

Aetiologic Factors of Anemia During Heart Failure in Brazzaville (The Republic of the Congo)

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Abstract

To contribute to improving the management of patients with heart failure and anemia in Brazzaville, a prospective and descriptive study was conducted in the University Hospital of Brazzaville for nine months (January 1st to September 30, 2017). Included 57 patients hospitalized for left or global heart failure and presenting anemia. Anemia was defined by an haemoglobin level < 12 g/dL in men and < 11 g/dL in women. Proportionings of the reticulocytes rate, serum iron, ferritin, erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP), electrophoresis of proteins, and evaluation of renal function by glomerular filtration rate (GFR), as well as the treatments of heart failure, and the auxiliary therapeutic ones, in particular the antithrombotic drugs, allowed aetiologic research. They were 20 men (35%) and 37 women (65%), old on average of 59 ± 17 years. The average rate of haemoglobin was 11.4 ± 1.4 g/dL. Heart failure was de novo in 24 cases (42.1%), old in 33 cases (57.9%); it was global in 54 cases (94.7%). The maintenance treatment associated diuretics in 32 cases (97%), angiotensin-converting enzyme inhibitor (ACEI) or angiotensin II receptor blocker (ARB) in 31 cases (94%), beta-blockers in two cases (6.1%), digoxin in four cases (12.1%), aspirin in five cases (15.1%) and anti-vitamin K in four cases (12.1%). Anemia was microcytic hypochromic in 30 cases (52.6%), normocytic normochromic in 20 cases (35.1%), and macrocytic normochromic in one case (1.7%). The main aetiologic factors were hemodilution in 46 cases (80.7%), renal insufficiency in 30 cases (52.3%), inflammation in 29 cases (50.8%), and iron deficiency in one case (1.7%). The HIV serology, carried out in 11 cases, was negative. Anemia

is a frequent comorbidity among heart failure patients. Aetiologic research remains difficult in our context, and its often multifactorial origin.

Keywords

Anemia, Heart Failure, Aetiologies, Congo

1. Introduction

Heart failure (HF) is the result of most cardiovascular diseases and is a significant burden on clinical and socioeconomic levels [1]. Heart failure is often accompanied by other health issues, such as anemia, which complicates management and worsens patient prognosis. In Congo Brazzaville, previous studies on anemia during HF did not focus on the underlying causes [2]. This study aims to improve the management of heart failure patients in Brazzaville, whose objective is to explore the aetiologic factors of anemia in this particular population.

2. Patients and Methods

A prospective study was conducted in the cardiology department of Brazzaville University Hospital from January 1 to September 30, 2017. On the 100 initially planned for better statistical power, the study included only 57 patients according to the selection criteria (patients who were hospitalized because of left or global heart failure and had anemia). The patients who met the screening criteria received blood testing for further evaluation to determine the aetiology of anemia. Heart failure was diagnosed through clinical signs and symptoms such as dyspnea, right ventricular insufficiency, jugular turgescence, hepatomegaly, and oedema in lower limbs. A hemogram was taken using an EDTA tube and the SYSMEX Sp-300 type machine was used for blood numeration. A rate of haemoglobin (Hb) < 12 g/dL in men and <11 g/dL in women made it possible to retain the diagnosis of anemia. Anemia was classified according to the patient's haemoglobin level as 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), or severe (when the Hb level was strictly below 6 g/dL). Variables studied included sociodemographic data ((frequency, age, sex, socio-economic level, educational level), clinical data such as cardiovascular risk factors, type of HF, and paraclinical data such as haemoglobin rate, reticulocytes rate, serum iron, ferritin, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), electrophoresis serum proteins, serum creatinin and glomerular filtration rate (GFR), and therapeutic data such as HF drugs and additives. To determine the cause of microcytic hypochromic anemia, it is recommended to check for an inflammatory process (by testing ESR and/or CRP levels and fibrinogen, as well as conducting protein electrophoresis). If there is no indication of an inflammatory syndrome, it is important to examine iron metabolism by mea-

suring serum iron and ferritin levels. For normocytic normochromic anemia, it is necessary to measure the reticulocyte count to distinguish between anemia caused by hemodilution (when the reticulocyte count is increased, typically over 120,000/mm³, due to edema that can be resolved with diuretic therapy) and anemia caused by renal insufficiency (when the reticulocyte count is decreased, typically below 80,000/mm³, due to deterioration of renal function with a glomerular filtration rate lower than 60 mL per minute, calculated using the Cockcroft and Gault equation).

Statistical analysis was conducted using Epi-info software version 7.1.5.2. Qualitative data were expressed as percentages, while quantitative data were presented as the mean \pm standard deviation.

3. Results

3.1. Socio-Demographic Aspects

The group of patients consisted of 20 men (35%) and 37 women (65%), resulting in a sex ratio of 0.5. Their average age was 59 ± 17 years, with the age range being from 22 to 90 years. **Table 1** presents the main characteristics of the patients.

Table 1. Patients characteristics.

