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Prevalence and Management of Anemia and Associated Factors among Patients with Heart Failure at Tertial Care Hospital, Dhaka, Bangladesh

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Abstract: ***Background and Aims:*** Heart Failure (HF) is a multi-faceted and life-threatening syndrome characterized by significant morbidity, mortality, poor functional capacity, poor quality of life and associated high costs. Anemia is a frequently encountered comorbid illness in heart failure. It develops due to the complex interaction of other associated comorbidities like chronic kidney diseases (CKDs), diabetes mellitus, hypertension, micronutrient deficiency and blood loss disorders. Hence, this study was aimed to find out the prevalence of anemia and associated factors among patients with heart failure at tertial care hospital, Dhaka, Bangladesh. ***Methods:*** A hospital based cross sectional study was conducted Department of Cardiology July 2017 August 2018 among consecutively selected 200 patients at BSM Medical University Hospital. Socio-demography, clinical features and laboratory parameters to evaluate anemia were obtained. Ethical clearance was taken from the Institutional Review Committee of institute. Collected data was entered in Microsoft Excel and analyzed by Statistical Package for Social Sciences version 23. Frequency, mean, percentage were calculated and chi square test at 0.05% level of significance was used to find the association. ***Results:*** The prevalence of anemia was 65%. Out of 200 patients, majority had iron deficiency anemia (40%), followed by anemia of chronic disease (10%). In this study population, majority (98%) of patients were above age more than 40 years of age and the mean age of the study participants was 65.4±12.5 yrs. More 104 (52%) were male. Among the various religion 87% were Muslim, Hindu (12%) and 1 % other ethnicity. Majority of the study population (61%) were illiterate. 60 percent had iron deficiency without anemia. Female patients 144 (72%) and patients with chronic obstructive pulmonary disease (COPD) 60 (30%) had significantly higher prevalence of anemia (p value <0.05). ***Conclusions:*** Nearly two third of heart failure patients had anemia among which iron deficiency anemia was the commonest. Female and patients with COPD had higher prevalence of anemia.

Keywords: Chronological Order, Heart Failure, Iron Deficiency Anemia, Prevalence of Anemia.

INTRODUCTION

Heart failure (HF) is a multifaceted, life-threatening syndrome characterized by significant morbidity, mortality, poor functional capacity, poor quality of life, and associated high costs [1]. Anemia is a comorbidity that frequently occurs in heart failure. Because of the complex interactions of other related comorbidities such as chronic kidney disease (CKDS), diabetes, hypertension, lack of micronutrients, and blood loss [2]. The prevalence of anemia in heart failure patients is in almost 46.8% of patients, compared to 29.5% of non-anaesthetized patients, with a higher risk of hospitalization and mortality [3]. Long-term anemia of any cause can cause left ventricular hypertrophy (LVH), which can lead to the death of cardiac cell death due to apoptosis, which can exacerbate CHF. Therefore, a vicious cycle is set in which CHF causes anemia, and anemia causes more CHF, both causing damage to the kidneys that worsen anemia and CHF. The challenges regarding optimal definition of iron absence in patients with heart failure are complex. The current definition of iron deficiency in international heart failure guidelines

is a serum ferritin of <100 µg/L, or 100–299 µg/L with a transferrin saturation (TSAT) of <20%. The prevalence of anemia in heart failure varies according to age, sex, severity of heart failure and presence of other comorbid illness [4]. It is related to improved frequency of hospitalization and better morbidities and mortalities, so its early correction improves the first-rate of existence and scientific outcome [2]. A look at from B. P. Koirala Institute of Health Sciences (BPKIHS) stated 82% incidence of anemia wherein 54% had iron deficiency popularity no matter presence or absence of anemia amongst coronary heart failure sufferers [5]. There are confined research executed in our a part of the sector to assess the superiority of anemia amongst sufferers identified with coronary heart failure. Hence, this look at became aimed to discover the superiority of anemia and related elements amongst sufferers with coronary heart failure at tertial care hospital, Dhaka, Bangladesh.

METHODS & MATERIALS

This was a hospital based cross sectional study conducted at Department of Cardiology July 2017 August 2018 among consecutively selected 200 patients at BSM Medical University Hospital. The study included patients with diagnosis of heart failure from outpatient departments and admitted patients at the department of cardiology and medical ward during the study period. Pregnant women, patients who were on iron supplementation or blood transfusion, hemodialysis and connective tissue disorder were excluded from the study.

