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Original Article

Clinical Manifestations, Immunological Profile and Short-Term Outcome in Pakistani Pediatric Lupus Patients

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ABSTRACT

Background: Childhood-onset systemic lupus erythematosus (cSLE) is a rare but clinically aggressive autoimmune disease with substantial variability in its presentation across different geographic and ethnic populations. Data on pediatric lupus in Pakistan, particularly in outpatient settings, remain limited, hindering timely diagnosis and targeted management strategies. Objective: To evaluate the clinical manifestations, immunological profile, and short-term outcomes in Pakistani pediatric lupus patients managed in specialized rheumatology outpatient clinics. Methods: This retrospective, cross-sectional study analyzed electronic medical records from three tertiary rheumatology centers in Lahore, Pakistan, between November 2021 and August 2024. Patients under 18 years of age meeting ACR/EULAR 2019 SLE classification criteria and followed for at least six months were included. Data on demographics, clinical features, immunological markers, treatment regimens, and disease outcomes were collected. Statistical analyses were performed using SPSS 23, with significance set at $p<0.05$. Results: A total of 34 patients were included, 85.3% of whom were female, with a mean age of 13.8 ± 2.91 years. Polyarthritis (64.7%) was the most common clinical feature, followed by nephritis and hematological involvement (44.1% each). Anti-dsDNA antibodies were positive in 79.4% of patients. At a mean follow-up of 17.1 ± 11.6 months, 44.1% achieved clinical remission (SLEDAI=0), with minimal serious complications or hospitalizations. Conclusion: Pediatric lupus in Pakistan presents with a distinctive clinical and immunological profile, with favorable short-term outcomes under specialist outpatient care. Early diagnosis and immunologically guided treatment can mitigate disease burden in this high-risk population.

Keywords: Pediatric lupus, systemic lupus erythematosus, childhood-onset SLE, lupus nephritis, immunological profile, remission, Pakistan.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic, multisystem autoimmune disorder that predominantly affects females of reproductive age. However, this paradigm has shifted in recent years as increasing recognition of pediatric-onset cases has expanded the understanding of its epidemiology and pathophysiology. Childhood-onset systemic lupus erythematosus (cSLE), defined as lupus presenting before 18 years of age, represents approximately 10–20% of all lupus cases (1). Although the core clinical features of SLE may overlap across age groups, cSLE often follows a more aggressive disease trajectory, with earlier and more severe multiorgan involvement, increased prevalence of nephritis, neuropsychiatric symptoms, and hematological abnormalities compared to adult-onset lupus (2, 3). These manifestations are frequently compounded by a higher risk of serious infections, prolonged hospitalization, and treatment-related adverse events, posing unique challenges in both diagnosis and management (4, 5).

Epidemiologically, the incidence of cSLE varies widely across different racial, ethnic, and geographic groups, ranging between 0.36 and 2.5 per 100,000 children annually (4). In South Asian countries, particularly in Pakistan, data on pediatric lupus remains scarce, limiting our understanding of disease behavior in this demographic context. Most available studies from the region are institution-based, often focused on inpatient populations, which tend to represent more severe phenotypes and may not reflect the broader spectrum of disease seen in outpatient settings. Moreover, these studies have largely excluded longitudinal follow-up or treatment outcomes, thereby narrowing insights into disease course and remission trends (9, 10). The complexity of cSLE in low-resource settings is further compounded by diagnostic delays, lack of pediatric rheumatology expertise, and poor access to immunological testing—factors that likely contribute to underreporting and suboptimal care (9). Despite mounting evidence from other regions emphasizing the distinct immuno-clinical features of cSLE, limited literature exists from Pakistan that characterizes pediatric lupus comprehensively. Previous studies conducted at Agha Khan University Hospital and Children's Hospital, Lahore, have provided preliminary descriptions of clinical and serological features (9, 10), but these findings are limited by their single-center scope and hospital-based recruitment, which may overrepresent acutely ill patients.

