

Lupus Nephritis; an Unrevealed Morbidity in Bangladeshi Population- A Clinical and Histomorphological Study

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Abstract

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder with multi-organ involvement. SLE affect on kidneys, mostly referred to as Lupus nephritis (LN) is of special interest for three reasons. First, lupus nephritis is one of the commonest types of organ involvement in this disorder, affecting as up to 45% of all patients with SLE. Second, it presents with a great variety of clinical and histopathological findings and thirdly, it greatly affects the morbidity and mortality of SLE patients. Thus, LN is one of the most serious SLE complications and the clinicopathological findings of LN are responsible for the ultimate prognosis of SLE. But these findings show geographical variation. Data on LN of Bangladeshi patients are rare in literature and most of them describe mostly clinical features rather than the histomorphologic findings.

Objectives: To evaluate demographic, clinical, laboratory and histomorphological characteristics of LN patient and analyze correlations across different ISN/RPS 2003 classes.

Method: A prospective, cross-sectional study was conducted at a tertiary diagnostic center in Dhaka from July 2024 to June 2025. Total fifty clinically diagnosed SLE cases with renal involvement were included in this study. The study group were underwent renal core biopsy. Histological evaluation and direct immunofluorescence (DIF) study were done on each specimen. Each case was classified according to the International Society for Nephrology/Renal Pathology Society (ISN/RPS) 2003 LN classification system and compared with the clinical, biochemical and immunological findings.

Results: The mean age was 28.3 ± 12.2 years (range: 9-70), with female predominance (M:F ratio 1:4.5). Proteinuria was the leading presentation (96%), followed by hematuria (56%). ISN/RPS classification revealed Class IV as most frequent (40%), followed by Class III (26%). Class II (22%), Class V (08%) and Class I (04%). Proliferative LN (Class III/IV) exhibited crescent formation (30%), wire loop formation (34%) and necrotizing change (36%). Full house Immunofluorescence deposits were present in 85% of evaluable cases. Higher activity and chronicity indices were observed in Class IV lesions, correlating with worse renal function.

Conclusion: Class IV LN was the predominant and most severe subtype, strongly associated with adverse clinical, biochemical and histological features. Early renal biopsy and clinicopathological correlation remain indispensable for prognosis and therapeutic planning in Bangladeshi patients.

[Journal of Histopathology and Cytopathology, 2026 Jul; 10 (2):86-95]

DOI: <https://www.doi.org/10.69950/jhc.2026.10.2.2>

Keywords: Systematic lupus erythematosus, Lupus nephritis, Histopathology, Immunofluorescence, ISN/RPS classification, Bangladesh.

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Introduction

Systemic lupus erythematosus (SLE) is a multisystemic autoimmune disease of unknown etiology and with high heterogeneity. The hallmark of SLE pathogenesis is the production of autoantibodies, which results from a combination of genetic, epigenetic, environmental, hormonal and immunoregulatory factors.¹ This disease is marked clinically by multisystemic inflammatory involvement.² Renal involvement is a common complication of SLE which is associated with significant morbidity and mortality.³ The renal manifestations are called as Lupus nephritis (LN) which often determine the course of the disease and it is characterized by the accumulation of immune complexes in glomeruli and often as an inflammatory response in all kidney compartments leading to varying degree of kidney damage, and in severe cases kidney failure.⁴ The frequency of LN varies between different regions of the world and different ethnicities. Overall, 30-60% of patients with SLE and 70% of young individual with SLE develop LN.⁵ It has been shown that LN is more frequent in the black population with SLE than in Asians and Hispanic populations and less common in Caucasians.⁶ A study reported that in India prevalence of SLE is 3.2 per 100,000. The prevalence of lupus nephritis (LN) is higher in Indo-Asians in comparison to the white population.⁷ In a study done by Das J et al in the north eastern India, the prevalence of paediatric and adolescent lupus nephritis was found to be 11.3%.⁸ Moreover, a cohort of SLE patients from Pakistan was found to have a 5-year survival of 80%. Organ damage including LN was present in 76% of the patients.⁹

