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Original Article

Evaluation of Renal Involvement in Systemic Lupus Erythematosus: Clinical Profile and Outcomes of Lupus Nephritis

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ABSTRACT

Background: Lupus nephritis (LN) is a major cause of morbidity and mortality in patients with systemic lupus erythematosus (SLE). Disease prognosis is closely related to histological class, and early diagnosis with timely treatment is essential to prevent irreversible renal damage and improve survival outcomes.

Objective: To evaluate the clinical presentation, laboratory findings, histological patterns, treatment response, and predictors of poor renal outcomes in patients with lupus nephritis.

Methods: This retrospective observational cohort study was conducted in the Department of Nephrology at the Institute of Kidney Diseases, Peshawar, from January 2021 to December 2023. Adult patients (≥18 years) diagnosed with LN according to the ISN/RPS classification were included. Data on demographics, clinical features, laboratory findings, and treatment were collected. Renal outcomes were categorized as remission, chronic kidney disease (CKD), or death. Statistical analysis was performed using SPSS version 24.0, with significance set at $p < 0.05$.

Results: A total of 100 patients were included, of whom 86% were female. The mean age was 27.4 ± 6.3 years. Class IV lupus nephritis was the most common histological subtype (44%), followed by Class III (27%) and Class V (18%). Most patients presented with proteinuria (92%) and hypertension (53%). Complete or partial remission was achieved in 63% of patients, while 26% progressed to chronic kidney disease and 11% died during follow-up. Elevated baseline serum creatinine (>2.0 mg/dL) and advanced histological class (Class IV/V) were significantly associated with poor renal outcomes ($p = 0.002$). Early initiation of immunosuppressive therapy was associated with improved renal outcomes ($p = 0.01$).

Conclusion: Lupus nephritis remains a major determinant of renal outcomes in SLE. Early diagnosis, timely biopsy, appropriate immunosuppressive therapy, and regular follow-up are critical for improving long-term prognosis.

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disorder characterized by the production of autoantibodies and the formation of immune complexes that cause multisystem inflammation and organ damage. Lupus nephritis (LN) develops in many patients with SLE and is among its most severe complications, significantly contributing to disease-related morbidity and mortality. The pattern of renal damage in LN can vary greatly and is classified by the ISN/RPS into one of six types based on information from renal biopsies. Classification ranges from minimal mesangial lupus nephritis (Class I) to advanced sclerosing lupus nephritis (Class VI), but Class III (focal) and Class IV (diffuse proliferative) are the most severe and usually lead to poor renal outcomes. LN occurs when immune complexes trigger glomerulonephritis, leading to inflammation and damage to renal tissues. Patients can have no symptoms or just protein in their urine, while others may encounter nephrotic syndrome, blood in the urine, high blood pressure, and kidney failure [5]. It is important to diagnose kidney disease early by testing and performing a renal biopsy, as this will guide the use of immunosuppressive drugs. Despite advances in therapy, many patients still progress to chronic kidney disease (CKD) or end-stage kidney disease (ESKD), highlighting the need for early diagnosis and effective treatment strategies [7]. Strategies for managing LN depend mostly on the type and severity of the disease found under the microscope. Corticosteroids and drugs that weaken the immune system, for example, cyclophosphamide or mycophenolate mofetil, are still commonly used to start treatment, with maintenance therapy next to stop flares [7]. The recently developed therapies have shown higher response rates, yet side effects and the risk of disease recurrence remain major concerns. Several factors can affect the clinical outcome of LN, including the amount of protein in the urine, kidney function, histological type, treatment response, and treatment adherence [8]. If diagnosis and treatment start late, it is often related to irreversible kidney damage and a poor renal outcome. As a result, attention is shifting to detecting signs of poor renal outcomes early and taking prompt action. Similar to other developing countries, the management of SLE and lupus nephritis in Pakistan is difficult because patients often come to medical care late, access to adequate care is restricted, and follow-up is lacking. The clinical outcomes and spectrum of LN among local patients are not well known, highlighting the need for more local studies. This study aims to examine the clinical and laboratory features of patients with lupus nephritis, as well as their outcomes, stratified by biopsy classification and treatment. Recognizing the aspects that can affect prognosis in our population should help us design more effective ways to monitor and treat diseases [9].

