Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Nephrology

Correlation of Serum Anti-C1q Antibody with Histological Characteristics in Lupus Nephritis

Dr. Sharmin Sultana[1*], Dr. Md. Aminul Haq[2], Dr. Abdullahil Baki[3], Dr. Mohammed Rubayat Al Matin[4], Dr. Mithun Barman[5], Dr. Mohammad Sumon Sarker[6], Dr. G. M. Hafizur Rahman[7], Prof. Dr. Abu Saleh Ahmed[8]

[1]Assistant Registrar, Department of Nephrology, Rangpur Medical College and Hospital, Rangpur, Bangladesh
[2]Assistant Surgeon, B- Nagar UHC, Faridpur, Pabna, Bangladesh
[3]IMO, Nephrology Department, Shaheed Suharawardy Medical College Hospital, Dhaka, Bangladesh
[4]Assistant Professor, Dhaka Medical College Hospital, Dhaka, Bangladesh
[5]Assistant Surgeon, Sirajdikhan UHC, Munshigonj, Bangladesh
[6]RMO, Baniyachong UHC, Hobigonj, Bangladesh
[7]Assistant Professor, Dhaka Medical College Hospital, Dhaka, Bangladesh
[8]Professor, Dhaka Medical College Hospital, Dhaka, Bangladesh

DOI: https://doi.org/10.36347/sjams.2025.v13i10.003 | **Received:** 21.08.2025 | **Accepted:** 06.10.2025 | **Published:** 15.10.2025

***Corresponding author:** Dr. Sharmin Sultana
Assistant Registrar, Department of Nephrology, Rangpur Medical College and Hospital, Rangpur, Bangladesh

Abstract **Original Research Article**

***Background*:** Lupus nephritis (LN) is a major determinant of morbidity and mortality in systemic lupus erythematosus (SLE), with renal biopsy serving as the gold standard for evaluating disease activity and chronicity. However, its invasive nature underscores the need for reliable non-invasive biomarkers. Among them, serum anti-C1q antibodies have been implicated in LN pathogenesis, yet their association with histological parameters remains incompletely defined. ***Objective*:** This study aimed to investigate the correlation between serum anti-C1q antibody levels and histological characteristics in patients with lupus nephritis. ***Methods*:** A cross-sectional study was conducted at Dhaka Medical College and Hospital between March 2022 and August 2023, enrolling 55 patients with biopsy-proven LN. Serum anti-C1q antibody levels were measured by ELISA, and renal biopsies were classified according to the ISN/RPS 2004 criteria. Histological activity and chronicity indices were assessed, and correlations between antibody levels and histopathological features were analyzed using Spearman's rank correlation. ***Results*:** The mean age of participants was 28.8 ± 9.03 years, with a female predominance (87.3%). Class IV LN was the most frequent subtype (34.5%), followed by class III (27.3%). Serum anti-C1q antibody levels were highest in proliferative classes (IV: 77.26 U/ml; III: 65.2 U/ml). Significant positive correlations were observed between anti-C1q levels and endocapillary hypercellularity (r=0.573, p=0.001), cellular crescents (r=0.632, p=0.001), interstitial infiltrates (r=0.450, p=0.001), and activity index score (r=0.765, p=0.001). No significant correlations were found with chronicity indices, including sclerosis, interstitial fibrosis, and tubular atrophy. ***Conclusion*:** Serum anti-C1q antibody levels strongly correlate with histological activity but not chronicity in lupus nephritis, particularly in proliferative classes. These findings suggest that anti-C1q may serve as a useful non-invasive biomarker for monitoring renal disease activity, though it cannot replace biopsy in assessing chronicity.

Keywords: Lupus Nephritis, Systemic Lupus Erythematosus, Anti-C1q Antibody, Histological Activity, Renal Biopsy, Biomarker.

INTRODUCTION

Lupus nephritis (LN) represents one of the most serious manifestations of systemic lupus erythematosus (SLE), significantly contributing to morbidity and mortality among affected patients. It is characterized by immune complex deposition, complement activation, and subsequent glomerular and tubulointerstitial injury [1-3]. Early and accurate assessment of renal involvement is essential, as timely diagnosis and appropriate therapy can improve long-term renal outcomes and overall survival. Despite advances in diagnostic modalities, renal biopsy remains the gold standard for evaluating histological activity and chronicity in LN. However, its invasive nature and associated risks necessitate the search for reliable, non-invasive biomarkers that can reflect underlying renal pathology [4].