LN is a classic example of immune complex induced microvascular injury which results

from the production of autoantibodies against autoantigens, with double-stranded DNA is the commonest target.¹⁰ There are two ways that anti-ds DNA antibodies exert their nephrogenic effect. First, immune complexes are formed in the circulation that are deposited to the glomeruli. Second, anti-ds DNA antibodies are connected to the glomeruli in situ either by binding to exposed chromatin fragments connected to glomerular membranes and mesangial matrices or by binding to non-DNA structures connected to the glomerulus that cross-react with anti-ds DNA antibodies.^{11,12}

The present classification of LN was published in 2004 jointly by the International Society of Nephrology (ISN) and Renal Pathology Society (RPS). According to this classification, LN is classified as Class I (minimal mesangial LN), Class II (mesangial proliferative GN), Class III (focal proliferative LN), and Class IV (diffuse proliferative LN). In Class V LN (membranous LN), continuous subepithelial deposits with or without mesangial alteration are seen. Class VI is advanced sclerosing GN, and it is diagnosed when more than 90% of glomeruli show global glomerulosclerosis.¹³

LN is the most common and serious manifestation of SLE and proliferative LN has poor outcome. Though some studies on Asian patients have suggested that they have an increased risk of developing lupus nephritis and it often present with more severe renal disease,^{14,15} patients from South Asia were not well represented till date. However, data on LN of Bangladeshi patients are extremely rare in the literature and most of them describe mostly clinical features rather than pathological findings. So this study was carried out in an effort to find out the histomorphologic patterns of LN and their clinical correlation.

Rationale

Systemic Lupus Erythematosus (SLE) is an autoimmune disease characterized by chronic immune complex formation and variable manifestations that include multi organ involvement. Among these, Renal involvement is the most serious complication of SLE accompanied by multiple laboratory abnormalities, and frequent exacerbations. Survival of patients with SLE has improved remarkably over the past decades. Earlier diagnosis, awareness of the vascular risk factors such as hypertension, nephrotic syndrome at presentation, and better approaches to treatment have undoubtedly contributed to the improved prognosis of patients with LN. The other factors which determine the outcomes are male gender, younger age, higher baseline creatinine, low socioeconomic status, resistant nephritic syndrome, severe anemia, low levels of complement, class IV histology, high activity and chronicity index etc. On the other hand, Chronic changes that occur as a result of delay in diagnosis and therapy are an important cause for failure to remit.

We aim in this study to compare the demographic, clinical, laboratory and histopathological findings in our patients with lupus nephritis and different classes of lupus nephritis according to the ISN/ RPS 2003 classifications.

Objective

We have designed this study to find out the demographic distribution and clinical and laboratory characteristics of LN patients and to compare the clinical and histologic characteristics with different classes of lupus nephritis patients from this region.

Methods

The study group comprised all biopsied renal core-needle biopsy specimens of known SLE patients having clinical evidence of renal

involvement received in a tertiary diagnostic center with all histo and cytopathological tests facility, Dhaka, from July 2024 to June 2025. A prospective, cross-sectional study was carried out during this one year duration.

A total 50 clinically diagnosed SLE cases were included in this study. The study group was comprised of all biopsied renal core-needle biopsy specimen of known SLE patients having clinical evidence of renal involvement in a tertiary diagnostic center Dhaka, from July 2024 to June 2025. A prospective, cross-sectional study was carried out during this 12 months duration. Renal involvement was defined by newly developed proteinuria, hematuria and/or increased serum creatinine level. Histological evaluation of each cases was done using standard histological techniques for renal biopsy.

Kidney biopsies were processed for light microscopy and also for Immunofluorescence microscopy (DIF) in all specimens. For each case, two biopsy sample was taken. One formalin fixed sample for light microscopy, and other was michels solution preserved sample for DIF study. All data related to the final diagnosis including age, gender, clinical and laboratory information were recorded. Each case was classified according to the ISN/RPS classification 2003 of LN.

