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Epidemiological and Prognostic Aspects of Anemia during Heart Failure in Brazzaville (The Republic of the Congo)

Stéphane Méo Ikama[1]*, Joffode Mobet Memougame[1], Thibaut Oko[2], Jospin Makani[1], Lydie Ocini Ngolet[3], Bijou Moualengue[1], Eric Gibrel Kimbally Kaky[1], Thibaut Gankama[1], Suzy Gisèle Kimbally Kaky[1]

[1]Department of Cardiology, University Hospital Center of Brazzaville, Brazzaville, The Republic of the Congo
[2]Department of Hematology Laboratory, University Hospital Center of Brazzaville, Brazzaville, The Republic of the Congo
[3]Department of Clinical Hematology, University Hospital Center of Brazzaville, Brazzaville, The Republic of the Congo
Email: *stephane.mikama@gmail.com

Abstract

To improve the management of patients with heart failure and anemia at the University Hospital of Brazzaville, a cross-sectional study of patients diagnosed with heart failure condition (left or global heart failure) was conducted over a period of nine months from January 1 to September 30, 2017. A total of 171 patients were included during the study period. Study participants were divided into two groups: Group A included patients with an additional anemic condition (n = 57) and Group NA patients without anemia (n = 114). Anemia was defined as a hemoglobin rate of < 12 g/dL for men and <11 g/dL for women. All eligible patients admitted to the Department of Cardiology were included in the study. The frequency of anemia was 33.3%, with a mean hemoglobin level of 9.4 ± 1.5 g/dL. Men accounted for 46.9% of cases (n = 79) and women 53.8% (n = 92). The mean age of eligible patients was 57.5 ± 16.5 years. Of these, 46.2% (n = 75) had a secondary educational level and 53.8% (n = 92) had a low socioeconomic status. Heart failure was global in 153 cases (89.5%). Patients were on NYHA III-IV functional class in 112 cases (65.5%), with a statistically significant difference between anemic and non-anemic patients (p = 0.0001). The main underlying heart diseases were dilated cardiomyopathy (75.1%), hypertensive heart disease (10.5%), ischemic heart disease (6.5%), and valvular disease (4.7%). The comparison between the two groups (A and NA) showed a longer hospital length of stay (18.4 ± 8.9 versus 12.9 ± 7.6 days; p = 0.00001) and a higher mortality rate (4 versus 2 deaths). The re-hospitalization rate was more important in group A (n = 4) than in group NA (n = 1). Anemia is a common condition in patients with heart failure. It worsens the clinical features and prognosis.

1. Introduction

Heart failure (HF) is the ultimate clinical expression of most cardiovascular diseases. It is characterized by an inability of the heart to meet the metabolic needs of the body under normal pressure conditions. It is a real burden both clinically and socioeconomically [1]. It is often associated with co-morbidities that make the management difficult and contribute to a worse prognosis. Anemia is often associated with HF. Its prevalence varies from 4% to 61% depending on the population studied [2] [3] [4] [5] [6], but also according to the definition used [7]. In the Republic of the Congo, a preliminary study carried out in 2010 estimated the prevalence of anemia in patients with heart failure at 42% [2]. To contribute to improving the management of patients with heart failure at the University Hospital of Brazzaville, we carried out the current study whose objectives are to estimate the frequency of anemia during the course of heart failure, and evaluate its prognosis.

2. Patients and Methods

A cross-sectional and analytical study was conducted in the cardiology department of the University Hospital of Brazzaville from January 1 to September 30, 2017 (9 months). Were included all patients admitted for left or global heart failure. Heart failure (HF) was defined by clinical arguments (dyspnea associated with signs of right ventricular insufficiency in particular, jugular turgescence, hepatomegaly and oedemas of the lower limbs). The Hemoglobin (Hb) rate was measured with the SYSMEX SP-300 type machine for each patient included. Anemia was diagnosed when the cell blood count shows a hemoglobin value less than 12 g/dL in men and 11 g/dL in women. All patients meeting the following inclusion criteria were considered for the study: clinical signs of heart failure and morphological examine as well as chest radiography, electrocardiogram, and echocardiography. A total of 171 meeting the selection criteria were included. They were divided into two groups: anemic patients or group A (n = 57) and non-anemic patients or group NA (n = 114). Anemia was considered mild when the Hb level was between 11 and 8 g/dL for men and between 10 and 8 g/dL for women; moderate when the Hb level was between 8 and 6 g/dL; and severe when the Hb level was strictly below 6 g/dL.

