

Clinical aspects and risk factors of lupus nephritis: a retrospective study of 156 adult patients

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Abstract

Objective: To analyze the clinical manifestations, laboratory indexes, disease activity, and pathological types of lupus nephritis (LN) in adult patients.

Methods: We retrospectively analyzed the clinical manifestations, laboratory indexes, and pathological classifications of 156 adult patients first diagnosed with LN between July 2013 and November 2017. Patients were categorized according to the following criteria: active or inactive LN, LN with or without renal damage, and mild or severe LN.

Results: Immunoglobulin G and A levels, 24-hour proteinuria, and anti-dsDNA, anti-Sm, and anti-ribosomal P protein antibody positivity rates were all significantly increased in patients with active LN compared with inactive LN. Anti-dsDNA antibody positivity and 24-hour proteinuria were significantly increased, whereas hemoglobin, serum albumin, and C3 and C4 levels were significantly decreased in patients with LN and renal damage compared with those without renal damage. Anti-dsDNA and anti-Sm antibody positivity rates and 24-hour proteinuria were significantly increased, while hemoglobin, serum albumin, C3 and C4 levels, and estimated glomerular filtration rate were significantly decreased in patients with severe LN compared with patients with mild LN.

Conclusions: LN can display various clinical manifestations, laboratory indexes, levels of disease activity, and pathological types in adult patients.

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Keywords

Systemic lupus erythematosus, clinical analysis, lupus nephritis, pathogenesis, disease activity, renal damage

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Introduction

Systemic lupus erythematosus (SLE) is a diffuse autoimmune-mediated connective tissue disease mainly manifested by immune inflammation, involving multiple systems and organs.¹ Previous studies showed that approximately 50% of patients with SLE experience renal damage, and histopathological studies confirmed that 100% of patients with SLE had varying degrees of renal pathological changes.² Lupus nephritis (LN) is the most severe form of organ damage in patients with SLE and one of the most common secondary glomerular diseases, accounting for approximately 70% of secondary glomerular diseases based on histopathological examination.³ Importantly, LN frequently remains unrecognized until it has developed into full-blown nephritic and/or nephrotic syndrome with renal failure.⁴

Changes in several indicators, including the presence or increase of protein in the urine, positive autoantibodies, and decreased hemoglobin and complement levels, may reflect SLE disease activity and renal damage. However, the sensitivity and specificity of these indicators and their relationships with clinical manifestations remain controversial. The associations between these indicators and disease activity, renal damage, and pathological lesions, and their clinical relevance thus remain unclear.

In this retrospective study, we analyzed the clinical and laboratory data for 156 patients with LN and analyzed the relationships among disease characteristics, including disease activity, degree of renal damage, and severity of pathological type.

Patients and methods

Subjects

Adult patients initially diagnosed with LN at the Affiliated Hospital of Youjiang Medical University for Nationalities between July 2013 and November 2017 were included in this study. All patients fulfilled the Systemic Lupus International Collaborating Clinics 2012 classification criteria for SLE.⁵ Patients were excluded if they had rheumatoid arthritis, skin inflammation, systemic sclerosis, nodular polyarteritis, epilepsy, organic brain disease, psychosis, idiopathic thrombocytopenic purpura, or a primary glomerular disease. The study protocol was approved by the ethics committee of Affiliated Hospital of Youjiang Medical University for Nationalities. Written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Diagnostic criteria

Disease activity was evaluated according to the SLE disease activity index 2000 (SLEDAI-2K).⁶ Patients fulfilling any of the following criteria were diagnosed with LN: 24-hour urine protein level >0.5 g or +++; tubules (erythrocyte tubules, granulatubules, or mixed tubules) and/or renal dysfunction (according to the pathological classification standard established by International Society of Nephrology/Renal Pathology Society in 2003 and the National Institutes of Health pathological index of lupus nephritis); and abnormal renal biopsy.

The pathological classification standard established by the International Society of Nephrology/Renal Pathology Society in 2003 was used for pathological classification of LN.

The following features were considered as clinical manifestations of LN: simple hematuria (gross or microscopic hematuria without proteinuria); simple proteinuria (proteinuria without hematuria); hematuria and proteinuria (main manifestations of hematuria and proteinuria); nephrotic syndrome (heavy proteinuria ≥ 3.5 g/24 hour, hypoproteinemia ≤ 30 g/L, hyperlipemia, and edema); and renal dysfunction (significantly increased blood urea nitrogen and creatinine, accompanied by anemia, hypertension, and edema).

