

The relationship between neutrophil-lymphocyte ratio and early renal affection in patients with lupus nephritis

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ABSTRACT

Lupus nephritis (LN) remains one of the most severe manifestations of systemic lupus erythematosus, driven by immune-complex deposition, complement activation, and persistent glomerular inflammation. Renal involvement develops in approximately 30.5% of SLE patients and significantly influences long-term morbidity and mortality. Early detection of renal injury is essential, yet conventional markers such as serum creatinine and proteinuria may not capture early inflammatory changes. The neutrophil-lymphocyte ratio (NLR), a simple and inexpensive marker derived from routine blood counts, reflects the combined effects of neutrophilia and lymphopenia associated with systemic inflammation. NLR correlates with classical inflammatory biomarkers including CRP, ESR, IL-6, and TNF- α , and is influenced by heightened neutrophil activation, impaired lymphocyte regulation, and cytokine-driven immune dysregulation characteristic of LN. The aim of this review is to evaluate the relationship between NLR and early renal affection in lupus nephritis, highlighting its pathophysiologic basis, its association with renal activity and fibrosis, and its potential utility as a predictive marker for early renal involvement...

Keywords: Neutrophil-lymphocyte ratio, Lupus nephritis, Systemic lupus erythematosus, Early renal affection.

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INTRODUCTION

Lupus nephritis (LN) is a major cause of mortality in systemic lupus erythematosus (SLE) patients. Immune complex deposition in glomeruli triggers activation of neutrophils, monocytes, and T lymphocytes, causing persistent renal inflammation and injury. The NOD-, LRR- and pyrin domain-containing protein 3 (NLRP3) inflammasome plays a critical role in LN pathogenesis; its activation is enhanced by immune complexes, interferon-I, and neutrophil extracellular traps (NETs). In SLE, macrophage overactivation further stimulates inflammasomes, elevating inflammatory cytokines and accelerating renal damage through increased autoantibody depletion (1).

The neutrophil-lymphocyte ratio (NLR), derived from a routine complete blood count, is a cost-effective inflammatory marker. Unlike total leukocyte count, NLR reflects both neutrophilia and lymphopenia caused by stress or immune dysregulation. Neutrophils adhere to vascular endothelium and secrete inflammatory mediators such as elastase and reactive oxygen species, promoting endothelial

injury and antigen presentation. Lymphocytes, which regulate inflammation, may have impaired signaling in autoimmune conditions (2).

NLR correlates with classical inflammatory markers such as C-reactive protein (CRP), tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6), and erythrocyte sedimentation rate (ESR), indicating its strong link with systemic inflammation (3). Several studies have explored the association of NLR with renal function, proteinuria, and baseline disease severity in LN; however, data on its predictive value for renal prognosis remain limited (4). Despite improved immunotherapies that have reduced overall SLE mortality, the incidence of end-stage renal disease (ESRD) remains unchanged, underscoring the need for reliable prognostic biomarkers. Therefore, assessing the relationship between NLR, early renal fibrosis, and renal prognosis in LN patients is of major clinical relevance (5).

Lupus Nephritis

Lupus nephritis (LN) is one of the most serious complications of systemic lupus erythematosus (SLE) and

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a major determinant of morbidity and mortality. It usually develops within 3–5 years after SLE onset, and histological evidence of renal involvement is found in most SLE patients, even when asymptomatic (6).

Early detection using serum creatinine, urine analysis, and urine albumin-to-creatinine ratio enables timely management to prevent progression to end-stage renal disease (ESRD) (7).

Etiology

LN results from a type III hypersensitivity reaction, where anti-double-stranded DNA (anti-dsDNA) antibodies form immune complexes that deposit in the mesangial, subendothelial, or subepithelial regions of the glomeruli (8). This activates the complement cascade, leading to inflammation and renal injury (6).

Genetic predisposition also plays a role. Polymorphisms in Fcγ receptor genes and Apolipoprotein L1 (APOL1) variants—notably in African Americans—are linked with increased LN susceptibility (9).

Genetic Factors

SLE and LN are polygenic autoimmune disorders. Key genes implicated include PTPN22, CRP, FCGR2A/B, FCGR3A/B, C1Q, C1R, C1S, C2, C4A/B, STAT4, CTLA4, HLA-DRB1 (DR2/1501, DR3/0301), TNF-α (-308), and MBL2 (6).

Familial SLE prevalence is 10–12%, with twin concordance rates of 24–58% in monozygotic versus 2–5% in dizygotic twins, supporting genetic contribution alongside environmental triggers (6).

Immunologic Factors

The immune response in LN is driven by autoantibody formation against nuclear antigens from apoptotic debris. Impaired clearance of apoptotic cells causes plasmacytoid dendritic cells to release interferon-α, amplifying inflammation (6).

Autoreactive B lymphocytes escape tolerance and generate anti-dsDNA and other autoantibodies via epitope spreading, which precedes clinical SLE by months to years (6).

