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TITLE:

A Study of Anemia in Hospitalized Patients of Heart Failure with Reduced Ejection

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ABSTRACT:

INTRODUCTION: Heart failure is a complex clinical syndrome resulting from structural and functional impairment of ventricular filling or ejection of blood, which in turn leads to the cardinal clinical symptoms of dyspnea and fatigue and signs of HF, namely edema and rales.[1] According to the World Health Organization (WHO), anemia is defined as hemoglobin (Hb) levels <12.0 g/dL in women and <13.0 g/dL in men.[2] Anemia in HF decreases the oxygen delivery to the tissues leading to dyspnea and fatigue which worsens the quality of lives of the patients. The guidelines of the American College of Cardiology Foundation/American Heart Association and the European Society of Cardiology both recognize anemia as an important comorbidity in patients with HF. [3,4] Management recommendations focus on determining the underlying etiology and subsequent treatment, although, often no specific cause is found. In this study, we evaluated the patients of heart failure for anemia.

AIMS AND OBJECTIVES: To study anemia in hospitalized patients of heart failure with reduced ejection fraction.

METHOD AND MATERIAL: This is a hospital based cross sectional study of 140 patients of heart failure with reduced ejection fraction admitted in the Department of General Medicine, NHL Medical college, Ahmedabad, Gujarat. The material for this study was formed by adult

patients admitted in the hospital between October 2019 to 2021 fulfilling the inclusion and the exclusion criteria.

RESULT: Out of 140 patients admitted heart with reduced ejection fraction, 58 (41.3%) had anemia with 59% being male. The mean age of patients in the anemic group was 58.5±9.95 years and iron deficiency anemia (53.44%) was the most common cause of anemia in patients of HFrEF with mean Hb being 8.42±1.62 g/dl. We found an inverse relationship between NYHA class grading and mean Hb but no correlation between EF severity and mean Hb.

CONCLUSION: Anemia is a common comorbid condition in patients with HFrEF and has been associated with poor clinical outcome. In this study, nutritional anemia is the most common cause, hence by providing adequate nutrition and awareness we can reduce the burden and can attenuate worse outcomes in patients of heart failure.

KEY WORDS: Anemia, Heart failure, Reduced ejection fraction, Nutrition.

INTRODUCTION:

Anemia in patients with heart failure is associated with increased symptoms severity and higher mortality. Even a small reduction in hemoglobin concentration is associated with less favorable outcomes. [1,2]The prevalence of anemia in patients with HF (defined as hemoglobin <13 g/dL in men and <12 g/dL in women) [3] is ≈30% in stable and ≈50% in hospitalized patients, regardless of whether patients have HFrEF (HF with reduced ejection fraction) or HF with preserved ejection fraction, compared with <10% in the general population (although prevalence increases with age, exceeding 20% in subjects ≥85 years old).[5]The following factors have been suggested to cause anemia in HF patients: iron deficiency, neurohormonal and proinflammatory activation, renal dysfunction, reduced erythropoiesis, hemodilution, and some medications [6,7].The unfavorable effects of anemia in HF patients may overlap with pre-existing pathologies. A rise in sympathetic and renin-angiotensin-aldosterone system activity provokes vasoconstriction and reduces renal perfusion. The heart is burdened with an increased volume workload as a result of water and salt retention [8]. Animal studies have revealed that chronic anemia leads to eccentric cardiac hypertrophy, interstitial fibrosis, increased left ventricular end-diastolic pressure, and decreased systolic functional reserve [9,10] Anemia-related hemodynamic and neurohormonal alterations could potentially result in reduced systolic function related to impaired Frank–Starling responses to preload, particularly in failing hearts [11].

AIMS AND OBJECTIVE:

AIM: To study anemia in hospitalized patients of heart failure with reduced ejection fraction.

OBJECTIVE: To study occurrence, etiology, and clinical profile of anemia in patients of heart failure with reduced ejection fraction.

METHODS: The present study was a cross sectional study conducted at tertiary care center, in the Department of General Medicine at NHL medical college, Ahmedabad extending over a period of 2 years in adult patients that met the inclusion and exclusion criteria. Heart failure was diagnosed based on history, signs and symptoms, clinical parameters, laboratory parameters and 2D ECHO used to measure ejection fraction.

