1], Chineme Ekeh[1], Ikejiofor Prudence[1], Maclean Akpa[1]**

[1] Department of Internal Medicine, University of Port Harcourt Teaching Hospital, Rivers State, Nigeria
[2] Department of Internal Medicine, Rivers State University Teaching Hospital, Port Harcourt, Nigeria

Abstract

Background. Iron deficiency (ID) is a common comorbidity in patients with heart failure (HF) and is associated with reduced functional capacity, diminished quality of life, and increased mortality. This study aimed to determine the prevalence of ID and its clinical characteristics.
Methods. This descriptive cross-sectional study involved 136 patients with chronic HF at the University of Port-Harcourt Teaching Hospital. Informed consent was obtained. Blood samples were collected for a full blood count and serum ferritin analysis, while echocardiography was performed for all study participants.
Results. The mean age was 59.2±14.9years, with 51% being males. Notably, 41% of the patients exhibited low ferritin levels (≤100ng/ml), indicating the presence of ID. Among patients with ID, 19.7% had anemia. Although patients aged 65 years and above tended to have lower ferritin levels, this difference was not statistically significant (p=0.141). In contrast, statistically significant associations were observed between ID and gender, with females being more susceptible to iron deficiency (p=0.036). However, normal levels of N-Terminal-prohormone-Brain Natriuretic Peptide (NT-Pro-BNP) and high sensitivity – C Reactive Protein(hs-CRP) were significantly linked to ID (p=0.001 & p=0.004, respectively), and there was no significant correlation between ejection fraction and ferritin levels.
Conclusion. Iron deficiency, with or without anemia, is prevalent in chronic heart failure patients, particularly among females and even in persons who have normal levels of markers of HF severity such as hs-CRP and NT-pro-BNP. Regular screening for ID is vital to identify and manage this comorbidity, as iron correction can lead to improved functional capacity and reduced morbidity and mortality associated with heart failure.

Keywords. Iron-deficiency, heart failure, anemia, ferritin, severity, NT-Pro-BNP, hs-CRP

***Correspondence:** Dr. Aisha O. Ajala, Department of Internal Medicine, University of Port Harcourt Teaching Hospital. Email: ajalabunmi@gmail.com

How to Cite: Ajala AO, Oyan B, Dodiyi-Manuel S, Julius E, Ekeh C, Prudence I, Akpa M. Clinical Characteristics of Iron Deficiency in Patients with Chronic Heart Failure at a Major Referral Centre in Southern Nigeria. Niger Med J 2026; 67 (2): 3284-3298. http://doi.org10./71480/nmj.v67i2.1040

Quick Response Code:

Introduction

Chronic heart failure (CHF) remains a significant global health challenge associated with substantial morbidity, mortality, and economic burden, particularly in low- and middle-income countries (LMICs) such as Nigeria. [1] It is estimated to have a global prevalence of about 37.7million, and accounts for about 9 to 33% of hospital cardiovascular-related mortalities in Africa. [2,3]

The pathophysiology of CHF is complex, involving neurohormonal activation, systemic inflammation, and metabolic dysregulation, all of which contribute to disease progression and poor quality of life. [4] Among the myriad complications associated with CHF, iron deficiency (ID) has emerged as a critical yet under-recognized comorbidity that exacerbates clinical outcomes and complicates management. Iron deficiency in CHF is multifactorial in origin, and arises from causes such as reduced dietary intake, impaired gastrointestinal absorption, chronic blood loss, and inflammation-driven sequestration of iron. It is defined clinically by low serum ferritin levels (<100 µg/L) or a combination of ferritin levels between 100–300 µg/L with reduced transferrin saturation (<20%). Notably, ID in CHF can occur with or without anemia, and its presence is associated with reduced exercise capacity, worsening symptoms, and increased risk of hospitalization and mortality. [5,6]

The prevalence of ID in CHF patients is estimated to range from 37% to over 70% globally, though data specific to sub-Saharan African populations, including Nigeria, remain sparse. [7,8] This knowledge gap is particularly concerning given the unique demographic, socioeconomic, and environmental factors in this region that may influence the epidemiology and clinical presentation of ID in CHF.

The significance of ID in CHF extends beyond its role as a comorbidity; it is a modifiable risk factor with proven therapeutic implications. Intravenous iron therapy, such as ferric carboxymaltose, has been shown to improve functional capacity, quality of life, and hospitalization rates in CHF patients with ID, as demonstrated in landmark trials like the Ferinject Assessment in Patients with Iron Deficiency and Chronic Heart Failure (FAIR-HF) and the Ferric Carboxymaltose evaluation on performance in patients with Iron deficiency in combination with chronic Heart Failure (CONFIRM-HF) trials. [9,10] However, these studies primarily involved populations from high-income countries, and their findings may not be directly applicable to African populations due to differences in healthcare infrastructure, patient demographics, and disease etiology. In Nigeria, where access to advanced diagnostics and treatments is often limited, the clinical characteristics of ID in CHF patients remain poorly characterized, which ultimately hinder the development of context-specific interventions.

To this end, this study aims to investigate the clinical characteristics of iron deficiency in patients with chronic heart failure attending a major referral center in Southern Nigeria.