Groups

All patients with LN were divided into the following subgroups: active LN (SLEDAI-2K score >10) and inactive LN (score ≤ 10); LN with renal damage (estimated glomerular filtration rate [eGFR] < 60 mL/minute) and without renal damage (eGFR ≥ 60 mL/minute), according to patients' renal function; and mild LN (pathological class I–II) and severe LN (pathological class III–V).

Data acquisition

Peripheral blood samples were obtained from patients with LN and fasting venous blood was obtained from all patients in the morning. The following laboratory data were recorded: hemoglobin level, white blood cell count, blood platelet count, routine urine analysis, serum albumin level, 24-hour proteinuria, immunoglobulin level, serum C3 and C4, autoantibodies (anti-dsDNA, anti-Sm, anti-U1RNP, anti-ribosomal P protein (anti-Rib), anti-SSA, anti-SSB, and anti-Scl-70), pathological classification results, and clinical data.

Statistical analysis

All statistical analyses were carried out using SPSS for Windows, Version 21.0 (IBM Corp., Armonk, NY, USA). Quantitative variables were expressed as mean \pm standard deviation. Non-parametric distribution data were expressed as median and interquartile range. Quantitative variables were compared using *t*-tests and non-parametric variables using χ^2 tests. All tests were two-tailed, and a *P* value < 0.05 was considered statistically significant. Patients with missing data were excluded.

Results

Clinical features of patients with LN

A total of 156 adult patients (136 women, 20 men; mean age 38.09 ± 14.98 years, range 18–80 years) were included in the study. The sex ratio was 6.8:1 (87.18% women, 12.82% men). The mean age of the women was 37.35 ± 14.32 years and that of the men was 41.86 ± 17.71 years. Hematological abnormalities were the most common clinical manifestations (76.28%), followed by arthritis (57.69%), malar rash (50.64%), serositis (36.54%), photosensitization (15.38%), and oral ulcers (10.90%). Renal pathology was class I in 19 cases (12.18%), class II in 20 cases (12.82%), class III in 29 cases (18.59%), class IV in 62 cases (39.74%), and class V in 26 cases (16.67%).

Comparison of clinical manifestations and laboratory parameters between patients with active and inactive LN

A total of 132 patients (84.62%) had active LN and 24 (15.38%) had inactive LN. The main clinical manifestations of active LN were hematological abnormalities (80.30%), arthritis (62.12%), serositis (37.88%), malar rash (32.58%), photosensitization (11.36%),

and oral ulcers (6.82%) (Table 1). The incidences of arthritis, photosensitization, and hematological abnormalities and the rates of anti-dsDNA antibody, anti-Sm antibody, and anti-Rib antibody positivity were significantly higher in patients with active LN compared with those with inactive LN (all $P < 0.05$). However, oral ulcers were significantly less frequent in patients

with active (6.82%) compared with inactive LN (33.33%).

Immunoglobulin G (IgG) and IgA levels and 24-hour proteinuria were significantly increased, while hemoglobin, serum albumin, C3 and C4 levels, and eGFR were significantly decreased in patients with active LN compared with those with inactive LN ($P < 0.05$) (Table 2).

Table 1. Comparison of clinical manifestations and antibodies between patients with active and inactive LN.