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INCLUSION CRITERIA: Consenting adult indoor patients with age 18 years and above; of either sex with Ejection Fraction ≤ 40%.

EXCLUSION CRITERIA: Nonconsenting patients; pregnant females and those not fulfilling the inclusion criteria.

SAMPLING METHODS AND DIAGNOSTIC TOOL: All patients were assessed for demographics such as age, gender and detailed history, clinical, physical, and hematological examination was done and recorded in the proforma. Complete blood count, serum iron, serum ferritin, TSAT, vitamin B12 were done along with other laboratory parameters. The following reference range for various parameters in our laboratory were considered: Hb- 12-18 g/dl, TLC- 5.2-12.4 KU/L, APC- 130-400 KU/L, Serum Iron = 65-175 ug/dl, Serum Ferritin= 30-400 ng/ml, Serum TIBC=240-450 mcg/dl, TSAT= Serum iron/TIBC*100=average 25%, Serum Vitamin B12 =211-946 pg/dl

STATISTICAL METHOD: The data was recorded and entered in Microsoft Excel Worksheet. IBM SPSS version 22 has been used for statistical analysis. Categorical variables were expressed in numbers and percentages, normally distributed data were presented as mean ± standard deviation. Unpaired t test, chi-square test and ANOVA (analysis of variance) were used to calculate p-value as appropriate. P value < 0.05 has been considered statistically significant.

RESULTS AND DISCUSSIONS: A total of 140 patients who fulfilled the inclusion criteria were studied. Among them 83 were males and 57 females. 58 patients were anemic out of which 34 were male and 24 were female. The mean age of patients in the anemic group was 58.5 ± 9.95 years and in non-anemic group was 59.31 ± 10.67 years. By using unpaired t test the above value was statistically insignificant as t value was 0.455 which equals *p* value 0.252 thus not significant. The commonest age group in our study was the 50-59 years age group in both anemic and non-anemics making up to 38% of our study patients. The 2nd most common age group was the 60-69 years group (29%).

TABLE 1: DISTRIBUTION OF PATIENTS IN ACCORDANCE WITH AGE:

Age	TOTAL NO OF PATIENTS	TOTAL ANEMIC PTS	TOTAL NON-ANEMIC PTS
30-39	03(2.14%)	01	02
40-49	21(15.00%)	09	12
50-59	53(37.86%)	23	30
60-69	41(29.29%)	17	24
70-79	16(11.43%)	06	10
80-89	06(4.29%)	02	04
Total	140(100%)	58	82
MEAN	**58.98**	**58.5**	**59.31**
SD	**10.35**	**9.95**	**10.67**
p-value	**0.252**		

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TABLE 2: DISTRIBUTION OF PATIENTS IN ACCORDANCE WITH GENDER:

SEX	NUMBER OF TOTAL PATIENT (%)	ANEMIC GROUP	NON-ANEMIC GROUP
MALE	83(59%)	34	49
FEMALE	57(41%)	24	33
TOTAL	140(100%)	58	82
RATIO M: F	1.4:1	1.4:1	1.5:1

TABLE 3: DISTRIBUTION OF PATIENTS IN ACCORDANCE WITH SYMPTOMS:

Symptoms	ANEMIC GROUP		NON-ANEMIC GROUP		Total (no. Of pts.) %	p-value
	MALE	FEMALE	MALE	FEMALE		
Cough	24 (17.14%)	15 (10.71%)	41 (29.28%)	22 (15.71%)	102 (72.86%)	0.72
Palpitation	29 (20.71%)	18 (12.86%)	32 (22.86%)	21 (15%)	100 (71.43%)	0.89
Dyspnea on Exertion	34 (24.29%)	24 (17.14%)	49 (35%)	33 (23.57%)	140 (100%)	0.89
Chest pain	11 (7.85%)	08 (5.71%)	20 (14.29%)	10 (7.14%)	49 (35.00%)	0.53
Fatigue	29 (20.71%)	22 (15.71%)	25 (17.86%)	22 (15.71%)	98 (70.00%)	0.90

In our study most common symptom in anemic as well as non-anemic patients was dyspnea on exertion 140 (100.00%) due to heart failure itself. In anemic group, most common symptom was dyspnea on exertion 58 (100.00%) followed by fatigue 51 (87.93%), palpitations 48(82.76%), cough 39 (67.24%), and chest pain 19 (32.76%). In non-anemic groups, most common symptoms were dyspnea on exertion 82 (100%) followed by cough 63 (76.83%), palpitation 53(63.41%), fatigue 47(57.32%) and chest pain 30(36.59%). There was no statistical significance for symptoms of both groups.

