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Original Article

Iron Status in Patients With Chronic Left Ventricular Systolic Failure

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Abstract

Background: Heart failure is one of the most important public health problems with an increasing prevalence and identifying its contributing factors is imperative. This study was conducted to evaluate the iron status in patients with chronic systolic heart failure in Shahid Mohammadi Hospital of Bandar Abbas.

Materials and Methods: A total of 80 patients with chronic left ventricular failure participated in this cross-sectional study. Data were collected using a researcher developed checklist containing demographic details and echocardiographic data (left ventricular ejection fraction, LVEF%). Additionally, the frequency and distribution of iron status were measured in the research population.

Results: The results showed that the prevalence of anemia was significantly high in patients with chronic heart failure (77.3%). The prevalence of iron deficiency (ID) was 77.33% based on iron level (<60 µg/dL), and it was 82.66% based on the mean ferritin level (ferritin<100, or ferritin of 100 to 299 ng/mL, and transferrin saturation<20%). The prevalence of total iron binding capacity (TIBC)>360 µg/dL was 26.66%, and the prevalence of mean corpuscular volume (MCV)<80 fL was 60%. Age less than 60 years, glomerular filtration rate (GFR) less than 60, and body mass index (BMI) less than 18.5 were also found to increase the risk of anemia in these patients.

Conclusion: Our study showed that the prevalence of anemia was significantly high in patients with chronic heart failure. Due to the high prevalence of anemia in patients with chronic systolic heart failure and the impact of anemia on the prognosis of the disease in these patients, effective treatment is necessary in high-risk patients to reduce the severity of their disease, compensate for their heart failure, and reduce their mortality.

Keywords: Systolic heart failure, Iron, Anemia

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Introduction

Heart failure is one of the most important public health problems that affects over 23 million people throughout the world (1). The spread of this disease will increase in the next decade due to the aging population and increased survival of patients with complications of coronary artery disease (2). Despite the new treatments and recent advances in chronic heart failure (CHF) management, functional limitations and restricting symptoms are common in treated patient. (3-5). Coronary artery disease is the cause of two-thirds of systolic heart failure cases, although hypertension and diabetes are contributing factors in many cases (6). The main symptoms of this disease, such as shortness of breath and fatigue, lead to an inability to carry out activities of daily living and affect the patient's health status (3). Despite the recent advances in the treatment of heart failure, the rate of hospitalization of heart failure patients has increased by 159% over the past decade (7). Fifty percent of patients with severe heart failure die in the first year after diagnosis and the other half die within the four years following diagnosis (8).

Anemia is the most common predisposing factor for failure to compensate for heart failure and re-hospitalization of patients refusing to comply with their treatment, whether in the form of nutritional adherence, proper intake of medications, or both (9), and iron

deficiency (ID) is the most common cause of anemia (10). ID is one of the most common nutritional deficiencies that affects over one-third of the world's population (11).

ID anemia occurs when the body iron stores are depleted and there is an insufficient amount of iron to produce the required hemoglobin of the body (12). ID is observed to be associated with poor dietary regimens, gastrointestinal hemorrhage, menstruation, and pregnancy (13).

ID is a complication of some chronic diseases (for instance, inflammatory bowel disease, rheumatic diseases, and chronic kidney disease), irrespective of its concomitance with anemia. The first report of ID in cardiovascular diseases was published over 50 years ago (11). ID anemia is widely present in patients with heart failure with an estimated prevalence of over 50% in ambulatory patients (13). Over the last decade, anemia has been identified as a destructive factor for HF that limits physical activity, reduces quality of life, predicts adverse outcomes, and is associated with increased mortality, and ID is considered a major factor causing anemia (2, 11, 14).

Untreated chronic anemia or ID can lead to an increased cardiac output, chronic increase in sympathetic activity, increased volume of extracellular and plasma fluids, exacerbated systolic or diastolic dysfunction, left ventricular hypertrophy and dilatation, renal dysfunction, and exacerbation and progression of the disease (15). Intravenous iron therapy improves the symptoms, physical capacity, and quality of life of heart failure patients with ID (16).

Given the prevalence of heart failure and ID anemia as an exacerbating factor and also the limited information in our local population on the rate of ID anemia in these patients, this research was conducted to investigate the iron status of heart failure patients.

Materials and Methods

This descriptive cross-sectional study was conducted on patients with left ventricular systolic failure referred to Cardiac Clinic of Shahid Mohammadi Hospital of Bandar Abbas during 2018-2019 with a diagnosis of CHF including compensated and decompensated failure.

The study population consisted of hospitalized patients with left ventricular systolic failure receiving standard treatment for heart failure with respect to clinical setting. All the patients were classified as New York Heart Association (NYHA) III-IV based on pre-admission history.

Inclusion and Exclusion Criteria

All patients admitted to the cardiology ward who had ejection fraction (EF) < 40% for at least 6 months, had no change in left ventricular function in spite of receiving standard treatment for heart failure, and were diagnosed with CHF were included in the study. Patients who had acute heart failure, acute renal failure, or any other acute disease (acute respiratory disease, sepsis, trauma, and surgery), critical patients requiring intensive care, patients with known thalassemia, acute hemorrhage or comorbidities (cancer, infection, and autoimmune and inflammatory diseases) were excluded.