Clinical manifestation or antibodies	Number (rate%)	Active LN	Inactive LN	χ^2 value	P value
Arthritis	90 (57.69)	82 (62.12) [#]	8 (33.33)	6.895	0.009
Photosensitization	24 (15.38)	15 (11.36) [#]	9 (37.50)	8.743	0.003
Malar rash	49 (50.64)	43 (32.58)	6 (25.00)	0.541	0.462
Neuropsychiatric disorders	9 (5.77)	7 (5.30)	2 (8.33)	0.012	0.913
Oral ulcer	17 (10.90)	9 (6.82) [#]	8 (33.33)	12.100	0.001
Hematological abnormality	119 (76.28)	106 (80.30) [#]	13 (54.17)	7.667	0.006
Serositis	58 (36.54)	50 (37.88)	8 (33.33)	0.180	0.672
Anti-ds DNA	78 (50.00)	73 (55.30) [#]	5 (20.83)	9.652	0.002
Anti-UIRNP	66 (42.31)	55 (41.67)	11 (45.83)	0.144	0.704
Anti-Sm	101 (64.74)	94 (71.21) [#]	7 (29.17)	15.728	<0.001
Anti-SSA	117 (75.00)	99 (75.00)	18 (75.00)	0.000	1.000
Anti-SSB	41 (26.28)	35 (26.52)	6 (25.00)	0.024	0.877
Anti-Rib	75 (44.08)	72 (54.55) [#]	3 (12.50)	14.381	<0.001
Anti-Scl-70	4 (2.56)	3 (2.27)	1 (4.17)	0.000	1.000

[#] $P < 0.05$ compared with inactive LN. LN, lupus nephritis.

Table 2. Comparison of routine laboratory parameters between patients with active and inactive LN.

Variable	Active LN	Inactive LN	t/Z value	P value
Hemoglobin (g/L)	96.04 ± 23.25 [#]	106.46 ± 23.27	2.019	0.045
Leukocytes ($\times 10^9/L$)	4.95 (3.30, 7.33)	6.05 (5.33, 7.55)	-1.901	0.057
Thrombocytes ($\times 10^9/L$)	197.42 ± 100.98	205.33 ± 84.44	0.361	0.718
Albumin (g/L)	28.95 ± 8.04 [#]	33.94 ± 8.24	2.788	0.006
Creatinine clearance rate (mL/minute)	53.67 (41.90, 70.25) [#]	77.32 (56.18, 101.50)	-3.592	<0.001
eGFR (mL/minute)	57.49 (34.88, 76.03) [#]	75.09 (50.71, 96.12)	-2.379	0.017
24-h proteinuria (g/24 h)	1.55 (0.44, 3.19) [#]	0.16 (0.06, 0.31)	-4.868	<0.001
C3 (mg/mL)	38.40 (21.15, 51.00) [#]	97.50 (72.75, 115.53)	-5.877	<0.001
C4 (mg/mL)	6.60 (3.25, 14.88) [#]	13.60 (6.55, 25.75)	-2.945	0.003
IgG (g/L)	18.17 ± 8.90 [#]	12.26 ± 7.83	-3.045	0.003
IgA (g/L)	2.87 ± 1.22 [#]	1.97 ± 1.56	-3.168	0.002
IgM (g/L)	1.27 (0.79, 1.82)	0.97 (0.79, 1.54)	-1.820	0.069

Values given as mean ± standard deviation or median (interquartile range). [#] $P < 0.05$ compared with inactive LN. LN, lupus nephritis; eGFR, estimated glomerular filtration rate.

Comparison of clinical manifestations and laboratory parameters between patients with LN with and without renal damage

Ninety-nine patients (63.46%) with LN had renal damage and 57 patients (36.54%) did not. The main clinical manifestations of LN with renal damage were hematological abnormalities (93.94%), arthritis (79.80%), serositis (49.49%), malar rash (33.33%), photosensitization (13.13%), and oral ulcers (10.10%) (Table 3). The incidences of arthritis, hematological abnormalities, and serositis, and anti-dsDNA antibody positivity were increased in patients LN with renal damage compared with those without renal damage ($P < 0.05$).

The level of 24-hour proteinuria was significantly increased, whereas hemoglobin, serum albumin, and C3 and C4 levels were significantly decreased in patients with LN with renal damage compared with those without renal damage ($P < 0.05$) (Table 4).

Comparison of clinical manifestations and laboratory parameters between patients with mild and severe LN

Thirty-nine patients (25.00%) had mild LN and 117 patients (75.00%) had severe LN. The various intrarenal manifestations included simple hematuria (25/156, 16.03%), simple proteinuria (56/156, 35.90%), hematuria combined with proteinuria (76/156, 48.72%), nephrotic syndrome (36/156, 23.08%), and renal failure (25/156, 16.03%) (Table 5). The main extrarenal manifestations in patients with severe LN were hematological abnormalities (76.92%), arthritis (62.39%), serositis (39.32%), malar rash (33.33%), photosensitization (11.97%), and oral ulcers (10.26%). The incidences of hematuria combined with proteinuria, nephrotic syndrome, renal failure, arthritis, photosensitization, and anti-dsDNA antibody and anti-Sm antibody positivity were increased in patients with severe LN compared with those with mild LN ($P < 0.05$).