Informed consent was obtained from each study participant prior to data collection. Data was collected by using structured questionnaires which includes, patient's personal history, diagnosis, New york heart association (NYHA) functional classification, other comorbidities and concomitant diseases, and findings from physical examination in the first part. In the second part, echocardiography was performed to identify left ventricular ejection fraction (LVEF). The diagnosis of heart failure was done after a detailed clinical examination, laboratory findings and measurement of left ventricular ejection fraction (LVEF) by echocardiography. The classification of Heart failure was done as Heart failure with reduced ejection fraction (EF) (HFrEF) [LVEF]: ≤40%), HF with mildly reduced EF (HFmrEF) (LVEF: 41% to 49%), HF with preserved EF (HFpEF) (LVEF: ≥50%), and HF with improved EF [6].

The clinical symptoms of heart failure were classified according to the New York Heart Association classification [7]. Blood samples were drawn for investigation on the day of presentation to the hospital. Hemoglobin, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), serum iron profile and other relevant investigations were performed. Laboratory estimation of hemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) was done via Yumizen H550 automated hematology analyzer. For the classification of anemia, Hb <13.0 g/dL in male adults and <12.0 g/dL in non-pregnant female adults as defined by WHO was used [8]. Red blood cells having equal to, less than or greater than given reference range of MCHC and MCH was considered normochromic, hypochromic and hyperchromic respectively [9]. Reticulocyte count, serum iron profile, and serum ferritin test was done via AU480 chemistry analyzer. After obtaining detailed clinical examination, presence or absence of comorbidities, laboratory reports and from other test procedures, patients were further classified into different types of anemia. Anemia of chronic disease was defined as the presence of a chronic inflammatory condition characterized by a microcytic or normocytic anemia, elevated serum ferritin and low hemoglobin concentration [10].

Iron deficiency (ID) was classified as absolute iron deficiency and relative iron deficiency based on serum ferritin and transferrin level. Absolute iron deficiency was defined as serum ferritin less than 100 µg/l. Relative iron deficiency was defined as serum ferritin levels of 100–300 µg/l and transferrin saturation (TSAT) levels below. Iron deficiency anemia (IDA) was defined as absolute or relative iron deficiency with low hemoglobin. Iron Deficiency without Anemia (IDWA) was operationalized as absolute or relative iron deficiency with normal hemoglobin [11,12].

Data was entered in Microsoft excel, checked for incompleteness, coded and transferred to the statistical package for social sciences (SPSS) version 21. Descriptive statistics such as frequency, mean and percentage were used. Chi square test at 5% level of significance was applied to find the statistical significant association.

RESULTS

Total 200 patients included in our study. Majority (98%) of patients were above age more than 40 years of age and the mean age of the study participants was 65.4±12.5 yrs. More 104 (52%) were male. Among the various religion 87% were Muslim, Hindu (12%) and 1 % other ethnicity. Majority of the study population (61%) were illiterate as shown in Table 1. Among the study population 62% patients were admitted with duration for 1-15 days while 38% were seen at outpatient department.

Table 1: Baseline characteristics (n=200)

Variable	n	%
<40	04	2.0
40-65	98	49.0
>65	09	49.0
Mean±SD	65.4±12.5	
Sex		
Male	104	52.0
Female	96	48.0
Religion		
Muslim	174	87.0
Hindu	24	12.0
Other	02	1.0
Education		
Illiterate	122	61.0
Literate	78	39.0

Table 2: Heart failure classification based on NYHA functional classification and Left Ventricular Ejection Fraction (n=200)

New York Heart Association Functional Classification	n	%
II	10	5.0
III	76	38.0
IV	114	57.0
Types of heart failure according to echocardiography findings of left ventricular ejection fraction (LVEF)		
HFmEF (41% to 49%)	24	12.0
HFrEF (≤40%)	176	88.0

In the study population, more than half (57%) had symptoms of New York heart association (NYHA) functional class IV, 38 % had NYHA class III symptoms and 5 % had NYHA class II symptoms. The majority of patients (88%) had heart failure with reduced ejection fraction (HFrEF) with LVEF (≤40%). (Table 2).

