High Neutrophil-Lymphocyte Ratio Predicts Serious Renal Insufficiency in Patients With Lupus Nephritis

Dijiao Tang

The First Affiliated Hospital of Chongqing Medical University

Qi Tang

Shandong Provincial Hospital, Cheeloo College of Medicine, Shandong University

Xiaojiong Jia

The First Affiliated Hospital of Chongqing Medical University

Long Zhang

People's Hospital of Jiulongpo District

Hongxu Wang (✉ wanghx502@163.com)

The First Affiliated Hospital of Chongqing Medical University

Research Article

Keywords: systemic lupus erythematosus, lupus nephritis, neutrophil-lymphocyte ratio, renal insufficiency

Posted Date: February 10th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-155572/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background

Recently, neutrophil-lymphocyte ratio (NLR), a biomarker used to monitor inflammation and immune response, has been shown to be a prognostic marker in systemic lupus erythematosus (SLE).

Objective

To investigate the association between pretreatment NLR and renal impairment in patients with lupus nephritis(LN).

Methods

This retrospective study included 88 LN patients, 51 SLE patients without renal involvement, 79 patients with primary chronic nephritis (CN) and 52 healthy controls (HC). The differentiation was analyzed among these four groups via Whitney U test, and correlations among variables were evaluated in LN patients. Finally, receiver operating characteristic curves (ROC) was performed to evaluate the diagnostic value of NLR in patients with LN.

Results

Pretreatment NLR of LN patients was significantly higher than that of the other three groups. The NLR was positively associated with complement 3(C3), C4, C-reactive protein (CRP) and serum creatinine (SCr) (C3: $r = 0.222$, $p = 0.042$; C4: $r = 0.230$, $p = 0.035$; CRP: $r = 0.337$, $p = 0.007$; SCr: $r = 0.408$, $p < 0.0001$) but inversely correlated with IgG ($r = -0.226$, $p = 0.041$). NLR level increased with severity of renal impairment. NLR (area under the curve (AUC): 0.785, 95% CI = 0.708–0.862) was useful for diagnosis of LN, and its optimal cutoff was 5.44 (sensitivity: 65.9%, specificity: 86.3%).

Conclusions

A high NLR was associated with severe renal function impairment in LN patients. NLR would be useful for diagnosis of LN and reflect severity of renal impairment. Thus, evaluating pretreatment NLR could help clinicians identify the potential renal involvement in SLE patients and distinguish LN from CN, so clinicians could conduct early triage and initiate effective management in time.

Introduction

Lupus nephritis (LN) is a form of glomerulonephritis that occurs in over half of patients with systemic lupus erythematosus (SLE) and is one of the most severe target-organ complications of SLE. Importantly, LN is also the initial manifestation of SLE. Therefore, it is critical to identify LN from general SLE and primary chronic nephritis. Multiple pathogenic pathways are involved in LN including autoantibody production, immune complex deposition, complement activation and aberrant apoptosis. Clearly, inflammation exerts a pivotal role in the pathophysiology of LN. Neutrophil-lymphocyte ratio (NLR), a biomarker used to monitor inflammation and immune response, has been shown to be associated with overall survival in patients with malignancies[1–3], cardiovascular disease[4], autoimmune diseases[5–7] and even general population[8]. While NLR has been shown to closely correlate with disease activity of SLE and is increased significantly in the LN group without infection as compared with those in healthy controls[6], there is limited understanding of the relationship between pretreatment NLR and renal impairment in LN. Moreover, the value of NLR in distinguishing LN with and primary chronic nephritis and SLE without renal impairment is not clear.

Patients And Methods

Clinical data on all patients was collected by reviewing medical records with permission from the Ethics Committee of The First Affiliated Hospital of Chongqing Medical University. LN patients admitted to the First Affiliated Hospital of Chongqing Medical University from 2015 to 2020 were included.

