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General Medicine

IRON PROFILE IN HEART FAILURE

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ABSTRACT

Introduction:- Anemia is fairly common among individuals with heart failure and is associated with poor outcomes. Our aim was to study the status of Iron in heart failure patients which in turn will help us in their better management.

Materials and Methods:- This was a prospective study and was conducted at a tertiary care hospital. Recruitment of the study subjects was done from August 2015, for a period of 2 years. After ethical approval from, 120 consecutive patients of heart failure and 202 controls were included in the study. Baseline investigations with iron profile was done in all patients.

Results:- In our study most of the patients (88.3%) belonged to the age group of 40-70 years while as most of controls (95%) belonged to age group of 30-70years. Mean age among cases was 54.3 years whereas mean age of controls was 51.9 years. Male to female ratio in our study was 1.5:1 and among controls Male to female ratio was 1.3:1. Anemia was present in 44 (36.7%) of study patients and 19(15.8%) of controls. Among anemic patients' Systolic HF was present in 29 (65.9%) and Diastolic HF was present in 15 (34.1%). Among non-anemic patients Diastolic heart failure was present in 43 (56.6%) and systolic heart failure was present in 33 (43.4%). Iron deficiency was found in 38 (31.7%) of cases and in 27 (13.4 %) among controls. Iron deficiency was more among anemic patients in 27(61.4%) where as non-anemic patients were also iron deficient in 11 (14.5%) of cases. Iron deficiency was found to be high in the age group > 60 years in 51.4% of cases and was more among females (35.4%).

Conclusion:- Iron deficiency is common and constitutes a predictor of unfavourable outcome, irrespective of the presence of anemia.

KEYWORDS : Iron deficiency, heart failure, iron stores, ferritin

INTRODUCTION:-

Heart Failure (HF) is a complex clinical syndrome resulting from structural and functional impairment of ventricular filling or ejection of blood.[1]

HF is a major public health issue with a current prevalence of over 5.8 million in the USA and over 26 million worldwide. The overall prevalence of heart failure is 3-20 per 1000 population, although this exceeds 100 per 1000 in those aged 65 years and over. The annual incidence of heart failure is 1-5 per 1000, and the relative incidence doubles for each decade of life after the age of 45years. Although the relative incidence of HF is lower in women than in men. A diagnosis of HF carries substantial risk of morbidity and nearly 300,000 deaths annually are directly attributable to HF.[1]

In addition to older age, male sex, and ethnicity multiple other factors indicate increased risk for development of HF. One of the important risk factor which plays a dualistic role in heart failure is **Iron**.

Both iron overload and iron deficiency (ID) are associated with heart failure, but in different circumstances. Iron can accumulate in cardiac muscles in hereditary iron metabolism diseases (e.g, primary hemochromatosis, Alpha and beta thalassemia, sickle cell anemia, myelodysplastic syndrome), Intravenous iron in ESRD patients, friedreichs ataxia or following multiple blood transfusions, leading to cell death via oxidative stress. This phenomenon is called iron-overload cardiomyopathy and is a major cause of heart failure in people with iron overload disorders. Another effect of iron deficiency on CHF patients is the consequent thrombocytosis. CHF is a hypercoagulable state where the co-existence with iron deficiency-related thrombocytosis increases the risk of thrombosis and the mortality rate. A blood test called transferrin saturation can be used to screen for iron overload. Physicians may test for iron excess in heart failure patients with a personal or family history of iron metabolism diseases, or if iron overload is suspected for another reason.[2]

On the other hand, individuals with heart failure may develop iron deficiency (ID) as their condition progresses. In an analysis of studies including more than 1500 heart failure patients, 50% of subjects were found to be iron deficient. Also, a 2013 study on 552 subjects with chronic heart failure found that iron deficiency was strongly associated with reduced quality of life.[3] Iron supplementation in heart failure patients with iron deficiency is associated with improved symptoms, functional capacity, quality of life and reduced hospital admissions.[4] The specific mechanisms by which iron deficiency negatively impacts heart failure outcomes are not clearly defined, but may be due to iron-deficiency related anemia in some cases, and to the direct effects of depleted iron stores in others. An iron and total iron binding capacity (TIBC) test can be used to screen for iron deficiency.[5]

