Original Article

Prevalence of anemia and iron deficiency among patients with heart failure admitted in a tertiary care hospital of sub-Himalayan Region in North India

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ABSTRACT

Objective: Anemia and iron deficiency (ID) are common in patients with chronic systolic heart failure (HF). The study was planned to find out the prevalence of anemia and ID in patients of chronic HF among patients admitted in a tertiary care hospital from Himachal Pradesh, India. **Methods:** This was a hospital-based open cohort observational descriptive study conducted on patients diagnosed with chronic HF. The study period was of 1 year. HF was defined on the basis of 2016 ESC Guidelines for diagnosis and treatment of acute and chronic HF. Anemia was diagnosed on the basis of WHO definitions (<13 g/dl in males and <12 g/dl in females). ID was diagnosed as serum ferritin <100 µg/dl (absolute ID) or serum ferritin 100–299 µ/dl and transferring saturation <20% (functional ID). **Results:** A total 61 patients (41 females and 20 males) were included in the study over 1 year. Out of 61 patients, 48 (78.7%) were found to be iron deficient. Thirty-four patients were having absolute ID, whereas 14 were having functional ID. Anemia was found in 29 patients (47.5%). Nineteen patients were having ID without anemia. **Conclusion:** Anemia and ID are common in patients with HF in the sub-Himalayan region in North India. Hemogram and iron profile should be included in the investigation protocol during management of HF in Indian patients.

KEYWORDS: *Anemia, ferritin, heart failure, hemoglobin, ID*

INTRODUCTION

Heart failure (HF) has reached epidemic proportions globally as well as in India. In India, as per the conservative estimates, the prevalence of HF is 1.3–4.6 million, and the incidence is 491,600–1.8 million.[1] Anemia and iron deficiency (ID) are commonly prevalent comorbidities in patients with HF and are associated with poor clinical status and increased mortality. The ID is either low iron storage (absolute) or defective iron utilization in the presence of normal/increased body iron (functional).[2,3] The prevalence of anemia in patients with HF (defined as haemoglobin [Hb] <13 g/dL in men and <12 g/dL in women) is 30% in stable and 50% in hospitalized patients. Nearly 50% of patients with HF with or without anemia have low levels of available iron.[2] The prevalence of ID is higher in the more advanced stages of HF (NYHA Class III and IV), in females, and in patients with high levels of inflammatory markers (such as C-reactive protein) as well as increased levels of NT-proBNP, but, even in patients at lower risk such as those with NYHA Class I or II, the prevalence remains >30%.[4] The clinical and prognostic significance of ID in HF is now recognized in international HF guidelines. The European Society of Cardiology HF guidelines recommend that all patients with HF should be tested for anemia and ID with serum ferritin and transferrin saturations.[5] Most of the studies available about this subject are from developed countries; the data on this subject is scanty from our country. The study was planned to determine the prevalence of anemia and ID among patients with chronic HF admitted in a tertiary care center from northern state of India.

METHODS

This was a hospital-based open cohort observational descriptive study which was conducted in a tertiary care referral hospital of Himachal Pradesh, India. Recruitment period was 1 year from July 2018 to June 2019, using an open cohort design. The inclusion criteria were patients above the age of 18 years presenting with HF. The exclusion criteria were (a) patients who had received intravenous iron within 3 months or on oral iron supplementation currently, (b) history of overt bleeding, (c) hematological disorders, (d) malignancy, (e) inflammatory disorders, (f) end-stage renal failure, and (g) acute HF due

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to acute coronary syndrome, accelerated hypertension, acute valve insufficiency, tachyarrhythmias, pulmonary embolism, or pericardial tamponade. All the newly diagnosed or on treatment patients of HF and fulfilling the inclusion and exclusion criteria were recruited as cases. Details of patient's demographic data including age and gender were recorded. Detailed clinical history was taken, and examination was performed in all cases. Functional status (NYHA class), cardiovascular risk factors, drug history, and relevant clinical details were obtained and recorded. Baseline echocardiogram was performed in all the cases. Blood biochemistry including renal and liver function tests were carried out. Hematological investigations including hemogram was done. Serum iron profile including serum ferritin, serum iron, total iron binding capacity, and percent transferrin saturation was done in all the recruited patients.