Patients with SLE satisfied the American College of Rheumatology (ACR) 1982 revised criteria for the classification of SLE[9]. Meanwhile, SLE patients accompanying with following conditions ((1) Albuminuria persistence > 0.5 g/24 h, or random urine test for urine protein+++, or Urine protein/creatinine > 500 mg/g (50 mg/mmol); (2) Cell casts includes red blood cell casts, hemoglobin casts, granular casts, or mixed casts; (3) Active urinary sediment (except urinary tract infection, urinary leucocyte > 5 /HPF, urinary red blood cell > 5 /HPF)) were excluded according to Chinese guidelines for the diagnosis and treatment of lupus nephritis. Entry criteria of LN: Enrolled patients of LN had autoantibody-positive SLE (antinuclear antibody titers $\geq 1:80$, anti-double-stranded DNA antibodies, or both) that fulfilled the 1982 American College of Rheumatology classification criteria for SLE, which were updated in 1997[9]. LN was biopsy-proven and classified based on the International Society of Nephrology-Renal Pathology Society 2003 classification system[10, 11]. Primary chronic glomerulonephritis (CN) was diagnosed according to Mayo clinic/renal pathology society consensus report on pathologic classification, diagnosis, and reporting of glomerulonephritis[10–12]. Subjects were excluded if they had one of the following situations: 1) other autoimmune diseases 2) malignant diseases, hematologic disease or pregnancy; 3) evidence of any concomitant inflammatory disease; 4) patients with cardiovascular/cerebrovascular disease, diabetes or hepatic disease. Healthy controls were collected from the Physical Examination Center of the First Affiliated Hospital of Chongqing Medical University and were excluded if they had some malignancies or previous immunosuppressive treatment.

Altogether, 88 patients with LN, 51 SLE patients without renal impairment, 79 patients with primary chronic nephritis (CN), and 52 healthy controls (HC) were enrolled in this retrospective study.

The data and the samples that were analyzed in the present study were obtained in accordance with the standards and approval of the Chongqing Medical University Institutional Review Board and Biomedical Ethics Committee. The ethics committee waived the need for written informed consent provided by participants due to the retrospective nature of the study. Because all patient data were analyzed in anonymity, no additional informed consent was required. All experimental protocols were approved by the Chongqing Medical University Institutional Review Board and Biomedical Ethics Committee.

Clinical And Laboratory Parameter

Clinical-laboratory information of each subject was extracted from clinical records. The pretherapeutic complete blood cell count (CBC) and serum indices were available for each patient. Samples for CBC were placed in tubes with EDTA-K2 anticoagulation and further analyzed via XN1000 Hematology Analyzer (Sysmex, Japan). NLR was calculated as the proportion of absolute neutrophil count to lymphocyte count from CBC. Assay of blood urea nitrogen (BUN) and serum creatinine (SCr) were tested by biochemical analyzer (Roche cobas701, Switzerland). Tests of erythrocyte sedimentation (ESR) were accomplished by TEST1 (ALIFAX, Italy). Beckman Coulter Immage-800 immunochemistry system was employed to detect serum levels of C3, C4, IgG and C-reactive protein (CRP). The levels of serum anti-dsDNA antibodies were measured by using fluorescence-enzyme immunoassay (Euroummun, Lubeck, Germany). Anti-ds DNA was quantified by enzyme-linked immunosorbent assay (ELISA) (YHLO Union, YHLO, China). Moreover, the operation processes were carried out in strict accordance with protocols of both manufacturer and laboratory.

Statistical analysis

Continuous variables in normal distribution were displayed in the form of Mean $\pm$ SD, while variables in skewed distribution (the Kolmogorov-Smirnov Test) were presented as median (interquartile range) (median (IQR)). Additionally, categorical data was outputted as the absolute count and percentage. Mann-Whitney U test was employed to analyze the differences among these four groups (LN, SLE, NE and HC). Spearman correlation analysis was used to analyze the relationship between NLR and other variables (Anti-dsDNA, C3, C4, IgG, CRP, ESR, SCr) in LN group. P-value of three groups with different degrees of kidney injury were calculated by analysis of Kruskal-wallis test. Finally, we estimated clinical performance of NLR in differentiating complication of LN in SLE patients by ROC curve.

Statistical analyses were performed via SPSS 21.0. A p value < 0.05 was considered statistically significant.

Results

The Demographic and Clinical Characteristics of Study Subjects

All subjects were divided into four groups (LN, SLE, CN, and HC). The basic clinical features of these four groups were demonstrated in Table 1, including age, gender, pathological classification, ANA, CRP, C3, C4, SCr, etc. There was no statistic difference in the aspect of age among these four groups. Also, there was no significant difference in both ANA titer and level of anti-dsDNA between LN and SLE. Levels of BUN, SCr and eGFR in LN were significantly elevated than that in SLE and HC ($p < 0.05$), but there was no statistical difference between LN and CN ($p > 0.05$).