Table 3: Iron deficiency status with or without anemia in patients with heart failure (n=154)

Iron deficiency category	Iron deficiency Anemia (IDA) n (%)	Iron deficiency without Anemia (IDWA) n (%)	Total
Relative iron deficiency (Transferrin saturation <20% when serum ferritin is 100-300 ng/ ml)	32(72.8)	12(27.2)	44(100)
Absolute iron deficiency (serum ferritin<100 ng/ml)	56(50.9)	54(49.1)	110(100)
Total	88(57.1)	66(42.9)	154(100)

The prevalence of iron deficiency (ID) in heart failure was 77%. Among them 88(57.1%) had iron deficiency anemia (IDA) and 66(42.9%) had iron deficiency without anemia (IDWA) (Table 3).

Table 4: Classification of Anemia among patients with heart failure (n=130)

Classification	n	%
Iron Deficiency Anemia	80	61.5
Anemia of Chronic Disease	20	15.4
Megaloblastic Anemia	8	6.5
Combined Megaloblastic and Iron deficiency Anemia	8	6.5
Combined Megaloblastic anemia with absolute iron deficiency	14	10.7

Among 65 anemic patients, the majority had iron deficiency anemia 40(61.5%) followed by anemia of chronic disease 10 (15.4%) and others as shown in Table 4.

Table 5: Association of baseline characteristics with Anemia among patients with heart failure (n=200)

Characteristics		Anemia		p-value
		Present (n%)	Absent (%)	
Age in years	<65 years	54(60)	36(40)	0.343
	≥65 years	76(69.1)	34(30.9)	
Sex	Female	72(75)	24(25)	0.044
	Male	58(55.8)	46(44.2)	
Diabetes Mellitus	Yes	56(68.3)	26(31.7)	0.565
	No	74(62.7)	44(37.3)	
Hypertension	Yes	46(67.6)	22(32.4)	0.690
	No	84(63.6)	48(36.4)	
Chronic obstructive pulmonary disease (COPD)	Yes	30(93.8)	2(6.3)	0.009
	No	100(59.5)	68(40.5)	
Coronary artery disease	Yes	62(68.9)	28(31.1)	0.461
	No	68(61.8)	42(38.2)	
Atrial fibrillation	Yes	4(66.7)	2(33.3)	1.000*
	No	126(64.9)	68(35.1)	
NYHA functional classification	II	4(40)	6(60)	0.471*
	III and IV	126(66.3)	64(33.7)	
Types of heart failure	HFmEF	12(50)	12(50)	0.402*
	HFrEF	118(67)	58(33)	

In this study on evaluating the various associated factors for prevalence of anemia in HF patients, only female patients and patients with a history of chronic obstructive pulmonary disease had increased prevalence of anemia among HF patients which were statistically significant (p value<0.05). The other factors such as age, diabetes mellitus, hypertension, coronary artery disease, atrial fibrillation, types of heart failure and NYHA classification were not found to statically significant with the prevalence of anemia in HF patients as shown in Table 5.

DISCUSSION

Iron deficiency (ID) is an extremely common comorbidity in patients with heart failure. One-third of HF patients are anaemic and almost 50% have ID. ID is associated with more HF symptoms, worse New York Heart Association (NYHA) functional status, greater risk of HF hospitalization and reduced survival. In our study, patients were relatively younger than in large series in developed countries where the mean age of patients was 57 years old and the mean age of patients was 70 years [13, 14]. In Africa, few studies have been conducted on the assessment of anemia in HF patients [15]. Among the different religions were 87% Muslims, Hindus (12%) and 1% of other ethnic groups. The majority (61%) of the study population were illiterate. Under the study population, 62% of patients were recorded for 1-15 days, and 38% were observed in the outpatient department. Two different studies by Brazzaville University Hospital in Brazil and Gondar University Transfer Hospital in Ethiopia found the prevalence of anemia as 42% and 41.9% [16]. Anemia in heart failure is a frequently occurring comorbidity, with its prevalence between 30% and 70°C for the limits used to define its presence and population under consideration [17]. Structural and/or functional abnormalities prevent the heart from functioning efficiently in patients with heart failure. The best medical care and devices are treatments, but the mortality rate is 50% over a five-year diagnosis. Complications are made by comorbidities such as anemia, oxygen delivery to tissues continues and reinforces symptoms of dyspnea and fatigue, along with deterioration in quality of life [18]. Anemia in heart failure was independently associated with decreased training tolerance, increased hospitalization, morbidity, and mortality [19]. In our study, there was a difference in the prevalence of anemia with different test procedures. Hb estimation alone diagnosed anemia in 55% while Hb along with serum iron level, serum ferritin, transferrin saturation, TIBC and RBC morphology diagnosed anemia in 65% of patients. Anemia has a multifactorial pathogenesis, most commonly occurring due to iron deficiency. Nutritional deficiencies (folate, vitamin B12 and vitamin A), inflammation, parasitic infections and inherited or acquired disorders affect hemoglobin synthesis, red blood cell production or red blood cell survival, and all can cause anemia. In such cases, serum ferritin is the most sensitive biomarker to test for early stages of iron deficiency as well as iron deficiency anemia [20]. More than three fourth (77%) patients had iron deficiency irrespective of the presence or absence of anemia in this study. A relatively lower percentage of prevalence was found in India in comparison to our study where 53.8% were diagnosed with iron deficiency [13]. Among 77% diagnosed for having iron deficiency, 88(57.1%) had