Epidemiology

Globally, 30.5% of SLE patients develop histologically confirmed LN. The mean age at diagnosis is 28.4 years, with higher prevalence among men, younger individuals, and those of African, Asian, or Hispanic descent. Use of antimalarial drugs significantly lowers LN risk (10, 11).

Age: LN commonly affects individuals 20–40 years old, and occurs earlier in children (6).

Sex: Female-to-male SLE ratio is 9:1, though men often present with more severe renal disease (6).

Race: LN is more prevalent in African Americans and Asians, though Asians show better 10-year survival rates (12).

Pathophysiology

LN involves immune complex formation and deposition in glomeruli, triggering complement activation and inflammatory infiltration. Autoantibodies—particularly anti-dsDNA—may cross-react with the glomerular basement membrane, leading to insitu immune complex formation (6). **Figure 1.**

Additionally, glomerular thrombosis is common in LN with antiphospholipid syndrome, due to antibody–phospholipid interactions. Gut microbiota may also contribute; SLE patients with renal involvement show increased RG-specific bacterial variants (13).

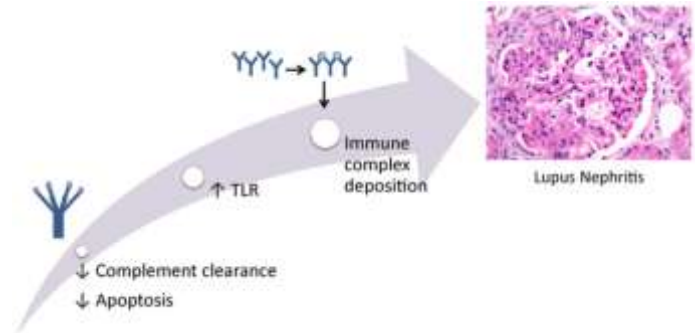


Figure (1): Proposed mechanism of immune complex deposition of lupus nephritis.

Diagnosis

Laboratory Findings

Active LN is characterized by low complement (C3, C4) levels and anti-dsDNA positivity. Proteinuria >3.5 g/day indicates nephrotic-range disease with low serum albumin. Screening for proteinuria and hematuria is recommended every 3 months in active SLE (6).

Radiologic Evaluation

Bilateral renal ultrasound helps exclude obstructive pathology such as hydronephrosis (14).

Renal Biopsy (Figure 2):

Indicated in nephrotic-range proteinuria or recurrent nephritis, biopsy defines the histologic class and disease activity (6). Prediction accuracy from clinical data alone is 70–80%.

Interpretation accuracy varies by center, with higher consistency in specialized institutions (6).

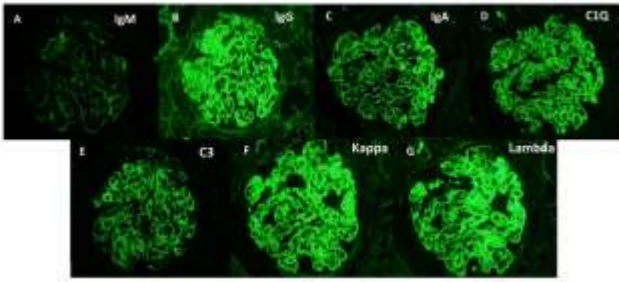


Figure (2): Immunofluorescence (IF) staining in lupus nephritis. (A-F) IF findings from a patient with LN with a full house pattern. Abbreviation: IgM, immunoglobulin M.

ISN/RPS Classification:

Class I: Normal light microscopy; mesangial deposits (6).

Class II: Mesangial hypercellularity or matrix expansion.

Class III: Focal (<50%) glomerular involvement.

Class IV: Diffuse (≥50%) segmental/global lesions with “wire loops.”

Class V: Membranous thickening with subepithelial deposits.

Class VI: Advanced sclerosis (>90% glomeruli), fibrosis, and atrophy (6).

Treatment

General Principles

Management involves immunosuppressive and steroid therapy, adjusted by class severity.

Classes III & IV: Require aggressive immunosuppression.

Class VI: Usually progresses to **renal replacement therapy** (6).

Therapy is divided into induction and maintenance phases. Induction aims for remission; maintenance prevents relapse. Pneumocystis prophylaxis and bone protection with DEXA scans and supplements are essential (15).

Class III–IV Induction Therapy

Initial regimen: Mycophenolate mofetil (MMF) for 6 months, plus 3 days IV glucocorticoids, then oral prednisone taper.

Responders continue low-dose MMF or azathioprine.

Nonresponders switch to cyclophosphamide + glucocorticoids.

Resistant cases may receive rituximab or calcineurin inhibitors.

This approach is particularly effective in Hispanic and African American patients (6).

Class V Induction Therapy

Treated with high-dose MMF + prednisone for 6 months. If

responsive, maintenance continues with low-dose MMF or azathioprine; otherwise, cyclophosphamide plus pulse steroids is used (6).

Adjunctive Therapy

All LN patients should receive hydroxychloroquine, which significantly reduces flare frequency. Combination therapy with glucocorticoids and either MMF or cyclophosphamide remains the cornerstone of treatment (16).