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TABLE 4: DISTRIBUTION OF STUDY PARTICIPANTS IN ACCORDANCE WITH SIGNS:

Signs	ANEMIC GROUP		NON-ANEMIC GROUP		Total (no. of pts) (%)	p-value
	MALE	FEMALE	MALE	FEMALE		
Tachypnoea	34 (23.94%)	24 (17.14%)	49 (35.35%)	33 (23.57%)	140 (100%)	0.89
Pedal Edema	30 (21.42%)	23 (16.42%)	43 (30.71%)	27 (19.28%)	123 (87.86%)	0.58
Neck vein engorgement	29 (20.71%)	22 (15.71%)	40 (28.57%)	29 (20.71%)	120 (85.71%)	0.90
Tachycardia	34 (24.28%)	24 (17.14%)	21 (15%)	12 (8.57%)	91 (65.00%)	0.63
Pallor	34 (24.28%)	24 (17.14%)	00	00	58 (41.43)%)	-
Jaundice	03 (2.14%)	03 (2.14%)	04 (2.85%)	05 (3.57%)	15 (10.71%)	0.83
Cyanosis	00	00	01 (0.71%)	00	01 (0.71%)	-

In this study, the most common signs were tachypnea 140 (100%) followed by pedal edema 123(87.86%), neck vein engorgement 120(85.71%), tachycardia 91(65%) pallor 58(41.43%) jaundice 15(10.71%) and cyanosis (0.71%). In the anemic group, the most common signs were tachypnea 58(100.00%) pallor 58(100.00%), tachycardia 58(100.00%) followed by pedal oedema 53(91.38%), neck vein engorgement 51(89.66%) and jaundice 6(10.34%). In the non-anemic group (82 patients), the most common signs were tachypnea 82(100.00%) followed by pedal oedema 70 (85.37%), neck vein engorgement 69 (71.95%), tachycardia 33(40.24%,) jaundice 9 (10.98%), and cyanosis 1 (1.22%). After using the chi square test and Fisher exact test, for the signs of anemic and non-anemic groups, there was no statistical significance between both groups. In our study most of the patients belonged to NYHA class III and IV on admission, so tachypnea and pedal edema were the most common signs in our study.

TABLE 5: DISTRIBUTION OF PATIENTS IN ACCORDANCE WITH RISK FACTORS:

Risk Factors	ANEMIC GROUP		NON-ANEMIC GROUP		Total (no. of pts) (%)	p-value
	MALE	FEMALE	MALE	FEMALE		
Dyslipidemia	20 (14.29%)	12 (8.57%)	28 (20.00%)	16 (11.43%)	76 (54.29%)	0.92
Obesity	04 (2.86%)	06 (4.29%)	06 (4.29%)	11 (7.86%)	27 (19.29%)	0.21
HTN	18 (12.86%)	10 (7.14%)	27 (19.29%)	18 (12.86%)	73 (52.14%)	0.71

DM	12 (8.57%)	07 (5.00%)	20 (14.29%)	13 (9.29%)	52 (37.14%)	0.85
CKD	07 (5.00%)	09 (6.43%)	01 (0.71%)	03 (2.14%)	20 (14.29%)	0.97
Alcohol	05 (3.57%)	05 (3.57%)	09 (6.43%)	04 (2.86%)	23 (16.43%)	0.34
Tobacco	23 (16.43%)	10 (7.14%)	26 (18.58%)	15 (10.71%)	74 (52.86%)	0.57
Smoking	13 (9.29%)	02 (1.43%)	17 (12.14%)	06 (4.29%)	38 (27.14%)	0.34