LN had significantly higher CRP than SLE ((median (IQR), 9.5(5.0-27.2) vs 4.48 (1.9-12.9), $p < 0.05$) (Figure 1(a)). In contrast, LN possessed remarkably lower levels of C3 ((median (IQR), 0.45(0.30-0.56) vs 0.79(0.55-1.00), $p < 0.05$) and C4((median (IQR), 0.12(0.06-0.17) vs 0.16(0.11-0.19), $p < 0.05$) than SLE (Figure 1 (b) and (c)).

NLR level was increased in LN patients

We analyzed indexes of CBC of these 4 groups (Table 2). Both groups of LN and CN got significantly elevated WBC count than SLE and HC, but there was no statistical difference between LN and CN. Meanwhile, LN patients had higher Neutrophil absolute values (5.25(3.63-7.36)) than both groups of SLE (3.75(2.33-5.47)) and HC (3.19(2.47-4.03)), but no significant difference between LN and CN was observed. However, LN had the lowest level of lymphocyte count, Hb and PLT among the four groups. LN patients had the highest NLR level (6.48(3.95-11.76)) and RDW (14.85(13.7-16.00)) value than the other three groups (Table 2, Figure 2).

Correlations between NLR and laboratory indexes of LN patients

To explore the relationship between NLR and inflammatory biomarkers in LN patients. We analyzed correlations of NLR with anti-dsDNA, IgG, C3, C4, CRP and SCr in LN group (Figure 3). NLR was positively correlated with C3 ($r = 0.222$, $p = 0.042$), C4 ($r = 0.230$, $p = 0.035$), CRP ($r = 0.337$, $p = 0.007$) and SCr ($r = 0.408$, $p < 0.0001$), but negatively correlated with IgG ($r = -0.226$, $p = 0.041$). However, there was no statistical correlation between NLR and anti-dsDNA. Therefore, NLR was closely associated with biomarkers of inflammation (C3, C4, CRP and IgG) and renal function (SCr) in LN patients.

Correlations of NLR level with renal function

To further explore relationship between NLR and renal function in LN patients. We divided LN patients into three groups according to the Chinese chronic renal failure staging: severely impaired group ($\text{SCr} \geq 442 \mu\text{mol/L}$), moderate impaired group ($177 \mu\text{mol/L} \leq \text{SCr} < 442 \mu\text{mol/L}$) and mild impaired group ($\text{SCr} < 177 \mu\text{mol/L}$). NLR level increased with severity of renal impairment (Table 3 and Figure 4).

The ROC curve of NLR for predicting LN in SLE patients

We performed ROC analyses to establish cutoff point for NLR and defined LN patients as "state variables". The area under the curve (AUC) of NLR was 0.785 (0.708-0.862) (Figure 5). NLR would be useful for diagnosis of LN, and its specificity and sensitivity were 86.30% and 65.90%, respectively.

Besides, the optimal cut-off value of NLR level for recognition of LN patients was 5.44(AUC=0.785, 95%CI = 0.708-0.862) (Figure 5).

Discussion

Lupus nephritis (LN) is frequent in patients with lupus and involved the kidneys in 30–75% of patients, presenting as proteinuria and cell tubules, and is observed both at the onset and during the course of the disease[13]. 10–30% of patients with lupus nephritis may progress to end-stage kidney disease [14]. This risk has remained unchanged during the past three decades[15]. The extra-renal involvement, presence of concomitant neurological, cardiac or pulmonary involvement showed association with the need for renal replacement therapy (RRT), including kidney dialysis and kidney transplantation[13]. These patients had poor quality of life and long-term prognosis. In addition, 27–66% of patients in remission have subsequent flares of lupus nephritis[16]. Therefore, more secure, convenient and rapid indicators are needed to indicate renal inflammation, hoping to prevent recurrence and protect renal function.

