

Research Article

Anatomoclinical Aspects and Progression of Lupus Nephritis in African Patients**Mbengue M¹, Faye M¹, Lemrabott AT¹, Cissé MM¹, Fall K¹, Keita A¹, Faye MO¹, Ba B¹, Diagne S¹, Keita N¹, Ba MA¹, Dieng A¹, Niang A¹, Diouf B¹, Ka EF¹**¹Department of Nephrology, Aristide Le Dantec University Hospital, Dakar, Senegal, 30, Avenue Pasteur, BP: 3001, Dakar, Senegal**Corresponding author:* Mansour Mbengue, Department of Nephrology, Aristide Le Dantec University Hospital, BP: 3001, Dakar, Senegal; Tel: 00221 77 444 32 75; Email: mansourmbengue92@gmail.com*Received Date:* 02-08-2019*Accepted Date:* 03-08-2019*Published Date:* 03-11-2019*Copyright:* © 2019 Mansour Mbengue**Abstract****Introduction:** Renal damage is one of the most severe manifestations of systemic lupus erythematosus, and affects 40-60% of patients. We conducted this study to evaluate the epidemiological, clinical, paraclinical and progression aspects of lupus nephritis in African patients.**Patients and Method:** This was a retrospective and descriptive study, conducted over a 10-year period from January 1, 2007 to December 31, 2016, in the nephrology department of Aristide Le Dantec Hospital. Patients with lupus nephritis were included. The studied parameters were epidemiological, clinical, paraclinical and progression.**Results:** In a total of 93 black patients with lupus, there were 64 cases of lupus nephritis, a prevalence of 69%. The mean age of the patients was 31.97 ± 10.44 years old. There were 81% women and 19% men, a sex ratio of 0.23. Hypertension was found in 34.3% of patients. Renal failure was present in 34.5% of patients. Nephrotic syndrome was found in 71.90% of cases. Class III was found in 24 (37.5%) patients, class IV in 20 (31.25%) patients, class V in 15 (23.4%) patients, class II in 4 (6.25%) patients and class I in 1 (1.6%) patient. The combination of corticosteroids and immunosuppressants was used in 56.25% of cases. After a follow-up of 6 months, 38.8% of the patients were in complete remission, 42.8% of the patients were resistant and 10.2% of the patients were in end-stage renal disease. The death was observed in 5 patients and the causes were pulmonary embolism, bacterial meningitis and pulmonary tuberculosis and indeterminate in 2 patients.**Conclusion:** the proliferative classes were the most frequent. The risk of progression to chronic renal failure was relatively high. The death was related to thromboembolic and infectious complications.**Keywords:** Renal failure; Nephrotic Syndrome; Immunosuppressants; African**Introduction**

Renal damage is one of the most severe manifestations of systemic lupus erythematosus (SLE). It affects 40 to 60% of patients with SLE [1, 2]. Two previous studies in Senegal reported a hospital prevalence of 56% and 72% [3, 4]. The risk of progression to end-stage renal disease is relatively low in all randomized studies published in recent years, estimated at less than 10% of patients after a follow-up of 5 to 10 years [5]. However, broader epidemiological studies

reveal a greater risk when one approaches the usual clinical practice, ranging from 19% in the Caucasian subject to 69% in the black subject [5]. As for the vital prognosis of lupus patients, it is strongly influenced by the existence or not of lupus nephritis. In a large European cohort [6], it was thus shown that the overall survival, measured at 10 years of the discovery of lupus, was 94% for patients without lupus nephritis against 88% for those who entered the disease with lupus nephritis [7]. Since the last studies on lupus nephritis in Senegal dating back ten years, there is a generalization of renal biopsy puncture and the use of immunosuppressant's, hence the need for a reevaluation of the lupus nephritis in Senegal. We conducted this study with the aim of determining the epidemiological, clinical, paraclinical, therapeutic and progression aspects of lupus nephritis.