Among the various immunological pathways implicated in LN, the complement system plays a central role. C1q, the first component of the classical complement pathway, is particularly important in immune complex clearance. Deficiency of C1q predisposes individuals to lupus-like disease, while antibodies directed against C1q (anti-C1q antibodies) have been increasingly recognized as potential mediators of renal damage in SLE [5, 6]. These antibodies may promote glomerular inflammation through enhanced deposition of immune complexes and direct interaction with resident renal cells, thereby perpetuating injury.

Serum anti-C1q antibodies have been detected in a substantial proportion of patients with SLE, with higher prevalence among those with nephritis. Several studies suggest that anti-C1q levels correlate with disease activity and renal involvement, yet their relationship with histological features of LN remains incompletely understood. Histological patterns in LN, classified by the International Society of Nephrology/Renal Pathology Society (ISN/RPS), range from mesangial proliferation to diffuse proliferative and sclerotic forms, each with different therapeutic implications and prognostic outcomes [7]. Understanding whether anti-C1q antibody levels reflect these histological distinctions could enhance their value as a biomarker.

Previous investigations have demonstrated variable associations between serum anti-C1q titers and specific histological parameters such as activity index, chronicity index, glomerular proliferation, and crescent formation [8, 9]. While some reports suggest a strong correlation between high anti-C1q levels and proliferative forms of LN, others have failed to confirm such associations, possibly due to heterogeneity in study populations, methodologies, or disease stages. This inconsistency highlights the need for further exploration in diverse patient cohorts [10].

Establishing a clear link between serum anti-C1q antibodies and renal histopathology could potentially reduce reliance on repeat biopsies and aid in non-invasive disease monitoring. Such an approach may provide clinicians with valuable insights for predicting disease flares, tailoring therapy, and monitoring response to treatment. Moreover, it could contribute to risk stratification and early identification of patients at higher risk for severe renal involvement.

OBJECTIVE

The study aims to investigate the correlation between serum anti-C1q antibody levels and histological characteristics in lupus nephritis.

METHODOLOGY

This study was designed as a cross-sectional investigation and was conducted at Dhaka Medical College and Hospital between March 2022 and August 2023. The study population comprised patients diagnosed with lupus nephritis (LN). Participants were selected using purposive sampling, and the final sample size was determined to be 55, based on statistical calculation using the correlation coefficient of anti-C1q antibody with glomerular leukocyte infiltration as reported by Zhu Chen *et al*., (2012).

55 Patients were recruited according to specific inclusion and exclusion criteria. Inclusion was restricted to individuals with lupus nephritis, while those younger than 18 years, those with a history of immunosuppressive therapy within the past six months, patients with anti-C1q vasculitis or hypocomplementemic urticarial vasculitis syndrome (HUVS), lupus nephritis in pregnancy, and other confounding conditions were excluded.

Data collection encompassed both demographic and laboratory variables. Demographic variables included age and sex, while laboratory variables included serum anti-C1q antibody levels and histological characteristics such as class, activity index, and chronicity index based on renal biopsy. Additional investigations performed were urinalysis (routine and microscopic, culture and sensitivity), 24-hour urinary total protein, complete blood count, peripheral blood film, serum creatinine, serum albumin, lipid profile, antinuclear antibody (ANA), anti-dsDNA, complement levels (C3, C4), extractable nuclear antigen (ENA) profile, ultrasonography of the kidneys, ureter, and bladder (KUB) region, as well as screening for viral infections (HBsAg, Anti-HCV, HIV-1, HIV-2) and coagulation tests (BT, CT, PT, APTT).

For measurement of serum anti-C1q antibody, 5 ml of venous blood was collected from each participant under aseptic precautions prior to renal biopsy. The samples were processed within 30 minutes and serum was stored at –30°C until analysis. Anti-C1q antibody levels were measured using an ELISA kit (DRG Diagnostics GmbH, Germany) following the manufacturer's instructions. The assay involved dilution of samples, incubation with enzyme conjugates, washing steps, and colorimetric detection at 450 nm with a reference wavelength between 620–650 nm.

Renal biopsy was performed on all participants with clinical features of LN and active urinary sediment. The procedure included counseling and informed consent, patient positioning in the prone posture, local anesthesia, ultrasound guidance, and collection of two cortical cores from the lower pole of the left kidney using a biopsy gun. Specimens were examined by light microscopy and direct immunofluorescence at accredited laboratories, including the Pathology Department of BSMMU, Armed Forces Institute of Pathology, and Kidney Foundation Research Institute of Bangladesh.

