Original Article

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Prevalence of anemia and associated factors among patients with heart failure at Birat Medical College Teaching Hospital

Madhab Bista[1], Ram Kumar Mehta[2], Surya B. Parajuli[3], Prashant Shah[1]

[1] Department of Cardiology, Birat Medical College Teaching Hospital
[2] Department of Internal Medicine, Birat Medical College Teaching Hospital
[3] Department of Community Medicine, Birat Medical College Teaching Hospital

Corresponding Author: Madhab Bista
Department of Cardiology, Birat Medical College Teaching Hospital, Morang, Nepal.
Phone: +977 9861171137

Email: bistamadhab10@gmail.com
ORCID ID NO: ***0000-0002-2900-2582***

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Abstract

Background and Aims: Anemia is a frequently encountered comorbid illness in heart failure and is associated with poor clinical outcomes. There are limited studies done in Nepal to evaluate its prevalence among patients diagnosed with heart failure. Hence, this study was aimed to find out the prevalence of anemia and associated factors among patients with heart failure at Birat Medical College Teaching Hospital.

Methods: A hospital based cross sectional study was conducted from 1st July 2022 to 30 February 2023 among consecutively selected 100 patients at Birat Medical College Teaching 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 100 patients, majority had iron deficiency anemia (40%), followed by anemia of chronic disease (10%). Thirty three percent had iron deficiency without anemia. Female patients 36(75%) and patients with chronic obstructive pulmonary disease (COPD) 15(93.8%) 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: Chronoligical order, Heart failure, Iron deficiency anemia, Prevalence of anemia

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Introduction

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.[1] 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.[2] The prevalence of anemia in heart failure varies according to age, sex, severity of heart failure and presence of other comorbid illness.[3] It is associated with increased frequency of hospitalization and higher morbidities and mortalities, so its early correction improves the quality of life and clinical outcome.[2] A study from B. P. Koirala Institute of Health Sciences (BPKIHS) reported 82% prevalence of anemia where 54% had iron deficiency status irrespective of presence or absence of anemia among heart failure patients.[4] There are limited studies done in our part of the world to evaluate the prevalence of anemia among patients diagnosed with heart failure. Hence, this study was aimed to find out the prevalence of anemia and associated factors among patients with heart failure at Birat Medical College Teaching Hospital.

Methods

This was a hospital based cross sectional study conducted with consecutive sampling of 100 patients from 1st July 2022 to 30 February 2023 in the department of cardiology and internal medicine at Birat Medical College Teaching 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. Ethical approval was obtained from the Institutional Review Committee of Birat Medical College Teaching Hospital (IRC-PA-206/2078-79).

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.[5] The clinical symptoms of heart failure were classified according to the New York Heart Association classification.[6] 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.[7] The reference range for MCV, MCH, and MCHC was 75-95fl, 25-32 pg, 30-35% respectively as per the standard given from the clinical laboratory department of Birat Medical College Teaching Hospital. Red blood cells having equal to, less than or greater than of given reference range of MCV was considered normocytic, microcytic and macrocytic red blood cells respectively. 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.[8] 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.[9]

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 20. 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.[10-12]

Megaloblastic anemia is defined as presence of Vitamin B12 or folate deficiency characterized by red cell morphology having high MCV (macrocytic), normal MCHC (normochromic) and increased MCH (hyperchromic).[13]

Data was entered in Microsoft excel 16, checked for incompleteness, coded and transferred to the statistical package for social sciences (SPSS) version 23. 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

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 than half (52%) were male. Among the various ethnicity 33% were Brahmin/chhetri, Janajati (33%), Madhesi 15 %, and Muslim 12%, Dalit 6% 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=100)

Variable	n (%)
Age (In Years) Mean±S.D.= 65.4±12.5	
<40	2(2)
40-65	49(49)
>65	49(49)
Sex	
Male	52(52)
Female	48(48)
Ethnicity	
Brahmin/Chhetri	33(33)
Dalit	6(6)
Janajati	33(33)
Madhesi	15(15)
Muslim	12(12)
Other	1(1)
Education	
Illiterate	61(61)
Literate	39(39)

Table 2: Heart failure classification based on NYHA functional classification and Left Ventricular Ejection Fraction (n=100)

New York Heart Association Functional Classification	n(%)
II	5(5)
III	38(38)
IV	57(57)
Types of heart failure according to echocardiography findings of left ventricular ejection fraction (LVEF)	
HFmEF (41% to 49%)	12(12)
HFrEF (≤40%)	88(88)

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=77)

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)	16(72.8)	6(27.2)	22(100)
Absolute iron deficiency (serum ferritin<100 ng/ml)	28(50.9)	27(49.1)	55(100)
Total	44(57.1)	33(42.9)	77(100)

The prevalence of iron deficiency (ID) in heart failure was 77%. Among them 44(57.1%) had iron deficiency anemia (IDA) and 33(42.9%) had iron deficiency without anemia (IDWA) (Table 3).

