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Hematological manifestations during Systemic Lupus Erythematosus : Experience from Libreville University Hospital

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Abstract— Hematological damage is common in Systemic Lupus Erythematosus and does not result from hemolytic anemia alone. In order to report the experience of the Libreville University Hospital, we conducted a study to determine the hematological manifestations that may be associated with systemic lupus erythematosus in patients followed in Gabon. Retrospective descriptive study , carried out on files of lupus patients hospitalized in the internal medicine department of Libreville University Hospital for 2 years. Was included: any patient aged over 15 years, regardless of sex, hospitalized for SLE. Data analysis by Epi-info version 3.5. A total of 51 lupus patient files were collected. There were 43 women and 8 men, giving a sex ratio of 0.19. The 20-29 year old age group, comprising 37.3% of the workforce, was the most representative. Lupus disease was found to be insidious in 78.4% and brutal in 21.6%. Anemia was present in 40 out of 51 patients. Anemia was severe in 18 patients with a mean hemoglobin level of 6.2g/dl, moderate in 16 patients and mild in 6 patients. It was microcytic normochrome in 50% of cases, normocytic normochrome in 22.5%. Inflammatory causes represented 37.5% of patients. Hematological damage remains common in lupus and must be carefully investigated. Our study showed that more than half of lupus patients had anemia and. its causes, probably multifactorial, are dominated by an inflammatory mechanism.

Keywords*:* Systemic lupus erythematosus, anemia, inflammation

1. Introduction

Systemic lupus erythematosus (SLE) is considered a model of autoimmune disease with multiple aspects. Its exact etiology remains unknown but is characterized by a significant production of autoantibodies and immune complexes. It probably involves complex interactions between hormonal, genetic and environmental factors [1]. It is a pathology with systemic expression whose clinical presentation is very polymorphous, andthe spontaneous evolution is characterized by flare-ups interspersed with remissions. Its prevalence varies from one country to another, ranging from 4 to 178 per 100,000 inhabitants and its incidence from 0.3 to 23.7 per 100,000 inhabitants per year [2]. SLE preferentially affects young women (the sex ratio being nine women to one man) of childbearing age. [2] The suggestion of hormonal, immunological and genetic factors in the physiopathology of this disease has been proposed by several studies, but the environmental character is poorly elucidated and few studies have been able to establish causal links, particularly in terms of solar exposure, geographical and seasonal distribution of the

different outbreaks [3]. Lupus can present in extremely variable forms, ranging from simple local skin damage to more severe forms, and where one or more internal organs or systems are affected, namely kidneys, lungs, serous membranes, nervous system, vascular , gastrointestinal, ophthalmological and hemato-lymphatic [1]. Hematological abnormalities are common and are part of the diagnostic criteria in patients with SLE. They are mainly manifested by cytopenias, which can affect all lineages. Isolated or associated with other manifestations, they usually have little clinical translation and rarely require specific treatment. Splenomegaly and peripheral lymphadenopathy are often associated with a flare-up of the disease. Other serious hematological disorders can be life-threatening in the short term, such as lymphohistiocytosis. hemophagocytic , thrombotic microangiopathy and exceptionally, myelofibrosis[4]. In sub-Saharan Africa, there is little work studying the hematological manifestations observed during SLE. The objective of this work was to report the experience of the Libreville University Hospital.

2. Patients and method

Study design, setting and population

This was a retrospective descriptive study involving all patients who had been hospitalized for SLE in the Internal Medicine department of the Libreville University Hospital Center (CHUL), and covered a period of activity of 2 years: January 1 2021 to December 31, 2022. Data was sought from the files of patients hospitalized for SLE during this period and collected on a form.
Was included: any patient hospitalized for SLE, aged over 15 years regardless of gender, having anemia. Allstages of LED evolution were taken into account. Incomplete files were not included.

