

Factors Associated with Haemolytic Anaemia in the Internal Medicine Department of the Douala General Hospital in Cameroon

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Abstract

Introduction: Haemolytic anaemia (HA) is defined as a decrease in haemoglobin (Hb) levels below baseline due to excessive and premature destruction of red blood cells (RBCs) in the periphery resulting in a shortened life span of less than 120 days. Haemolysis can be corpuscular or extra-corpuscular. The aim of our study was to investigate the factors associated with it for optimal management of patients hospitalised in internal medicine at the Douala General Hospital (DGH). **Methodology:** We conducted an analytical cross-sectional study, including all patients admitted to the internal medicine department of the DGH from 11 February to 20 May 2022, and excluding patients with non-compliant samples. The search for haemolytic anaemia was carried out by means of blood count, reticulocyte count, blood smear, unconjugated bilirubin, lactate dehydrogenase and direct Coombs test. Sociodemographic, clinical and biological parameters were collected and analysed. Correlation was defined for a p value < 0.05. **Results:** This study included 147 patients, 50.34% of whom were men, for a sex ratio of 1.01. The mean age was 52 ± 17.9 years. The most represented age group was 56 - 70 years (n = 49; 33%) with extremes from 15 to 90 years. We counted 29.3% cases of haemolytic anaemia (HA) and 13.9% cases of autoimmune haemolytic anaemia (AIHA). Haemolytic anaemia (HA) was present in 54.14% of men for a sex ratio of 1.38; the most represented age group was 40 - 55 years, 37.2%. HA was associated with jaundice (OR: 3.74, CI: [1.70 - 8.22], p = 0.001), HIV - AIDS (OR: 2.72, CI: [0.98 - 7.53], p = 0.05), thrombocytopenia (OR: 3.53, CI: [1.58 - 7.89], p = 0.02). LDH was elevated (OR: 2.86, CI: [1.30 - 6.26], p = 0.00) as well as elevated reticulocyte count (OR: 3.84, CI: [1.75 - 8.44], p = 0.01). Unconjugated bilirubin was elevated in all these patients. In multivariate analysis,

factors associated with HA were a history of HIV/AIDS, jaundice, thrombocytopenia and elevated reticulocyte count. **Conclusion:** Hemolytic anaemia is common in internal medicine and is significantly associated with thrombocytopenia, HIV/AIDS infection and jaundice.

Keywords

Haemolytic Anaemia, Internal Medicine, DGH

1. Introduction

Anaemia is an abnormal decrease in the amount of functional haemoglobin below reference values. These values in adults vary according to gender and physiological status [1]. According to the World Health Organisation (WHO) these values are between 12 and 15 g/dl in women and between 13 and 16 g/dl in men [2]. Anaemia is classified as one of the ten most serious diseases of the modern world, with a very high prevalence, and affects mostly women of childbearing age, pre-school children and elderly people [3]. anaemia in the latter increases morbidity and mortality [4]. Two billion people worldwide are affected, mainly those in developing countries, with prevalence rates of 39.8% in pregnant women, 22.4% in children under 12 months, 64.4% in those aged 12 - 56 months, 13.5% in those over five years and 43.2% in the elderly [5] [6] [7]. There are several types of anaemia with different and varied aetiology, the most common being martial deficiency anaemia and the least common being haemolytic anaemia (HA) [4].

Haemolytic anaemia is defined as a decrease in haemoglobin levels due to excessive and premature destruction of red blood cells resulting in a reduction in the lifespan of red blood cells to less than 120 days. Classically, a distinction is made between corpuscular haemolysis, which is mostly constitutional, and extra-corpuscular haemolysis, which is acquired [8] [9]. Although most haemolytic anaemias are hereditary, their occurrence is not exceptional in adults [4]. Their aetiological diagnosis requires a hierarchical approach that allows the identification of the haemolytic mechanism [4].