Recent work has revealed that the mechanism of LN is caused by the effect of the disturbed immune system on passive target organs and non-immune factors on the end organ damage through the combination of target organ resistance and regulation of local inflammatory response[13, 16, 17]. Also, imbalance of neutrophil and lymphocyte contribute to SLE development. NLR has been reported elevated in SLE patients and could reflect inflammatory response and disease activity in SLE patients[6, 18–21]. Neutrophils and lymphocytes have been reported playing important roles in LN and their levels change with aggravation and remission of systemic inflammatory response[17, 22–24]. Importantly, neutrophil and lymphocyte count have been routinely applied in clinical practice and their detections were relatively simply to perform. NLR level was automatically calculated and regularly provided in CBC report. This current retrospective study enrolled four groups of study subjects: LN (lupus nephritis), SLE (systemic lupus erythematosus patients without LN), CN (chronic nephritis patients) and HC (healthy controls). To clearly illustrating correlations of NLR with LN, we specially set up two conditional groups of control (SLE and CN).

Firstly, we found that LN got the highest level of NLR which was consistent with several previous reports[6, 19]. Moreover, we identified that NLR increases with severity of renal dysfunction. In a cohort of 99 LN patients and 151 controls, Qin et al. demonstrated that NLR was effective in predicting SLE and NLR level of 2.065 was determined as predictive cut-off value of SLE (sensitivity: 74.7%, specificity: 77.5% and AUC = 0.828)[19]. The current study turned out that the optimal predictive cutoff value of NLR for LN was 5.44 (sensitivity: 86.30%, specificity: 65.90% and AUC = 0.785). Thus, it suggests that pretreatment NLR could be an indicator of renal impairment in LN.

To our knowledge, it is the first time to systematically evaluate correlations of NLR with renal function in LN and investigate difference of LNR between LN and CN. To assess correlations of LNR level with clinical indexes of LN patients. Variables of both systemic immune markers and renal function related

were included in the current study. Our data revealed that NLR was correlated with biomarkers of inflammation (C3, C4, CRP and IgG) and renal function (SCr) in LN patients.

However, this was a single-center and small sample-size study. As clinical follow-ups were not regularly carried out, associations of NLR level with prognosis were not well estimated.

In conclusion, the present study found that NLR was rather high in LN patients than SLE patients without LN and CN and it was aggressively increased with the degree of renal dysfunction. These findings suggested that NLR could be a potential marker in predicting LN and assessing renal injury severity.

Abbreviations

NLR:neutrophil-lymphocyte ratio ;LN:lupus nephritis;SLE:systemic lupus erythematosus;CN:primary chronic nephritis;HC:healthy controls;ROC:receiver operating characteristic curves;C3:complement 3;C4:complement 4;CRP:C-reactive protein; SCr :serum creatinine;CBC: complete blood cell count ;BUN:blood urea nitrogen ;ESR:erythrocyte sedimentation;ELISA:enzyme-linked immunsorbent assay;WBC:white blood cell;RBC:red blood cell; Hb:hemoglobin; PLT:platelet; RDW:red cell distribution width;RRT:renal replacement therapy.

Declarations

Authors' contributions

HXW and DJT designed the study, wrote the article, and consulted literature.QT and LZ performed experiment and statistical data. XJJ revised manuscript. All authors contributed to the article and approved the submitted version.

Availability of data and materials

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The data and the samples that were analyzed in the present study were obtained in accordance with the standards and approval of the Chongqing Medical University Institutional Review Board and Biomedical Ethics Committee. The ethics committee waived the need for written informed consent provided by participants due to the retrospective nature of the study. Because all patient data were analyzed in anonymity, no additional informed consent was required.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests

Author details

1 Department of Laboratory Medicine, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China

2 Department of Clinical Laboratory, Shandong Provincial Hospital, Cheeloo College of Medicine, Shandong University, Jinan, Shandong, China

