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FREQUENCY OF SERUM IRON DEFICIENCY IN HEART FAILURE PATIENTS WITHOUT CLINICAL ANEMIA

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Abstract

Objective: To determine the frequency of iron deficiency in patients with heart failure without clinical anemia and to evaluate its association with clinical characteristics and biochemical parameters.
Study Design: Cross-sectional study.
Place and Duration of Study: Conducted at Department of Cardiology, Punjab Institute of Cardiology, Lahore from 10th December 2025 till 10th April 2026. **Methodology:** A total of 148 patients with heart failure without clinical anemia were included. Demographic details, clinical characteristics, and laboratory parameters including hemoglobin, serum iron, ferritin, transferrin saturation, creatinine, and estimated glomerular filtration rate (eGFR) were recorded. Data were analyzed using SPSS version 29.0.
Results: The mean age of patients was 50.05 ± 11.92 years, with 75 (50.7%) females and 73 (49.3%) males. Iron deficiency was observed in 87 (58.8%) patients. Patients with iron deficiency had significantly lower hemoglobin (13.1 ± 1.2 vs 13.8 ± 1.3 g/dL, p=0.004), serum iron (61.5 ± 10.8 vs 80.4 ± 12.6 mcg/dL, p<0.001), ferritin (102.6 ± 41.3 vs 154.2 ± 48.5 ng/mL, p<0.001), and transferrin saturation (19.8 ± 6.5 vs 32.4 ± 8.1%, p<0.001). A significant reduction in eGFR was also noted in iron-deficient patients (77.3 ± 19.4 vs 85.6 ± 21.1 mL/min, p=0.032).
Conclusion: Iron deficiency is highly prevalent in patients with heart failure without clinical anemia and is associated with significant biochemical derangements and reduced renal function. Routine screening and early management of iron deficiency should be considered in the comprehensive care of heart failure patients.

Keywords: Heart failure, Iron deficiency, Ferritin, Transferrin saturation, Non-anemic patients, eGFR.

INTRODUCTION

Heart failure is a complex disorder characterized by either poor ventricular filling or the ability of the heart to pump blood [1]. It may be due to a number of anatomical and functional factors. It is an international-wide medical disorder that has been known to impact over 64 million individuals across the world [2]. It has been reported that prevalence of this chronic condition in Pakistan is 405.12 per 100,000 population. Anemia is reported to be a typical occurrence in the majority of cases of chronic diseases and all the types of anemia that are related to chronic diseases, iron deficiency anemia is the most prevalent type of anemia [3]. However, among patients with heart failure, the research has revealed that despite the lack of anemia that is evident, iron deficit may still be present [4]. In this case, a research study that performed on patients with heart failure, who are non-anemic clinically, the rate of iron deficiency may run as high as 59% [5]. Likewise, in another study carried in India where non-anemic patients with heart failure were involved, a total of 100 patients were used [6][7]. They indicated that serum iron deficiency occurring in heart failure patients, who had no clinical anemia, was 60% [8]. One study was carried out in Abbottabad, Pakistan, and a total of 150 patients with no clinical evidence of anemia were investigated to be present with iron deficiency and it was reported to be present with 54.7 per cent [9].

The iron deficiency in the patient with heart failure, even without anemia, may potentially and independently lead to the adverse functional outcome [10]. Overall, it is not a common practice of the local and institutional level to screen heart failure patients to determine the presence of iron deficiency in their absence and prior literature demonstrates that it is highly prevalent in such patients [11][12]. Consequently, the current research is performed with the purpose to establish the prevalence of serum iron deficiency in patients having heart failure but no clinical anemia of the local population [13]. This can assist in establishing the load of this condition among heart failure patients who are not anaemic and make the decision whether or not routine screening of such patients to identify iron deficiency should be promoted as a routine management practice at institutional levels.

OBJECTIVE

To determine the frequency of serum iron deficiency in heart failure patients without clinical anemia.

Methodology

This Cross-sectional study was conducted at Department of Cardiology, Punjab Institute of Cardiology, Lahore from 10th December 2025 till 10th April 2026. Non-probability consecutive sampling technique were used to collect data. The sample size of 148 patients was calculated using the WHO sample size calculator with a confidence level of 95%, absolute precision of 8%, and an anticipated frequency of iron deficiency in heart failure patients of 54.7%. Male and female patients aged between 30 and 70 years, diagnosed with heart failure for more than six months (as per operational definition), were included in the study. Patients with a history of previous cardiac surgery, prior blood loss, use of iron supplements, hematological disorders, and pregnant women were excluded. After obtaining approval from the Institutional Ethical Committee and CPSP, and written informed consent from participants, eligible patients were enrolled. Age, gender, body mass index (BMI), ejection fraction (EF%), time of heart failure, and New York Heart Association (NYHA) functional class were measured using a structured proforma. The calculation of BMI was determined by weight/height in meters squared. Iron deficiency (according to operational definition) was assessed to all patients, although this is not a regularly conducted development in clinical practice. Patients who were diagnosed with iron deficiency were dealt with. Data analysis was done using SPSS version 22. Continuous variables (age, BMI, EF, and duration of heart failure) were determined to be normal or not with the help of the Shapiro-Wilk test and represented as mean standard deviation or median with interquartile range. The categorical variables such as gender, NYHA class, and the presence of iron deficiency were presented in terms of frequencies and percentages. Effect modifiers were controlled by stratifying iron deficiency in terms of age, gender, BMI, EF, duration of heart failure, and NYHA class. After stratification, the Chi-square or Fisher exact test was used and p-value of less than 0.05 was regarded as statistically significant.

