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Prevalence of iron deficiency among patients with chronic heart failure attending Rizgary and Hawler teaching hospitals in Erbil City

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Abstract

Background and objectives: Iron deficiency is an emerging problem in patients with chronic heart failure and could be a potential therapeutic target. This study aimed to determine the prevalence, severity, and type of iron deficiency among patients with chronic heart failure.

Methods: This study was conducted in Rizgary and Hawler teaching hospitals in Erbil from April 2015 to January 2016. A total of 60 patients with heart failure for more than six months with an ejection fraction less than 55% were enrolled. These patients were evaluated for iron status and hematological indices.

Results: The prevalence of iron deficiency was 76.7% with 52% of them having severe iron deficiency. Absolute iron deficiency was detected in 41% of patients. The prevalence of anemia was 41.7%. There was a significant difference between those with chronic heart failure with iron deficiency and those with no iron deficiency in the hemoglobin (P = 0.001), mean cell volume (P = 0.001), mean corpuscular hemoglobin (P = 0.002), serum iron (P <0.001) and transferrin saturation (P <0.001).

Conclusion: Iron deficiency is common in chronic heart failure. It is the most common cause of anemia in such patients. Serum ferritin alone was not a reliable marker of iron deficiency in such patients.

Keywords: Chronic heart failure; Iron deficiency; Anemia.

Introduction

Iron deficiency, with or without anemia, and chronic kidney disease are the most prevalent comorbidities in chronic heart failure and worsen prognosis, decrease aerobic performance and exercise intolerance.[1] chronic heart failure is a multisystem disease resulting from the inability of the heart to fill and /or pump adequate amount of blood to meet metabolic need of the body due to the functional or structural abnormality of the heart, and it is chronic inflammatory process affecting functional capacity of many organs for example liver, kidney, and skeletal muscle.[2] Iron is an essential trace element present in our body in reduced and oxidized form. About 67% of total body iron present in erythrocyte (as hemoglobin) and in muscle cell (as myoglobin), 30% stored in macrophage and liver cell and 3% losses in urine, sweat, bile, and enterocytes.[3] Since iron is not metabolized in the body (actively excreted from the body), iron homeostasis is mostly regulated by iron absorption in the gut[4] and average iron intake is 10–20 mg/day, but only 10–20% of dietary iron absorbed.[5,6] Hepcidin is a protein produced by liver cell in response to infection and inflammation (especially chronic inflammation like cancer, rheumatoid arthritis, renal failure and heart failure, in such conditions there will be inflammatory cytokine-like interleukin 6 act on liver leads to release of Hepcidin which acts on ferroportin in macrophage, liver cells and enterocyte leads to decrease in iron absorption by enterocyte and decrease iron mobilization from enterocyte, macrophage, liver cells to

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blood stream.[7,8] Iron deficiency anemia (IDA) is reduction in hemoglobin (Hb) concentration (Hb<12 g/dL in women and <13 g/dL in men) or hematocrit or red blood cell as a result of depletion of iron store, either due to decrease iron intake or decrease iron absorption or excess iron loss, there are two types of iron deficiency in chronic heart failure; absolute iron deficiency (depletion of iron store) and functional iron deficiency (impairment of iron mobilization from liver, macrophage and enterocytes by Hepcidin and hence iron in bone marrow gradually depleted by new erythrocyte formation and leads to IDA).[9] Causes of iron deficiency in chronic heart failure may be due to decrease iron intake (anorexia or decrease protein intake due to associated kidney disease), gastrointestinal blood loss (uremia cause platelet dysfunction, antiplatelet drugs, anticoagulation), decrease iron absorption either due to intestinal mucosal edema or by effect of hepcidin on enterocyte in case of chronic inflammation. Also, iron deficiency in chronic heart failure may be due to decreased erythropoietin production if there is associated renal failure or bone marrow resistance to erythropoietin when there is no adequate amount of iron store. Hemodilution due to sodium and water retention may be another cause.[10] Diagnosis and treatment of iron deficiency in chronic heart failure patients is important because iron plays important role in oxygen uptake, transport, storage and in the oxidative metabolism in the erythropoiesis, heart and skeletal muscle hence affecting functional capacity and prognosis of the patients with chronic heart failure.[11] Anemia is present in about 40% of heart failure patients, iron deficiency is present in about 60% of the patients with anemia (which form about 24% of all heart failure patients) and in about 40% of patients without anemia (about 24% of all heart failure patients); thus iron deficiency is present in about half the patients with heart failure.[10] This study aimed to determine the prevalence, severity and type of iron deficiency among patients with chronic heart failure in Erbil city and the relation with the serum iron, ferritin level in anemic and non-anemic patients. This study also aimed to compare number and percentage of some studied variable between those patients having chronic heart failure with iron deficiency and those with no iron deficiency. It also aimed to compare the mean ± SD of the same studied variable between those patients having chronic heart failure with anemia and those who are not anemic, between those patients having chronic heart failure with no iron deficiency, mildiron deficiency and severe iron deficiency and between those patients having chronic heart failure with absoluteiron deficiency and those with functional iron deficiency.