Data gathering

The demographic characteristics of the patients (age and sex), the mode of revelation of SLE, the clinical manifestations of SLE, the hemogram parameters (leukocytes, neutrophils , lymphocytes, eosinophils, monocytes, hemoglobin, platelets) were studied. The form, type and etiopathogenic factors associated with anemia were also studied.
Mean corpuscular volume (MCV), Mean corpuscular hemoglobin concentration (MCHC) have been used to characterize anemia. The etiological factors of anemia were retained from the analysis of clinical and paraclinical signs. The additional tests analyzed to focus on one cause or another of the anemia were: reticulocytes, indirect bilirubin, lactate dehydrogenases (LDH), haptoglobin, C-reactive protein (CRP) , serum iron , transferrinemia , ferritinemia, iron saturation coefficient, creatinemia, glomerular filtration rate.

Definitions

Patients were classified as anemic according to the World Health Organization (WHO) criteria (Hb <12 g/dlfor women and <13 g/dl for men) [5].
Anemia was mild if Hb in women between 10.9 and 11.9 g/dl and in men between 10.9 and 12.9 g/dl, moderateif Hb between 8 and 10.9 g/dl and severe if Hb <8g/dl.
Excluded : patient file having received a blood transfusion within 4 months, incomplete file and patient file having an associated hematological disease.

Based on mean corpuscular volume (MCV), anemia was classified as microcytic (MCV <80 fl), normocytic (MCV between 80 and 100 fl), or macrocytic (MCV >100 fl). Mean corpuscular hemoglobin concentration (MCHC) was used to characterize anemia as hypochromic (MCHC <32 g/dl) or normochromic (MCHC ≥ 32 g/dl). Anemia was central if the reticulocyte count was < 120,000/mm3. A positive Coombs test associated with a normochromic normocytic or macrocytic character of the anemia pointed to an autoimmune origin. A C-reactive protein >10 mg/l was in favor of an inflammatory origin, iron deficiency was retained when the ferritin level was less than 30 µg/L and serum iron < 100 mg/l. Estimated glomerular filtration rate (eGFR) (ml/min/1.73 m2) was calculated using the abbreviated formula modification of diet in kidney disease as eGFR = 186 × [serum creatinine (mg/l)] − 1.154 × [age (years)] - 0.203 × 0.192 × (0.742 for women) [14].

Statistical analyzes

Data were presented as mean and standard deviation for continuous variables and as numbers and percentages for categorical variables. Data were tested for normality using histograms, comparison of means and medians. data were analyzed with SPSS for Windows: EPI-INFO version 3.5.

3. Results

Epidemiological data

Age and Sex

Over a period of 2 years, 51 SLE files were identified. There were 43 women and 8 men, with a sex ratio of

0.19. The mean age of these patients was 30.4 ± 11.8 years with extremes of 15 and 59 years. There is nosignificant age difference between men and women (p = 0.683). The 20-29 year old age group, comprising

37.3% of the workforce, was the most representative (figure 1).

