ORIGINAL ARTICLE

Anti-C1q antibodies as a specific serological marker In patients with active lupus nephritis

Aml Ahmed Sayed[1*], Sahar Abd Elgaber Hassan[1], Islam Fathy Mohamed[2], Omaima Mohamed Ali[1]

[1.] Internal Medicine Department, Faculty of Medicine, Aswan University, Aswan, Egypt
[2.] Clinical Pathology Department, Faculty of Medicine, Aswan University, Aswan, Egypt

ABSTRACT

Background: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease, lupus nephritis (LN) is a widespread and serious complication and it is responsible for morbidity and mortality. This study aimed to detect the correlation between anti-C1q antibodies and LN activity. **Patients and Methods**: A case-control study was conducted from September 2021 to September 2022, consisted of 30 healthy controls and 60 patients with SLE. The patients were divided into two groups: group 1 with active LN and group 2 with absent LN. **Results:** The current study consisted of 72 females and 18 males. Regarding the renal biopsy, there were 8 (26.7%) patients in class I, 3 (10.0%) patients in class II, 11 (36.7%) patients in class III and 8 (26.7%) patients in class IV. Our study found a significant difference between groups 1, 2 and the control group regarding Albumin/creatinine ratio, e GFR, SLEDAI score, and anti-C1q. We also revealed a significant positive correlation between anti-C1q and SLEDAI score, Urea, Creat, and Albumin/creatinine ratio in all studied groups. **Conclusion:** Anti-C1q antibodies may serve as a reliable serological indicator for identifying SLE individuals with active LN and active SLE disease.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune connective tissue disorder affecting multiple systems with unknown causes. However, the etiology of SLE may be affected by several genetic, immunological, endocrinal, and environmental factors [1]. Autoantibodies, immunological complexes, complement stimulation, and tissue inflammations are all produced due to immunological dysfunction, which results in clinical conditions with multi-organ affection and unexpected outcomes [2]. SLE affects several systemic organs, such as the musculoskeletal, mucocutaneous, cardiovascular, renal, and hematological systems [3]. Exacerbations or flares of SLE may vary in intensity from minor episodes that may be treated in the clinics to major episodes that require hospitalization. Due to these flare-ups, individuals usually carry the risk of serious complications and permanent organ damage [4].

LN is a widespread, significant consequence and a key indicator of poor outcomes, a report of five-year survival with treatments varying from 46 to 95%. The earlier detection and immunosuppressive therapy initiation are essential for improving outcomes of a patient with LN and hence long-term survival in SLE patients [5]. Moreover, the clinical and serological heterogeneity make a very early diagnosis of SLE and LN and obtaining a reliable evaluation of the disease's progression remains a great challenge [6].

Over 160 autoantibodies, particularly antibodies to complement C1q, histone, chromatin, nuclear and double-stranded DNA (ds DNA), have been reported in SLE patients[7]. Anti-C1q antibodies showed a substantial correlation with the clinical signs of active SLE, especially with renal involvement [8]. The starting molecule of the classical complement pathway activation is C1q complement, which is crucial for removing immune complexes and debris of apoptotic cells. Autoantibodies to C1q are often found in conjunction with inadequate amounts of C1q, which are present in up to 100% of those suffering from SLE with active proliferative LN and in 20-50% of unselected individuals with SLE [9]. As a result, anti-C1q antibodies not only have a high negative predictive value for severe LN occurrence but are necessary for proliferative LN development. Anti-C1q antibody could also be used as an indicator for LN activity [10].

Clinical consequences are usually preceded by the activation of immune system pathways and the formation of pathogenic autoantibodies [11]. Accordingly, anti-C1q titers precede renal flares by 2-6 months. On the other hand, its titers were reduced with treatment in SLE patients with proliferation LN, with a greater fall seen in treatment responders compared to non-responders, 77% and 38%, respectively. The identification of therapy responders and people at risk of renal relapse might be aided by serial anti-C1q detection in SLE individuals who have renal flares [12].

PATIENTS AND METHODS

Study Design, Setting, and Patients:

The ninety participants involved in the present case-control study were divided into; 30 healthy controls (HCs) (group 3) and 60 patients suffering from SLE from the rheumatology and nephrology departments of Aswan University Hospital (the Egyptian Middle Eastern community). Participants with SLE who met at least four of the American College of Rheumatology (ACR) criteria for diagnosis of SLE were included in the study. Individuals with SLE and LN were diagnosed and categorized using the revised ACR criteria and Kidney Disease Improving Global Outcomes (KDIGO) criteria for glomerulonephritis, respectively. Based on renal involvement, the patients were divided into two subgroups: absence and active LN. The term "renal involvement" was used to describe both laboratory and clinical manifestations. SLE patients with active LN (group 1 = 30 patients) were defined as biopsy-proven LN with proteinuria (exceeding 0.5 g/day) or active urinary sediment (hematuria, RBCs casts). While the absent LN (group 2 = 30 patients) were identified as the SLE patients without previous history of renal involvement and normal proteinuria (below 150 mg/day) for at least 5 years.

