Clinicopathological Correlation in Pediatric Lupus Nephritis: Insights from a Tertiary Pediatric Care Center in Nepal

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ABSTRACT

Background

Lupus nephritis (LN) is a severe manifestation of childhood-onset systemic lupus erythematosus (cSLE) and a major cause of morbidity. Given the variability in clinical features and histological grades, renal biopsy plays a pivotal role in diagnosis and management. This study aims to evaluate the clinical-pathological correlations in children with biopsy-proven renal involvement.

Method

A hospital-based retrospective descriptive study was conducted at Kanti Children's Hospital from March 1, 2019, to February 28, 2025. Children aged ≤14 years with biopsy-proven LN were included. Demographic, clinical, laboratory, and histopathological data were analyzed.

Result

Among 30 children (25 females, 5 males), Class IV LN was the most common (63.3%), followed by Class V and Class IV+V (each 10%). Nephrotic-range proteinuria (70%), hematuria (80%), and ANA positivity (100%) were prominent. Class IV LN strongly correlated with proteinuria, elevated creatinine, and hematuria (r=0.664). Class III LN showed negative correlations and mixed classes displayed variable associations.

Conclusion

Class IV LN was associated with the most severe clinical features, reaffirming the importance of histopathological classification. Discordant clinicopathological findings in other classes underscore the necessity of biopsy in all pediatric LN cases prior to treatment initiation.

Keywords: Lupus erythematosus, systemic; Lupus nephritis; Renal biopsy.

Introduction

Systemic lupus erythematosus (SLE) is a multisystem, chronic inflammatory disorder of autoimmune origin, predominantly affecting the skin, joints, heart, lungs, and, importantly, the kidneys.[1] Childhood-onset SLE (cSLE) demonstrates wide variability in incidence and prevalence, with higher frequency reported among Asians, African Americans, Hispanics, and Native Americans.[2] Although rare, cSLE accounts for approximately 15–20% of all SLE diagnoses, with an incidence ranging from 0.3 to 0.9 per 100,000 children per year and a prevalence of 3.3 to 8.8 per 100,000. The female predominance in cSLE increases with age and parallels that observed in adults.[3]

Lupus nephritis (LN), a consequence of SLE, presents with a broad clinical spectrum ranging from mild, asymptomatic proteinuria to end-stage renal disease (ESRD) and contributes to significant morbidity and mortality. Pediatric SLE often presents

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with less overt systemic symptoms compared to adults, with some children manifesting severe renal involvement at disease onset without fulfilling the complete diagnostic criteria for SLE.[3,4]

The International Society of Nephrology/Renal Pathology Society (ISN/RPS) classifies LN into six histopathological classes. Kidney biopsy remains a cornerstone in diagnosing LN, assessing disease activity, predicting prognosis, and guiding treatment decisions. Up to 50% of pediatric SLE cases develop LN, with Classes III and IV being most prevalent and associated with worse outcomes.[5] Clinical indicators such as nephrotic-range proteinuria, active urinary sediments, and hypocomplementemia may suggest active disease but often do not correlate reliably with histological severity.[6]

Therefore, several studies recommend renal biopsy in all pediatric lupus patients with urinary abnormalities. The aim of this study is to determine the distribution of histopathological LN classes in our pediatric cohort and to evaluate clinico-pathological correlations in biopsy-proven cases of LN. To our knowledge, this is the first such study conducted at Kanti Children's Hospital, Kathmandu, Nepal, focusing on the clinical, immunological, and pathological spectrum of cSLE. This study provides valuable insight into pediatric LN patterns and their clinico-pathological correlations in a South Asian tertiary care setting.

Material and Methods

This hospital-based retrospective descriptive study was conducted at Kanti Children's Hospital, Kathmandu, Nepal, spanning six years from March 1, 2019, to February 28, 2025. Demographic, clinical, and laboratory data were retrieved from the hospital medical records and the lupus nephritis registry maintained by the nephrology unit.

