Health Sciences & Disease
The Journal of Medicine and Biomedical Sciences

Original Article

Prevalence, Correlates and Outcome of Anemia in Hospitalized Patients with Heart Failure at the Buea Regional Hospital, South West Region of Cameroon

Prévalence, Déterminants et Pronostic de l'Anémie, chez les Patients Hospitalisés pour Insuffisance Cardiaque à l'Hôpital Général de Buea, Région du Sud-Ouest du Cameroun

Siddikatou Djibrilla[1,2], Clovis Nkoke[1, 2], Denis Teuwafeu[1, 2], Cyrille Nkouonlack[1, 2,] Ahmadou Musa Jingi[3], Ronald Gobina[1, 2,] Jean Jacques Noubiap[4]

Affiliations
1. Faculty of Health Sciences, University of Buea, Buea, Cameroon
2. Buea Regional hospital, Buea, Cameroon
3. Faculty of Health Sciences, University of Bamenda
4. Center for Heart Rhythm Disorders, University of Adelaide, Adelaide, SA, Australia

Corresponding author : Dr Siddikatou Djibrilla Faculty of Health Sciences, University of Buea
Tel : +237694942028 E-mail : djibrillasid@yahoo.fr

Keywords: Heart failure, anemia, mortality, outcome, Cameroon

ABSTRACT

Background. Anemia is a common co-morbidity in heart failure (HF). It is associated with poor clinical status and worse outcomes. There is paucity of data on prognostic impact of anemia in patients admitted for acute decompensated heart failure in Cameroon. **Objectives.** The aim of this study was to determine the prevalence of anemia, associated factors and its impact on outcome in patients hospitalized with acute decompensated heart failure. **Methods**. We conducted a cross-sectional study in consecutive patients hospitalized with HF between June 2016 and November 2017. Anemia was defined as hemoglobin < 12 g/dl in women and < 13 g/dl in men. **Results.** During the study period, 86 patients were hospitalized with heart failure. Of these, 68 patients had hemoglobin recorded and were included in this study. There were 31 (46.4%) males. Mean age (SD) was 59.4 ± 17.7 years. The mean (SD) hemoglobin concentration was 12.3 (2.4) g/dL. Anemia was present in 42.7%, [95% CI: 30.7 – 55.2]) of the patients, of which it was mild in 31%, moderate in 62.1%, and severe in 6.9% patients. Those with anemia had significantly elevated creatinine>13mg/l (p=0.016), left ventricular hypertrophy (p=0.018), and left atrial dilation (p=0.045). In bivariate analyses, serum creatinine > 13 mg/L (aOR=3.1, 95%CI: 1.1-8.9) was associated with anemia. All deaths (100%) occurred in patients without anemia. **Conclusion**. Anemia was frequent in hospitalized patients with heart failure. Elevated serum creatinine, left ventricular hypertrophy and left atrial enlargement were significantly associated with anemia. Anemia might not be a driver of poor outcome. There is need for larger studies to assess the prognostic impact of anemia in hospitalized heart failure patients in our setting.