Definitions

Heart failure

Heart failure defined as per 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic HF.[5]

Iron deficiency

(a) Serum ferritin level <100 µg/l (absolute ID) anf (b) if serum ferritin level 100–299 µg/l with transferrin saturation <20% (functional ID).[6]

Anemia

Anemia diagnosed on the basis of WHO definitions (Hb <13 g/dl for males and <12 g/dl for females).[7]

Data were analyzed in Microsoft Excel 2010. Quantitative variables were expressed as mean with standard deviation and categorical variables as frequencies and percentage. For analysis of quantitative variables, *t*-test was applied, and Chi-square test was applied for categorical variables. $P < 0.05$ was considered statistically significant.

Results

Between July 1, 2018 and June 30, 2019, 61 patients of chronic HF were recruited in this observational study. The distribution of age, gender, hemoglobin, and prevalence of ID of the patients is shown in Table 1. The youngest patient was 31 years old, and oldest was 96 years old. Majority of the patients were in the age group of 50–80 years.

Patients were divided into three groups on the basis of ejection fraction on echocardiography. Group I: HFpEF (HF with preserved ejection fraction, EF ≥50%),

Group II: HFmrEF (HF with midrange ejection fraction, EF: 40–49%),

Group III: HFrEF (HF with reduced ejection fraction, EF <40%.)

The distribution of patients into various HF groups and prevalence of ID is shown in Table 2. The prevalence of anemia and ID among study subjects is shown in Table 1. Out of total 61 patients taken in the study, 48 patients (78.7%) were found to be iron deficient. ID was not present in 13 patients (21.3%). The distribution of ID according to the etiology of HF is shown in Table 3. The distribution of ID among anemic patients and anemia among ID patients is shown in Table 4. ID was not present in five patients with anemia. Hence, 50% of patients with ID were having anemia, whereas 82% of all patients with anemia were having ID ($P = 0.62$). No statistically significant relation was observed between anemia and ID in chronic HF.

Discussion

In recent years, the presence of ID and its pharmacological management in HF have received greater attention. In the absence of standard definition, ID has been defined by the diagnostic criteria as used in the FAIR-HF study in most of the observational studies.[6] Anemia is common in HF patients, especially in elderly. In most of the recent studies on anemia in HF, WHO criteria for the definition of anemia has been used.[7]

The mean age of the HF group in our study was 65.2 ± 13.9 years. This is higher in comparison to the mean age reported in previous studies from other parts of India.[8-11] However, in a study on prevalence and spectrum of ID in HF from South Rajasthan, India, the mean age of the subjects was 63.3 ± 14.4 years.[12] In another study on anemia profile in patients with congestive HF, the mean age of the patients observed was 62.7 ± 13.6 years.[13] The mean age in both the studies from India is consistent with our study and with HF patients in Europe and the USA.[14-18] Thus, we did not observe the trend of HF presenting at a younger age in Indian patients in this study. ID anemia is widely present in patients with HF. It is an independent predictor of worse functional capacity and survival. The prevalence of anemia in our study population was 47.5%. The prevalence of anemia in HF reported from India, Europe, USA, and Singapore is variable. Applying the WHO definition for anemia, the prevalence of anemia reported in studies from India varies from 35% to 76.7% and 12% to 47.5% from studies on the subjects belonging to Europe, USA, and Singapore.[8-18]

Table 1: Distribution of age, gender, hemoglobin, and prevalence of anemia and iron deficiency among study subjects