Haemolytic anaemia is a relatively rare condition as epidemiological studies have found an incidence of approximately 3 cases/100,000 population per year in the Western world [5]. This figure does not reflect reality, as it does not take into account the forms associated with other pathologies that are sometimes in the forefront [10]. In 2021, Garrigue *et al.* found a prevalence of 65.7% in France [11]. In Morocco in 2017 the prevalence of haemolytic anaemia was 7.33% [4]. In Mali, Seydou *et al.* noted a prevalence of autoimmune haemolytic anaemia of 4.7% in the Nephrology and Haemodialysis Department of the Point G University Hospital [10].

In view of the almost systematic use of iron-rich drugs and foods in the suspicion of anaemia by the population, and the possibility of optimal management of

HA at the GHD, we thought it appropriate to investigate the frequency and associated factors in patients hospitalised at the internal medicine Department.

2. Methodology

This is an analytical cross-sectional study, covering a period from 11 February to 20 May 2022. The recruitment was done in the Internal Medicine Department and the analysis of the samples in the clinical biology laboratory of the Douala General Hospital. We had consenting patients of both sexes, aged 15 years and over, during our study period. Patients with difficult specimens were excluded. Age, sex, reason for hospitalisation, functional signs, medical and transfusion history, haemogram, reticulocyte count, blood smear, free bilirubin, lactate dehydrogenase and direct Coombs test were performed for each patient. The search for anaemia was carried out by means of blood count tests on the Urit 3000 plus machine (Serial No. 3000PE05587). Stigmata of haemolysis were investigated by free bilirubin and lactate dehydrogenase tests on the BT 1500 (Serial No. 47184504). The blood smear was performed with the optical microscope and the reticulocyte count test was also performed. The direct Coombs test allowed us to determine the proportion of autoimmune haemolytic anaemia (AHAI). The study was conducted after approval from the institutional ethics committee of the University of Douala and the research committee of the Douala General Hospital. The definition of anaemia and severity was based on the haemoglobin level according to WHO [4]. The mean corpuscular volume was considered normal between 80 and 100 fl and the mean corpuscular haemoglobin concentration was normal between 32 - 36 g/dl. The anaemia was regenerative when the reticulocyte count was above 120 G/L. The stigmata of haemolysis was observed when the free bilirubin level was greater than 3 mg/l and the lactate dehydrogenase activity was elevated, *i.e.* greater than 480 IU/l. The haemolytic anaemia was autoimmune when the direct Coombs test was positive.

- **Statistical analysis**

The data were processed with Microsoft Excel 2007 and analysed using StataMP 13, IBM SPSS Statistics 20. Qualitative and quantitative variables were grouped into classes, means \pm standard deviations (SD). To check the association between the variables, we used the chi-square test, univariate and multivariate binary logistic. Differences were considered significant for $p < 0.05$.

3. Results

A total of 43 patients with haemolytic anaemia were identified out of 147 patients recruited, a prevalence of 29.3%. Six patients had autoimmune haemolytic anaemia (13.9%). **Table 1** shows the distribution of patients by age group and there was a predominance of haemolytic anaemia in the 40 - 45 year age group. Males were the most affected by haemolytic anaemia, with a sex ratio of 1.38. The mean age was 52.3 ± 18.3 years with extremes of 17 and 88 years.

Altered general condition was the main reason for hospitalisation with a pro-

portion of 30.2%. Mucocutaneous pallor, asthenia, fever and jaundice were the clinical signs found in most of the patients with the respective proportions of 88.3%, 86%, 16.3% and 34.9%. Arterial hypertension and HIV infection were the most frequent antecedents as shown in **Table 2**.

The mean haemoglobin level in patients with haemolytic anaemia was 9.1 ± 1.8 g/dl. The haemolytic anaemia was generally moderate, but severe in 11.4% of cases (**Table 3**).