For light microscopy, hematoxylin and eosin, periodic acid-Schiff, Masson trichrome and Jones methenamine silver stains were used. For direct immunofluorescence (DIF) study, IgG, IgA, IgM, C3, C1q, kappa and lamda antibodies were done. The degree of fluorescence was graded on an arbitrary scale from (+) to (+++).

We have included known SLE patients of different age group having clinical evidence of renal involvement in this study. Renal involvement was defined by newly developed

proteinuria, hematuria and/or increased serum creatinine level. Patients having inadequate renal biopsy, poorly preserved tissue or previously diagnosed LN already undergoing therapy were excluded from this study. Biopsies from renal transplant kidneys were also excluded from this study.

Results

In our study, a total 50 cases were diagnosed as LN among the non-neoplastic renal biopsy specimens received during the mentioned time period in our centre and were included in our study. Among the LN cases the mean age was 28.1 ± 12.16 years with 9 males (18%) and 41 females (82%). The age distribution has shown in Figure 1; 30% was from below 20 years, 42% was from 21 to 30 years and 16% from 31 to 40 years group. The demographic features are shown in Table I.

The most common indication for renal biopsy was proteinuria in total 48 (96%) cases, followed by hematuria in 28 (56%), and renal impairment (increased serum creatinine).

Among all the cases, 16 (32%) had nephrotic range proteinuria and 14 (28%) had nephritic presentation. Others presented with isolated proteinuria or hematuria or renal dysfunction. The mean serum creatinine was 1.67 ± 1.30 (mg/dl) and urinary total protein (UTP) was 3.9 ± 3 (g/24 hr).

Table I: Demographic Characteristics of Lupus Nephritis patients (n=50)

Characteristics	Value
Mean age	28.3 ± 12.16 years
Age range	9-70 years
Age distribution	
≤20 years	15 (30%)
21-30 years	21 (42%)
31-40 years	8 (16%)
41-50 years	3 (6%)
>50 years	3 (6%)
Gender	
Male	9 (18%)
Female	41 (82%)
Male:Female	1:4.5

Table II: Clinical and Laboratory Characteristics of Lupus Nephritis Patients (n=50)

Characteristics	All patients (n=50)	Class I (n=2)	Class II (n=11)	Class III (n=13)	Class IV (n=20)	Class V (n=4)
Clinical presentation						
Proteinuria	48 (96%)	2 (100%)	11 (100%)	12 (92%)	19 (95%)	4 (100%)
Hematuria	28 (56%)	0 (0%)	3 (27%)	5 (38%)	17 (85%)	3 (75%)
Generalized edema	21 (42%)	0 (0%)	3 (27%)	3 (23%)	11 (55%)	2 (50%)
Hypertension	12 (24%)	0 (0%)	1 (9%)	3 (23%)	6 (30%)	2 (50%)
Laboratory findings						
Mean serum creatinine (mg/dL)	1.67 ± 1.30	0.65 ± 0.20	1.50 ± 1.48	1.70 ± 1.50	1.90 ± 1.12	1.65 ± 0.95
Mean urinary protein (g/24h)	3.95 ± 3.0	2.70 ± 2.35	3.55 ± 2.45	3.45 ± 2.40	4.60 ± 4.45	4.05 ± 1.70
Nephrotic-range proteinuria	16 (32%)	0 (0%)	5 (45%)	4 (31%)	5 (25%)	2 (50%)
Nephritic presentation	14 (28%)	0 (0%)	0 (0%)	3 (23%)	10 (50%)	1 (25%)
Anti-dsDNA positive	47 (94%)	2 (100%)	10 (91%)	12 (92%)	19 (95%)	4 (100%)
Low serum C3	30 (60%)	1 (50%)	6 (55%)	7 (54%)	14 (70%)	2 (50%)