Methods

This cross-sectional study was conducted in Rizgary, and Hawler teaching hospitals in Erbil from April 2015 to January 2016. A total of 60 patients (41 male and 19 female) were enrolled by purposive non-random sampling, and informed consent was taken. The criteria for inclusion included chronic heart failure (more than six months) with left ventricular ejection fraction less than 55% proved by echocardiography (Echo). Those with history of acute coronary syndrome, coronary revascularization or any major surgery within three months preceding the study, any acute/chronic illness including malignancy, those with history of anemia and / or iron deficiency treatment either at the time of the study or in past 12 months, those who received erythropoietin therapy, or blood transfusions at the time of the study were excluded. A thorough history was taken for symptoms of heart failure and anemia, and all of them were examined for signs of anemia and heart failure. We also reviewed associated comorbidities like hypertension (HTN), diabetes mellitus (DM), ischemic heart disease (IHD) and some of them unknown to have comorbidities. Chest

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x-ray and electrocardiography (ECG) were taken. LVEF was assessed by Echo that was graded to: (normal ejection fraction> 55%, mildly reduced 40-55%, moderately reduced 20-39%, and severely reduced ejection fraction< 20%) 12. We assessed the functional capacity of the patient by the New York Heart Association (NYHA) classification. The body mass index (BMI) and estimated glomerular filtration rate (eGFR) were assessed by measuring creatinine clearance by Cockcroft-Gault equation. According to eGFR, the stages of chronic kidney disease are classified as; Stage 1: Kidney damage with normal or increased GFR (>90 mL/min/1.73 m2). Stage 2: Mild reduction in GFR (60-89 mL/ min/1.73 m2), Stage 3a: Moderate reduction in GFR (45-59 mL/min/1.73 m2,Stage 3b: Moderate reduction in GFR (30-44 mL/min/1.73 m2,Stage 4: Severe reduction in GFR (15-29 mL/min/1.73 m2,Stage 5: Kidney failure (GFR <15 mL/ min/1.73 m2 or dialysis.[13] A total of 5 ml peripheral venous blood samples were collected from each patient and sent for investigation, 2 ml of blood was collected into EDTA-containing tubes for complete blood count (CBC) including; Hemoglobin (Hb), Hematocrit (Hct), Mean corpuscular volume (MCV), White cell count (WBC), platelets count, Red cell distribution (RDW) and ESR, the remaining 3ml of blood was used for preparing of serum to determine iron status by serum ferritin (µg/dl), serum iron, total iron binding capacity (TIBC) with and unsaturated iron binding capacity (UIBC)(UIBC = S.TIBC - serum iron). Transferrin saturation (TSAT %) which was defined as a ratio of serum iron (µg/dl) and total iron binding capacity (µg/dl) multiplied by 100 (TSAT%= serum iron /TIBC X100). Reduced TSAT % less than (20%) is indicate insufficient iron available for metabolizing cells. In healthy persons, serum ferritin cut-off level can be used to diagnose absolute iron deficiency are 30 µg/ dl. In the inflammatory conditions, diagnosis of iron deficiency needs higher serum ferritin cut off level. In the current study, absolute iron deficiency in chronic heart failure is defined as serum ferritin less than 100 µg /dl in combination with a TSAT less than 20% while functional iron deficiency in chronic heart failure serum ferritin is between 100-300 µg/dl in combination with a TSAT less than 20%.[14] Mild iron deficiency defined as TSAT% between10.1- 19.9% while Severe iron deficiency defined as TSAT% between 0.1- 10%.[15]