Anemia is fairly common among individuals with heart failure and is associated with poor outcomes. ID is a prominent cause of anemia in many situations, but anemia can occur independently of iron deficiency in heart failure. Excluding iron deficiency, other possible causes of anemia in heart failure include impaired production of erythropoietin (a hormone that controls red blood cell production), kidney problems, and problems with fluid retention.[6] Recognition and management of anemia is increasingly recognized as an important component of heart failure care, but the best treatment strategies are still being investigated.[16]

The following mechanisms are presumed to be involved in the development of absolute ID in HF:

(i) Insufficient dietary intake.
(ii) Poor GI absorption, impaired duodenal iron transport, drug interactions (e.g. omeprazole), or food reducing absorption, and
(iii) GI blood loss.

Some studies demonstrate suboptimal dietary iron supply, particularly in patients with advanced HF. Based on a 4-day food diary, Hughes *et al*. showed that 46% of patients with stable HF consumed less iron than the dietary reference value, and average daily iron intake was markedly reduced in patients in NYHA class III–IV when compared with NYHA class II.[7]

In our general population where iron stores are usually low, knowing the status of Iron in heart failure patients will help us in their better management and may improve their morbidity and mortality. With this in mind, our main aim was to study Iron Profile in patients with Heart Failure.

MATERIALS AND METHODS

This was a prospective study and was conducted in the Department of Cardiology at Sher-i-Kashmir Institute of Medical Sciences (SKIMS),

Srinagar, Jammu & Kashmir. Recruitment of the study subjects was done from August 2015, for a period of 2 years. After ethical approval from institutional Ethical Committee, 120 consecutive patients of heart failure and 202 controls were included in the study. Apparently healthy volunteers/attendants well matched with age, sex, residence and dietary habits were taken as controls. Heart failure patients irrespective of aetiology were included in study excluding any acute or chronic illness that might influence iron metabolism like malignancy, T_2DM, infection, CKD on RRT, haematological diseases, or any major surgery in recent past (3 months) or on Iron/erythropoietin therapy.

All patients with HF based on Framingham criteria underwent thorough history (including dietary history) and clinical evaluation including health related quality of life, blood sampling and comprehensive transthoracic echocardiography. Patients were characterized as having Preserved Ejection Fraction (EF ≥ 50%) and Reduced EF <40%). Apart from routine hemogram, these patients were assessed for their iron status by measuring complete iron profile, including serum iron, serum ferritin, total iron binding capacity, and transferrin saturation (TSAT).

After proper consent, Peripheral venous blood sample was taken in the morning following an overnight fast and supine rest of at least 15min in a EDTA vial (red stoppered tube) by standard venepuncture procedure. After centrifugation, serum was collected and frozen at -20^{0}C until being analysed.

Anemia was defined as a hemoglobin level < 12 g/dl in women and < 13g/dl in men, based on WHO definition.[8] The following biomarkers reflecting iron status were measured as: serum iron (microgram per decilitre), serum ferritin (nanogram per decilitre), total iron binding capacity (microgram per decilitre) and transferrin saturation (%). Transferrin saturation was measured as ratio of serum iron and TIBC multiplied by 100. Serum iron was measured using calorimetric method (Manual Rx Monza). Serum ferritin was measured by direct immunoenzymatic assay based on electrochemiluminescence (DiaMetra, Calabria, Italy). TIBC was also measured using calorimetric method.

Iron deficiency was defined as a serum ferritin level of < 20 ng/dl and serum iron level of < 50 ug/dl or normal serum ferritin with transferrin saturation <20%. Iron overload was defined as serum ferritin level > 400 ng/ml and serum iron >150 ug/dl.