Classification of LN was performed according to the International Society of Nephrology/Renal Pathology Society (ISN/RPS) 2004 guidelines, and in addition to class assignment, specimens were stained for C1q, C3, and IgG. Histological features including activity and chronicity indices were recorded.

All laboratory investigations were conducted in collaboration with the Departments of Biochemistry, Microbiology, Hematology, and Transfusion Medicine at Dhaka Medical College, BSMMU, and Sheikh Hasina National Institute of Burn and Plastic Surgery. Data were collected using a pre-tested structured questionnaire by the principal investigator. Following data collection, accuracy and completeness were verified before entry into SPSS version 27 (IBM Corp., Armonk, NY) for analysis. Descriptive statistics were used to summarize demographic and clinical characteristics. Continuous variables were expressed as mean, median, and standard deviation, while categorical variables were presented as frequencies and percentages. Spearman's correlation test was employed to examine associations between serum anti-C1q antibody levels and histological parameters. A *p*-value < 0.05 was considered statistically significant.

RESULTS

Table I shows the distribution of the study subjects by demographic profile. It was observed that more than half (54.6 %) patients belonged to age 21-30 years. The mean age 28.8 ± 9.03 years with ranged from 18 to 60 years. Majority (87.3%) patients were female and female to male ratio is 7:1.

Table I: Distribution of the study subjects by demographic profile (N=55)

	Number	Percentage
Age		
≤20	9	16.4
21-30	30	54.6
31-40	12	21.7
>40	4	7.2
Mean ± SD	28.8 ± 9.03	
Range (min, max)	18, 60	
Sex		
Male	7	12.7
Female	48	87.3

Table II shows the distribution of the study subjects by LN Class. It was observed that more than one third (34.5%) patients had LN class IV followed by 15(27.3%) class III, 11(20.0%) class II and 10(18.2%) class V.

Table II: Distribution of the study subjects by LN Class (N=55)

LN Class	Number	Percentage (%)
Class II	11	20.0
Class III	15	27.3
Class IV	19	34.5
Class V	10	18.2

This figure describes serum level of anti-C1q antibody (U/ml) was highest in LN class IV (77.26 U/ml) followed in class III (65.2 U/ml).

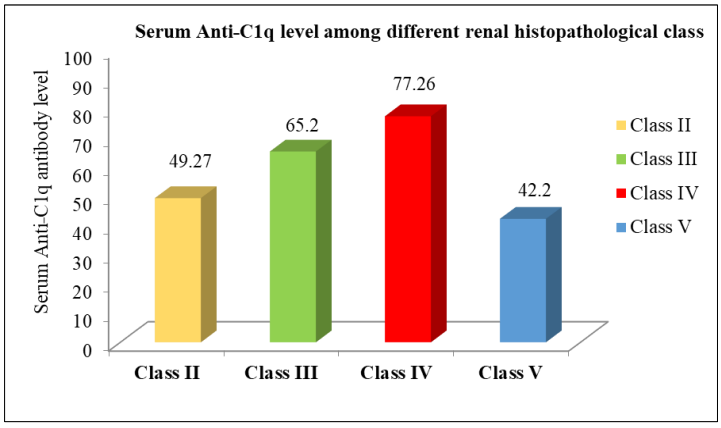

Figure 1: Bar-diagram showing distribution of the study subjects by Anti-C1q antibody level (U/ml)

Table III shows there were positive significant correlation between the level of anti- C1q antibody with endocapillary hypercellularity (r=0.573, p=0.001), neutrophils/karyorrhexis (r=0.332, p=0.013), hyaline deposits (r=0.390, p=0.003), cellular crescents (r=0.632, p=0.001), interstitial infiltrates (r=0.450, p=0.001) and AI score (r=0.765, p=0.001).

Table III: Correlation analysis between serum level of anti-C1q antibody (U/mL) and renal histological activity indices (N=55)

Histological features	ρ (r)	p value
Endocapillary hypercellularity	0.573	0.001
Neutrophils/Karyorrhexis	0.332	0.013
Fibrinoid necrosis	0.214	0.117
Hyaline deposits	0.390	0.003
Cellular crescents	0.632	0.001
Interstitial infiltrates	0.450	0.001
Activity indices (AI) score	0.765	0.001

Spearman‘s rank correlation test were performed

Table IV shows there were positive correlation found between the level of anti-C1q antibody with interstitial fibrosis (r=0.041, p=0.766) and tubular atrophy (r=0.097, p=0.481) which was found statistically not significant. A negative correlation was found between anti-C1q antibody level with total (global/segmental) sclerosis (r=- 0.168, p=0. 219) and CI score (r=-0.021, p=0.877) which was found statistically not significant.

