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Original Article

Prevalence of Iron Deficiency in Patients with Heart Failure

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Abstract

Background: Heart failure (HF) is a common health issue with the prevalence between 1% and 2% in public; in addition, it is a major risk factor for mortality, morbidity, and low quality of life. The prevalence of iron deficiency (ID) in patients with chronic HF (CHF) was examined in the present study. **Materials and Methods:** In the present cross-sectional, iron parameters of patients hospitalized for CHF decompensation were prospectively assessed within the 72 h following admission to hospital. ID was established as serum ferritin <100 μg/ml (absolute ID) and serum ferritin between 100 and 299 μg/ml with transferrin saturation <20% (functional ID) in accordance with the European Society of Cardiology HF Guidelines 2012. **Results:** The present study showed that the prevalence of absolute and functional iron deficiencies in patients with CHF was 44.9% and 18.8%, respectively, and 36.2% did not have the ID. The study did not find a significant difference in ID between male and female patients and between the patients with and without comorbidities. **Conclusions:** The present study suggests that ID is very common in patients admitted for CHF.

Keywords: Chronic heart failure, Iron deficiency, patients, serum ferritin

Introduction

Heart failure (HF) is a common health issue with the prevalence between 1% and 2% in public, in addition, it is a major risk factor for mortality, morbidity, and low quality of life (QoL).[1,2] There is a frequent anemia in patients with stable HF,[3,4] which enable to raise morbidity with respect to hospital admissions, low level of QoL, high mortality, and impaired exercise capacity. Iron deficiency (ID) and anemia are common comorbidities that coexist in patients diagnosed with HF. These commodities, together or independently, are related to poor clinical outcomes.[5] Chronic HF (CHF) is considered a severe disease with poor clinical outcomes despite new therapies.[6] This disease has a large number of comorbidities, including diabetes mellitus, renal diseases, coronary artery disease, anemia, hypertension, obesity, sleep apnea, and depression which were shown to contribute to poor patient outcomes.

The European Society of Cardiology (ESC) guidelines for the diagnosis and treatment of acute and CHF identified ID as a comorbidity in HF for the first time. The guidelines suggested that the HF diagnosis be made according to iron parameters in all patients skeptical with HF.[7]

ID is an emerging problem in patients with CHF and can be a potential therapeutic target. The majority of the studies conducted in association of ID with HF originated from western countries, and there is dearth on this regard in the Asian region in particular in Iraq. This issue has been examined in a few studies in Asian patients.[8,9] Currently, the estimation of prevalence of ID in patients with HF has not been examined in Iraq and no any information is available about this issue. In addition, not much is known about the prevalence, predictors of ID in patients with CHF.

Iron efficiency has been shown to associate with poor outcome in patients attended the hospital for CHF decompensation. However, the prevalence of ID whether absolute or functional has not been examined in this region. The prevalence of ID in patients with CHF was examined in the present study.

Materials and Methods

Study design and patients' recruitment

In the current cross-sectional study, the patients visited the outpatient and inpatient clinics of the Department of Medicine at the Azadi Teaching Hospital, Duhok, Iraq, were

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consecutively screened by a specialist for eligibility criteria. In this study, 69 patients aged 30–90 years old and diagnosed with CHF through clinical and biochemical investigations were included in the study. The data collection was performed between September 1, 2017 and December 15, 2017. The recruited patients were assessed for the ID.

The patients were eligible for the present study if they were males or females, aged 25 years and older, diagnosed with CHF. The Pregnant patients or those who were taking iron supplements within/prior 72 h of admission, were excluded from the study.

The information was taken from the patients through self-reported technique were age, gender, and comorbidity and regardless of their sociodemographic aspects. In addition, the venous blood sample of them was taken for assessment of iron categories through biochemical investigations. Patients with noncardiac comorbid conditions causing ID such as hemorrhoids, malignancy, or patients with end-stage renal failure, and patients with specific etiologies such congenital heart disease were excluded from the study.

Measurement and diagnostic criteria

Diagnosis of HF was established according to the validated criteria of the ESC Guidelines[7] taking into consideration of HF with preserved ejection fraction (EF)[10] and the Framingham criteria.[11] The patients were underwent thorough history taking and clinical evaluation, blood sampling, and comprehensive transthoracic echocardiography using standardized equipment.

Patients were characterized as having normal (EF ≥ 50%) or mild (EF 45%–50%), moderate (EF 31%–44%), or severe (EF ≤30%) LV systolic dysfunction. The patients' blood samples were assessed for iron status through complete iron profiles, including serum iron, serum ferritin, total iron binding capacity (TIBC), and transferrin saturation (TSAT).