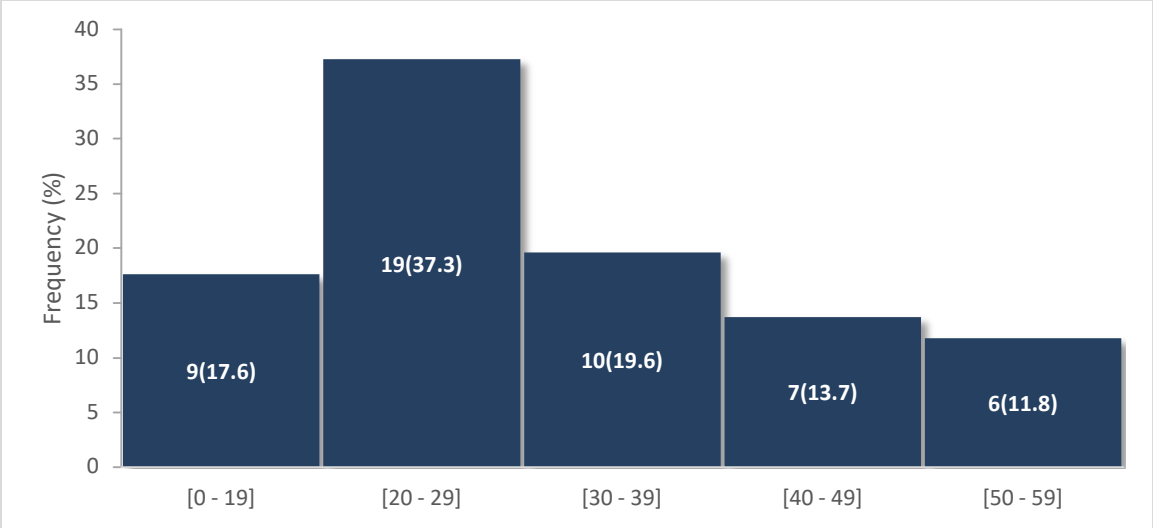

Figure 1: Distribution of patients by age

LED scalable mode

During hospitalization, lupus disease presented insidiously in 78.4% (Figure 2).

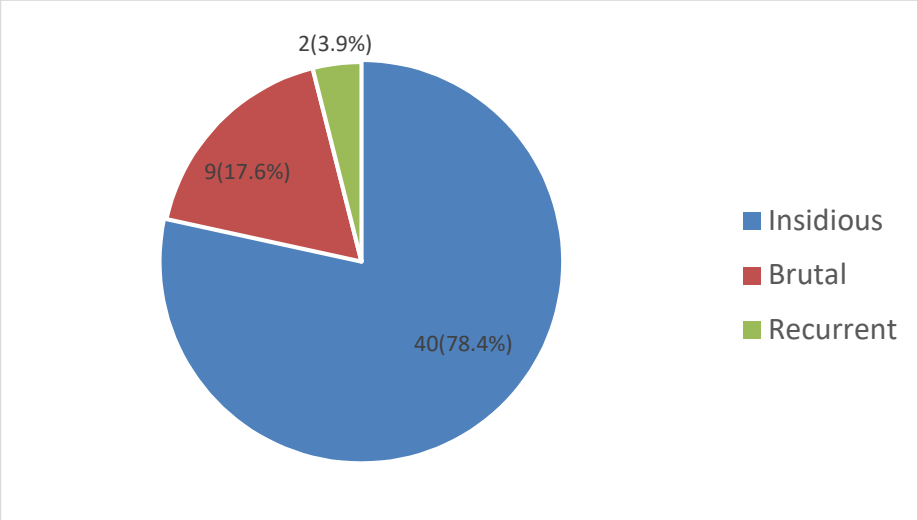

Figure 2: Distribution according to mode of appearance

The reason for hospitalization

The reasons for hospitalization of the patients are presented in Figure 3. Polyarthralgias were present in 26 patients, general signs in 13, rash in 8, cardiorespiratory signs such as dyspnea, palpitations in 5.9%. Three patients presented an altered general condition and 2…