3 Department of Urinary Surgery, People's Hospital of Jiulongpo District, Chongqing, China.

References

1. Templeton AJ, McNamara MG, Seruga B, Vera-Badillo FE, Aneja P, Ocana A, Leibowitz-Amit R, Sonpavde G, Knox JJ, Tran B *et al*: **Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: a systematic review and meta-analysis.** *J Natl Cancer Inst* 2014, **106**(6):dju124.
2. Patel A, Ravaud A, Motzer RJ, Pantuck AJ, Staehler M, Escudier B, Martini JF, Lechuga M, Lin X, George DJ: **Neutrophil-to-Lymphocyte Ratio as a Prognostic Factor of Disease-free Survival in Postnephrectomy High-risk Locoregional Renal Cell Carcinoma: Analysis of the S-TRAC Trial.** *Clin Cancer Res* 2020, **26**(18):4863–4868.
3. Gemenetzi G, Bagante F, Griffin JF, Rezaee N, Javed AA, Manos LL, Lennon AM, Wood LD, Hruban RH, Zheng L *et al*: **Neutrophil-to-lymphocyte Ratio is a Predictive Marker for Invasive Malignancy in Intraductal Papillary Mucinous Neoplasms of the Pancreas.** *Ann Surg* 2017, **266**(2):339–345.
4. Kim S, Eliot M, Koestler DC, Wu WC, Kelsey KT: **Association of Neutrophil-to-Lymphocyte Ratio With Mortality and Cardiovascular Disease in the Jackson Heart Study and Modification by the Duffy Antigen Variant.** *JAMA Cardiol* 2018, **3**(6):455–462.
5. Wu Y, Chen Y, Yang X, Chen L, Yang Y: **Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were associated with disease activity in patients with systemic lupus erythematosus.** *Int Immunopharmacol* 2016, **36**:94–99.
6. Liu P, Li P, Peng Z, Xiang Y, Xia C, Wu J, Yang B, He Z: **Predictive value of the neutrophil-to-lymphocyte ratio, monocyte-to-lymphocyte ratio, platelet-to-neutrophil ratio, and neutrophil-to-monocyte ratio in lupus nephritis.** *Lupus* 2020, **29**(9):1031–1039.
7. D'Amico E, Zanghi A, Romano A, Sciandra M, Palumbo GAM, Patti F: **The Neutrophil-to-Lymphocyte Ratio is Related to Disease Activity in Relapsing Remitting Multiple Sclerosis.** *Cells* 2019, **8**(10).
8. Fest J, Ruiter TR, Groot Koerkamp B, Rizopoulos D, Ikram MA, van Eijck CHJ, Stricker BH: **The neutrophil-to-lymphocyte ratio is associated with mortality in the general population: The Rotterdam Study.** *Eur J Epidemiol* 2019, **34**(5):463–470.

9. Tan EM, Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfield NF, Schaller JG, Talal N, Winchester RJ: **The 1982 revised criteria for the classification of systemic lupus erythematosus.** *Arthritis Rheum* 1982, **25**(11):1271–1277.
10. Weening JJ, D'Agati VD, Schwartz MM, Seshan SV, Alpers CE, Appel GB, Balow JE, Bruijn JA, Cook T, Ferrario F *et al*: **The classification of glomerulonephritis in systemic lupus erythematosus revisited.** *J Am Soc Nephrol* 2004, **15**(2):241–250.
11. Yu F, Haas M, Glasscock R, Zhao MH: **Redefining lupus nephritis: clinical implications of pathophysiologic subtypes.** *Nat Rev Nephrol* 2017, **13**(8):483–495.
12. Sethi S, Haas M, Markowitz GS, D'Agati VD, Rennke HG, Jennette JC, Bajema IM, Alpers CE, Chang A, Cornell LD *et al*: **Mayo Clinic/Renal Pathology Society Consensus Report on Pathologic Classification, Diagnosis, and Reporting of GN.** *J Am Soc Nephrol* 2016, **27**(5):1278–1287.
13. Anders HJ, Saxena R, Zhao MH, Parodis I, Salmon JE, Mohan C: **Lupus nephritis.** *Nat Rev Dis Primers* 2020, **6**(1):7.
14. Mohan C, Putterman C: **Genetics and pathogenesis of systemic lupus erythematosus and lupus nephritis.** *Nat Rev Nephrol* 2015, **11**(6):329–341.
15. Illei GG, Austin HA, Crane M, Collins L, Gourley MF, Yarboro CH, Vaughan EM, Kuroiwa T, Danning CL, Steinberg AD *et al*: **Combination therapy with pulse cyclophosphamide plus pulse methylprednisolone improves long-term renal outcome without adding toxicity in patients with lupus nephritis.** *Ann Intern Med* 2001, **135**(4):248–257.
16. Chan TM: **Treatment of severe lupus nephritis: the new horizon.** *Nat Rev Nephrol* 2015, **11**(1):46–61.
17. Flores-Mendoza G, Sanson SP, Rodriguez-Castro S, Crispin JC, Rosetti F: **Mechanisms of Tissue Injury in Lupus Nephritis.** *Trends Mol Med* 2018, **24**(4):364–378.
18. Broca-Garcia BE, Saavedra MA, Martinez-Bencomo MA, Montes-Cortes DH, Jara LJ, Medina G, Vera-Lastra O, Cruz-Dominguez MP: **Utility of neutrophil-to-lymphocyte ratio plus C-reactive protein for infection in systemic lupus erythematosus.** *Lupus* 2019, **28**(2):217–222.
19. Qin B, Ma N, Tang Q, Wei T, Yang M, Fu H, Hu Z, Liang Y, Yang Z, Zhong R: **Neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) were useful markers in assessment of inflammatory response and disease activity in SLE patients.** *Mod Rheumatol* 2016, **26**(3):372–376.
20. Yang Z, Zhang Z, Lin F, Ren Y, Liu D, Zhong R, Liang Y: **Comparisons of neutrophil-, monocyte-, eosinophil-, and basophil- lymphocyte ratios among various systemic autoimmune rheumatic diseases.** *APMIS* 2017, **125**(10):863–871.
21. Kim HA, Jung JY, Suh CH: **Usefulness of neutrophil-to-lymphocyte ratio as a biomarker for diagnosing infections in patients with systemic lupus erythematosus.** *Clin Rheumatol* 2017, **36**(11):2479–2485.
22. Nishi H, Mayadas TN: **Neutrophils in lupus nephritis.** *Curr Opin Rheumatol* 2019, **31**(2):193–200.
23. Lech M, Anders HJ: **The pathogenesis of lupus nephritis.** *J Am Soc Nephrol* 2013, **24**(9):1357–1366.