CONCLUSION

Lupus nephritis is a major determinant of SLE prognosis, requiring early identification of renal inflammation to prevent progression to irreversible damage. Evidence shows that the neutrophil-lymphocyte ratio reflects key immunologic processes in LN including neutrophil activation, lymphocyte depletion and cytokine-mediated injury. Its strong correlation with inflammatory markers and renal disease activity suggests that NLR may serve as a practical tool for early detection of renal affection in SLE. Although current data indicate promising diagnostic and prognostic value, further studies are needed to establish standardized NLR thresholds, validate its predictive accuracy and integrate it alongside traditional clinical and histopathological assessments for optimal early management of lupus nephritis..

REFERENCE

1. Parikh SV, Almaani S, Brodsky S, Rovin BH. (2020). Update on lupus nephritis: core curriculum 2020. *American Journal of Kidney Diseases*, 76(2): 265–281.
2. Shumilah AM, Othman AM, Al-Madhagi AK. (2021). Accuracy of neutrophil to lymphocyte and monocyte to lymphocyte ratios as new inflammatory markers in acute coronary syndrome. *BMC Cardiovascular Disorders*, 21(1): 1-6.
3. Ferencova N, Visnovcova Z, Ondrejka I, Hrtanek I, Bujnakova I, Kovacova V, et al. (2023). Peripheral inflammatory markers in autism spectrum disorder and attention deficit/hyperactivity disorder at adolescent age. *International Journal of Molecular Sciences*, 24(14): 1-27.
4. Himmelfarb J, Vanholder R, Mehrotra R, Tonelli M. (2020). The current and future landscape of dialysis. *Nature Reviews Nephrology*, 16(10): 573–585.
5. Abd El-Monem SA, Agaiby ASZ, Hassan MH. (2025). The correlation between insulin resistance and fatty liver disease in Qena University Hospital: cross-sectional study. *SVU-International Journal of Medical Sciences*, 8(2): 160–173. DOI: 10.21608/SVUIJM.2025.398267.2208.
6. Musa R, Rout P, Qurie A. (2025). Lupus nephritis. *StatPearls*, 1(1): 1-2.
7. Gabr AASM, Khalil MA, Mogahed MM, Eltaweel BA, Marei YM, El Hammady AM, et al. (2025). Assessment of the relationship between vitamin D status

- and graft function in living-related kidney transplant recipients. *SVU-International Journal of Medical Sciences*, 8(1): 1–11. DOI: 10.21608/SVUIJM.2025.342302.2047.
8. Liu G, Wang H, Le J, Lan L, Xu Y, Yang Y, et al. (2019). Early-stage predictors for treatment responses in patients with active lupus nephritis. *Lupus*, 28(3): 283–289.
9. Jorge A, Wallace ZS, Lu N, Zhang Y, Choi HK. (2019). Renal transplantation and survival among patients with lupus nephritis: a cohort study. *Annals of Internal Medicine*, 170(4): 240–247.
10. Galindo-Izquierdo M, Rodriguez-Almaraz E, Pego-Reigosa JM, López-Longo FJ, Calvo-Alén J, Olivé A, et al. (2016). Characterization of patients with lupus nephritis included in a large cohort from the Spanish Society of Rheumatology Registry of Patients With Systemic Lupus Erythematosus (RELESSER). *Medicine*, 95(9): 1-11.
11. Elbahy DA, Bassit AS, Ahmed SAE, Aboueilla AMA. (2025). Mitigative effect of L-carnitine and simvastatin against dexamethasone-induced hepato-renal damage in rats. *SVU-International Journal of Medical Sciences*, 8(1): 388–404. DOI: 10.21608/SVUIJM.2025.340154.2035.
12. Yap DY, Chan TM. (2015). Lupus nephritis in Asia: clinical features and management. *Kidney Diseases*, 1(2): 100–109.
13. Azzouz D, Omarbekova A, Heguy A, Schwudke D, Gisch N, Rovin BH, et al. (2019). Lupus nephritis is linked to disease-activity associated expansions and immunity to a gut commensal. *Annals of the Rheumatic Diseases*, 78(7): 947–956.
14. Abdel Baseer KA, Soliman NA, Elmonem MA, Abdelbaset EA, Sakhr HM. (2025). Risk factors for recurrence of pediatric renal stones in Qena Governorate. *SVU-International Journal of Medical Sciences*, 8(2): 360–370. DOI: 10.21608/SVUIJM.2024.271053.1812.
15. Wirestam L, Enocsson H, Skogh T, Padyukov L, Jönsen A, Urowitz MB, et al. (2019). Osteopontin and disease activity in patients with recent-onset systemic lupus erythematosus: results from the SLICC inception cohort. *The Journal of Rheumatology*, 46(5): 492–500.
16. Abass NM, Abdelhady M, El-Rashidy MH. (2025). Atrial fibrillation as an independent risk factor for CKD progression. *SVU-International Journal of Medical Sciences*, 8(1): 417–430. DOI: 10.21608/SVUIJM.2025.352103.2077..