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Prevalence of Iron Deficiency in Patients with Chronic Heart Failure and its Relationship with Left Ventricular Ejection Fraction: A Single-Centered Observation

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Abstract
Background: *The relationship between serum iron status and cardiac function in chronic heart failure (CHF) has been a topic of interest in the field of clinical research. This study aimed to assess iron status in CHF patients attending a tertiary center of Bangladesh and its relationship with left ventricular ejection fraction (LVEF).*
Methods: *This study was a cross-sectional study conducted in the Department of Medicine, Rajshahi medical college hospital over a period of 18 months. The study comprised 68 adult patients with a confirmed history of CHF for more than 6 months. Iron profile and LVEF were assessed for each patient through blood test and echocardiogram. Data collection involved a semi-structured questionnaire. Face-to-face interview and thorough clinical assessment were conducted. Data was analyzed by SPSS V 25.*
Results: *The mean age of the study patients was 53.54±10.61 (SD) years with male predominance (54.42%). Approximately 85.3% of the patients had iron deficiency (ID), with absolute iron deficiency being more prevalent (64.7% absolute and 20.6% functional deficiency). No significant difference in LVEF was found between patients with and without iron deficiency (p>.05). However, patients with absolute iron deficiency demonstrated significantly lower LVEF than those with functional iron deficiency (p<.05). Female gender, longer duration of CHF, and higher NYHA class (III or IV) were associated with increased odds of iron deficiency (p<.05).*
Conclusion: *The study revealed a higher prevalence of iron deficiency among CHF patients in Bangladesh. The issue needs to be addressed during dealing with chronic heart failure patient.*
Keywords: *Chronic Heart Failure, CHF, Iron deficiency, Serum ferritin, Left Ventricular Ejection Fraction, LVEF*

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I. Introduction

As an essential micronutrient, iron plays key roles in various physiological processes of human body including oxygen transport, energy metabolism, and cellular function [1]. For the past decade, there has been growing interest in the potential impact of iron status on cardiac function [1] and its implications for patients with chronic heart failure (CHF) [2]. CHF, a progressive heart condition characterized by inability to pump blood efficiently which results in reduced oxygen in tissues and organs [3]. CHF is often associated with significant morbidity and even mortality, posing a substantial burden on the affected individuals physically,

emotionally and economically along with the associated peers [4]. Iron deficiency has been evident as a common comorbidity in CHF patients and associated with adverse outcomes across the globe [5–13]. So, it is necessary to explore further the relationship between serum iron profile and cardiac function parameters of CHF.

Left ventricular ejection fraction (LVEF) is a key indicator of cardiac function and is commonly used to assess left ventricular performance of an individual suspected to have cardiac incompetency. LVEF has been considered as an important prognostic factor in CHF and other heart diseases [14]. Though iron deficiency has started to be considered as a prognostic indicator of CHF [15], but the mechanism responsible is still to unveil properly. Moreover, effect of iron deficiency in the disease prognosis and quality of life of the CHF patients have been observed prominent irrespective of the status of anemia [16]. Hence, identifying any correlations between LVEF and iron profile might help to intensify the implications for risk stratification of CHF patients for further disease progression. If any specific patterns between LVEF and iron profile could be captured, existing risk assessment strategy might be upgraded and refined. The findings may offer insights into the role of iron metabolism in cardiac remodeling and function, potentially guiding the development of targeted therapeutic interventions aimed at optimizing iron status to improve cardiac outcomes in CHF.

So, the present study aimed to explore the relationship between LVEF and iron status among the patients with CHF. This single-centered observational study was conducted in Bangladesh, which holds particular significance due to the growing prevalence of chronic heart failure (CHF) and its associated burden on affected individuals and healthcare systems in the region [17]. By evaluating the association between serum iron status and left ventricular ejection fraction (LVEF) in patients with stable CHF, this study sought to address a critical gap in the understanding of CHF management within the Bangladeshi population. The findings from this research could provide valuable insights into the role of iron metabolism in cardiac function, potentially informing tailored approaches for risk assessment, prognosis, and therapeutic interventions for CHF patients in Bangladesh.