Table IV: Correlation analysis between serum level of anti-C1q antibody (U/mL) and renal histological chronicity indices (N=55)

Histopathological features	ρ (r)	p value
Total (global/segmental) sclerosis	-0.168	0.219
Interstitial fibrosis	0.041	0.766
Tubular atrophy	0.097	0.481
Chronicity indices (CI) score	-0.021	0.877

Spearman‘s rank correlation test were performed

Table shows the association between Anti-ds DNA and anti C1q study patients. It was observed that majority (91.1%) patients had anti-ds DNA positive in anti C1q positive and 8(80.0%) in anti C1q negative. The difference was statistically not significant (p>0.05) between two group.

Table V: Association between anti-ds DNA and anti C1q study patients (N=55)

Anti-ds DNA	Anti C1q Positive (n=45)		Anti C1q Negative (n=10)		P value
	n	%	n	%	0.308[ns]
Positive	41	91.1	8	80.0	
Negative	4	8.9	2	20.0	

ns= not significant p value reached from Chi-square test

DISCUSSION

In the present study, the mean age of patients with lupus nephritis was 28.8 years, with the majority (54.6%) belonging to the age group of 21–30 years. A striking female predominance was observed, with a female-to-male ratio of 7:1. These findings are consistent with the well-documented epidemiological profile of lupus nephritis, which predominantly affects young women of reproductive age. Previous studies have similarly reported higher prevalence among women, highlighting the role of hormonal and immunological factors in disease susceptibility [10, 11]. The mean age of our patients also closely aligns with that reported where the average age of LN onset was in the late twenties, reinforcing the observation that LN is primarily a disease of young adulthood [12].

Regarding histological distribution, class IV lupus nephritis was the most common subtype in our cohort (34.5%), followed by class III (27.3%) and class II (20.0%). This is consistent with the findings who reported proliferative classes (III and IV) as the predominant forms associated with active disease and worse renal outcomes [13]. A Bangladeshi study also reported class IV as the most frequent subtype, indicating a similar disease pattern in our population [14]. The higher anti-C1q antibody levels in patients with class IV (77.26 U/ml) and class III (65.2 U/ml) in the present

study further support the association of anti-C1q antibodies with proliferative and severe histological classes of LN, as described by other study [15].

Our study demonstrated a strong positive correlation between serum anti-C1q antibody levels and several histological activity indices, including endocapillary hypercellularity, hyaline deposits, cellular crescents, interstitial infiltrates, and activity index score. Notably, the correlation with activity index was particularly strong ($r = 0.765$, $p = 0.001$). These findings corroborate earlier studies which demonstrated that elevated anti-C1q antibodies are strongly associated with active renal inflammation and proliferative lesions [14]. Together, these observations highlight the potential role of anti-C1q antibody as a biomarker reflecting ongoing renal immunopathology.

Conversely, we found no significant correlation between anti-C1q antibody levels and histological chronicity indices, including total sclerosis, interstitial fibrosis, tubular atrophy, and overall chronicity score. This finding is in agreement with other study who noted that anti-C1q antibody levels are primarily elevated during periods of active inflammation rather than in chronic or sclerotic stages of disease [15]. This distinction has important clinical implications, as anti-C1q antibody may be more useful in monitoring disease flares than in predicting long-term scarring.

The present study also evaluated the association between anti-C1q antibody and anti-dsDNA antibody. While most anti-C1q positive patients were also positive for anti-dsDNA (91.1%), the difference compared to anti-C1q negative patients was not statistically significant. This result diverges slightly from findings who demonstrated synergistic diagnostic value when anti-C1q and anti-dsDNA were used together to predict LN flares [13]. The discrepancy may be due to differences in sample size, patient ethnicity, or disease activity at the time of sampling. Nonetheless, the high proportion of patients positive for both antibodies in our cohort still suggests overlapping but not identical pathogenic mechanisms.

Taken together, our findings support the growing body of evidence that serum anti-C1q antibody levels correlate with histological activity but not chronicity in lupus nephritis. The predominance of young female patients, higher antibody titers in proliferative classes, and significant association with activity indices are consistent with international studies, although the lack of strong association with anti-dsDNA requires further evaluation in larger cohorts. These results reinforce the potential of anti-C1q antibody as a non-invasive biomarker for disease activity monitoring, though it cannot substitute for renal biopsy in evaluating chronicity and long-term prognosis.

