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RESEARCH ARTICLE
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A PROSPECTIVE STUDY ON CHARACTERIZATION OF IRON DEFICIENCY IN PATIENTS WITH CHRONIC HEART FAILURE

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Abstract

Background and Aim: Heart failure (HF) is a prevalent medical issue affecting 1-2% population and significantly contributes to morbidity and mortality. Similarly, anemia is another condition that leads to frequent hospitalizations promoting morbidity and mortality. The present study aimed to assess different characterization of iron deficiency in chronic heart failure patients.

Patients and Methods: A prospective study was conducted on 146 heart failure patients in National Institute of Cardiovascular Diseases, Karachi from November 2022 to June 2023. The study enrolled hospitalized patients who received a clinical diagnosis of cardiac failure established using accepted medical criteria. Iron deficiency (ID) was determined by serum ferritin. Anemia was defined for men (<13 g/dL) and women (<12 g/dL) as per World Health Organization (WHO) criteria. Absolute iron deficiency was indicated by serum ferritin (<100 mg/L) and iron deficiency serum ferritin levels (100–300 mg/L) in combination with low TSAT (<20%). Descriptive statistic was done using SPSS version 27.

Results: The overall mean age was 58.7 ± 12.6 years. There were 96 (65.8%) male and 50 (34.2%) female. Age-wise distribution of patients was as follows: 40 (27.4%) in 30-40 years, 68 (46.6%) in 41-50 years, and 38 (26%) in >51 years. The prevalence of iron deficiency was 78.1% (n=114) with 46.6% (n=68) having absolute ID and 31.5% (n=46) having functional ID. Male patients were less prone to ID than female. Different comorbidities such as diabetes, hypertension, ischemic heart disease, atrial fibrillation, primary valvular heart diseases, and secondary mitral regurgitation was found in 26 (17.8%), 68 (46.6%), 78 (53.4%), 34 (23.3%), 22 (15.1%), and 54 (37%) respectively.

Conclusion: The incidence of iron deficiency was 78.1% among the studied population. The prevalence of iron deficiency was significantly higher in females compared to males. In an actual patient population with congestive heart failure (CHF) and increasing prevalence of heart failure with preserved ejection fraction, iron deficiency (ID) did not serve as a predictive factor for mortality or hospitalizations.

Keywords: Chronic heart failure, Iron deficiency, Characterization

INTRODUCTION

Iron deficiency is a health-related medical issue with insufficient amount of iron availability for human body needs and could be evident with or without anemia [1]. The incidence of iron deficiency as a common comorbidity varies from 36% to 60% among chronic heart failure patients [2, 3]. Chronic heart failure patients suffering from iron deficiency caused by multiple factors such as chronic inflammation, increase loss of GI blood, lower intake of iron, and partially because of antiplatelet and anticoagulant medications [4, 5]. Iron deficiency developed in approximately 50% cases of CHF, which is recognized as a poor prognostic factor independent of anemia and chronic kidney disease (CKD) [6]. In chronic HF, ID frequently coexists with anemia and/or CKD, and the presence of ID significantly increases the risk of death, either alone or with anemia including CKD [7]. However, in another study there was no observed association between ID and overall or cardiovascular mortality. Instead, predictors of worse survival included hemoglobin and C-reactive protein [8].

The significance improvements in heart failure pathogenesis understanding have paved the way for rational treatment, leading to significant improvements in patient outcomes [9]. Despite these advances, the prognosis of HF remains dismal two comorbidities common in HF patients, such as anemia and iron deficiency (ID), is associated with poor clinical outcomes [10]. Patients with chronic heart failure (CHF) typically exhibit characteristic traits such as exercise intolerance and fatigue. An earlier study indicated that individuals with chronic heart failure (CHF) might experience significant iron deficiency even prior to the development of anemia [11]. This increases the underlying morbidity and adversely affects symptoms and clinical outcome, carrying the risk of mortality away high 40–60% [12–14]. Most studies investigating the prevalence of iron deficiency (ID) associated with heart failure (HF) have been conducted in the Europe but limited regarding the association of iron deficiency with CHF in Asian patients [15, 16]. Presently, there is a lack of data from Pakistan to facilitate estimation of ID prevalence for HF. The aim of this study was to assess the prevalence of ID in HF in the Pakistani population.

