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Male lupus: experience of Gabon, a country in sub-Saharan Africa

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Summary

Introduction
Systemic lupus erythematosus (SLE) is an autoimmune disease mainly affecting young women, rarely in men. The objective of this study was to analyze the clinicobiological particularities of male SLE.

Patients and Methods
This was a retrospective, descriptive study carried out in the Internal Medicine Department of CHUL, over a period of 6 years, from 01/01/2016 to 05/31/2022. All patients met ACR criteria.

Results
A total of 24 patients were registered with an average age of 29.33 years (range: 18-52 years). An insidious onset was observed in 83.33% of cases. Hematological signs were more frequent and represented 70.83% of patients. Anemia was present in 15 patients or 88.23% with 3 cases of hemolytic anemia, lymphopenia in 6 patients or 35.29%, leukopenia in 4 (23.53%) and thrombocytopenia in 3 patients or 17 .65%. Kidney damage accounted for 66.65% or 16 patients. General signs, joint damage and heart damage accounted for 54.17%, 45.83% and 20.83% respectively. Photosensitivity, facial erythema, and discoid lupus accounted for 25%, 20.83%, and 8.33%, respectively. Hair loss was present in 5 patients as well as lung involvement. 3 patients had lymphadenopathy, 2 neuropsychiatric signs and 2 also had digestive manifestations. Raynaud's phenomenon was objectified in one patient. Antinuclear autoantibodies were performed in 17 patients and were positive in 66.67% of cases, native anti-DNA antibodies performed in 15 patients and were positive in 9 of them. Soluble antigen antibodies were produced in 8 patients and were found positive in 3 of them. Anti-phospholipid antibodies made in 5 patients and positive in one case. All patients had received oral corticosteroid therapy and hydroxychloroquine.

Thirteen out of 24 (54.17%) had previously received intravenous corticosteroid therapy. Cyclophosphamide was administered in 3 patients and other immunosuppressants were administered in 3 patients as well. Five cases of death were recorded, i.e. 20.83% of cases.

Conclusion
SLE is rare in humans, nevertheless it correlates with higher mortality in front of the most frequent association with renal impairment, which requires a better knowledge of these clinicobiological particularities.

Keywords: Lupus, Man, Gabon

Introduction

lupus erythematosus (SLE) is a syndrome characterized clinically by the association of protean manifestations and biologically by the almost constant presence of antibodies directed against various constituents of the nucleus (antinuclear antibodies).The epidemiology of SLE varies greatly from one territory to another, sometimes including within the same country or the same geographical region.[1] Globally, the prevalence of SLE varies from 4 to 178 per 100,000 inhabitants and its incidence from 0.3 to 23.7 per 100,000 inhabitants per year.[1] This reflects ethnic and possibly environmental variations as much as differences in the methodology of obtaining the data. In Africa, several series of cases are described. In Gabon, the number of cases of lupus diagnosed and/or followed on an outpatient basis in the Internal Medicine Department of the Libreville University Hospital Center (CHUL) was estimated at 120 in 1018.[2] Lupus is rare in men depending on the series. Several studies have focused on the particularity of this disease in male subjects. This is the case in France where 159 cases from a series of 1979 lupus patients were studied.[3] In Tunisia, 25 cases were reported in 2016[4] then 27 in 2020.[5] Morocco released a series of 44 in 2021.[6] There also seem to be significant differences in the clinical expression of Lupus in men compared to women[3,4,6] but this is highly variable from one series to another. Few data exist on the subject in sub-Saharan Africa. The objective of our study is to report the experience of the Internal Medicine Department of the CHUL (Gabon, country of sub-Saharan Africa) in the management and evolution of male patients with SLE.

Patients and Method

This was a retrospective, descriptive study carried out in the Internal Medicine Department of the CHUL, a reference service for the management of autoimmune diseases, over a period of 6 years, from 01/01/2016 to 31 /05/2022 and supported by diagnostic lupus files, supported and/or regularly monitored on an outpatient basis. Per patient, were specified on a data collection sheet, identity, date of birth, age, nationality, mode of onset, general signs (fever, asthenia, weight loss), clinical manifestations such as: cutaneous-phanerial signs (Photosensitivity, facial erythema**,** hair loss**,** discoid lupus), joint damage (oligo and polyarthralgia), lung damage, hematology damage (anemia, Coombs test, leukopenia, lymphopenia, thrombocytopenia), heart damage, neuropsychiatric impairment, digestive involvement, presence of lymphadenopathy and Raynaud's phenomenon. Immunological manifestations were also listed there, in particular antinuclear antibodies, native anti-DNA antibodies, soluble antigen antibodies and anti-phospholipid antibodies, as well as the various treatments received by patients to treat lupus disease. The mode of evolution was also specified there.