24. Boulos D, Proudman SM, Metcalf RG, McWilliams L, Hall C, Wicks IP: **The neutrophil-lymphocyte ratio in early rheumatoid arthritis and its ability to predict subsequent failure of triple therapy.** *Semin Arthritis Rheum* 2019, **49**(3):373–376.

Tables

Table 1 Basic Clinical characteristics of four study groups (LN, SLE, CN and HC).

Features	LN(n=88)	SLE(n=51)	CN(n=79)	HC(n=52)
Age, year	45(30-53)	46(30-55)	50(39-61)	43(29-49)
Gender, M/F	14/74 ^{2,3}	6/45 ^{4,5}	22/57	7/45
ANA, titer	320(100-1000)	320(100-1000)		
Anti-dsDNA,	50.2(7.8-492)	48.6(6.8-563)	/	/
ESR, mm/h	36(20-61)	34.5(20-54)	50.0(38-61)	/
CRP, mg/L	9.5(5.0-27.2) ¹	4.48(1.9-12.9) ⁴	13.21(5-36.22)	/
C3, g/L	0.45(0.30-0.56) ^{1,2}	0.79(0.55-1.00)	0.81(0.66-0.93)	/
C4, g/L	0.12(0.06-0.17) ^{1,2}	0.16(0.11-0.19) ⁴	0.23(0.18-0.27)	/
BUN, mmol/L	12.85(6.50-20.25) ^{1,3}	4.6(3.7-5.3) ⁴	8.95(5.325-18.73) ⁵	4.8(3.925-5.65)
SCr, umol/L	174.5(74.25-320.8) ^{1,3}	58(51-65) ⁴	210(65.25-653.0) ⁵	61.5(55.00-66.00)
eGFR, mL/(min*1.73m ²)	36.50(15.10-80.40) ¹	112.9(99.90-124.0) ⁴	13.3(5.85-50.48)	/
Renal biopsy I	2			
II	13			
III	17			
IV	40			
V	16			

Note: All variables are shown in form of median (interquartile range) except with Male/Female; LN: lupus nephritis; SLE: systemic lupus erythematosus (SLE) patients without LN; CN: chronic nephritis patients; HC: healthy controls; M/F: male/female; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; C3: Complement C3; C4: complement C4; BUN: blood urea nitrogen; SCr: Serum creatinine; GFR: Glomerular

filtration rate. 1: $p < 0.05$ LN vs SLE; 2: $p < 0.05$ LN vs CN; 3: $p < 0.05$ LN vs HC; 4: $p < 0.05$ SLE vs CN; 5: $p < 0.05$ CN vs HC.

Table 2 Indexes of complete blood cell count (CBC) among LN, SLE, CN and HC.