RÉSUMÉ

Introduction. L'anémie est une comorbidité fréquente de l'insuffisance cardiaque (IC). Elle est associée à une aggravation de l'état clinique et un mauvais pronostic. Il existe peu de données sur l'impact pronostique de l'anémie chez les patients admis pour insuffisance cardiaque aiguë décompensée au Cameroun. **Objectifs.** Le but de cette étude était de déterminer la prévalence de l'anémie, les facteurs associés et son impact sur le pronostic chez les patients hospitalisés pour insuffisance cardiaque. **Méthodologie**. Nous avons mené une étude transversale chez des patients hospitalisés pour IC entre juin 2016 et novembre 2017. L'anémie était définie comme un taux d'hémoglobine < 12 g/dl chez la femme et < 13 g/dl chez l'homme. **Résultats.** Au cours de la période d'étude, 86 patients ont été hospitalisés pour insuffisance cardiaque. Parmi eux, 68 patients ont eu un taux d'hémoglobine enregistré et ont été inclus dans cette étude. Il y avait 31 (46,4 %) hommes. L'âge moyen était de 59,4 ± 17,7 ans. Le taux moyen d'hémoglobine était de 12,3 g/dL. L'anémie était présente chez 42,7 % [IC 95 % : 30,7 – 55,2]) des patients ; elle était légère chez 31 %, modérée chez 62,1 % et sévère chez 6,9 % des patients. Les personnes souffrant d'anémie présentaient une créatininémie significativement élevée > 13 mg/l (p = 0,016), une hypertrophie ventriculaire gauche (p = 0,018) et une dilatation auriculaire gauche (p = 0,045). En analyse bivariée, une créatinine sérique > 13 mg/L (aOR=3,1, IC 95 % : 1,1-8,9) était associée à une anémie. Tous les décès (100 %) sont survenus chez des patients sans anémie. **Conclusion**. L'anémie était fréquente chez les patients hospitalisés pour insuffisance cardiaque. Une créatininémie élevée, une hypertrophie ventriculaire gauche et une dilatation de l'oreillette gauche étaient associées de manière significative à l'anémie. L'anémie n'est peut-être pas un facteur de mauvais résultats. Des études plus vastes sont nécessaires pour évaluer l'impact pronostique de l'anémie chez les patients hospitalisés pour insuffisance cardiaque dans notre contexte.

HIGHLIGHTS OF THE STUDY

What is already known on this topic
Anemia is a common co-morbidity in heart failure (HF). It is associated with poor clinical status and worse outcomes. Few data are available in Buea.
What question this study addressed
prevalence, associated factors and outcome of anemia in patients with acute decompensated heart failure in Buea
What this study adds to our knowledge
1. The prevalence of anemia in the study populatin was 42.7%.
2. Those with anemia had significantly elevated creatinine>13mg/l (p=0.016), left ventricular hypertrophy (p=0.018), and left atrial dilation (p=0.045).
3. However, anemia was not a driver of poor outcome of patients.

How this is relevant to practice, policy or further research.
There is need for larger studies to assess the prognostic impact of anemia in hospitalized heart failure patients in our setting

INTRODUCTION

Heart failure (HF) is growing public health problem of global magnitude affecting about of 26 millions people worldwide including sub-Saharan Africa (1). The prevalence of heart failure in developed countries is 1-2% and it is expected to rise (2-4). In Africa, HF accounted for 9.4–42.5% and 25.6–30.0% of all admissions to medical, and cardiology units, respectively (5). Heart failure in SSA is different from HF patients in high income countries. While heart failure patients from SSA are 10 years younger, with heart failure etiology dominated by hypertension, heart failure in high income countries is dominated by ischemic cardiomyopathy (6). The morbidity and mortality associated with heart failure is high despite improvements in heart failure treatment in the last two decades (7).

Co-morbidities frequently accompany heart failure and lead to increased morbidity and mortality, and a further decrease in quality of life (8-12). Anemia is one of the most frequent co-morbidities associated with heart failure. In patients with HF, studies have reported a wide range of anemia prevalence of about 30% in stable patients and about 50% in hospitalized patients regardless of the ejection fraction (13-17). Anemia in heart failure patients is associated with poor clinical status and poor outcomes (13-15). Anemia in patients hospitalized for acute decompensated heart failure is poorly characterized in Cameroon. The aim of this study was to determine the prevalence of anemia in patients admitted with acute heart failure, correlates and its impact on in-hospital outcomes in a semi-urban setting in Cameroon.

METHODS

Study design and setting

Between June 2016 and November 2017, we carried out a cross-sectional descriptive and analytic study in the Buea Regional Hospital. This is a secondary level Hospital and serves as one of the two main referral centers in the region, with a bed capacity of 111 beds, and a catchment population of about 200,000 inhabitants. The Hospital also serves as one of the teaching hospitals of the University of Buea. Facilities for cardiac evaluation at the center include; chest radiography, 12-lead electrocardiograph, and echocardiography.