Included were patients aged 17 or over, hospitalized and/or followed in the Internal Medicine Department of CHUL, in whom the diagnosis of systemic lupus was established on the criteria of the American College of Rheumatology (ACR)[7] retaining at least 4 out of 11 criteria (Table 1). For better data homogeneity, patients whose records were incomplete were excluded. The analysis software used was R version 3.4 and Excel 2016.

Results

A total of 24 patient files were studied on 177 lupus identified during our study period. The average age was 29.33 years with extremes ranging from 18 to 52 years and the most represented age group was that of 18 to 28 years (10 patients) followed by those of 28-38 years (7 patients), 38-48 years old (4 patients) and 48-58 years old (1 patient). The mode of entry into the disease was insidious in 83.33% (N=20) and sudden in 4 patients.

Regarding clinical manifestations (Table 2), hematological signs were more frequent and represented 70.83% of patients. Of the 17 haematological manifestations, anemia was present in 15 patients or 88.23% with 3 cases of haemolytic anemia, lymphopenia in 6 patients or 35.29%, leukopenia in 4 (23.53%) and thrombocytopenia in 3 patients or 17.65%. Kidney damage accounted for 66.65% or 16 patients. It was made of proteinuria (15/16 patients), nephritic syndrome (11/16 patients) and renal failure

Table 1: SLE diagnostic criteria: ACR[7]

1.Malar rash	
2. Discoid lupus	
3.Photosensitivity	
4. Oral ulcers	
5. Non-erosive arthritis	
6. Effusion	Pleurisy
	Pericarditis
7. Kidney damage	Proteinuria > 0.5 g/d
	Cylinders
8.Neurological impairment	Comitiality
	Psychosis
9. Hematological abnormality	Hemolytic anemia
	Leukopenia < 4000
	Lymphopenia < 1500
	Thrombocytopenia < 10000
10. Immunological disorder	LE+ or native anti-DNA cells
	Anti- Sm
	False syphilitic serology
11. Antinuclear antibodies (in the absence of inducing drugs) Ac antinuclei	

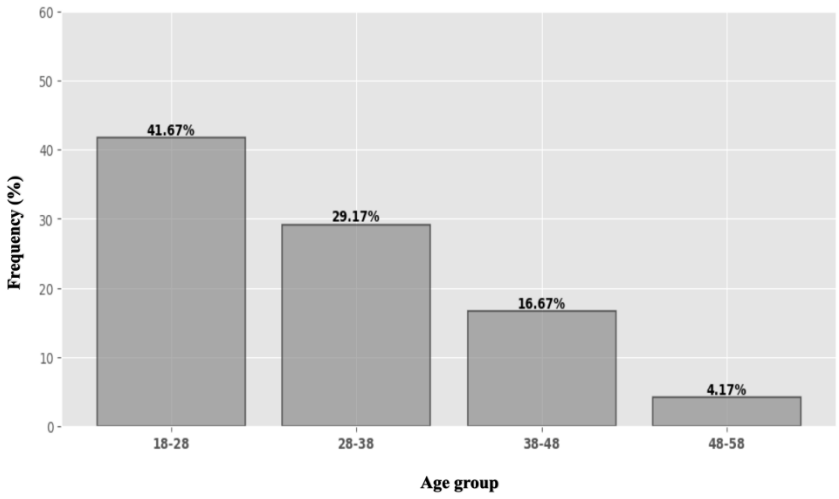

Figure 1: Breakdown by age.