METHODOLOGY

A prospective study was conducted on 146 heart failure patients in National Institute of Cardiovascular Diseases, Karachi from November 2022 to June 2023. The study enrolled hospitalized patients who received a clinical diagnosis of cardiac failure established using accepted medical criteria. Patients with coexisting non-cardiac conditions and those with intellectual disability (e.g., stroke, malignancy, etc.) or urinary excess occurs complex (e.g., end-stage psychosis) were excluded. All participants underwent a comprehensive evaluation that included dietary information, as well as clinical examination, blood draws, and advanced transthoracic echocardiography with standard equipment was used. Participants were classified as having normal (≥ 50%) or mild EF (EF 45) based

on their Ejection Fraction (EF), moderate (EF 31–44%), or severe (EF ≤ 30%) left ventricle. In addition to routine hemograms, the iron status of the participants was assessed by comprehensive iron profile measurements of iron data serum ferritin. Anemia for men (<13 g/dL) and women (<12 g/dL) was defined as per World Health Organization (WHO) criteria. Although the generally accepted serum ferritin cutoff level for the diagnosis of complete iron deficiency (ID) is 30 mg/L, in the case of heart failure (HF), intracellular iron accumulation and inflammation can cause arterial ferritin more likely, later for and blood can be levels. In such cases, a serum ferritin cutoff value as high as 100 mg/L was used to diagnose complete iron deficiency. Descriptive statistic was done using SPSS version 27. Numbers and percentages represent distributional variables, while normally distributed data were presented as mean ± standard deviation. The p-value was calculated using the Chi-square test, as appropriate.

RESULTS

The overall mean age was 58.7 ± 12.6 years. There were 96 (65.8%) male and 50 (34.2%) female. Age-wise distribution of patients was as follows: 40 (27.4%) in 30-40 years, 68 (46.6%) in 41-50 years, and 38 (26%) in >51 years. The prevalence of iron deficiency was 78.1% (n=114) with 46.6% (n=68) having absolute ID and 31.5% (n=46) having functional ID. Male patients were less prone to ID than female. Different comorbidities such as diabetes, hypertension, ischemic heart disease, atrial fibrillation, primary valvular heart diseases, and secondary mitral regurgitation was found in 26 (17.8%), 68 (46.6%), 78 (53.4%), 34 (23.3%), 22 (15.1%), and 54 (37%) respectively.

Patients were categorized based on their hemoglobin (g/dL) measured; total were 82 (56.2%) which comprised 10–13 g/dL for males and 10–12 g/dL for females 58 (70.7%), 8-10 g/dL 16 (19.5%), and <8 g/dL 8 (9.8%). Baseline characteristics are shown in Table-I. Table-II represents the age-wise distribution of patients. Severity of iron deficiency based on their Ejection fraction is illustrated in Figure-1. Figure-2 depicts different comorbidities. Distribution of patients based on their hemoglobin level is illustrated in Figure-3. Table-III represents the characterization and categorization of ID patients in both gender based on their hemoglobin, functional class and LV function.

Table-I Baseline details of patients (N=146)

Parameters	**Value [Mean ± SD]**
Age (years)	58.7 ± 12.6
Gender	
Male	96 (65.8%)
Female	50 (34.2%)
NYHA class	
I	17 (11.6%)
II	29 (19.9%)
III	66 (45.2%)
IV	34 (23.3%)
Iron deficiency	114 (78.1%)
Absolute	68 (46.6%)
Functional	46 (31.5%)

Table-II Age-wise distribution of patients (N=146)

Age groups (years)	**N (%)**
30-40	40 (27.4%)
41-50	68 (46.6%)
>51	38 (26%)
Total	146 (100%)