According to the ISN/RPS 2003 classification in this study, most of the LN cases belong to class IV 20, 40%), followed by class III (13, 26%), class II (11, 22%), class V (4, 8%) and class I (2, 4%) (Figure 2)

The common presentation of class IV was nephritic presentation in 10 (50%) and 5 (25%) cases had nephrotic-range proteinuria. Overall 19 (95%) cases had proteinuria and the mean urinary total protein (UTP) was 4.60 ± 4.45 g/24h. The mean serum creatinine

was 1.90 ± 1.12 mg/dl. On histopathology, 10 (50%) had crescent formation, of which 3 (15%) involved $>50\%$ glomeruli (crescentic LN), 12 (60%) had wire loop formation and 14 (70%) had necrotizing lesions. Interstitial fibrosis and tubular atrophy (IFTA) was $\geq 25\%$ in 4 (25%) cases of class IV LN. In 2 (4%) cases, there was an association of class V lesions with class IV.

In class III LN, 3 (23%) cases had nephritic presentation, 4 (31%) cases had nephrotic range proteinuria. The mean UTP was 3.45 ± 2.40 g/24h and mean serum creatinine was 1.70 ± 1.50 mg/dl in class III LN. Among class III LN cases, crescent formation was observed in 4 (31%) cases, wireloop formation in 5 (38%) cases and necrotizing lesion in 4 (31%) cases. IFTA was $\geq 25\%$ in 2 (15%) cases of class III LN. One class III LN had an association with class V lupus nephritis.

The most common presentation of class II LN was isolated proteinuria in 11 (100%) cases, nephrotic range proteinuria in 5 (45%) cases and hematuria in 3 (27%) cases. The mean UTP was 3.55 ± 2.45 g/24h and mean serum creatinine was 1.50 ± 1.48 mg/dl in class II LN. Histologically these cases had focal/diffuse mesangial proliferation with $\geq 25\%$ IFTA in 1 (9%) cases. In class V LN, 4 (100%) cases had isolated proteinuria and 2 (50%) cases had nephrotic range proteinuria. 3 (75%) cases of class V LN patient had hematuria. The mean UTP was 4.05 ± 1.70 g/24h and mean serum creatinine was 1.65 ± 0.95 mg/dl. Histologically all had spikes and crater formation in silver staining and 1 (25%) had $>25\%$ IFTA. Among class I LN cases, 2 (50%) cases had isolated proteinuria. The mean UTP was 2.70 ± 2.35 g/24h and mean serum creatinine was 0.65 ± 0.20 mg/dl. No class VI LN case was found in our study. The clinical and laboratory characteristics of different classes are shown in Table II.

Table III: Histological Characteristics of Lupus Nephritis Patients (n=50)

Histological Characteristics	All patients (n=50)	Class I (n=2)	Class II (n=11)	Class III (n=13)	Class IV (n=20)	Class V (n=4)
Crescent formation	15 (30%)	0 (0%)	0 (0%)	4 (31%)	10 (50%)	1 (25%)
Diffuse crescentic ($>50\%$)	3 (6%)	0 (0%)	0 (0%)	0 (0%)	3 (15%)	0 (0%)
Wire loop lesions	17 (34%)	0 (0%)	0 (0%)	5 (38%)	12 (60%)	0 (0%)
Necrotizing lesions	18 (36%)	0 (0%)	0 (0%)	4 (31%)	14 (70%)	0 (0%)
IFTA $>25\%$	8 (16%)	0 (0%)	1 (9%)	2 (15%)	4 (20%)	1 (25%)
Immune deposits (n=48)						
Full-house pattern	41 (85%)	0 (0%)	8 (73%)	11 (85%)	18 (90%)	4 (100%)
IgG deposits	48 (96%)	2 (100%)	11 (100%)	13 (100%)	20 (100%)	2 (50%)
IgA deposits	44 (92%)	1 (50%)	9 (82%)	12 (92%)	19 (95%)	4 (100%)
IgM deposits	43 (90%)	1 (50%)	9 (82%)	12 (92%)	18 (90%)	3 (75%)
C3 deposits	46 (96%)	2 (100%)	10 (91%)	12 (92%)	19 (95%)	4 (100%)
C1q deposits	43 (90%)	1 (50%)	9 (82%)	12 (92%)	17 (85%)	4 (100%)
K deposits	48 (96%)	1 (50%)	11 (100%)	13 (100%)	20 (100%)	3 (75%)
L deposits	48 (96%)	1 (50%)	11 (100%)	13 (100%)	20 (100%)	3 (75%)
Special features						
Mean activity index (III+IV)				4.60 $\pm$ 2.05	8.70 $\pm$ 3.40	
Mean chronicity index (III+IV)				2.75 $\pm$ 1.30	3.55 $\pm$ 1.60	