Table 3. Comparison of clinical manifestations and antibodies between patients with LN with and without renal damage.

Clinical manifestation or antibodies	Number (rate%)	LN with renal damage	LN without renal damage	χ^2 value	P value
Arthritis	90 (57.69)	79 (79.80) [#]	11 (19.30)	54.244	<0.001
Photosensitization	24 (15.38)	13 (13.13)	11 (19.30)	1.057	0.304
Malar rash	49 (50.64)	33 (33.33)	16 (28.07)	0.465	0.495
Neuropsychiatric disorders	9 (5.77)	5 (5.05)	4 (7.02)	0.257	0.612
Oral ulcer	17 (10.90)	10 (10.10)	7 (12.28)	0.177	0.674
Hematological abnormality	119 (76.28)	93 (93.94) [#]	26 (45.61)	46.691	<0.001
Serositis	58 (36.54)	49 (49.49) [#]	9 (15.79)	17.595	<0.001
Anti-dsDNA	78 (50.00)	57 (57.58) [#]	21 (36.84)	6.220	0.013
Anti-U1RNP	66 (42.31)	40 (40.40)	26 (45.61)	0.402	0.526
Anti-Sm	101 (64.74)	67 (67.68)	34 (59.65)	1.021	0.312
Anti-SSA	117 (75.00)	75 (75.76)	42 (73.68)	0.083	0.773
Anti-SSB	41 (26.28)	27 (27.27)	14 (24.56)	0.137	0.711
Anti-Rib	75 (44.08)	52 (52.53)	23 (40.35)	2.148	0.143
Anti-Scl-70	4 (2.56)	2 (2.02)	2 (3.51)	0.321	0.571

[#] $P < 0.05$ compared with LN without renal damage. LN, lupus nephritis.

Table 4. Comparison of routine laboratory parameters between patients with LN with and without renal damage.

Variable	LN with renal damage	LN without renal damage	t/Z value	P value
Hemoglobin (g/L)	89.01 ± 21.58 [#]	112.63 ± 18.73	6.899	<0.001
Leukocyte (× 10 ⁹ /L)	5.10 (3.20, 7.40)	5.30 (4.15, 7.10)	-0.847	0.397
Thrombocyte (× 10 ⁹ /L)	196.68 ± 105.80	202.05 ± 84.84	0.328	0.744
Albumin (g/L)	27.45 ± 7.60 [#]	33.66 ± 7.88	4.846	<0.001
24-h proteinuria (g/24 h)	1.56 (0.51, 3.15) [#]	0.31 (0.12, 2.51)	-2.621	0.009
C3 (mg/ml)	35.80 (19.60, 51.00) [#]	50.00 (34.75, 77.60)	-3.620	<0.001
C4 (mg/ml)	6.40 (2.80, 14.00) [#]	12.00 (5.10, 21.00)	-3.370	0.001
IgG (g/L)	16.75 ± 8.21	18.15 ± 10.20	0.932	0.353
IgA (g/L)	2.62 ± 1.23	2.91 ± 1.44	1.320	0.189
IgM (g/L)	1.18 (0.77, 1.64)	1.28 (0.87, 2.15)	-1.581	0.114

Values given as mean ± standard deviation or median (interquartile range). [#]*P* < 0.05 compared with LN without renal damage. LN, lupus nephritis.

Table 5. Comparison of clinical manifestations and antibodies between patients with mild and severe LN.