II. Methods

Study design and study participants

This study is a single-center observational study, conducted at Rajshahi Medical College Hospital- a tertiary hospital of Bangladesh from September 2020 to February 2022.

A total of 68 adult patients presented at the Department of Cardiology with a >6 months history of CHF and LVEF of <55% were included following informed written consent. The diagnosis of CHF was established through a comprehensive and repeated assessment of clinical features (signs and symptoms), physical examinations, and laboratory investigations (such as cardiac biomarkers and imaging) [18]. A team of expert physicians from mid-level to professors were engaged during diagnosis and management of these patients. Excluded patients were those who had comorbid noncardiac conditions causing iron deficiency (current diagnosis or suspicion of any malignancy, infection, severe renal diseases and hematological diseases), history of acute coronary syndrome, coronary revascularization within the three months prior to the study and unplanned hospitalization due to worsening cardiac condition within one month prior to the study.

Clinical assessment and data collection

A face-to-face interview was conducted for each patient following physical examination, laboratory and radio-imaging investigations. Laboratory investigations included serum iron profile (total iron, ferritin, total iron binding capacity; TIBC). Serum iron and TIBC were measured from collected blood sample using spectrochlorometric method. Serum ferritin was measured by Chemiluminescent Microparticle Immunoassay (CMIA) method. All patients were subjected to Electrocardiogram (ECG) & Echocardiography by Cardiologist for screening of any acute cardiac condition and assessment of LVEF at present.

Severity of CHF was assessed through LVEF where Ejection Fraction of 41%-51% was defined as mild, 30-40% was defined as moderate and less than 30% was defined as severe severe [19]. New York Heart Association (NYHA) Classification of Heart Failure was also assessed [20]**.**

Functional iron deficiency was considered with a ferritin level from 100 ng/ml to 299 ng/L and a transferrin saturation <20% [21]. Patients with ferritin level less than 100 ng/ml were considered to have absolute iron deficiency [22].

A semi-structured questionnaire was developed containing necessary information including baseline demographic and clinical characteristics of the patients.

Statistical analysis

Statistical analysis was conducted using the SPSS V 25. The difference of LVEF between the patients with iron deficiency and without iron deficiency was assessed using the independent student t-test considering

p<.05 as the level of significance. Univariate and multivariate logistic regression were conducted to assess the factors responsible for iron deficiency among the study patients.

Ethical considerations

Before the study began, ethical approval was secured from the RMCH Ethical Review Committee. Participants underwent a thorough explanation of the study in their local language along with a printed handout before final enrollment. Written consent was obtained from each participant. The study was conducted adhering to the 'Declaration of Helsinki' guidelines.

III. Result

The mean age of the study patients was 53.54±10.61(SD) years where more than half were over 50 years. Male patients comprised 54.42% of study patients while female comprised 45.58%. About 14.79% patients were obese and 29.41% were overweight according to body mass index (BMI). Almost half of the patients reported a positive family history of heart disease. By occupation mostly the patients were housewives, farmer, service holders and businessmen. The mean duration of chronic heart failure (CHF) was 2.74±1.41 (SD) years. (Table 1)

Regarding the type of HF- ischemic cardiomyopathy and dilated cardiomyopathy were most common followed by multiple valvular heart disease and hypertensive heart failure. Few patients had thyrotoxic heart disease and marfan syndrome. (Table 1)

The New York Heart Association (NYHA) class distribution revealed that most patients were classified as class IV & III (59.4%). The severity according to left ventricular ejection fraction (LVEF) was predominantly severe (51.5%) and moderate (45.6%) with a mean LVEF of 29.82±5.74% (SD). **(Table 1)**