All patients were requested to sign a consent form prior to answering questions that were part of a standard questionnaire. This questionnaire was used to collect data on all variables of interest for the study. These included anemic and non-anemic data, socio-demographic data, history of heart failure, clinical and paraclinical data, treatments and outcome data.

The variables studied were socio-demographic (frequency, age, sex, socioeconomic level, educational level), clinical (associated comorbidities, nature and type of HF, underlying heart disease), and paraclinical (radiographic, electrocardiographic, echocardiographic, and biological data), as well as evolutionary modalities. Statistical analysis was performed with Epi-info software version 7.1.5.2; Pearson's Chi 2 and ANOVA tests allowed comparison of the variables. The significance threshold was set at $p < 0.05$.

3. Results

3.1. Epidemiological and Socio-Demographic Aspects of the Patients

One hundred seventy one (171) patients with heart failure condition were included in the study. Among them, 57 had anemia (33.3%); 20 were men (35.1%) and 37 women (64.9%). The mean age was 59 ± 17 years (range: 22 - 90 years). The main characteristics of the study population are presented in Table 1.

3.2. Clinical Aspects

Hypertension was the most frequent (71.9%) for anemic patients versus 69.3% for non-anemic patients ($p = 0.72$), followed by diabetes mellitus (28.1% vs. 15.8%; $p = 0.06$), and renal failure (19.3% vs. 1.8%; $p = 0.00001$). Heart failure (HF) was de novo in 79 patients (46.2%), and old in 92 patients (53.8%) with no statistically significant difference between the two groups ($p = 0.34$). Dyspnea was graded per the NYHA class III and IV in 112 participants (65.5%), with a significant difference between anemic and non-anemic patients ($p = 0.0001$). Heart failure was global in 153 patients (89.5%), and left in 18 patients (10.5%), with no statistically significant difference between the two groups ($p = 0.113$).

Table 1. Patient characteristics.

	Patients (N = 171)
Female gender, n (%)	92 (53.8)
Age (years), SD (range)	58 ± 16.5 (22 - 90)
Secondary educational level, n (%)	75 (44)
Low socio-economic level, n (%)	92 (53.8)
Biventricular HF, (%)	153 (89.4)
NYHA class III-IV, n (%)	112 (65.5)
Atrial fibrillation, n (%)	18 (10.5)
Aspirin, n (%)	16 (6.4)*
Oral anticoagulation, n (%)	17 (10)**
LVEF (%), SD (range)	48.7 ± 15.4 (23 - 80)
Hospitalization stay (days), SD	15.6 ± 8.2 (3 - 44)
Re-hospitalization rate, n (%)	5 (3)
Mortality rate, n (%)	6 (3.5)

*(A: 5; NA: 11; $p = 0.983$), **(A: 4; NA: 13; $p = 0.328$); A: anemic patients; HF: heart failure; LVEF: left ventricular ejection fraction; NA: non-anemic patients; NYHA: New York Heart Association.