In our study, the most common risk factor was Dyslipidemia 76 (54.29%), followed by tobacco chewing 74 (52.86%,) Hypertension 73 (52.14%), DM 52 (37.14%), Smoking 38 (27.14%), Obesity 27 (19.29%) Alcohol 23 (16.43%), ,CKD 20 (14.29%). In the anemic group, the most common risk factor was Tobacco chewing 33 (58.90%) followed by dyslipidemia 32 (55.17%), hypertension 28 (48.28%), DM 19 (32.76%), CKD 16 (27.58%), smoking 15 (58.87%), alcohol 10 (17.24%), obesity 10 (17.24%). In the non-anemic group the most common risk factor was Hypertension 45 (54.88%) followed by Dyslipidemia 44 (53.66%), Tobacco chewing 41 (50.00%), DM 33 (41.25%), smoking 23 (28.05%), obesity 17 (20.73%), alcohol 13 (15.85%), CKD 4 (4.88%). By using the chi square test and Fisher exact test for the Risk factors of anemic and non-anemic groups there was no statistical significance between both groups. Dyslipidemia and tobacco can cause atherosclerotic changes which ultimately lead to coronary artery disease which is emerging as the single most common cause of heart failure[1].

TABLE 6: OCCURRENCE OF ANEMIA IN PATIENTS OF HEART FAILURE WITH REDUCED EJECTION FRACTION:

	TOTAL ANEMIC PT	**TOTAL NON-ANEMIC PT**	**TOTAL**
MALE	34(24.29%)	49(35.00%)	83(59.29%)
FEMALE	24(17.14%)	33(23.57%)	57(40.71%)
TOTAL	**58(41.43%)**	**82(58.57%)**	**140(100%)**

TABLE 7: COMPARISON OF DIFFERENT STUDIES CONSIDERING OCCURANCE OF ANEMIA IN HFrEF :

|STUDY	**OCCURRENCE OF ANEMIA IN HFrEF**
STAMINA – HFP Study[12]	**34%**
Ikama et al study[13]	**42%**
OUR STUDY	**41.43%**

In STAMINA -HFP study[12] and Ikama et al study[13] the prevalence of anemia was 34% and 42% respectively. In our study total 58(41.43%) patients were anemic in which 34 were male and 24

were female.

TABLE 8: GENDER DISTRIBUTION AND ANEMIA SEVERITY

GENDER	No. of ANEMIC PT	MEAN Hb	SD Hb
MALE	34	8.64	1.65
FEMALE	24	8.10	1.55
P value	0.07		

In our study, the mean Hb value of male patients was 8.64 ± 1.65 g/dl and in female patients was 8.10 ± 1.55 g/dl. By using unpaired t test the above value was not statistically significant. In this study, most of the females were above 50 years of age and postmenopausal, so difference of mean Hb value between male and female was not significant.

TABLE 9: DIFFERENT CAUSES OF ANEMIA IN PATIENTS WITH HErEF:

ANEMIA	MALE	FEMALE	TOTAL
Anemia of chronic disease	07	09	16(27.58%)
Iron deficiency	21	10	31(53.44%)
B12 deficiency	02	02	04(6.89%)
Others	04	03	07(12.09%)
Total	**34**	**24**	**58(100%)**

In this study, the most common cause of anemia in HFrEF was Iron deficiency anemia 31 (53.44%) followed by Anemia of chronic disease 16(27.58%). Vitamin B12 deficiency contributed to 4 (6.89%); and 07 patients (12.09%) had other causes.

TABLE 10: COMPARISON OF DIFFERENT STUDIES IN ACCORDANCE TO CAUSES OF ANEMIA IN HF.

