

## Clinicopathological Presentation of Lupus Nephritis

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### Abstract

#### Background:

Despite great improvement in the management of lupus nephritis, it remains the most frequent cause of SLE-related mortality. It has diversities of clinical and histological presentations.

#### Objective:

The aim of this study was to observe the most common clinicopathological presentations of lupus nephritis (LN).

#### Methods:

This cross-sectional observational study was conducted among thirty patients with lupus nephritis, admitted into department of Medicine, Rangpur Medical College and Hospital during June, 2023 to May, 2024 through convenient sampling. After written consent, all patients were undergone renal biopsy and tissue was analyzed for histopathological examination. After compilation data was analyzed by SPSS version 25.0.

#### Results:

Out of thirty patients female were 27(90%) and male 3(10%), most of them 21(70.00%) were at childbearing age between 18 and 35 years, the mean age was 24.16±4.23 years. The most frequent clinical features were edema (100%), joint pain/arthralgia 18(60.00%), fever 16(53.33%) and oral ulceration 11(36.66%). On examination 21(70%) patients were anaemic, 18(60%) patients had microscopic hematuria and proteinuria >0.5 gm/24 hours was noticed in all patients. Among the respondents 18(60.00%) patients had nephrotic range of proteinuria. 10(33.33%) patients had serum creatinine >1.40 mg/dl. On serological test 28(93.3%) patients had a positive ANA, 27(90%) patients had a positive anti-ds DNA. The most common histological feature was class IV in 17(56.70%) patients, followed by 6(20.00%) patients had Class II, 4(13%) patients had Class V and 2(6.7%) patients had Class III lupus nephritis.

#### Conclusion:

Generalized swelling/ edema was the commonest clinical presentation with class IV lupus nephritis on histology .

**Keywords:** Lupus nephritis, Clinical presentation, Histological feature

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### Introduction:

Systemic lupus erythematosus is the paradigm of systemic autoimmune disease. Lupus nephritis develops in most of the SLE patients with their disease process.<sup>1</sup> Near about 50% of patients with SLE develop lupus nephritis; Male SLE patient are at increased risk of aggressive disease having higher rates of kidney involvement and increase risk of developing renal failure than female.<sup>2</sup>Lupus nephritis mainly develops early in the disease

course, within the first six to thirty six months, and can present at initial diagnosis. Risk factors for the developing lupus nephritis are male sex, early age; and non-European ancestry. In the USA, the incidence of lupus nephritis is higher in Asian people (33%-55%) black people (34%-51%), Hispanic people (31%-43%), and then white (14%-23%) patients. Hispanic and Black people have adverse outcomes and are most likely to develop renal failure than white people.<sup>2</sup>

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The overall incidence ranges from 1.8 to 7.6 cases per 100,000 people.<sup>3</sup> Clinically identification of LN can be challenging because patients often presented without overt signs of kidney disease, especially in early stage.<sup>2</sup>

The clinical presentations of lupus nephritis are variable, ranging from proteinuria to overt proteinuria, nephrotic syndrome or nephritic syndrome, and renal failure may be asymptomatic. Sometimes patients can present with “silent” LN, where patients do not have any findings of clinical renal disease but have histopathological changes on kidney biopsy consistent with lupus nephritis.<sup>4,5</sup> Renal involvement in lupus nephritis is assumed by an abnormal urinary finding and raised serum creatinine and confirmed by histological findings on kidney biopsy.<sup>6</sup> The histopathological class of LN; the degree of disease activity, chronicity and the presence of other complications like as interstitial nephritis and thrombotic microangiopathy have been suggested as the main histological features indicating further management.<sup>7</sup> Proteinuria is found in 100% of people with lupus nephritis and nephrotic range proteinuria is found in 50% of total patients with lupus nephritis.<sup>8-10</sup>

Despite progress in the discovery of diagnostic and prognostic biomarkers, renal biopsy remains essential in clinical practice to diagnose lupus nephritis. Renal biopsy gives evidence of disease prognosis, chronicity activity, and treatment planning. Management of lupus nephritis includes potentially toxic medications; it can be; not beneficial into the treatment without definitive diagnosis. The common indications for doing first renal biopsy are proteinuria >500 mg/day, active urinary sediments ( $\geq 5$  RBC cast or WBC cast/HPF, mainly dysmorphic without evidence of infection) or elevated serum creatinine.<sup>11,12</sup>

The recent approach for managing lupus nephritis and researching new treatment modalities is mainly guided by ISN/RPS, classification. Lupus nephritis is a disabling disease in patients with systemic lupus erythematosus. Despite difference biochemical and laboratory tools are used for diagnosing lupus nephritis, renal biopsy is still gold standard. Management of lupus nephritis depends upon - its histological classification, as we used mainly toxic medications; it can be not beneficial into the treatment without definitive diagnosis. So, it is important to specify histological pattern of lupus nephritis for specific treatment and

better outcome. Several studies are done in different parts of our country, especially Dhaka based. But in our northern area we have limited data related to clinicopathological presentations of lupus nephritis. That's why this study aimed to determine clinicopathological presentations of lupus nephritis.