3.3. Paraclinical Aspects

Cardiomegaly was diagnosed in 166 patients (97.1%), with no difference between the two groups (p = 0.212). The electrocardiogram showed a sinus rhythm in 147 cases (86%), and atrial fibrillation in 18 patients (10.5%). The left ventricle was dilated in 113 cases (66.1%), with respectively a mean left ventricular end-diastolic diameter (LVEDD) of 57.2 ± 13.9 vs. 69.9 ± 37.9 mm (p = 0.002) in anemic and non-anemic groups. The mean left ventricular ejection fraction (LVEF) was 35.5% ± 16.9% in anemic patients and 34.1 ± 11% in non-anemic patients (p = 0.534). The LVEF was normal in 16 patients (9.4%) and reduced in 155 patients (90.6%). The mean hemoglobin rate was 9.4 ± 1.5 g/dL (range: 4.3 - 11.6 g/dL). The anemia was mild in 32 cases (56.1%), moderate in 22 cases (38.6%) and severe in three cases (5.3%). Anemia was microcytic hypochromic in 30 cases (52.6%), normocytic normochromic in 20 (35.1%), and normochromic macrocytic in one case (1.8%). The mean hematocrit level was 30.3 ± 5.3%; 47 patients (82.5%) had regenerative anemia, and ten (17.5%) had a non regenerative one. Sedimentation rate (SR) and/or C-reactive protein (CRP), was noted in anemic patients compared with non-anemic patients: 40.4 ± 33 versus 20.7 ± 33.3 mg/L (p = 0.00001), and 40 ± 36 versus 26 ± 9 mm (p = 0.0007), respectively for CRP and SR. Ferritin levels were normal or high in 57 patients (100% of men and 97.3% of women). It was low in 2.7% of women. The main underlying heart diseases found in both anemic and non-anemic patients were dilated cardiomyopathy (61.8% versus 81.6%), hypertensive heart disease (23.6% versus 3.5%), ischemic heart disease (3.6% versus 7.9%), and valvular disease (5.5% versus 4.4%). Table 2 shows additional clinical and paraclinical aspects of studied patients.

3.4. Treatment of Heart Failure and Anemia

Only 33 of 57 anemic patients and 68 of 114 non-anemic patients were treated for heart failure. The most commonly used therapeutic classes were diuretics (95% versus 97.1%; p = 0.98) and angiotensin converting enzyme inhibitor

Table 2. Clinical and paraclinical aspects.

	A (n = 57)	NA (n = 114)	p
Hypertension, n (%)	41 (71.9)	79 (69.3)	0.72
Diabetes, n (%)	16 (28.1)	18 (15.8)	0.06
Renal insufficiency, n (%)	11 (19.3)	2 (1.8)	**0.0001**
NYHA class III, n (%)	21 (36.8)	43 (37.7)	0.91
NYHA class IV, n (%)	35 (61.4)	13 (11.4)	0.0001
Atrial fibrillation, n (%)	5 (8.8)	13 (11.5)	0.58
Hypertensive heart disease, n (%)	13 (23.6)	4 (3.5)	**0.001**
Dilated cardiomyopathy, n (%)	34 (61.8)	81.6 (93)	
Ischemic heart disease, n (%)	2 (3.6)	9 (7.9)	

A: anemic patients; NA: non-anemic patients; NYHA: New York Heart Association.

(ACEI) or angiotensin II receptor blocker (ARB) [93.9% versus 97.1%; p = 0.45]. Thirteen patients (22.8%) received martial therapy and ten (17.5%) received blood transfusions.

3.5. Course and Prognosis

The average length of hospital stay was 15.6 ± 8.2 days. It was longer in anemic patients compared to non-anemic patients (18.4 ± 8.9 days versus 12.9 ± 7.6 days; p = 0.00001). The re-hospitalization rate at day 15 was 2.9%, including four anemic patients and one non-anemic. The case fatality rate was 3.5%, including four (04) anemic patients and two (02) non-anemic patients. Furthermore, a strong correlation was noted between anemia, renal function and NYHA functional class (stages III and IV) as illustrated in Table 3.

4. Discussion

The prevalence of anemia was 33% in our study. This prevalence is similar to that found by Groenveld in the United States [4], 37.2%. It is lower than those reported in previous series by Ikama in the Republic of the Congo [2], Abassade in France [3] and Makubi in Tanzania [5], 42%, 49% and 57%, respectively. According to the literature, the prevalence of anemia in heart failure varies between 4% and 61% in most published studies [2] [3] [4] [5]. These large variations can be explained, on the one hand, by differences in the heart failure populations studied, and on the other hand, by methodological differences in the thresholds for defining anemia. This threshold is defined either on the basis of hemoglobin level, as in most studies [6] [7] [8] [9], or on the basis of hematocrit level, as reported by some authors [10] [11] [12]. Indeed, if we take into account the

Table 3. Prognostic factors.