Parameter	Study population (*n*=61)	Male	Female
Sex, *n* (%)	61	20 (32.8)	41 (67.2)
Mean age (years±SD)	65.2±13.9	65.1±14.5	65.3±14
Mean hemoglobin (g/dl)	12.3±2.6	12.92±3.7	12±1.9
Prevalence of anemia, *n* (%)	29 (47.5)	12 (19.6)	17 (27.8)
Prevalence of iron deficiency, *n* (%)	48 (78.6)	18 (29.5)	30 (49.1)
Absolute iron deficiency, *n* (%)	34 (55.7)	12 (19.6)	22 (36)
Functional iron deficiency, *n* (%)	14 (22.9)	6 (9.8)	8 (13.1)

SD=Standard deviation

The prevalence of ID in this study population was 78.7%. The prevalence of ID in HF reported from India, Europe, USA, and Singapore is variable. Applying the FAIR-HF definition for ID, the prevalence of ID reported in studies from India varies from 53.8% to 76% and 36% to 61.4% from studies on the subjects belonging to Europe, USA, and Singapore as shown in Table 5.[8-10,12-18] At 78.7%, the prevalence of ID in patients with HF demonstrated in our study is one of the highest figures among current data and highlights the burden of this condition. Yeo *et al*. in their multiethnic study found percentage of iron deficient to be 61% in total patients, but it was 81.6% in Indians.[14] More male patients of chronic HF are ID in comparison to females in our study, though the difference is not statistically significant. This is in contrast to the previous studies. Sharma *et al*. found ID prevalence higher in females (91.6%) in comparison to males (68.6%).[12] Similarly, Yeo *et al*. found high percentage in females (70.5%) than in males (58.5%).[14] The possible explanation could be the difference in the sample size among male and female patients. Absolute ID was more common than functional ID in this study. Out of 48 iron deficient patients, 34 (70%) were having

Table 2: Distribution of type heart failure and prevalence of iron deficiency

Parameter Type of HF	Value (*n*=61), *n* (%)	Iron deficiency (*n*=48), *n* (%)
HFrEF	35 (57.4)	27 (77)
HFmrEF	8 (13.1)	6 (75)
HFpEF	18 (29.5)	15 (83)

HF=Heart failure, HFrEF=HF with reduced ejection fraction, HFmrEF=HF with midrange ejection fraction, HFpEF=HF with preserved ejection fraction

Table 3: Distribution of the etiology of heart failure and prevalence of iron deficiency

Type of HF	Number (*n*=61), *n* (%)	Iron deficiency (*n*=48), *n* (%)	Absolute iron deficiency, *n* (%)	Functional iron deficiency, *n* (%)
Dilated cardiomyopathy	27 (44.3)	21 (43)	15 (31.2)	6 (12.5)
Ischemic cardiomyopathy	7 (11.5)	5 (10.4)	3 (6.2)	2 (4.1)
COPD-RHF	18 (29.5)	14 (29.1)	10 (20.8)	4 (8.3)
Hypertensive heart disease	1 (1.6)	1 (2)	1 (2)	0
Restrictive cardiomyopathy	1 (1.6)	1 (2)	1 (2)	0
Rheumatic heart disease	6 (9.8)	5 (10.4)	3 (6.2)	2 (4.1)
Nonrheumatic valvular heart disease	1 (1.6)	1 (2)	1 (2)	0

COPD=Chronic obstructive pulmonary disease, HF: Heart failure , RHF=Right HF

Table 4: Distribution of patients with iron deficiency and with or without anemia

Iron status	With anemia, *n* (%)	Without anemia, *n* (%)	Total, *n* (%)
Absolute iron deficiency	16 (26.2)	18 (29.5)	34 (55.7)
Functional iron deficiency	8 (13.1)	6 (9.8)	14 (22.9)
Non-ID	5 (8.1)	8 (13.1)	13 (21.3)
Total	29 (47.5)	32 (52.5)	61 (100)