Statistical Analysis:

The results were analyzed with the statistical package for the social sciences (version 19). Data are expressed as means ± SD when normally distributed and as numbers and percentages when data are categorical. We analyzed parametric variables with independent samples t-tests in comparing variables between (anemic andnon-anemic patients, absolute and functional iron deficiency patients) and one-way ANOVA in comparing variables between (no iron deficiency, mild iron deficiency, and severe iron deficiency patients). Non-parametric variables analyzed with Chi-square tests in comparing categorized variable between iron deficiency and no iron deficiency patients. A *P* value of ≤0.05 was considered statistically significant.

Results

Our study population includes 60 patients having chronic heart failure consisting of 41 (68.3%) male and 19 (31.7%) female, with a male: female ratio of (2.15:1). The Mean of age (± SD) was 61± 13 years ranging from 31- 90 years. The ejection fraction of patients ranges from (20-45%) with the mean (± SD) of 35±7 % Estimated glomerular filtration rate (eGFR) of the patients ranged from (8-200%) with the mean (± SD) was 79.7 ±32.8. According to NYHA functional classification of heart failure, 27 (45%) of patients were of class III, and 17 (28%) of them were class IV. Prevalence of iron deficiency among chronic heart failure patients in the current study was 76.7% (46 patients: 29 male and

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17 female). Among 41 male patients, 29 (70.7%)had an iron deficiency, and among 19 female patients, 17(89.5%) had iron deficiency. Among 46 iron deficiency patients, 22 (47.8%) had mild iron deficiency (13 males, nine females) and the remaining 24 (52.2%) had severe iron deficiency (16 males and eight females). Among 46 iron deficiency patients, 19 (41.3%) had absolute iron deficiency (13 males, six females) and the remaining 27 (58.7%) had functional iron deficiency(16 male, 11 female). Although five patients of these 27 patients had serum ferritin more than 300 µg/dl, they had TSAT less than 20%. The mean (± SD) of Hb was 12.9 (±2.12) gm/dl (range 7.4-17.1 gm/dl). The prevalence of anemia among the studied patients was 25 (41.7%) including 16 males and nine females, and there was no significant difference between male and female patients (*P* = 0.542). Among 19 absolute iron deficiency patients, 12 (63.2%) had severe iron deficiency including seven anemic, and the remaining seven patients (36.8%) had mild iron deficiency including four anemic. Among 27 functional iron deficiency patients, 12 (44.4%) had severe iron deficiency including seven anemic, and the remaining 15 (55.6%) had mild iron deficiency including six anemic. Among 14 patients with normal iron status, only one (7.2%) was anemic. The MCV of RBC ranged from 60.4 to 108.4 ft with a mean (± SD) of 86.7±8.7, and MCH ranged from 19.1 to 34.6 pg with the mean (± SD) of 27.7 ±3.4. Fifteen out of 60 (25%) patients were hypochromic, in whom nine of 15 patients were microcytic hypochromic including seven anemic. The remaining two of nine patients were non-anemic patients. The remaining six of 15 hypochromic patients were hypochromic normocytic, in whom five were anemic while the remaining one was non-anemic patient. In 39 out of 60 (65%) patients were normocytic normochromic, in whom 12 of 39 patients were anemic while the remaining 27 of 39 patients were not anemic. The remaining six out of 60 (10%) patients had macrocytosis with MCV between 97 and 108.4 ft, in which one out of six was anemic and mild absolute iron deficiency, while the remaining five had normal iron status and were not anemic. Macrocytosis means that they may have other hematinic deficiency. The serum iron ranged from 4 to 161 µg/dl with the mean (± SD) of 31.6 ±27.7 µg/dl. The mean (± SD) TIBC was 327.5 ±92.1 ranging from 149 to 614 µg/dl. The serum ferritin range was from 14.6 to 1041 µg/dl with the mean (± SD) of 175.48 ±166 µg/dl and TSAT was ranging from 0.97 to 41.6% with the mean (± SD) of 15.1% ±10.8. Among 24 patients with severe iron deficiency, 23 (95.8%) had low serum iron, while among 22 mild iron deficiency patients, 13 (59%) had low serum iron. Out of 60 chronic heart failure enrolled patients,16 (26.6%) had moderate to severe chronic renal disease (eGFR less than 60 mL/min/1.73 m^2) which possibly increase the risk of anemia. Among these 16 (100%) patients with chronic kidney disease, seven (43.8%) were anemic in which two had severe iron deficiency (one absolute iron deficiency and other functional iron deficiency), four had mild iron deficiency (one absolute iron deficiency and three functional iron deficiency) and one normal iron status. The remaining nine (56.2%) patients were not anemic in whom two had severe iron deficiency (one absolute iron deficiency and other functional iron deficiency), five had mild iron deficiency (one absolute iron deficiency and four functional iron deficiency), and two had normal iron status. Tables 1, 2 and 3 show the frequency and percentage of the category of each studied variable among iron deficiency and no iron deficiency patients with chronic heart failure together and a comparative study between them. Tables 4,5 and 6 show a comparative study of mean (± SD) of same variables between those patients having chronic heart failure with no iron deficiency, severe iron deficiency and those with mild iron