IDA (40% IDA only and 4% combined iron deficiency and megaloblastic anemia) and 66(42.9%) had IDWA in our study. In a study from Dharan, 48% had IDA which is higher than our study and 6% had IDWA which is lower than our study [3]. A higher prevalence was found in which 47.2% patients had iron deficiency anemia in a study from India and 36 (6.54%) had IDWA which is lower than our study [13]. The prevalence of iron deficiency among patients with heart failure varies from 37 to 61% and it increases as the disease advances [21]. Ten percent of patients had anemia of chronic disease in our study. Among these group we found that the red cell morphology showed microcytic (3 patients) or normocytic anemia (7 patients), hemoglobin concentration showing mild (1%), moderate (7%) and severe anemia (2%), increased serum ferritin greater than 300 ng/ ml (10%) and increased serum transferrin (10%). All the patients with anemia of chronic disease were in NYHA III and IV and 18 patients had HFrEF in this study. Fifteen patients had megaloblastic anemia in which 4 patients had megaloblastic anemia only, 14 patients had combined absolute iron deficiency and megaloblastic anemia and four patients had combined megaloblastic and iron deficiency anemia in this study. Deficiency of Vitamin B12 and folate results in megaloblastic anemia characterized by macrocytic red blood cells. Megaloblastic anemia is often overlooked in HF due to concomittant iron deficiency. Megaloblastic is a nutritional deficiency anemia that occurs alone or concomitant with other types of anemia and increases with advancing age and disease severity. So, evaluating it is also as important as other test procedures [23]. In our study females patients and patients with COPD had higher prevalence of anemia compared to others which was statistically significant. Female patients having higher prevalence were found in other studies too [24]. COPD and heart failure frequently coexist in clinical practice [25]. Studies reveal that 10-30% of patients with COPD had anemia. Anemia of chronic disease is considered the most common cause for presence of anemia in patients with coexisting COPD and heart failure [26]. Our study shows increased prevalence of anemia among comorbidities like diabetes, hypertension, concomitant disease like coronary artery disease, atrial fibrillation, age above 65 years, NYHA III and IV, and HFrEF however there was no statistically significant association. Study from Dharan also identified the same pattern but there was no statistical linkage mentioned in that study [3]. Serum iron level also changes frequently throughout the day so serum ferritin should be considered the best biomarker for identifying the patients having anemia which is supported by the recent guidelines [27]. The limitations of our study is the generalizability of the findings. This is a single centered hospital based study with small sample size so findings from this study may not represent the population at large. Another limitation might be related to the presence of other comorbid illness which are not studied in this study. We recommend conducting a community based cross sectional study or a case control study to find the prevalence of anemia so that the findings are more generalizable.

CONCLUSION

Anemia with low iron reserve on the basis of low transferrin saturation and relatively higher levels of ferritin identifies the two most common causes of anemia in patients with heart failure, namely anemia of chronic disease (AOCD) and iron deficiency anemia (IDA). Nearly two third patients with heart failure had anemia. Iron deficiency anemia was the most common occurrence. Iron deficiency without anemia was seen in one third of patients. Female and patients with COPD had an increased percentage of anemia compared to others.

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