

Assessment of Ferritin Deficiency in Patients with Heart Failure

Sanket Sinha¹, Fauzia Rehman Khan², Zoya Akbar³

¹Consultant Medicine, Swastik Hospital, Karnal, Haryana, India. Email: swastiktpa6@gmail.com, ORCID ID: 0000-0002-3506-3752.

²Associate Professor, Department of Anaesthesia, KCGMC, Karnal, Haryana, India. Email: fauzia79@gmail.com, ORCID ID: 0000-0003-4446-2621.

³RMO, Swastik Hospital, Karnal, Haryana, India. Email: zoyaakbarali6295@gmail.com, ORCID ID: 0000-0002-6284-8678.

Abstract

Background: To assess ferritin deficiency in patients with heart failure. **Subjects and Methods:** Eighty six chronic heart failure patients of either gender were selected and based on iron status, group I and II were formed. Group I had iron deficiency patients and group II were without it. Prospective, observational study was done. Parameters such as ferritin, serum iron, and transferrin saturation (TSAT) were measured. **Results:** Out of 86 patients, males comprised of 50 and females 36. Group I comprise of 20 males and 23 females and group II 18 males and 25 females. The difference was non-significant ($P>0.05$). The mean hemoglobin in group I patients was 11.6 g/dl and in group II was 13.2 g/dl. Iron level was 57.8 $\mu\text{g/L}$ and 97.5 $\mu\text{g/L}$, MCV was 82.1 fl and 91.6 fl, TSAT was 13.1% and 28.5% and ferritin was 76.4 $\mu\text{g/L}$ and 262.1 $\mu\text{g/L}$ respectively. The difference in ferritin level was significant ($P<0.05$). **Conclusion:** Serum ferritin was significantly reduced in chronic heart failure patients. Anaemia is common comorbid condition in patients of heart failure.

Keywords: Anaemia, Serum ferritin, Iron deficiency.

Corresponding Author: Dr. Zoya Akbar, RMO, Swastik Hospital, Karnal, Haryana, India.

Received: 02 June 2021

Revised: 08 July 2021

Accepted: 21 July 2021

Published: 30 November 2021

Introduction

Iron deficiency anemia is widely present in patients with heart failure with an estimated prevalence of over 50% in ambulatory patients. It is an independent predictor of worse functional capacity and survival.^[1] Risk factors for iron deficiency include female sex, advanced heart failure, and higher levels of N-terminal pro-B-type natriuretic peptide and C-reactive protein. Populations at high risk include infants, young children, adolescents, elderly persons, and women, the last particularly during menstrual periods and pregnancy.^[2] The past decades have seen tremendous research effort into iron deficiency (ID) in patients with chronic diseases with underlying inflammatory activation, and these efforts have finally yielded the understanding that patients with heart failure (HF), chronic kidney disease, cancer, and inflammatory bowel disease are likewise at increased risk of developing ID.^[3]

Different pathophysiological mechanism can explain the association between low ferritin levels and incident HF. In conditions of iron deficiency, there is a reduction in concentration and activity of muscular oxidative enzymes and respiratory proteins, causing impairment in cellular energetics.^[4] Concomitantly, structural alterations such as mitochondrial swelling and irregularities in sarcomere organization could develop. Also, iron deprivation affects the cell proliferation cycle, triggering G1/S phase mitotic arrest and apoptosis, altering myocardial composition.^[5] Independently of presence of anemia, it might increase catecholamines levels, contributing to cardiac hypertrophy. Altogether, these intracellular and neurohormonal

disarrangements might contribute to the development of HF in patients with iron deficiency.^[6] Considering this, we assessed ferritin deficiency in patients with heart failure.

Subjects and Methods

Eighty six chronic heart failure patients of either gender were selected for this prospective, observational study. Approval from ethical review committee of the institute was obtained. Written consent from patients or their family member was obtained.

Demographic characteristics was recorded in case sheet. 5 ml of venous blood was collected. Iron deficiency (ID) was defined as absolute (ferritin $<100 \mu\text{g/L}$) or functional (transferrin Saturation index $<20\%$ and ferritin between 100 and 299 $\mu\text{g/L}$). Hematologic indices were measured in venous blood collected in EDTA tubes. Parameter such as ferritin, serum iron, total iron binding capacity, transferrin and transferrin saturation (TSAT) were measured. A serum ferritin in the range of 30–300 $\mu\text{g/L}$ was considered to be normal. Based on iron status, group I and II were formed. Group I had iron deficiency patients and group II were without it. The results were compiled and subjected for statistical analysis using Mann Whitney U test. P value less than 0.05 was set as significant.

Results

Out of 86 patients, males comprised of 50 and females 36 [Table 1].

Group I comprise of 20 males and 23 females and group II

18 males and 25 females. The difference was non-significant ($P>0.05$). [Table 2]

The mean hemoglobin in group I patients was 11.6 g/dl and in group II was 13.2 g/dl. Iron level was 57.8 $\mu\text{g/L}$ and 97.5 $\mu\text{g/L}$, MCV was 82.1 fl and 91.6 fl, TSAT was 13.1% and

28.5% and ferritin was 76.4 $\mu\text{g/L}$ and 262.1 $\mu\text{g/L}$ respectively. The difference was significant ($P<0.05$) [Table 3, Figure 1].