ID=Iron deficiency

Table 5: Comparison between previous studies and present study

Study	Number of patients	Mean age (years)	Anemia, *n* (%)	ID, *n* (%)	ID in anemic, *n* (%)	ID non anemic, *n* (%)	Anemia without ID, *n* (%)
Negi *et al*.[8]	226	58.2±14.1	81 (35.8)	133 (58.8)	74 (55.6)	59 (40.6)	7 (7.5)
Verma *et al*.[9]	40	46.7±16.9	14 (35)	27 (67.5)	8 (30)	19 (70.3)	6 (46.1)
Jain *et al*.[10]	584	56.6±14.5	290 (49.6)	314 (53.8)	167 (57.6)	139 (44.3)	123 (62.8)
Chopra *et al*.[11]	5590	59.1±11.8	- (65.8)	-	-	-	-
Sharma *et al*.[12]	150	63.3±14.4	77 (51.3)	114 (76)	77 (51.3)	37 (24.7)	-
Arora *et al*.[13]	275	62.7±13.6	211 (76.7)	148 (53.8)	130 (61.6)	18 (28.1)	81 (63.7)
Yeo *et al*.[14]	751	62.0±12.2	308 (47.4)	- (61.4)	- (65.3)		
Chobufo *et al*.[15]	187	65.4	- (12.0)	- (48.1)	- (47.4)	- (48.2)	- (52.5)
Klip *et al*.[16]	1506	64±13	426 (28.3)	753 (50)	- (61.2)	- (45.6)	- (22)
Jankowska *et al*.[17]	546	55±11	-	199 (36.4)	- (57)	- (32)	-
Okonko *et al*.[18]	157	71±12	61 (39)	68 (43)	- (64)	- (30)	-
Present study	61	65.2±13.9	29 (47.5)	48 (78.7)	24 (50)	24 (50)	5 (38.4)

absolute ID, whereas 14 (22.9%) were having functional ID. Among iron deficient patients, 50% (24/48) were found to have anemia and 50% (24/48) of patients were without anemia. Previous reports from our country have found the prevalence of ID in anemia from 30% to 61% and prevalence of ID without anemia from 24.7% to 70.3%.[8-10,12,13] Similarly, studies from Europe, USA, and Singapore have reported on the prevalence of ID with anemia from 47.4% to 65.3% and prevalence of ID without anemia from 30% to 48.2%.[14-18] The high prevalence of ID in nonanaemic patients is an important finding. The observation has a clinical implication in that patient should be evaluated for possible ID with or without comorbid anemia. Among the patients with anemia, 82.7% (24/29) were having the presence of ID. Interestingly, the prevalence of ID did not differ between patients with and without anemia in our study.

In this study, we analyzed the distribution of ID with type of HF based on left ventricular (LV) ejection fraction. Majority of patients (35/61) belonged to HFrEF group and 77% (27/35) of them were found to be iron deficient. The prevalence of ID among patients with HFmEF and HFpEF was 75% and 83%, respectively. Scanty literature is available where ID has been assessed as per the LV ejection fraction in patients with HF and etiological diagnosis.

Limitations

There are several limitations in this study. First, having more female patients in comparison to male patients in this study is an observation. The design was open cohort observational descriptive study for 1 year. We recruited patients who fulfilled the inclusion and exclusion criteria. This observation can be explained as a random error due to small sample size. Second, the study did not rule out worm infestations as a likely cause of ID or anemia.

Summary

Anemia and ID are common comorbidities associated with HF of various etiologies and LV ejection fraction. ID with and without anemia is common. Absolute ID was more common compared to functional ID in our patients, and percentage of ID was more among males compared to females. Universal screening for ID in patients with HF should be performed irrespective of the presence or absence of anemia.

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Conflicts of interest

There are no conflicts of interest.