Methodology

Study Design and Setting: This was a hospital-based, cross-sectional study conducted at the University of Port Harcourt Teaching Hospital (UPTH), a major tertiary healthcare center located in South-South Nigeria. The study was carried out in the Heart Failure and Cardiology Clinic of the department of Internal Medicine, which serves a diverse population across several states in the Niger Delta region. The clinic manages a wide range of cardiovascular diseases, including chronic heart failure, and provides both follow-up and specialist care.

Study Population and Sampling: The study population comprised adult patients diagnosed with heart failure who were attending follow-up appointments at the cardiology outpatient clinic. The minimum sample size was estimated using a validated formula[11] (Cochran formula for proportion): $n_0 = Z^2pq/e^2$, where Z = 1.96 (95% confidence level), p = 0.34 (prevalence of iron deficiency among Nigerian chronic

heart failure patients, as reported by Amaechi et al. **[12]**), q = 0.66, and e = 0.10 (10% margin of error, appropriate for a single-centre descriptive prevalence study). This yielded a minimum required sample size of 87. Eligible participants were then recruited consecutively over a six-month period to ensure inclusion of all patients meeting the eligibility criteria within the study duration. A total of 136 patients were enrolled on the study period.

The study included patients aged 18 years and above with a confirmed clinical diagnosis of heart failure based on the Framingham criteria and echocardiographic evidence of systolic or diastolic dysfunction. Patients were required to be stable, ambulatory, and attending the clinic for routine follow-up. Exclusion criteria included individuals with acute decompensated heart failure requiring hospitalization, known active infection or malignancy, recent blood transfusion (within the last three months), or any condition known to significantly affect iron metabolism such as chronic kidney disease on dialysis or chronic inflammatory disorders.

Ethical Considerations: Ethical approval for the study was obtained from the Ethics and Research Committee of the University of Port Harcourt Teaching Hospital. (UPTH/ADM/90/S. II/VOL. XI/1479) Informed written consent was obtained from each participant prior to enrolment. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki.

Data Collection: Data were collected through interviewer-administered structured questionnaires and review of clinical records. Sociodemographic data collected included age, sex, occupation, level of education, and marital status. Clinical data included New York Heart Association (NYHA) functional class, comorbidities, ongoing medications, and prior hospitalizations. Anthropometric measurements (weight, height, and body mass index) were also obtained.

Venous blood samples were drawn from each participant under aseptic conditions for full blood count, serum ferritin, high-sensitivity C-reactive protein (hs-CRP), and N-terminal pro-B-type natriuretic peptide (NT-pro-BNP) levels. Iron deficiency was defined according to the European Society of Cardiology (ESC) criteria for patients with chronic heart failure as serum ferritin <100 ng/mL. [13] Anaemia was defined as a haemoglobin concentration <11g/dl, microcytosis as a low mean corpuscular volume (MCV) less than 80.0 fL and hypochromia as a low mean corpuscular haemoglobin concentration (MCHC) less than 32.0 g/dl. [14] Elevated hs-CRP levels were defined as levels >3 mg/l, [15] and NT-Pro-BNP levels ≥ 125 pg/ml were categorized as elevated. [16] All laboratory investigations were conducted at the UPTH central laboratory, and standardized operating procedures were followed to ensure reliability and reproducibility of results.

Echocardiography, adhering to the Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults, was performed for all study participants. The ejection fraction was assessed using the biplane Simpsons method. Heart failure with preserved ejection fraction (HFpEF) was defined as an ejection fraction (EF) of ≥ 50, whereas heart failure with reduced ejection fraction (HFrEF) was defined as an EF of < 50%. [17,18]

Data Management and Statistical Analysis: The collected data were entered into the Microsoft excel spreadsheet, and data cleaning was also performed using the same software. Data analysis was performed using the Statistical Package for Social Sciences (SPSS) version 25.0 (IBM Corporation, Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. The prevalence of iron deficiency was determined, and its association with clinical and demographic variables was examined. Comparisons between categorical variables were made using the Chi-square test and correlation between ejection fraction and iron levels was done using Spearman's test.

Results

A total of 136 patients with heart failure were enrolled in the study. The mean age was 59.2±14.9years, ranging from 25 to 92years and most patients were middle-aged (45–64 years) (43.4%). The cohort included 66 females (48.5%) and 70 males (51.5%) and a significant proportion (33.8%) had attained tertiary education. Over half of the participants were engaged in business activities.

Hypertension was the most prevalent comorbidity, identified in 102 patients (75.0%), followed by diabetes mellitus in 21 patients (15.4%). Table 1 summarizes the sociodemographic characteristics of the study population

Table 1. Sociodemographic characteristics of patients in the study

Variables	Frequency (Percentage) n=136
Age groups	
Young adults (<44 years)	26(19.1)
Middle aged (45-64 years)	59(43.4)
Elderly (≥ 65 years)	51(37.5)
Sex	
Female	66(48.5)
Male	70(51.5)
Marital status	
Married	123(89.7)
Single	3(2.2)
Widowed/divorced	10(7.4)
Level of Education	
None	5(3.7)
Primary	24(17.6)
Secondary	61(44.9)
Tertiary	46(33.8)
Occupation	
Artisan	3(2.2)
Business	73(53.7)
Civil servant	26(19.1)
Farmer	5(3.7)

Professional	9(6.6)
Retired	20(14.7)

As shown in Table 2, hypertensive heart disease was the most common etiology of heart failure, accounting for 70 patients (50.7%). This was followed by dilated cardiomyopathy (20.3%) and valvular heart disease (15.2%). Less common causes included rheumatic heart disease (9.4%), restrictive cardiomyopathy (2.2%), and isolated diastolic dysfunction (2.2%). With regards to the phenotypes of heart failure, 58.1% of patients were diagnosed with heart failure with reduced ejection fraction (HFrEF), while 41.9% had preserved ejection fraction (HFpEF). Just over half of the participants (69 persons) were in New York Heart Association functional class 2.

