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Original Article

Correlation of proteinuria and quantitative anti-dsDNA level in patients of Lupus Nephritis after treatment of pulse cyclophosphamide therapy

Raisul Islam Sejan[1*], Kazi Shihab Uddin[2], Ehsan Mahmud[3], Kazi Rakib Uddin[3]

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*Corresponding author

ABSTRACT

Background: Lupus nephritis is a frequent and severe renal complication of systemic lupus erythematosus (SLE), driving significant morbidity and progression to chronic kidney disease, especially in resource-limited settings. Timely assessment of clinical, urinary, and immunological markers and their response to therapy is vital for evaluating disease activity and treatment effectiveness. **Objective:** To assess the correlation of proteinuria and quantitative anti-dsDNA level in patients with lupus nephritis after treatment of pulse cyclophosphamide therapy. **Methods & Material:** This prospective cross-sectional study was conducted at Khwaja Yunus Ali Medical College & Hospital, Sirajganj, Bangladesh, from January 2023 to December 2023. This prospective study enrolled 47 SLE patients with renal involvement via purposive sampling. Baseline demographic, clinical, urinary, and immunological data were collected. Serial follow-up of urine protein, RBC, and quantitative anti-dsDNA levels was performed for six months. Data analysis was conducted using MS Office. **Results:** The cohort (n=47) was predominantly young females (91.5%). At baseline, 61.7% had heavy proteinuria (+++) and 68.1% had anti-dsDNA >400 IU/ml. After cyclophosphamide-based therapy, 76.6% achieved urine protein ≤+ by three months. By six months, 87.2% had minimal proteinuria and 55.4% had anti-dsDNA <200 IU/ml, demonstrating a correlated improvement in both key parameters. **Conclusion:** Pulse cyclophosphamide therapy effectively reduced both proteinuria and anti-dsDNA levels in lupus nephritis patients within six months, demonstrating a strong correlation between clinical and serological response. This supports the utility of combined monitoring in assessing treatment efficacy.

Keywords: *Anti-dsDNA, Lupus nephritis, Proteinuria, Urine RBC, Young adults*

1. *Assistant professor, Department of Medicine, Khwaja Yunus Ali Medical College & Hospital, Sirajganj, Bangladesh (ORCID: 0009-0005-7233-6480)*
2. *Associate Professor, Department of Medicine, Khwaja Yunus Ali Medical College & Hospital, Sirajganj, Bangladesh*
3. *Assistant Registrar, Department of Medicine, Khwaja Yunus Ali Medical College & Hospital, Sirajganj, Bangladesh*

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder characterized by multisystem involvement and the production of pathogenic autoantibodies against nuclear components [1]. The disease follows a relapsing–remitting course and predominantly affects women of reproductive age. Among the various organ systems involved, renal involvement in the form of lupus nephritis (LN) represents one of the most severe and prognostically important manifestations of SLE [2]. It has been reported that approximately 40–60% of adult patients with SLE develop lupus nephritis, with higher incidence and more aggressive disease observed in Asian and African populations [3,4]. The pathogenesis of lupus nephritis involves the deposition of immune complexes in the renal glomeruli, activation of the complement system, and subsequent inflammatory injury to renal tissue [5]. These immunopathological processes result in a wide spectrum of clinical presentations, ranging from asymptomatic urinary abnormalities to rapidly progressive glomerulonephritis and nephrotic syndrome. Common clinical and laboratory features include proteinuria, microscopic hematuria, active urinary sediment, hypertension, and varying degrees of renal dysfunction. Disease activity is frequently associated with elevated anti–anti-double-stranded DNA (anti-dsDNA) antibody levels and reduced complement levels, which are widely used markers for assessing renal involvement and disease severity [6]. Early identification and appropriate management of lupus nephritis are crucial, as delayed diagnosis and inadequate treatment are strongly associated with poor renal outcomes, including progression to chronic kidney disease and end-stage renal disease [7]. Routine monitoring of urinary parameters such as proteinuria and urine red blood cell (RBC) count, along with serological markers like anti-dsDNA antibodies, plays a central role in evaluating disease activity and therapeutic response [8]. Several studies have demonstrated that a reduction in proteinuria within the first six months of treatment is a reliable predictor of long-term renal survival, underscoring the importance of short-term outcome assessment [9]. Immunosuppressive therapy remains the cornerstone of lupus nephritis treatment. Current international guidelines recommend induction therapy with high-dose corticosteroids combined with immunosuppressive agents, most commonly cyclophosphamide or mycophenolate mofetil, followed by maintenance therapy to sustain remission [10]. Despite the increasing use of mycophenolate in many settings, cyclophosphamide continues to be widely utilized in low-resource countries because of its affordability, availability, and established efficacy in severe disease [11]. However, treatment-related toxicity and variability in response necessitate close clinical and laboratory monitoring. In low- and middle-income countries such as Bangladesh, the management of lupus nephritis is further complicated by late presentation, limited access to renal biopsy facilities, and heterogeneity in treatment practices [12,13]. Local data regarding the clinical spectrum, laboratory characteristics, treatment approaches, and short-term outcomes of lupus nephritis remain scarce. Generating context-specific evidence is essential for optimizing patient care and improving prognostic assessment in such healthcare settings. Therefore, this study was undertaken to assess the clinical profile, laboratory findings, treatment modalities, and short-term renal and immunological outcomes of patients with SLE-associated lupus nephritis attending a tertiary care hospital in Bangladesh. The

