

CLINICAL AND HISTOPATHOLOGICAL CHARACTERIZATION OF LUPUS NEPHRITIS IN A TERTIARY HEALTH CENTRE, NORTH-EASTERN NIGERIA: REPORT OF FIVE CASES.

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ABSTRACT

Background: Lupus nephritis (LN) is an immune complex glomerulonephritis that complicates up to 40% of SLE patients. A kidney biopsy is required for diagnosis and staging of the disease.

Case report: We report a cohort of five patients with LN from a tertiary health facility in northeastern Nigeria. The five patients were all women with age ranging from 26 to 55 years, and eGFR of between 6 to 154ml/minute. Four patients had normal kidney size and were biopsied whereas 1 patient had contracted kidney. Diffuse proliferative LN (Class IV) was seen in two patients while the other two patients had glomerular sclerosis (Class VI). Patients were given induction with methylprednisolone and mycophenolate mofetil (MMF). At one year follow up 2(40%) patients were in remission, 1(20%) was on maintenance hemodialysis and 2(40%) patients had died. **Conclusion:** Lupus nephritis is a common complication of SLE in northeastern Nigeria. Patients have features of advanced kidney disease at presentation.

Key words: *Histopathologic features, Lupus nephritis, North-eastern Nigeria*

INTRODUCTION

Lupus nephritis (LN) is an immune complex glomerulonephritis that develops as one of the severe organ manifestation of systemic lupus erythematosus (SLE) with ample morbidity and mortality. The pathogenesis is complex and involves immunological, environmental and genetic factors.¹ SLE predominantly affects women of childbearing age, with a female to male ratio of 8:1 to 15:1; the incidence and prevalence of LN is, however, variable.^{2,3} The disease occurs in 40 -75% of patients with SLE usually within five years of disease onset and can be an initial manifestation of SLE in most cases.² SLE patients that are most likely

to develop LN are of younger age, males and black, Hispanic or of Asian ethnicity. Studies have shown that 60% of black SLE patients develop LN, with 25-50% having LN as an initial manifestation of SLE.⁴

The clinical presentation of LN is variable with most patients presenting with mild proteinuria and haematuria. Some patients will present with 'silent' LN (normal renal function and urinalysis), severe proteinuria (nephrotic syndrome), acute nephritic syndrome and/or acute kidney failure. Renal involvement in SLE is defined by persistent proteinuria (more than 0.5 g of protein per day, 3+ on dipstick or a urinary protein to creatinine ratio or 24h urinary protein excretion corresponding to 0.5 g daily) or the presence of cellular casts (either red blood cell, haemoglobin, granular, tubular or mixed) in urinary sediment.^{5,6}

Definitive diagnosis of LN is by kidney biopsy in which, LN is categorized into various histological

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patterns. The histological classification has evolved from the 1982 World Health Organization (WHO) classification to the 2003 International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification class.^{7, 8} Renal biopsy not only diagnoses LN, but also determines levels of activity, predicts prognosis and guides treatment protocols.^{9,10} All compartments of the kidney are affected in SLE-associated renal disease giving rise to a wide range of morphological changes which includes, mesangial or endocapillary proliferation, tubulointerstitial nephritis and thrombosis or necrotizing arteritis.⁹

In a series of 79 LN patients seen in Jordan, the commonest presentations were asymptomatic proteinuria and haematuria accounting for 59.5%, followed by nephrotic syndrome (22.8%) and nephritic syndrome (17.7%).¹¹ The most common histopathological types of LN were class IV (46.8%), class V (19.0%) and class III (12.7%).² Few cases of overlapping patterns have also been reported.⁹⁻¹¹

Diagnosis of LN in developing countries is challenging due to delay in patients' presentation, lack of reliability of clinical features alone, difficulties performing biopsies, poor correlation between histopathologic and clinical features of the disease; and where biopsies are performed, there are difficulties in differentiating LN from overlapping conditions such as thrombotic microangiopathy, non-steroidal anti-inflammatory drugs (NSAIDs) interstitial nephritis, focal segmental glomerulosclerosis from other causes, and IgA nephropathy.¹²

Despite the reports on the increased disease severity of LN among Blacks and African Americans, there are few reports of biopsy-proven lupus nephritis in Nigeria. In addition, the role of genetics in the pathogenesis of LN in black Africans and the clinical outcomes of the diseases are largely underreported.^{13,14} A systematic review conducted on the standard of treatment and outcomes of LN in Africa revealed that only 18.8% used recent criteria to report renal histopathology and more than 90% used cyclophosphamide (CYC) for induction therapy, highlighting the diagnostic challenges in LN in Africa.

We report the clinical and renal histopathologic findings in five patients managed for LN in UMTH Maiduguri, Nigeria.