Study population

These were adults of both sexes aged ≥ 18 years who were hospitalized for heart failure during the study period. The participants were prospectively recruited.

Procedure and measurements: This is sub-study of previously collected data. The methods involved in this study have been previously described (18). We collected demographic data (age and sex), medical history (previous diagnosis of heart failure, hypertension, diabetes, alcohol consumption, tobacco use, atrial fibrillation). Each patient underwent complete clinical evaluation for symptoms and signs of heart failure. We measured the blood pressure according to standard procedures and blood was collected for biochemical analysis (serum creatinine, hemoglobin, sodium, potassium, and fasting blood glucose). Each patient then underwent a 12-lead resting ECG and a comprehensive cardiac ultrasound by a trained Cardiologist (CN) with a Sonoscape S8 ultrasound machine (Sonoscape China).

Outcome variables: The main outcome variable was the proportion of anemia in patients with heart failure according to WHO (Hemoglobin< 13 g/dL in males and <12 g/dL in females) (19). Secondary outcome measures were in-hospital death or hospital stay > 7 days and the association with anemia.

Sample size and Statistical analyses: A convenient sample of all patients fulfilling the inclusion criteria was considered for this study. The data were analyzed using IBM SPSS version 26. Continuous variables are presented as means (SD) and discrete variables as frequencies and proportions (95% confidence interval). We have compared the means with independent sample T-test and proportions with Chi-squared or Fischer exact test where appropriate. We assessed for factors associated with anemia in patients with heart failure in bivariate analyses and then adjusted for sex using stratification multivariate analyses. A p-value < 0.05 was considered statistically significant.

RESULTS

General characteristics

During the study period, 86 patients were hospitalized with heart failure. Of these, 68 patients had a hemoglobin recorded and were considered for this study. There were 31 (46.4%) males and 37 (54.4%) females (p=0.873). Their mean age (SD) was 59.4 ± 17.7 years, and ranged from 22 to 100 years. The clinical characteristics are shown in Table 1. Hypertension was the most frequent cardiovascular risk factor seen in 39 (57.4%) patients. Most of the patients were in NYHA class 3 and 4. Fatigue was a constant symptom at presentation. The echocardiographic and biochemical characteristics are shown in Table 2. Dilation of the left atrium was the most frequent echocardiographic finding. Biventricular heart failure was the most frequent type seen in 39 (57.4%) patients.

Prevalence of anemia, its determinants and outcome

Anemia was present in 29 (42.7%, [95% CI: 30.7 – 55.2]) patients, of which it was mild in 9 (31%), moderate in 18 (62.1%), and severe in 2 (6.9%) patients. The mean (SD) hemoglobin concentration was 12.3 (2.4) g/dL. There was no significant difference of anemia between sexes (males 51.6% versus females 35.1%, p=0.171), past history, and clinical presentation (Table 1).

Table 1 : Clinical characteristics of participants: overall and by anemia (WHO criteria)

