**Original Research Article**

# A study to evaluate the correlation between serological profile and histopathology of lupus nephritis

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## Abstract

**Background:** Systemic lupus erythematosus is an autoimmune disease of unknown etiology, characterized by the involvement of multiple organ systems. Organ damage is mediated by tissue binding autoantibodies and immune complexes. High anti-dsDNA titer and low serum complement levels (C3, C4) correlate with disease activity of SLE, especially with lupus nephritis (LN).
**Aim of the study:** To evaluate the correlation between a serological profile (anti-dsDNA, serum C3, and C4) and histopathology of lupus nephritis and to find out the class of LN which has a significant correlation with the serological profile.
**Materials and methods:** This retrospective study was conducted in the Department of Nephrology, Kilpauk Medical College and Hospital, Chennai between 2013-2017 with 50 ANA positive female SLE patients with evidence of lupus nephritis (proteinuria, microscopic hematuria or increased serum creatinine). Serological profile (anti-dsDNA, serum C3, and C4) and renal biopsy were done in all patients.
**Results:** Of 50 patients, 35 (70%) had class IV lupus nephritis, 7 (14%) class II, 4(8%) class V and 4 patients (8%) had class IV and V on renal biopsy. The prevalence of anti dsDNA was 97.1% in LN and 97.4% (38 of 39 pts) in proliferative LN ($p<0.001$). The C3 level was low in 68% of patients with LN and 84.6% with proliferative LN ($p <0.001$). C4 level was low in 74% of patients with LN and 87.2% with proliferative LN ($p <0.001$). In our study, 72% (28 of 39 pts) of the patients with

proliferative LN (class IV, IV and V) had the combination of anti-dsDNA positivity, low C3,and low C4 levels but none of the patients with class II or class V LN had this combination of serology.

**Conclusion:** In our study, the serological profile of SLE had a significant correlation with histopathology of lupus nephritis. Anti-dsDNA, low C3, and low C4 had a significant independent correlation ($p<0.05$) with proliferative LN (class IV, IV and V).

## Key words

Lupus nephritis, Anti-dsDNA, Complements, Renal biopsy.

## Introduction

Systemic lupus erythematosus is an autoimmune disease of unknown etiology, characterized by the involvement of multiple organ systems.Organ damage is mediated by tissue binding autoantibodies and immune complexes [1]. The hallmark of SLE is the presence of serum autoantibodies directed to nuclear constituents (i.e., antinuclear antibodies, ANA).In most of the patients, these autoantibodies are present for a few years before the first clinical symptoms appear. The clinical presentation and course of SLE are extremely variable [2]. Some patients have spontaneous remissions; others may have mild musculoskeletal involvement which response to therapy and a few dies from progressive severe multisystem disease unresponsive to immunosuppressive therapy. SLE commonly involves skin, joints, kidneys, serosal surfaces including pleura and pericardium, CNS and hematopoietic system [3]. Lupus nephritis is one of the common manifestations of SLE. Diagnosis of SLE is based on the 11 criteria defined by the American Rheumatism Association (ARA). SLE patients develop a wide range of autoantibodies [4]. ANA is the most sensitive test for SLE and is present in more than 90% of patients but not specific for SLE. Anti dsDNA is a more specific but less sensitive marker of SLE [5]. High titer of anti dsDNA correlates with disease activity and especially with lupus nephritis Serum levels of complements C3 and C4 are usually decreased in active SLE and in active lupus nephritis. Most of the patients with active proliferative lupus nephritis have a hightiter of anti dsDNA and low C3 and C4 levels [6].

## Materials and methods

This retrospective study was conducted in the Department of Nephrology, Kilpauk Medical College and Hospital Chennai from 2013-2017. All ANA positive female patients with evidence of renal involvement were admitted in our Dept. of Nephrology. All ANA positive female SLE patients fulfilling ARA criteria between 15 and 45 years of age group with any one of the following abnormalities-Proteinuria (spot urine PCR >0.5), microscopic hematuria (≥ 3RBCs/HPF), increased serum creatinine (>1.2mg/dl) were included. Male SLE patients, patients below 15 and above 45 years of age group and ANA-negative lupus patients were excluded. All the patients who fulfilled the study criteria were included in the study after getting informed consent for renal biopsy. A well designed proforma was used to collect the demographic and clinical details of the patients. Apart from basic workups like urine analysis, CBC, RFT, LFT, ECG, X-ray chest and USG KUB, the following other investigations had been done in all patients. Anti-dsDNA antibody – done by Immunofluorescence method using the DNA of the kinetoplast of Crithidialuciliae and serum complement levels C3 and C4 – by the nephelometric method. ANA has been done already before enrolling the patient into the study – by indirect immunofluorescence method using Hep 2 cells. Percutaneous USG guided renal biopsy was done for all the patients and the specimen was analyzed by Light Microscopy and Immunofluorescence study.