Variables	LN	SLE	CN	HC
WBC, $\times 10^9/L$	6.24(5.18-8.64) ¹	5.52(4.02-6.99) ⁴	6.47(5.24-8.76)	5.79(5.02-6.68)
Hb, g/L	91.5(76.3-111.8) ^{1,2,3}	125.0(118.0-131.0) ^{4,5}	106.0(85.0-130.0) ⁶	140.0(133.3-148.8)
PLT, $\times 10^9/L$	162.0(121.0-224.8) ^{2,3}	180(128.0-235.0)	209.0(154.0-262.0)	211.5(178.0-240.0)
Neu#, $\times 10^9/L$	5.25(3.63-7.36) ^{1,3}	3.75(2.33-5.47)	4.67(3.42-6.38) ⁶	3.19(2.47-4.03)
Lym#, $\times 10^9/L$	0.82(0.63-1.15) ^{1,2,3}	1.32(0.80-1.98) ⁵	1.24(0.99-1.69) ⁶	2.03(1.65-2.28)
Mon#, $\times 10^9/L$	0.41(0.29-0.58)	0.45(0.31-0.60)	0.42(0.32-0.55)	0.37(0.29-0.43)
RDW	14.85(13.7-16.00) ^{1,2,3}	13.5(12.70-14.20) ⁵	13.50(12.70-15.30) ⁶	12.80(12.23-13.35)
NLR	6.48(3.95-11.76) ^{1,2,3}	3.03(2.02-4.42) ⁵	3.57(2.65-5.41) ⁶	1.53(1.24-2.22)

Note: Variables are demonstrated in the pattern of median (interquartile range). LN: lupus nephritis; SLE: systemic lupus erythematosus (SLE) patients without LN; CN: chronic nephritis patients; HC: healthy controls; CBC: complete blood cell count; WBC: white blood cell count; Hb: hemoglobin; PLT: platelet; Neu#: Neutrophil absolute value; Lym#: Lymphocyte absolute value; Mon#: Monocyte absolute value; RDW: Erythrocyte distribution width; NLR: Neutrophils/lymphocytes; 1: $p < 0.05$ LN vs SLE; 2: $p < 0.05$ LN vs CN; 3: $p < 0.05$ LN vs HC; 4: $p < 0.05$ SLE vs CN; 5: $p < 0.05$ SLE vs HC; 6: $p < 0.05$ CN vs HC.

Table 3. Relationship between NLR and renal function in LN patients.

Variables	SCr<177 (n=35)	177≤ SCr <442 (n=27)	SCr ≥442 (n=26)	<i>P</i>
Age	45(28-52)	51(40-55)	43(27-48)	0.055
Gender: M/F	5/30	2/25	7/19	0.143
CRP	11.85(5.00-44.08)	9.410(5.90-25.30)	9.200(6.29-20.85)	0.999
ESR	30(18.5-57.0)	41(23.5-66)	36(11-50.50)	0.356
eGFR	81.40(58.15-109.0)	24.10(16.80-33.20)	9.50(9.00-15.10)	<0.0001
NLR	5.463(2.344-7.200)	5.926(3.882-11.79)	10.31(6.816-20.36)	<0.0001

Note: Variables are demonstrated in the pattern of median (interquartile range).

LN: lupus nephritis; NLR: Neutrophils/lymphocytes; M/F: male/female; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; SCr: Serum creatinine; GFR: Glomerular filtration rate.

Figures

Figure 1

Comparison of CRP (a), C3 (b) and C4 (c) among groups of LN, SLE and CN. Note: LN: lupus nephritis; SLE: systemic lupus erythematosus (SLE) patients without LN; CN: chronic nephritis patients; HC: healthy controls; CRP: C-reactive protein; C3: Complement 3; C4: complement 4.

Figure 2

Comparison of NLR levels among groups of LN, SLE, CN and HC. NLR: neutrophil-lymphocyte ratio; LN: lupus nephritis; SLE: systemic lupus erythematosus (SLE) patients without LN; CN: chronic nephritis patients; HC: healthy controls.

Figure 3

Correlations of NLR with anti-dsDNA (a), IgG(b), C3(c), C4 (d), CRP(e) and SCr (f) in LN patients. LN: lupus nephritis; NLR: neutrophil-lymphocyte ratio; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; C3: Complement C3; C4: complement C4; BUN: blood urea nitrogen; SCr: Serum creatinine.

Figure 4

Relationship between NLR and LN group with different degrees of kidney injury Note: NLR: neutrophil-lymphocyte ratio.

Figure 5

ROC curves of NLR (a), Crea (b), and serum urea nitrogen (c) in LN patients were compared with SLE patients