### Methods:

A cross-sectional study was carried out in the Department of Medicine at Rangpur Medical College Hospital from June, 2023 to May, 2024 for a period of 12 months. Ethical clearance was obtained from ethical approval committee (ERC) of Rangpur Medical College. Informed written consent was taken from each eligible person. Then total 30 lupus nephritis patients aged  $\geq 18$  years were enrolled in study according to inclusion & exclusion criteria who were admitted in the department of Medicine and department of Nephrology of Rangpur medical college hospital. After enrolment, comprehensive history, physical findings and laboratory reports collected through direct interview. All patients were undergone renal biopsy and tissue was analyzed for histopathological examination. Lupus nephritis is staged according to the classification revised by the International Society of Nephrology (ISN) and the Renal Pathology Society (RPS) in 2004.<sup>13</sup> After compilation data was analyzed by SPSS version 25.0 and presented in tabulated form.

### Results:

Among 30 patients with lupus nephritis, the mean age of the study patient was  $24.16 \pm 4.23$  (SD) years, 18-25 years was the most prevalent group. Total female was 27(90%) and male were 3(10%). Mean age of female and male was  $23.11 \pm 3.22$  and  $30.83 \pm 4.12$  years respectively (Table-I).

**Table-I: Age and sex distribution of the respondents (N=30)**

Age (years)	Male no. (%)	Female no. (%)	Total
18 – 25	2(6.66)	11(36.66)	13(43.33)
26 - 35	1(3.33)	10(33.33)	11(36.66)
36 - 45	0(0.0)	5(16.66)	5(16.66)
>45	0(0.00)	1(3.3)	1(3.3)
Total	3(10.00)	27(90.0)	30(30)
Mean $\pm$ SD	30.83 $\pm$ 4.12	23.11 $\pm$ 3.22	24.16 $\pm$ 4.23

Most of the study subjects resided in rural area 26(86.66%). Maximum of the study subject occupation was housewife 20(66.66%). Most of the study subject religion was Islam 22(73.33 %). Most of the respondents belongs from 16(53.33%) low socioeconomic status are shown in Table- II.

**Table-II: Demographic profile of the study subjects (N=30)**

Demographic profile	no. (%)
<b>Residence</b>	
Urban	4(13.33)
Rural	26(86.66)
<b>Occupation</b>	
Service	3(10.0)
Housewife	20(66.66)
Others	7(23.33)
<b>Religion</b>	
Islam	22(73.33)
Hindu	8(26.66)
<b>Socioeconomic status (monthly income in taka)</b>	
Low( $\leq$ 10000)	16(53.33)
Average(11000-20000)	11(36.66)
High(>20000)	3(10)

The most frequent clinical features were edema 30(100%), Joint pain /arthralgia 18(60.00%), serositis 17(56.7%), fever 16(53.33%) and skin rash 14(46.7%). The other clinical manifestations were oral ulceration 11(36.66%), gross haematuria 9(30%), headache 9(30%) and most common symptoms was edema, shown in Figure-1.

At the time of renal biopsy 21(70%) patients were anaemic, 18(60%) patients had microscopic hematuria and Proteinuria  $>0.5$  gm/ 24 hours was notices in all patients. Among them 18(60.00%) patients had nephrotic range of proteinuria. ANA was positive in 28(93.3%) patients, 27(90%) patients had a positive anti-dsDNA. These are shown in Table- IV.

Most common histological class of lupus nephritis in this study was class IV found in 17(56.7%) respondents followed by Class II, 6(20%) patients;

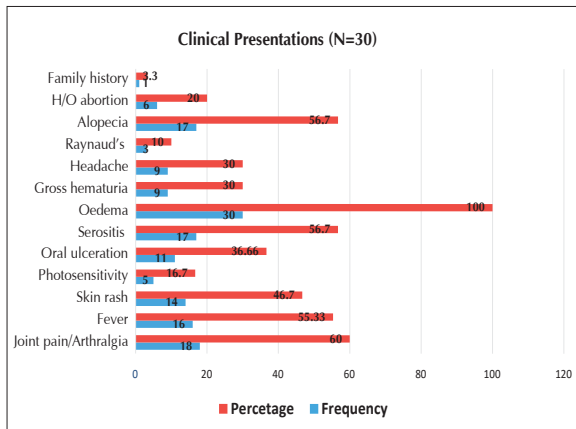
Class V, 4(13.3%) patients; Class III, 2(6.7%) patients; Class VI, 1(3.3%) patient are described in Table-V.