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deficiency, between those patients having chronic heart failure with absolute iron deficiency and those with functional iron deficiency, also between patients with chronic heart failure with anemia and those have no anemic. Table 1 shows no significant differences in age, gender, BMI, comorbidities, NYHA functional classification, ejection fraction and stages of chronic kidney disease between 46 patients having chronic heart failure with iron deficiency and 14 patients having chronic heart failure with no iron deficiency.

Table 1: Frequency, percentage and comparative study of age, gender, BMI, comorbidities, NYHA functional classification, ejection fraction and stage of chronic kidney disease between 46 patients with chronic heart failure and iron deficiency and 14 patients with chronic heart failure and no iron deficiency.

Variables	Categories	iron deficiency		No iron deficiency		Total		*P* value
		No.	%	No.	%	No.	%	
Gender	Female	17	89.5%	2	10.5%	19	100%	0.189
	Male	29	70.7%	12	29.3%	41	100%	
Age Groups (Years)	30-39	4	100%	0	0.00%	4	100%	0.416
	40-49	5	71.4%	2	28.6%	7	100%	
	50-59	8	66.7%	4	33.3%	12	100%	
	60-69	13	86.7%	2	13.3%	15	100%	
	70-79	13	68.4%	6	31.6%	19	100%	
	80-89	2	100%	0	0.0%	2	100%	
	90-99	1	100%	0	0.0%	1	100%	
Body Mass Index (Kg/m^2)	Below Normal weight	1	100%	0	0.0%	1	100%	0.903
	Normal weight	14	77.8%	4	22.2%	18	100%	
	Overweight	19	73.1%	7	26.9%	26	100%	
	Mild obesity	9	81.8%	2	18.2%	11	100%	
	Moderate Obesity	1	100%	0	0.0%	1	100%	
	severe Obesity	2	66.7%	1	33.3%	3	100%	
Comorbidities	DM	4	80%	1	20%	5	100%	0.809
	DM+IHD	4	66.7%	2	33.3%	6	100%	
	HTN	4	66.7%	2	33.3%	6	100%	
	HTN+DM	2	100%	0	0.0%	2	100%	
	HTN+IHD	5	71.4%	2	28.6%	7	100%	
	HTN+IHD+DM	13	86.7%	2	13.3%	15	100%	
	IHD	9	81.8%	2	18.2%	11	100%	
	No comorbidities	5	62.5%	3	37.5%	8	100%	
NYHA Functional Classification	I	1	50%	1	50%	2	100%	0.433
	II	11	78.6%	3	21.4%	14	100%	
	III	19	70.4%	8	29.6%	27	100%	
	IV	15	88.2%	2	11.8%	17	100%	
Ejection Fraction (%)	Mild LV Dysfunction	17	77.3%	5	22.7%	22	100%	0.933
	Moderate LV Dysfunction	29	76.3%	9	23.7%	38	100%	
	Severe LV Dysfunction	0	0.0%	0	0.0%	0	0.0%	
eGFR (mL/min/1.73 m2)	Stage 1	11	64.7%	6	35.3%	17	100%	0.586
	Stage 2	22	81.5%	5	18.5%	27	100%	
	Stage 3A	9	75.0%	3	25.0%	12	100%	
	Stage 3B	2	100%	0	0.0%	2	100%	
	Stage 4	1	100%	0	0.0%	1	100%	
	Stage 5	1	100%	0	0.0%	1	100%	