We included all children aged ≤ 14 years with biopsy-proven lupus nephritis. A minimum of 10 glomeruli was considered adequate for inclusion in the biopsy analysis. Only native kidney biopsies were analyzed; transplant biopsies were excluded. Renal biopsies were evaluated by experienced nephropathologists using light microscopy and immunofluorescence techniques, including assessment of IgA, IgG, IgM, C3, C1q, kappa, and lambda deposits.

Data were analyzed using IBM SPSS Statistics version 21. Descriptive statistics were calculated for categorical variables as percentages. Correlation analyses were performed using Spearman's correlation coefficient. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 30 patients with varying histopathological classes of lupus nephritis (LN) were included in this study, conducted over 6 years from March 1, 2019, to February 28, 2025. The cohort consisted predominantly of females, with a male-to-female ratio of 1:5 (5 males, 25 females). The majority of patients (n = 24; 80%) were above 10 years of age, while 6 patients (20%) were below 10 years of age.

At presentation, renal function tests showed that 26 patients (86.7%) had serum creatinine levels below 1 mg/dL, whereas 4 patients (13.3%) had levels above 1 mg/dL. Nephrotic range proteinuria was observed in 21 patients (70%), while 9 patients (30%) had non-nephrotic range proteinuria. Hematuria was present in 24 patients (80%), with only 6 patients showing no hematuria. Edema was a universal clinical finding noted in all 30 patients (100%). Serologically, antinuclear antibody (ANA) positivity was seen in all patients (Table 1).

Among the 30 patients, the most common histopathological class was Class IV lupus nephritis, observed in 19 patients (63.3%). This was followed by Class V and Class IV+V, each identified in 3 patients (10%). Mixed Class III+V was seen in 2 patients (6.7%), while isolated Class III and Class II were observed in 1 (3.3%) and 2 (6.7%) patients, respectively. (Table 1).

Correlation analysis was conducted using Spearman's rank correlation coefficient to assess the association between histopathological classes and clinical variables: proteinuria, serum creatinine, and hematuria.

Class IV lupus nephritis demonstrated the strongest positive correlations with proteinuria (r = 0.664), serum creatinine (r = 0.664), and hematuria (r = 0.664), although these did not reach statistical significance (p = 0.15 for all). Class III lupus nephritis showed negative correlations with all three variables—proteinuria and creatinine (r = -0.531) and hematuria (r = -0.664)—but these also lacked statistical significance (p > 0.05). (Table 2)

Mixed classes, particularly Class IV+V, showed variable correlation patterns: proteinuria (r = -0.133), serum creatinine (r = -0.531), and hematuria (r = 0.133), indicating clinical heterogeneity. Classes

Table 1 : Demographic, clinical, biochemical, and serological findings across different histopathological classes of lupus nephritis.

Histopathological Class	II	III	IV	V	III+V	IV+V	Total Patients
Age							
<10 years	0	4	0	1	1	0	6
>10 years	2	1	15	3	1	2	24
Serum Creatinine							
<1 mg/dL	2	1	17	3	2	1	26
>1 mg/dL	0	2	0	0	0	2	4
Proteinuria							
Nephrotic range	1	0	16	0	2	2	21
Non-nephrotic range	1	1	3	3	0	1	9
Hematuria							
Present	1	0	15	3	2	3	24
Absent	1	1	4	0	0	0	6
Edema							
Present	2	1	19	3	2	3	30
ANA							
Positive	2	1	19	3	2	3	30

II and V exhibited weaker correlations ranging from -0.531 to 0.399, none of which were statistically significant ($p > 0.05$). (Table 2).

Discussion

This study analyzed the clinical, biochemical, serological, and histopathological features of pediatric lupus nephritis (LN) in 30 patients admitted to Kanti Children's Hospital over six years. While the etiopathogenesis of LN in children mirrors that of adults, the disease tends to be more severe in the pediatric population, with notable heterogeneity in clinical presentation and histopathological classes. We aimed to evaluate the correlation between clinical findings and histopathological classes in this cohort.

Demographically, the predominance of females (83.3%) and patients older than 10 years aligns with epidemiologic trends seen in SLE.[7] This reaffirms the need for close monitoring of adolescent and young adult SLE females for renal involvement.