Variable	Overall (n=68)	Anemia (WHO criteria)		*p*-value
		Yes (n=29)	No (n=39)	
Age (years), mean (SD)	59.4 (17.7)	59 (18.6)	59.7 (17.2)	0.873
Male sex, n(%)	31 (45.6)	16 (55.2)	15 (38.5)	0.171
Medical History, n(%)				
Chronic Heart Failure	12 (17.6)	3 (10.3)	9 (23.1)	0.212
Hypertension	39 (57.4)	16 (55.2)	23 (59)	0.754
Diabetes	9 (13.3)	6 (20.7)	3 (7.7)	0.156
Current smoking	4 (5.9)	1 (3.4)	3 (7.7)	0.631
Atrial Fibrillation	2 (2.9)	0 (0)	2 (5.1)	0.504
Chronic Kidney Disease	5 (7.4)	4 (13.8)	1 (2.6)	0.155
Alcohol consumption	8 (11.8)	4 (13.8)	4 (10.3)	0.715
Symptoms, n (%)				
NYHA Class				
II	5 (7.4)	1 (3.4)	4 (10.3)	0.241
III	35 (51.5)	13 (44.8)	22 (56.4)	
IV	28 (41.2)	15 (51.7)	13 (33.3)	
Fatigue	68 (100)	29 (100)	39 (100)	NA
Orthopnea	65 (95.6)	29 (100)	36 (92.3)	0.255
Physical findings				
Systolic BP, mean (SD)	143.5 (36.9)	149 (38.1)	139.4 (35.9)	0.295
Diastolic BP, mean (SD)	94.4 (29.5)	91.9 (27.2)	96.3 (31.3)	0.549
Heart Rate, mean (SD)	94.7 (18)	93 (21.4)	96 (15.3)	0.497
Pedal edema, n(%)	60 (88.2)	27 (93.1)	33 (84.6)	0.451
Rales, n (%)	53 (77.9)	24 (82.8)	29 (74.4)	0.409

Those with anemia had significantly higher rates of impaired kidney function, left ventricular hypertrophy, and left atrial dilation (Table 2).

Table 2 : Echocardiographic and biochemical characteristics in participants: overall and by anemia status (WHO criteria).

Variable	Overall (n=68)	Anemia (WHO criteria)		*p*-value
		Yes (n=29)	No (n=39)	
Mean (SD) values				
Septum (mm)	10.4 (2.9)	10.7 (3.1)	10.1 (2.7)	0.394
Posterior wall (mm)	10.4 (2.8)	11 (2.9)	10 (2.6)	0.105
LV End-diastolic diameter (mm)	57.8 (11.2)	58.2 (8.8)	57.6 (12.9)	0.828
LV End-systolic diameter (mm)	47.2 (13.3)	47.5 (10.5)	46.9 (15.2)	0.864
Relative Wall Thickness	0.38 (0.16)	0.39 (0.2)	0.38 (0.2)	0.691
LV Mass (g)	252.3 (104.7)	265.2 (95.3)	242.7 (111.4)	0.383
LV Ejection fraction (%)	37.8 (19.5)	38 (15.3)	37.7 (22.3)	0.943
LV Fractional shortening (%)	19.1 (11.9)	18.9 (9.1)	19.2 (13.7)	0.910
LA Area (cm^2)	24.96 (7.1)	25.5 (5.3)	24.6 (8.2)	0.606
LA Diameter (mm)	41.9 (8.4)	42.9 (6.4)	41.1 (9.6)	0.377
RA Area (cm^2)	20.8 (7)	19.1 (6.1)	22.1 (7.4)	0.087
TAPSE	15.5 (2.1)	15.9 (1.6)	15.1 (2.3)	0.131
E-wave Deceleration time (ms)	117.1 (36.3)	119.4 (32)	115.4 (39.6)	0.662
E/A ratio	1.91 (0.96)	2.12 (1.1)	1.73 (0.8)	0.138
PASP (mmHg)	63.4 (4)	57.4 (17.1)	68.8 (22.2)	0.042

Table 2 : Echocardiographic and biochemical characteristics in participants: overall and by anemia status (WHO criteria).