Additionally, none have systematically addressed short-term treatment responses, immunosuppressive use, or remission outcomes in an outpatient setting. This creates a critical gap in knowledge, particularly as outpatient rheumatology clinics are increasingly becoming the primary site for diagnosis and ongoing care. To address this deficit, the present study investigates the clinical presentation, immunological profile, and short-term outcomes of Pakistani pediatric lupus patients attending specialized rheumatology outpatient clinics across three major centers in Lahore. By leveraging data from National Hospital and Medical Centre, Arthritis Care Clinic, and the Arthritis Care Foundation, we aim to provide a broader, more representative understanding of cSLE in a resource-limited yet clinically diverse setting. Our study specifically explores organ involvement at presentation, autoantibody profiles, immunosuppressive usage patterns, and early disease outcomes using the SLE Disease Activity Index (SLEDAI). Through this multicenter, retrospective cohort, we seek to identify patterns that may inform early recognition, improve clinical care pathways, and guide national policy in pediatric rheumatology (11). The primary objective of this study is to evaluate the clinical and immunological characteristics of pediatric SLE in outpatient settings and to assess short-term disease outcomes following standard immunosuppressive therapy. We hypothesize that pediatric lupus in Pakistan, while sharing some universal features with global cohorts, exhibits region-specific patterns in organ involvement and immunological markers that influence disease trajectory and treatment response

MATERIAL AND METHODS

This study employed a retrospective, cross-sectional observational design to evaluate the clinical manifestations, immunological profile, and short-term outcomes in pediatric patients diagnosed with systemic lupus erythematosus (SLE) in an outpatient rheumatology setting. The design was chosen to provide a descriptive epidemiological snapshot of pediatric lupus across multiple specialized rheumatology clinics in Pakistan, offering insight into disease characteristics outside inpatient facilities where more severe phenotypes are typically overrepresented. The study was conducted across three urban, tertiary-care rheumatology outpatient centers in Lahore: National Hospital & Medical Centre, Arthritis Care Clinic, and Arthritis Care Foundation. Data collection spanned from November 2021 to August 2024, with all eligible cases identified through the combined electronic medical record systems of these institutions.

The study population consisted of patients diagnosed with SLE according to the 2019 classification criteria jointly proposed by the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) (6). Inclusion criteria were patients under the age of 18 years at their last recorded follow-up, who fulfilled the ACR/EULAR 2019 criteria for SLE and had a minimum follow-up duration of six months. Exclusion criteria included patients with drug-induced lupus, overlap connective tissue disorders, isolated cutaneous lupus, or incomplete follow-up data. Patients were identified through systematic filtering of outpatient diagnostic codes for SLE and further confirmed via detailed chart review. Only those patients managed and monitored in the outpatient setting were included, and any hospitalization during follow-up was documented as an outcome variable rather than an inclusion determinant.

All patients included in the study were managed under standard clinical care pathways at each site. Informed consent was deemed waived by the Institutional Review Board (IRB) due to the retrospective nature of the study and anonymized data analysis. Ethical approval was obtained from the IRB of National Hospital & Medical Centre, Lahore, under compliance with the Declaration of Helsinki and local regulatory guidelines.

Data was collected from structured clinical records, laboratory results, and pharmacy dispensing logs. Clinical manifestations including mucocutaneous, musculoskeletal, renal, neuropsychiatric, hematologic, and serosal involvement were recorded based on physician documentation corroborated with relevant laboratory and radiological findings. Immunological markers such as antinuclear antibodies (ANA), anti-double stranded DNA (dsDNA), anti-Smith (Sm), anti-RNP, anti-Ro, anti-La, and antiphospholipid antibodies (aPLAs) were recorded from standard laboratory assays. Disease activity was assessed using the SLE Disease Activity Index (SLEDAI), calculated at each follow-up, with remission defined as a SLEDAI score of zero without immunosuppressive escalation. Variables were operationalized using standardized definitions: lupus nephritis required either biopsy confirmation or persistent proteinuria with active urinary sediment; polyarthritis was defined as synovitis involving two or more joints documented on examination; hematologic involvement encompassed leukopenia (<4,000/mm³), thrombocytopenia (<100,000/mm³), or autoimmune hemolytic anemia confirmed by positive Coombs test and laboratory indices.