Patients and Method

This was a retrospective, descriptive study conducted over a 10-year period from January 1, 2007 to December 31, 2016, in the nephrology department of Aristide Le Dantec University Hospital in Dakar. All patients with lupus nephritis were included. The diagnosis of lupus nephritis was retained in the presence of concordant renal biopsy with proteinuria greater than 0.5 g / 24h or active urinary sediment [8]. For each selected patient, epidemiological, clinical, biological, histological, therapeutic and evolutionary data were studied. The glomerular filtration rate was estimated according to the MDRD (The Modification of Diet in Renal Disease) formula. Histological lesions were established on the basis of the ISN / RSP classification of 2003. The evolutionary modalities were recorded after a follow-up of 6 months. Partial or complete remission, relapse and resistance were defined according to the 2012 EULAR / ERA / EDTA criteria [9]. The collected data were entered into "The sphinx" version 5.1.0.2.

Results

In a total of 93 black patients with lupus, there were 64 cases of lupus nephritis, a prevalence of 69%. The mean age of the patients was 31.97 ± 10.44 years. There were 52 (81%) women and 12 (19%) men, a sex ratio of 0.23. Edema was the main reason for consultation, found in 57.68% of cases. Oliguria was found in 2 patients and anuria in 1 patient. Hypertension was found in 34.37% of patients (Table 1).

Table 1: Renal Signs of Lupus Nephritis

Renal signs	Absolute frequency (N=64)	Percentages (%)
Edema	49	76.5
Oliguria	2	3.2
Anuria	1	1.6
Macroscopic hematuria	1	1.6
Proteinuria	60	93.7
Microscopic Hematuria	29	45.3
Leukocyturia	15	23.4
Systolic hypertension	22	34.3
Diastolic hypertension	17	26.5

The most extrarenal signs were alopecia in 26.5% of cases and malar erythema in 26.5% of cases, polyarthralgia in 42.2% of cases. Mean serum creatinine was $19.27 \text{ mg / L} \pm 20.72$ and renal failure was present in 34.5% of patients. mean serum protein was $55.65 \text{ g / l} \pm 11.8$ and the mean serum albumin was $24.65 \text{ g / l} \pm 22.09$. The mean proteinuria was $3.99 \text{ g / 24h} \pm 3.09$. Nephrotic syndrome was found in 71.90% of cases and was impure in 69.56% (Table 2).

Table 2: The Main Nephrological Syndromes

Nephrological syndromes	Absolute frequency (N=64)	Percentages (%)
Chronic glomerulonephritis syndrome at stage chronic renal failure	2	3.1
Glomerulonephritis rapidly progressive	1	1.6
Isolated non-nephrotic proteinuria	12	18.8
Acute nephritic syndrome	3	4.7
Nephrotic syndrome	46	71.9
Total	64	100.0

The complement was dosed in 11 patients and C3 and CH50 hypocomplementemia were noted in 2 patients and the C4 fraction was normal in all patients. Antinuclear antibodies (ANA) were dosed in 15 patients and positive in all patients. Anti-ENA were positive in 92.59% of cases and were anti-Sm in 72% of cases (Table 4). Native anti-DNA antibodies were positive in 43.47% of cases. Anti-Neutrophil cytoplasmic antibodies (ANCA) were dosed and positive in 2 patients. They were pANCA. The direct Coombs test was performed in 8 patients (12.5%) and was positive in 3 cases. Anticardiolipin, anti-B2 glycoprotein and circulating lupus anticoagulant (ACL) were dosed and positive in one patient. Class III was found in 24 (37.5%) patients, class IV in 20 (31.25%) patients, class V in 15 (23.4%) patients, class II in 4 (6.25%) patients and class I in 1 (1.6%) patients (Figure 1).