Class IV lupus nephritis emerged as the most prevalent histopathological subtype, representing 63.3% of cases, consistent with prior studies reporting Class IV as the most common and clinically severe form of LN.[8] This class also demonstrated the strongest positive correlations with proteinuria,

Table 2: Spearman's correlation coefficients between lupus nephritis classes and clinical variables

Class	Variable	Spearman r	p-value
II	Proteinuria	-0.531	0.27
	Creatinine	-0.133	0.80
	Hematuria	-0.266	0.61
III	Proteinuria	-0.531	0.27
	Creatinine	-0.531	0.27
	Hematuria	-0.664	0.15
IV	Proteinuria	0.664	0.15
	Creatinine	0.664	0.15
	Hematuria	0.664	0.15
V	Proteinuria	0.399	0.43
	Creatinine	0.399	0.43
	Hematuria	0.399	0.43
III+V	Proteinuria	0.133	0.80
	Creatinine	0.133	0.80
	Hematuria	-0.266	0.61
IV+V	Proteinuria	-0.133	0.80
	Creatinine	-0.531	0.27
	Hematuria	0.133	0.80

serum creatinine, and hematuria (Spearman's r = 0.664 for all), highlighting its association with more severe renal involvement and active disease. Similar observations have been reported where Class IV lesions were the most frequent, and initial renal function did not reliably predict histological class or outcomes.[9]

In contrast, Class II LN, typically characterized by mesangial involvement, exhibited negative correlations with proteinuria (r = –0.531), serum creatinine (r = –0.133), and hematuria (r = –0.266), reflecting its milder clinical course. These findings align with pediatric LN guidelines and cohort studies, which indicate that Class I and II diseases often follow a favorable natural history and typically require minimal or no immunosuppressive therapy.[10] Also, Class III LN, representing focal proliferative disease, showed negative correlations, particularly with hematuria (r = –0.664), suggesting that isolated hematuria may not reliably predict segmental proliferative pathology. These findings align with earlier studies indicating that clinical markers such as serum creatinine and proteinuria do not consistently predict histologic severity or outcomes in Class III lesions.[11]

Class V lupus nephritis demonstrated moderate positive correlations with clinical parameters (r = 0.399 for proteinuria, creatinine, and hematuria), consistent with its known association with heavy proteinuria and variable degrees of renal impairment.[12,13] Mixed classes, especially Class IV+V, showed discordant correlation patterns—negative with proteinuria (r = –0.133) and serum creatinine (r = –0.531) but mildly positive with hematuria (r = 0.133). This variability reflects the heterogeneity of mixed-class LN and underscores the critical need for renal biopsy to classify disease and guide therapy accurately. Supporting this, prior multinational studies have shown that kidney damage can be present even when urinary abnormalities are mild, highlighting that severe symptoms are not always necessary to indicate serious disease, which can significantly impact treatment decisions. [14]

In line with previous studies emphasizing the importance of early renal biopsy, our findings further support the notion that clinical and laboratory parameters may underestimate the underlying histological severity in pediatric lupus nephritis, thereby underscoring the necessity of early biopsy for accurate diagnosis and informed therapeutic planning.[15,16] While Class IV correlates with more severe renal dysfunction, less aggressive classes may still present with significant proteinuria or hematuria, potentially leading to misclassification without biopsy confirmation.

Despite observed correlations, all had a P value of less than 0.05, i.e., none reached statistical significance, likely due to the limited sample size. This highlights that clinical features alone are insufficient to predict histopathological class, emphasizing the indispensable role of renal biopsy in guiding diagnosis and treatment decisions in pediatric lupus nephritis.

Conclusion

In conclusion, our study reinforces the critical role of histopathological evaluation in the management of lupus nephritis. It highlights that Class IV LN correlates most strongly with markers of disease severity. The weak or negative correlations in other classes, particularly mixed classes, reflect the complex and often unpredictable nature of lupus nephritis. Further prospective studies of larger cohorts are warranted to validate these findings and refine prognostic markers.

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