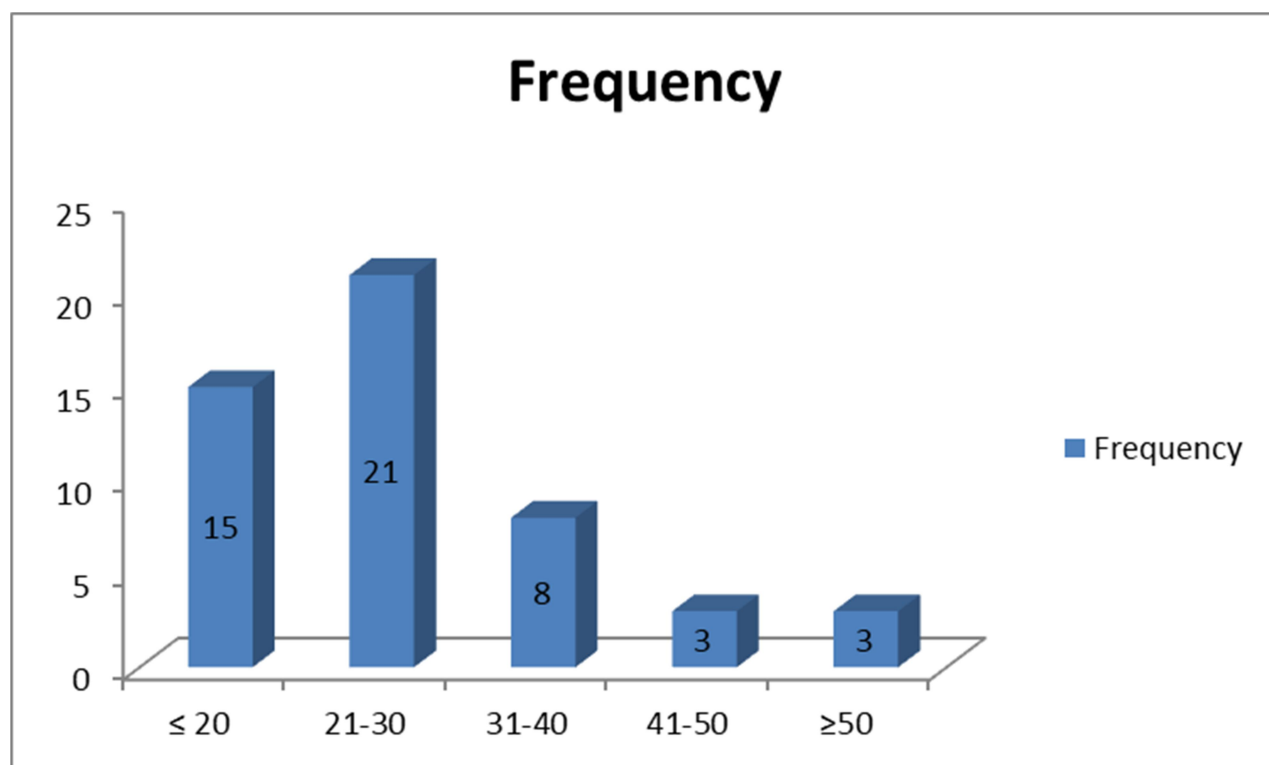


Figure 1. Age distribution (n=50)