	A (n = 57)	NA (n = 114)	p
Age (years)	59.2 ± 17.2	56.2 ± 15.5	0.245
Haemoglobin rate (g/dL)	9.4 ± 1.5	13.4 ± 1.4	**0.00001**
GFR (ml/min)	68.6 ± 44.2	76.0 ± 50.0	0.494
Sodium (mEq/l)	136 ± 10.2	136.1 ± 13.1	0.909
Heart rate (bpm)	114.1 ± 74.9	104.2 ± 75.7	0.482
NYHA class III-IV, n (%)	56 (98.2)	56 (49.1)	**0.00001**
LVEF (%)	35.5 ± 16.9	34.1 ± 11.0	0.534
LVEDD (mm)	57.2 ± 14.0	70.0 ± 37.9	0.002
Hospitalization stay (days)	18.4 ± 8.9	12.9 ± 7.6	**0.00001**
Rehospitalization rate, n (%)	4 (7.0)	1 (0.9)	**0.001**
Mortality rate, n (%)	4 (7.0)	2 (1.8)	**0.003**

A: anemic patients; GFR: glomerular filtration rate; LVEF: left ventricular ejection fraction; LVTDD: left ventricular end diastolic diameter; NA: non-anemic patients; NYHA: New York Heart Association.

World Health Organization definition of anemia as a hemoglobin level < 13 g/dL in men and <12 g/dL in women [13], this prevalence was underestimated. As for age and sex, no influence clearly appears in our series, with both sexes affected, with no significant difference in age between anemic and non-anemic patients, all of whom were relatively younger in our series. However, some data in the literature have reported a higher prevalence of anemia in heart failure patients aged 70 years or older, between 55.6% and 46.8% respectively [6] [11]. This is certainly a simple coincidence, heart failure being rather commonly observed in elderly subjects, especially in the West. Our study showed an increase in the prevalence of anemia with the severity of heart failure symptoms. Almost all anemic patients in our series were in NYHA class III-IV, reflecting the severity of the heart failure. Similar results were also found by other authors [6] [8] [14] [15], who highlighted the direct correlation between the degree of anemia and the severity of heart failure, as evidenced by the functional class. This association may stipulate either an increase in the prevalence of anemia with the severity of heart failure, or a worsening of heart failure symptoms when there is associated anemia.

Furthermore, due to the age of patients with heart failure, comorbidities are often associated and various treatments used (acetyl salicylic acid, anti-vitamin K, angiotensin converting enzyme inhibitor). In our series, hypertension, diabetes, and renal failure were the main comorbidities, with a preponderance of the latter in anemic patients. The use of acetyl salicylic acid and anti-vitamin K, which are both more likely to cause bleeding and therefore to favor the occurrence of anemia, is not widespread in our study population. It was found in less than 10% of the patients in the study.

Anemia is a poor prognostic factor in patients with heart failure. In a large Canadian cohort of heart failure patients, Ezekowitz *et al.* [16] showed that one-year survival was worse in anemic patients compared to non-anemic patients (62% versus 73% respectively).

This finding was also noted by Anand *et al.* [14], in the large RENAISSANCE study of heart failure patients with severe systolic dysfunction (LVEF < 30%) and NYHA class III-IV, where it was found that patient survival was proportional to the baseline hemoglobin level of the patients, thus to the degree of severity of the anemia. In our study, because of the short follow-up time, the prognosis was analyzed in terms of length of hospital stay (longer in anemic patients), the re-hospitalization rate (more important in anemic patients), and number of deaths. A large number of studies have confirmed that anemia is a strong and independent predictor of increased mortality and hospital stay in heart failure patients with anemia [14] [17] [18]. These data make anemia a poor prognostic factor in heart failure patients, highlighting its pejorative role.

5. Conclusion

This study shows that anemia is a frequent comorbidity in heart failure patients. Also, the presence of anemia is a marker of the severity of heart failure, and a

factor of poor prognosis in terms of longer hospitalization, the re-hospitalization rate and higher mortality. It is therefore necessary to systematically screen patients with decompensated or uncompensated heart failure and to have a multidisciplinary collaboration involving cardiologists, hematologists and biologists to improve the management of patients with heart failure and anemia.

Study Limitations

The selection of heart failure and anemic patients was done only in the cardiology department of Brazzaville university center hospital. This led to the exclusion of patients with similar characteristics administer in other departments such as the Hematology Department resulting more likely in possible under or overestimation of the frequency of anemia in patients with heart failure. The small proportion of heart failure and anemic patients included, 57 on the 100 initially planned for better statistical power, can also influence the external validity of the study.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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