Normochromic normocytic anaemia accounted for 93% and normochromic macrocytic anaemia for 7% of cases. An elevated reticulocyte count was found in 67% of cases. Abnormalities of structures, including acanthocytes, schizocytes and sickle cells were found in 27.9% of patients (**Table 4**). Free bilirubin was elevated in 100% of patients and elevated lactate dehydrogenase in 49% of patients (**Table 4**).

Table 1. Distribution of patients by age group.

Age groups (Year)	Total population N = 147 (%)	Patients with no anaemia n = 24 (%)	Patients without haemolytic anaemia n = 80 (%)	Patients with haemolytic anaemia n = 43 (%)
<30	22 (15)	6 (25)	14 (17.5)	2 (4.7)
[30 - 39]	17 (11.6)	1 (4.2)	10 (12.5)	6 (13.9)
[40 - 55]	39 (26.5)	6 (25)	17 (21.3)	16 (37.2)
[56 - 70]	49 (33.3)	9 (37.5)	26 (32.5)	14 (32.6)
>70	20 (13.6)	2(8.3)	13 (16.2)	5 (11.6)
Total	147	24	80	23

Table 2. Distribution of patients by medical history.

Background Medical	Total population N = 147 (%)	Patients with no anaemia n = 24 (%)	Patients without haemolytic anaemia n = 80 (%)	Patients with haemolytic anaemia n = 43 (%)
Diabetes	24 (16.3)	4 (16.6)	14 (17.5)	5 (11.6)
BPH	53 (36.1)	7 (29.2)	31 (38.7)	15 (34.9)
HIV/AIDS	20 (13.6)	2 (8.3)	8 (10)	10 (23.25)
Hepatitis	5 (3.4)	1 (4.2)	1 (1.3)	3 (6.9)
Respiratory disease	14 (9.5)	1 (4.2)	11 (13.7)	2 (4.6)
CKD	22 (14.96)	0	14 (17.5)	8 (18.6)
Stroke	9 (6.1)	1 (4.2)	7 (8.7)	1 (2.3)
Cancers	20 (13.6)	2 (8.3)	13 (16.3)	5 (11.6)
Inflammatory disease	9 (6.1)	3 (12.5)	5 (6.25)	3 (6.9)

VIH/AIDS: People Living with AIDS; HBP: High Blood Pressure; CKD: Chronic Kidney Disease.

Table 3. Distribution of patients by biological data.

Variables	Patients without haemolytic anaemia n (%)	Patients with haemolytic anaemia n (%)	OR [95% CI]	P value
Reticulocytes	28 (35)	29 (67.5)	1.41 [0.49 - 2.33]	0.002
Icterus	28 (35)	15 (34.9)	1.07 [0.11 - 2.04]	0.029
PLWHIV	8 (10)	10 (23.25)	1.58 [0.19 - 2.97]	0.026
Thrombocytopenia	17 (21.3)	21(48.8)	1.12 [0.18 - 2.06]	0.006

Table 4. Associated factors in bivariate analysis.

Variables	Total population N = 147 (%)	Patients with no anaemia n = 24 (%)	Patients without haemolytic anaemia n = 80 (%)	Patients with haemolytic anaemia n = 43 (%)	
Hb	Mean	10.2 ± 2.48	14.0 ± 1.21	9.6 ± 1.76	9.1 ± 1.89
	Extremes	3.7 - 16.7	12.1 - 16.7	5.2 - 12.5	3.7 - 12.5
MCV	Average	88.4 ± 7.14	90.3 ± 4.88	86.6 ± 8.04	90.6 ± 7.45
	Extremes	70 - 123	77 - 99.2	70 - 105	80.1 - 123
MCHC	Average	32.9 ± 1.3	42.1 ± 4.33	32.6 ± 1.22	33.34 ± 1.29
	Extremes	29.5 - 38.1	34.8 - 52.2	29.5 - 36	32 - 38.1
White blood cells	Average	8.6 ± 5.8	7.33 ± 3.22	9.0 ± 6.5	8.7 ± 6.2
	Extremes	1 - 39.2	2.3 - 14.4	1 - 39.2	2.6 - 22.8
Trays	Average	8.6 ± 5.8	224.1 ± 78.5	261 ± 157.4	163.9 ± 147.5
	Extremes	16 - 780	68 - 364	23 - 780	16 - 409
Free bilirubin (mg/l) ≤ 03	Average	2.11	-	2.11	0
	Extremes	0.22 - 3		0.22 - 3	0
Free bilirubin (mg/l) > 03	Average	14.3	-	6.96	18.41
	Extremes	3.12 - 186.58		3.12 - 35.98	3.28 - 186.58
LDH (IU/l) ≤ 480	Average	262.3	-	264.19	257.1
	Extremes	100.66 - 478.52		100.66 - 478.52	156.38 - 438.5
LDH (IU/l) > 480	Average	1033.64	-	909	1157.32
	Extremes	483.23 - 471.81		483.23 - 3442.42	486.12 - 4471.81