To reduce bias, only patients with complete immunological and clinical datasets were included. Verification of diagnoses was performed independently by two rheumatologists reviewing the records to ensure consistency in classification and data abstraction. Confounding was minimized by restricting analysis to a homogenous cohort (pediatric SLE without overlap syndromes) and excluding patients with insufficient follow-up, which could skew remission or outcome analyses. While the sample size was not based on a formal statistical power calculation, all eligible patients fulfilling inclusion criteria within the defined period were enrolled, representing a complete census of cases across participating centers. Data were entered and analyzed using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used for categorical variables, presented as frequencies and percentages, and for continuous variables, as means with standard deviations. Bivariate analyses were performed using chi-square or Fisher's exact tests for categorical variables and t-tests for continuous data. A p-value of less than 0.05 was considered statistically significant. Missing data were handled using case-wise deletion where necessary, with sensitivity analyses confirming the stability of findings.

All study records were anonymized at the point of data extraction, and data management was conducted with strict adherence to institutional confidentiality protocols. To ensure reproducibility, all data abstraction was done using a standardized template, and variables were coded based on predefined criteria, which are available upon request. Audit trails of data abstraction, de-identification, and analysis processes were maintained to ensure data integrity and enable full replication of study procedures by independent researchers.

RESULTS

Among 34 pediatric SLE patients, the mean age was 13.8 years (SD 2.91), and the mean age at diagnosis was 9.88 years (SD 4.42). Females comprised 85.3% (n=29), with a female-to-male ratio of 5.8:1. The mean duration of follow-up was 17.1 months (SD 11.6). A positive family history of lupus was present at 5.9% (n=2).

Table 1. Demographic and Baseline Characteristics of Pediatric SLE Patients (n = 34)

Variable	Value (n = 34)
Mean age (years)	13.8 ± 2.91
Mean age at diagnosis (years)	9.88 ± 4.42
Female, n (%)	29 (85.3%)
Male, n (%)	5 (14.7%)
Mean duration of follow-up (months)	17.1 ± 11.6
Family history of lupus, n (%)	2 (5.9%)

Table 2. Clinical Manifestations and Immunological Profile

Variable	n (%)	95% CI
Polyarthritis	22 (64.7)	47.9–78.5
Nephritis	15 (44.1)	28.7–60.7
Hematological involvement	15 (44.1)	28.7–60.7
Skin rash	13 (38.2)	23.8–54.4
Alopecia	10 (29.4)	16.7–46.0
Oral ulcers	7 (20.6)	10.2–37.4
Pulmonary involvement	4 (11.8)	4.2–27.4
Neurological involvement	4 (11.8)	4.2–27.4
Photosensitivity	3 (8.8)	2.3–24.2
Vasculitis	2 (5.9)	1.0–20.3
Cardiac involvement	1 (2.9)	0.1–15.3
ANA positive	34 (100)	89.7–100
Anti-dsDNA positive	27 (79.4)	63.2–90.1
Anti-Ro positive	7 (20.6)	10.2–37.4
Anti-La positive	4 (11.8)	4.2–27.4
aPLA positive	4 (11.8)	4.2–27.4
Biopsy-proven nephritis	9 (26.5)	14.0–44.0
Class IV nephritis	4 (11.8)	4.2–27.4

Polyarthritis was the most prevalent manifestation (64.7%), followed by nephritis (44.1%) and hematological involvement (44.1%). Skin rash and alopecia were reported in 38.2% and 29.4% of patients, respectively. ANA positivity was universal (100%), and anti-dsDNA antibodies were present in 79.4%. Other immunological markers such as anti-Ro, anti-La, and aPLA were less frequently positive (20.6%, 11.8%, and 11.8%, respectively). Of those with nephritis, 9 had biopsy confirmation, with Class IV nephritis being the most common class (11.8%).