The mean values for serum iron, serum ferritin, total iron binding capacity, and percentage saturation were 50.35±20.24 (SD) µg/dl, 70.47±25.56 (SD) ng/ml, 305.48±101.53 (SD) mcg/dl, and 17.84±8.34% (SD) respectively. **(Table 1)**

Table 1: Demographic and clinical characteristics of the study patients along with iron profile (n=68)

Parameter	n (%)
Age group (years)	
< 50	31 (45.58)
≥ 50	37 (54.42)
Mean±SD	53.54±10.61
Gender	
Male	37 (54.42)
Female	31 (45.58)
Occupation	
Housewives	22 (32.4)
Farmer	14 (20.6)
Service holders	12 (17.6)
Businessmen	10 (14.7)
Labour	3 (4.4)
Others	7 (10.3)
BMI category	
Underweight	4 (5.88)
Normal	34 (50)
Overweight	20 (29.41)
Obese	10 (14.79)
Mean±SD (kg/m^2)	24.94±6.18
Family history of heart disease	33 (48.52)
Duration of CHF (years) (mean±SD)	2.74±1.41
Types of HF	
Ischemic cardiomyopathy	20 (29.4)
Dilated cardiomyopathy	20 (29.4)
Hypertensive heart failure	10 (14.7)
Multiple valvular heart disease	12 (17.7)
Thyrotoxic heart disease	4 (5.9)
Marfan syndrome	2 (2.9)
NYHA class	
Class I	13 (19.1)
Class II	17 (25)

Class III	18 (26.5)
Class IV	20 (29.4)
Severity according to ejection fraction	
Mild	2 (2.9)
Moderate	31 (45.6)
Severe	35 (51.5)
Mean±SD	29.82±5.74
Iron profile	
Serum iron (µg/dl)	50.35±20.24
Serum ferritin (ng/ml)	70.47±25.56
Total Iron Binding Capacity(mcg/dl)	305.48±101.53
Percentage saturation (%)	17.84±8.34

BMI: Body Mass Index, CHF: Chronic Heart Failure, NYHA class: New York Heart Association

About 85.3% of the study patients with CHF had iron deficiency and among them absolute iron deficiency was most common (64.7%). **(Figure 1)**