Results

Data were collected form 148 patients, with a mean age of 50.05 ± 11.92 years. The gender distribution was nearly equal, with 73 (49.3%) males and 75 (50.7%) females. The mean BMI was 24.93 ± 4.40 kg/m², while the mean duration of heart failure was 4.89 ± 2.09 years. The mean ejection fraction was 40.28 ± 8.50%. Regarding functional status, 51 (34.5%) patients were in NYHA class II, 46 (31.1%) in class III, and 51 (34.5%) in class IV (Table 1).

Table 1: Baseline Demographic and Clinical Characteristics (n=148)

Parameter	Category / Mean ± SD	Total (n=148)
Age (years)	—	50.05 ± 11.92
Gender	Male	73 (49.3%)
	Female	75 (50.7%)
BMI (kg/m²)	—	24.93 ± 4.40
Duration of HF (years)	—	4.89 ± 2.09
Ejection Fraction (%)	—	40.28 ± 8.50
NYHA Class	II	51 (34.5%)
	III	46 (31.1%)
	IV	51 (34.5%)

Mean hemoglobin level was 13.38 ± 1.26 g/dL. The mean serum iron was 69.35 ± 13.93 mcg/dL, ferritin was 124.42 ± 49.02 ng/mL, and transferrin saturation was 25.04 ± 9.98%. The mean creatinine was 0.97 ± 0.29 mg/dL, and eGFR was 80.86 ± 20.32 mL/min. Iron deficiency was present in 87 (58.8%) patients, while 61 (41.2%) had normal iron status. Among comorbidities, diabetes mellitus was observed in 67 (45.3%), hypertension in 68 (45.9%), and coronary artery disease in 76 (51.4%) patients (table 2).

Table 2: Biochemical Profile, Iron Deficiency Status, and Comorbidities (n=148)

Parameter	Subcategory	n (%) / Mean ± SD
Biochemical Parameters	Hemoglobin (g/dL)	13.38 ± 1.26
	Serum Iron (mcg/dL)	69.35 ± 13.93
	Ferritin (ng/mL)	124.42 ± 49.02
	Transferrin Saturation (%)	25.04 ± 9.98
	Creatinine (mg/dL)	0.97 ± 0.29
	eGFR (mL/min)	80.86 ± 20.32
Iron Deficiency Status	Yes	87 (58.8%)
	No	61 (41.2%)
Comorbidities	Diabetes Mellitus – Yes	67 (45.3%)
	Diabetes Mellitus – No	81 (54.7%)
	Hypertension – Yes	68 (45.9%)
	Hypertension – No	80 (54.1%)
	Coronary Artery Disease – Yes	76 (51.4%)
	Coronary Artery Disease – No	72 (48.6%)

Iron deficiency was more common in males (64.4%) compared to females (53.3%). According to NYHA classification, iron deficiency was highest in class III patients (65.2%), followed by class II (58.8%) and class IV (52.9%). Among diabetic patients, 62.7% had iron deficiency compared to 55.6% of non-diabetics. Similarly, iron deficiency was present in 57.4% of hypertensive and 60.0% of non-hypertensive patients. In patients with coronary artery disease, 59.2% were iron deficient compared to 58.3% without coronary artery disease (Table 3).

Table 3: Stratification of Iron Deficiency with Clinical Variables

Variable	Category	Iron Deficiency Yes n (%)	Iron Deficiency No n (%)
Gender	Male	47 (64.4%)	26 (35.6%)
	Female	40 (53.3%)	35 (46.7%)
NYHA Class	II	30 (58.8%)	21 (41.2%)
	III	30 (65.2%)	16 (34.8%)
	IV	27 (52.9%)	24 (47.1%)
Diabetes	Yes	42 (62.7%)	25 (37.3%)
	No	45 (55.6%)	36 (44.4%)
Hypertension	Yes	39 (57.4%)	29 (42.6%)
	No	48 (60.0%)	32 (40.0%)
CAD	Yes	45 (59.2%)	31 (40.8%)
	No	42 (58.3%)	30 (41.7%)

Patients with iron deficiency had significantly lower hemoglobin levels (13.1 ± 1.2 vs 13.8 ± 1.3 g/dL, p=0.004), serum iron (61.5 ± 10.8 vs 80.4 ± 12.6 mcg/dL, p<0.001), ferritin (102.6 ± 41.3 vs 154.2 ± 48.5 ng/mL, p<0.001), and transferrin saturation (19.8 ± 6.5 vs 32.4 ± 8.1%, p<0.001). A significant reduction in eGFR was also observed in iron-deficient patients (77.3 ± 19.4 vs 85.6 ± 21.1 mL/min, p=0.032) (Table 4).