**Table-IV: Frequency of main laboratory variables (N=30)**

Name of test	no. (%)
<b>Hematological</b>	
Anemia (Hb-<10gm/dl)	21(70.0)
Leucopenia (<4 $\times$ 10 <sup>9</sup> /L)	2(6.66)
Thrombocytopenia (p<100 $\times$ 10 <sup>9</sup> /L)	3(10.00)
Raised ESR (>60)	24(80.0)
<b>Renal</b>	
Microscopic hematuria	18(60)
Nephrotic syndrome >3.50gm/24 hours	18(60.00)
Serum creatinine - $\leq$ 1.40 mg/dl	20(66.66)
Serum creatinine - >1.40 mg /dl	10(33.33)
<b>Immunological</b>	
ANA (positive)	28(93.3)
Anti-ds DNA (Positive)	27(90.0)

**Table-V: Histological classifications of lupus nephritis (N=30)**

Class of LN	no. (%)
Class I	0(0.00)
Class II	6(20.0)
Class III	2(6.7)
Class IV	17(56.7)
Class V	4(13.3)
Class VI	1(3.3)
Total	30(100.0)



**Figure-1: Frequency of main clinical presentations (N=30)**

**Discussion:**

In this study the mean age was 24.16±4.23 years and male: female sex ratio is 1:9. Similar studies were carried out in Singapore and China showed that the mean age of the patient was 35.4 years and 33±14 years, respectively.<sup>14,15</sup> A study in Iran showed that the mean age was 25.6±10.3 years and in other studies the mean age varied from 33.5±14 years to 36.8±13.8 years.<sup>16,17</sup> Another study conducted in Bangladesh showed mean age of the patients was 26±11.97 years and the age range was 10 to 60 years.<sup>18</sup>

This study was conducted among 3(10%) male and 27(90%) female. It was observed that female patients were more than the male. A hospital-based study done in Bangladesh showed that 31(91.18%) patients were females and only 3(8.82%) patients were male.<sup>18</sup> This study showed that male: female ratio of 1:9 which is similar with a previous study from Iran with a male: female ratio 1:13.<sup>19</sup> In this study, most of the respondents resided in rural area 26(86.66%) and most common occupation was housewife 20(66.66%). Another study showed that 61.3% patient's occupation was housewife.<sup>20</sup> The most common clinical symptom was generalized swelling/ edema reported in 30(100%) cases in this study followed by joint pain /arthralgia 18(60.00%), serositis 17(56.7%) fever 16(53.33%) oral ulcer 11(36.66%) and gross hematuria 9(30%) which is similar with a previous study that showed edema in 52.46% cases, fever in 47.54% , joint pain in 42.62%, photosensitivity/rash in 40.98%, oral ulcer in 22.95%, and central nervous system involvement in 11.48% cases.<sup>20</sup> Another study

conducted in Bangladesh showed that edema in 76.3% cases, joint pain 51.6%, skin rash 41.95% and fever, 33.4% cases.<sup>20</sup> This study showed that 21(70%) patient was anemic, 3(10%) patient had thrombocytopenia and 2(6.66%) patient had leucopenia. In another study it was found mean Hb 9.87±1.78 gm/dl.<sup>20</sup> In this study, 9(30.0%) patients had gross haematuria and 18(60%) had microscopic haematuria, which was similar to those reported by some authors.<sup>22</sup> Most common histological class of lupus nephritis in this study was class IV found in 17(56.7%) respondents followed by Class II, 6(20%) patients; Class V, 4(13.3%) patients; Class III, 2(6.7%) patients; Class VI, 1(3.3%) patient. In other study most common histological class of lupus nephritis was Class IV 52.7%, Class III 21.5%, class II- 14%, class V- 7.5% and class VI- 1.1% which was consistent to this study.<sup>20</sup>

**Limitation:**

Small sample size was a major limitation of this study. Conducted in a single center. Moreover, patients were not selected randomly.

**Conclusion:**

Most respondents were female and aged 18-25, primarily from rural areas, housewives, and Muslim. Lupus nephritis has varied clinical features with different histological type. Common symptoms included edema, joint pain, and fever. Nephrotic range proteinuria occurred in 18(60%) and elevated serum creatinine was noted in 10(33.33%) patients. The majority had Class IV histology. Renal biopsy aids in evaluating renal status and lupus nephritis classification.

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