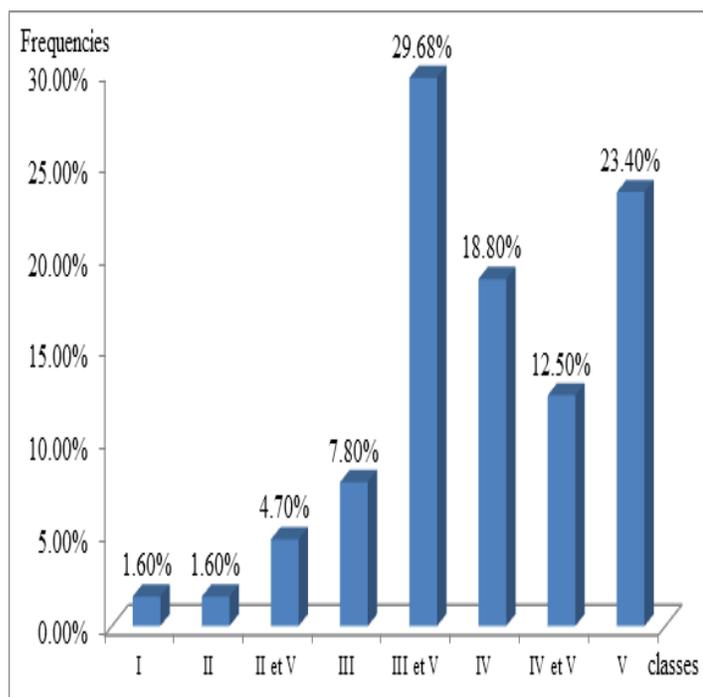


Figure 1: Distribution of Patients according to the Histological Class

The most frequent associated vascular lesions were fibrous endarteritis in 31.3% of cases and arteriosclerosis in 23.4% of cases. The most frequent associated tubulointerstitial lesions were interstitial fibrosis in 43.8% of cases, tubular atrophy in 31.25% of cases and interstitial lymphocyte infiltration in 28.1% of cases. In the induction treat-

ment of patients with proliferative lupus nephritis, cyclophosphamide was used in 19 cases, mycophenolate mofetil in 10 cases and azathioprine in 3 cases. This immunosuppressive treatment was associated with steroids in all cases. In patients with pure class V, cyclophosphamide combined with corticosteroid therapy was used in 4 cases. The other patients received steroids alone. Hydroxychloroquine was used in all patients. After a follow-up of 6 months, there were 15 lost to follow-up, 38.8% of patients were in complete remission, 18.4% of patients were in partial remission, 42.8% of patients were resistant to treatment and relapse were found in 2% of cases (Figure 2).

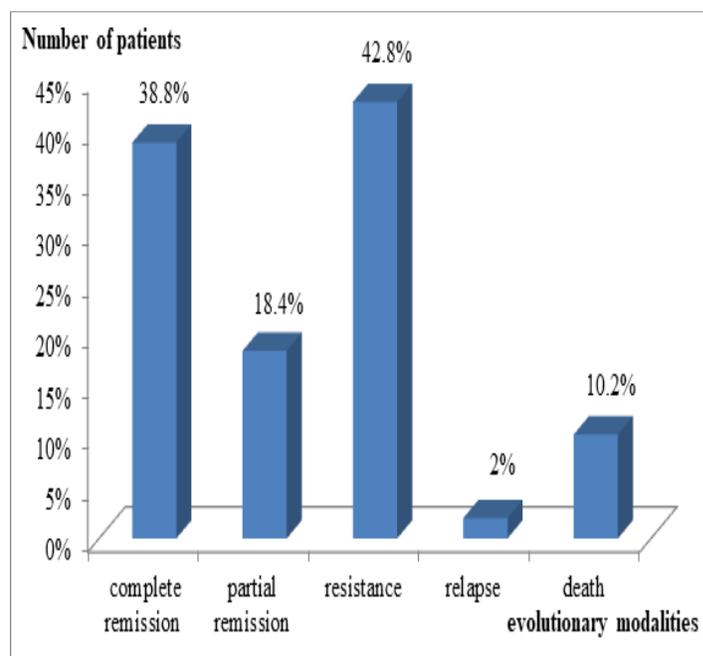


Figure 2: Distribution of Patients according to the Evolutionary Modalities.

End-stage renal disease was found in 10.2 % of patients. Death was observed in 5 patients and the causes were pulmonary embolism, bacterial meningitis and pulmonary tuberculosis and indeterminate in 2 patients.