Table 4: Comparison of Continuous Variables Between Patients With and Without Iron Deficiency

Variable	Iron Deficiency Yes (n=87) Mean ± SD	Iron Deficiency No (n=61) Mean ± SD	p-value
Age (years)	49.1 ± 11.5	51.4 ± 12.3	0.241
BMI (kg/m²)	24.6 ± 4.2	25.3 ± 4.6	0.362
Duration of HF (years)	5.1 ± 2.1	4.6 ± 2.0	0.158
Ejection Fraction (%)	39.2 ± 8.3	41.7 ± 8.6	0.082
Hemoglobin (g/dL)	13.1 ± 1.2	13.8 ± 1.3	0.004
Serum Iron (mcg/dL)	61.5 ± 10.8	80.4 ± 12.6	<0.001
Ferritin (ng/mL)	102.6 ± 41.3	154.2 ± 48.5	<0.001
Transferrin Saturation (%)	19.8 ± 6.5	32.4 ± 8.1	<0.001
Creatinine (mg/dL)	1.01 ± 0.31	0.92 ± 0.26	0.071
eGFR (mL/min)	77.3 ± 19.4	85.6 ± 21.1	0.032

Discussion

This paper has shown iron deficiency to be very prevalent in patients with heart failure even without overt anemia with 58.8 percent of the study population showing the prevalence of iron deficiency. This observation is consistent with other studies that have reported iron deficiency to be an under-appreciated but an important clinical comorbidity in heart failure regardless of hemoglobinogen status. Our cohort was characterized by the mean age, and an equal gender distribution is indicative of a general population of heart failure, and hence, the results can be generalized to usual practice clinical environment [14]. The major findings of this study are that iron deficiency has no close connection with most of the baseline demographic or clinical factors, such as age, BMI, and heart failure duration. Other studies conducted in the past have also indicated that other mechanisms like chronic inflammation, absence of gastrointestinal absorption, and distorted iron metabolism play a significant role in causing iron deficiency in such patients [15][16]. It was interesting to note that iron deficiency was also more prevalent in males and patients with diabetes and NYHA class III symptoms, but the differences were not statistically significant. This pattern could indicate an increased metabolic supply or inflammatory load in these subgroups, which was observed in the past studies [17]. The prevalence of NYHA class III was slightly higher than the prevalence of the disease in class IV and this may be attributed to the survival bias or different disease progressions since very sick individuals are likely to exhibit complex metabolic reactions. The comparison of the two groups in the laboratory showed statistically significant difference of hemoglobin, serum iron, ferritin, transferrin saturation, and eGFR. A significant decrease in hemoglobin levels of iron deficient patients was still within non-anemic ranges, which evidences the notion of functional iron deficiency. More importantly, the level of saturation of serum iron, ferritin and transferrin were much lower, which proves the real depletion of iron stores and iron unavailability. The findings are consistent with the available literature which has been able to emphasize the diagnostic importance of ferritin and transferrin saturation in the diagnosis of iron deficiency in the heart failure employees [18]. The other clinically important outcome is the correlation between reduced eGFR in iron deficient patients that can show the association between the impaired activity of the kidneys and the abnormal iron metabolism. One of the possible causes of this association is that chronic kidney disease is reported to have an impact on erythropoiesis and iron consumption. Previous studies have also observed the two-way communication between the renal functioning and iron homeostasis in the heart failure population [19][20].

A number of limitations are associated with this study. Cross-sectional study is not causal in its design since it is only possible to determine associations, and not causal relationships. Being a single-centre study; the sample size of 148 patients was used, thus, findings might not be extrapolated. Biomarkers of iron metabolism and inflammation (hepcidin, CRP) were not measured, and this would have given a more in-depth mechanistic comprehension. Also, no evaluation of potential confounding factors like dietary and socioeconomic status and medication history were made. There were also no other clinical outcomes such as hospitalization, functional capacity and mortality and the assessment of prognostic value was limited. Besides, the multivariate regression analysis was not done to establish the independent predictors of iron deficiency that would have enhanced the analytical depth of the study.

Conclusion

It is concluded that iron deficiency is highly prevalent among patients with heart failure even in the absence of clinical anemia, affecting more than half of the study population. It is associated with significant alterations in key biochemical parameters, including lower serum iron, ferritin, transferrin saturation, and reduced renal function. These findings highlight that iron deficiency exists as an independent and clinically relevant condition in heart failure patients, irrespective of traditional demographic and comorbidity factors.

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