Table 4: Classification of Anemia among patients with heart failure (n=65)

Classification	**n(%)**
Iron Deficiency Anemia	40(61.5)
Anemia of Chronic Disease	10(15.4)
Megaloblastic Anemia	4(6.5)
Combined Megaloblastic and Iron deficiency Anemia	4(6.5)
Combined Megaloblastic anemia with absolute iron deficiency	7(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=100)

Characteristics		**Anemia**		**P value**
		Present (n%)	Absent (%)	
Age in years	<65 years	27(60)	18(40)	0.343
	≥65 years	38(69.1)	17(30.9)	
Sex	Female	36(75)	12(25)	0.044
	Male	29(55.8)	23(44.2)	
Diabetes Mellitus	Yes	28(68.3)	13(31.7)	0.565
	No	37(62.7)	22(37.3)	
Hypertension	Yes	23(67.6)	11(32.4)	0.690
	No	42(63.6)	24(36.4)	
Chronic obstructive pulmonary disease (COPD)	Yes	15(93.8)	1(6.3)	0.009
	No	50(59.5)	34(40.5)	
Coronary artery disease	Yes	31(68.9)	14(31.1)	0.461
	No	34(61.8)	21(38.2)	
Atrial fibrillation	Yes	2(66.7)	1(33.3)	1.000*
	No	63(64.9)	34(35.1)	
NYHA functional classification	II	2(40)	3(60)	0.471*
	III and IV	63(66.3)	32(33.7)	
Types of heart failure	HFmEF	6(50)	6(50)	0.402*
	HFrEF	59(67)	29(33)	

P value<0.05 was considered statistically significant.

**continuity correction was applied.*

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

We found that nearly two third (65%) patients had anemia. Compared to our study, a significantly higher prevalence was found in a study from Dharan where every four in five (82%) patients had anemia.[4] A study from India found that more than three fourth (76.7%) patients with heart failure had anemia which is higher from our study.[14] Two different study from Brazzaville University Hospital, Brazil and Gondar University Referral Hospital, ethiopia found the prevalence of anemia as 42% and 41.9% respectively.[15,16]

Anemia in heart failure is a commonly occurring comorbidity and its prevalence ranged from 30% to 70% depending on the cutoff value used to define its presence and on the population considered.[17] In patients with heart failure, heart is unable to perform circulatory function efficiently due to structural and/or functional abnormalities. The mortality rate is 50% at 5 years of diagnosis despite having the best medical and device therapies. When it is complicated by comorbidity like anemia, the oxygen delivery to the tissue further decreases and aggravates the symptoms of dyspnea and fatigue with worsening quality of life.[18] Anemia in heart failure has been independently associated with reduced exercise tolerance, increased hospitalization, morbidity and mortality.[17]

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. Screening for iron deficiency using a hemoglobin test only identifies the most severe cases. Hemoglobin is not a specific marker for diagnosing iron deficiency or iron deficiency 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.[19,20]

More than three fourth (77%) patients had iron deficiency irrespective of the presence or absence of anemia in this study. Contrast to our finding, the prevalence of iron deficiency was 46.67% and 54% respectively irrespective of the presence or absence of anemia in studies from Dharan conducted in 2019 and 2021.[21,4] A relatively lower percentage of prevalence was found in India in comparison to our study where 53.8% were diagnosed with iron deficiency.[14]

Among 77% diagnosed for having iron deficiency, 44(57.1%) had IDA (40% IDA only and 4% combined iron deficiency and megaloblastic anemia) and 33(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.[4] A higher prevalence was found in which 47.2% patients had iron deficiency anemia in a study from India and 18(6.54%) had IDWA which is lower than our study.[14] The prevalence of iron deficiency among patients with heart failure varies from 37 to 61% and it increases as the disease advances.[22] Iron deficiency and heart failure have almost similar presentation (fatigue, exercise intolerance) which may sometimes be misdiagnosed or delay the diagnosis.[11] Iron deficiency anemia is the most common presentation in patients with heart failure with an estimated prevalence of over 50% in ambulatory patients. It is an independent predictor of worse functional capacity, survival and increased mortality.[11,16,23] IDWA is twice as common as iron deficiency anemia but is poorly recognised probably because of suboptimal screening recommendations. IDWA has increased risk of mortality in patients with chronic infection such as heart failure and recognizing it as a clinical diagnosis is crucial to ensuring adequate management and to improve quality of life.[12]

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 9 patients had HFrEF in this study. Fifteen patients had megaloblastic anemia in which 4 patients had megaloblastic anemia only, 7 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. [24]

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.[21,25] COPD and heart failure frequently coexist in clinical practice.[26] 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.[27, 28] 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.[4] The strength of this study is that we conducted a study which is of great significance in clinical practice to treat patients with heart failure and anemia. We performed a timely detailed investigation so as not to miss a single case of patients with anemia. We also performed a bivariate analysis to find the association of demographic variables, comorbidities in causing anemia. The findings from this study state that every suspected patient with anemia must undergo serum iron profile (serum ferritin test, TSAT,TIBC, serum iron) peripheral smear test, reticulocyte counts along with the Hemoglobin estimation. 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.[10,12] 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

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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