Clinical manifestation or antibodies	Number (rate%)	Mild LN	Severe LN	χ ² value	P value
Simple hematuria	25 (16.03)	10 (25.64)	15 (12.82)	3.573	0.059
Simple proteinuria	56 (35.90)	18 (46.15)	38 (32.48)	2.377	0.123
Hematuria and proteinuria	76 (48.72)	13 (33.33)	63 (53.85) [#]	4.926	0.026
Nephritic syndrome	36 (23.08)	1 (2.56)	35 (29.91) [#]	12.326	<0.001
Renal hypofunction	25 (16.03)	1 (5.26)	24 (20.51) [#]	7.002	0.008
Arthritis	90 (57.69)	17 (43.59)	73 (62.39) [#]	4.237	0.040
Photosensitization	24 (15.38)	10 (25.64)	14 (11.97) [#]	4.202	0.040
Malar rash	49 (50.64)	10 (25.64)	39 (33.33)	0.803	0.370
Neuropsychiatric disorders	9 (5.77)	3 (7.69)	6 (5.13)	0.039	0.843
Oral ulcer	17 (10.90)	5 (12.82)	12 (10.26)	0.022	0.882
Hematological abnormality	119 (76.28)	29 (74.36)	90 (76.92)	0.106	0.744
Serositis	58 (36.54)	12 (30.77)	46 (39.32)	0.915	0.339
Anti-dsDNA	78 (50.00)	9 (23.08)	69 (58.97) [#]	15.077	<0.001
Anti-U1RNP	66 (42.31)	15 (38.46)	51 (43.59)	0.315	0.575
Anti-Sm	101 (64.74)	20 (51.28)	81 (69.23) [#]	4.128	0.042
Anti-SSA	117 (75.00)	29 (74.36)	88 (75.21)	0.011	0.915
Anti-SSB	41 (26.28)	7 (17.95)	34 (29.06)	1.864	0.172
Anti-Rib	75 (44.08)	16 (41.03)	59 (50.43)	1.036	0.309
Anti-Scl-70	4 (2.56)	0 (0.00)	4 (3.42)		
I (3.85)	0.342	0.559			

[#]*P* < 0.05 compared with mild LN. LN, lupus nephritis.

The level of 24-hour proteinuria was significantly increased, whereas hemoglobin, serum albumin, C3 and C4 levels, and eGFR were significantly decreased in patients with severe LN compared with those with mild LN (Table 6) (*P* < 0.05).

Discussion

SLE is characterized by the production of multiple autoantibodies that form an immune complex, which is the main pathogenic factor of the disease. LN is a renal

Table 6. Comparison of routine laboratory parameters between patients with mild and severe LN.

Variable	Mild LN	Severe LN	t/Z value	P value
Hemoglobin (g/L)	114.36 ± 20.57	92.07 ± 21.75 [#]	5.617	<0.001
Leukocyte (× 10 ⁹ /L)	5.30 (3.60, 7.80)	5.30 (3.35, 7.05)	-0.483	0.629
Thrombocyte (× 10 ⁹ /L)	192.15 ± 84.98	200.80 ± 102.75	-0.474	0.636
Albumin (g/L)	35.69 ± 8.59	27.73 ± 7.12 [#]	5.735	<0.001
eGFR (mL/minute)	84.96 (73.69, 96.12)	53.07 (33.05, 68.73) [#]	-6.965	<0.001
24-h proteinuria (g/24 h)	0.23 (0.08, 2.61)	1.51 (0.40, 2.91) [#]	-2.963	0.003
C3 (mg/mL)	60.00 (41.00, 104.00)	36.00 (20.55, 51.00) [#]	-4.541	<0.001
C4 (mg/mL)	17.00 (11.00, 27.00)	6.00 (3.05, 13.10) [#]	-4.943	<0.001
IgG (g/L)	15.80 ± 8.09	17.75 ± 9.24	-1.176	0.242
IgA (g/L)	2.81 ± 1.42	2.70 ± 1.28	0.440	0.660
IgM (g/L)	1.25 (0.85, 1.82)	1.23 (0.79, 1.73)	-0.061	0.951

Values given as mean ± standard deviation or median (interquartile range). [#]P < 0.05 compared with mild LN. LN, lupus nephritis; eGFR, estimated glomerular filtration rate.

disease associated with high mortality,⁷ characterized by severe organ damage in patients SLE. It is difficult to determine the activity status of LN and the associated renal damage because of the diversity and complexity of the clinical manifestations of SLE. However, evaluating disease activity, the degree of renal damage, and the relationships between renal pathology and laboratory indicators is essential to improve treatment protocols and prognosis.