### Statistical analysis

Data analysis was done by using SPSS 17 software. Univariate analysis was done by chi-

square test. Multivariate analysis was done by logistic regression method.

## Results

Of 50 patients, 25 (50%) were in the age group of 15 to 25 years, 17 in 26 to 35 years and 8 were in 36 to 45 years (**Table – 1**).

**Table – 1:** Age distribution.

| Age (Years) | Frequency | Percent |
|---|---|---|
| 15-25 | 25 | 50.0 |
| 26-35 | 17 | 34.0 |
| 36-45 | 8 | 16.0 |
| Total | 50 | 100.0 |

**Table – 2:** Class of LN in renal biopsy.

| Class | Frequency | Percent |
|---|---|---|
| II | 7 | 14.0 |
| IV | 35 | 70.0 |
| V | 4 | 8.0 |
| IV and V | 4 | 8.0 |
| Total | 50 | 100.0 |

35 patients (70%) had class IV lupus nephritis, 7 (14%) class II, 4(8%) class V and 4 patients (8%) had class IV and V on renal biopsy. No one had class III LN in our study. Totally 39 patients (78%) had proliferative LN (class IV and class IV and V) as per **Table - 2**.

Of 50 patients with LN, 41(82%) had anti dsDNA positivity. 34 of 35 patients (97.1%) with class IV, all the 4 patients (100%) with class IV&V, 1 of 7 patients (14.3%) with class II and 2of 4 patients (50%) with class V LN had anti dsDNA positivity. Totally 38 of 39 patients (97.4%) with proliferative LN had anti dsDNA positivity (P Value <0.001) as per **Table – 3, 4**.

Of 50 patients with LN, 34(68%) had a low C3 level in serum. 29 of 35 patients (82.9%) with class IV, all the 4 patients (100%) with class IV&V and 1 of 4 patients (25%) with class V LN had a low C3 level in serum. But none of the patients with class II LN had low C3 level. Totally 33 of 39 patients (84.6%) with proliferative LN had low C3 level (P Value < 0.001) as per **Table – 5, 6**.

**Table – 3:** Anti dsDNA and its correlation with the histopathology of LN.

| Renal Biopsy | | Anti dsDNA | | Total | P Value |
|---|---|---|---|---|---|
| | | Negative | Positive | | |
| II | Count | 6 | 1 | 7 | <0.001 |
| | % within Renal Biopsy | 85.7% | 14.3% | 100.0% | |
| IV | Count | 1 | 34 | 35 | |
| | % within Renal Biopsy | 2.9% | 97.1% | 100.0% | |
| V | Count | 2 | 2 | 4 | |
| | % within Renal Biopsy | 50.0% | 50.0% | 100.0% | |
| IV and V | Count | 0 | 4 | 4 | |
| | % within Renal Biopsy | 0% | 100.0% | 100.0% | |
| Total | Count | 9 | 41 | 50 | |
| | % within Renal Biopsy | 18.0% | 82.0% | 100.0% | |

Of 50 patients with LN, 37(74%) had a low C4 level in serum. 30 of 35 patients (85.7%) with class IV, all the 4 patients (100%) with class IV and V and 3 of 4 patients (75%) with class V LN had a low C4 level in serum. But none of the patients with class II LN had low C4 level. Totally 34 of 39 patients (87.2%) with proliferative LN had low C4 level (P Value < 0.001) as per **Table – 7, 8**.

## Discussion

We have studied 50 ANA positive female SLE patients with any one of the evidence of LN (proteinuria, microscopic hematuria or increased

serum creatinine) to evaluate the correlation between serological profile and histopathology of LN [7, 8]. Majority (25 patients, 50%) were in the age group between 15 and 25 years. All patients had significant proteinuria (>500 mg/day) [9]. Tutuncu ZN, et al, reported that 83.8% (31 of 37 pts) of patients had class IV LN on biopsy. In our study, 70% (35 pts) had class IV and 8% (4 pts) had combined class IV & V. Totally 78% (39 of 50 pts) had proliferative LN [10]. Harley JB, et al. reported that 86.2% (50 of 58 pts) with proliferative LN had microscopic hematuria. In our study, 82% (32 of 39 pts) of patients with proliferative LN had microscopichematuria [11]. In our study, it was 34% (17 of 50 pts). Waldman Metal found that 67% (25 of 37 pts) of patients with proliferative LN had renal insufficiency [12]. In our study, 41% (16 of 39 pts) of patients with proliferative LN had increased serum creatinine. Clatworthy, et al., also reported a high prevalence of anti dsDNA antibodies (94.3%) in SLE patients with active proliferative LN and it was statistically significant when compared to non LN group ($p<0.001$) [13]. Ng KP, et al. reported that 84.5% (49 of 58 pts) with proliferative LN had anti dsDNA positivity. In our study, the prevalence of anti dsDNA was 97.1% in LN and 97.4% (38 of 39 pts) in proliferative LN ($p<0.001$). In a study conducted by Carlos Franco, et al., the prevalence of hypocomplementemia was 91.4% with class IV LN ($p = 0.05$) [14]. Hahn BH, et al. also reported high prevalence (91.2%) of hypocomplementemia with proliferative LN. In our study, the C3 level was low in 68% of patients with LN and 84.6% with proliferative LN ($p <0.001$). C4 level was low in 74% of patients with LN and 87.2% with proliferative LN ($p <0.001$). In our study, 72% (28 of 39 pts) of the patients with active proliferative LN (class IV, IV & V) had the combination of anti-dsDNA positivity, low C3, and low C4 levels but none of the patients with class II or class V LN had this combination of serology [15].