Discussion

The prevalence of lupus nephritis in our series was 69%. In the literature, it varies from 50 to 80%. In an earlier study in Senegal, it was 72% [3]. In our series, hypertension was observed in 34.37% of patients. In the literature, the frequency of hypertension varies from 20 to 30% in studies performed in black patients [3,10] and from 50 to 70% in

studies performed in caucasian [11,12,13]. Based on these results, it was found that the prevalence of hypertension in our study was similar to that of other studies in black patients and was lower than of studies in caucasian. This fact deserves a reflexion because hypertension in general and particularly in patients with glomerulopathy, is more common in black because of the genetic predisposition related to the presence of a polymorphism of the gene Apol 1 which codes for the apolipoprotein 1 [14]. Further studies are needed to answer this question.

Mean serum creatinine was 19.27 mg / l in our series. This result was similar to results of Ka [3] and Okpechi [10], which were respectively equal to 21 and 20,25mg / l. However, Contreras [11] and Martin-Gomez [12] found lower values that were respectively 14.3 and 13.8 mg / l. Mean serum creatinine in our series was similar to other studies in blacks and was higher than studies in Caucasian patients.

This could be explained by the more severe nature of lupus nephritis in black patients [11]. In fact, other studies performed in the past mentioned this severity in black of lupus and in particular lupus nephritis. This is the case of the study conducted by Contreras in the USA and the LUMINA study (Lupus in Minorities, nature vs nurture) which showed a more severe involvement in black patients. And this would be associated with the presence of the HLA-DRB1 * 1503 (DR2) group in these subjects [11]. In our series nephrotic syndrome was found in 71.90% of cases. Its frequency in the literature varied between 40 to 70% [3, 11, 12, 10].

In our series, proliferative classes were the most common, found in 68.75% of cases, followed by class V found in 23.5% of cases. This distribution was similar to that of the other series, where diffuse proliferative forms are predominant reaching 27 and 53% of cases, classes I and II reach a maximum of 19% and class V varies between 7 and 25% [15,16, 17]. In an earlier study in Senegal, Ka et al found a higher frequency of class V [3]. This difference with our series could be explained by the fact that in the Ka series, biopsy was not performed in all patients.

In our series, the rate of resistance to immunosuppressive therapy was high, found in 42.8% of cases. This high rate of resistance was found by Mokoli, Beji, Tannor and Ka [18,15,19,3]. This could be explained by a delay in

the management, by the lack of therapeutic observance in our patients related to the lack of means, by the high frequency of the proliferative classes which are the most severe [20], and probably by the genetic predisposition with severe forms [11]. The prevalence of end-stage renal disease varies in the literature between 5 and 26% of cases [15]. End-stage renal disease was observed in 10.2% of our patients. The relatively high percentage of end-stage renal disease in our series could be explained by the high frequency of proliferative classes, which are factor of poor renal prognosis [20], by the non-observance of treatment in our patients, by taking of Herbal medicine which is a factor of acceleration of the chronic kidney disease and by the delay diagnosis.

The death rate in our series was 10.2% and was related to infectious and thromboembolic complications. The frequency of death from renal failure has decreased last 30 years from 60 to 10% with an increase in deaths from infectious and cardiovascular complications currently reaching 70% [15]. This is explained on the one hand by a better management of the renal insufficiency and on the other hand by the generalization of the immunosuppressive treatment which is associated important infectious complications.

Conclusion

The proliferative classes were the most frequent. The rate of resistance to treatment was high. The risk of progression to end-stage renal disease was relatively high. Death was related to thromboembolic and infectious complications.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Ethical statement

The local ethics committee approved the study.

Informed consent

This research involve human participant, they have signed the informed consent.