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Table 2 shows a significant difference in Hb (P = 0.003), Hct (P = 0.018), MCV (P = 0.003), MCH (P = 0.020) between 46 patients having chronic heart failure with iron deficiency and 14 patients having chronic heart failure with no iron deficiency.

Table 2: Frequency, percentage and comparative study of hemoglobin, red cell indices and ESR between 46 patients with chronic heart failure and iron deficiency and 14 patients with chronic heart failure and no iron deficiency.

Variables	Categories	iron deficiency		No iron deficiency		Total		*P* value
		No.	%	No.	%	No.	%	
Hb (gm/dl)	*Anemia*	*24*	*96%*	*1*	*4%*	*25*	100%	*0.003*
	No-Anemia	*22*	*62.9%*	*13*	*37.1%*	*35*	100%	
Hct (%)	*Low Hct*	*18*	*94.7%*	*1*	*5.3%*	*19*	100%	*0.018*
	High Hct	*2*	*40%*	*3*	*60%*	*5*	100%	
	Normal Hct	*26*	*72.2%*	*10*	*27.8%*	*36*	100%	
MCV (fl)	*Low MCV*	*8*	*88.9%*	*1*	*11.1%*	*9*	100%	*0.003*
	High MCV	*1*	*16.7%*	*5*	*83.3%*	*6*	100%	
	Normal MCV	*37*	*82.2%*	*8*	*17.8%*	*45*	100%	
MCH (Pg)	*Low MCH*	*14*	*93.3%*	*1*	*6.7%*	*15*	100%	*0.020*
	High MCH	*1*	*25%*	*3*	*75%*	*4*	100%	
	Normal MCH	*31*	*75.6%*	*10*	*24.4%*	*41*	100%	
WBC (c/mm^3)	Low WBC count	2	100%	0	0.0%	2	100%	0.294
	High WBC count	4	57.1%	3	42.9%	7	100%	
	Normal WBC count	40	78.4%	11	21.6%	51	100%	
Platelet (c/mm^3)	Low Platelet count	11	91.7%	1	8.3%	12	100%	0.171
	High Platelet count	2	100%	0	0.0%	2	100%	
	Normal platelet count	33	71.7%	13	28.3%	46	100%	
RDW%	Low RDW%	0	0.0%	1	100%	1	100%	0.171
	High RDW%	32	80%	8	20%	40	100%	
	Unknown RDW%	5	83.3%	1	16.7%	6	100%	
	Normal RDW%	9	69.2%	4	30.8%	13	100%	
ESR (mm/hr)	High ESR	16	72.7%	6	27.3%	22	100%	0.240
	Unknown ESR titer	11	64.7%	6	35.3%	17	100%	
	Normal ESR	19	90.5%	2	9.5%	21	100%	

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Table 4 shows a significant differences in age (P = 0.044), Hb (P = 0.002), Hct (P = 0.005), MCV (P = 0.002), MCH (P = 0.004), serum iron (P <0.001), UIBC (P <0.004) and TSAT (P <0.001) between 24 patients having chronic heart failure with severe iron deficiency, 22 patients having chronic heart failure with mild iron deficiency and 14 patients with normal iron status, i.e. with no iron deficiency.

Table 4: Comparing mean±SD, frequency, and percentage of some variables between patients with chronic heart failure with mild iron deficiency, those with severe iron deficiency and those with No iron deficiency.