The Minnesota Living with Heart Failure Questionnaire (MLHFQ) is a self-administered questionnaire consisting of 21 individual items. For each item in the MLHFQ, Health related quality of life (HRQoL) was defined as Good (MLHFQ score < 24), Moderate (MLHFQ score 24-45) and Poor (MLHFQ score >45). Responses were scored from 0 (no impact on HRQoL) to 5 (maximum impact on HRQoL).[9]

Data was collected, compiled in (Microsoft Excel) and then analysed through SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Data obtained from case study were compared with controls.

RESULTS: -

In our study we enrolled 120 patients of heart failure and 202 controls. Most of the patients (88.3%) belonged to the age group of 40-70 years while as most of controls (95%) belonged to age group of 30-70years. Mean age among cases was 54.3 years (40-70 years) whereas mean age of controls was 51.9 years (40- 62years) with statistically insignificant p-value (p= 0.064). Out of 120 patients of heart failure, 72 (60%) were males and 48(40%) were females. Among controls 58.4 % were males and 41.6% were females. Male to female ratio in our study was 1.5:1 and among controls Male to female ratio was 1.3:1. Most of our patients (70%) belonged to rural areas while 30% were from urban areas. Whereas most (71.3%) of our controls also belonged to rural areas and 28.7% were from urban areas. Most of cases 91 (75.8%) were non-vegetarian and 29 (24.2%) were vegetarians. Most of our controls were also non-vegetarian 92.6% and 7.4% were vegetarians with a statistically non-significant p value, as shown in table 1.

Table 1: Comparison based on demographic profile among cases and controls

Demographic Profile		Cases		Controls		P-value
		No.	%age	No.	%age	
Age (years)	20-29	2	1.7	10	5.0	0.064
	30-39	12	10.0	39	19.3	
	40-49	26	21.7	49	24.3	
	50-59	43	35.8	51	25.2	
	≥ 60	37	30.8	53	26.2	
	Mean ±SD	54.3±11.06		51.9±11.29		
Gender	Male	72	60.0	118	58.4	0.779
	Female	48	40.0	84	41.6	
Residence	Rural	84	70.0	144	71.3	0.806
	Urban	36	30.0	58	28.7	
Dietary Habit	Vegetarian	13	10.8	15	7.4	0.294
	Non-vegetarian	107	89.2	187	92.6	

Patients of heart failure usually presented with typical symptom and signs. Most common symptoms were Fatigue (86.7) and Dyspnoea (75.8%) whereas most common signs were Tachypnoea (61.6%) and Tachycardia (58.3%) as shown in table 2 below.

Table 2: Clinical presentation of study patients

Symptoms	Frequency	Percentage
Fatigue	104	86.7
Dyspnea	91	75.8
Orthopnea	62	51.7
Anorexia	47	39.2
Nausea	38	31.7
RHC Pain	29	24.2
Cough	24	20.0
Nocturia	14	11.6
PND	11	9.2
Insomnia	8	6.7
Confusion	6	5.0
Signs		
Tachypnea	74	61.6
Tachycardia	70	58.3
Edema	69	57.5
Elevated JVP	62	51.7
Rales	42	35.0
S3, S4 Heart Sound	25	20.8
Anasarca	22	18.3
Parasternal Lift	13	10.8
Hepatomegaly	7	5.8

Overall HTN (46.7%) and CAD (31.8%) constituted the most common aetiology for heart failure. Other causes of heart failure were Dilated cardiomyopathy (13.3%) and Valvular heart diseases (8.3%).

Most common type of heart failure was Systolic heart failure (HFrEF with an EF of <40) present in 62 (51.7%).

Among cases most of patients 80 (66.6%) were having higher NYHA functional class (class 3 and 4). Stratification on the basis of NYHA functional class revealed that study patients showed Class 1 in 2 (1.7%), Class 2 in 38 (31.7%), Class 3 in 51 (42.4%) and Class 4 in 29 (24.2%) of cases.

