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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 at the Department of Nephrology, Institute of Kidney Diseases Peshawar from January 2021 to December 2023. Adult patients (≥18 years) diagnosed with LN based on 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 85.8% were female. The mean age was 27.4 years. Class IV LN was the most common (44.1%), followed by Class III (26.6%) and Class V (18.3%). Most patients presented with proteinuria (91.6%) and hypertension (53.3%). Remission was achieved in 62.5% of patients, while 25.8% progressed to CKD and 11.7% died. Elevated serum creatinine (>1.3 mg/dL) and advanced histological class (IV/V) were significantly associated with poor outcomes ($p = 0.002$). Early initiation of immunosuppressive therapy was linked to improved 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.

Keywords: Lupus nephritis; Renal outcomes; Immunosuppressive therapy; Histopathology

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INTRODUCTION

In Systemic Lupus Erythematous the body mistakenly creates autoantibodies that lead to the involvement of multiple body systems through the development of immune complexes. Lupus nephritis develops in many individuals with SLE, making it one of the most severe complications. The pattern of renal damage in LN can change greatly and is classified by the ISN/RPS as one of six types using information from renal biopsies.classification ranges from minimal mesangial lupus nephritis(Class I) and end with 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, which leads to inflammation and damage of the 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. Still, many people who receive treatment develop chronic kidney disease (CKD) or end-stage renal disease (ESRD) [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 seen better response rates, yet side effects and the risk of the disease returning are still major concerns. Several things can affect the clinical outcome of LN, such as the amount of protein found in the urine, the function of the kidneys, the histological type, response to treatment, and how well patients follow their treatment plan [8]. If diagnosis and treatment start late, it is often related to irreversible kidney damage and a bad outcome. As a result, attention is shifting to detecting signs of poor renal outcomes early and taking prompt action. Similar to 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 for local patients are not well-known, highlighting the need for more local studies. This study aims to examine clinical and laboratory features of patients with lupus nephritis, as well as their outcomes based on how their biopsy results were classified and how they were treated. Recognizing the aspects that can affect prognosis in our population should help us design more effective ways to monitor and treat diseases [9].

MATERIALS AND METHODS

This retrospective observational cohort study conducted in the Department of Nephrology Institute of Kidney Diseases Peshawar between January 2021 and December 2023. Patients were included who met the ACR criteria for SLE and also had kidney involvement, confirmed through biopsy. Each patient went through various examinations: clinical evaluation, urine protein, serum creatinine, ANA, anti-dsDNA, and complement levels in the blood, and analysis of renal tissue. Treatment was given using immunosuppressive drugs and corticosteroids that were chosen according to the severity of the disease. Follow-up included checking for improvement, worsening kidney function, or death in patients.

ETHICAL APPROVAL STATEMENT

Ethical approval was obtained from the Institute of Kidney Diseases ERB, Peshawar **(Ref: 2040-ERB-1740/2020.**All participants Provided written informed consent. Procedures adhered to the Declaration of Helsinki; confidentiality and data security were maintained. No inducements were offered. The ERB approved the protocol and data collection tools.

INCLUSION CRITERIA

Individuals who were 18 years or older, had validly diagnosed SLE, and exhibited biopsy-proven lupus nephritis upon arrival at the nephrology department were considered for the study.

EXCLUSION CRITERIA

The study included only patients who fully had their records available, did not have a previous kidney transplant, did not have any unrelated glomerular diseases, and agreed to the renal biopsy.

DATA COLLECTION

All relevant data such as age, medical signs, blood values, biopsy findings, and treatments were recorded using the data collection sheet. Patients were checked again every three months. Key outcomes tracked in the two-year follow-up were complete and partial remission, progression to CKD, and death.

STATISTICAL ANALYSIS

The data were explored and organized using SPSS 20.0. Statistical data was shown as mean ± standard deviation for continuous variables and as percentages for categorical ones. For associations, chi-square test and independent t-tests were used. Logistic regression was applied to determine what factors were linked to poor kidney outcomes. The result was considered statistically significant if the p-value was below 0.05.

