A STUDY OF IRON PROFILE IN PATIENTS WITH HEART FAILURE WITH PRESERVED AND REDUCED EJECTION FRACTION

TYPE OF ARTICLE: ORIGINAL RESEARCH ARTICLE

ABSTRACT

BACKGROUND: Heart failure is a complex clinical syndrome that results from any structural of functional impairement of ventricular filling or ejection of blood leading to cardinal manifestations of dyspnoea ,fatigue ,and fluid retention. In developed countries, the prevalence of known heart failure is generally estimated at 1% to 2% of the general adult population.

Heart failure is a major cause of morbidity and mortality worldwide. Iron deficiency (ID) with or without anemia has been commonly associated with HF. In view of this, the current study was undertaken to assess the iron profile in patients with heart failure (HF).

Objectives: This study aims at studying the prevalence, clinical correlates fuctional significance of iron deficiency in heart failure patients and to **highlight the importance of iron deficiency in heart failure.**

MATERIALS AND METHODS: In this study , we have taken 60 patients who are above 18 years diagnosed to have heart failure , 30 patients had preserved ejection fraction, 30 patients had reduced ejection fraction , BNP ,ECG, 2DECHO, haemogram, iron profile were done. This study is being undertaken to evaluate the prevalance of iron deficiency in heart failure with preserved or reduced ejection fraction , Correlating iron levels with stage of heart failure , Correlating iron levels with length of stay in hospital.

RESULTS: 22 patients of 30 patients in preserved ejection fraction group had iron deficiency. 23 patients of 30 patients in reduced ejection fraction had iron deficiency. The mean serum iron levels of the study participants with length of stay in hospital between 1-5 days, 6 – 10 days and 11 – 15 days were found to be 28.99 $\pm$ 17.55, 31.82 $\pm$ 17.15 and 35.37 $\pm$ 23.58 respectively. The association was found to be statistically significant between with length of stay in hospital and serum iron levels of the study participants.

The mean serum iron levels of the study participants in stage B, stage C and Stage D of heart failure were found to be 30.21 $\pm$ 20.57, 30.23 $\pm$ 17.02 and 20.63 $\pm$ 18.28 respectively. The association between stages of heart failure and serum iron levels of the study participants was not found to be statistically significant .

CONCLUSION AND INTERPRETATION

In this study 73.33% in preserved EF group and 76.66% in reduced EF group had iron deficiency. The association was found to be statistically significant between with length of stay in hospital and serum iron levels of the study participants. The association between stages of heart failure and serum iron levels of the study participants was not found to be statistically significant.

Keywords: Heart Failure , Iron Deficiency Anemia, ejection fraction(EF)

INTRODUCTION

"Heart failure is a complex clinical syndrome that results from any structural of functional impairement of ventricular filling or ejection of blood leading to cardinal manifestations of dyspnoea ,fatigue ,and fluid retention" [1].

"Coronary artery disease is currently the leading cause of death in India and its prevalence is projected to rise. The prevalence of iron deficiency in heart failure in Indian population was 76% as per the articles published in Indian heart journal in 2015" [2-5].

HF once was thought to arise primarily in the setting of reduced left ventricular (LV) ejection fraction (EF) . Accordingly, HF patients are now broadly categorized into one of two groups:

1. HF with a reduced EF
2. HF with a preserved EF

"Heart failure with preserved ejection fraction (HFpEF) is a clinical syndrome in which patients have signs and symptoms of HF as the result of high left ventricular (LV) filling pressure despite normal or near normal LV ejection fraction (LVEF; ≥50 percent)". (6, 7-9)

"Heart failure with reduced ejection fraction (HFrEF), also called systolic heart failure is when the ejection fraction is ≤ 40%" (10). "Typical symptoms include dyspnea, orthopnea, paroxysmal nocturnal dyspnea, fatigue, and ankle swelling. Other symptoms of right-sided heart failure that may be present but are more nonspecific include abdominal bloating, right upper-quadrant discomfort, and early satiety" (11)

Anemia is a frequent comorbidity in stable HF patients and it increases morbidity in terms of frequent hospital admissions, impaired exercise capacity, poor QoL, and increased mortality . Iron deficiency (ID) with or without anemia has been commonly associated with HF. As iron supplementation improves prognosis in patients with HF,

ID is an attractive therapeutic target – a hypothesis that has recently been tested in clinical studies .