The venous blood sample was drawn from all patients within 72 h following hospital admission for the measurement of the following biochemical parameters: serum ferritin, serum iron, TIBC, and TSAT. The biochemical investigations were performed in the biomedical laboratory of the hospital. ID was established as serum ferritin <100 μg/ml (absolute ID) and serum ferritin between 100 and 299 μg/ml with TSAT <20% (functional ID) in accordance with the ESC HF Guidelines 2012.[7]

Statistical analysis

The Statistical Package for the Social Sciences version 25 (SPSS, IBM Company, Chicago, USA) was used for statistical analysis. The frequency percentage and mean standard deviation (SD) were performed for descriptive purposes such as prevalence of ID in patients with HF. The prevalence of absolute and functional ID was determined in frequency and percentage. The difference in prevalence of ID between male and female patients and between the patients with and without comorbidities was determined in Chi-Squared and Fishers' Exact tests, respectively. The predictors of ID were examined through binary logistic regression. The level of <0.05 was considered as statistically significant difference.

Ethical considerations

In the current study, no any intervention was applied to the patients. The patients had right to reject to not participate in the study. The patients were guaranteed the confidentiality of their personal information. The ethical approval of the present investigation was obtained from the Kurdistan Board for Medical Specialties (KBMS). The study was conducted in line with the Declaration of Helsinki as confirmed by the KBMS ethical committee.

Results

The mean age of the patients was 65.79 (SD: 12.34 year). Of the total 69 patients included in the study, the number of the male and female patients was similar, 36 and 33, respectively. In addition, the majority of the patients included in this study had at least one comorbidity apart from HF (87.0%) [Table 1].

The mean concentration of serum iron was 45.13 (SD: 23.04) ranged 15.00–116.0 g/dL. In addition, the means of total iron, serum ferritin, and transferrin were 280.13 (SD: 75.36 mg/dL), 121.50 (interquartile range: 186.0 ng/mL), and 17.49 (SD: 9.99%), respectively [Table 1].

The study showed an absolute ID was 44.9%, functional ID was 18.8%, and 36.2% did not have ID. The study did not show that the significant difference in prevalence of ID between male and female patients ($P = 0.728$) and between the patients with and without comorbidities ($P = 0.809$), [Table 2].

The total ID was considered as dependent variables and other patients' characteristics as preceptors in binary logistic regression. The study showed that lower serum ferritin and transferrin are independently associated with ID in our sample size, $P = 0.006$ and $P = 0.007$, respectively [Table 3].

Discussion

The author's aim in conducting the present study was to evaluate the prevalence of absolute and functional ID in a sample population with CHF.

The overall absolute and functional iron deficiencies were 44.9% and 18.8% in this study. The prevalence of ID has been investigated in other studies as well. For example Cohen-Solal *et al*.[12] reported that the prevalence of ID was 69% in men and 75% in women. The prevalence of absolute ID and function ID was 41% and 49%, respectively. They found that the prevalence of anemia was 68% in men and 52% in women as determined <13 g/dL for men and <12 g/dL in women according to the World Health Organization. The prevalence of ID in nonanemic patients was 57% in men and 79% in women. In our study, the prevalence of absolute and functional ID was 44.9% and 18.8%, respectively. We did not examine the prevalence of ID in anemic and nonanemic patients. Kalra *et al*.[13] reported that the prevalence of ID was 50% in a cohort

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Table 1: Baseline information of study patients

General information ($n=69$)	Frequency distribution	
	Mean	SD
Age (year)	65.79	11.94
Serum iron (μg/dL)	45.13	23.04; range: 15.00-116.00
Total iron (mg/dL)	280.13	75.36; range: 22.00-426.00
Serum ferritin (ng/mL)*	121.50	186.0; range: 4.00-2000.00
Transferrin (%)	17.49	9.99; range: 1.10-47.00
Gender		
Male	36	52.2
Female	33	47.8
Comorbidity	60	87.0

*The numbers for serum ferritin are median (IQR). SD: Standard deviation, IQR: Interquartile range

Table 2: Overall iron deficiency and its prevalence bases on the gender and comorbidities