Data were collected using a researcher-developed checklist containing demographic details and echocardiographic data (LVEF%). The checklist was completed by the researcher.

Data were collected by reviewing the recorded history and test results in the patients' records, and the frequency and distribution of iron status were measured in the research population.

Data Analysis

Data were presented as mean (SD) and frequency (percent). Intergroup comparisons were done using Student's *t* test, Pearson's Chi-square test, the Mann-Whitney U test. IBM-SPSS version 22 was used for the analysis of data. A *P* value of less than 0.05 was considered statistically significant.

Results

A total of 80 patients with CHF entered the study, but five were excluded as a result of missing data and 75 remained until the end of the research. The results showed that the prevalence of anemia was significantly high in patients with CHF. The mean age of the participants was 64.73 ± 11.69 years (range: 39 to 90 years). Of the 75 participating patients, 52 (69.3%) were men and 23 (30.7%) were women.

The mean serum iron level was significantly lower in the patients younger than 60 years of age compared to those older than 60 years (36.36 vs. 50.68 µg/dL; $P = 0.015$), and similarly, the mean transferrin saturation was significantly lower in the patients younger than 60 years of age compared to those older than 60 years (11.88 vs. 18.06; $P = 0.014$). As shown in Table 1, there was no significant difference between genders in the mean and standard deviation of the variables assessed in the patients with HF ($P > 0.05$).

The mean hemoglobin level (10.97 g/dL), serum iron level (30.5 µg/dL), and transferrin

saturation (8.48%) were significantly lower in the patients with body mass index (BMI) < 18.5 compared to the other BMI groups, while total iron binding capacity (TIBC) was significantly higher in this group of patients compared to the other BMI groups (352.5 µg/dL; $P < 0.05$).

No significant differences were found between DHF patients in terms of the NYHA class and EF ($P > 0.05$) . The mean Hb level was significantly lower in the patients with a glomerular filtration rate (GFR) < 60 compared to the other group (11.39 vs. 12.38 g/dL; $P < 0.05$).

Discussion

The present findings showed that the mean serum iron level was significantly lower in the patients younger

Table 1. The Association of Study Variables With Age, Gender, NYHA Class, EF, GFR in Anemic Patients

Variables	Hemoglobin	MCV	RDW	Ferritin	Iron	TIBC	TS
Age							
≤60	11.12 ± 2.4	78.4 ± 8.5	17.3 ± 3.8	129.3 ± 47.7	36.6 ± 15.7	313.1 ± 77	11.8 ± 4.2
>60	11.73 ± 1.6	77.4 ± 7.7	16.5 ± 2.5	126.9 ± 46	50.6 ± 23.9	298.4 ± 74	18.6 ± 9.5
P value	0.43	0.62	0.73	0.66	0.15	0.44	0.014
Gender							
Men	11.9 + 2.1	78.7 ± 8.4	17.07 ± 3.1	125.9 + 49.8	44.8 ± 21	292 +71.3	16.2 ± 7.4
Women	11.29 ± 1.9	75.5 ± 6.2	16.1 ± 2.3	131.4 + 36.9	50.2 ± 25.8	327 ± 78.9	16.21 ± 9.8
P value	0.38	0.107	0.28	0.91	0.49	0.6	0.82
NYHA III							
II	11.9 + 1.4	76.4 + 7.8	16.4 ± 2.4	130.8 + 46	48.4 ± 22.7	284 ± 83	18.2 ± 9.7
III	11.2 + 1.9	78.2 ± 7.4	17.01 ± 3.4	117 ± 48	45.8 ± 23.2	321 ± 62	15.9 ± 8.3
IV	12.7 + 3.1	90.9 + 9.6	17.1 + 3.06	151 ± 23.6	41.1 ± 22.4	304 ± 73	12.8 ± 4.6
P value	0.09	0.3	0.88	0.21	0.64	0.13	0.203
EF							
<30	11.7 ± 2.1	78.2 ± 7.4	16.9 + 38	128 + 47.4	44.3 + 20.5	298.8 ± 68	15.2 ± 6.6
≥30	11.70 ± 1.3	76.6 + 9.1	16.3 ± 1.7	136.7 ± 43	51.5 ± 27	312 ± 89.6	18.7 ± 12.4
P value	0.72	0.43	0.85	0.76	0.31	0.49	0.58
GFR							
<60	11.3 ± 1.5	77.5 ± 8.2	16.5 ± 2.4	126 ± 45	46.1 ± 24	299.6 ± 81	16.4 + 9.8
≥60	12.3 ± 2.4	77.9 ± 7.3	17.3 ± 3.7	136 ± 46	47.2 + 19	303 ± 61	15.7 ± 6.3
P value	0.03	0.97	0.27	0.18	0.83	0.65	0.73

Abbreviations: EF, ejection fraction; MCV, Mean corpuscular volume; TIBC, total iron binding capacity; NYHA, New York Heart Association; TS, transferrin saturation; RDW, red cell distribution width.

than age 60 years compared to those older than 60 years. The mean transferrin saturation was also found to be significantly lower in the patients below age 60 years compared to those older than this age, which disagrees with the results of other studies; however, the researchers could not find any explanations for it.