RESULTS

All the five cases were females with a mean age of 34 ± 11.9 years, referred to renal clinic University of Maiduguri Teaching Hospital from July to October 2020, and the median duration of disease before presentation was 8 months IQR (3 - 18). Three (60%) had a clinical diagnosis of chronic glomerulonephritis and 4 (80%) were hypertensive at presentation. They all had positive ANA with a median eGFR of 28ml/min IQR (10 - 95) and normal kidney sizes. Two (40%) were in class IV, and one (20%) was in class V, the remainder were in end-stage (class VI). Two (40%) died during treatment of which one was in Class IV and the other in class V. (Table 1)

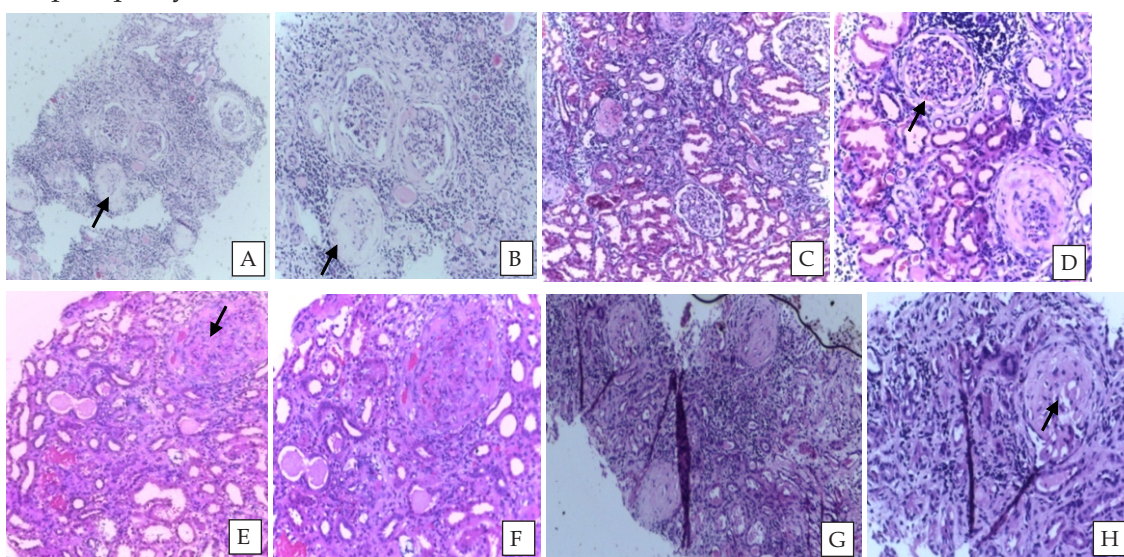


Figure 1: Photomicrographs of the four cases of LN; A, B and C, D show class IV LN with glomerulosclerosis (black arrows); E, F is class V LN and G, H shows class VI LN; H and E x100 and x200 each respectively.

Table1: Clinical and laboratory characteristics of patients with Lupus nephritis

| Characteristics | Cases | | | | | Mean±SD/ median (IQR) |
|-------------------------------|--------------------------|--------------------------|---------------|-------------------|-------------------|--------------------------|
| | 1 | 2 | 3 | 4 | 5 | |
| Age (years) | 30 | 26 | 55 | 28 | 31 | 34±11.9 |
| Sex | F | F | F | F | F | |
| Duration of symptoms (months) | 4 | 2 | 12 | 24 | 8 | 8.0 (3-18) |
| Clinical Diagnosis | CGN | NS | CGN | NS | CGN | |
| Hypertension | Yes | No | Yes | Yes | Yes | |
| PCV (%) | 24 | 31 | 34 | 26 | 33 | 29±4.3 |
| ESR (mm/Hour) | 43 | 127 | 55 | 84 | 39 | 55.0 (41-105) |
| ANA | Positive | Positive | Positive | Positive | Positive | |
| Total Protein(g/dl) | 70 | 46 | 64 | 55 | 60 | 59±9.11 |
| Albumin (g/dl) | 12 | 14 | 21 | 18 | 26 | 18.2±5.6 |
| Creatinine (µmol/l) | 840 | 45 | 159 | 230 | 400 | 230.0 (102-620) |
| Urea(mmol/l) | 30 | 2.6 | 8.8 | 10.1 | 15.4 | 10.1 (5.7-22.7) |
| Proteinuria | 3+ | 2+ | 2+ | 3+ | 2+ | |
| Haematuria | 1+ | 2+ | 1+ | 2+ | 2+ | |
| eGFR | 6 | 154 | 36 | 28 | 14 | 28.0 (10-95) |
| ISN/RPS | IV | IV | N/A | VI | VI | |
| Kidney size (cm) | 11.9 | 10.4 | 8.8 | 10.5 | 9.7 | 10.2±1.1 |
| Right | | | | | | |
| Left | 11.8 | 9.7 | 8.2 | 10.4 | 10.0 | 10.0±1.3 |
| Induction therapy | MP/MMF | MP/MMF | M P / M MF | M P / M MF | MP/MMF | |
| Histopathologic diagnosis | Diffuse proliferative LN | Diffuse proliferative LN | N/A | Diffuse sclerosis | Diffuse sclerosis | |
| Outcome | Remission | Died | Died | Partial Remission | Dialysis | |