References

1. Feldman CH, Hiraki LT, Liu J et al. Epidemiology and socio-demographics of systemic lupus erythematosus and lupus nephritis among US adults with medicaid coverage,

- 2000–2004. *Arthritis Rheum.* 2013; 65:753–63.
2. Seligman VA, Lum RF, Olson JL et al. Demographic differences in the development of lupus nephritis: a retrospective analysis. *Am J Med.* 2002; 112 (9): 726–9.
 3. Ka E.F, Cisse M.M, Lemrabott A.T et al. Néphropathie lupique chez les sujets génétiquement pigmentés vivant au Sénégal : à propos de quarante-trois cas. *Med Sante Trop.* 2013; 23:328-331.
 4. Niang A, Ka EF, Dia D, Pouye A, et al. Lupus Nephritis in Senegal: A study of 42 cases. *Saudi J Kidney Dis Transpl.* 2008;19: 470-4.
 5. Adler M, Chambers S, Edwards C et al. An assessment of renal failure in an SLE cohort with special reference to ethnicity, over a 25-year period. *Rheumatology (Oxford).* 2006;45:1144–7.
 6. Cervera R, Khamashta MA, Font J et al. Morbidity and mortality in systemic lupus erythematosus during a 10-year-period: a comparison of early and late manifestations in a cohort of 1000 patients. *Medicine (Baltimore).* 2003; 82:299–308.
 7. Mok CC, Kwok RC, Yip PS. Effect of renal disease on the standardized mortality ratio and life expectancy of patients with systemic lupus erythematosus. *Arthritis Rheum.* 2013; 65(8): 2154–60.
 8. Hahn BH, McMahon MA, Wilkinson A et al. American College of Rheumatology guidelines for screening, treatment, and management of lupus nephritis. *Arthritis Care Res.* 2012; 64:797–808.
 9. Bertsias GK, Tektonidou M, Amoura Z et al. Joint European League Against Rheumatism and European Renal Association–European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of adult and paediatric lupus nephritis. *Ann Rheum Dis.* 2012; 71:1771–1782.
 10. Okpechi IG, Swanepoel N, Tiffin N et al. Clinicopathological insights into lupus nephritis in South Africans: a study of 251 patients. *Lupus.* 2012; 21(9):1017–1024.
 11. Contreras G, Lenz O, Pardo V et al. Outcomes in African Americans and Hispanics with lupus nephritis. *kidney Int.* 2006; 69 (10) :1846–1851.
 12. Martin-Gomez MA, Frutos Sanz MA, De Ramon Garrido E et al. Malaga Study: 25 Year Background in Lupus Nephritis in South of Spain. *Lupus Open Access.* 2016; 1:103.
 13. Aoudia R, Omrane M, Gaied H et al. Profil histologique et évolutif de l’hypertension artérielle chez les patients atteints d’une néphropathie lupique. *Néph-Thér.* 2017;13: 296–310.
 14. Larsen CP, Beggs ML, Saeed M, et al. Apolipoprotein L1 risk variants associate with systemic lupus erythematosus-associated collapsing glomerulopathy. *J Am Soc Nephrol.* 2013; 24:722–5.
 15. Béji S, Kaaroud H, Ben Moussa F et al. Néphropathie lupique: à propos de 211 cas. *La Rev Med interne.* 2005; 26: 8–12.
 16. Cervera R, Khamashta MA, Font J, et al. Systemic lupus erythematosus: clinical and immunologic patterns of disease expression in a cohort of 1000 patients. *Medicine (Baltimore).* 1993; 72:113-124.
 17. Le Thi Huong D, Papo T, Beaufils H, et al. Renal involvement in systemic lupus erythematosus: a study of 180 patients from a single center. *Medicine.* 1999; 78:148-66.
 18. Mokoli VM, Sumaili EK, Lepira FB et al. Aspects anatomo-cliniques et évolution des patients suivis pour néphropathie lupique aux Cliniques Universitaires de Kinshasa. *Ann. Afr. Med.* 2009; 2(3).
 19. Tannor EK, WD Bates, MR Moosa et al. The clinical relevance of repeat renal biopsies in the management of lupus nephritis: a South African experience. *Lupus.* 2018 ;27(4):525-535.
 20. Korbet SM, Lewis EJ, Schwartz MM et al. Factors predictive of outcome in severe lupus nephritis. *Am J Kidney Dis.* 2000; 35: 904–14.
-