METHODS

Source of data:

All patients with heart failure admitted in General Medicine, Cardiology Department at KIMS hospital Bangalore will be taken up for the study after considering the inclusion and exclusion criteria.

Methods of Collection Of Data:

A. Study design: CROSS SECTIONAL study

B. Study period: 1.5 years

C. Place of study: KEMPEGOWDA INSTITUTE OF MEDICAL SCIENCE AND RESEARCH CENTRE, BANGALORE

D. Sample size: **Total:60 patients**

SAMPLING METHOD: PURPOSIVE SAMPLING

E. Inclusion Criteria:

1.Age more than 18 years of age.

2. All cases of heart failure with preserved or reduced ejection fraction

E. Exclusion Criteria:

1.Conditions that cause confounding in assignment of etiology for fluid overload (example: end stage renal disease)

2.Patients with congenital heart disease

3.Patient with erythropoietin supplementation and iron supplementation

F.Methodology:

- It is a cross sectional study. Subjects will be enrolled in the study based on the inclusion and exclusion criteria. The selected subjects will be briefed about the nature of the study and a written informed consent will be obtained before the subject study.
- Demographic data like gender, age etc. will be collected along with the relevant history and recorded in predesigned proforma.
- A thorough clinical examination will be conducted and findings will be recorded.

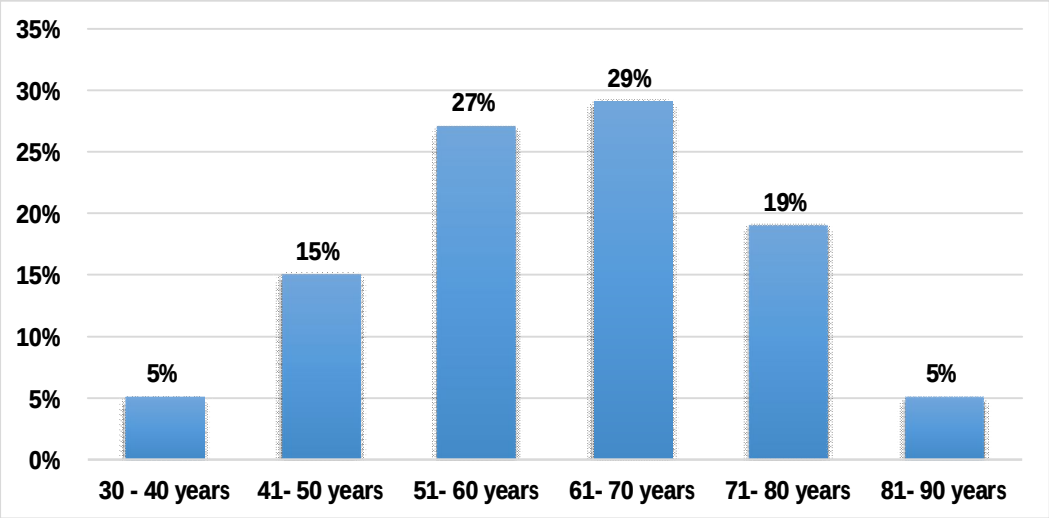
- Patients will be evaluated for iron deficiency using iron profile and 2D ECHO studies.

Assessment tools:

Iron profile ,2D ECHO,ECG ,complete haemogram, BNP levels

RESULTS

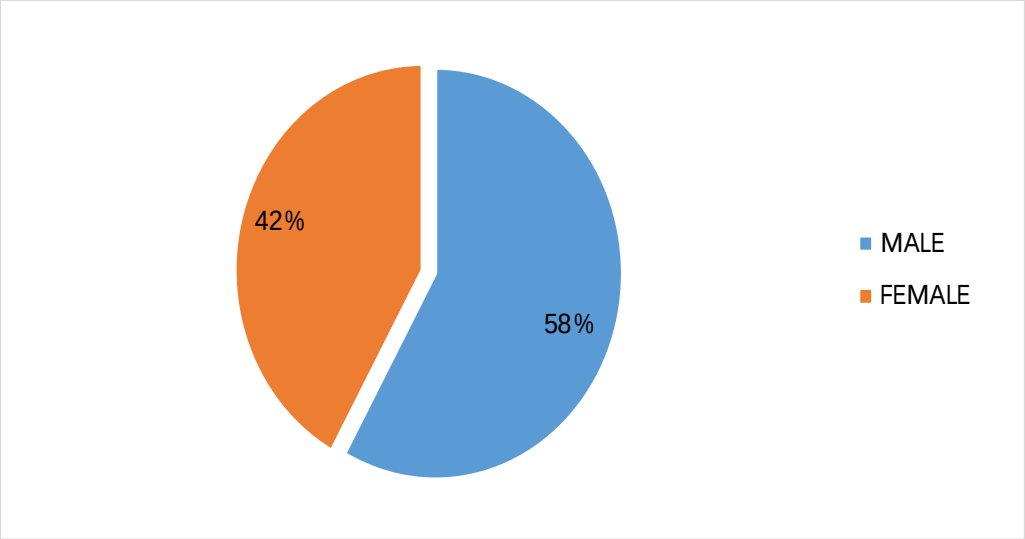
Figure 1: Distribution of the study participants according to their age group



50% of the study participants belonged to the age group 51-60 years of age.

The mean age of the study participants was found to be 55.85 $\pm$ 7.64 years of age.

Figure 2 showing distribution of the study participants according to their gender:



58% of the study participants were males with females contributing to 42% of study population.

Figure 3 showing distribution of the study participants according to their comorbidity profile:

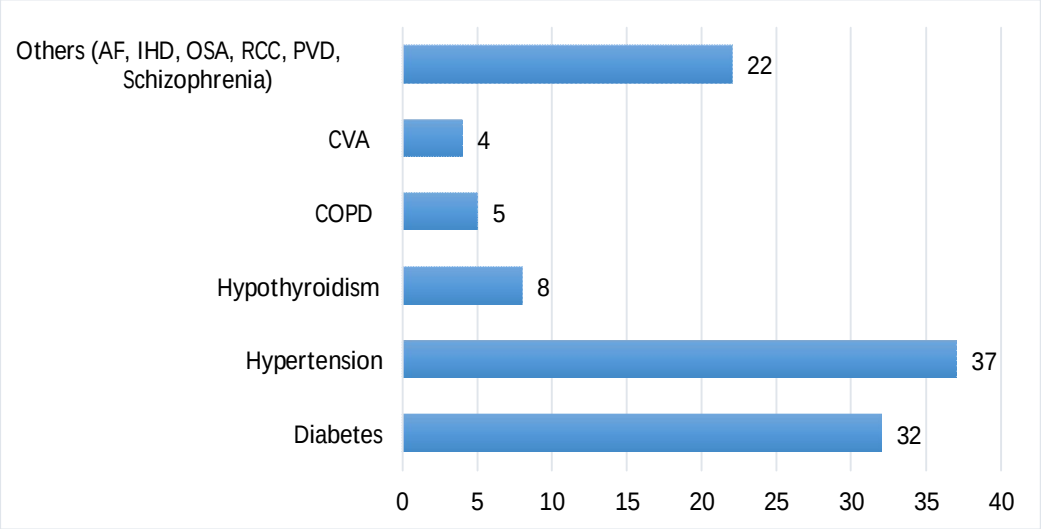


Figure 4 showing distribution of the study participants according to their staging of heart failure:

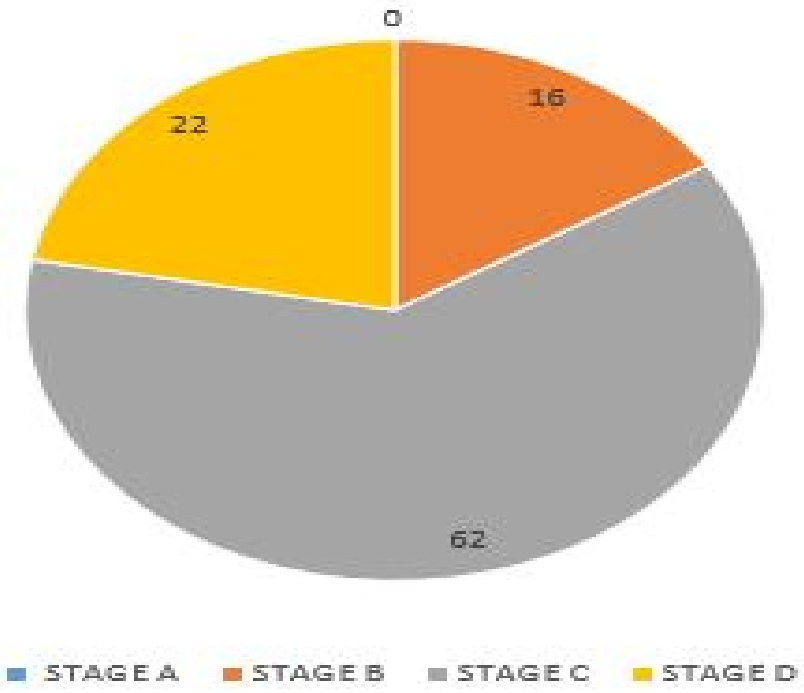


Figure 5 showing Ejection fraction among the study participants:

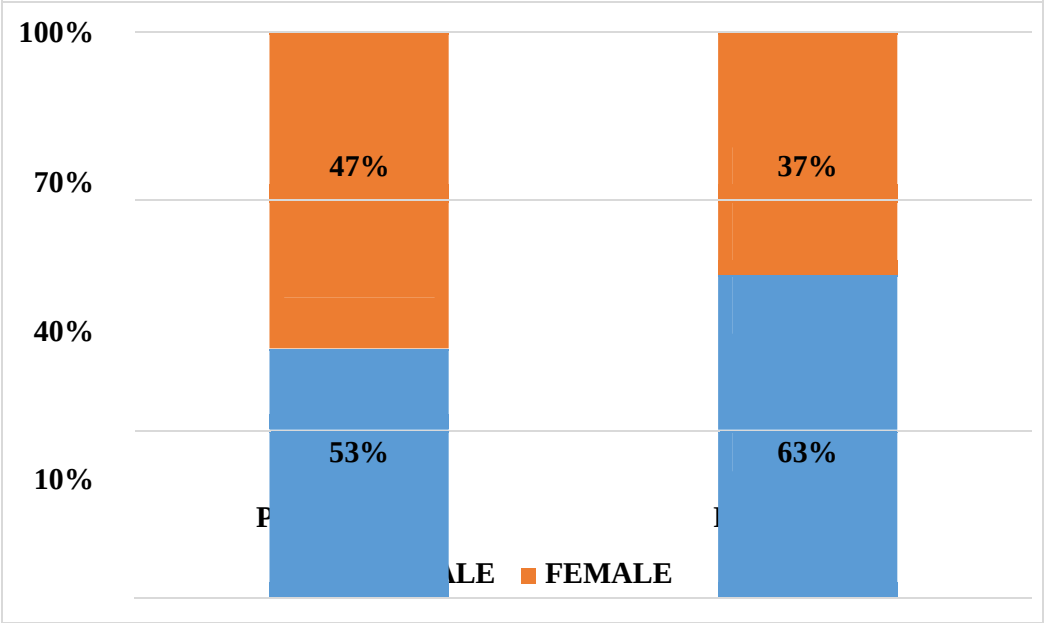


Table 1: Distribution of ejection fraction among the study participants:

Ejection Fraction	Frequency N	Percentage %
10 – 20	7	12%
20 – 30	15	25%
30 - 40	12	20%
40 - 50	14	23%
50 - 60	12	20%

25% of the study participants had Ejection fraction in the range of 20 – 30 with 23% having ejection fraction in the range of 40 – 50.

Table 2: Mean and SD of the study participants according to their Laboratory parameters:

Laboratory parameters	Mean ± SD
Ejection Fraction	39.02 $\pm$ 13.02
Hb (gm %)	10.86 $\pm$ 0.81