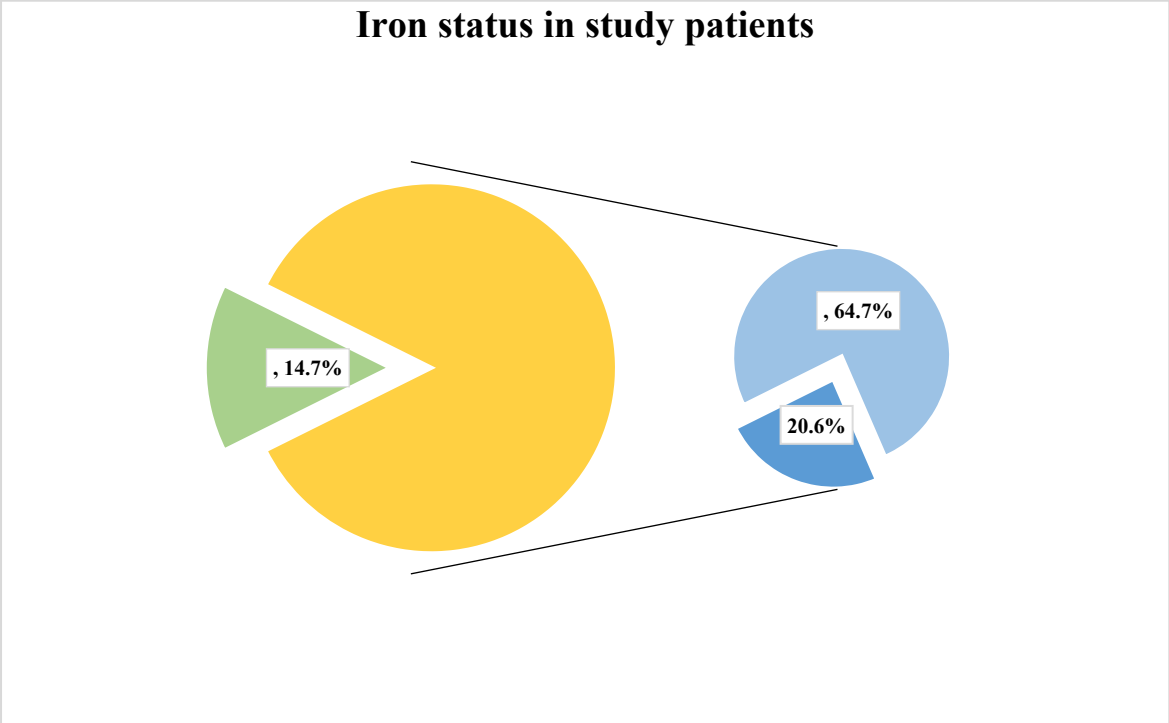

Figure 1: Frequency and type of iron deficiency among study patients (n=68)

The study found no significant difference in LVEF between patients with and without iron deficiency. But duration of CHF was significantly longer in patients with iron deficiency. **(Table 2)**

LVEF was significantly lesser in patients with absolute iron deficiency compared to those with functional iron deficiency. **(Table 3)**

Table 2: Difference of left ventricular ejection fraction (LVEF) and duration of CHF between patients with iron deficiency and patient without iron deficiency (n=68)

	Patients with iron deficiency n=58	**Patients without iron deficiency n=10**	**p value**
Duration of CHF (in years)	2.78±1.41	1.78±0.84	.023
LVEF	29.25±8.74	30.00±9.14	.854

p value was determined by independent student t test

Table 3: Difference of left ventricular ejection fraction (LVEF) between patients with absolute iron deficiency and patient functional iron deficiency (n=68)

	Absolute iron deficiency n=58	Functional iron deficiency n=10	p value
LVEF	28.74±5.28	33.60±5.84	.034

p value was determined by independent student t test

The univariate and multivariate logistic regression analyses revealed that female gender, duration of CHF, and NYHA class (III, IV) were associated with increased odds of iron deficiency among the studied patients. **(Table 4)**

Table 4: Univariate and multivariate logistic regression for the predictors of iron deficiency among the studied patients (n=68)

Variables	Univariate		• Multivariate	
	Odds Ratio	95% CI (Lower-Upper)	Odds Ratio	95% CI (Lower-Upper)
Age	1.16	.41-.3.95	1.97	.92-3.03
Gender (female)	1.3*	1.1-2.54	1.25*	1.10-1.45
Duration of CHF	2.24*	1.02-2.89	1.85*	1.03-3.30
NYHA class (III, IV)	2.01*	1.57-3.25	1.84*	1.02-1.9
LVEF	1.03	.95-1.43	1.98	.87-2.1

p-value was determined by univariate and univariate logistic regression analysis, *denotes statistical significance.

IV. Discussion

The relationship between chronic heart failure (CHF) and iron deficiency is a focal point of current medical research due to its significant impact on patient outcomes. This study aimed to assess the prevalence of iron deficiency in adults with CHF and its impact on disease progression and severity, focusing particularly on the relationship with left ventricular ejection fraction (LVEF).

The average age of the study patients with CHF was 53 years with a male predominance which aligns with other similar study [23]. Nearly half of the participants were overweight or obese, which is concerning given the independent association between obesity and cardiovascular diseases, including heart failure [24]. Almost half of the patients had family history of heart disease.

Nearly more than half of the patients were in class IV and III of NYHA classification indicating higher number of patients with more severe form of CHF. The duration of CHF was found to be significantly longer in patients with iron deficiency compared to those without iron deficiency which indicates iron deficiency may develop or worsen over time in CHF patients [25]. The chronic inflammatory state and increased oxidative stress associated with heart failure may contribute to the development of iron deficiency. Understanding the temporal relationship between CHF and iron deficiency can help inform strategies for early detection and intervention.