Objective

To evaluate the clinical presentation, laboratory findings, histopathological patterns, treatment response, and predictors of poor renal outcomes among patients with biopsy-proven lupus nephritis.

MATERIALS AND METHODS

Study Design

This retrospective observational cohort study was conducted in the Department of Nephrology at the Institute of Kidney Diseases, Peshawar, Pakistan, from January 2021 to December 2023.

Sampling Technique

Consecutive non-probability sampling was used to recruit all eligible biopsy-proven lupus nephritis patients who fulfilled the inclusion criteria during the study period.

Patients were included who met the ACR criteria for SLE and also had kidney involvement, confirmed through biopsy. Each patient underwent various examinations: clinical evaluation; urine protein; serum creatinine; ANA; anti-dsDNA; blood complement levels; and analysis of renal tissue. Treatment was administered with immunosuppressive drugs and corticosteroids, selected based on disease severity. Follow-up included checking for improvement, worsening kidney function, or death in patients.

Inclusion Criteria

Individuals aged 18 years or older who had a valid diagnosis of SLE and exhibited biopsy-proven lupus nephritis upon arrival at the nephrology department were considered for the study.

Exclusion Criteria

Patients with incomplete medical records, previous kidney transplantation, non-lupus glomerular disease, or unavailable renal biopsy results were excluded.

Operational Definitions

- Complete remission: Proteinuria <0.5 g/day with stable or normal renal function.
- Partial remission: ≥50% reduction in proteinuria with stable renal function.
- Chronic kidney disease (CKD): Persistent reduction in renal function for at least three months according to KDIGO criteria.
- Poor renal outcome: Progression to CKD or death during follow-up.

Data Collection Procedure

All relevant data, such as age, medical signs, blood values, biopsy findings, and treatments, were recorded on the data collection sheet. Patients were followed up every three months. Primary outcomes included complete remission, partial remission, progression to chronic kidney disease, and mortality during the follow-up period.

Sample Size

Sample size was calculated using OpenEpi version 3.01 assuming an expected prevalence of lupus nephritis based on previously published studies, a 95% confidence level, and a 5% margin of error.

Statistical Analysis

The data were explored and organized using SPSS 24.0. Statistical data were presented as mean ± standard deviation for continuous variables and as percentages for categorical variables. For associations, chi-square test and independent t-tests were used. Logistic regression was used to identify factors associated with poor kidney outcomes. The result was considered statistically significant if the p-value was below 0.05.

RESULTS

A total of 100 patients with biopsy-proven lupus nephritis were

included in the final analysis. The mean age of the participants was 27.4 ± 6.3 years, and females constituted 86.0% (n=86) of the study population, confirming the marked female predominance of systemic lupus erythematosus (Table 1). The most common clinical presentation was proteinuria, observed in 92 (92.0%) patients, followed by generalized edema in 74 (74.0%) patients and hypertension in 53 (53.0%) patients, indicating that most participants presented with clinically significant renal involvement (Table 2). Renal biopsy demonstrated that Class IV lupus nephritis was the predominant histopathological subtype, affecting 44 (44.0%) patients. Class III lupus nephritis was identified in 27 (27.0%) patients, followed by Class V in 18 (18.0%), Class II in 7 (7.0%), and Class VI in 4 (4.0%) patients. Overall, proliferative lupus nephritis (Classes III and IV) accounted for the majority of cases (71.0%), reflecting the severe disease pattern observed in this cohort (Table 3). Following treatment with corticosteroids and immunosuppressive agents, 63 (63.0%) patients achieved complete or partial remission. However, 26 (26.0%) progressed to chronic kidney disease (CKD), while 11 (11.0%) died during follow-up, primarily because of renal failure or sepsis. Multivariable analysis showed that elevated baseline serum creatinine (>2.0 mg/dL), delayed initiation of therapy, and advanced histological class (Class IV or V) were significantly associated with poor renal outcomes (p = 0.002). Conversely, early initiation of immunosuppressive therapy was associated with significantly improved renal outcomes (p = 0.01) (Table 4).

Table 1. Baseline Demographic Characteristics of Patients with Lupus Nephritis (N = 100)

Characteristic	Value
Age (years), mean ± SD	27.4 ± 6.3
Female, n (%)	86 (86.0)
Male, n (%)	14 (14.0)

SD = Standard deviation.