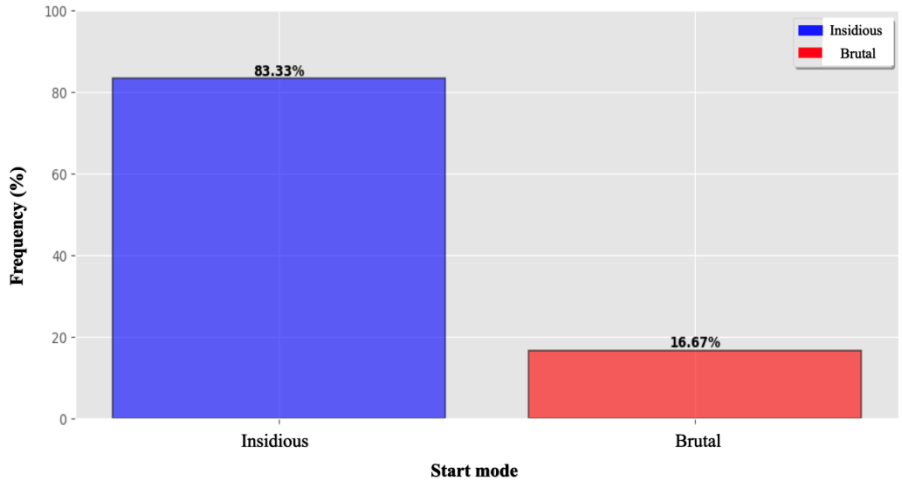

Figure 2: Distribution according to mode of entry into the disease.

Table 2: Distribution according to clinical manifestations

Clinical manifestations	Effective	%	pvalue
Hematological impairment	**17**	70.83	2.80e-21
Anemia	15	62.50	
Lymphopenia	6	25.00	
Leukopenia	4	16.65	
Thrombocytopenia	3	12.50	
Hemolytic anemia	**3**	12.50	
Kidney damage	**16**	**66.65**	
Proteinuria	15	62.50	
Nephrotic syndrome	11	45.83	
Renal failure	8	33.33	
General signs	**13**	**54.17**	
Joint damage	**11**	**45.83**	
Heart attack	**5**	**20.83**	
Pericardial effusion	3	12.50	

	7	29.17
Cutaneo-phanerial involvement		
Photosensitivity	6	**25.00**
Facial erythema	5	**20.83**
Hair loss	5	20.83
Discoid lupus	3	8.33
Lung involvement	**5**	**20.83**
Lymphadenopathy	**3**	**8.33**
Neuropsychiatric impairment	**2**	**8.33**
Digestive impairment	**2**	**8.33**
Raynaud's phenomenon	1	**4.17**

Table 3: Distribution according to immunological tests

Testing	Achieved	%	Positives	%
Anti-nuclear antibodies	17	70.83	16	66.65
Native anti-DNA antibodies	15	62.50	9	37.50
Soluble Antigen Antibodies	8	33.33	3	12.50
Anti-phospholipid antibodies	2	8.33	1	4.17

Table 4: Repair according to treatment

Treatment	Effective	%	pvalue
Oral corticosteroid therapy	24	100	1.65e-37
Hydroxychloroquine	24	100	
Intravenous corticosteroid therapy	13	54.17	
Cyclophosphamide	3	12.5	
Other immsuppressors	3	12.5	

8/16 patients). General signs, articular involvement, cardiac involvement (dominated by pericardial effusion: 3/5 patients) represented 54.17%, 45.83% and 20.83% respectively. Cutaneous signs, namely photosensitivity, facial erythema and discoid lupus accounted for 25%, 20.83% and 8.33% respectively. Hair loss was present in 5 patients as well as pulmonary involvement represented by pleural effusion. There were 3 cases of adenopathy. Two patients had neuropsychiatric manifestations. Digestive manifestations such as peritoneal effusion were also found in 2 patients. Raynaud's phenomenon was objectified in one patient.

Immunologically (Table 3), antinuclear autoantibodies were produced in 17 patients and were positive in 66.67% of cases (16 patients), native anti-DNA antibodies produced in 15 patients and were positive in 9 of them, i.e. 37% of patients. Soluble antigen antibodies were produced in 8 patients and were found positive in 3 of them. Anti-phospholipid antibodies made in 5 patients and positive in one case.

Therapeutically (Table 4), all patients had received oral corticosteroid therapy and hydroxychloroquine. Thirteen out of 24 (54.17%) received prior intravenous corticosteroid therapy in the form of a bolus of methylprednisolone. Cyclophosphamide was administered in 3 patients and other immunosuppressants such as azathioprine and mycophenolatemofetil were administered in 3 patients as well. Five cases of death were recorded, i.e. 20.83% of cases. All the cases of death were pictures of renal insufficiency with ion disorder and hemodynamic failure.