	Patients (N = 57)
Women, n (%)	37 (65)
Age (years)	59 ± 17 (22 - 90)
Secondary educational level, n (%)	22 (38.6)
Low socioeconomic level, n (%)	31 (54.4)
Hypertension, n (%)	41 (72)
Diabetes mellitus, n (%)	16 (28.1)
Renal insufficiency, n (%)	11 (19.3)
Global heart failure, n (%)	54 (94.7)
NYHA class III-IV, n (%)	56 (98.2)
Atrial fibrillation, n (%)	5 (8.8)
Aspirin, n (%)	5 (15.1)*
Anti-vitamin K, n (%)	4 (12.1)*
ACEI/ARB, n (%)	31 (94)*
LVEF, (%)	35.5 ± 16.9 (23 - 80)
Hospitalization stay (days)	18.4 ± 8.9 (3 - 44)
Rehospitalization rate, n (%)	4 (7)
In hospital mortality rate, n (%)	4 (7)

*Maintenance treatment in 33 patients with chronic heart failure; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin II receptor blocker; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association.

3.2. Heart Failure Characteristics

Regarding heart failure characteristics, it was newly diagnosed in 24 cases (42.1%) and pre-existing in 33 cases (57.9%). Of the patients, 3 (5.3%) had left-sided heart failure, while 54 (94.7%) had global heart failure. Dyspnea was classified per NYHA class II, III, and IV among 1 patient (1.8%), 21 patients (36.8%), and 35 patients (61.4%), respectively. Diuretics were used as maintenance treatment in 32 cases (97%), along with an angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker (ARB) in 31 cases (94%), beta-blocker in two cases (6.1%), digoxin in four cases (12.1%), aspirin in five cases (15.1%) and anti-vitamin K in four cases (12.1%).

3.3. Anemia Characteristics

The average haemoglobin level was 9.4 ± 1.5 g/dL, ranging from 4.3 to 11.6 g/dL. Anemia severity was categorized as mild in 32 cases (56.1%), moderate in 22 cases (38.6%), and severe in three cases (5.3%). Of the cases, 30 (52.6%) were microcytic hypochromic, 20 (35.1%) were normocytic normochromic, and one (1.8%) was macrocytic normochromic. The average hematocrit level was $30.3 \pm 5.3\%$. Regenerative anemia was observed in 47 patients (82.5%) while non-regenerative anemia was observed in 10 patients (17.5%). Ferritin levels were normal or high in 56 patients (98.2%), including 100% of men and 97.3% of women. Low ferritin levels were observed in only 2.7% of women, and low serum iron levels were observed in 2.7% of women. The average erythrocyte sedimentation rate (ESR) was 40 ± 36 mm, and it was high in 20 patients (35.1%). In addition, C-reactive protein (CRP) had an average rate of 40.4 ± 33 mg/L and was high in 29 patients (50.8%). The inflammation was indicated in 56 patients who underwent electrophoresis serum protein testing. The interpretation of the patients' electrophoresis profile is shown in **Figure 1**. The average glomerular filtration rate was 68.6 ± 74.2 mL/min and was lower in 30 patients (52.3%).

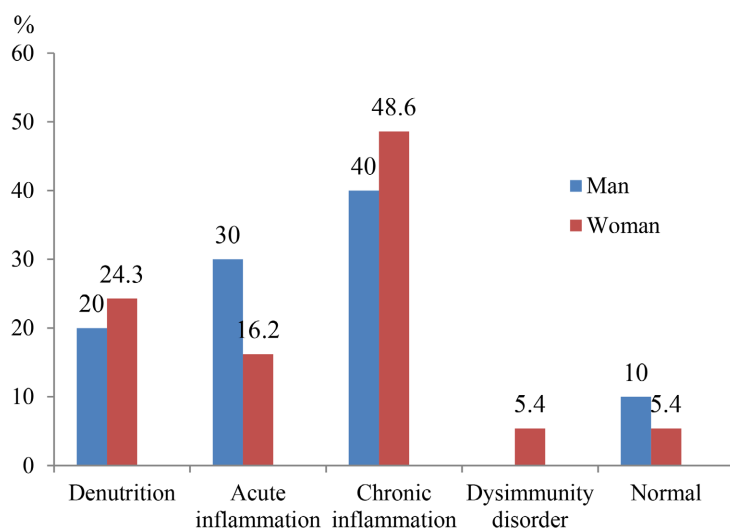


Figure 1. Patients electrophoresis profile according gender.

3.4. Underlying Heart Diseases and Aetiologic Factors of Anemia

Underlying heart diseases found in anemic patients were dilated cardiomyopathy in 34 patients (61.8%), hypertensive heart disease in 13 patients (23.6%), valvular disease in three patients (4.4%), and ischemic heart disease in two patients (3.6%). The most common aetiologic factors of anemia were hemodilution in 46 cases (80.7%), renal insufficiency in 30 cases (52.3%), inflammation in 28 cases (50%), and iron deficiency in one case (1.7%) (Figure 2). The HIV serology test performed in 11 patients was negative.