findings are expected to contribute valuable regional data and enhance understanding of lupus nephritis management in resource-constrained environments.

METHODS & MATERIALS

This prospective cross-sectional study was conducted at Khwaja Yunus Ali Medical College & Hospital, Sirajganj, Bangladesh, from January to December 2023. A total of 47 patients with SLE and renal involvement were enrolled using purposive sampling.

Inclusion criteria: Patients of all genders aged 18 years and above with a confirmed diagnosis of SLE according to SLICC/ACR criteria, who had clinical evidence of lupus nephritis (proteinuria >0.5 g/day or active urinary sediment) and were eligible to receive pulse cyclophosphamide therapy, were included.

Exclusion criteria: Patients with pre-existing chronic kidney disease from other etiologies, active severe infection, malignancy, or pregnancy were excluded. Those unwilling to provide informed consent or to complete the six-month follow-up were also excluded.

Study procedure: Demographic, clinical, and laboratory data were recorded at baseline. All patients received standard immunosuppressive therapy. Follow-up assessments for 24-hour urine protein (semi-quantitatively graded as +, ++, +++) and quantitative anti-dsDNA antibody levels (via ELISA) were performed at diagnosis and at one, three-, and six-months post-treatment initiation.

Data analysis: Collected data were analyzed using MS Office tools (Excel). Descriptive statistics were used to present demographic and clinical variables as frequencies and percentages. The correlation between trends in proteinuria reduction and anti-dsDNA levels over time was analyzed.

RESULTS

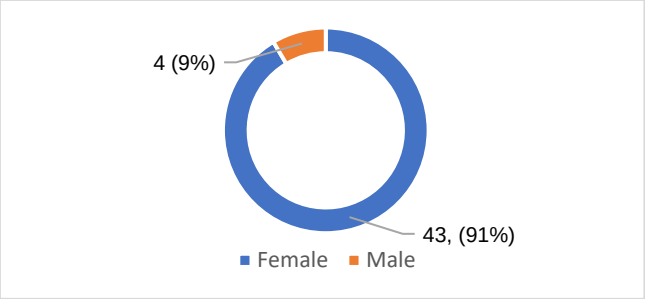

Figure 1 Gender distribution of cases (*n*=47).

The figure shows the gender distribution of the patients, where it is clear that females (43, 91%) dominate over males (4, 9%), showing that lupus nephritis is predominantly found in females (*Figure 1*).