On the basis of Minnesota Living with Heart Failure questionnaire (MLHFQ), Health related quality of life (HRQoL) was impaired in 85% of study patients. HRQoL was good in 18 (15%), moderate in 36 (30%) and poor in 66 (55%) of study patients.

In our study Anemia was present in 44 (36.7%) of study patients and 19(15.8%) of controls. Anemia was absent in 76(63.6%) of cases and 101(84.2%) of controls with a statistically significant p value (p<0.001). Most common type of anemia was normocytic normochromic in 27(61.4%) of patients. Second most common type of anemia was microcytic hypochromic in 17 (38.6%) of patients and in 4(21.1%) of controls with a statistically insignificant p value. Most of study patients 23 (52.3%) were having severe anemia, 15 (34.1%) were having moderate and 6 (13.6%) were having mild anemia. Among controls Mild to Moderate anemia predominates in 13(68.4%) followed by severe anemia in 6 (31.8%) which was statistically significant (p-value<0.05) as shown in table 3.

Table 3: Comparison based on anemia among cases and controls

		Cases		Controls		P-value
		No.	%age	No.	%age	
Anemia	Present	44	36.7	19	15.8	<0.001*
	Absent	76	63.3	101	84.2	

Type of Anemia	Microcytic	17	38.6	4	21.1	0.174
	Normocytic	27	61.4	15	78.9	
	Macrocytic	0	0.0	0	0.0	
Severity of Anemia	Mild	6	13.6	10	52.6	0.022*
	Moderate	15	34.1	6	31.6	
	Severe	23	52.3	3	15.8	

Statistically Significant Difference (P-value<0.05)

Among anemic patients' Systolic HF was present in 29 (65.9%) and Diastolic HF was present in 15 (34.1%). Among non-anemic patients Diastolic heart failure was present in 43 (56.6%) and systolic heart failure was present in 33 (43.4%) with statistically significant difference (p-value < 0.05).

Among anemic patients 31(70.5%) were having poor, 11 (25%) were having moderate and 2(4.5%) were having good HRQoL. whereas among non-anemic patients 41(54%) were having good-moderate HRQoL, with a statistically significant difference (p-value <0.05). Mean HRQoL among anemic patients was 48.5±12.17 and among non-anemic patients mean HRQoL was 34.7±11.2. Patients having severe anemia (95.7%) were found to have poor QoL whereas patients with Mild to Moderate anemia were having Good to Moderate QoL with statistically significant difference (p-value < 0.05, Chi-square= 42.43).

Among anemic patients, 35 (79.6%) were having higher NYHA Class (Class 3 and 4) whereas 8(18.2%) were having NYHA Class 2 and 1 (2.3%) was having NYHA Class 1. Among non-anemic patients NYHA Class 2 and 3 predominates in 62(81.6%). So Anemic patients were having Higher NYHA Class as compared to non-anemic patients with a statistically significant difference (p-value<0.05) as shown in table 4.

Table 4: Comparison based on NYHA classification among anemic and non-anemic patients

NYHA Class	Anemic Patients		Non-Anemic Patients		P-value
	No.	%age	No.	%age	
Class 1	1	2.3	1	1.3	0.038*
Class 2	8	18.2	30	39.5	
Class 3	19	43.2	32	42.1	
Class 4	16	36.4	13	17.1	
Total	44	100	76	100	

Statistically Significant Difference (P-value<0.05)

Iron deficiency was found in 38 (31.7%) of cases. Among controls Iron deficiency was found in 27 (13.4 %). However, iron profile was normal in 81 (67.5%) of cases and 175 (86.6%) of controls, with statistically significant (p- value < 0.05). Iron overload was present in 1(0.8%) of cases. Serum iron was <50 µg/dl in 38 (31.7%), 50-150 µg/dl in 81 (67.5%) and >150 in 1 (0.8%) of cases. Serum ferritin was < 20 ng/dl in 38 (31.7%), 20-400 ng/dl in 81 (67.0%) and > 400ng/dl in 1 (0.8%) of cases. TIBC was > 400µg/dl in 50 (41.7%) and between 250-400 µg/dl in 70 (58.3%) of cases, with a significant statistical difference (p-value of < 0.05) among controls serum iron was <50 µg/dl in 29 (14.4%) and 50 -150 µg/dl in 173 (85.6%). Serum Ferritin was <20ng/dl in 28 (13.9 %) and between 20-400 ng/dl in 174 (86.1%) of controls, with serum TIBC between 250-400µg/dl in 29 (14.4%), having significant statistical difference p value < 0. 0002. as shown in table 5 and 6.