4. Discussion

When a person has anemia, it is important to investigate possible causes or factors involved in its occurrence, in particular of the heart failure condition. Our study found that as markers of inflammation increased, the level of hemoglobin decreased. This relationship has been reported by other studies, such as those conducted by Bolger and Abromeit [3] [4]. However, some studies, like the one by Abassad *et al.* [5], have found differing results. Despite these discrepancies, all authors agree that there are multiple factors contributing to anemia in heart failure patients, including hemodilution, inflammation, iron deficiency, renal insufficiency, and medication toxicity [6] [7] [8] [9].

Our study found that nearly 90% of anemic patients had hemodilution, which is higher than the 46% reported by Androne in the United States [10]. This could be due to the fact that in decompensated heart failure patients, it is important to wait for congestion signs to disappear before diagnosing anemia. The interpretation of hematocrit is also more sensitive to hemodilution than the rate of hemoglobin. In our study, patients were often in congestive heart failure, which was not the case in the study by Androne [10]. Additionally, the sample size of our study was larger, with 57 patients compared to 37 in Androne's study [10].

Out of our sample of 57 patients, only one had iron deficiency (1.7%). This

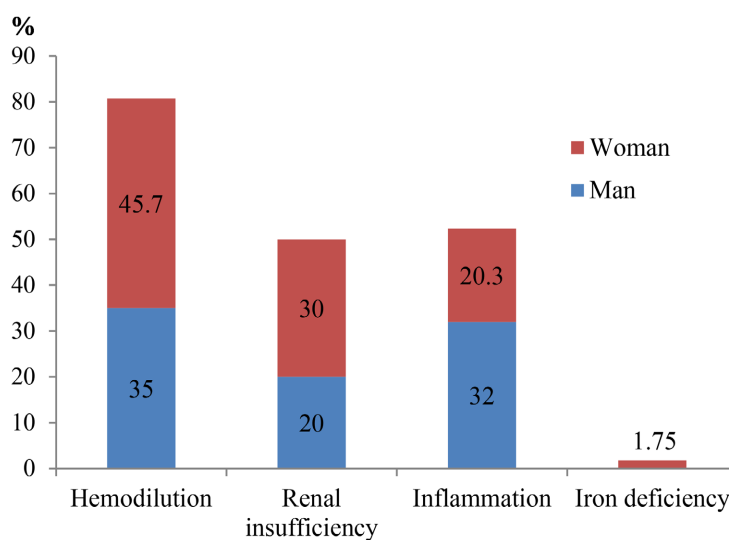


Figure 2. Main aetiologic factors according gender.

percentage is much lower than what was found in previous studies by Cromie [9], Wittle [11], and Ezekowitz [12], located between 14% and 21%. The small size of our sample ($n = 57$), compared with the great series of Ezekowitz ($n = 2051$), can be the explanation for it. The prevalence of renal insufficiency in our patients was 52.3%, which may be due to their advanced age and comorbidities, such as hypertension and diabetes mellitus, that are often associated with renal disease. We observed signs of inflammation in 50% of our patients through measurements of ESR, CRP, and protein electrophoresis. Some studies suggest that inflammation can be a cause of anemia, but we were unable to test for specific markers such as IL6 and TNF α [13] [14] [15] due to technical limitations. Additionally, we were unable to determine the prevalence of HIV infection in our study population, as HIV serology was only performed on a small percentage of patients with dilated cardiomyopathy; HIV serology which should have been performed systematically in this population of heart failure patients with like dominant a dilated cardiomyopathy. Aside from the underlying causes and related conditions, certain medications can also contribute to the development or worsening of anemia in patients with heart failure. Among these medications are angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin II receptor blockers (ARBs), as well as anti-thrombotic drugs like acetylsalicylic acid. Studies show that ACEIs can decrease the production of erythropoietin (EPO) by the kidney [16], and when used in high doses, they can worsen anemia by inhibiting angiotensin II, red blood cell precursors, and the use of EPO by the bone marrow [13] [17]. Our own study found that almost all heart failure and anemic patients had been treated with ACEI/ARB for several years, with more than half of them suffering from chronic heart failure. As for acetylsalicylic acid, although it was only slightly used among our patients, it is known to harm the gastric mucous membrane and cause occult bleeding, which can lead to anemia.

5. Conclusion

The combination of heart failure and anemia is a clinical situation that merits further investigation. If the positive diagnosis of anemia in heart failure is an easy rule, the more difficult the etiological search remains. Anemia during heart failure is often of multifactorial origin, caused by hemodilution, inflammation, renal insufficiency, iron deficiency, and medication toxicity. Identifying the specific factors at play can lead to better correction of anemia and improve outcomes for heart failure patients.

6. Study Limitations

Possible limitations of this study include the lack of some basic and useful diagnostic tests for investigating the underlying causes of anemia, such as direct examination of stool samples for intestinal parasites which are common in our region. Additionally, more specialized tests like measuring chronic inflammation markers (such as IL6 and TNF-alpha), bone marrow examination (myelogram),

and HIV screening could have helped to better understand the etiology of anemia in heart failure patients.

Conflicts of Interest

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

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