Scientific Research Publishing

Open Journal of Gastroenterology, 2021, 11, 194-202
https://www.scirp.org/journal/ojgas
ISSN Online: 2163-9469
ISSN Print: 2163-9450

Hematological Profile of Anemia in Hospitalized Cirrhotics in the Hepato-Gastroenterology Unit of the University Hospital Campus of Lome (Togo)

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How to cite this paper: Lawson-Ananissoh, L.M., Kogoe, L.R.-M., Redah, V.D., Bouglouga, O., El-Hadji Yakoubou, R., Kaaga, L. and Bagny, A. (2021) Hematological Profile of Anemia in Hospitalized Cirrhotics in the Hepato-Gastroenterology Unit of the University Hospital Campus of Lome (Togo). *Open Journal of Gastroenterology*, **11**, 194-202.
https://doi.org/10.4236/ojgas.2021.1110020

Received: September 5, 2021
Accepted: October 25, 2021
Published: October 28, 2021

Abstract

Background: Anemia is multifactorial and very frequently observed in the evolution of cirrhosis. Only biological investigations can clarify its mechanisms. **Objective:** To determine the frequency of anemia in cirrhosis patients and to identify the different types of anemia encountered. **Patients and Methods:** Descriptive and analytical study based on the retrospective collection of data was carried out over 12 months in the hepato-gastroenterology unit of the University Hospital Campus of Lome (Togo). This study included hospitalized cirrhotic patients with a complete medical file including a blood count and presenting anemia. **Results:** During the study period, we collected 253 cases of cirrhosis, of which 153 patients had anemia (60.5%); there was a male predominance of 73.2%. The mean age was 51 ± 13 years. The B viral origin of cirrhosis was the most common (60.1%). Oedemato-ascitic decompensation (82.4%) and hepatocellular carcinoma (34%) were the main complications. The Child-Pugh B score was the most represented (74.5%). Hypochromic microcytic anemia was noted (48.4%) followed by normochromic normocytic anemia (46.4%); 82 patients (53.6%) had thrombocytopenia; pancytopenia was noted in 17 patients (11.1%). Hepatitis B virus was most commonly found with 50% hypochromic microcytic anemia followed by 46.7% normochromic normocytic anemia ($p = 0.311$). Hepatic encephalopathy was significantly more frequent in patients with hypochromic microcytic anemia (45.5%) ($p = 0.025$); hepatocellular carcinoma was significantly noted with 63.5% hypochromic microcytic anemia ($p = 0.016$). Child-Pugh C score with 47.4% hypochromic microcytic anemia was more frequent ($p = 0.673$). **Conclusion:** Hy-

pochromic microcytic anemia was the most common type of anemia noted in our study. Hepatic encephalopathy and hepatocellular carcinoma were the major complications of cirrhosis significantly associated with the hypochromic microcytic anemia.

Keywords

Anemia, Blood Count, Cirrhosis, Hepatitis B Virus, Togo

1. Introduction

Anemia is very frequently observed in the evolution of cirrhosis [1] [2] [3] [4] and only biological investigations can clarify its mechanisms. Anemia in cirrhosis is multifactorial: hypersplenism, hemodilution, hemolysis, vitamin B12 and folic acid deficiency [2]. In Togo, several studies have been conducted on cirrhosis and its complications [5] [6] [7] [8] but none has really focused on anemia in cirrhotics. Among these various studies, the one conducted on transfusion practices in the hepato-gastroenterology department of the Campus University Hospital had identified cirrhosis and hepatocellular carcinoma as the first pathologies associated with blood transfusion and therefore associated with anemia [8]. The aim of this study was to determine the frequency of anemia in cirrhosis patients and to identify the different types of anemia encountered.

2. Patients and Method

It was a descriptive and analytical study based on the retrospective collection of data carried out over 12 months in the hepato-gastroenterology unit of the University Hospital Campus of Lome (Togo). The study population consisted of all patients hospitalized for cirrhosis and its complications. This study included hospitalized cirrhotic patients with a complete medical file including a blood count and presenting anemia. Patients with other causes of anemia were not included: chronic renal failure, heart failure, major sickle cell disease, malignant hemopathy.