Previous studies showed that women accounted for the majority of SLE cases, with a female:male ratio of approximately 7:1 to 9:1.^{8,9} The ratio in the current study was 6.8:1, which was similar to that reported by Boodhoo et al.¹⁰ (6.5:1). Hematological abnormalities are the most common clinical manifestations of LN. Hemocytosis typically occurs in SLE with clinical manifestations including anemia, leukopenia, and thrombocytopenia, which can easily be misdiagnosed as blood system diseases. However, the hematological abnormalities in SLE are generally believed to be related to immunological abnormalities.¹¹ The current study demonstrated correlations between hematological abnormalities and disease activity and renal damage, consistent with previous results.¹²

Anemia is the most common hematological abnormality in patients with SLE. This may be related to the presence of autoantibodies, which were previously found in bone marrow hematopoietic cells and erythrocytes in patients with SLE, resulting in pancytopenia or anemia.¹³ Alternatively, the anemia may be caused by a combination of erythropoietin deficiency and anti-erythropoietin antibodies.^{14,15}

The incidences of arthritis and photosensitization in the present study were 57.69% and 15.38%, respectively, which were lower than previously reported.¹⁶ This apparent discrepancy could be because the subjects underwent renal biopsy and therefore had limited movement.

A previous study reported that nephrotic syndrome was the main clinical phenotype in patients with severe LN,¹⁷ as a result of severe Sertoli cell damage.¹⁸ Nephrotic syndrome in LN is usually non-simple and combined with hematuria and even renal failure.¹⁹

The current study found no significant differences in IgG, IgA, and IgM levels between patients with LN with and without renal damage, and between patients with mild and severe LN. However, the mean immunoglobulin levels were lower in

patients with LN with renal damage and in patients with severe LN. This may be due to large amounts of immunoglobulins being deposited in the glomerulus in patients with LN with renal damage and those with severe LN, resulting in decreased serum immunoglobulin levels.

Although there are several criteria for assessing the activity of SLE, no gold standard has yet been established. Immune complexes are widely accepted to play an important role in the progression of kidney disease in LN.²⁰ Furthermore, some previous studies suggested that serum IgG, C3, and C4 levels were associated with disease activity in SLE,²¹ while others reported that decreased serum C4 level was not closely related to disease activity in SLE.²² A correlation between hypocomplementemia and active LN has been reported, with normal complement levels associated with stable renal function, while long-term hypocomplementemia could lead to deteriorating renal function.²³ In the present study, C3 and C4 levels were significantly decreased in patients with LN with renal damage compared with those without renal damage, and in patients with severe LN compared with patients with mild LN. These findings were similar to those of our previous study.²⁴ This suggests that patients with LN and renal damage were more prone to hypocomplementemia, indicating that lower serum complement levels were associated with more severe pathological lesions.

Anti-dsDNA antibodies are exclusive to patients with SLE and thus represent an SLE-specific antibody. Numerous studies have demonstrated correlations between anti-dsDNA antibody levels and clinical manifestations, illness severity, and disease activity, suggesting a potential role in assessing patient condition and prognosis.²⁵ Renal damage usually occurs in the active stage of the disease, and anti-dsDNA antibodies were found to play an important

pathogenic role and to be a risk factor for LN.²⁶ Consistent with this finding, 55.56% of patients with LN with anti-dsDNA antibodies in the present study had renal damage.

Several studies have found no correlation between anti-dsDNA antibody levels and the presence and severity of renal damage.²⁷ Recent studies found that 30% of patients with LN were negative for anti-dsDNA antibodies, while 25% of patients with SLE were positive for anti-dsDNA antibodies but did not have LN.²⁸ In the current study, 36.84% of patients were positive for anti-dsDNA antibodies but did not have renal damage. Further studies are therefore needed to explore the role of pathogenic antibodies in the injury mechanism of LN. Nucleosomes and their antibody molecules have also become increasingly significant in the pathogenesis of LN.²⁹ Napirei et al.³⁰ found that the activity of anti-dsDNA antibodies disappeared after removal of the nucleosomes and their antibody molecules, suggesting that these may mediate the binding of antigens, possibly initiating the pathological process of LN. The severity of LN should thus be assessed based on the level of organ damage rather than on antibody levels. Further studies are needed to clarify the relationship between anti-dsDNA antibodies and renal damage.