STUDY GROUP	MAJOR CAUSES OF ANEMIA
Opasich et al[14]	Anemia of chronic disease (57.4%)
Sharma et al[15]	Iron deficiency anemia (51.3%)
Our study	Iron deficiency anemia (53.44%)

In our study, the most common cause of anemia was Iron deficiency anemia (53.44%) followed by Anemia of chronic disease (27.58%). With a mean age of 58.98+_10.35 years, the women we studied were mostly post-menopausal, making blood loss from menstruation a very unlikely cause of ID. The factors include dietary habits—there are high proportions of vegetarians among Indian communities as many Indian. A combination of tea consumption and vegetarianism may further promote ID as black tea has been shown to reduce iron absorption by more than 50% in participants with and without anemia.[16] A study by Yeo et al. done in a multiethnic Asian population, suggested HF patients of Indian ethnicity had highest rates of ID, also supports our findings.[17] In the present study iron deficiency anemia was diagnosed by low s.iron levels, low ferritin levels, normal to high TIBC levels, low TSAT levels and hypochromic microcytic RBCs on peripheral smear. In this study among anemic patients 53.44% patients had iron deficiency anemia, out of which 34 were male and 24 females.

For ID diagnosis serum ferritin <30 ng/ml considered to be a criteria but as HF is chronic inflammatory condition, both intracellular iron accumulation and inflammation stimulate the tissue expression of ferritin and increase its blood level so serum ferritin level may come high. In our study, ID was considered if serum ferritin < 100 μg/L and or normal serum ferritin (100–300 μg/L) with low TSAT (<20%).

Vitamin B12 deficiency anemia was diagnosed by low S.Vitamin B 12 levels , raised MCV and Macrocytosis on peripheral blood smear. It was present in 6.89% of anemic patients with heart failure with reduced ejection fraction.

Anemia of chronic disease was diagnosed by low serum iron levels, normal to high s.ferritin levels, normal TSAT levels and low to normal s.TIBC levels. It was found in 27.58% of anemic patients with heart failure with reduced ejection fraction.

TABLE 11: COMPARISON OF MEAN IRON AND MEAN FERRITIN VALUE IN DIFFERENT TYPES OF ANEMIC PTS IN HFrEF:

TYPES	MEAN IRON(mcg/dl)	MEAN FERRITIN(ng/ml)
Iron deficiency anemia	51.16±40.59	20.04±7.18
Anemia of chronic disease	74.07±17.13	557.80±98.78
B12 deficiency	83.05±22.45	102.70±91.39
Others	214.69±37.59	769.26±156.40
Total Mean	63.56±33.27	219.97±251.27

In our study mean iron value of all anemic patients was 63.56mcg/dl, while mean iron value in Iron deficiency anemia and anemia of chronic disease were 51.16 ± 40.59 mcg/dl and 74.07 ± 17.13 mcg/dl respectively. Serum iron value is decreased in both iron deficiency anemia and anemia of chronic disease [1]. Mean ferritin value of anemic patients was 219.97±251.27 ng/ml while mean ferritin value in Iron deficiency anemia and anemia of chronic disease was 20.04±7.18 ng/ml and 557.80±98.78 ng/ml respectively. Serum ferritin value decreases in iron deficiency anemia and increases or remains normal in anemia of chronic disease. Serum ferritin is an acute marker of inflammation and the increased inflammation in these HF patients with Anemia of chronic disease may lead to higher ferritin value.[1]

TABLE 12: COMPARISON OF MEAN HB, MEAN IRON AND FERRITIN VALUES IN ANEMIC AND NON-ANEMIC PATIENTS:

	ANEMIC GROUP	NON-ANEMIC GROUP	p-value
MEAN HB(g/dl)	8.42±1.62	14.25±0.79	<0.0001
MEAN IRON (mcg/dl)	63.56±33.27	123.13±63.62	<0.0001
MEAN FERRITIN (ng/ml)	219.97±251.57	212.11±220.20	0.84

The t value of unpaired t test for mean Hb was 28.502 and corresponding p value was <0.0001, suggesting significant difference in anemic group and non-anemic groups. The t value of unpaired t test for mean iron was 6.523 and corresponding p value was <0.0001, suggesting

significant difference in anemic group and non-anemic groups. The p value for mean ferritin was 0.84, suggesting no significant difference in the anemic group and non-anemic groups due to inflammation or any other cause as HF itself is a high inflammatory state.