References

1. Huffman MD, Prabhakaran D. Heart failure: Epidemiology and prevention in India. Natl Med J India 2010;23:283-8.
2. Anand IS, Gupta P. Anemia and iron deficiency in heart failure: Current concepts and emerging therapies. Circulation 2018;138:80-98.
3. Grote Beverborg N, van der Wal HH, Klip IT, Anker SD, Cleland J, Dickstein K, *et al.* Differences in clinical profile and outcomes of low iron storage vs defective iron utilization in patients with heart failure: Results from the DEFINE-HF and BIOSTAT-CHF studies. JAMA Cardiol 2019;4:696-701.
4. McDonagh T, Macdougall IC. Iron therapy for the treatment of iron deficiency in chronic heart failure: Intravenous or oral? Eur J Heart Fail 2015;17:248-62.
5. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, *et al.* 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J 2016;37:2129-200.
6. Anker SD, Comin Colet J, Filippatos G, Willenheimer R, Dickstein K, Drexler H, *et al.* Ferric carboxymaltose in patients with heart failure and iron deficiency. N Engl J Med 2009;361:2436-48.
7. WHO. Haemoglobin Concentrations for the Diagnosis of Anaemia and Assessment of Severity. Vitamin and Mineral Nutrition Information System. Geneva: World Health Organization; 2011 (WHO/NMH/NHD/MNM/11.1). Available from: http://www.who.int/vmnis/indicators/haemoglobin.pdf. [Last accessed on 2018 Jul 01].
8. Negi PC, Dev M, Paul P, Pal Singh D, Rathoure S, Kumar R, *et al.* Prevalence, risk factors, and significance of iron deficiency and anemia in nonischemic heart failure patients with reduced ejection fraction from a Himachal Pradesh heart failure registry. Indian Heart J 2018;70 Suppl 3:S182-8.
9. Verma S, Dua P, Saini A, Chakraborty P. Iron deficiency in chronic systolic heart failure (INDIC Study). J Pract Cardiovasc Sci 2016;2:99-102.
10. Jain D, Desai BN, Rathi RK, Shekhar C, Sahoo PK, Burkule N, *et al.* Characterization of Iron deficiency in patients with chronic heart failure: A prospective, multicentric, observational study from India. J Indian Coll Cardiol 2020;10:30-6.
11. Chopra VK, Mittal S, Bansal M, Singh B, Trehan N. Clinical profile and one-year survival of patients with heart failure with reduced ejection fraction: The largest report from India. Indian Heart J 2019;71:242-8.
12. Sharma SK, Agarwal SK, Bhargava K, Sharma M, Chopra K, Arumugam G. Prevalence and spectrum of iron deficiency in heart failure patients in south Rajasthan. Indian Heart J 2016;68:493-7.
13. Arora H, Sawhney JP, Mehta A, Mohanty A. Anemia profile in patients with congestive heart failure a hospital based observational study. Indian Heart J 2018;70 Suppl 3:S101-4.
14. Yeo TJ, Yeo PS, Ching-Chiew Wong R, Ong HY, Leong KT, Jaufeerally F, *et al.* Iron deficiency in a multi-ethnic Asian population with and without heart failure: prevalence, clinical correlates, functional significance and prognosis. Eur J Heart Fail 2014;16:1125-32.
15. Chobufo MD, Rahman E, Gayam V, Bei Foryoung J, Agbor VN, Farah F, *et al.* Prevalence and association of iron deficiency with anemia among patients with heart failure in the USA: NHANES 2017-2018. J Community Hosp Intern Med Perspect 2021;11:124-7.
16. Klip IT, Comin-Colet J, Voors AA, Ponikowski P, Enjuanes C, Banasiak W, *et al.* Iron deficiency in chronic heart failure: An international pooled analysis. Am Heart J 2013;165:575-82.e3.
17. Jankowska EA, Rozentryt P, Witkowska A, Nowak J, Hartmann O, Ponikowska B, *et al.* Iron deficiency: An ominous sign in patients with systolic chronic heart failure. Eur Heart J 2010;31:1872-80.
18. Okonko DO, Mandal AK, Missouris CG, Poole-Wilson PA. Disordered iron homeostasis in chronic heart failure: prevalence, predictors, and relation to anemia, exercise capacity, and survival. J Am Coll Cardiol 2011;58:1241-51.