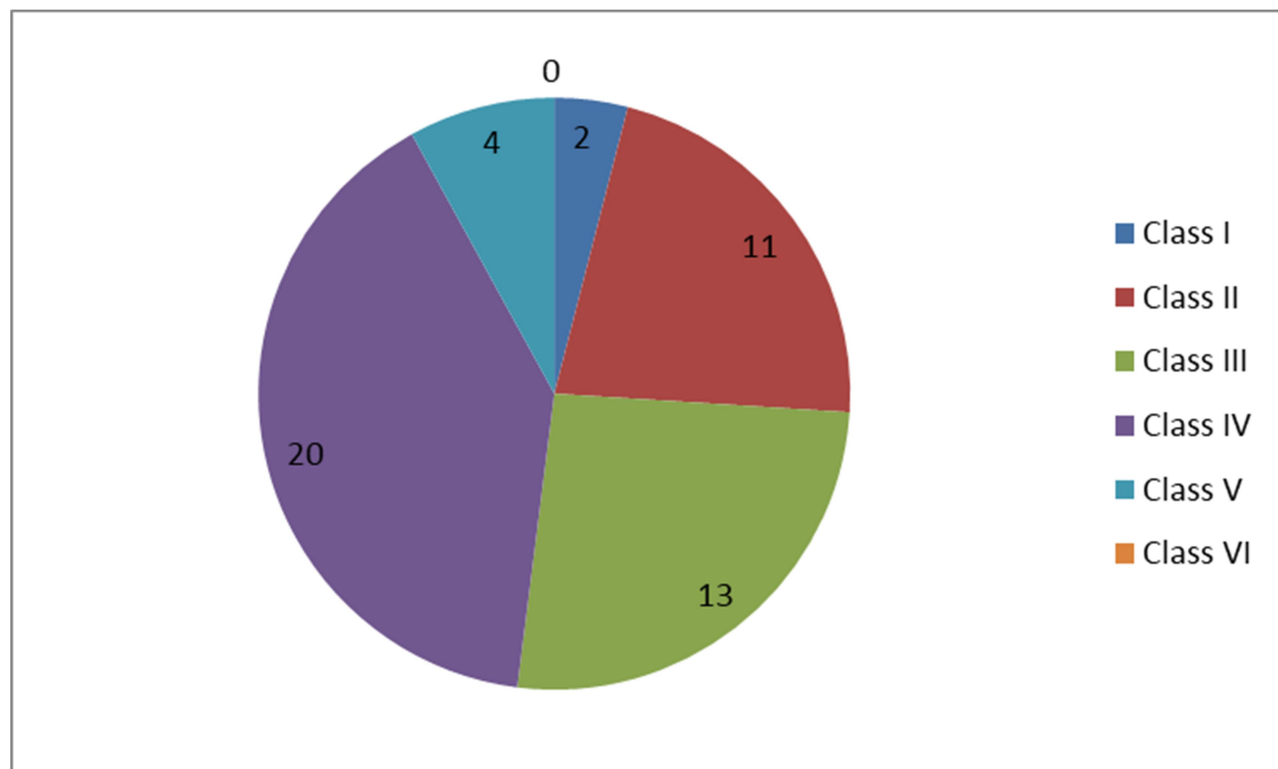
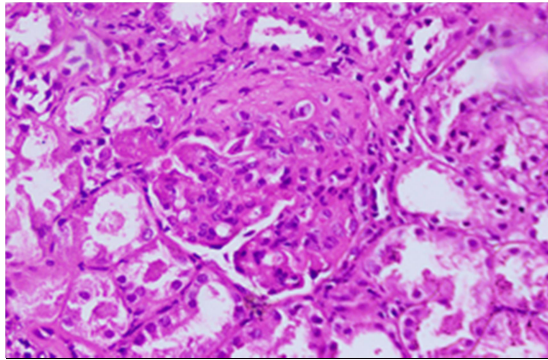
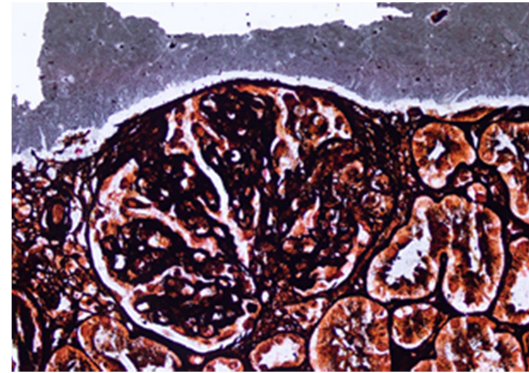