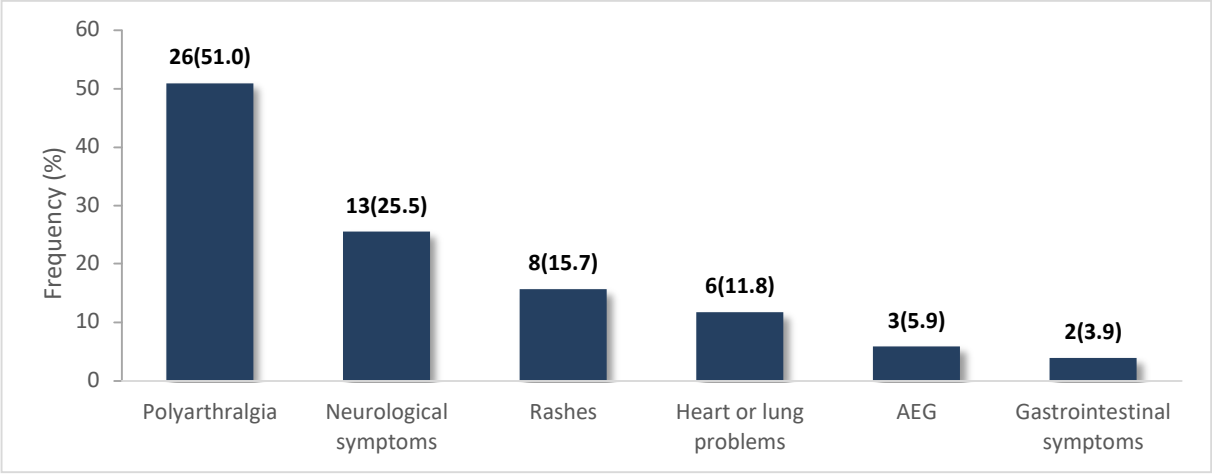

Figure 3: Distribution according to discovery mode

Clinical manifestations

General signs were present in 78.4% of patients, proteinuria in 76.5% of patients and arthralgia in 60.8% of patients. Other clinical manifestations are presented in Figure 4.

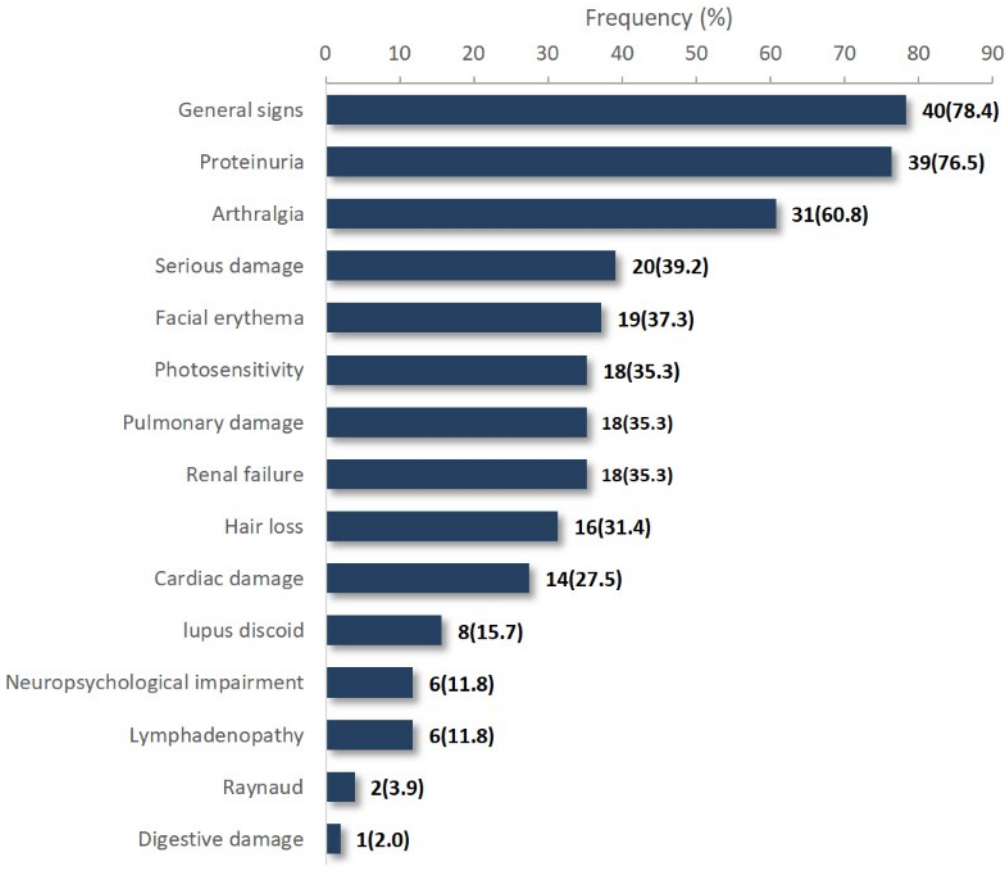

Figure 4: Distribution according to clinical manifestations

Hematological manifestations

When the hematological manifestations were studied in general, anemia was present in 40 out of 51 patients,