This study explored the iron profile status among adult patients with chronic heart failure (CHF) and found a high prevalence with an approximate percentage of 85.3%. Iron deficiency has been observed in variable frequencies in different studies conducted across the world ranging from 20%-85% [5, 23, 26–28]. Among the patients with iron deficiency, absolute iron deficiency was more common involving almost two-third of the study patients while rest had functional iron deficiency.

The pathophysiology of iron deficiency in CHF is multifactorial. Reduced iron intake, low bioavailability of dietary iron, and gastrointestinal malabsorption contribute to iron deficiency in CHF patients [29, 30]. Additionally, clinical consequences of CHF such as intestinal interstitial edema and certain therapeutic medications further exacerbate the mechanism [31]. Increased iron loss is associated with several gastrointestinal disorders such as peptic ulceration, esophagitis, gastritis, and duodenitis and this chronic inflammatory states including heart failure itself, also play significant role in impairing the absorption, recycling, and release of iron. The mean value of iron parameters were also shows an overall iron depletion corroborating with pervious study [23]. Iron deficiency can have a significant impact on the prognosis and quality of life of CHF patients, as it is associated with increased symptoms, hospitalizations, and mortality rates [32]. Therefore, identifying and managing iron deficiency is crucial in the management of CHF.

This study found no significant difference in left ventricular ejection fraction (LVEF) between patients with and without iron deficiency. LVEF is a measure of cardiac function and is commonly used to assess the severity of heart failure. The finding suggests that iron deficiency may not directly influence cardiac function as

measured by LVEF. Similar observation was reported by Amaechi et al. and Ramashree et al [33, 34]. But this study observed significantly lower LVEF in patients with absolute iron deficiency compared to those with functional iron deficiency. This finding suggests that absolute iron deficiency may be associated with more severe cardiac dysfunction in CHF patients. Identifying different types of iron deficiency can help guide targeted interventions for CHF patients. However, LVEF is just one parameter of cardiac function, and other measures such as exercise capacity and symptoms may be influenced by iron deficiency. Further research is needed to explore the impact of iron deficiency on various aspects of cardiac function in CHF patients.

The univariate and multivariate logistic regression analyses revealed several factors associated with increased odds of iron deficiency among the studied patients. Female gender, longer duration of CHF, and higher NYHA class (III or IV) were found to be significant predictors of iron deficiency. These findings are consistent with previous research showing that female gender and disease severity are risk factors for iron deficiency in CHF patients [35]. The association between longer duration of CHF and iron deficiency suggests that ongoing monitoring and management of iron levels are necessary throughout the course of the disease.

Given the high prevalence of iron deficiency among CHF patients, routine screening for iron status should be considered as part of the management strategy for these patients. Early detection and appropriate treatment of iron deficiency can potentially improve symptoms, quality of life, and outcomes in CHF patients.

However, there were some limitations of this study. This study included only the stable CHF patients and the sample size was relatively small, which may limit the generalizability of the findings. Additionally, being a cross-sectional study, long term observations could not be done. Longitudinal studies are needed to further investigate the temporal relationship between CHF and iron deficiency.

V. Conclusion

In conclusion, this study observed a high prevalence of iron deficiency in patients with CHF which highlights the importance of routine screening for iron deficiency in CHF patients aiming an early detection and prompt management. But no relation between LVEF and iron status was observed within the study patients. Further research is needed to explore the underlying mechanisms linking iron deficiency and heart failure and to evaluate the impact of iron supplementation on clinical outcomes in this population.

Declarations

Ethics approval: The study protocol was reviewed and approved by the Ethical Review Committee of Rajshahi Medical College. Ethical issues were maintained in accordance with the Helsinki Declaration.

Consent for publication: None

Availability of data and materials: The data and other necessary details are available and can be found upon reasonable request to the corresponding authors.

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