RESULTS

100 patients who had lupus nephritis. The average age was 27.4 years, and females made up 85.8% of patients. Most patients presented with proteinuria (91.6%), while many also experienced generalized edema (74.1%) and hypertension (53.3%). Among the renal biopsies, 53 (44.1%) patients had Class IV lupus nephritis, 32 (26.6%) had Class III, 22 (18.3%) had Class V, and the remaining patients had Class II or Class VI. Corticosteroids and either cyclophosphamide or mycophenolate mofetil were given in the first round, based on

what class the disease belonged to. At the end of the follow-up period, out of 100 patients, 75 (62.5%) experienced remission of any degree. Of the 100 patients, 31 (25.8%) suffered chronic kidney disease (CKD), and ten patients (11.7%) passed away due to renal failure or sepsis. The multivariate analysis found that patients who had a high baseline serum creatinine (over 2.0 mg/dL), started treatment late, and had advanced nephritis (Classes IV or V) showed worse renal outcomes. Diagnosing the disease early and treating with powerful immunosuppression resulted in much higher remission rates ($p = 0.01$). Individuals who stick to follow-up care tend to have a better survival rate for their kidneys.

Table 1. Baseline demographic characteristics (N = 100)

Characteristic	Value
Age, years — mean ± SD (range)	**27.4 ± 6.3 (18.9–35.2)**
Female sex — n (%)	**86 (85.8)**

SD: standard deviation.

Table 2. Baseline clinical presentation (N = 100)

Clinical feature	n (%)
Proteinuria present	**92 (91.6)**
Generalized edema	**74 (74.1)**
Hypertension	**53 (53.3)**

Percentages are as reported. "Edema" refers to generalized edema at presentation.

Table 3. Histopathological classification by ISN/RPS (percent distribution)

Class	% of patients
Class II	**6.7**
Class III	**26.6**
Class IV	**44.1**
Class V	**18.3**
Class VI	**4.3**

Percentages are those provided. Underlying raw counts were inconsistently reported; therefore, only percentages are shown.

Table 4. Renal outcomes at last follow-up

Outcome	% of patients
Complete or partial remission	**62.5**
Progression to chronic kidney disease (CKD)	**25.8**
Death (all-cause, in-hospital)	**11.7**

Outcomes reflect the proportions reported for the study cohort. CKD criteria were not specified in the source text.

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; 85.8% 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 (44.1%) being the most frequent, followed by Class III (26.6%) and Class V (18.3%). 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 (91.6%) and hypertension (53.3%). 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 62.5% of patients achieved remission (complete or partial), while 25.8% progressed to chronic kidney disease (CKD), and 11.7% died, predominantly due to renal failure or sepsis. These remission rates are comparable to contemporary studies reporting 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, while 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[19.20].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[21,22].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.

LIMITATIONS

This study was limited because it only looked at one medical center, had a small number of patients, and followed them for only two years. Additionally, since people didn't have as much access to well- developed immune and genetic tests back then, they couldn't do as much detailed work. Socioeconomic barriers and whether patients followed their treatment were not looked at, so that might have affected how well patients responded.

CONCLUSION

Lupus nephritis is still a serious complication of lupus, and Class IV is the most common and dangerous type. Early diagnosis, figuring out the type of lymphoma with a test called histology, and starting treatment early and strongly to suppress immune-mediated disease activity can really affect how well people do with lymphoma. Comprehensive patient education and sticking to the treatment are really important for keeping people with kidney disease alive longer and reducing long-term renal morbidity.

AUTHORS CONTRIBUTION

Concept & Design of Study: Mazhar Ul Haq

Drafting: Mohmmand Shahzad

Data Collection & Critical Review:Najmuddin

Final Approval of Version: All Authors

CONFLICT OF INTEREST: Nil.

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ETHICAL STATEMENT

Ref: 2040-ERB-1740/2020

AI USAGE STATEMENT

AI tools (**e.g., ChatGPT**) were used for language editing and structuring of the manuscript. The authors take full responsibility for the content and accuracy of the manuscript.