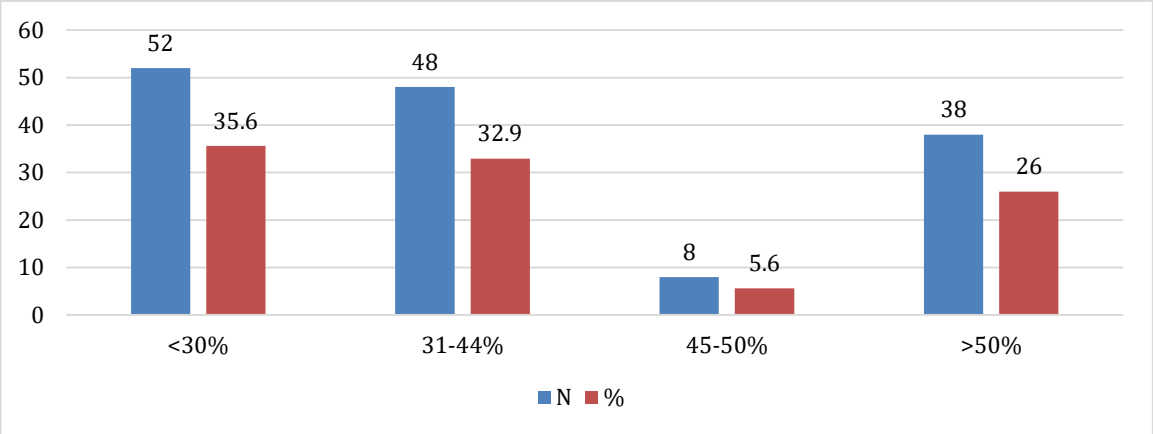

Figure-1 Severity of iron deficiency based on their Ejection fraction (N=146)

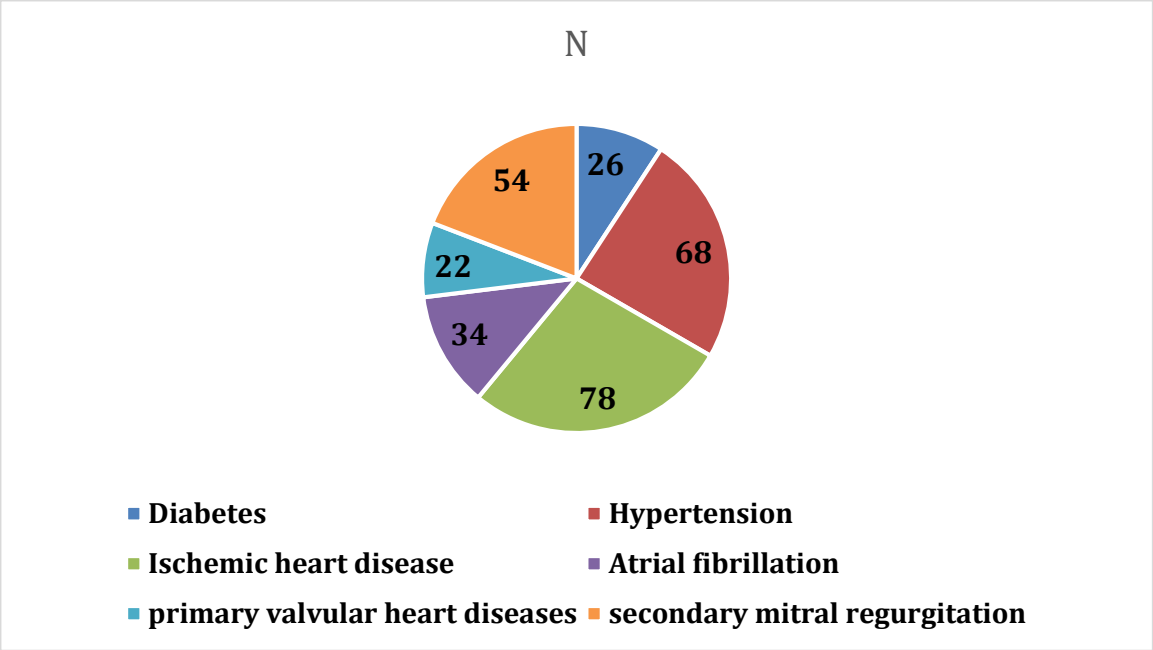

Figure-2 Comorbidities (N=146)