Table 5: Showing Iron deficiency and iron overload among cases and controls

Iron Profile	Cases [n=120]		Controls [n= 202]		P-value
	No.	%age	No.	%age	
Normal	81	67.5	175	86.6	<0.001*
Iron Deficiency	38	31.7	27	13.4	
Iron Overload	1	0.8	0	0.0	
Total	120	100	202	100	

Statistically Significant Difference (P-value<0.05)

Table 6: Comparison based on iron profile among cases and controls

Iron Profile		Cases [n=120]		Controls [n= 202]		P-value
		No.	%age	No.	%age	
Serum Iron (µg/dl)	< 50	38	31.7	29	14.4	0.0004*
	50-150	81	67.5	173	85.6	
	> 150	1	0.8	0	0.0	
Serum Ferritin (ng/dl)	< 20	38	31.7	28	13.9	0.0002*
	20-400	81	67.5	174	86.1	
	> 400	1	0.8	0	0.0	
Serum TIBC (µg/dl)	< 250	0	0.0	173	85.6	<0.001*
	250-400	70	58.3	29	14.4	
	> 400	50	41.7	0	0.0	
% Saturation	< 20%	20	16.7	15	7.4	0.0004*
	20%-55%	97	80.8	160	79.2	
	> 55%	3	2.5	27	13.4	

statistically Significant Difference (P-value<0.05)

Iron deficiency was more among anemic patients in 27(61.4%) where as non-anemic patients were also iron deficient in 11 (14.5%) of cases. Among anemic patients 17 (38.6%) were having normal iron profile and among non-anemic patients 65(85.5%) were iron sufficient with statistically significant difference (p-value<0.005). Iron deficiency was higher among patients with systolic HF (45.2%) and was found in 17.2% of patients having Diastolic HF. 82.8% of Diastolic HF were iron sufficient and 54.4% of systolic HF were having normal iron profile with a statistically significant p-value <0.05. Patients with ID were having poor QoL as compared to iron sufficient cases. ID patients were having poor QoL in 45.2%, moderate in 25% and good in 5.6% of cases. Whereas QoL was good in 94.4% of iron sufficient cases with a statistically significant p-value <0.05. ID patients were having higher NYHA Class as compared to iron sufficient patients. NYHA Class 3 and 4 was present in 77.6% of ID patients whereas iron sufficient patients were having predominantly NHYA Class of 1 and 2 with a statistically significant p-value<0.05, as shown in table 7.

Table 7: Showing association of Iron profile with anemia, type of heart failure, quality of life and NYHA classification

Parameter		Iron Deficient		P-value
		No.	%age	
Anemia	Present	27	61.4	<0.001*
	Absent	11	14.5	
Type of heart failure	HFrEF (Systolic HF)	28	45.2	0.001*
	HFpEF (Diastolic HF)	10	17.2	
Quality of life	Good	1	5.6	0.007*
	Moderate	9	25.0	
	Poor	28	42.4	
NYHA Classification	Class 1	0	0.0	0.036*
	Class 2	6	15.8	
	Class 3	22	43.1	
	Class 4	10	34.5	

Statistically Significant Difference (P-value<0.05)

ID was found to be high in the age group > 60 years in 51.4% of cases. ID was found to be more as age advances. Age < 50 were found to be more Iron Sufficient than higher age groups with a significant p value <0.05. ID was more among females in 35.4% and among males ID was found in 29.2% of cases. Whereas males were more Iron sufficient than females (70.8% vs 64.6%), respectively. ID was found to be higher among rural areas in 33.3% of case and 27.8% in urban areas. ID was found to be more among vegetarians 46.2% than non-vegetarians in 29.9%. Non-veg were found to have more Iron sufficient than vegetarians (70.1% vs 53.8%), respectively. ID was found to be higher among patients having CAD (32.6%), DCM (24.1%), HTN (19.6%) and Valvular Heart Disease in 16%, respectively. As shown in table 8.