Table 3. Treatment Modalities and Remission Outcomes

Variable	n (%)	95% CI
Mycophenolic acid analogues	15 (44.1)	28.7–60.7
Azathioprine	9 (26.5)	14.0–44.0
Rituximab	6 (17.6)	7.1–34.4
Cyclophosphamide	5 (14.7)	5.8–31.0
Calcineurin inhibitors	5 (14.7)	5.8–31.0
Oral corticosteroids (last follow-up)	21 (61.8)	44.6–76.6
Corticosteroid dose >10 mg/day	4 (11.8)	4.2–27.4
Lupus in remission (SLEDAI = 0)	15 (44.1)	28.7–60.7
Stable lupus nephritis (GFR/proteinuria)	14 (41.1)	25.8–57.9
Hemodialysis required	1 (2.9)	0.1–15.3

Mycophenolic acid analogues were the most prescribed immunosuppressants (44.1%), followed by azathioprine (26.5%) and rituximab (17.6%). At last follow-up, 61.8% of patients were still receiving corticosteroids, though only 11.8% were on high-dose therapy (>10 mg/day). Remission (SLEDAI=0) was achieved in 44.1%, while 41.1% of those with nephritis maintained stable renal function. Only one patient progressed to hemodialysis.

Table 4. Complications and Adverse Outcomes

Variable	n (%)	95% CI
Hospitalization	6 (17.6)	7.1–34.4
ICU admission	1 (2.9)	0.1–15.3
Macrophage Activation Syndrome (MAS)	1 (2.9)	0.1–15.3
Tuberculous brain abscess	1 (2.9)	0.1–15.3
CMV infection	1 (2.9)	0.1–15.3
Herpes zoster infection	1 (2.9)	0.1–15.3
Deaths	0 (0)	0–10.3

During follow-up, 17.6% of patients required hospitalization, with only one ICU admission. Notable complications included one case each of MAS, tuberculous brain abscess, CMV infection, and herpes zoster. No deaths occurred during the study period.

Table 5. Comparison of Selected Features by Gender

Variable	Female (n=29)	Male (n=5)	p-value	Odds Ratio (95% CI)
Polyarthritis	19 (65.5%)	3 (60.0%)	1.000	1.25 (0.13–11.65)
Nephritis	13 (44.8%)	2 (40.0%)	1.000	1.21 (0.18–8.21)
Hematological involvement	13 (44.8%)	2 (40.0%)	1.000	1.21 (0.18–8.21)
Remission (SLEDAI=0)	12 (41.4%)	3 (60.0%)	0.629	0.46 (0.06–3.87)

No statistically significant differences were detected in major clinical features or remission rates between female and male patients (all $p > 0.05$).

Table 6. Predictors of Remission at Last Follow-up (Univariate Analysis)

Variable	Remission (n=15)	No Remission (n=19)	p-value	Odds Ratio (95% CI)
Biopsy-proven nephritis	3 (20.0%)	6 (31.6%)	0.692	0.53 (0.10–2.85)
Use of Mycophenolic acid	7 (46.7%)	8 (42.1%)	0.799	1.20 (0.30–4.77)
Female sex	12 (80.0%)	17 (89.5%)	0.605	0.43 (0.07–2.75)
Steroid use (current)	8 (53.3%)	13 (68.4%)	0.494	0.53 (0.13–2.19)

On univariate analysis, none of the evaluated clinical or treatment-related variables were significantly associated with remission status at last follow-up (all $p > 0.05$). All p-values are two-tailed, with statistical significance set at $p < 0.05$. Confidence intervals are at 95% level. Odds ratios (OR) are calculated using Fisher's exact test for small sample sizes. The cohort was predominantly female, with a high frequency of polyarthritis and nephritis. Immunological markers such as ANA and anti-dsDNA were frequently positive. Mycophenolic acid analogues were the most utilized immunosuppressant. Remission was achieved 44.1% at short-term follow-up. No statistically significant differences were found between genders or with respect to clinical variables predicting remission. The hospitalization rate was relatively low and there were no deaths in the follow-up period.

DISCUSSION

The findings of this multicenter observational study provide valuable insight into the clinical and immunological spectrum of pediatric systemic lupus erythematosus (SLE) in a South Asian outpatient context, a domain where regional data remains markedly scarce. The predominance of polyarthritis, nephritis, and hematological manifestations aligns with global literature indicating the aggressive nature of childhood-onset lupus (cSLE) (7,8). However, our cohort revealed a comparatively lower frequency of constitutional symptoms such as fever (29.4%), diverging from previous Pakistani studies where fever was reported in over 80% of pediatric SLE cases (9,10). This discrepancy may reflect earlier diagnosis and immunosuppressive initiation in outpatient rheumatology clinics, which contrasts with inpatient samples often characterized by more advanced disease. Our study's remission rate of 44.1% within 17.1 months of follow-up demonstrates promising short-term outcomes in a resource-constrained setting, underscoring the clinical effectiveness of standardized treatment algorithms and specialist care access.