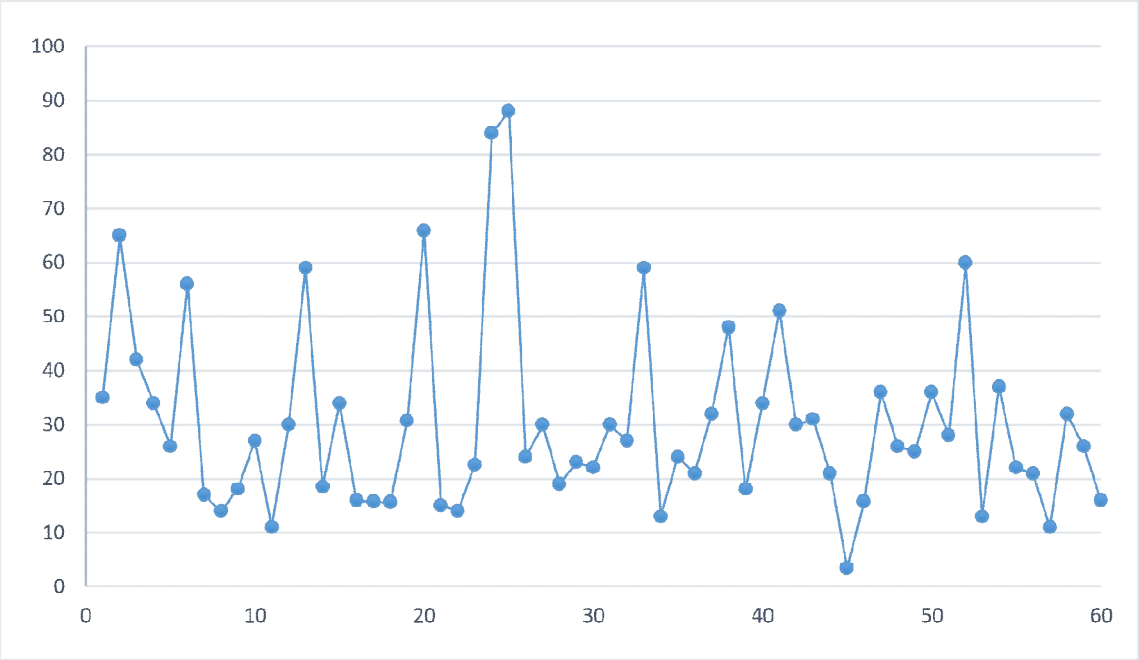
The Mean ejection fraction and Haemoglobin (gm %) among the study participants were found to be 39.02 $\pm$ 13.02 and 10.86 $\pm$ 0.81 respectively.

Table 3: Mean and SD of the study participants according to their according to their iron levels:

Iron levels	Mean	SD
Serum Iron	30.31	17.59
Total iron-binding capacity (TIBC)	280.35	76.29

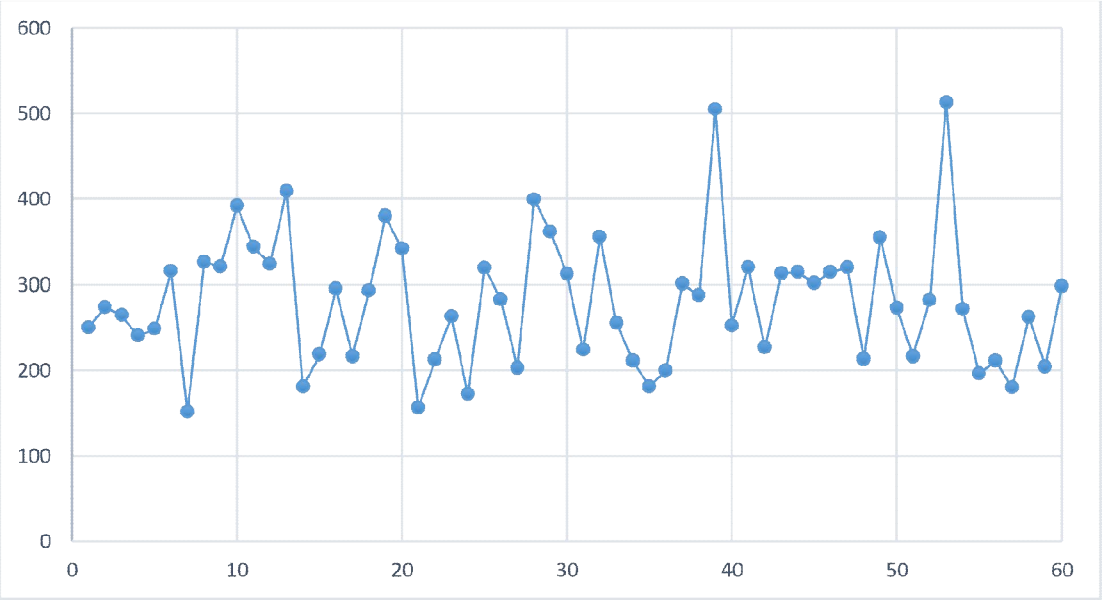
The Mean serum iron and TIBC among the study participants were found to be 30.31 ± 17.59 and 280.35 ± 76.29 respectively.