Variable	Overall (n=68)	Anemia (WHO criteria)		*p*-value
		Yes (n=29)	No (n=39)	
Hemoglobin (g/dL)	12.3 (2.4)	10.1 (1.5)	13.99 (1.3)	<0.001
Creatinine (mg/L)	18.9 (21.3)	25.9 (30)	13.7 (8.4)	0.018
Natriemia (mmol/L)	138.7 (8.3)	139.8 (6.8)	138 (9.2)	0.425
Proportion, n(%) values				
LV Hypertrophy	36 (52.9)	20 (69)	16 (41)	0.018
LA Dilation	53 (77.9)	26 (89.7)	27 (69.2)	0.045
RA Dilation	37 (54.4)	13 (44.8)	24 (61.5)	0.223
Type of HF syndrome				
Left Ventricular Failure	21 (30.9)	11 (39.7)	10 (25.6)	0.031
Right Ventricular Failure	8 (11.8)	0 (0)	8 (20.5)	
Bi-ventricular Failure	39 (57.4)	18 (62.1)	21 (53.8)	
LV Ejection Fraction < 40%	41 (60.3)	18 (62.1)	23 (59)	0.796
TAPSE < 17mm	47 (69.1)	18 (62.1)	29 (74.4)	0.278
PASP > 35 mmHg	49 (72.1)	23 (79.3)	26 (66.7)	0.250
Creatinine > 13 mg/L	33 (48.5)	19 (65.5)	14 (35.9)	0.016
Natriemia< 135 mmol/L	12 (17.6)	3 (10.3)	9 (23.1)	0.099

LV: Left Ventricle. TAPSE: LA: Left Atrium. RA: Right Atrium. HF: Heart Failure. Tricuspid Annular Plane Systolic Excursion. PASP: Pulmonary Artery Systolic Pressure.

In Bivariate analyses, serum creatinine > 13 mg/L associated with anemia in heart failure. After adjusting for sex, serum creatinine was still associated with anemia in HF (Table 3).

Table 3: Factors associated with anemia in patients with heart failure (bivariate analyses and adjusting for sex).

Variable	N (%)	Unadjusted		Adjusted	
		OR (95% CI)	*p*-value	aOR (95%CI)	*p*-value
Male sex					
Yes	16 (51.6)	1.97(0.7-5.2)	0.171	-	
No	13 (35.1)	1			
Diabetes					
Yes	6 (66.7)	3.1 (0.7-13.8)	0.156	2.5 (0.5-12)	0.442
No	23 (39)	1		1	
Chronic Kidney Disease					
Yes	4 (80)	6.1 (0.6-57.6)	0.156	5.5(0.5-68)	0.242
No	25 (39.7)	1		1	
Creatinine >13 mg/L					
Yes	19 (57.6)	3.4 (1.2-9.3)	0.016	3.1(1.1-8.9)	0.039
No	10 (28.6)	1		1	
Left Ventricular Hypertrophy					
Yes	22(45.8)	1.57(0.5-4.6)	0.411	-	
No	7(35)	1			
Left Atrial Dilation					
Yes	26(49.1)	3.9(1-15.2)	0.074	3.4 (0.8-13.7)	0.086
No	3(20)	1		1	
Left Heart failure					
Yes	29(100)	NA	0.017	NA	
No	0(0)				
NYHA Stage 4					
Yes	15(53.6)	2.1(0.8-5.7)	0.128	2.1 (0.7-6.5)	0.133
No	14(35)	1			

The mean (SD) duration of hospitalization was 8.7 (4.3) days and ranged from 3 to 21 days. Duration of hospitalization > 7 days was seen in 33 (48.5%, [95% CI: 36.2 – 70]) patients. Anemia in HF was not significantly associated with duration of hospitalization> 7 days (OR: 2.04, [0.8 – 5.4], p=0.151). A total of 7 (10.3%, [95% CI: 4.2 – 20.1]) in hospital deaths were recorded. All deaths (100%) occurred in patients without anemia (p=0.018).

DISCUSSION

The aim of this study was to determine the prevalence of anemia in patients hospitalized with acute decompensated heart failure, its correlates and its impact on outcomes. Our results show that 42.7% of patients had anemia. Elevated serum creatinine, left ventricular hypertrophy and left atrial enlargement were significantly associated

with anemia. Anemia was however not associated with poor outcome.