	Frequency	Male	Female	*P* (two-sided)
Absolute iron deficiency	31 (44.9)	16 (44.4)	15 (45.5)	0.728 Chi-square test
Functional iron deficiency	13 (18.8)	8 (22.2)	5 (15.2)	
Normal iron level	25 (36.2)	12 (33.3)	13 (39.4)	
	Comorbidity			*P* (two-sided)
	Yes	No		
Absolute iron deficiency	26 (43.3)	5 (55.6)		0.809 Fisher's exact test
Functional iron deficiency	12 (20.0)	1 (11.1)		
Normal iron level	22 (36.7)	3 (33.3)		

The numbers are in frequency (%)

Table 3: Logistic regression of total iron deficiency

Predictors	*B*	SE	Wald	*P*	OR	95% CI	
						Lower	Upper
Age	0.055	0.053	1.082	0.298	1.057	0.952	1.173
Gender	−1.776	1.385	1.644	0.200	0.169	0.011	2.557
Comorbidity	−1.455	2.230	0.426	0.514	0.233	0.003	18.467
Serum iron (microgram/dL)	−0.011	0.028	0.163	0.686	0.989	0.936	1.044
Total iron (mg/dl)	0.013	0.008	2.567	0.109	1.013	0.997	1.029
Serum ferritin (microgram/dL)	0.043	0.016	7.563	0.006	1.044	1.013	1.077
Transferritin (%)	0.458	0.170	7.305	0.007	1.581	1.134	2.205

OR: Odds ratio, SE: Standard error, CI: Confidence interval

of 1506 CHF patients. The ID is related to disease severity and it is a greater predictive value for the outcome compared to the anemia. Klip *et al*.[4] reported a 50% for prevalence of ID in a much larger sample of 1506 patients.

We did not find a significant difference in prevalence of ID between male and female patients. Cohen-Solal *et al*.[12] reported a slightly higher ID prevalence in women (48.9%) compared to 40.6% in men.

We did not examine the prevalence of ID in several points of the patient admission in this study. While Cohen-Solal *et al*.[12] showed that the prevalence of ID remained high during the entire hospitalization period. The prevalence rates of ID in 1st, 2nd, 3rd, 4th, and 5th day of admission were 82%, 70.3%, 72.4%, 75.3%, and 58.7%, respectively.

We did not include the patients were taking iron supplementations within the 72 h of the hospital admission to avoid the measurement bias. Clinical trials have approved that fictional status and QoL was improved in patients with CHF following ID correction with intravenous (IV) iron.[14-16] Anker *et al*.[16] showed the improvement in health-related QoL and 6 min distance in patients with CHF following IC iron supplementation compared to the placebo, even in anemic and nonanemic patients. Therefore, it is so important to assess the ID in CHF patients for the iron prescription. There is evidence that IV route is more efficient for iron supplementation for its retention pathway.[17]

The present study showed that the lower conceptions of serum ferritin and transferrin are the only predictors of ID in patients with CHF. Other studies showed that anemia and antiplatelet treatment in men, low C-reactive protein in women, and diabetes as independent predictors of ID.[12] We did not measure any other clinical features in this study; however, the study did not find that comorbidity is a predictor possibly due to small sample size. Klip *et al*.[4] reported that being female, lower mean corpuscular volume, anemia, higher NT-proBNP level, and higher New York Heart Association functional class as a predictor. We did not find the gender as a predictor for ID in this study. Possibly, the clinical characteristics of females, such as body mass index, biochemical indicators, and comorbidities, have the role in this difference. In addition, the severity of CHF was not measured in this study precluding us to establish the contribution of the predictors to the disease severity.

With the strong possibility, ID is the outcome of HF or coexist comorbidities rather than the cause of disease. ID in CHF patients may be associated with gradual iron depletion (absolute ID) owing to gastrointestinal blood loss (antiplatelet therapy or oral anticoagulation), malabsorption, or poor nutrition.[18] Chronic systemic inflammation is frequently seen in CHF, which is contributed to the reduction in intestinal absorption of iron and the reduction in recycled iron availability in blood cells in the reticuloendothelial system (functional ID).[19] The role of iron in the CHF pathophysiology and its causal pathway between ID and disease severity remains unclear. However, the ID has shown to associate with worsening of chronic diseases, even after adjustment for anemia.[20] Iron is required for energy production in cells of mitochondrial chain.[21] Iron is immobilized owing to the chronic inflammation in patients with chronic illnesses resulting in functional ID.[22]

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Conclusions

The study showed that ID is very common in patients admitted for CHF. The authors suggest the iron assessment during the hospital admission for these kinds of patients.

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Conflicts of interest

There are no conflicts of interest.

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