Figure 6: Scatter plot showing the serum iron levels among the study participants:



The above Scatter plot shows the serum iron levels among the study participants.

Figure 7: Scatter plot showing the TIBC levels among the study participants:



The above Scatter plot shows the TIBC levels among the study participants.

Table 4: Distribution of the study participants according to their length of stay in hospital:

Length of stay in hospital	Frequency N	Percentage %
1 – 5 days	37	62
6 – 10 days	19	31
11 – 15 days	4	7

62% of the study participants having length of stay in hospital between 1 – 5 days with 31% of the study participants having length of stay in hospital between 6 – 10 days.

Table 5: Serum iron levels of the study participants with their stages of heart failure:

Staging of Heart failure	Mean	SD	P value
Stage A	**0**	**0**	
Stage B	30.21	20.57	0.371
Stage C	30.23	17.02	
Stage D	20.63	18.28	

The mean serum iron levels of the study participants in stage B, stage C and Stage D of heart failure were found to be 30.21 $\pm$ 20.57, 30.23 $\pm$ 17.02 and 20.63 $\pm$ 18.28 respectively. The association between stages of heart failure and serum iron levels of the study participants was not found to be statistically significant.

Table 6: Serum iron levels of the study participants with their length of stay in hospital:

Length of stay in hospital	Serum iron levels		P value
	Mean	**SD**	
1 – 5 days	28.99	17.55	**0.000**
6 – 10 days	31.82	17.15	
11 – 15 days	35.37	23.58	

*paired t-test

The mean serum iron levels of the study participants with length of stay in hospital between 1-5 days, 6 – 10 days and 11 – 15 days were found to be 28.99 $\pm$ 17.55, 31.82 $\pm$ 17.15 and 35.37 $\pm$ 23.58 respectively. The association was found to be statistically significant between with length of stay in hospital and serum iron levels of the study participants.

Table 7: Correlation between Serum iron levels and length of stay in hospital of the study participants:

Length of stay in hospital	Serum iron levels		Pearson Correlation	P value
	Mean	SD		
1 – 5 days	28.99	17.55	**+1**	0.373
6 – 10 days	31.82	17.15		
11 – 15 days	35.37	23.58		

When serum iron levels of the study participants were correlated with the length of stay in hospital, serum iron levels showed strong positive correlation with length of stay in hospital and the correlation was not found to be statistically significant between serum iron levels and length of stay in hospital of the study participants.

DISCUSSION

Heart failure is a leading cause of morbidity and mortality. Iron metabolism is disrupted in CHF, resulting in low circulation and functional iron levels despite apparently ample reserves. Anemia is a serious comorbidity. ID is frequent in people with heart failure. Targeting the ID can help alleviate the negative symptoms of heart failure. In our study among 60 patients ,22 patients of 30 patients in preserved ejection fraction group had iron deficiency that is 73 % of patients had iron deficiency in preserved EF group. 23 patients of 30 patients in reduced ejection fraction had iron deficiency, 76% of patients had iron deficiency in reduced EF group.

The mean serum iron levels of the study participants with length of stay in hospital between 1-5 days, 6 – 10 days and 11 – 15 days were found to be 28.99 $\pm$ 17.55, 31.82 $\pm$ 17.15 and 35.37 $\pm$ 23.58 respectively. The association was found to be statistically significant between with length of stay in hospital and serum iron levels of the study participants.

The mean serum iron levels of the study participants in stage B, stage C and Stage D of heart failure were found to be 30.21 $\pm$ 20.57, 30.23 $\pm$ 17.02 and 20.63 $\pm$ 18.28 respectively. The association between stages of heart failure and serum iron levels of the study participants was not found to be statistically significant .

Conclusion:

Our study highlights the yet underestimated and neglected burden of ID in HF patients in India. This study suggests further large-scale studies to better characterize this easily treatable condition and considering routine testing in future Indian guidelines.

