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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 reason for the illness and death among patients with systemic lupus erythematous (SLE). Prognosis depends on the kidney tumor subtype, so catching it early and treating it properly can help avoid lasting kidney damage and improve the patient's survival.

Objectives: To assess the features of lupus nephritis, how patients present in the clinic, their laboratory results, and their responses to treatment, and to find risk factors for a poor renal outcome.

Study Design: A Prospective observational cohort study.

Methods: this study conducted at Department Of Nephrology Institute Of Kidney Diseases Peshawar between January 2021 and December 2023. age of 18 with lupus nephritis as diagnosed by ISN/RPS were considered for this study. Information about the patients' demographics, health problems, laboratory findings, and treatments were documented. Results for the kidneys were determined as remission, chronic kidney disease (CKD), or deceased. SPSS version 24.0 was used for statistical analysis, and results were considered significant if p was less than 0.05.

Results:100 patients, and 85.8% of those were women. On average, participants were 27.4 years old with a range of 18.9 to 35.2 years. Among all patients, Class IV (44.1%) accounted for the greatest number, and Class III (26.6%) was the second-highest frequency, followed by Class V (18.3%). Most patients showed proteinuria (91.6%), had enema used (74.1%), and experienced hypertension (53.3%). The disease went into full or partial remission in 62.5%, whereas 25.8% progressed to advanced kidney disease and 11.7% died. Serum creatinine higher than 1.3 mg/dL and Class IV or V histology were both linked to worse results in patients (p = 0.002). Those who started immunosuppressive therapy quickly had better outcomes (p = 0.01).

Conclusion: Many cases of chronic kidney disease in SLE are strongly influenced by lupus nephritis. Most patients have Class IV, which can cause chronic kidney disease and leads to poor outcomes if left untreated. Quick biopsy, accurate classification of the tissue, and right treatment with immunosuppressants boost the chances of survival for the kidneys. Regular check-ups are important to recognize any relapses and help patients with lupus nephritis achieve better long-term results.

Keywords: Outcome in renal disease, recovery, treatment with immunosuppressants, study of the organ tissue

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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. They start with barely noticeable 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 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 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 Prospective 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** Author Dr. Mazar Khan). All participantsProvided 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 enemata (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 120 patients, 75 (62.5%) experienced remission of any degree. Of the 118 patients, 31 (25.8%) suffered chronic kidney disease (CKD), and s=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.

Table 5. Predictors of poor renal outcome (CKD or death) — multivariable analysis

Predictor	Direction of association	p-value
Elevated baseline serum creatinine†	Higher risk	0.002
ISN/RPS Class IV or V	Higher risk	<0.05
Early initiation of immunosuppression	Lower risk (protective)	0.01

Discussion

We found a relatively young, largely female proportion of patients (mean age 27.4 years; 85.8% women), a histologic distribution profile heavily deployed with Class IV (44.1%) followed by Class III (26.6) and Class V histologic classes (18.3) and very high levels of proteinuria (91.6%) and hypertension (53.3%) in our single-center cohort of biopsy-proven lupus nephritis (LN) in Peshawar, Pakistan. Such characteristics reflect the well-characterized epidemiology of systemic lupus erythematosus (SLE) and LN in which women who have reached childbearing age are overrepresented and proliferative classes (III / IV) are the most prevalent at presentation [10,11]. Our series histologic spectrum also concurs with previous reports on South Asians who describe a high load of proliferative disease and a high baseline burden of substantial nephritic-range proteinuria [12].Follow-up outcomes in the form of complete or partial remission, progression to chronic kidney disease (CKD) or even death were experienced in 62.5%, 25.8% and 11.7% of cases, respectively, mostly due to renal failure or sepsis. Between 50 and 70 percent remissions after cyclophosphamide or mycophenolate mofetil-based induction rates are thus common in modern series, implying that the performance of our center is generalizable despite resource limitations [13,14]. The rate of CKD evolution underlines persistent danger of incurable damage despite the treatment and emphasizes the importance of careful risk stratification and follow-up [15]. An overall mortality around 1015% has been reported in a variety of series in low and middle income settings typically due to infection and active disease; our results are compatible with this and further underline the importance of