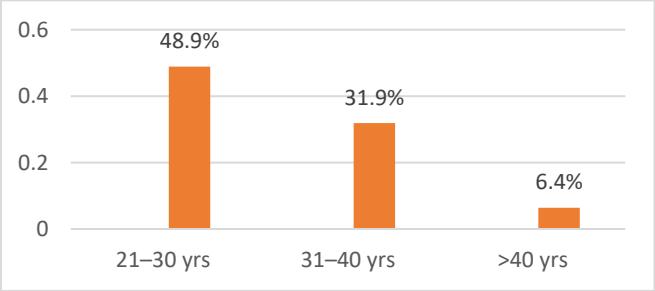

Figure 2 Age distribution of cases.

A total of 47 patients with systemic lupus erythematosus–associated renal involvement were included in the analysis. Most patients were young adults, with nearly 49% aged between 21 and 30 years, and a clear female predominance (91.5%) was observed (*Figure 2*).

The most frequent clinical diagnosis was SLE with lupus nephritis, accounting for approximately 72.3% of cases, while the remaining patients had associated hypertension, central nervous system involvement, rapidly progressive nephritis, or nephrotic syndrome (*Table I*).

Table I
Clinical diagnosis at presentation

Diagnosis	n	%
SLE with lupus nephritis	34	72.3
SLE with lupus nephritis + hypertension	5	10.6
SLE with lupus nephritis + CNS involvement	4	8.5
Rapidly progressive lupus nephritis	2	4.3
Lupus nephritis with nephrotic syndrome	2	4.3

At the time of diagnosis, renal disease activity was considerable in the majority of patients. Heavy proteinuria (+++) was present in about 61.7% of cases, while the remaining patients had moderate proteinuria (++). Hematuria was also prominent, with 36.2% of patients exhibiting urine red blood cell (RBC) counts greater than 20/HPF or described as "plenty." Immunological activity was marked, as anti-dsDNA levels exceeded 400 IU/ml in 68.1% of patients, and antinuclear antibody positivity was detected in all patients (100%) *Table II*.

Table II
Baseline laboratory findings at diagnosis.

Parameter	n	%
Urine protein		
++	18	38.3
+++	29	61.7
Urine RBC (/HPF)		
≤10	7	14.9
11–20	23	48.9
>20 / plenty	17	36.2
Anti-dsDNA (IU/ml)		
>400	32	68.1
200–400	9	19.1
<200	6	12.8

With regard to management, combined cyclophosphamide and high-dose corticosteroid therapy was the most frequently employed treatment modality, administered to 66.0% of patients. Cyclophosphamide alone was used in approximately 25.5%, while the remaining patients received supportive therapy based on clinical indication (*Table III*).

Table III
Treatment modalities used.

Treatment regimen	n	%
Cyclophosphamide + high-dose steroids	31	66.0
Cyclophosphamide alone	12	25.5
Supportive therapy only	4	8.5

Follow-up evaluation revealed a progressive improvement in urinary findings. After one month of treatment, 38.3% of patients showed a reduction of urine protein to ≤+. This proportion increased to 61.7% at two months and further to 76.6% by three months. A parallel trend was observed in hematuria, with urine RBC counts ≤5/HPF noted in 34.0% of patients at one month, rising to 57.4% at two months and 74.5% by three months. By six months, near-normal urinary parameters were achieved in more than 85% of patients, indicating substantial renal recovery (*Table IV*).

Table IV
Changes in urinary findings over follow-up.

Follow-up period	Urine protein/RBC	
	Urine protein (≤ +)	Urine RBC (≤ 5/HPF)
After 1 month	18 (38.3%)	16 (34.0%)
After 2 months	29 (61.7%)	27 (57.4%)
After 3 months	36 (76.6%)	35 (74.5%)
After 6 months	41 (87.2%)	40 (85.1%)

Serological response followed a similar pattern. While high anti-dsDNA titers were predominant at baseline, a marked decline was observed at six months. The proportion of patients with anti-dsDNA levels below 200 IU/ml increased from 12.8% at baseline to 55.4% at final follow-up, reflecting effective disease control (*Table V*).

Table V
Immunological response during follow-up (Anti-dsDNA levels).