Table 8: Showing association of Iron profile with age, gender, residence, dietary habit and comorbidities

Parameter		Iron Deficient		P-value
		No.	%age	
Age (years)	20-29	0	0.0	0.017*
	30-39	2	16.7	
	40-49	4	15.4	
	50-59	13	30.2	
	≥ 60	19	51.4	
Gender	Male	17	23.6	0.020*

	Female	21	43.8	
Residence	Rural	28	33.3	0.549
	Urban	10	27.8	
Dietary Habit	Vegetarian	6	46.2	0.234
	Non-vegetarian	32	29.9	
Comorbidities	Hypertension	11	19.6	0.281
	CAD	14	32.6	
	DCM	9	31.0	
	Valvular Heart Disease	4	16.0	

Statistically Significant Difference (P-value<0.05)

DISCUSSION: -

In this study we enrolled 120 patients of Heart Failure and 202 controls with no known medical illness. The cases and controls were well matched in terms of age, sex, residence and dietary habits.

Anemia, a common comorbidity in HF, is associated with increases disease severity and contributed to a worse outcome. Recent studies have shown that patients with HF are more susceptible to become iron deficient. This could be explained by gradual depletion of iron stores due to low iron intake, iron malabsorption, reduced iron absorption due to chronic inflammation, gastrointestinal blood loss and drug and food interactions. Many Western studies have shown that nearly one third of patients with heart failure had Iron deficiency (37% by **Jankowska et al[10],** 36% by **Opasich et al[11]**, 43% by **Okonko et al[12]** and 26% by **Adlbrecht et al[13]**). A recent study by **Sohan et al[14]** from Indian state Rajasthan also showed that nearly one third (**31.3%**) of HF patients were iron deficient. Similar results were shown by our study where nearly one third (**31.7%)** patients of HF were Iron deficient.

In our study Iron deficiency was more among anemic patients in 27(61.4%) where as non-anemic patients were also iron deficient in 11 (14.5%) of cases with statistically significant difference (p-value<0.05). Similar results were seen in other studies (62.5% and 35.4%, respectively by **von Haehling S. et al[1]** and (61.2% and 45.6%, respectively by **Ijsbrand T Klip et al[10]).** Thus ID is clinically relevant in presence of anemia in patients with HF. But even in non-anemic heart failure patients with iron deficiency, ID is an independent risk factor for HF and contributes significantly toward clinical outcome. These findings lay emphasis on getting a complete iron profile in HF patients, a practice still missing in the developing world, including India.

In our study most common type of anemia among HF was normocytic normochromic (61.4%). Similar observations were shown by other studies (**57% by Opasich et al[11]** and **54% by Adlbecht et al[13]**). As anemia of chronic disease is usually mild but can be severe. It is usually **normocytic**, but can be **microcytic**.[15] The presence of both anemia of chronic disease and dietary iron deficiency in the same patient results in a more severe anemia.

Both anemia and ID was more prevalent in patients having systolic HF (HFrEF) than Diastolic heart failure (65.9% vs 34.1% and 45.2% vs 17.2%) respectively. Similar data was shown by a western study who concluded that nearly ID was present more in patients with systolic HF (40% by **Jankowska et al[10]** and 37% by **Okonko DO et al[16]**). Another study by Julio nunez **et al[17]** showed that anemia was present in 50% of patients with systolic HF (HFrEF). Experimental data showed that ID induces cardiac dysfunction, fatigue, reduce exercise capacity and leads to cardiac hypertrophy, characterized by aberrant mitochondrial and irregular sarcomere organization [18,19]. In these patients treatment with intravenous iron has shown to improve symptoms, functional capacity, and quality of life regardless of anemic status[20,21].