Variables		Iron deficiency			*P* value
		No iron deficiency N=14	Chronic heart failure with mild iron deficiency N=22	Chronic heart failure with severe iron deficiency N=24	
Age		61±10	66±12	57±13	0.852
Gender	Male (41)(68.3%)	12 (20%)	13 (21.6%)	16 (26.7%)	0.096
	Female (19)(31.7%)	2 (3.3%)	9 (15%)	8 (13.3%)	
IHD (39)(100%)		8 (20.5%)	16 (41%)	15 (38.5%)	0.6
Hypertension (30) (100%)		6 (42.9%)	13 (59.1%)	11 (45.8%)	0.554
Diabetes mellitus (28)(100%)		5 (41.7%)	11 (50%)	12 (50%)	0.644
Ejection Fraction		36±7	35±7	35±7	0.896
Hemoglobin (Hb)		14.59±1.71	12.86±2.02	12.18±1.97	0.002
Hct		45.34±6.14	39.97±6.32	38.46±5.70	0.005
MCV		93.19±7.38	86.60±7.36	83.04±8.80	0.002
MCH		30.06±2.73	27.89±3.09	26.33±3.48	0.004
WBC		8.64±2.91	6.84±2.14	8.11±2.15	0.061
Platelet		205±45	184±91	238±79	0.07
RDW		26.09±44.50	16.81±2.94	16.71±3.21	0.36
ESR		18.10±23.82	32.47±30.22	39.25±25.49	0.166
Serum iron		103.36±23.29	47.25±17.83	18.92±11.37	<0.001
TIBC		334.99±75.05	303.70±80.97	345.12±108.18	0.3
UIBC		231.63±63.69	264.18±70.80	326.20±104.73	0.004
TSAT		31.52±6.49	15.33±3.03	5.48±2.78	<0.001
Serum ferritin		221.24±122.28	152.58±128.49	169.77±213.08	0.478
NYHA classification (60)(100%)	I (2) (3.4%)	1 (1.7%)	0 (0.0%)	1 (1.7%)	0.616
	II (14) (23.3%)	3 (5%)	5 (8.3%)	6 (10%)	
	III (27) (45%)	8 (13.3%)	11 (18.3%)	8 (13.3%)	
	IV (17) (28.3%)	2 (3.3%)	6 (10%)	9 (15%)	
eGFR		85.72±22.35	71.87±36.31	83.36±34.42	0.37
BMI		27.77±5.07	27.92±5.39	26.87±6.52	0.81

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Table 5 shows a significant difference in TIBC (*P* <0.001), UIBC (*P* <0.001) and serum ferritin (*P* <0.001) between 19 patients having chronic heart failure with absolute iron deficiency and 27 patients having chronic heart failure with functional iron deficiency.

Table 5: Comparing mean±SD, frequency, and percentage of some variables between patients with chronic heart failure and absolute iron deficiency and those with functional iron deficiency

Variables		No iron deficiency N=14	Chronic heart failure with absolute iron deficiency n= 19	Chronic heart failure with functional iron deficiency n= 27	*P* value
Age		61±10	62.16±12.75	60.07±14.01	0.603
Gender (60) (100%)	Male (41)(68.3%)	12 (20%)	13 (21.6%)	16 (26.7%)	0.526
	Female (19)(31.7%)	2 (3.3%)	6 (10%)	11 (18.4%)	
IHD (39) (100%)		8 (20.5%)	13 (33.3%)	18 (46.2%)	0.901
Hypertension (30) (100%)		6 (20%)	10 (33.3%)	14 (46.7%)	0.958
Diabetes mellitus (28) (100%)		5 (17.9%)	8 (28.6%)	15 (53.5%)	0.369
Ejection Fraction		36±7	34.84±6.69	35.30±7.51	0.371
Hemoglobin (Hb)		14.59±1.71	12.75±1.66	12.34±2.22	0.478
Hct		45.34±6.14	40.86±5.48	38.00±6.14	0.106
MCV		93.19±7.38	84.83±8.05	84.68±8.54	0.951
MCH		30.06±2.73	26.54±3.31	27.46±3.39	0.365
WBC		8.64±2.91	7.45±1.95	7.55±2.43	0.881
Platelet		205±45	221.63±77.35	205.81±95.90	0.54
RDW		26.09±44.50	17.52±3.18	16.22±2.88	0.189
ESR		18.10±23.82	32.54±31.04	37.85±26.11	0.615
Serum iron		103.36±23.29	30.06±2.73	29.56±16.93	0.288
TIBC		*334.99±75.05*	*394.05±96.03*	*276.49±63.46*	*<0.001*
UIBC		*231.63±63.69*	*358.09±99.17*	*253.22±62.65*	*<0.001*
TSAT		31.52±6.49	9.66±6.31	10.56±5.40	0.618
Serum ferritin		*221.24±122.28*	*51.54±17.46*	*239.03±195.77*	*<0.001*
NYHA classification (60) (100%)	I (2) (3.3%)	1 (1.65%)	0 (0.0%)	1 (1.65%)	0.23
	II (14) (23.3%)	3 (5%)	2 (3.3%)	9 (15%)	
	III (27) (45%)	8 (13.3%)	9 (15%)	10 (16.7%)	
	IV (17) (28.3%)	2 (3.3%)	8 (13.3%)	7 (11.7%)	
(eGFR)		85.72±22.35	90.94±44.24	68.66±24.56	0.057
BMI		27.77±5.07	28.90±7.68	26.29±4.21	0.191