TABLE 13: **DISTRIBUTION OF PATIENTS IN ACCORDANCE WITH NYHA CLASS:**

NYHA Class	Male (no. of pts)	Female (no. of pts)	Total (no. of pts) (%)
Class 1	0	01	01(0.71%)
Class 2	21	08	29(20.71%)
Class 3	32	31	63(45.00%)
Class 4	30	17	47(33.57%)
Total	**83**	**57**	**140(100%)**

In our study, the most common class was NYHA III which includes 63 (45.00%) of patients, while class I, II and IV included 01(0.71%),29 (20.71%) and 47 (33.57%) of patients respectively. Thus, most of the patients belonged to class III and IV. As our study includes only hospitalized patients, the severity of heart failure was higher in our study.

TABLE 14: CORRELATION OF DIFFERENT NYHA CLASS AND ANEMIA SEVERITY

NYHA Class	Male	Female	Total	MEAN Hb	SD Hb
Class 1	0	0	0	-	-
Class 2	10	3	13	10.36	0.36
Class 3	12	14	26	8.53	0.98
Class 4	12	7	19	6.94	1.36
Total	**34**	**24**	**58**	**8.42**	**1.62**

Mean Hb value of NYHA Class II was 10.36 ± 0.36 while mean Hb values of NYHA Class III and IV were 8.53 ± 0.98 and 6.94 ± 1.36, respectively. Mean Hb value and NYHA class have inverse relationship. ANOVA test (analysis of variance) was used for correlation between different NYHA CLASS and MEAN Hb value. The values of anova test was 42.345 and corresponding p value was <0.00001, suggesting significant difference of mean Hb values in different NYHA class patients and showed inverse relation between mean Hb and NYHA class of HF patients. Similar relationship between NYHA class and mean Hb had also been demonstrated in study done by Anand et al.[18]

TABLE 15: CORRELATION BETWEEN EJECTION FRACTION IN 2D ECHO AND ANEMIA SEVERITY.

Mean EF of anemic patients in our study was 27.07 ± 5.99%. We split our study patients in two groups based on EF, 10-24% EF and 25-40% EF and studied the correlation of mean Hb value with EF.

EJECTION FRACTION	EF=10-24%	EF=25-40%
MEAN Hb(g/dl)	8.50	8.39
SD	1.55	1.66

NO. OF PATIENTS	15	43
P-value	0.82	

The t value of the Unpaired t test was 0.0956 and corresponding *p* value was 0.82, which was statistically not significant in our study so the mean Hb value in different groups of ejection fraction patients were insignificant.

CONCLUSION: Our study highlights the importance of treating anemia in all HF patients; effectively find ways of establishing the various etiologies of anemia in heart failure and managing the same in the most appropriate and feasible manner. At least 59% of anemia patients had nutritional deficiency-based anemias as seen in our study and those can be effectively managed if we care to look into it.

REFERENCES:

[1] Harrison's Principles of Internal Medicine,20e

[2] World Health Organization. The World Health Report 2005: Global database on anemia survey 2005. (DEFINITION OF ANEMIA)

[3] Theresa A McDonagh, Marco Metra, Marianna Adamo, Roy S Gardner, Andreas Baumbach, Michael Böhm, Haran Burri, Javed Butler, Jelena Čelutkienė, Ovidiu Chioncel, John G F Cleland, Andrew J S Coats, Maria G Crespo-Leiro, Dimitrios Farmakis, Martine Gilard, Stephane Heymans, Arno W Hoes, Tiny Jaarsma, Ewa A Jankowska, Mitja Lainscak, Carolyn S P Lam, Alexander R Lyon, John J V McMurray, Alexandre Mebazaa, Richard Mindham, Claudio Muneretto, Massimo Francesco Piepoli, Susanna Price, Giuseppe M C Rosano, Frank Ruschitzka, Anne Kathrine Skibelund, ESC Scientific Document Group, 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC, European Heart Journal, Volume 42, Issue 36, 21 September 2021, Pages 3599–3726

[4] Yancy C.W., Jessup M., Bozkurt B.et al. : "2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines". J Am Coll Cardiol 2013; 62: e147.

[5] Tang YD, Katz SD. The prevalence of anemia in chronic heart failure and its impact on the clinical outcomes. Heart Fail Rev. 2008; 13:387–392.