Table 1: Patients distribution

Total- 86		
Gender	Males	Females
Number	50	36

Table 2: Distribution of patients based on iron status

Iron status	Group I (43)	Group II (43)	P value
Male	20	18	0.91
Female	23	25	0.82

Table 3: Assessment of parameters

Parameters	Group I	Group II	P value
Hb (g/dl)	11.6	13.2	0.05
Iron ($\mu\text{g/L}$)	57.8	97.5	0.02
MCV (fl)	82.1	91.6	0.96
TSAT (%)	13.1	28.5	0.01
Ferritin ($\mu\text{g/L}$)	76.4	262.1	0.001

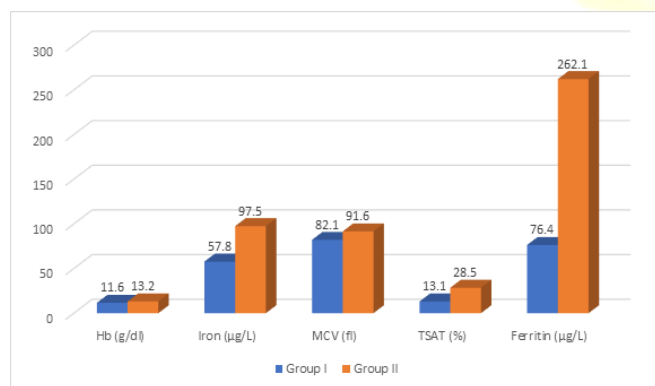


Figure 1: Assessment of parameters

Discussion

Disorders of iron metabolism, either deficiency or overload, have been associated with increased cardiovascular morbidity and mortality.^[7] Severe iron overload, due to acquired and genetic hemochromatosis, has been consistently associated with cardiomyopathy and higher incidence of heart failure (HF). Anaemia is defined by WHO as Hb < 13.0 g/dL in male adults and <12.0 g/dL in female adults.^[8] It is one of the commonest associations in patients of HF and has been shown to be associated with increased mortality in both acute and chronic heart failure.^[9] The aetiology is varied, especially in countries like India where apart from other mechanisms, nutritional deficiency and worm infestations also play a part.^[10] Iron deficiency has emerged as one of the most important causes of anaemia in patients of heart failure.^[11] Considering this, we assessed ferritin deficiency in patients with heart failure.

Our results showed that out of 86 patients, there were 50 males and 36 females. Kulkarni et al,^[12] determined if iron deficiency (ID) was a predictor of death or hospitalization

due to heart failure or any cause using univariate and multivariate cox regression analysis. There were 67.5% (27/40) patients who had ID with a mean serum ferritin level of 76.4 $\mu\text{g/L}$. Of the 27 iron deficient patients, 22 (55%) had an absolute ID, and 5 had a functional ID. Eight out of 27 of the iron deficient patients were anaemic (20% of the total cohort, 30% of the iron deficient patients). Anemia was seen in 6 other patients, which was possibly anemia of chronic disease.

Group I comprise of 20 males and 23 females and group II 18 males and 25 females. The mean hemoglobin in group I patients was 11.6 g/dl and in group II was 13.2 g/dl. Iron level was 57.8 $\mu\text{g/L}$ and 97.5 $\mu\text{g/L}$, MCV was 82.1 fl and 91.6 fl, TSAT was 13.1% and 28.5% and ferritin was 76.4 $\mu\text{g/L}$ and 262.1 $\mu\text{g/L}$ respectively. Silvestre et al,^[13] assessed the relationship between ferritin, a marker of iron status, and the incidence of HF in 1,063 participants. The participants were categorized in low (<30 ng/mL; n=153), normal (30–200 ng/mL in women and 30–300 ng/mL in men; n=663) and high (>200 ng/mL in women and >300 ng/mL in men; n=247) ferritin levels. Participants with low ferritin levels had a higher risk of HF as did those with high ferritin levels when compared to participants with normal ferritin levels. Low ferritin levels remained associated with incident HF even after excluding subjects with anemia.

Iron overload cardiomyopathy has been described in patients with primary hemochromatosis and also in transfusion-dependent anemias. Ferritin serum levels higher than 2500 ng/mL were associated with a higher risk of HF in a study by Kirk et al.^[14] As recently reported by Klip et al,^[15] hemoglobin serum levels < 11 g/dL for men and <10 g/dL for women were associated with an increased incidence of HF in eight years of follow-up when compared with normal hemoglobin level concentrations. It is possible that anemia plays a role in the mechanism linking iron deficiency and incident HF.

Conclusion

Serum ferritin was significantly reduced in chronic heart failure patients. Anaemia is common comorbid condition in patients of heart failure.