Anti-dsDNA	Baseline	After 6 months
>400 IU/ml	32 (68.1%)	9 (19.1%)
200–400 IU/ml	9 (19.1%)	12 (25.5%)
<200 IU/ml	6 (12.8%)	26 (55.4%)

DISCUSSION

This study provides a focused insight into the clinical-renal profile and short-term outcomes of lupus nephritis patients treated with pulse cyclophosphamide therapy in a Bangladeshi tertiary care setting. The findings reaffirm the well-established demographic pattern of SLE, with a striking female predominance (91.5%) and a peak incidence in young adulthood (21-30 years) [1,2]. This demographic concentration underscores the significant socioeconomic and reproductive age burden of the disease. At presentation, our cohort exhibited high disease activity. The majority (61.7%) had heavy proteinuria (+++), and a significant proportion (68.1%) had markedly elevated anti-dsDNA levels (>400 IU/ml). This aligns with the known pathogenic role of anti-dsDNA antibodies in immune complex deposition and complement activation within the glomeruli [14]. The strong association between high anti-dsDNA titers and severe renal involvement at baseline highlights its utility as a marker of renal activity, consistent with other studies [15]. The treatment response observed over six months is the central finding of this study. The use of cyclophosphamide-based induction therapy (in 91.5% of patients, either alone or with steroids) led to substantial improvement. A progressive decline in proteinuria was noted, with 76.6% of patients achieving proteinuria ≤+ by three months and 87.2% by six months. This rapid reduction is critically important, as an early decrease in proteinuria is a well-validated predictor of favorable long-term renal survival [16]. Similarly, hematuria resolved in 85.1% of patients by six months, indicating a reduction in glomerular inflammatory activity. Concurrently, a significant serological response was observed. The proportion of patients with anti-dsDNA levels <200 IU/ml increased from 12.8% at baseline to 55.4% at six months. This parallel

improvement in proteinuria and anti-dsDNA titers reinforces the concept that these parameters are interconnected biomarkers of disease activity. The correlation suggests that effective immunosuppression reduces autoantibody production, leading to decreased immune complex-mediated renal injury and, consequently, lower protein excretion [17,18]. Our findings support the practice of using serial anti-dsDNA and proteinuria measurements to monitor therapeutic efficacy, as recommended by current management guidelines [19]. The continued reliance on cyclophosphamide in our setting, as opposed to mycophenolate mofetil, which is increasingly used as a first-line agent globally, reflects resource constraints and drug availability common in low- and middle-income countries [12]. Despite its known toxicity profile, our data demonstrate that cyclophosphamide remains highly effective for inducing remission, a finding consistent with historical clinical trials and real-world data from similar regions [20,21]. However, the study is not without limitations. The lack of renal biopsy data in all patients precludes correlation of outcomes with histological class, which is a key prognostic factor [22]. The relatively small sample size and short follow-up period limit the assessment of long-term outcomes, relapse rates, and drug-related adverse events. Furthermore, the absence of a control group or comparison with other immunosuppressive regimens prevents definitive conclusions about the superiority of the used protocol. Nevertheless, our results contribute valuable context-specific data from Bangladesh. They demonstrate that with available standard therapy, significant short-term renal and immunological remission can be achieved in most patients. Future studies with longer follow-up, histological correlation, and cost-effectiveness analyses comparing different induction regimens are needed to optimize lupus nephritis management in resource-limited environments.

LIMITATIONS

This study is limited by its single-center design, small sample size, and lack of histopathological correlation due to limited renal biopsy data. The short six-month follow-up period precludes assessment of long-term outcomes and relapse rates.

CONCLUSION

This study confirms that lupus nephritis predominantly affects young females in Bangladesh, presenting with significant proteinuria and high anti-dsDNA levels. Pulse cyclophosphamide-based therapy resulted in substantial short-term improvement, with a strong correlation observed between the reduction of proteinuria and anti-dsDNA titers within six months. These findings support the effectiveness of available immunosuppressive regimens and underscore the value of monitoring both parameters to assess treatment response in resource-constrained settings.

RECOMMENDATION

Based on the findings, we recommend routine serial monitoring of both proteinuria and quantitative anti-dsDNA levels to assess treatment response in lupus nephritis. Larger, multicenter studies with histological correlation and longer follow-up are needed to establish local management guidelines.

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CONFLICT OF INTEREST

None declared

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