[6] D. Magr`ı, F. De Martino, F. Moscucci, P. Agostoni, and S. Sciomer, "Anemia and iron deficiency in heart failure," Heart Failure Clinics, vol. 15, no. 3, pp. 359–369, 2019.

[7] O. Sˆırbu, M. Floria, P. Dascalita et al., "Anemia in heart failure—from guidelines to controversies and challenges," Anatolian Journal of Cardiology, vol. 20, no. 20, pp. 52–59, 2018

[8] M. Tominaga, M. Kawai, K. Minai et al., "Association between plasma B-type natriuretic peptide and anaemia in heart failure with or without ischaemic heart disease: a retrospective study," BMJ Open, vol. 9, no. 3, Article ID e024194, 2019

ISSN 2515-8260 Volume 09, Issue 06, 2022

[9] S. Yamashita, N. Matsumiya, T. Fujii, and H. Yamaguchi, "A case of progressive congestive heart failure secondary to severe anemia in a patient presenting with uterine hemorrhage," Resuscitation, vol. 42, no. 1, pp. 69–72, 1999

[10] G. Olivetti, F. Quaini, C. Lagrasta et al., "Myocyte cellular hypertrophy and hyperplasia contribute to ventricular wall remodeling in anemia-induced cardiac hypertrophy in rats," 6e American Journal of Pathology, vol. 141, no. 1, pp. 227– 239, 1992.

[11] K. Rakusan, N. Cicutti, and F. Kolar, "Effect of anemia on cardiac function, microvascular structure, and capillary hematocrit in rat hearts," American Journal of Physiology-Heart and Circulatory Physiology, vol. 280, no. 3, pp. H1407–H1414, 2001

[12] Kirkwood F Adams Jr 1, James H Patterson, Ron M Oren, Mandeep R Mehra, Christopher M O'Connor, Ileana L Piña, Alan B Miller, Jun R Chiong, Stephanie H Dunlap, William G Cotts, Gary M Felker, Douglas D Schocken, Todd A Schwartz, Jalal K Ghali, STAMINA-HFP Registry Investigators, STAMINA-HFP Study. Am Heart J. 2009 May;157(5):926-32.doi: 10.1016/j.ahj.2009.01.012.

[13] Méo Stéphane Ikama, MD, Bernice Mesmer Nsitou, MD, Ngamami Solange Mongo, MD, Gisèle Kimbally-Kaky, PhD, Jean Louis Nkoua, PhD, and Innocent Kocko, MD Prevalence of anemia among patients with heart failure at the Brazzaville University Hospital Cardiovasc J Afr. 2015 May-Jun; 26(3): 140–142.

[14] Opasich C, Cazzola M, Scelsi L, De Feo S, Bosimini E, Lagioia R, et al. Blunted erythropoietin production and defective iron supply for erythropoiesis as major causes of anaemia in patients with chronic heart failure. Eur Heart J. 2005;26:2232–2237. doi: 10.1093/eurheartj/ehi388.

[15] Sharma SK, Agarwal SK, Bhargava K, Sharma M, Chopra K, Arumugam G. Prevalence and spectrum of iron deficiency in heart failure patients in southRajasthan. Indian Heart J. 2016 Jul-Aug;68(4):493-7. doi: 10.1016/j.ihj.2015.10.387. Epub 2016 Jan 11.PMID: 275434

[16] Nelson M, Poulter J. Impact of tea drinking on iron status in the UK: a review. J Hum Nutr Diet 2004;17:43–54.

17] Yeo TJ, Yeo PS, Ching-Chiew Wong R, Ong HY, Leong KT, Jaufeerally F, Sim D, Santhanakrishnan R, Lim SL, M Y Chan M, Chai P, Low AF, Ling LH, Ng TP, Richards AM, Lam CS. 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 Oct;16(10):1125-32.

[18] Inder Anand, John J.V. McMurray, James Whitmore, Marshelle Warren, Anemia and Its Relationship to Clinical Outcome in Heart Failure 21 Jun 2004 https://doi.org/10.1161/01.CIR.0000134279.79571.73 Circulation. 2004;110:149–154