i.e. a percentage of 78.4%, leukopenia in 62% of cases, lymphopenia in 56.9% of cases, thrombocytopenia in 25 patients and neutropenia in 2 patients. Two cases of splenomegaly and 1 case of lymphadenopathy were observed. The hematological manifestations are presented in the table. The characteristics of the hematological markers corresponding to the abnormalities in Table II. The average hemoglobin level was 8.0
± 2.0g/dl with extremes ranging from 3.8g/dl to 11.8g/dl and a median of 8.1g/dl.

Table 1: Distribution of patients according to hematological manifestations

Hematological manifestations	Number (N= 51)	Percentage (%)
Anemia	40	78.4
Leukopenia	32	62.7
Lymphopenia	29	56.9
Thrombocytopenia	25	49.0
Neutropenia	2	3.9
Splenomegaly	2	3.9
Lymphadenopathy	1	2.0

Table 2: Hematological characteristics according to manifestations

	mev . ± sd	**Minimum**	**Maximum**	**Median**
Hemoglobin(g/dl)	8.0 ± 2.0	3.8	11.8	8.1
Leukocytes (/mm3)	7,549.7 ± 5,300.8	1,800.0	28,230.0	5,920.0
Lymphocytes(/mm3)	1452.6 ± 791.4	150.0	3,190.7	1,353.0
Platelets(/mm3)	274,825.0 ± 119,829.6	66,000.0	584,000.0	257,500.0

Anemia, present in 40 out of 51 patients , was severe in 18 patients with an average hemoglobin level of 6.2g/dl, moderate in 16 patients and mild in 6 patients . The distribution of patients according to the severity of anemia is presented in Table III and the corresponding average hemoglobin levels in Figure 5.

Table 3: Distribution of patients according to severity of anemia

Anemia	Effective	%
Severe	18	45.0
Moderate	16	40.0
Light	6	15.0
Total	40	100.0

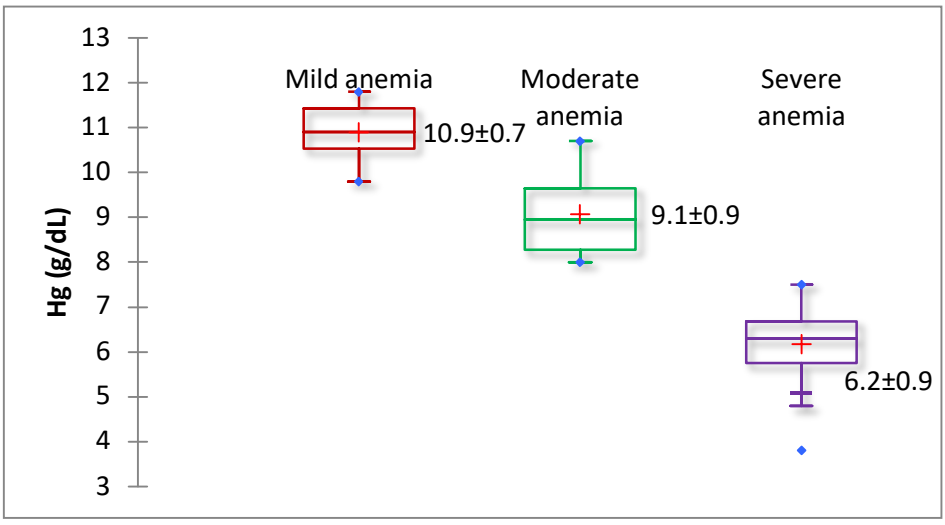

Figure 5: hemoglobin level according to severity of anemia

Type of anemia

The anemia was normochromic microcytic in 50% of cases, normochromic normocytic in 22.5% (Table 4).