NB: TIN=Tubulointerstitial nephritis, ESRD=End stage renal disease, MPGN=Membranoproliferative glomerulonephritis, N/A= Not available.

Tables 2: Histopathological findings among patients with lupus nephritis

| Type of lesion | Number of patients (n=4) | Percentage (%) |
|---------------------------|--------------------------|----------------|
| No of glomeruli | | |
| >10 | 2 | 40 |
| <10 | 2 | 40 |
| Glomerular sclerosis | 2 | 40 |
| MPGN | 2 | 40 |
| Tubular dilatation | 4 | 90 |
| Interstitial fibrosis | 3 | 60 |
| Interstitial inflammation | 3 | 60 |
| Vascular changes | 1 | 20 |

DISCUSSION

This case series is the first reported biopsy confirmed LN in northeastern Nigeria and it showed that LN is common in our region. Our reported cases presented with advanced stages of kidney disease probably due to delayed diagnosis. This report highlights the need for an enhanced index of suspicion among health care providers as well as increased awareness of the inherent dangers of LN and SLE. Lupus nephritis can smoulder without symptoms in many SLE patients.¹⁶ Kidney biopsy is needed to provide accurate diagnosis and prognosis of kidney involvement in SLE patients.¹⁷

Lupus nephritis is the most feared complication of systemic lupus erythematosus. The contribution of SLE to the burden of end-stage renal disease in Nigeria is becoming more apparent. However, challenges remain due to the non-availability of diagnostic tests in many centres and the long turnaround time for the results of diagnostic investigations to become available. Patients are often diagnosed late because they usually spend time seeking care from traditional healers. This has resulted in a delay in the initiation of essential life-saving disease-modifying treatment. Our patient cohort had a mean duration of symptoms of 8 months with a range between 2 to 24 months. This is similar to the study reported by Adelowo *et al*¹⁴ and Umezudike *et al*¹⁵ in southern Nigeria.

Lupus nephritis predominantly affects women in their reproductive age with female: male ratio between 10-15:1. Males often lack typical features of SLE and coupled with lack of suspicion, many cases tend to be misdiagnosed. All our reported cases were females.

Our patients had a mean age of 30.0±11.9 years similar to findings by Adelowo *et al*¹⁵ whose patient cohort had a mean age of 30.4 years.

Nephrotic syndrome is a common clinical presentation of lupus nephritis especially among women of childbearing age. Other workers also reported that nephrotic syndrome is the commonest presentation of lupus nephritis.¹⁴⁻¹⁶ Our patients presented with a clinical diagnosis of CGN whereas 40% presented with features of nephritic syndrome. The majority of our patients have been diagnosed with hypertension. This is consistent with the histologic class they presented with at the time of diagnosis. Patients with class III, IV and VI usually have hypertension.

Diffuse proliferative lupus nephritis (RPS/ISN stage IV) is the commonest histologic abnormality seen from biopsy of LN patients and requires aggressive treatment with immunosuppressive drugs. Half of our patients had diffuse proliferative LN.

The management and prognosis of LN is determined by the underlying histopathologic stage and the extent of interstitial fibrosis. All our patients were treated with corticosteroids and MMF as induction therapy to avoid the side effects of cyclophosphamide therapy in childbearing young women. This contrast with the report by Ameh *et al*¹³ which showed that corticosteroid/cyclophosphamide combination was the most common drug combination used in lupus nephritis in Africa.

Two (40%) of our patients died; one from complications of COVID-19 and the second from pulmonary embolism. The mortality rate in lupus nephritis was shown to range between 7.9-34.9% among African patients.¹⁹ Infections, cardiopulmonary involvement, and neurologic complications have been reported as the commonest causes of death in lupus patients.²⁰

Our study is limited by the lack of immunofluorescence study of the biopsy specimen to define type and pattern of complement factor and antibody deposition in the kidneys. Assay of anti-double stranded DNA was not done due to its non-availability in our centre.

CONCLUSION

Lupus nephritis is a common complication of SLE among patients in northeastern Nigeria. We reported five patients with biopsy-confirmed lupus nephritis and their outcome will be improved with early diagnosis and prompt institution of immunosuppressive treatment.

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