2.1. Operational Definition

The diagnosis of cirrhosis was made on the basis of:

- Clinical arguments including ascites and edema; morphological changes in liver, portal hypertension and hepatocellular insufficiency;
- Biological arguments with hepatocellular insufficiency (in particular prothrombin rate less than 60%, albuminemia less than 35 g/liter, beta-gamma block in the protidogram);
- And/or echographic and possibly endoscopic arguments.

Anemia was defined when the hemoglobin rate value was below 12 g/dl. We were able to characterize anemia using erythrocyte constants:

- A hypochromic microcytic anemia for a Mean Corpuscular Volume (MCV) value < 80 femtoliters and the Mean Corpuscular Hemoglobin Content (MCHC) < to 27 picograms;
- A macrocytic anemia for a MCV value greater than 100 femtoliters;
- A normochromic normocytic anemia for a MCV value between 80 and 100 femtoliters and MCHC between 27 and 31 picograms.

2.2. Statistical Analysis

Descriptive statistics were performed and the results were presented in the form of effective and proportion tables for the categorical variables. Quantitative variables were presented as means with their standard deviation and extreme values. Qualitative variables were compared using the chi-square and/or Fisher test. Analyzes were carried out using R version 3.3.2 software. The significance level was set at 5%.

3. Results

3.1. Epidemiological Data

During the study period, we collected 253 cases of cirrhosis, of which 153 patients had anemia (60.5%); there was a male predominance (73.2%) with an M/F sex ratio of 2.64. The mean age was 51 ± 13 years with extremes of 20 to 99 years. The B viral origin of cirrhosis was the most common (60.1%) (Table 1).

3.2. Complications and Prognosis of Cirrhosis

The main complication was oedemato-ascitic decompensation (82.4%) followed by hepatocellular carcinoma (34%). The Child-Pugh B score was the most represented (74.5%). Complication data, Child-Pugh score are noted in Table 1. Of the 33 patients with hepatic encephalopathy, 15 (45.5%) had hepatocellular carcinoma.

3.3. Hematological Data

Hypochromic microcytic anemia was noted (48.4%) followed by normochromic normocytic anemia (46.4%) as shown in Table 1. The mean values of the various parameters of the complete blood count are noted in Table 2; 82 patients (53.6%) had thrombocytopenia; 12 patients (7.8%) had neutropenia; pancytopenia was noted in 17 patients (11.1%).

3.4. Types of Anemia and Epidemiological Data

Macrocytic anemia has been noted in men than in women (p = 0.486) and normochromic normocytic anemia has been noted in patients over 50 years of age (p = 0.664) as shown in Table 3. Hepatitis B virus was most commonly found with 50% hypochromic microcytic anemia followed by 46.7% normochromic normocytic anemia (p = 0.311) as shown in Table 3. The ethylic cause was noted in 50% of patients with macrocytic anemia (p = 0.311).

Table 1. Etiologies, complications, Child-Pugh score and types of anemia.

	n	%
Etiologies		
Hepatitis B Virus	92	60.1
Hepatitis C Virus	16	10.5
Alcohol	45	29.4
Complications		
Oedemato-ascitic decompensation	126	82.4
Jaundice	67	43.8
Hepatocellular carcinoma	52	34.0
Hepatic encephalopathy	33	21.6
Splenomegaly	32	20.9
Esophageal varices	29	19.0
Gastrointestinal bleedings	4	2.6
Ascites fluid infection	4	2.6
Acute renal failure	3	2.0
Child-Pugh score		
A	1	0.7
B	114	74.6
C	38	24.8
Types of anemia		
Hypochromic microcytic anemia	74	48.4
Normochromic normocytic anemia	71	46.4
Macrocytic anemia	8	5.2

Table 2. Different parameters of the blood count.

Parameters	Mean value	Standard deviation	Extreme values
Hematocrit (%)	30	7	9 - 52
Hemoglobin (g/dl)	9	2	4 - 11
Mean corpuscular volume (fl)	83	11	29 - 129
Mean corpuscular hemoglobin content (pg)	28	4	18 - 39
White cells (/mm^3)	9509	5716	1000 - 31,000
Polynuclear neutrophils (/mm^3)	6474	4725	720 - 24,000
Lymphocytes (/mm^3)	1899	1152	210 - 7500
Platelets (/mm^3)	174,065	105,615	5820 - 516,000

3.5. Types of Anemia and Complications of Cirrhosis

Hepatic encephalopathy was significantly more frequent in patients with hypochromic microcytic anemia (45.5%) ($p = 0.025$); hepatocellular carcinoma was significantly noted with 63.5% hypochromic microcytic anemia ($p = 0.016$) as shown in Table 3.