The rate of anti-Sm antibody positivity in patients with SLE is 10% to 30%.³¹ Although the detection rate is low (30%–40%),³² the specificity is as high as 92.2% to 99%, and anti-Sm antibody positivity is thus included in the diagnostic criteria for SLE. The anti-Sm positivity rate in the current study was 64.74%. Although the relationship between anti-Sm antibodies and disease activity remains controversial, the current study demonstrated that anti-Sm antibodies were a major indicator of disease activity. Furthermore, previous studies showed that the incidence of renal damage was higher in patients with SLE who were

positive for anti-Sm antibodies compared with those without anti-Sm antibodies, especially in patients who were also positive for anti-dsDNA antibodies.³³ Consistently, the anti-Sm antibody positivity rate in the present study was significantly increased in patients with severe LN compared with patients with mild LN, suggesting that anti-Sm antibodies are associated with LN as well as its pathological lesions, and that higher anti-Sm antibody titers correlate with more severe pathological lesions.

Anti-U1RNP antibody is an essential serological indicator for the diagnosis of mixed connective tissue disease.³⁴ The positivity rate for anti-U1RNP in SLE is 30% to 40%, but it may also be positive in other rheumatoid diseases, and its specificity is therefore not high.³⁵ Previous studies showed a higher incidence of renal damage in patients with SLE who were positive for anti-U1RNP antibodies compared with those who were negative.³⁶ However, the current study did not identify anti-U1RNP antibodies as a factor affecting disease activity, renal damage, or pathological lesions.

Anti-Rib antibody mainly targets P0, P1, and P2, which comprise the cytoplasmic subunit of phosphoric acid protein. Its positivity rate in SLE is 14.0% to 22.0%³⁷ and its specificity is high, with patients positive for anti-Rib antibody often having neurological damage. Moreover, anti-Rib antibodies are often present throughout the duration of SLE, and their degradation is similar to that of anti-dsDNA antibodies, except that they do not disappear immediately with remission of the disease. In addition, the anti-Rib positivity rate was significantly higher in the cerebrospinal fluid of patients with SLE and diffuse psychiatric syndromes compared with those with neurological syndromes or peripheral neuropathy, as well as in those with non-inflammatory neurological disease.³⁸ However, other reports found no

association between anti-Rib antibodies and SLE neurological damage.³⁹ Anti-Rib antibodies were also shown to be correlated with disease activity, and their positivity rate and titer were significantly increased in patients with active SLE.⁴⁰ Some studies have suggested that anti-Rib antibodies and LN are closely related,⁴¹ while other studies found that the correlation was more significant when both anti-Rib and anti-dsDNA antibodies were present, compared with either antibody alone.⁴² Although anti-Rib antibody levels were not related to renal damage or pathological lesions in the present study, anti-Rib antibody was suggested to be a factor affecting disease activity. Nevertheless, more studies are required to explore the mechanism underlying the role of anti-Rib antibody in patients with LN.

The rate of anti-SSA antibody positivity in patients with SLE was 30% to 50% and that of anti-SSB antibody was 10% to 15%,⁴³ with higher positivity rates in patients with active compared with inactive SLE.³⁶ Few patients with LN had both types of antibodies or only anti-SSB antibodies, whereas anti-SSA antibodies alone were detected in many patients.⁴⁴ Neither anti-SSA nor anti-SSB antibodies were found to affect disease activity, renal damage, or pathological lesions in the present study.

The clinical manifestations and laboratory parameters differed among the groups in the current study. Clinicians need to evaluate disease activity, the degree of renal damage, and the severity of the pathological lesions to develop a reasonable therapeutic strategy for LN. This requires an analysis of the clinical manifestations and laboratory indicators of LN, especially when renal biopsy cannot be performed for various reasons.

The main limitation of this study was the lack of a prospective design in terms of the correlations between the various indicators and treatment and prognosis.

In conclusion, the results of this study suggest that increased 24-hour proteinuria and IgG level, decreased C3, hemoglobin level, and eGFR, and the presence of anti-Sm and anti-dsDNA antibodies are involved in the pathogenesis of LN in adult patients. For patients who cannot undergo renal biopsy for various reasons, observation of their clinical manifestations and analysis of laboratory indicators can help to evaluate the activity of LN, the degree of renal function damage, and the severity of pathological damage, to allow the development of a reasonable diagnosis and treatment plan.

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Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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