Recommendations

Recommendations worldwide are being changed to incorporate the need to assess and treat ID in patients with chronic HF. As our study indicates, ID is a common neglected burden in Indian HF patients, and this requires the need for more routine testing in future Indian guidelines

Ethical Approval:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

Consent

As per international standard or university standard, Parental written consent has been collected and preserved by the author(s).

REFERENCES

1. Micheal M. Givertz, Mandeep R .Mehra, Heart Failure: Pathophysiology and diagnosis. 21st Edition, volume 1, Mc Graw Hill publishing , 2022.
2. Loehr LR, Rosamond WD, Chang PP, Folsom AR, Chambless LE. Heart failure incidence and survival(From the atherosclerosis risk in communities study). The American Journal of Cardiology [Internet]. 2008 Apr [cited 2022 Sep 29];101(7):1016–22. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0002914907023636
3. Yeung DF, Boom NK, Guo H, Lee DS, Schultz SE, Tu JV. Trends in the incidence and outcomes of heart failure in Ontario, Canada: 1997 to 2007. CMAJ. 2012 Oct 2;184(14):E765-773.
4. Christiansen MN, Køber L, Weeke P, Vasan RS, Jeppesen JL, Smith JG, et al. Agespecific trends in incidence, mortality, and comorbidities of heart failure in denmark, 1995 to 2012. Circulation. 2017 Mar 28;135(13):1214–23.
5. Christ M, Störk S, Dörr M, Heppner HJ, Müller C, Wachter R, et al. Heart failure epidemiology 2000-2013: insights from the German Federal Health Monitoring System: Heart failure in Germany (2000-2013). Eur J Heart Fail [Internet]. 2016 Aug [cited 2022 Sep29];18(8):1009–18.Availablefrom: https://onlinelibrary.wiley.com/doi/10.1002/ejhf.567
6. Sharma K, Kass DA. Heart failure with preserved ejection fraction: mechanisms, clinical features, and therapies. Circ Res 2014; 115:79.

7. Zile MR, Bennett TD, St John Sutton M, et al. Transition from chronic compensated to acute decompensated heart failure: pathophysiological insights obtained from continuous monitoring of intracardiac pressures. Circulation 2008; 118:1433.
8. Zile MR, Bourge RC, Bennett TD, et al. Application of implantable hemodynamic monitoring in the management of patients with diastolic heart failure: a subgroup analysis of the COMPASS-HF trial. J Card Fail 2008; 14:816.
9. Redfield MM. Heart Failure with Preserved Ejection Fraction. N Engl J Med 2017; 376:897.
10. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Drazner MH, et al. 2013 accf/aha guideline for the management of heart failure. Journal of the American College of Cardiology [Internet]. 2013 Oct [cited 2022 Sep 30];62(16):e147–239. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0735109713021141
11. Murphy SP, Ibrahim NE, Januzzi JL. Heart failure with reduced ejection fraction: a review. JAMA [Internet]. 2020 Aug 4 [cited 2022 Sep 30];324(5):488. Available from: https://jamanetwork.com/journals/jama/fullarticle/2768982

12.Iron deficiency in a multi-ethnic Asian population with and without heart failure: prevalence, clinical correlates, functional significance and prognosis Tee Joo Yeo1†, Poh Shuan Daniel Yeo2†, Raymond Ching-ChiewWong1, Hean Yee Ong3, Kui Toh Gerard Leong4, Fazlur Jaufeerally5,6, David Sim7, Rajalakshmi Santhanakrishnan8,9, Shir Lynn Lim1, Michelle M.Y. Chan6, 8, Ping Chai1, Adrian F.Low1,9, Lieng H. Ling1,8,9, Tze Pin Ng9, A. Mark Richards1,8,9, and Carolyn S.P. Lam1,8,9* 1National University Heart Centre Singapore, National University Health System, Tower Block Level 9, 1E Kent Ridge Road, Singapore 119228, Singapore

Conclusions**:** ID was highly prevalent and independently related to functional capacity and outcomes in our cohort. These findings suggest a pathophysiological role of ID in HF and support its importance as a therapeutic target in Southeast Asian patients with HF.