Table 2. Clinical characteristics of heart failure among participants

Variables	Frequency (n=136)	Percentage
Aetiology of heart failure		
Dilated cardiomyopathy	28	20.3
Diastolic dysfunction	3	2.2
Hypertensive heart disease	70	50.7
Restrictive cardiomyopathy	3	2.2
Rheumatic heart disease	11	9.4
Valvular heart disease	21	15.2
Stage of heart failure		
HFrEF	79	58.1
HFpEF	57	41.9
New York Heart Association class		
Class 1	28	20.6
Class 2	69	50.7
Class 3	34	25.0
Class 4	5	3.8

Key: HFrEF=heart failure with reduced ejection fraction, HFpEF=heart failure with preserved ejection fraction

The mean BMI of the study participants was 26.3±5.1kg/m². The mean systolic and diastolic blood pressures as well as the pulse rate were within normal ranges as shown in table 3.

Microcytosis (low MCV) was observed in 21 (15.4%) patients, 87 (64.0%) patients had low MCHC values, and 27 (19.9%) patients were anemic. The mean haemoglobin level, mean corpuscular volume (MCV) and mean corpuscular haemoglobin concentration (MCHC) are shown in table 3.

The median serum ferritin level was 137.5 ng/mL (IQR=79.3 to 137.5 ng/mL) and 56(41.2%) had reduced ferritin levels as shown in figure 1. N-terminal pro-B-type Natriuretic Peptide (NT-proBNP) was increased in 22(16.2%) persons while high sensitivity C-reactive peptide was increased in 91(66.9%) persons.

Table 3. Characteristics of Study Participants

Variable	Mean ± SD	Range
Clinical characteristics		
Body mass index (kg/m²)	26.3 ± 5.1	18.0 – 45.2
Systolic blood pressure (mmHg)	122.8 ± 17.9	80 – 170
Diastolic blood pressure (mmHg)	77.1 ± 11.7	50 – 110
Pulse rate (bpm)	84.4 ± 17.4	42 – 140
Hematologic characteristics		
Ferritin (ng/mL) *	137.5	79.3 – 137.5
Hemoglobin (g/dL)	12.6 ± 2.3	7.3 – 19.6
Mean corpuscular volume (fL)	86.2 ± 7.5	66.2 – 112.5
Mean corpuscular hemoglobin concentration (g/dL)	24.4 ± 1.6	24.4 – 34.3
Biochemical characteristics		
NT-proBNP (ng/ml) *	67.0	44.0 – 90.0
Hs C reactive peptide (mg/l)	4.73 ± 3.0	0.5 – 11.2

Key: *= Median (interquartile range), NT-proBNP =N-terminal pro-B-type Natriuretic Peptide, hs= high sensitivity

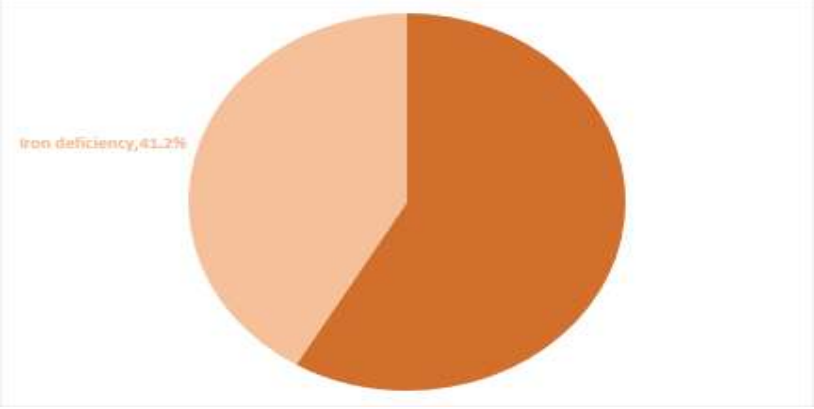

Figure 1. Prevalence of Iron deficiency in the study population

Characteristics of patients with and without Iron Deficiency

Table 4 compares the socio-demographic and clinical characteristics of patients with low ferritin (iron deficiency) and those with normal ferritin levels. The prevalence of iron deficiency did not significantly differ across age categories (p = 0.141), although it was more common among elderly patients (51.0%) compared to young adults (42.3%). Sex distribution however, showed a statistically significant association, with females representing a higher proportion of those with iron deficiency (60.7%) compared to males (39.3%), p = 0.036. Educational status, occupational grouping, and marital status did not demonstrate significant associations with ferritin levels.