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Table 6 shows significant differences, ischemic heart disease (*P* = 0.033), Hb (*P* <0.001), Hct (*P* <0.001), MCV (*P* = 0.024), MCH (*P* = 0.02), serum iron (*P* <0.001), TSAT (*P* <0.001), between 25 patient having chronic heart failure with anemia and 35 patients having chronic heart failure with no anemia.

Table 6: Comparing mean±SD, frequency, and percentage of some variables between patients with chronic heart failure and anemia and those with no anemia

Variables		All patients N=60	Chronic heart failure and Anemia N=25	Chronic heart failure and No Anemia N=35	P value
Age		61±13	60.6±13.12	61.22±12.39	0.852
Gender	Male	41 (100%)	14 (34.1%)	27 (65.9%)	0.096
	Female	19(100%)	11 (57.9%)	8(42.1%)	
IHD		39 (100%)	20 (51.3%)	19 (48.7%)	0.033
Hypertension		30 (100%)	13 (43.3%)	17 (56.7%)	0.797
Diabetes mellitus		28 (100%)	14 (50%)	14 (50%)	0.23
Ejection Fraction		35±7	35.08±7.04	35.42±7.00	0.85
Hemoglobin (Hb)		12.99±2.12	11.00±1.32	14.40±1.26	<0.001
Hct		40.62±6.52	34.8±3.75	44.78±4.60	<0.001
MCV		86.71±8.77	83.56±9.65	88.96±7.42	0.024
MCH		27.77±3.44	26.48±3.88	28.69±2.79	0.02
WBC		7.77±2.42	7.10±2.13	8.24±2.52	0.065
Platelet		211±80	216.64±84.54	206.28±77.23	0.63
RDW		19.00±20.30	16.82±3.99	20.19±25.10	0.443
ESR		31.65±27.70	33.43±31.52	30.59±25.75	0.762
Serum iron		49.01±36.79	29.44±27.36	62.98±36.57	<0.001
TIBC		327.57±92.13	312.90±122.40	338.05±62.29	0.352
UIBC		281.39±92.03	290.25±117.83	275.06±69.26	0.567
TSAT		15.17±10.83	9.53±7.03	19.19±11.33	<0.001
Serum ferritin		175.48±166.06	178.06±220.67	173.63±116.04	0.927
NYHA classification	I	2 (100%)	1 (50%)	1 (50%)	0.853
	II	14 (100%)	6 (42.9%)	8 (57.1%)	
	III	27 (100%)	11 (40.7%)	16 (59.3%)	
	IV	17 (100%)	7 (41.2%)	10 (58.8%)	
eGFR		79.70±32.83	78.87±39.48	80.28±27.73	0.878
BMI		27.46±5.73	26.23±4.31	28.34±6.46	0.135