Compared with cohorts from Sri Lanka, China, and Egypt, the rates of neuropsychiatric involvement, mucocutaneous features, and serositis in our cohort were lower (16,18,19). These differences may be attributable to environmental, genetic, and diagnostic thresholds across populations. For instance, while nephritis occurred in 44.1% of our patients—lower than in most international cohorts reporting rates exceeding 60%—Class IV histological involvement was still the predominant subtype, reinforcing the aggressive renal phenotype characteristic of cSLE (14,17). This supports the pathophysiological understanding that pediatric patients experience a more severe disease phenotype due to a stronger type I interferon response and immature immune regulation mechanisms compared to adults (6). The immunological profile of our cohort, particularly the high prevalence of anti-dsDNA (79.4%) and relatively lower anti-Ro/La positivity, aligns closely with patterns seen in South Asian and Middle Eastern populations (15,18), yet diverges from Western data that often report a higher anti-Ro prevalence (17,19). Such variation highlights the immuno-epidemiological diversity of cSLE and emphasizes the need for geographically tailored diagnostic approaches.

The use of mycophenolic acid analogues as the most common immunosuppressant in 44.1% of patients reflects evolving treatment preferences toward agents with a favorable toxicity profile and proven efficacy in lupus nephritis (8). Our analysis found no serious drug-related adverse events, and only one patient required dialysis, further reinforcing the utility of immunosuppressants in sustaining remission. The hospitalization rate of 17.6%, with only a single ICU admission, appears significantly lower than in most tertiary center-based studies (10,13), suggesting that regular outpatient monitoring may mitigate disease-related complications. Nonetheless, the occurrence of rare complications such as macrophage activation syndrome and CNS infections highlights the persistent risk of morbidity even in non-hospitalized populations.

A major strength of this study is its focus on outpatient clinics, offering a broader and possibly more representative picture of cSLE than inpatient-only studies. Additionally, this is one of the first local efforts to integrate clinical features, immunological profiles, treatment patterns, and short-term remission outcomes in a single analysis. However, limitations include a relatively small sample size and the retrospective design, which restricts the ability to draw causal inferences or track long-term outcomes. Data regarding treatment adherence, socioeconomic variables, and quality-of-life indices were unavailable, limiting a more nuanced interpretation of remission predictors. The generalizability of findings may also be constrained due to the urban, specialist nature of participating clinics, potentially underrepresenting rural populations or those without rheumatology access. Future research should involve prospective, multicentric studies with larger sample sizes and longer follow-up durations to validate these findings and assess sustained remission and damage accrual. Studies incorporating

biomarkers of disease activity, pharmacogenomic profiling, and patient-reported outcomes are also needed to deepen our understanding of disease heterogeneity and optimize personalized care strategies. Addressing barriers to early referral and standardizing pediatric rheumatology training in resource-limited settings remain critical steps toward improving pediatric lupus outcomes regionally and globally.

CONCLUSION

This multicenter study on clinical manifestations, immunological profile, and short-term outcomes in Pakistani pediatric lupus patients reveals that childhood-onset SLE presents with a distinct phenotype, predominantly featuring polyarthritis, nephritis, and hematological involvement, alongside a high prevalence of anti-dsDNA antibodies. Despite the aggressive disease nature, a remission rate of 44.1% was achieved within a mean follow-up of 17.1 months, highlighting the effectiveness of early, immunologically guided interventions in specialized outpatient settings. These findings underscore the critical need for early diagnosis, structured follow-up, and access to pediatric rheumatology expertise to reduce morbidity in this vulnerable population. Clinically, the study supports risk stratification and individualized treatment planning, while from a research perspective, it lays the groundwork for larger, prospective studies aimed at optimizing long-term outcomes and refining therapeutic algorithms in diverse pediatric SLE populations.

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