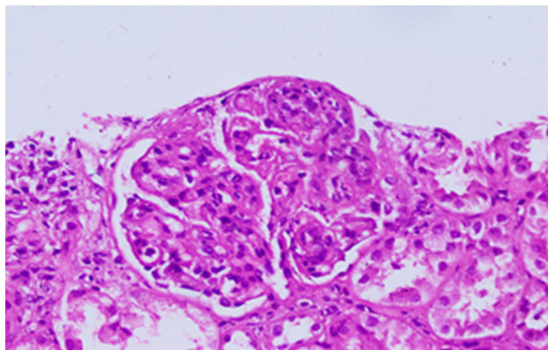
Figure 2. LN Renal Pathology Society/International Society of Nephrology classes (n=50)



A

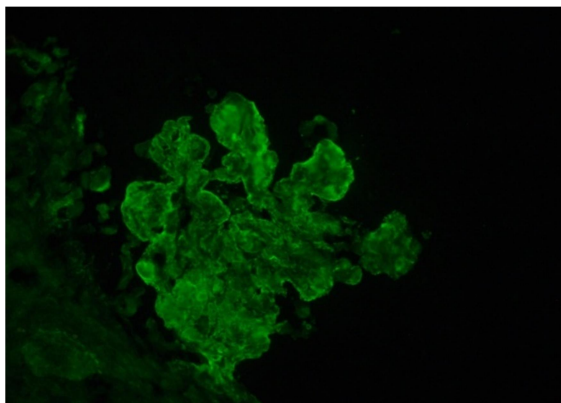


B

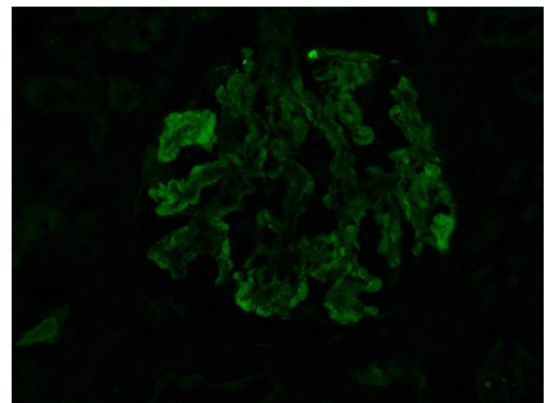


C

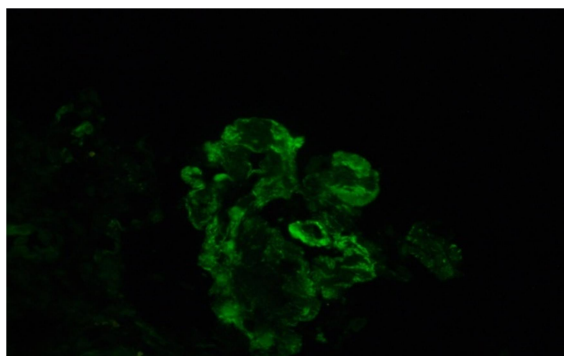
Figure 3: Renal pathology Society/International Society of Nephrology Class IV Lupus Nephritis with microscopic active changes, (A) Cellular crescent formation, (B) Wire loop changes in silver stain, (C) Endocapillary proliferation