Table 3. Different types of anemia according to etiologies, complications and Child-Pugh score.

	Normochromic normocytic anemia	Hypochromic microcytic anemia	Macrocytic anemia	Total	p
	N = 71 (%)	N = 74 (%)	N = 8 (%)	N = 153 (%)	
Sex					0.486
Male	49 (43.8)	56 (50.0)	7 (6.2)	112 (100.0)	
Female	22 (53.7)	18 (43.9)	1 (2.4)	41 (100.0)	
Age (years)					0.664
Less than 50	31 (42.5)	38 (52.1)	4 (5.5)	73 (100.0)	
50 and more	40 (50.0)	36 (45.0)	4 (5.0)	80 (100.0)	
Gastrointestinal bleedings	0 (0.0)	4 (100.0)	0 (0.0)	4 (100.0)	0.155
Acute renal failure	0 (0.0)	2 (66.7)	1 (33.3)	3 (100.0)	0.078
Hepatic encephalopathy	13 (39.4)	15 (45.5)	5 (15.2)	33 (100.0)	0.025
Ascites fluid infection	1 (25.0)	3 (75.0)	0 (0.0)	4 (100.0)	0.694
Hepatocellular carcinoma	16 (30.8)	33 (63.5)	3 (5.8)	52 (100.0)	0.016
Esophageal varices	15 (51.7)	14 (48.3)	0 (0.0)	29 (100.0)	0.482
Splenomegaly	13 (40.6)	18 (56.2)	1 (3.1)	32 (100.0)	0.630
Jaundice	32 (47.8)	30 (44.8)	5 (7.5)	67 (100.0)	0.452
Child-Pugh score					0.673
A and B	54 (47.0)	56 (48.7)	5 (4.3)	115 (100.0)	
C	17 (44.7)	18 (47.4)	3 (7.9)	38 (100.0)	

3.6. Types of Anemia and Child-Pugh Score

Child-Pugh C score with 47.4% hypochromic microcytic anemia was more frequent (p = 0.673).

4. Discussion

Some data on the causes and identification of the type of anemia are not found in the medical records: dosage of vitamins B12 and B9, reticulocytes count, iron metabolism and data on hemolytic anemia. Our study, like that of Nacoulma *et al.* in Burkina Faso [3], included only hospitalized cirrhotic patients, unlike the studies by Denie *et al.* in France [2] and Sack et al in Cameroon [4]. Anemia is frequently noted in cirrhotic patients but at a lower rate than that of Nacoulma *et al.* [3] (74.5%) and Sack *et al.* [4] (96.9%) but at a higher rate than that of Denie *et al.* [2] (54%); the Sack *et al.* [4] study was a comparative case-control study. For Sack *et al.* [4], cirrhosis is an exposure factor for anemia and people suffering from cirrhosis and/or hepatocellular carcinoma are 94 times more likely to develop anemia than controls (Odds ratio = 94, 1) in their study. In addition, gender and age have no influence on the different types of anemia noted in our study.

4.1. Hypochromic Microcytic Anemia

No case of hypochromic microcytic anemia in our study performed workup to

evaluate iron metabolism for iron deficiency. In our study, this was the first type of anemia found in cirrhotic patients. Its frequency in our study is higher than that of Nacoulma *et al*. [3] (20%), Denie *et al*. [2] (38%). Even minimal and chronic digestive haemorrhages, chronic inflammation, hypotransferrinemia [9] [10] by limitation of transferrin synthesis due to hepatocellular insufficiency could explain the microcytic hypochromic anemia during cirrhosis.

4.2. Normochromic Normocytic Anemia

It would have been useful in our study to have the reticulocyte count in order to judge the regenerative or non-regenerative nature of normochromic normocytic anemia. Digestive hemorrhage, hypersplenism frequently encountered in cirrhosis, and hemolysis [11] could explain the normochromic normocytic anemia encountered in cirrhosis. Bone marrow dysfunction due to hepatitis viruses has also been suggested as a cause of aplastic anemia [12]. In our series, hepatitis B and C viruses are the main causes of cirrhosis and nearly 75% of patients with normochromic normocytic anemia had a B or C viral cause. The frequency of normochromic normocytic anemia in our study was higher than that found in the studies by Nacoulma *et al*. [3] (43.3%), Denie *et al*. [2] (12%). In our study 51.7% of patients with normochromic normocytic anemia had esophageal varices; however, none of them had digestive hemorrhage during hospitalization.