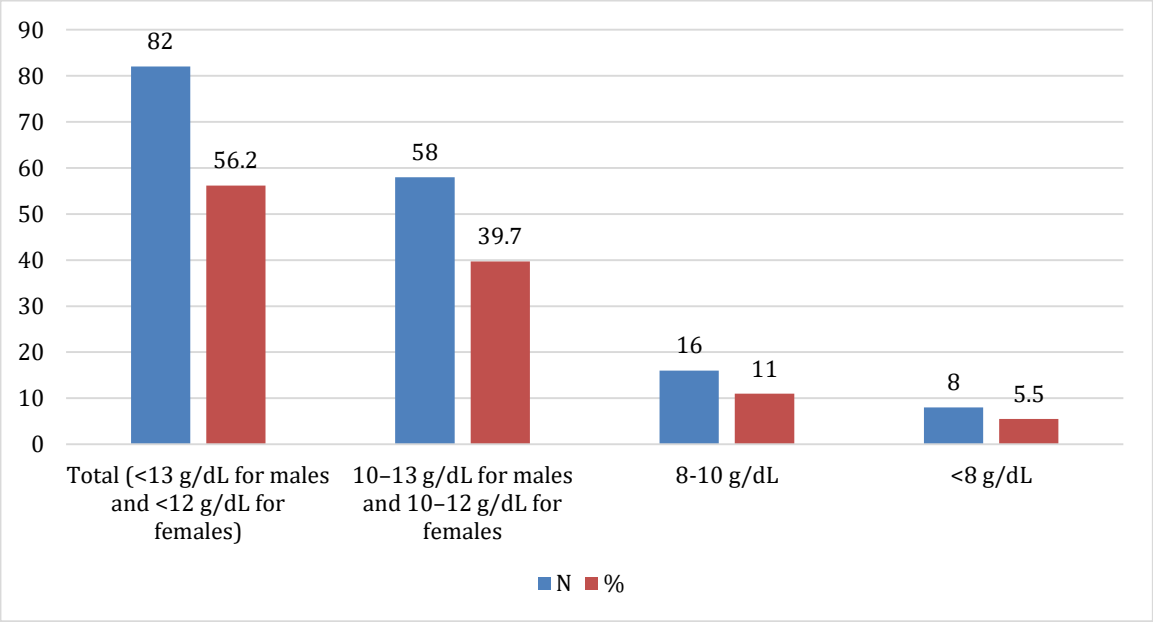

Figure-3 Distribution of patients based on their hemoglobin level (N=82)

DISCUSSION

The present study mainly focused on the characterization of iron deficiency in chronic heart failure patients and reported that Iron deficiency (ID) was highly prevalent in our cohort of chronic heart failure (HF) patients, mainly due to complete ID. The different predictors of ID included female sex, higher body mass index, more advanced functional group, higher systolic blood pressure, and lower hemoglobin levels. The prevalence of iron deficiency was 78.1% among the studied population. The prevalence of iron deficiency was significantly higher in females compared to males. In an actual patient population with congestive heart failure (CHF), iron deficiency (ID) did not serve as a predictive factor for mortality or hospitalizations after accounting for comorbidities, functional class, and neuro-hormonal treatment. Nevertheless, hemoglobin remained a significant predictor of mortality. These data are consumed are consistent with previous findings reported by other research groups [17-19].

Heart failure (HF)-related hospitalizations are common in chronic HF and result in increased mortality, decreased patient quality of life, and financial burden on the health system. Despite the diagnosis of iron deficiency (ID), it is an important determinant of health-related quality of life. Notably, predictors of hospitalization for HF are similar to predictors of low mortality, except that low serum sodium and low hemoglobin predict mortality but not hospitalization due to HF [20].

The results of our study highlight the prevalence of iron deficiency (ID) in heart failure (HF) patients. Importantly, the iron deficiency (ID) was observed in anemic heart failure patients, representing a negative prognostic indicator. In a prospective study on heart failure (HF), the incidence was reported at 62% with reported figures ranging from 37% to 50% in Europe [21, 22]. Patently, our study revealed an unexpectedly elevated prevalence of iron deficiency (ID) at 78.1%, surpassing these figures. These findings resemble an earlier study result [23].

In this study, 78.1% of patients were found to have iron deficiency (ID). Notably, a substantial proportion of patients had anemic ID. Thus, relying solely on hemoglobin (Hb) levels to assess ID in patients with heart failure (HF) may overlook a substantial proportion of cases. This subgroup of patients were not be identified unless careful consideration given to including serum ferritin and transferrin saturation in the diagnostic tests. Klip et al. [24] emphasizes the importance of a functional ID and its relationship to symptoms, regardless of ejection fraction. If ferritin levels are high, transferrin saturation (TSAT) (<20%) can be used to detect iron deficiency (function).

In our study, no significant differences were found between patients with heart failure (HF) with or without iron deficiency (ID) within the NYHA functional group. Previous detailed studies have established an association between ID and NYHA functional group in HF patients, as well as patient functional capacity [25, 26]. The absence of noteworthy differences in our study could be attributed to the high baseline New York Heart Association (NYHA) group of our patients. Additionally, as an observational study, we were unable to investigate the potential impact of iron supplementation on improving NYHA class. Numerous studies, comprising two open-label, uncontrolled trials, and four randomized, placebo-controlled trials, have documented the positive effects of iron supplementation in heart failure (HF) [27, 28].

CONCLUSION

The incidence of iron deficiency was 78.1% among the studied population. The prevalence of iron deficiency was significantly higher in females compared to males. In an actual patient population with congestive heart failure (CHF) and increasing prevalence of heart failure with preserved ejection fraction, iron deficiency (ID) did not serve as a predictive factor for mortality or hospitalizations.

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