References

1. Marantz PR, Tobin JN, Wassertheil-Smoller S, Steingart RM, Wexler JP, Budner N, et al. The relationship between left ventricular systolic function and congestive heart failure diagnosed by clinical criteria. *Circulation*. 1988;77(3):607-12. doi: 10.1161/01.cir.77.3.607.
2. Parikh A, Natarajan S, Lipsitz SR, Katz SD. Iron deficiency in community-dwelling US adults with self-reported heart failure in the National Health and Nutrition Examination Survey III: prevalence and associations with anemia and inflammation. *Circ Heart Fail*. 2011;4(5):599-606. doi: 10.1161/CIRCHEARTFAILURE.111.960906.
3. Mohan G, Mohan G, Chandey M, Kaur A, Sikand TS, Kaur R. Prevalence and spectrum of iron deficiency anaemia in heart failure patients. *Int J Adv Med*. 2020;7:132-7.
4. Krum H, Jelinek MV, Stewart S, Sindone A, Atherton JJ. 2011 update to National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand Guidelines for the prevention, detection and management of chronic heart failure in Australia, 2006. *Med J Aust*. 2011;194(8):405-9. doi: 10.5694/j.1326-5377.2011.tb03031.x.
5. Bolger AP, Bartlett FR, Penston HS, O'Leary J, Pollock N, Kaprielian R, et al. Intravenous iron alone for the treatment of anemia in patients with chronic heart failure. *J Am Coll Cardiol*. 2006;48(6):1225-7. doi: 10.1016/j.jacc.2006.07.015.
6. Usmanov RI, Zueva EB, Silverberg DS, Shaked M. Intravenous iron without erythropoietin for the treatment of iron deficiency anemia in patients with moderate to severe congestive heart failure and chronic kidney insufficiency. *J Nephrol*. 2008;21(2):236-42.
7. Okonko DO, Grzeslo A, Witkowski T, Mandal AK, Slater RM, Roughton M, et al. Effect of intravenous iron sucrose on exercise tolerance in anemic and nonanemic patients with symptomatic chronic heart failure and iron deficiency FERRIC-HF: a randomized, controlled, observer-blinded trial. *J Am Coll Cardiol*. 2008;51(2):103-12. doi: 10.1016/j.jacc.2007.09.036.
8. Toblli JE, Lombraña A, Duarte P, Di Gennaro F. Intravenous iron reduces NT-pro-brain natriuretic peptide in anemic patients with chronic heart failure and renal insufficiency. *J Am Coll Cardiol*. 2007;50(17):1657-65. doi: 10.1016/j.jacc.2007.07.029.
9. Ponikowski P, van Veldhuisen DJ, Comin-Colet J, Ertl G, Komajda M, Mareev V, et al. Beneficial effects of long-term intravenous iron therapy with ferric carboxymaltose in patients with symptomatic heart failure and iron deficiency†. *Eur Heart J*. 2015;36(11):657-68. doi: 10.1093/eurheartj/ehu385.
10. Gaber R, Kotb NA, Ghazy M, Nagy HM, Salama M, Elhendy A. Tissue Doppler and strain rate imaging detect improvement of myocardial function in iron deficient patients with congestive heart failure after iron replacement therapy. *Echocardiography*. 2012;29(1):13-8. doi: 10.1111/j.1540-8175.2011.01532.x.
11. Folsom AR, Yamagishi K, Hozawa A, Chambless LE; Atherosclerosis Risk in Communities Study Investigators.

Absolute and attributable risks of heart failure incidence in relation to optimal risk factors. *Circ Heart Fail*. 2009;2(1):11-7. doi: 10.1161/CIRCHEARTFAILURE.108.794933.

12. Kulkarni V, Bijapur S, Chincholi AS, Patil V. A Prospective Study on Ferritin Deficiency in Heart Failure in North Karnataka Patients. *EJMCM*. 2022;9-1.
13. Silvestre OM, Gonçalves A, Nadruz W Jr, Claggett B, Couper D, Eckfeldt JH, et al. Ferritin levels and risk of heart failure-the Atherosclerosis Risk in Communities Study. *Eur J Heart Fail*. 2017;19(3):340-347. doi: 10.1002/ejhf.701.
14. Kirk P, Roughton M, Porter JB, Walker JM, Tanner MA, Patel J, et al. Cardiac T2* magnetic resonance for prediction of cardiac complications in thalassemia major. *Circulation*. 2009;120(20):1961-8. doi: 10.1161/CIRCULATIONAHA.109.874487.
15. Klip IT, Postmus D, Voors AA, Brouwers FP, Gansevoort RT, Bakker SJ, et al. Hemoglobin levels and new-onset heart failure in the community. *Am Heart J*. 2015;169(1):94-101.e2. doi: 10.1016/j.ahj.2014.09.010.

Copyright: © the author(s), 2021. It is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), which permits authors to retain ownership of the copyright for their content, and allow anyone to download, reuse, reprint, modify, distribute and/or copy the content as long as the original authors and source are cited.

How to cite this article: Sinha S, Khan FR, Akbar Z. Assessment of Ferritin Deficiency in Patients with Heart Failure. *Asian J. Med. Res*. 2021;10(4):28-30.

DOI: [dx.doi.org/10.47009/ajmr.2021.10.4.ME7](https://doi.org/10.47009/ajmr.2021.10.4.ME7)

Source of Support: Nil, **Conflict of Interest:** None declared.