13 . Effect of ferric carboxymaltose on hospitalization and mortality outcomes in chronic heart failure: A meta-analysis Jamshed Dalala, Vijay Katekhayeb, Rishi Jainc,* a Centre for Cardiac Sciences, Kokilaben Dhirubhai Ambani Hospital, Rao Saheb Achutrao Patwardhan Marg, Four Bunglows, Andheri West, Mumbai, Maharashtra 400053, India b Dev Clinic, Opp. Bhosala Vedh School, Ayachit Mandir Road, Mahal, Nagpur, Maharashtra 440032, India c Medical Services Dept., Emcure Pharmaceuticals Ltd., Survey No. 255/2, Phase-I, M.I.D.C., Hinjawadi, Pune, Maharshtra 411057, India

Conclusion: FCM reduces hospitalization rates in CHF but may not reduce mortality outcome. This finding needs further evaluation in a large, prospective, randomized controlled trial. © 2017 Published by Elsevier B.V. on behalf of Cardiological Society of India.

14 . Anemia profile in patients with congestive heart failure a hospital based observational study Himanshu Arora*, J.P.S. Sawhney, Ashwani Mehta, Arun Mohanty Department of Cardiology, Sir Ganga Ram Hospital, New Delhi 110060, India

Results: Two hundred and seventy-five patients with heart failure (mean age - 62.72, mean Hb- 10.54 g/dl, 188 males [68.36%] and 87 females [31.64%]) were enrolled in the study. 211 out of 275 (76.7%) were found to be anemic. Out of 275 patients. 148 (53.8%) were diagnosed with iron deficiency. 12.7% (n = 35) were B12 deficient and 5.1% (n = 14) were folate deficient. In the anemic group, ID was present in 130 patients (61.61%), B12 deficiency in 32 patients (15.16%) and folate deficiency in 12 patients (5.68%). In the group of patients without anemia, ID was present in 18 patients (28.12%) while B12 and folate deficiency was present in 3 (4.68%) and 2 (3.12%) patients, respectively. Conclusion: Iron deficiency is present in substantial number while B12 and folate account for a few number of cases. Substantial number of patients without anemia were found to be iron deficient. © 2018 Published by Elsevier B.V. on behalf of Cardiological Society of India. This is an open access article

15 . Iron deficiency in chronic heart failure: An international pooled analysis IJsbrand T. Klip, MD, a Josep Comin-Colet, MD, PhD, b Adriaan A. Voors, MD, PhD, a Piotr Ponikowski, MD, PhD, c Cristina Enjuanes,MD, b Waldemar Banasiak,MD, PhD, c Dirk J. Lok, MD, d Piotr Rosentryt,MD, e Ainhoa Torrens,MD, b Lech Polonski, MD, PhD, e Dirk J. van Veldhuisen, MD, PhD, e Peter van der Meer, MD, PhD, a and

Ewa A. Jankowska, MD, PhDb Groningen, and Deventer, The Netherlands; Barcelona, Spain; and Wroclaw, and Zabrze,Poland

Conclusions Iron deficiency is common in patients with chronic HF, relates to disease severity, and is a strong and independent predictor of outcome. In this study, ID appears to have greater predictive power than anemia. (Am Heart J 2013;165:575-582.e3.)

16 .Disordered Iron Homeostasis in Chronic Heart Failure Prevalence, Predictors, and Relation to Anemia, Exercise Capacity, and Survival Darlington O. Okonko, MBBS,* Amit K. J. Mandal, MBBS,† Constantinos G. Missouris, MD,† Philip A. Poole-Wilson, MD, FMEDSCI*

London and Slough, United Kingdom Conclusions Disordered iron homeostasis in patients with CHF relates to impaired exercise capacity and survival and appears prognostically more ominous than anemia

17. Prevalence and spectrum of iron deficiency in heart failure patients in south Rajasthan Sohan Kumar Sharma a , Shalabh Kumar Agarwal b, *, Kapil Bhargava c , Mukesh Sharma d , Karan Chopra b , Gopinath Arumugam b

18 . Harikrishnan S1*, Abraham Oomman2 , Uday M Jadhav3 , Bagirath Raghuraman4, PP Mohanan5 , Mangesh Tiwaskar6 , GS Wander7 , VK Chopra8 Received: 31 December 2021; Accepted: 13 May 2022