A Study of Iron Profile in Patients with Heart Failure with Preserved and Reduced Ejection Fraction

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Authors’ contributions
This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

ABSTRACT

Background: Heart failure is a complex clinical syndrome that results from any structural or functional impairment 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 functional 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 prevalence 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 ± 17.55, 31.82 ± 17.15 and 35.37 ± 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 ± 20.57, 30.23 ± 17.02 and 20.63 ± 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).

1. INTRODUCTION

“Heart failure is a complex clinical syndrome that results from any structural or functional impairment 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.

2. METHODS

2.1 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.

2.2 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

2.3 Sampling Methods: Purposive Sampling

2.3.1 Inclusion criteria
1. Age more than 18 years of age.
2. All cases of heart failure with preserved or reduced ejection fraction

2.3.2 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. Patients with erythropoietin supplementation and iron supplementation

2.4 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.

2.4.1 Assessment tools
Iron profile, 2D ECHO, ECG, complete haemogram, BNP levels

3. RESULTS AND DISCUSSION

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 [12-15].

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.

Fig. 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 ± 7.64 years of age
Fig. 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

Fig. 3. Showing distribution of the study participants according to their comorbidity profile

Table 1. Distribution of ejection fraction among the study participants

<table>
<thead>
<tr>
<th>Ejection Fraction</th>
<th>Frequency N</th>
<th>Percentage %</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 – 20</td>
<td>7</td>
<td>12%</td>
</tr>
<tr>
<td>20 – 30</td>
<td>15</td>
<td>25%</td>
</tr>
<tr>
<td>30 - 40</td>
<td>12</td>
<td>20%</td>
</tr>
<tr>
<td>40 - 50</td>
<td>14</td>
<td>23%</td>
</tr>
<tr>
<td>50 - 60</td>
<td>12</td>
<td>20%</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Laboratory parameters</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejection Fraction</td>
<td>39.02 ± 13.02</td>
</tr>
<tr>
<td>Hb (gm %)</td>
<td>10.86 ± 0.81</td>
</tr>
</tbody>
</table>

The Mean ejection fraction and Haemoglobin (gm %) among the study participants were found to be 39.02 ± 13.02 and 10.86 ± 0.81 respectively
Fig. 4. Showing distribution of the study participants according to their staging of heart failure

Fig. 5. Showing Ejection fraction among the study participants

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

<table>
<thead>
<tr>
<th>Iron levels</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Iron</td>
<td>30.31</td>
<td>17.59</td>
</tr>
<tr>
<td>Total iron-binding capacity (TIBC)</td>
<td>280.35</td>
<td>76.29</td>
</tr>
</tbody>
</table>

*The Mean serum iron and TIBC among the study participants were found to be $30.31 \pm 17.59$ and $280.35 \pm 76.29$ respectively*
Fig. 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

Fig. 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

<table>
<thead>
<tr>
<th>Length of stay in hospital</th>
<th>Frequency N</th>
<th>Percentage %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 – 5 days</td>
<td>37</td>
<td>62</td>
</tr>
<tr>
<td>6 – 10 days</td>
<td>19</td>
<td>31</td>
</tr>
<tr>
<td>11 – 15 days</td>
<td>4</td>
<td>7</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Staging of Heart failure</th>
<th>Mean</th>
<th>SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage A</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Stage B</td>
<td>30.21</td>
<td>20.57</td>
<td>0.371</td>
</tr>
<tr>
<td>Stage C</td>
<td>30.23</td>
<td>17.02</td>
<td></td>
</tr>
<tr>
<td>Stage D</td>
<td>20.63</td>
<td>18.28</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Length of stay in hospital</th>
<th>Serum iron levels</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>1 – 5 days</td>
<td>28.99</td>
<td>17.55</td>
</tr>
<tr>
<td>6 – 10 days</td>
<td>31.82</td>
<td>17.15</td>
</tr>
<tr>
<td>11 – 15 days</td>
<td>35.37</td>
<td>23.58</td>
</tr>
</tbody>
</table>

*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

<table>
<thead>
<tr>
<th>Length of stay in hospital</th>
<th>Serum iron levels</th>
<th>Pearson Correlation</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td></td>
</tr>
<tr>
<td>1 – 5 days</td>
<td>28.99</td>
<td>17.55</td>
<td>+1</td>
</tr>
<tr>
<td>6 – 10 days</td>
<td>31.82</td>
<td>17.15</td>
<td></td>
</tr>
<tr>
<td>11 – 15 days</td>
<td>35.37</td>
<td>23.58</td>
<td></td>
</tr>
</tbody>
</table>

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.

4. 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.

5. 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.

CONSENT

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

ETHICAL APPROVAL

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

Authors have declared that no competing interests exist.

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