Table 4: Distribution of patients according to type of anemia

Type of anemia	Effective	%
Microcytic normochrome	20	50.0
Normocytic normochrome	9	22.5
Microcytic hypochrome	8	20.0
Normocytic hypochromia	3	7.5
Total	40	100.0

The etiopathogenic factors of anemia are presented in Table V. Inflammatory causes accounted for 37.5% of patients. The cause was not determined in 22.5% of cases. Iron deficiency and kidney failure accounted for 15% and 12%, respectively. In 4 patients, anemia was attributed to an autoimmune mechanism

Table 5: Distribution of patients according to the causes of anemia

Causes of anemia	Effective	%
Inflammatory anemia	15	37.5
Undetermined causes	9	22.5
Iron deficiency	6	15.0
Renal failure	5	12.5
Autoimmune Hemolytic Anemia	4	10.0
hemorrhages	1	2.5
Total	40	100.0

4. Discussion

SLE is a pathology with a clear female predominance. The peak prevalence is observed in women between 40 and 49 years old (138.8/100,000). The sex ratio (F/M) gradually increases with age, going from 1 for the youngest patients, to a maximum of 13 in young adults, to drop to 3 in patients aged 70 to 79 years, highlighting the hormonal influence on this pathology [6]. In this series, there were 43 women out of 51 patients, or 84.3% of the entire population studied, or a female/male sex ratio of 5.4. This result is close to that of Marrakech (out of a series of 35 patients, 30 were female (86%)). A sex ratio of 12, higher than in this series, was found in Tunisia in 2018 [7]. SLE mainly affects young women between 30 and 40 years old [1,2,4,7]. Our results confirm this observation. The average age in our study is 30.4 ± 11.8 years 39.62 years with extremes with extremes of 15 and 59 years of 15 years. The hematological manifestations encountered during SLE are numerous, varied and well established in the literature (inflammatory anemia-type cytopenias, AHAI, Evans syndrome, ITP, pancytopenia, hemolysis, or even macrophage activation, etc.). Their expressions are clinical and/or biological. Some of them constitute diagnostic or even prognostic criteria. The complexity of hematological events is generated by the multifactorial nature of the often intricate mechanisms (inflammatory process, runaway immune system, hypersplenism, etc.) characterizing SLE. These hematological disturbances require close collaboration between clinicians and biologists. The hematological damage indicates a progression, even a seriousness of the underlying condition, in this case SLE, and requires specific, sometimes aggressive therapy. It must therefore be quickly identified and analyzed in this context in the same way as other visceral damage determining the immediate prognosis (kidneys, central nervous system, etc.) of lupus disease . In this study, 42 out of 51 patients (82.3%) had hematological damage. This result is close to that of. Samai et al. In a series of 134 patients, hematological damage was present in 89.33% [4]. Oubelkacem et al observed a lower prevalence of 67.3% [8]. Anemia was predominant (40 out of 51 patients or 78.4%) followed by leukopenia (62% of cases), lymphopenia (56.9% of cases) and thrombocytopenia which was present in 25 patients or 49% of cases. case. Samai et al. Found 58.9% anemia, 41% leukopenia, 67.1% lymphopenia, 5% neutropenia and 15.6% thrombocytopenia [4]. The systemic manifestations associated with hematological damage were mainly general signs present in 78.4% of patients, proteinuria in 76.5% of patients and arthralgia in 60.8% of patients. These manifestations may appear differently depending on the region. The Tunisian team found a predominance of joint damage (67.7%), photosensitivity (59.7%), malar rash (42.5%) and kidney damage (40%). Anemia is the most common hematological manifestation in lupus and can be classified into two main categories: immune and non-immune. Nonimmune anemia includes inflammatory anemia, iron deficiency anemia, sideroblastic anemia , anemia of renal failure, anemia induced by certain drugs), and hemoglobinopathies. Immune anemia includes autoimmune hemolytic anemia (AIHA), drug-induced hemolytic anemia, aplastic anemia, red cell aplasia , and pernicious anemia. The discovery of anemia in the blood count is therefore usual. In our series, we report anemia in 40 out of 51 patients, representing a prevalence of 78.4%. 80% of cases. A similar result was noted in the series from the internal medicine department of Fez