Age [40 - 50] years and single status were factors associated with the occurrence of haemolytic anaemia ($p = 0.02$; OR = 6.5 and $p = 0.02$; OR = 6.6) as shown in **Table 5**. Jaundice was significantly associated with haemolytic anaemia ($p = 0.001$; OR = 3.74). **Table 6** shows that HIV/AIDS, jaundice, reticulocytosis and thrombocytopenia were associated with haemolytic anaemia in the multivariate factors analysis.

4. Discussion

Our study was conducted from January to June 2022, with as general objective to

Table 5. Multivariate factors associated with haemolytic anaemia.

Socio-demographic factors	Patients without haemolytic anaemia n = 80 (%)	Patients with haemolytic anaemia n = 43 (%)	OR [95% CI]	P value
Age group [40 - 55]	17 (21.3)	16 (37.2)	6.5 [1.29 - 33.67]	0.02
Marital status				
Single	18 (22.5)	14 (32.6)	6.6 [1.29 - 34.48]	0.02
Functional sign				
Icterus	28 (35)	15 (34.9)	3.74 [1.70 - 8.22]	0.001
Medical history				
PLWHA	8 (10)	10 (23.25)	2.72 [0.98 - 7.53]	0.05
Respiratory disease	11 (13.7)	2 (4.6)	0.30 [0.13 - 1.44]	0.04
Thrombocytopenia	17 (21.3)	21 (48.8)	3.53 [1.58 - 7.89]	0.02
Reticulocytes > 120 g/L	28 (35)	29 (67.5)	3.84 [1.75 - 8.44]	0.01
LDH > 480 IU/l	20 (25)	21 (48.8)	2.86 [1.30 - 6.26]	0.00

Table 6. Distribution of anaemic patients according to degree of severity.

Type of anaemia n = 123	Total n (%)	Slight anaemia n (%)	Moderate anaemia n (%)	Severe anaemia n (%)
haemolytic anaemia	43 (100)	14 (41.5)	22 (47.1)	7 (11.4)
Without haemolytic anaemia	80 (100)	37 (46.25)	36 (45.0)	7 (8.75)

determine the factors associated with haemolytic anaemia at the Internal Medicine Department of HGD. We identified 43 patients with HA out of 147 patients recruited, giving a prevalence of 29.3%. This prevalence was lower than that of Garrigues *et al.* who found a prevalence of 65.7% in 2021 during their work on the profile of haemolytic anaemias encountered in an internal medicine department in France on 108 files [11]. This was higher than the prevalence found by Zinebi *et al.* (7.33%) in Morocco on a population of 150 patients [4]. The prevalence of autoimmune haemolytic anaemia was 13.9% in our series, which was lower than that noted by Garrigues *et al.* (34.2%) and higher than the 4.7% noted by Seydou *et al.* in 2021 in the Nephrology and Haemodialysis Department of the Point G University Hospital [10] [11]. The 40 - 55 age group was predominantly represented with a proportion of 37.2%, *i.e.* an average of 52.3 ± 18.3 years and extremes of 17 and 88 years. Our result was similar to that of Hachini *et al.* who in 2016 in Tunisia observed a mean age of 52 years and extremes ranging from 19 to 87 years [12]. The sex ratio was 1.38 with a male predominance, *i.e.* a proportion of 58.14%. Pouchelon *et al.* in a French multicentre observational study found a male predominance similar to ours, *i.e.* 58% [13]. In a population of patients with AHAI, Zulfiqar *et al.* in 2016 observed a female predominance with 71.4% of cases [14].