COPYRIGHT STATEMENT

DATA AVAILABILITY STATEMENT

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

REFERENCES

1. Akca UK, Batu ED, Kisaarslan AP, Poyrazoglu H, Ayaz NA, Sozeri B, et al. Hematological involvement in pediatric systemic lupus erythematosus: a multicenter,study.Lupus.2021;30:1983–90. doi:10.1177/09612033211038824.
2. Anders HJ, Saxena R, Zhao MH, Parodis I, Salmon JE, Mohan C. Lupus nephritis. Nat Rev Dis Primers. 2020;6:7. doi:10.1038/s41572-019-0141-9.
3. Antonini L, Le Mauff B, Marcelli C, Aouba A, de Boysson H. Rhupus: a systematic literature review. Autoimmun Rev. 2020;19:102612. doi:10.1016/j.autrev.2020.102612.
4. Aringer M. Inflammatory markers in systemic lupus erythematosus. J Autoimmun. 2020;110:102374. doi:10.1016/j.jaut.2019.102374.
5. Athanassiou L, Kostoglou-Athanassiou I, Koutsilieris M, Shoenfeld Y. Vitamin D and autoimmune rheumatic diseases. Biomolecules. 2023;13:709. doi:10.3390/biom13040709.
6. Chandwar K, Aggarwal A. Systemic lupus erythematosus in children. Indian J Pediatr. 2024;91:1032–40. doi:10.1007/s12098-023-04833-0.
7. Dong Y, Wang G, Yan X, Ye W, Qiao X, Deng X, et al. Ponatinib exacerbates renal injury in SLE mouse model via PDGFR-PI3K/AKT pathway. Biochem Pharmacol. 2024;230:116578. doi:10.1016/j.bcp.2024.116578.
8. Dowsett T, Oni L. Renal manifestations of paediatric systemic lupus erythematosus. Curr Opin Pediatr. 2022;34:203–8. doi:10.1097/MOP.0000000000001101.
9. Greenan-Barrett J, Doolan G, Shah D, Virdee S, Robinson GA, Choida V, et al. Biomarkers associated with organ-specific involvement in juvenile SLE. Int J Mol Sci. 2021;22:7619. doi:10.3390/ijms22147619.
10. Kaneko M, Jackson SW. Recent advances in immunotherapies for lupus nephritis. Pediatr Nephrol. 2023;38:1001–12. doi:10.1007/s00467-022-05670-7.
11. Lichtnekert J, Anders HJ. Lupus nephritis-related chronic kidney disease. Nat Rev Rheumatol. 2024;20:699–711. doi:10.1038/s41584-024-01158-w.
12. Liu L, de Leeuw K, van Goor H, Doornbos-van der Meer B, Arends S, Westra J. Neutrophil extracellular traps and oxidative stress in SLE. Arthritis Res Ther. 2024;26:220. doi:10.1186/s13075-024-03454-y.
13. Liu Y, Wang X, Huang M, Luo A, Liu S, Cai M, et al. METTL3 facilitates kidney injury in SLE. BMC Med. 2024;22:511. doi:10.1186/s12916-024-03735-y.
14. Mockel T, Basta F, Weinmann-Menke J, Schwarting A. BAFF in SLE: structure and clinical implications. Autoimmun Rev. 2021;20:102736. doi:10.1016/j.autrev.2020.102736.
15. Pennesi M, Benvenuto S. Lupus nephritis in children: novel perspectives. Medicina (Kaunas). 2023;59:1841. doi:10.3390/medicina59101841.
16. Rovin BH, Teng YKO, Ginzler EM, Arriens C, Caster DJ, Romero-Diaz J, et al. Voclosporin for lupus nephritis (AURORA 1 trial). Lancet. 2021;397:2070–80. doi:10.1016/S0140-6736(21)00578-X.
17. Sahu D, Saha S, Bhattacherjee S, Datta S, Banik S. Pulmonary involvement in SLE patients. J Assoc Physicians India. 2022;70:11–2. doi:10.5005/japi-11001-0148.
18. Sciascia S, Cozzi M, Barinotti A, Radin M, Cecchi I, Fenoglio R, et al. Renal fibrosis in lupus nephritis. Int J Mol Sci. 2022;23:14317. doi:10.3390/ijms232214317.
19. Silver R, Craigo S, Porter F, Osmundson SS, Kuller JA, Norton ME. SLE in pregnancy. Am J Obstet Gynecol. 2023;228:B41–60. doi:10.1016/j.ajog.2022.09.001.
20. Wang Z, Hu D, Pei G, Zeng R, Yao Y. Driver genes in lupus nephritis. Front Immunol. 2023;14:1288699. doi:10.3389/fimmu.2023.1288699.
21. Xiao L, Xiao W, Lin S. Biomarkers for renal involvement in SLE. Front Med (Lausanne). 2022;9:995103. doi:10.3389/fmed.2022.995103.
22. Zhang Y, Cai M, Huang X, Zhang L, Wen L, Zhu Z, et al. ELF1 as biomarker in SLE. Sci Rep. 2024;14:26590. doi:10.1038/s41598-024-78593-y.