**Table – 4:** Proliferative LN classes IV, IV and V and anti dsDNA- correlation.

| **Renal Biopsy – IV, IV & V** | | **Anti dsDNA** | | **Total** | **P Value** |
|---|---|---|---|---|---|
| | | **Negative** | **Positive** | | |
| Absent | Count | 8 | 3 | 11 | <0.001 |
| | % within Renal Biopsy - IV | 72.7% | 27.3% | 100.0% | |
| Present | Count | 1 | 38 | 39 | |
| | % within Renal Biopsy - IV | 2.6% | 97.4% | 100.0% | |
| Total | Count | 9 | 41 | 50 | |
| | % within Renal Biopsy - IV | 18.0% | 82.0% | 100.0% | |

**Table - 5:** Serum C3 and its correlation with the histopathology of LN.

| **Renal Biopsy** | | **C3** | | **Total** | **P Value** |
|---|---|---|---|---|---|
| | | **Normal** | **Decreased** | | |
| II | Count | 7 | 0 | 7 | <0.001 |
| | % within Renal Biopsy | 100.0% | 0% | 100.0% | |
| IV | Count | 6 | 29 | 35 | |
| | % within Renal Biopsy | 17.1% | 82.9% | 100.0% | |
| V | Count | 3 | 1 | 4 | |
| | % within Renal Biopsy | 75.0% | 25.0% | 100.0% | |
| IV and V | Count | 0 | 4 | 4 | |
| | % within Renal Biopsy | 0% | 100.0% | 100.0% | |
| Total | Count | 16 | 34 | 50 | |
| | % within Renal Biopsy | 32.0% | 68.0% | 100.0% | |

**Table – 6:** Proliferative LN classes IV, IV and V and serum C3- correlation.

| Renal Biopsy – IV, IV & V | | C3 | | Total | P Value |
|---|---|---|---|---|---|
| | | Normal | Decreased | | |
| Absent | Count | 10 | 1 | 11 | <0.001 |
| | % within Renal Biopsy - IV | 90.9% | 9.1% | 100.0% | |
| Present | Count | 6 | 33 | 39 | |
| | % within Renal Biopsy - IV | 15.4% | 84.6% | 100.0% | |
| Total | Count | 16 | 34 | 50 | |
| | % within Renal Biopsy - IV | 32.0% | 68.0% | 100.0% | |

**Table - 7:** Serum C4 and its correlation with the histopathology of LN.

| Renal Biopsy | | C4 | | Total | P Value |
|---|---|---|---|---|---|
| | | Normal | Decreased | | |
| II | Count | 7 | 0 | 7 | <0.001 |
| | % within Renal Biopsy | 100.0% | 0% | 100.0% | |
| IV | Count | 5 | 30 | 35 | |
| | % within Renal Biopsy | 14.3% | 85.7% | 100.0% | |
| V | Count | 1 | 3 | 4 | |
| | % within Renal Biopsy | 25.0% | 75.0% | 100.0% | |
| IV and V | Count | 0 | 4 | 4 | |
| | % within Renal Biopsy | 0% | 100.0% | 100.0% | |
| Total | Count | 13 | 37 | 50 | |
| | % within Renal Biopsy | 26.0% | 74.0% | 100.0% | |

**Table – 8:** Proliferative LN Classes IV, IV and V and serum C4 – correlation.

| Renal Biopsy – IV, IV & V | | C4 | | Total | P Value |
|---|---|---|---|---|---|
| | | Normal | Decreased | | |
| Absent | Count | 8 | 3 | 11 | <0.001 |
| | % within Renal Biopsy - IV | 72.7% | 27.3% | 100.0% | |
| Present | Count | 5 | 34 | 39 | |
| | % within Renal Biopsy - IV | 12.8% | 87.2% | 100.0% | |
| Total | Count | 13 | 37 | 50 | |
| | % within Renal Biopsy - IV | 26.0% | 74.0% | 100.0% | |

## Conclusion

In our study, the serological profile of SLE had a significant correlation with histopathology of lupus nephritis. Anti dsDNA, low C3 and low C4 had a significant independent correlation ($p<0.05$) with proliferative LN (class IV, IV & V).

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