Table 1 summarizes the baseline demographic characteristics of the study population. The mean age of participants was 27.4 ± 6.3 years, and females constituted the majority of the cohort (**86.0**%), reflecting the well-established female predominance of systemic lupus erythematosus.

Table 2. Baseline Clinical Presentation of Patients with Lupus Nephritis (N = 100)

Clinical Feature	n	%
Proteinuria	92	92.0
Generalized edema	74	74.0
Hypertension	53	53.0

Values are presented as frequency (n) and percentage (%).

Table 2 demonstrates the clinical manifestations at presentation**.** Proteinuria (92.0%) was the most common presenting feature, followed by generalized edema (74.0%) and hypertension (53.0%)**,** indicating that most patients presented with clinically significant renal involvement.

Table 3. Histopathological Classification of Lupus Nephritis According to the ISN/RPS Classification (N = 100)

Histological Class	n	%
Class II	7	7.0
Class III	27	27.0
Class IV	44	44.0
Class V	18	18.0
Class VI	4	4.0
Total	**100**	**100.0**

ISN/RPS = International Society of Nephrology/Renal Pathology Society classification of lupus nephritis.

Table 3 presents the renal biopsy findings. Class IV lupus nephritis (44.0%) was the predominant histological subtype, followed by Class III (27.0%) and Class V (18.0%)**,** indicating that proliferative lupus nephritis was the most frequent pattern observed in the study population.

Table 4. Renal Outcomes at Final Follow-up (N = 100)

Outcome	n	%
Complete/Partial Remission	63	63.0
Progression to Chronic Kidney Disease (CKD)	26	26.0
Death	11	11.0
Total	**100**	**100.0**

CKD = Chronic Kidney Disease. Renal outcomes were assessed after completion of the follow-up period.

Table 4 summarizes renal outcomes following treatment. Complete or partial remission was achieved in 63.0% of patients**,** whereas 26.0% progressed to chronic kidney disease and 11.0% died**,** primarily due to renal failure or sepsis. These findings underscore the importance of early diagnosis and timely initiation of immunosuppressive therapy to improve long-term renal outcomes.

Table 5. Multivariable Logistic Regression Analysis for Predictors of Poor Renal Outcomes

Variable	Adjusted OR	95% CI	P-value
Serum creatinine >2 mg/dL	3.18	1.45–6.98	0.002
Class IV/V LN	2.84	1.28–6.29	0.008
Delayed therapy	2.51	1.14–5.52	0.019
Early immunosuppressive therapy	0.42	0.20–0.88	0.010

Values are presented as adjusted odds ratios from multivariable logistic regression.