University Hospital, where anemia was found in 71.6% [9]. Somai et al [7] as well as Rachdi et al. [10] found a lower prevalence of anemia, 58.9% and 57.1 %. Delay in the management of lupus disease can often lead to worsening of anemia. In this study, anemia was severe in 18 patients with a mean hemoglobin level of 6.2g/dl, moderate in 16 patients and mild in 6 patients. This series noted a predominance of microcytosis with a frequency of microcytic normochromic character in 50% of cases, microcytic hypochromic in 22.5% of cases and microcytic hypochromic in 20% of cases. In other series of literature, we note rather a predominance of normochromic normocytic anemia most often linked to the autoimmune origin, 78.1% by Rachdi et al [9], 62.5% by Zbadi [8]. In this series, inflammatory causes represented 37.5% of patients, the cause was undetermined in 22.5% of cases, iron deficiency and renal failure represented 15% and 12% respectively. In 4 patients, anemia was attributed to an autoimmune mechanism. Our results are close to those of Rachdi et al [7]. Out of 32 cases of anemia, 13 were of inflammatory origin in 13 cases (40.6%), hemolytic in 3 cases (9.3%), iron deficiency in 6 cases (18.75%) and secondary to renalinsufficiency chronic in 4 cases (12.5%). The high prevalence of inflammatory causes found in these studies can be explained by the delay in treatment. In our regions, the diagnosis of SLE is often made late and patients present with a significant and chronic inflammatory syndrome. The predominance of the microcytic form in our population may also suggest the importance of deficiency causes, notably iron deficiency, which is probably underestimated in our population (15%). This low proportion results from the inaccessibility of patients to all additional examinations despite the availability of health insurance which only partially coversthe costs of medical care in Gabon. This also explains the absence of etiology in several cases in this work (22.5%). It is possible that these cases of microcytosis have a multifactorial etiopathogenic mechanism . Anemia is common in systemic lupus erythematosus (SLE), autoimmune hemolytic anemia (AIHA), which is a diagnostic criterion for SLE, only concerns 10% of patients. Our results are consistent with these data from the literature.

We acknowledge the following potential limitations of our study: despite being conducted in a tertiary care hospital, the results may underestimate some actual causes of anemia in hospitalized SLE patients. The number of reticulocytes and the vitamin dosage (vitamin B12 and folic acid) were not evaluated and the search for hemoglobinopathies was not carried out. Additionally, this study did not consider non-Lupus patients to identify causes that may be specific to SLE, indicating the need for continued research in this area.

5. Conclusion

Hematological manifestations are common in SLE and are dominated by anemia, the causes of which are variable and diverse. Our study showed that more than half of lupus patients had anemia. Its causes, probably multifactorial, are dominated by an inflammatory mechanism. These results need to be confirmed by carrying out a prospective study.

6. Abbreviation

CHUL: University Hospital Center of LibrevilleCRP: C-Reactive Protein

eGFR : estimated glomerular filtration rate SLE: Systemic Lupus Erythematosus
MCHC: Mean Corpuscular Hemoglobin Concentration WHO: World Health Organization
MCV: Mean Globular Volume

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