Considering hemoglobin values > 13 g/dL and 12 g/dL acceptable for men and women, respectively, the prevalence of anemia was found to be 77.3%.

The prevalence of anemia in patients with heart failure (hemoglobin values > 13 g/dL for men and > 12 g/dL for women) was 30% in clinically stable patients and it was 50% in the hospitalized patients (16). In the study by Ikama et al, the prevalence of anemia in patients with heart failure was about 42 (17).

The review of other studies showed that the prevalence of anemia varied from 4% to

61%, and mostly from 18% to 20%. Such a wide range may be due to the differences in the research methods and essentially the definition of anemia, as most studies have used the definition provided by the World Health Organization, i.e., hemoglobin > 13 g/dL for men and > 12 g/dL for women, while some studies have divided the patients based on the definition of National Kidney Foundation, i.e., hemoglobin > 12 g/dL for men and < 11 g/dL for women (18).

In the present study, the prevalence of anemia was found to be 77.3%, which is higher than that in the study by Ikama et al since the WHO definition was used for anemia in the present study and the NKF definition in the study by Ikama et al (17).

In the present study, the mean ferritin level was 127.65 ng/mL, mean iron level was 46.48 µg/dL, mean TIBC was 302.75 µg/dL, and transferrin saturation was 16.25%. The prevalence of ID was found to be 77.33% based on the iron level (< 60 µg/dL) and 82.66% based on the ferritin level (ferritin < 100, or ferritin of 100 to 299 ng/mL, and transferrin saturation < 20%), and the prevalence of TIBC > 360 µg/dL was 26.66%.

In chronic HF, ID has a known effect on the morbidity of 37%-61% of the patients. ID has a multifactorial etiology. Previous studies have shown that ID can be severe in patients with CHF even before the onset of anemia and aggravate the underlying disease (19).

In a study conducted by Mistry et al to investigate anemia in HF patients, the prevalence of ID was estimated to be 30-83%. ID in HF is thus seldom diagnosed unless actively sought. ID has been shown to directly contribute to increased mortality and hospitalization in HF patients compared to cases without ID or those with anemia without ID (18). In the present study, the prevalence of ID based on the serum iron was 77.3%, which agrees with the aforementioned study, but this issue was not investigated in the study conducted by Ikama et al (17). In

the present study, the prevalence of ID was 82.66% based on the ferritin level (ferritin < 100, or ferritin of 100 to 299 ng/mL, and transferrin saturation < 20%). Meanwhile, Mistry et al reported a prevalence of 30-50% for ID in patients with CHF, and the reason for this difference is the definitions used for ID and the different inclusion criteria applied (18). In agreement with the present study, in the study conducted by Nanas et al, ID was confirmed by bone marrow aspiration in 73% of the patients (20).

There were no significant differences in the mean and standard deviation of the variables assessed in the patients with DHF between genders ($P > 0.05$). This finding may have been due to the fact that fewer women participated in the study than men.

There was also no significant difference between the patients with DHF in terms of EF, which agrees with the study conducted by Ikama et al reporting no significant difference between the anemic and non-anemic groups in terms of EF (17).

In the present study, the prevalence of anemia in HF patients was high, but NYHA was not found to have any relationships with iron and other laboratory variables.

In the study by Ikama et al, no significant difference was observed between the anemic and non-anemic groups in terms of NYHA classification III-IV (17).

Moreover, in the present study, the mean levels of hemoglobin, serum iron, and transferrin saturation were significantly lower in the patients with BMI < 18.5 compared to the other BMI groups, while TIBC was significantly higher in this group compared to the other BMI groups. This result could have been due to the patients' nutritional deficiency.

The mean Hb level was significantly lower in patients with GFR < 60 than in the other group (11.39 vs. 12.38 g/dL; $P < 0.05$), which concurs with most studies, including the study by Ikama et al in which a significant difference ($P < 0.004$) was observed between the anemic and non-anemic groups in terms of GFR (17).

Conclusion

Our study showed that the prevalence of anemia was significantly high in patients with CHF.

Given the high prevalence of anemia in patients with compensated systolic heart failure and the impact of anemia on the prognosis of the disease in these patients, effective treatment is necessary in high-risk patients in order to reduce the severity of their disease, compensate for their heart failure, and reduce their mortality.

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Authors' Contributions

The idea of this research: MN and MH; data collection: FN; original draft preparation: MK and MA; final approval of article: MN and SM; data analysis: EB.

Conflict of Interest Disclosures

The authors state that they have no conflict of interest.

Ethical Statement

All records were anonymized and de-identified prior to the analysis. This study was approved by the Ethics Committee of Hormozgan University of Medical Sciences (IR.HUMS.REC.1398.108).

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Informed Cosnent

The present study was carried out after obtaining informed consent

Study Highlights

Anemia is the most common predisposing factor for decompensation and rehospitalization of CHF patients. However, the evaluation and treatment of anemia in these patients have not yet found their proper place.

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