Anemia usually affects females more than males because of regular menstrual bleeding, lactation and less dietary intake. In women over 50 years old, the most common cause of iron-deficiency anemia is chronic gastrointestinal bleeding from nonparasitic causes, such as **gastric ulcers** and **duodenal ulcers**. Anemia has been also found to be more in rural areas because of poor hygiene, more parasitic infections and malnutrition[22]. On gender and residence-based analysis, we found that Anemia was more common in females and patients from rural areas (68.1% and 43.8%) respectively. Similar observations were shown by **Jankowska et al[10]** who concluded that anemia affects females more than males and patients from rural areas. The women in our study were mostly post-menopausal, making blood loss of menstruation (an otherwise common cause of ID in women) a very unlikely cause of ID. This finding is in accordance with previous studies that suggested female gender as an independent correlate of ID in HF[23]. Among demographic parameters ID was found to be more common in female sex than males (43.8% vs 23.6%) respectively in our study. Similar results have been shown by other studies (49.6 vs 31.4% % by **Josep comin-colet et al[24]**, 91.6% vs 68.6% **Sohan et al[14]**). In women, the most common cause of iron deficiency anemia is a loss of iron in the blood due to heavy menstruation. A poor diet or certain intestinal diseases that affect how the body absorbs iron can also cause iron deficiency anemia[25].

In our study anemic patients were more likely to present with advanced NYHA Class (Class 3/4) and had poor Quality of life as compared to non-anemic patients. There was a significant graded association between severity of anemia, NYHA Class as well as Quality of Life. Many western studies also shown similar association of anemia with advanced NYHA Class and poor Quality of life (**Jankowska et al[10], Witte Ezekowitz JA et al[26] and** Enjuanes C **et al[24]). Sohan et al[14]** also showed that anemic patients were having advanced NYHA Class (Class3/4 in 69.4%), and poor quality of life.

Our study revealed that ID was significantly associated with worse clinical presentation in terms of NYHA class and Quality of life, independent of presence of anemia .ID patients were having poor QoL in 45.2%. ID patients were having higher NYHA Class as compared to iron sufficient patients. NYHA Class 3 and 4 was present in 77.6% of ID patients whereas iron sufficient patients were having predominantly NHYA Class 1 and 2. Similar results were also observed in other studies[10,26,24].

Apart from NYHA class and QoL, Iron supplementation has been shown to improve echocardiographic parameters of myocardial performance [27,28]. Unfortunately, such trials are lacking in Indian patients. Our study tries to lay foundation for future large-scale multicentre observational as well as randomized interventional studies of iron replacement in heart failure with ID in Indian subjects.

Few of the limitations of our study are described as follows. This study is a single-centre study conducted at a tertiary care centre in Srinagar, J&K. India being a vast country with different cultures and food habits, it is difficult to generalize the findings necessitating multicentre larger studies. Secondly, the observational character of our study needs to be acknowledged. The study was not designed to elucidate the underlying detrimental mechanisms of ID in patients with HF. Thirdly, this study had no follow up regarding treatment of deficiencies like iron replacement. Finally, there is no clear-cut definition of ID in HF and using criteria standard of bone marrow iron staining in all patients with suspected ID is feasible, as a result most studies relay on serum markers reflecting a disordered iron status.

CONCLUSION: -

ID is common and constitutes a predictor of unfavourable outcome, irrespective of the presence of anemia. 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 consider routine testing in future Indian guidelines. Despite concerns about potential adverse effect of chronic iron overload, there are accumulating data indicating that short term administration of intravenous iron is associated with improved symptoms, Quality of life and mortality in HF. Pharmacological interventions aimed to optimally replete ID in patients with HF will be a challenging task.

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