Among clinical variables, patients with heart failure with reduced ejection fraction (HFrEF) comprised a slightly larger proportion of the iron-deficient group (44.3%) relative to those with preserved ejection fraction (HFpEF), although this difference was not statistically significant (p = 0.544). NYHA functional class distribution was similar between both groups (p = 0.553).

No significant differences were observed in the prevalence of comorbid hypertension, diabetes, or anemia between patients with and without iron deficiency. However, significant differences were found in relation to N-terminal pro-B-type Natriuretic Peptide (NT-proBNP) and high sensitivity C-reactive protein (hs-CRP) levels. Elevated NT-proBNP was significantly more frequent among the patients with normal ferritin levels (46.5% vs 13.6%, p = 0.004). Similarly, elevated hs-CRP levels were observed in 76.5% of patients with normal ferritin, compared to 24.2% among those with low ferritin, and this finding was statistically significant (p < 0.001).

Table 4. Characteristics of patients with and without Iron deficiency

Variable	Low ferritin frequency (%) n=56	Normal ferritin frequency (%) n=80	Statistic	p-value
Age groups				
Young adults (<44 years)	11(42.3)	15(57.7)	3.999	0.141
Middle-aged (45-64 years)	19(32.2)	40(57.8)		
Elderly (≥ 65 years)	26(51.0)	25(49.0)		
Sex				
Female	34(60.7)	33(41.2)	4.993	0.036*
Male	22(39.3)	47(58.8)		
Level of Education				
None	2(40.0)	3(60.0)	1.503	0.682
Primary	10(41.7)	14(58.3)		
Secondary	22(36.1)	39(63.9)		
Tertiary	22(47.8)	24(52.2)		
Occupation				

Artisan	1(33.3)	2(66.6)	8.243	0.143
Business	24(32.9)	49(67.1)		
Civil servant	15(57.7)	11(42.3)		
Farmer	4(80.0)	1(20.0)		
Professional	4(44.4)	5(55.6)		
Retired	8(40.0)	12(60.0)		
Marital Status				
Married	49(39.8)	74(60.2)	1.739	0.449
Single	1(33.3)	2(66.7)		
Widowed/divorced	6(60.0)	4(44.0)		
Stage of heart failure				
HFpEF	21(36.8)	36(63.2)	1.223	0.544
HFrEF	35(44.3)	44(55.7)		
NYHA class				
Class 1	10(35.7)	18(64.3)	2.099	0.553
Class 2	31(44.9)	38(55.1)		
Class 3	12(35.3)	22(64.7)		
Class 4	3(60.0)	2(40.0)		
History of hypertension			1.457	0.227
Yes	45(44.1)	57(55.9)		
No	11(32.4)	23(67.6)		
History of diabetes			0.029	0.524
Yes	9(42.9)	12(57.1)		
No	47(40.9)	68(59.1)		
Anaemia			1.003	0.569
Present	11(40.7)	16(59.3)		
Absent	45(41.3)	64(58.7)		
NT pro BNP			8.218	0.004*
Normal levels	53(46.5)	61(53.5)		
Increased	3(13.6)	19(86.4)		

Hs C reactive protein			32.82	<0.001*
Normal levels	34(75.6)	11(24.4)		
Increased	22(24.2)	69(75.8)		

Key: *=statistically significant, NYHA=New York Heart Association, HFrEF=heart failure with reduced ejection fraction, HFpEF=heart failure with preserved ejection fraction, NT-proBNP =N-terminal pro-B-type Natriuretic Peptide

Relationship between ejection fraction and iron levels in patients with heart failure

No linear relationship could be established between the ejection fractions and ferritin levels in patients with heart failure in this study.