CONCLUSION

Based on our results, the findings indicate a significant correlation between serum anti-C1q antibody levels and the histological characteristics of lupus nephritis, particularly with disease activity and severity of renal involvement. Elevated anti-C1q antibody titers were more frequently observed in patients with active proliferative classes and higher activity indices, suggesting that this biomarker may serve as a valuable indicator of ongoing immunological injury within the kidney. However, no consistent association was observed with chronicity indices, implying that anti-C1q primarily reflects active disease processes rather than irreversible damage. These observations highlight the potential role of anti-C1q antibody as a non-invasive adjunct in monitoring renal disease activity in lupus nephritis, complementing histopathological evaluation while reducing reliance on repeated invasive biopsies.

REFERENCE

1. Faurschou M, Starklint H, Halberg P, Jacobsen S. Prognostic factors in lupus nephritis: diagnostic and therapeutic delay increases the risk of terminal renal failure. J Rheumatol 2006;33:1563–9.Abstract/FREE Full TextGoogle Scholar
2. Uwatoko S, Mannik M. Low-molecular weight C1q-binding immunoglobulin G in patients with systemic lupus erythematosus consists of autoantibodies to the collagen-like region of C1q. J Clin Invest 1988;82:816–24.PubMedGoogle Scholar
3. Horvath L, Czirijak L, Fekete B, Jakab L, Pozsonyi T, Kalabay L, et al. High levels of antibodies against C1q are associated with disease activity and nephritis but not with other organ manifestations in SLE patients. Clin Exp Rheumatol 2001;19:667–72.PubMedGoogle Scholar
4. Trendelenburg M, Marfurt J, Gerber I, Tyndall A, Schifferli JA. Lack of occurrence of severe lupus nephritis among anti-C1q autoantibody-negative patients. Arthritis Rheum 1999;42:187–8.CrossRefPubMedGoogle Scholar
5. Moroni G, Trendelenburg M, Del Papa N, Quaqlini S, Raschi E, Panzeri P, et al. Anti-C1q antibodies may help in diagnosing a renal flare in lupus nephritis. Am J Kidney Dis 2001;37:490–8.PubMedGoogle Scholar
6. Fremeaux-Bacchi V, Noel LH, Schifferli JA. No lupus nephritis in the absence of anti C1q autoantibodies? Nephrol Dial Transplant 2002;17:2041–3.FREE Full TextGoogle Scholar
7. Trouw LA, Seelen MA, Visseren R, Duijs JM, Benediktsson H, de Heer E, et al. Anti-C1q autoantibodies in murine lupus nephritis. Clin Exp Immunol 2004;135:41–8.CrossRefPubMedGoogle Scholar
8. Trouw LA, Groeneveld TW, Seelen MA, Duijs JM, Bajema IM, Prins FA, et al. Anti-C1q autoantibodies deposit in glomeruli but are only pathogenic in

combination with glomerular C1q-containing immune complexes. J Clin Invest 2004; 114:679–88. CrossRefPubMedGoogle Scholar

9. Bigler C, Schaller M, Perahud I, Osthoff M, Trendelenburg M. Autoantibodies against complement C1q specifically target C1q bound on early apoptotic cells. J Immunol 2009;183:3512–21.Abstract/FREE Full TextGoogle Scholar
10. Walport MJ. Complement and systemic lupus erythematosus. Arthritis Res 2002;4 Suppl 3:S279–93.CrossRefPubMedGoogle Scholar
11. Coremans IE, Spronk PE, Bootsma H, Daha MR, van der Voort EA, Kater L, et al. Changes in antibodies to C1q predict renal relapses in systemic lupus erythematosus. Am J Kidney Dis 1995;26:595–601.PubMedGoogle Scholar
12. Gunnarsson I, Sundelin B, Heimbürger M, Forslid J, van Vollenhoven R, Lundberg I, et al. Repeated renal biopsy in proliferative lupus nephritis — predictive role of serum C1q and albuminuria. J Rheumatol 2002;29:698–9.Google Scholar
13. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1997;40:1725.PubMedGoogle Scholar
14. Churg J, Bernstein J, Glassock RJ. Renal disease: classification and atlas of glomerular disease. 2nd ed. New York, Tokyo: Igaky-Shoin; 1995.Google Scholar
15. Austin HA 3rd, Muenz LR, Joyce KM, Antonovych TT, Balow JE. Diffuse proliferative lupus nephritis: identification of specific pathologic features affecting renal outcome. Kidney Int 1984;25:689–95.PubMedGoogle Scholar.