A



B



C

Figure 4. DIF stain show deposition of IgG, IgA & C3 Antibody

On DIF study, 2 cases could not be evaluated due to a lack of glomerulus. Among the rest 48 cases, 41 (85%) cases were found with full-house immune deposits of different intensities. Among others, IgA deposits was lacking in 4 cases, IgM was lacking in 5 cases and C3 deposits was lacking in 2 cases. The mean activity score in class III LN was 4.60 ± 2.05 and in class IV LN was 8.70 ± 3.40 . The mean chronicity score in class III LN was 2.75 ± 1.30 and in class IV LN was 3.55 ± 1.60 . Histological characteristics of different classes of LN are shown in table III.

Discussion

The renal biopsy in SLE patients performed therapeutic and prognostic purpose. The renal complication in SLE is very common. Autopsy study shows that 75% of SLE patient have LN.¹⁶

The mean age of LN cases in our study was 28.3 ± 12.2 years, with a male:female ratio of 1:4.45. Baqui et al in Sir Salimullah Medical College and Mitford Hospital, Dhaka found the mean age of 26 ± 11.97 years with a male:female ratio of 1:10.33.¹⁷ In India, Sharma et al found male-female ratio as 1:8.7 with predominant age group 20–40 years.¹⁸

In this study, the nephrotic range of proteinuria was observed in 32% and nephritic presentation was seen in 28% of

cases. While Singh et al reported nephrotic-range proteinuria in 51% of cases in a study in India.¹⁶ Gor et al. reported hematuria in 88.6% of cases of LN, while Sharma et al reported microscopic hematuria in 78.4% of cases.¹⁸ In this study, hematuria observed in 56% of patients. It was also observed that 60% of cases had low serum C3 level, while Farah et al reported low C3 concentration in 75% of cases.¹⁹

In this study, according to the ISN/RPS 2003 classification, most of the LN belong to class IV (20,40%), followed by class III (13, 26%), class II (11, 22%), class V (4, 8%) and class I (2, 4%). Studies carried out in India, Nepal, Saudi Arabia as well as Bangladesh also found LN class IV as the predominant histological class of LN, ranging from 40% to 76%.²⁰

Among different classes of LN, the mean serum creatinine level and mean UTP were highest in class IV LN in our study. However, except in class I LN, in all the classes, UTP was >3 g/25 h and serum creatinine was >1.5 mg/dl. Farah et al also found higher mean serum creatinine level in class IV LN, but there was no significant between class III and class IV in mean UTP level.¹⁹

In this study, crescent formation was found in proliferative lesions. In our study, crescent formation was found in 50% of class IV LN, of which 15% were crescentic LN, and in class III LN, 31% had crescent formation. Among the proliferative lesions, wire loop formation was seen in 60% and 38% in class IV and III lesions, respectively. Singh et al in their study reported crescentic LN in 10 out of 28 (35.71%) class IV LN.¹⁶ Nasri et al. reported crescent formation in 42.86% of cases of class III and IV LN, while Zoshima et al reported wire loop lesion in 36% of cases among class III and class IV LN.^{21, 22} There was no significant difference in IFTA among class III, IV, and V in our study. Overlapping features were present in three cases in this series which include LN IV + V in two and LN III+V in one case.

Conclusion

In our study, the correlations of clinical manifestations and laboratory findings with ISN/RPS classes of LN in a group of Bangladeshi patients were analyzed. This correlation may help to determine the prognosis and the need for immediate immunosuppressive treatment. Clinical manifestations and laboratory results are helpful in the prognosis and prediction of clinical courses. Renal biopsy remains the cornerstone for identifying treatment options for LN patients. This study provides more information about LN in Bangladesh and future clinical research.

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