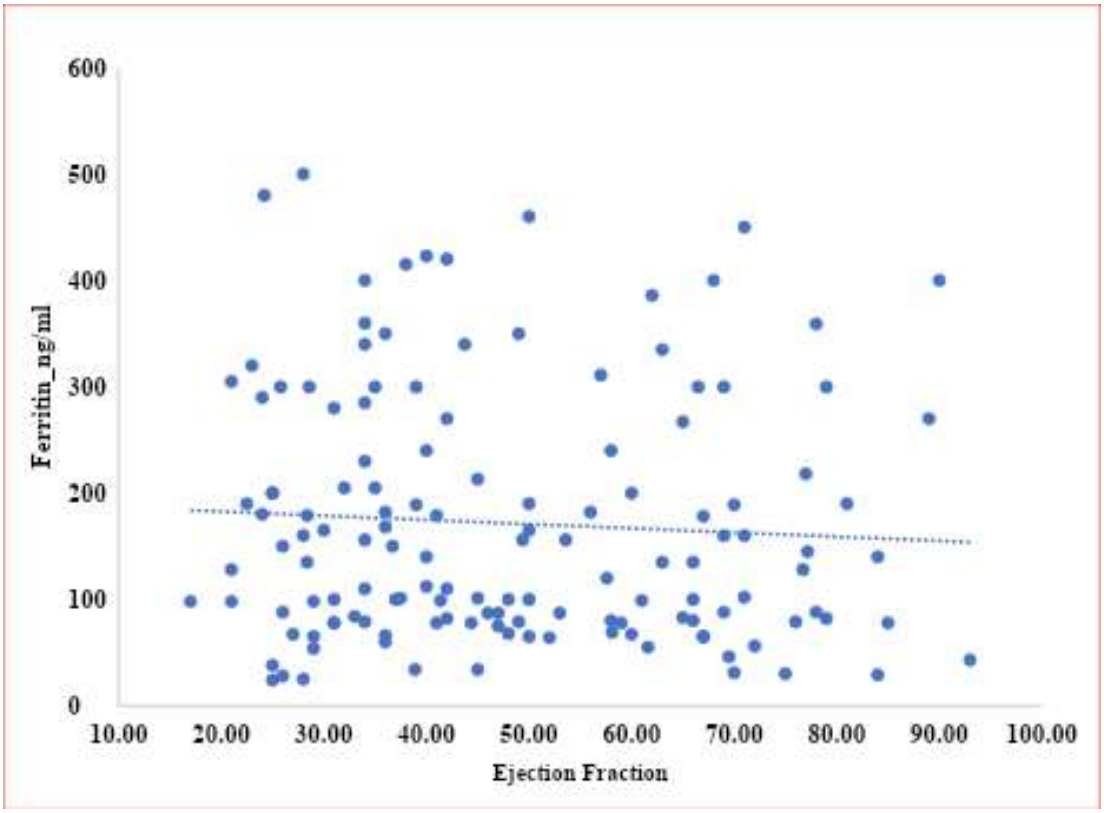

Fig 2. Correlation between ejection fraction and iron levels in heart failure patients (Spearman's rho=-0.084; p=0.328)

As shown in Table 5 below, binary logistic regression analysis identified three independent predictors of iron deficiency status. Female sex was associated with approximately 2.6 times the odds of iron deficiency compared with male sex (adjusted OR 2.60; 95% CI 1.134–5.977; p = 0.024). Elevated hs-CRP was independently and inversely associated with iron deficiency (adjusted OR 0.102; 95% CI 0.042–0.248; p <0.001), as was elevated NT-proBNP (adjusted OR 0.192; 95% CI 0.048–0.761; p = 0.019), indicating that patients with elevated inflammatory and natriuretic markers had significantly lower odds of iron deficiency after adjustment.

Table 5: Independent predictors of iron deficiency in patients with chronic heart failure

Variable	Adjusted odds ratio	95% CI	p value
Sex			
Male	Reference	1.134-5.977	0.024
Female	2.60		
Hs C reactive protein			
Normal levels	Reference	0.042-0.248	<0.001
Increased	0.102		
NT pro BNP			
Normal levels	Reference	0.048-0.761	0.019
Increased	0.192		

Key: OR = odds ratio; CI = confidence interval; hs-CRP = high-sensitivity C-reactive protein; NT-proBNP = N-terminal pro-B-type natriuretic peptide. Adjusted OR for elevated hs-CRP and elevated NT-proBNP represent the odds of iron deficiency compared to the reference category (normal levels). * statistically significant ($p < 0.05$). Binary logistic regression model adjusted for sex, hs-CRP status, and NT-proBNP status.

Discussion

Iron deficiency is a well-recognized comorbidity in chronic heart failure and has been linked to adverse clinical outcomes, including reduced exercise capacity, impaired quality of life, and increased mortality, irrespective of the presence of anaemia.[19] This study contributes region-specific evidence from sub-Saharan Africa, revealing that iron deficiency is prevalent among heart failure patients and is associated with distinct demographic and biochemical profiles.

The overall prevalence of iron deficiency in our cohort was 41.2%, with 56 people having iron deficiency anemia. These figures are consistent with the broad range reported in international literature (33.9%–74%) and comparable to previous studies from sub-Saharan Africa, including the THESUS-HF registry and other regional cohorts. [14, 20, 12, 21, 22]

A noteworthy feature of this study was the high prevalence of ID in the absence of anemia. Only one-fifth of iron-deficient patients had haemoglobin levels consistent with anaemia, challenging the traditional assumption that low haemoglobin is a surrogate marker of iron status in CHF. This finding aligns with evolving evidence that functional iron deficiency, characterized by inadequate iron availability despite normal or elevated ferritin, can exist independently and impair oxygen delivery, mitochondrial metabolism, and muscular function. [5] This highlights the inadequacy of haemoglobin-based screening as the sole criterion for iron assessment in this population.

Evidently, gender-specific patterns were observed in this study, with females exhibiting a significantly higher burden of iron deficiency in the univariate analysis (60.7% vs. 39.3%). On binary logistic regression,

female sex remained an independent predictor of iron deficiency (adjusted OR 2.60; 95% CI 1.134–5.977; p = 0.024), after adjustment for inflammatory and neurohormonal markers (Table 5). This gender disparity is consistent with findings from previous studies in comparable populations. [23,24] The mechanisms underlying this association were not directly evaluated in the present study; however, published literature has proposed lower baseline iron stores, menstrual blood loss in premenopausal women, and hormonal influences on hepcidin regulation as potential contributors. [23,24] The persistence of this association on multivariate analysis supports the value of sex-stratified screening for iron deficiency in clinical practice.