4.3. Macrocytic Anemia

The low frequency of macrocytic anemia in our study is probably related to the etiology of cirrhosis which is dominated by hepatitis B and C viruses. This frequency is lower than that found by Dénie *et al*. in France (48%) [2]; this could be explained by the fact that the causes of cirrhosis in France are dominated by alcohol [13]. Macrocytic anemias could be explained on the one hand by vitamin deficiencies, in particular folates and vitamin B12 relating to their uptake and storage [14]; data on these vitamin deficiencies were not available in our patients' medical records; sometimes the financial difficulties of the patients explain the non-realization of these dosages; however, it seems clear that their dosage is necessary for the care of cirrhotic patients who are at risk of malnutrition and on the other hand by chronic ethylism which frequently leads to macrocytosis. In our study, alcohol was noted in 50% of cases of macrocytosis. This explanation is confirmed by Belaiche *et al*. [15] for whom, blood macrocytosis in cirrhosis is linked not only to the toxic effect of alcohol on hematopoiesis but also to folate deficiency. The bone marrow toxicity of alcohol and its metabolite acetaldehyde is responsible for bone marrow failure in alcoholics [1].

4.4. Other Hematological Abnormalities

In our study, more than half of the patients had thrombocytopenia. Thrombocytopenia was found in 66.67% of cirrhotic patients significantly in the study by Sack *et al*. [4] and people suffering from cirrhosis and/or hepatocellular carci-

noma are 43 times more likely to develop thrombocytopenia than controls (Odds ratio = 42.66) [4]. In the study by Nacoulma *et al*. [3], thrombocytopenia was found in 59.50% of cirrhotics. Pancytopenia was noted in our study in 11.1% of cases; hypersplenism is one of the identified causes of pancytopenia [16]. In our study, 20.9% of patients had splenomegaly. The mechanism of this pancytopenia could be either a peripheral destruction of the various blood lines or a lack of bone marrow production. Sack *et al*. [4] in their study noted erythrocyte morphological abnormalities such as anisocytosis, erythrocyte poikilocytosis, presence of stomatocytes, target red blood cells. Our study did not do so because data regarding these erythrocyte abnormalities were not available in the patients' medical records.

4.5. Complications, Child-Pugh Score of Cirrhosis and Types of Anemia

Hepatic encephalopathy was significantly more frequent in patients with hypochromic microcytic anemia; this could be explained by the fact that in our study, all cases of digestive hemorrhage (gastrointestinal bleeding) had hypochromic microcytic anemia and digestive hemorrhage is well known to be one of the causes of hepatic encephalopathy in cirrhotic patients; this alone could not explain this significant link as there were only 4 cases of gastrointestinal bleeding in our sample. The Child-Pugh C score with 47.4% hypochromic microcytic anemia was more frequent but not significantly. Hepatic encephalopathy is one of the parameters of the Child-Pugh score; this could also explain the fact that hepatic encephalopathy is found among patients with microcytic hypochromic anemia because the latter have a poor prognosis Child-Pugh C score. Hepatocellular carcinoma was significantly noted with 63.5% hypochromic microcytic anemia as well as hepatic encephalopathy was significantly noted with hypochromic microcytic anemia; this correlates with the fact that of the 33 patients with hepatic encephalopathy, 15 (45.5%) had hepatocellular carcinoma.

5. Conclusion

Hypochromic microcytic anemia was the most common type of anemia noted in our study. Hepatic encephalopathy and hepatocellular carcinoma were the major complications of cirrhosis significantly associated with hypochromic microcytic anemia. The assessment of iron metabolism, vitamins B12, B9 and reticulocytes assays to determine the mechanism of anemia occurrence, were not carried out in the patients. The blood smear for erythrocytes morphological abnormalities was not performed in our patients either. This assessment is necessary because if there is a deficit of these different parameters, their correction would be necessary for taking charge of anemia in cirrhotic patients.

Conflicts of Interest

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

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