infection prevention in the face of immunosuppression [16,17].Baseline serum creatinine, above a certain threshold in multivariable analyses (>2.0 mg/d), and advanced histologic class (IV or V) were predictors of adverse renal outcome in our analysis. Initial renal dysfunction is a known prognosis indicator, showing cumulative inflammatory and ischemic damage, and proliferative and membranous lesions are also much more likely to be associated with chronic activity, chronicity lesions, and resistance to treatment [18-19]. On the other hand, the earlier start of immunosuppressive medication was accompanied by better outcomes (p=0.01), which is biologically and clinically understandable and shares the logic of prompt biopsy-based induction and maintenance to circumvent relapses recommended in the guidelines [20]. All these observations can be summarized to guide a strategy of accelerated diagnostic assessment (such as early-onset biopsy), fast-track risk-adapted induction, intensive infection-prevention surveillance and monitoring. It is worth highlighting the clinical picture of the presentation: high (and in fact, extremely high) prevalence of proteinuria and common hypertension. Proteinuria is an index of activity as well as an independent cause of tubulointerstitial damage; decreases in proteinuria are closely linked to long term renal survival in LN cohorts [21]. Likewise, management of blood pressure is required to maintain renal function and went hand in hand with immunosuppression, preferably renin angiotensin aldosterone system blockade where tolerated. Many of our patients are young, so even aggressive risk-factor modification has great lifetime benefit. Our proportion of remission indicates successful induction in general, but the ratio of cyclophosphamide and mycophenolate and various regimen dosing and compliance was not comprehensively reported. In contexts rather like ours, mycophenolate would be preferred over Class III/IV LN thanks to efficacy and a superior profile of gonad toxicity, whereas cyclophosphamide could be picked over crescent disease, rapid-progressive manifestations, or financial/market factors [22]. A protocol-based protocol induction based on biopsy class and chronicity index, whose maintene is mycophenolate or azathioprine at least 2436 months, would probably lead to a decreased risk of relapses and CKD progression [13,20,21]. The variation in our rate of mortality due to infection illustrates the requirement of vaccination, latent tuberculosis screening in epidemiologically relevant areas, Pneumocystis prophylaxis at high doses and close monitoring of neutropenia and opportunistic diseases [16,17].Multiple surrounding factors are likely to have contributed toward burden of advanced disease at presentation in Pakistan not least delayed referral, inaccessibility of nephrology/rheumatology services, economic barrier in acquiring biopsy and immunosuppressant, and difficulty with sustained follow-up. Their closures will demand interventions upstream: standard referral systems through the primary care, enhancing biopsy capacity, access to steroid-sparing agents via formulary, and initiatives based on patient education with the aim to improve adherence and early detection of symptoms [10-15]. Our setting may have better outcomes with multidisciplinary LN clinics with nephrology, rheumatology, nursing, and pharmacy care [14-20].Adequate strengths of this study are that the LN has been confirmed using biopsy; there was systematic recording of important clinical variables and multivariable analysis has also been provided to deduce independent predictors. The relative youth and proliferative disease are strengths as the findings are directly applicable to the regional practice because of this cohort. However, a number of limitations need to be discussed. First, the denominators of results reported are internally contradictory (e.g. remission/out of 120, CKD/118, v. stated cohort of 100); final tables should be harmonized to have the same number of persons in the analytic population because this reduces uncertainty of reporting bias. Second, this is an observational study and confounding due to indication cannot be ruled out; patients with more advanced disease were probably treated with differing induction regimen and closer management. Third, compliance, time to therapy, and total doses of steroids were not measured although they have a significant impact in causing remission and Adverse effects. Fourth, we did not have uniform activity/chronicity indices and cumulative proteinuria trajectories which are strong prognosticators of long run outcomes. Lastly, single-center design might be non-generalizable, but the demographic and the histologic represent similar to other South Asian groups. Prospective studies to compare this type of care, with protocol zed pathways (guided by biopsy results), predetermined regimens of induction and maintenance, infection bundle, and strict focus on blood pressure and proteinuria control are needed. Risk-Adapted Therapy intensification would be possible through the incorporation of treat-to-target milestones (e.g. reduction of proteinuria 50 per cent

or more by 6 months) and standardized activity/chronicity scores. In our population, mycophenolate-based versus cyclophosphamide-based induction could be compared in pragmatic trials, with cost-effectiveness analyses, and translate into local guidelines. Also, the inclusion of patient-reported outcome measures and adherence supports to support the remission and minimize CKD progression and death will be established. To conclude, our cohort highlights the heavy burden of proliferative LN in young women, and remission can be offered in the majority of patients despite permanent risks of CKD development and mortality. Patients with a high baseline creatinine and advanced histology should be exposed to an early and intensive treatment therapy period and a close follow up whereas early application of immunosuppression can improve outcomes. Leveraging early diagnostic paths, reproducibility of induction/maintenance, and focusing on preventing infection are some of the viable options to enhance renal survival in our setting [22].

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 calm down the immune system 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 helping them avoid serious health problems in the future.

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.

Future Findings

Future multicenter studies should look at longer-term results in people with lupus nephritis, use more detailed blood or urine tests, and try to find genetic clues that can help doctors know if a treatment is working well. Evaluating the role of biologics and making specific treatment plans for each person can help manage these tough cases. Real-world data about whether patients follow their recommended treatment and how money and financial situations affect them also needs more careful study.

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Authors Contribution

Concept & Design of Study: Mazhar Ul Haq[1]

Drafting: Mohmmand Shahzad[2]

Data Collection & Data Analysis: Najmuddin[3]

Critical Review: Mazhar Ul Haq[1]

Final Approval of version: All Mention Authors Approved the Final Version .

All authors contributed significantly to the study's conception, data collection, analysis,Manuscript writing, and final approval of the manuscript as per **ICMJE Criteria**

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