A particularly striking and counterintuitive finding was the inverse association between elevated inflammatory markers and iron deficiency status. Both elevated hs-CRP (76.5% vs. 24.2%; p < 0.001) and elevated NT-proBNP (46.5% vs. 13.6%; p = 0.004) were significantly more common among patients with normal ferritin levels than among those with iron deficiency. On binary logistic regression, the presence of elevated hs-CRP was independently and inversely associated with iron deficiency (adjusted OR 0.102; 95% CI 0.042–0.248; p < 0.001), and elevated NT-proBNP similarly retained an independent inverse association (adjusted OR 0.192; 95% CI 0.048–0.761; p = 0.019). These associations are mechanistically explicable in the context of ferritin's established role as a positive acute-phase reactant, whose hepatic synthesis is upregulated by pro-inflammatory cytokines including interleukin-1, interleukin-6, and tumour necrosis factor-alpha. [25,26] Consequently, patients with greater systemic inflammatory burden may exhibit disproportionately elevated ferritin levels that meet or exceed the diagnostic threshold of 100 ng/mL, thereby potentially masking underlying iron depletion. This represents a recognised limitation of ferritin-only diagnostic criteria in populations with active inflammation. [27]

With respect to heart failure phenotype, patients with HFrEF accounted for a higher proportion of the iron-deficient group (44.3%) than those with HFpEF (36.8%), though this difference did not reach statistical significance (p = 0.544). These results are directionally consistent with Singh et al. [28], who reported high prevalence of iron deficiency in HFrEF, and with the broader evidence base linking neurohormonal activation, oxidative stress, and systemic inflammation in HFrEF to progressive impairment of iron metabolism and myocardial energetics. [29,30] Iron deficiency in HFrEF has been specifically associated with reduced peak VO_2, impaired cardiac output, and greater risks of hospitalisation and mortality. [31,32,33] The absence of a statistically significant difference between phenotypes in the present study may reflect the limited sample size available for this subgroup comparison, and should be interpreted accordingly.

Elderly patients (≥65 years) exhibited a numerically higher prevalence of iron deficiency (51.0%) compared with younger age groups, though this did not achieve statistical significance (p = 0.141). This pattern is consistent with published literature attributing higher iron deficiency rates in the elderly to age-related nutritional inadequacy, reduced gastrointestinal iron absorption, and chronic low-grade inflammatory states that upregulate hepcidin and impair iron recycling. [34,35] The observed haematologic indices further illustrate the sub-clinical haematological impact of iron depletion in this cohort: microcytosis (low MCV) was identified in 15.4% of patients, while hypochromia (low MCHC) was present in 64.0%. These indices are consistent with iron-restricted erythropoiesis and have been associated with adverse outcomes in CHF. [36]

No significant associations were observed between iron deficiency and other socio-demographic variables including educational level, occupation, marital status, or alcohol use. The study was not designed to evaluate the determinants of this pattern, and future studies with broader sociodemographic sampling are needed to clarify the relationship between these variables and iron status in CHF populations in this setting.

The high prevalence of iron deficiency identified in this study, particularly in the absence of anaemia in the majority of affected patients, underscores the importance of routine iron status assessment in CHF patients in this setting. Given the demonstrated benefits of intravenous iron therapy in improving functional outcomes in iron-deficient CHF patients [9,10], these findings provide a rationale for future studies

evaluating the feasibility and impact of systematic iron deficiency screening and treatment within cardiac care pathways in sub-Saharan Africa

This study has several limitations that should be considered when interpreting the findings. First, the cross-sectional design permits the identification of associations only; temporal and causal relationships between iron deficiency, inflammatory markers, and clinical outcomes cannot be established from these data. Second, iron deficiency was defined solely by serum ferritin (<100 ng/mL), without concurrent measurement of transferrin saturation or serum iron. This precluded the assessment of functional iron deficiency and, given ferritin's behaviour as an acute-phase reactant, may have resulted in misclassification of iron status in patients with concomitant systemic inflammation. Third, the study was conducted at a single tertiary referral centre, which may limit the generalisability of findings to primary and secondary care settings, community populations, or other geopolitical regions of Nigeria. Fourth, although the enrolled sample of 136 participants exceeded the estimated minimum sample size of 87, the overall sample size is modest and may constrain the statistical power of subgroup analyses, particularly for associations with less prevalent clinical variables. These limitations notwithstanding, this study provides valuable preliminary data on the prevalence and clinical correlates of iron deficiency in a CHF population in Southern Nigeria, and highlights the need for prospective, multicentre studies incorporating comprehensive iron panels and longitudinal follow-up to address the identified gaps.

Conclusion

Iron deficiency is prevalent among patients with chronic heart failure in this tertiary setting, affecting over two-fifths of the cohort, and occurs predominantly in the absence of anaemia. Female sex was independently associated with iron deficiency on multivariate analysis. Notably, iron deficiency was more commonly identified in patients without elevated inflammatory and natriuretic markers, highlighting the diagnostic limitations of ferritin-only assessment in populations with systemic inflammation. These findings underscore the importance of routine iron status assessment in CHF patients beyond haemoglobin-based screening alone, and provide a basis for future studies evaluating systematic iron deficiency screening and treatment strategies within cardiac care pathways in sub-Saharan Africa.