Discussion

SLE is a systemic disease that affects more women, nine women for one man according to the Reference Center for rare systemic autoimmune diseases in the East and South-West of France (Reference Center for Autoimmune.[8] It is the imputability of estrogens that has been evoked in view of this high prevalence of the disease in young women and the notion of flare-ups during pregnancy, postpartum, and when taking the estrogen-progestogen pill. SLE is therefore rare in males. In our series, we recorded 24 cases out of all patients followed at CHUL since 2016.

The average age of our patients was 29.33 years. This average age is that found in the French series (30 years)[3] is less. In the Maghreb series, the age at diagnosis seems a little older: 40 years for the Moroccan series,[6] 34 years and 33.4 years for the Tunisian series.[9] The insidious onset mode in the majority of our patients (20/24) was also found in the Tunisian series (17/21).[9]

The clinical manifestations during SLE are variable in their expression and duration. They are variously associated from one patient to another and over time in the same patient. Each clinical sign can be the first sign of lupus.[10] Thus, in our series the hematological manifestations were found to be the majority up to 70.83%. This result is consistent with other studies, in particular that of Barakat et al in Morocco, which found hematological involvement in 56% of cases[6] and that of Sayhi in Tunisia (50% of cases). Other damage was found in the majority by different teams: joint damage (95%) was by a Tunisian team in 2018[11] and general signs, i.e. 61.9% of cases, by another Tunisian team in 2019.[9] The most common hematological abnormality in our series was anemia (88.23%) although the cause was not always sought. In the African context, this cause can be inflammatory, haemolytic, iron deficient and secondary to chronic renal failure.[12] The Coombs test to determine the haemolytic origin was performed in only 3 cases and was positive in 100% of cases. The Moroccan series found hemolytic anemia in half of the anemia cases. Lymphopenia was the hematological manifestation found in the greatest proportion by the Kefi (49.6%)[9] and Keita (15/25 cases).[4]

Renal involvement was also significant in our series (16/24 cases). This agrees with the data from other studies: 16/21.[11] For lack of anatomopathological analysis, the precision on the nephropathy had not been made. However, 11 cases of nephrotic syndrome and 8 cases of renal failure were noted, 2 of which required hemodialysis which not only suggests a particularly severe renal expression of the disease.

The less frequent cutaneous manifestations in our series are consistent with the French series.[3] They were higher in the Maghreb studies: 55% and 71%.[6,11]

In our series, antinuclear autoantibodies were produced in 17 out of 24 of our patients and were positive in 16. Native anti-DNA antibodies were positive in 9 of these patients. This may suggest a strong immunological expression of the disease in the male subject, but the immunological assessment in Africa is very expensive and therefore not accessible to all patients, which may explain the lack of these data in several African studies. However, our data agree with the results of Keita's team, which found positive anti-nuclear antibodies in 22/25 patients and native anti-DNA antibodies were positive in 18 patients.[4]

All our patients had received oral corticosteroid therapy and hydroxychloroquine with recourse to solumedrol boli in 13 cases. This treatment was associated or not with the administration of another immunosuppressant depending on the clinical context. These immunosuppressants were either cyclophosphamide, azathioprine, or mycophenolatemofetil. This support is similar to that received by the patients recruited in the other studies.[4,11] None of our patients received biotherapy. Five cases of death were recorded during the follow-up of our patients. This result is consistent with the Tunisian study by Kefi, which also found 5 cases of death in a series of 21 patients.[9] Deaths were lower in other series: 3/44 by the Morocco team[6] Sayhi team[11] and Keita.[4]

Conclusion

SLE is a rare disease in men with clinical manifestations as diverse as in women. Our series showed a predominance of hematological and renal signs as well as high mortality. Improving the management of these patients requires a better knowledge of these clinicobiological particularities.

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Conflict of Interest

The authors have no conflict of interest to declare.

Abbreviations

ACR: American College of Rheumatology**;**
CHUL: Libreville University Hospital Center;
DNA: DeoxyriboNucleic Acid**;**
SLE: Systemic Lupus Erythematosus**;**
SLE: Systemic Lupus Erythematosus

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