Anemia is a common co-morbidity in heart failure. The prevalence of anemia in our study was close to that reported by Nganou et al in an urban setting in Cameroon who had a prevalence of 49.5% (20). The prevalence of anemia in this study was also close to that reported in a large multinational pooled dataset of prospectively enrolled heart failure subjects, in which the prevalence of anemia was similar among those with HFrEF and HFpEF (42.8% vs. 41.6%) (21). It is however lower than that reported by some authors in Africa. In Nigeria, Akintunde et all reported a high prevalence of anemia of 75.7% among patients with heart failure recruited in cardiology clinics (22). The patients in their study were much older compared to the patients in the present study. The mean age in our study was 59.4 years compared to 67 years. This suggests that anemia becomes more frequent with increasing age. This may be because increasing age is a risk factor for conditions that can contribute to anemia, including kidney dysfunction, nutritional deficiency, recurrent infections, and progressive blood loss. Arora et al. in India also reported a higher prevalence of anemia in 76.7% of a cohort of 275 patients being followed up in a hospital-based study (23). Anemia is one of the most frequent co-morbidities associated with heart failure. In patients with HF, studies have reported a wide range of anemia prevalence of about 30% in stable patients and about 50% in hospitalized patients regardless of the ejection fraction (13-17). This wide range of anemia prevalence may be due may be the result of differences in anemia definition, patient demographic characteristics, co-morbidities, study type, and HF severity. Patients with concomitant chronic kidney disease (CKD) or diabetes mellitus, higher age, and more advanced disease are at the highest risk of anemia (24,25)

There was no significant age difference between patients with anemia and those without anemia contrary to Akintunde et al who reported a significant age difference, with patients with anemia being older (22). In our study, there was no significant difference in demographic characteristics and co-morbidity between patients with and without anemia. Other studies have shown that compared with non anemic patients with HF, anemic patients are older and more likely to be female and to have diabetes, chronic kidney disease (22, 16, 26).

In our study, there was no difference in clinical characteristics between patients with anemia and those without anemia. This is contrary to the findings of Akintunde et al who reported significantly higher heart rate, lower systolic and lower diastolic blood pressures among heart failure patients with anemia (22). Also, there was no difference in the severity of New York Heart Association functional classification in our study. Some studies have reported that the prevalence of anemia increases with severity of New York Heart Association functional classification (27, 28). Anemia worsens heart failure symptoms and is associated with poor quality of life (22). Regarding echocardiographic characteristics, heart failure patients with anemia in our study had higher proportions of left ventricular hypertrophy and left atrial dilation but there was no difference in left ventricular ejection fraction between the two groups. This contrasts from a previous study in Nigeria where heart failure patients with anemia had significantly lower left ventricular ejection fraction and higher proportion of pulmonary hypertension (22). Other studies have shown that the mean ejection fraction and fractional shortening were significantly lower among heart failure patients with anemia compared to those without anemia (29, 30). Anemia was significantly associated with creatinine in our study. Patients with anemia had a significant elevation in creatinine compared to patients without anemia. Impaired kidney function is one the major contributing factors to anemia in patients with heart failure (31). Patients with chronic kidney disease are at higher risk of anemia (25). In our study, patients with anemia had a higher proportion of chronic kidney disease although the difference was not statistically significant. In this study, there was no significant difference in in-hospital mortality and length of hospital stay between patients with and without anemia. However, several studies have also shown that anemia with the presence of heart failure was a predictor of poor outcome and greater hospital expenditure (28, 32-34).

Our study is limited by the small sample size. Also we did not investigate the etiologies of anemia in our study. Despite these limitations, our study is one of the few studies that have examined the association of anemia with heart failure in hospitalized heart failure patients in our setting and can serve as a preliminary study for larger studies.

CONCLUSION

Anemia was frequent in hospitalized patients with heart failure. Elevated serum creatinine, left ventricular hypertrophy and left atrial enlargement were significantly associated with anemia. Anemia was however not associated with poor outcomes.

DECLARATIONS

Ethical considerations: The study was approved by the institutional board review of the Buea Regional Hospital
Conflict of Interest: None to declare
Funding: None received for this study

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