References

1. Ogah OS, Kushimo OA, Adebiyi A, Onyema CT, Uchenna OC, Adebayo BE, et al. Heart failure in Nigeria: protocol for a systematic review and meta-analysis. African Health Sciences [Internet]. 2023 Jul 13 [cited 2023 Nov 28];23(2):530–6. Available from: https://www.ajol.info/index.php/ahs/article/view/250750

2. Savarese G, Becher PM, Lund LH, Seferovic P, Rosano GMC, Coats AJS. Global Burden of Heart failure: a Comprehensive and Updated Review of Epidemiology. Cardiovascular Research [Internet]. 2023 Feb 12;118(17). Available from: https://pubmed.ncbi.nlm.nih.gov/35150240/

3. Oyan B, Abere S, Ajala AO, Orupabo F, Nyeche OE, Nwosu JC, et al. Patterns and outcomes of cardiovascular disease admissions in the medical wards of the Rivers State University Teaching Hospital, Port Harcourt, Nigeria: A two-year review. PubMed [Internet]. 2024 Oct 14 [cited 2024 Nov 18];65(4):479–89. Available from: https://nigerianmedjournal.org/index.php/nmj/article/view/467

4. Malik A, Chhabra L, Shams P. Congestive heart failure [Internet]. National Library of Medicine. StatPearls Publishing; 2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430873/

5. Anghel L, Dinu C, Patraș D, Ciubară A, Chiscop I. Iron Deficiency Treatment in Heart Failure—Challenges and Therapeutic Solutions. Journal of Clinical Medicine [Internet]. 2025 Apr 24 [cited 2025 Apr 28];14(9):2934. Available from: https://www.mdpi.com/2077-0383/14/9/2934

6. von Haehling S, Ebner N, Evertz R, Ponikowski P, Anker SD. Iron Deficiency in Heart Failure. JACC: Heart Failure. 2019 Jan;7(1):36–46.

7. Sun H, Wang Q, Han W, Chen C, Wang T, Zhong J. Iron deficiency: prevalence, mortality risk, and dietary relationships in general and heart failure populations. Frontiers in Cardiovascular Medicine [Internet]. 2024 Mar 18 [cited 2024 Nov 21];11. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC10982413/#s1

8. Nwako OF, Ogah OS, Odia OJ, Nwako CA, Nwako AB, Iheanacho MC, et al. Prevalence of Iron Deficiency Anaemia among Chronic Heart Failure Patients in Owerri, Nigeria. PubMed [Internet]. 2025 Jul 24 [cited 2025 Jul 29];66(2):480–8. Available from: https://www.nigerianmedjournal.org/index.php/nmj/article/view/630

9. Anker SD, Comin Colet J, Filippatos G, Willenheimer R, Dickstein K, Drexler H, et al. Ferric Carboxymaltose in Patients with Heart Failure and Iron Deficiency. New England Journal of Medicine [Internet]. 2009 Dec 17;361(25):2436–48. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa0908355

10. Ponikowski P, van Veldhuisen DJ, Comin-Colet J, Ertl G, Komajda M, Mareev V, et al. Beneficial effects of long-term intravenous iron therapy with ferric carboxymaltose in patients with symptomatic heart failure and iron deficiency. European Heart Journal [Internet]. 2015 Mar 14;36(11):657–68. Available from: https://academic.oup.com/eurheartj/article/36/11/657/491882

11. Pourhoseingholi MA, Vahedi M, Rahimzadeh M. Sample size calculation in medical studies. Gastroenterology and Hepatology From Bed to Bench [Internet]. 2024;6(1):14. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC4017493/#CIT0004

12. Amaechi UM, Aiwuyo HO, Ewelukwa C, Ilerhunmwuwa N, Osarenkhoe JO, Kweki AG, et al. Assessing Iron Status in Chronic Heart Failure Patients by Using Serum Ferritin and Transferrin Saturation Levels: A Cross-Sectional Descriptive Study. Cureus [Internet]. 2023 Winter;15(5):e39425. Available from: https://pubmed.ncbi.nlm.nih.gov/37362450/

13. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. European Journal of Heart Failure [Internet]. 2022 Jan;24(1):4–131. Available from: https://onlinelibrary.wiley.com/doi/full/10.1002/ejhf.2333

14. Makubi A, Hage C, Lwakatare J, Mmbando B, Kisenge P, Lund LH, et al. Prevalence and prognostic implications of anaemia and iron deficiency in Tanzanian patients with heart failure. Heart. 2014 Dec 24;101(8):592–9.

15. Johns I, Moschonas KE, Medina J, Ossei-Gerning N, Kassianos G, Halcox JP. Risk classification in primary prevention of CVD according to QRISK2 and JBS3 “heart age”, and prevalence of elevated high-sensitivity C reactive protein in the UK cohort of the EURIKA study. Open Heart. 2018 Nov;5(2):e000849.

16. Welsh P, Campbell RT, Mooney L, Kimenai DM, Hayward C, Campbell A, et al. Reference Ranges for NT-proBNP (N-Terminal Pro-B-Type Natriuretic Peptide) and Risk Factors for Higher NT-proBNP Concentrations in a Large General Population Cohort. Circulation: Heart Failure. 2022 Oct;15(10).

17. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. European Heart Journal. 2023 Aug 25;44(37).

18. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Journal of the American Society of Echocardiography [Internet]. 2015 Jan;28(1):1-39.e14. Available from: https://asecho.org/wp-content/uploads/2015/01/ChamberQuantification2015.pdf

19. Singer CE, Vasile CM, Popescu M, Popescu AIS, Marginean IC, Iacob GA, et al. Role of Iron Deficiency in Heart Failure—Clinical and Treatment Approach: An Overview. Diagnostics. 2023 Jan 13;13(2):304.

20. Pezel T, Audureau E, Mansourati J, Baudry G, Ben Driss A, Durup F, et al. Diagnosis and Treatment of Iron Deficiency in Heart Failure: OFICSel study by the French Heart Failure Working Group. ESC Heart Failure. 2021 Feb 22;8(2):1509–21.

21. Przybylowski P, Wasilewski G, Golabek K, Bachorzewska-Gajewska H, Dobrzycki S, Koc-Zorawska E, et al. Absolute and Functional Iron Deficiency Is a Common Finding in Patients With Heart Failure and After Heart Transplantation. Transplantation Proceedings [Internet]. 2016;48(1):173–6. Available from: https://pubmed.ncbi.nlm.nih.gov/26915864/#:~:text=Functional%20iron%20deficiency%20(defined%20as

22. Núñez J, Comín-Colet J, Miñana G, Núñez E, Santas E, Mollar A, et al. Iron deficiency and risk of early readmission following a hospitalization for acute heart failure. European Journal of Heart Failure. 2016 Mar 30;18(7):798–802.

23. Sharma SK, Agarwal SK, Bhargava K, Sharma M, Chopra K, Arumugam G. Prevalence and spectrum of iron deficiency in heart failure patients in south Rajasthan. Indian Heart Journal. 2016 Jul;68(4):493–7.

24. Cohen-Solal A, Damy T, Terbah M, Kerebel S, Baguet JP, Hanon O, et al. High prevalence of iron deficiency in patients with acute decompensated heart failure. European Journal of Heart Failure. 2014 Jul 28;16(9):984–91.

25. Moreira AC, Mesquita G, Gomes MS. Ferritin: An Inflammatory Player Keeping Iron at the Core of Pathogen-Host Interactions. Microorganisms. 2020 Apr 18;8(4):589.

26. Vanarsa K, Ye Y, Han J, Xie C, Mohan C, Wu T. Inflammation associated anemia and ferritin as disease markers in systemic lupus erythematosus. Arthritis Research & Therapy. 2012;14(4):R182.

27. Lismawati N, Yusra N, Effendy D, Kurniawan L, Lydia A. Role of soluble transferrin receptor – An Iron marker in hemodialysis patients. Indian journal of nephrology/Indian Journal of Nephrology. 2022 Jan 1;32(6):555–5.

28. Singh B, Bajaj N, Singh P, Kumar Ghosh A, Anathakrishnan R, Singh N. Iron deficiency in patients of heart failure with reduced ejection fraction. Medical Journal Armed Forces India. 2022 Oct;78(4):463–8.

29. Hartupee J, Mann DL. Neurohormonal activation in heart failure with reduced ejection fraction. Nature Reviews Cardiology [Internet]. 2018 Oct 6;14(1):30–8. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5286912/

30. Packer M, Anker SD, Butler J, Cleland JGF, Kalra PR, Mentz RJ, et al. Identification of three mechanistic pathways for iron-deficient heart failure. European Heart Journal. 2024 May 11;45(26):2281–93.

31. Jankowska EA, Rozentryt P, Witkowska A, Nowak J, Hartmann O, Ponikowska B, et al. Iron Deficiency Predicts Impaired Exercise Capacity in Patients With Systolic Chronic Heart Failure. Journal of Cardiac Failure. 2011 Nov;17(11):899–906.

32. Klip IjT, Comin-Colet J, Voors AA, Ponikowski P, Enjuanes C, Banasiak W, et al. Iron deficiency in chronic heart failure: An international pooled analysis. American Heart Journal. 2013 Apr;165(4):575-582.e3.

33. Beale AL, Warren JL, Roberts N, Meyer P, Townsend NP, Kaye D. Iron deficiency in heart failure with preserved ejection fraction: a systematic review and meta-analysis. Open Heart. 2019 Apr;6(1):e001012.

34. Petrosyan I, Blaison G, Andrès E, Federici L. Anaemia in the elderly: An aetiologic profile of a prospective cohort of 95 hospitalised patients. European Journal of Internal Medicine. 2012 Sep;23(6):524–8.

35. Andrès E, Serraj K, Federici L, Vogel T, Kaltenbach G. Anemia in elderly patients: New insight into an old disorder. Geriatrics & Gerontology International. 2012 Dec 17;13(3):519–27.

36. Tkaczyszyn M, Comín-Colet J, Voors AA, van Veldhuisen DJ, Enjuanes C, Moliner-Borja P, et al. Iron deficiency and red cell indices in patients with heart failure. European Journal of Heart Failure [Internet]. 2018 Jan 1 [cited 2020 Sep 19];20(1):114–22. Available from: https://pubmed.ncbi.nlm.nih.gov/28386910/