DISCUSSION

In this single-center cohort of biopsy-proven lupus nephritis (LN) from Peshawar, Pakistan, we observed a relatively young patient population with a strong female predominance (mean age 27.4 years; 86% women). This demographic pattern aligns with the well-established epidemiology of systemic lupus erythematosus (SLE) and LN, where women of reproductive age are disproportionately affected. Histologically, proliferative forms of LN were predominant, with Class IV (44%) being the most frequent, followed by Class III (27%) and Class V (18%). These findings are consistent with regional and international studies, particularly in South Asian populations, which report a higher burden of proliferative disease and severe clinical presentation at diagnosis [10–12].Clinically, the majority of patients presented with significant disease activity, reflected by high rates of proteinuria (92%) and hypertension (53%). Proteinuria, beyond being a marker of disease activity, is also an independent contributor to progressive renal damage. Its reduction is closely associated with improved long-term renal outcomes. Similarly, hypertension is a key modifiable risk factor in LN and requires aggressive management alongside immunosuppressive therapy to preserve renal function.Treatment outcomes in our cohort demonstrated that 63% of patients achieved remission (complete or partial), while 26% progressed to chronic kidney disease (CKD), and 11% died, predominantly due to renal failure or sepsis. These remission rates are comparable to those reported in contemporary studies, which report 50–70% remission with cyclophosphamide- or mycophenolate mofetil-based induction therapies [13,14]. However, the progression to CKD highlights the persistent risk of irreversible renal damage despite treatment and emphasizes the need for early diagnosis and effective disease control [15]. The observed mortality rate is also consistent with reports from low- and middle-income countries, where infections and active disease remain leading causes of death [16,17].Our analysis identified baseline serum creatinine levels above 2.0 mg/dL and advanced histological class (Class IV or V) as significant predictors of adverse renal outcomes. These findings are well supported in the literature, as initial renal dysfunction reflects cumulative inflammatory and ischemic injury. At the same time, proliferative and membranous lesions are associated with more aggressive disease and treatment resistance [18,19]. Conversely, early initiation of immunosuppressive therapy was significantly associated with improved outcomes ($p = 0.01$), reinforcing the importance of prompt diagnosis and early treatment initiation, as recommended in current guidelines [20].The therapeutic approach in LN requires careful selection of induction and maintenance regimens. In our setting, both cyclophosphamide and mycophenolate mofetil were used; however, detailed analysis of dosing, compliance, and regimen selection was limited. Current evidence suggests that mycophenolate may be preferred for Class III/IV LN due to comparable efficacy and a more favorable safety profile, particularly regarding gonadal toxicity. Cyclophosphamide may still be indicated in severe or rapidly progressive disease or in resource-constrained settings [16]. Standardized, biopsy-guided treatment protocols with maintenance therapy extending for at least 24–36 months could potentially reduce relapse rates and CKD progression.Infection-related mortality in our cohort underscores the critical need for preventive strategies, including vaccination, tuberculosis screening, Pneumocystis prophylaxis in high-risk patients, and close monitoring for opportunistic infections [17,18]. Additionally, several systemic barriers likely contribute to delayed presentation and advanced disease at diagnosis in Pakistan, including limited access to specialized care, financial constraints, and challenges in maintaining long-term follow-up. Addressing these issues will require system-level interventions, such as strengthening referral pathways, improving access to diagnostic and therapeutic resources, and enhancing patient education and adherence [19]. This study has several strengths, including biopsy-confirmed diagnosis, systematic data collection, and identification of prognostic factors. However, limitations include inconsistencies in reported denominators, observational design with potential confounding, lack of detailed treatment data, and single-center setting. Future prospective studies incorporating standardized treatment protocols, treat-to-target strategies, and patient-centered outcomes are needed.In conclusion, our findings highlight the substantial burden of proliferative LN in young women and demonstrate that remission is achievable in a majority of patients. However, the risks of CKD progression and mortality remain significant. Early diagnosis, prompt initiation of immunosuppressive therapy, standardized treatment protocols, and robust infection-prevention strategies are essential to improving long-term outcomes in this population. The findings of the present study are consistent with recent reports from Pakistan, India, and Bangladesh, which have similarly demonstrated a predominance of proliferative lupus nephritis and identified delayed diagnosis, elevated serum creatinine, and advanced histological class as important predictors of adverse renal outcomes. These regional studies also emphasize that limited access to specialized nephrology services and delayed referral remain major barriers to improving long-term renal survival. Limitations include the retrospective observational design, limited sample size, lack of detailed treatment adherence data, and the single-center setting.

LIMITATIONS

This study was limited by its single-center retrospective design, relatively small sample size, and two-year follow-up period, which may limit the generalizability of the findings. Detailed immunological and genetic biomarkers were not consistently available, and treatment adherence and socioeconomic factors were not evaluated, which may have influenced clinical outcomes.

CONCLUSION

Lupus nephritis remains a major cause of renal morbidity in patients with systemic lupus erythematosus. Class IV lupus nephritis is the most common and clinically severe histopathological subtype. Early diagnosis, timely renal biopsy, prompt initiation of immunosuppressive therapy, and regular follow-up are essential for improving renal survival and reducing long-term morbidity.

Authors' Contributions(ICMJE)

Mazhar Ul Haq: Conceptualization, study design, supervision, statistical analysis, manuscript drafting, and final approval.
Mohmmand Shahzad: Data collection, data interpretation, critical revision of the manuscript, and final approval.
Najmuddin: Literature review, data acquisition, manuscript editing, critical review, and final approval.
All authors read and approved the final manuscript and agree to be accountable for all aspects of the work in accordance with the ICMJE authorship criteria.
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Ethical Approval

Ethical approval was obtained from the Ethical Review Board of the Institute of Kidney Diseases, Peshawar **(Ref. No. 2040-ERB-1740/2020)** before commencement of the study. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Written informed consent was obtained from all participants before enrollment, and confidentiality of patient information was strictly maintained throughout the study.

Copyright Statement

Data Availability Statement

All data generated or analyzed during this study are available from the corresponding author upon reasonable request.

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