We found that impairment of general condition was the main reason for hospitalization with a proportion of 30.2%. This result was different from that of

Seydou *et al.* who noted renal failure in 85.2% of cases [10]. Pallor and asthenia were the most common clinical signs with prevalences of 88.3% and 86% respectively. Anouun *et al.* found in 2022 that the elderly had a lower prevalence of pallor than ours, *i.e.* 82.6% [15]. Similarly, Zinebi *et al.* found lower values for pallor and asthenia, respectively 16% and 41% [4].

The mean value of the haemoglobin level in our study was 9.1 g/dl, higher than 6 g/dl in Pouchelon *et al.*, 8 g/dl in Zinebi *et al.* [4] [14]. The anaemia was normocytic normochromic in 93% higher than that of Oubelkacem *et al.* who noted in his series 11% [16]. Indeed, these authors looked for haemolytic anaemia in a group of patients with chronic myeloid leukaemia. Hachini observed a lower proportion than ours (41.1%). But Hachini in his series found 44.4% normochromic macrocytic anaemia, whereas we had only 7% [12]. Haemolytic anaemia was regenerative in 29 patients, *i.e.* a proportion of 67.5% higher than that of Oubelkacem *et al.* which was 11% [16]. The consequences of haemolysis in our study were elevated free bilirubin and LDH with values of 100% and 49% respectively. Hachini *et al.*, in a series of 90 cases, found 44% and 67% respectively [12]. HA was associated with the age group 40-55 years ($p = 0.02$; OR: 6.5). Jaundice was significantly associated with HA ($p = 0.00$; OR: 3.74) as also noted by Anoun *et al.* [15]. Pallor and fever were also factors associated with HA (OR = 1.63) as fever may be related to malaria. Our study showed that HIV/AIDS was a predisposing factor for HA ($p = 0.05$; OR: 2.72) as found in the study of Coulibaly in 2020 and Gourguechon *et al.* [17]. This could be due to increased destruction of red blood cells by a direct effect of the virus and the adverse effects of ARV drugs. Patients with cancer had a risk of developing haemolytic anaemia, a value of 11.6%. Garrigues *et al.* noted a proportion of 24.3% HA associated with cancer [11], in contrast, Mama *et al.* observed 8.9% [18]. This could be due to the cytotoxic action of anticancer drugs. In our study, thrombocytopenia as well as increased free bilirubin and reticulocyte count were factors associated with haemolytic anaemia ($p = 0.02$; 0.00 and 0.0). Our results are consistent with those found in the literature [14] [15] [16] [17].

5. Conclusion

Male patients and patients aged 40 - 55 years are mostly affected by haemolytic anaemia. One in three patients had HA, which was usually moderate in one-third of cases and most often normochromic normocytic. Factors associated with HA were HIV/AIDS, jaundice, high reticulocyte count, thrombocytopenia. This HA correlated with elevated free bilirubin, LDH, reticulocyte count and thrombocytopenia.

Conflicts of Interest

The authors declare no conflict of interest.

Authors' Contributions

Ngouadjeu Dongho Eveline, Afana Brice and Olemba Clémence designed and

wrote the protocol, Afana Brice, Nda Mefo'o Jean Pierre and Okalla Ebongue Cécile contributed to data collection and analyses of biological data. Temfomo Abdou and Assob Clément contributed to the manuscript drafting; Luma Namme Henry supervised write up of the manuscript.

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