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Discussion

The current study reveals that iron deficiency is a common comorbidity among chronic heart failure patients with a prevalence of (76.6%) in Erbil city. Our result is in agreement with a cohort study done in Alberta, Canada[16] which concluded that "irrespective of the presence of anemia, iron deficiency whether absolute or functional, is a frequent finding in chronic heart failure patients presenting with anemia as well, affecting up to 80% of these individuals" nearly have the same prevalence. In our study, anemia was present in 25 (41.6%) patients with chronic heart failure, iron deficiency was present in 96% of patients with anemia (which form about 40% of all chronic heart failure patients) while iron deficiency was present in about 63% of non-anemic patients (which form about 36.7% of all chronic heart failure patients). Comparing our finding with Silverberg study[10] in correction of iron deficiency which stated that "anemia is present in about 40% of heart failure patients, iron deficiency is present in about 60% of the patients with anemia (which form about 24% of all heart failure patients) and in about 40% of patients without anemia (about 24% of all heart failure patients). Thus, iron deficiency is present in about half the patients with heart failure." There was an agreement about the frequency of anemia in heart failure, but on the other side, there was a clear difference in frequency of iron deficiency among both anemic and non- anemic patients. According to the OPTIME-HF trial,[17] "the prevalence of anemia in heart failure patients was 50%-60%; IDA constituted 21% of all cases of anemia in heart failure patients. The difference in the frequency of anemia and iron deficiency between these studies may be due to the difference in the sample size of enrolled patients. Among 41 male patients with chronic heart failure, 70.7% had iron deficiency, and 39% of them were anemic. Among 19 female patients with chronic heart failure, 89.5% had iron deficiency, and 47.4% of them were anemic, so female patient with chronic heart failure are more anemic and more iron deficient than male patients, and this is maybe related to menstruation, obstetric problems and frequent pregnancies that already lead to iron deficiency before developing heart failure, which become more worse during heart failure. Serum iron concentration is strongly related to iron deficiency; 36 (78.3%) out of 46 iron deficiency patients had low serum iron; among 24 severe iron deficiency patients (95.8%) had low serum iron while among 22 mild iron deficiency patients (59%) had low serum iron, but in patients with normal iron status (100%) has normal serum iron. So normal serum iron may be present in both iron deficiency state and normal iron status patients while low serum iron indicates iron deficiency. There was a significant difference in each of Hb, Hct, MCV, MCH, serum iron, and TSAT % between patients having chronic heart failure with iron deficiency especially severe iron deficiency, and chronic heart failure with anemia in comparison with patients having chronic heart failure with no iron deficiency or mild iron deficiency, and chronic heart failure with non-anemic patients, respectively. This is because iron deficiency is present in about 96% of the patients with anemia. S.TIBC and serum ferritin have only significant differences between patients having chronic heart failure with absolute and functional iron deficiency. Serum ferritin concentration was significantly lower in patients having chronic heart failure with absolute iron deficiency (with the mean of serum ferritin less 100 µg/dl which was about 51.5 µg/dl) than patients having chronic heart failure with functional iron deficiency (with the mean serum ferritin less than 300 µg/dl which was 239 µg/dl). In this study, there was no significant association of ejection fraction, NYHA classification and eGFR between chronic heart failure with iron deficiency and no iron deficiency patients and between chronic heart failure with

anemia and those without anemia, while in an international pooled analysis which includes a larger sample number there was a significant association between NYHA functional staging and ejection fraction with severity of iron deficiency anemia in which both improve after iron therapy.[18] Body mass index was fluctuating in patients with chronic heart failure due to the effect of diuretic. Diuretic also may cause an increase in hemoglobin concentration and decrease hemodilution. Therefore, it was expected to not have a significant difference in the comparative study in this study. This study was limited by having a small sample size, limited time, uncooperative patients and a small number of female patients.

Conclusion

Iron deficiency is common in chronic heart failure, and it is the most common cause of anemia in chronic heart failure. In general, chronic heart failure is more common in male than female (M:F ratio = 1.7:1), while anemia and iron deficiency are more frequent in female patients with chronic heart failure. Hb, MCV, MCH, serum iron, UIBC and TSAT% more strongly associated with iron deficiency (mild or severe) and anemia in chronic heart failure than serum ferritin and TIBC concentration; while serum ferritin and TIBC level more strongly associated with types of iron deficiency (absolute or functional) in chronic heart failure. Serum ferritin alone is not a reliable marker for the diagnosis of iron deficiency in chronic heart failure it should be combined with serum iron, TIBC, and TSAT%. Normal serum iron may be present in iron deficiency patients and normal iron status patients while low serum iron indicates iron deficiency.

Competing interests

The authors declare that they have no competing interests.

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