Exclusion criteria

- Patients with other autoimmune diseases or did not meet four of the revised ACR criteria for SLE.
- Patients who developed end-stage renal disease and received renal replacement therapy.
- Patients with diabetes mellitus and chronic kidney disease (CKD) due to any cause rather than SLE.

Data collection:

The following data were collected from every eligible patient: demographic data, SLE activity detection**,** clinical examination to detect blood pressure, Body Mass Index (BMI), or any signs of SLE activity, such as malar flush, arthritis, alopecia, oral ulcers, or Raynaud's phenomenon, and

laboratory tests that included (complete blood count (CBC), urine analysis, Albumin/Creatinine (Alb/creat) ratio, erythrocyte sedimentation rate (ESR), urea, creatinine, albumin, antinuclear antibody (ANA), anti-double stranded DNA (anti- ds DNA), C3, C4, anti-C1q, e GFR, and renal biopsy for group 1.

Disease activity was assessed based on SLE Disease Activity Index 2000 **(SLEDAI 2K) Score:**

SLEDAI scores were used to define activity categories: no activity (SLEDAI = 0), mild activity (SLEDAI = 1 to 5), moderate activity (SLEDAI = 6 to 10), high activity (SLEDAI = 11 to 19), and extremely high activity (SLEDAI > 20)

Weight	SLEDAI SCORE	Descriptor	Definition
8	_____	Seizure	Recent onset, exclude metabolic, infectious or drug causes.
8	_____	Psychosis	Altered ability to function in normal activity due to severe disturbance in the perception of reality. Include hallucinations, incoherence, marked loose associations, impoverished thought content, marked illogical thinking, bizarre, disorganized, or catatonic behavior. Exclude uremia and drug causes.
8	_____	Organic brain syndrome	Altered mental function with impaired orientation, memory, or other intellectual function, with rapid onset and fluctuating clinical features, inability to sustain attention to environment, plus at least 2 of the following: perceptual disturbance, incoherent speech, insomnia or daytime drowsiness, or increased or decreased psychomotor activity. Exclude metabolic, infectious, or drug causes.
8	_____	Visual disturbance	Retinal changes of SLE. Include cytoid bodies, retinal hemorrhages, serous exudate or hemorrhages in the choroid, or optic neuritis. Exclude hypertension, infection, or drug causes.
8	_____	Cranial nerve disorder	New onset of sensory or motor neuropathy involving cranial nerves.
8	_____	Lupus headache	Severe, persistent headache; may be migrainous, but must be nonresponsive to narcotic analgesia.
8	_____	CVA	New onset of cerebrovascular accident(s). Exclude arteriosclerosis.
8	_____	Vasculitis	Ulceration, gangrene, tender finger nodules, periungual infarction, splinter hemorrhages, or biopsy or angiogram proof of vasculitis.
4	_____	Arthritis	≥ 2 joints with pain and signs of inflammation (i.e., tenderness, swelling or effusion).
4	_____	Myositis	Proximal muscle aching/weakness, associated with elevated creatine phosphokinase/aldolase or electromyogram changes or a biopsy showing myositis.
4	_____	Urinary casts	Heme-granular or red blood cell casts.
4	_____	Hematuria	>5 red blood cells/high power field. Exclude stone, infection or other cause.
4	_____	Proteinuria	>0.5 gram/24 hours
4	_____	Pyuria	>5 white blood cells/high power field. Exclude infection.
2	_____	Rash	Inflammatory type rash.
2	_____	Alopecia	Abnormal, patchy or diffuse loss of hair.
2	_____	Mucosal ulcers	Oral or nasal ulcerations.
2	_____	Pleurisy	Pleuritic chest pain with pleural rub or effusion, or pleural thickening.
2	_____	Pericarditis	Pericardial pain with at least 1 of the following: rub, effusion, or electrocardiogram or echocardiogram confirmation.
2	_____	Low complement	Decrease in CH50, C3, or C4 below the lower limit of normal for testing laboratory
2	_____	Increased DNA binding	Increased DNA binding by Farr assay above normal range for testing laboratory.
1	_____	Fever	>38°C. Exclude infectious cause.
1	_____	Thrombocytopenia	<100,000 platelets / x10⁹/L, exclude drug causes.
1	_____	Leukopenia	< 3,000 white blood cells / x10⁹/L, exclude drug causes.

TOTAL SLEDAI SCORE

Measurement of anti-C1q:

Principle: The ELISA kit uses purified antigen to coat the microtiter plate, makes solid phase antigen, then anti-C1q antibody is added to the wells along with anti-C1q antibody, after that the non-combinative antibody and other components are washed and removed. Then the HRP-labeled antibody is combined to become a complex of an antigen-antibody-enzyme-antibody, after washing completely, the TMB substrate solution is added so that the TMB substrate becomes blue when stimulating the HRP enzyme. After that, the reaction is terminated by adding a sulfuric acid solution, and the color change is measured by spectrophotometry at a wave length of 450 nm, then a comparison is made with the CUT OFF value to judge the presence of anti-C1q Ab in the sample or not.

Ethical Statement

We certify that the study adheres to the national and the global ethical guidelines. Regarding any of the following: physical, psychological, social, legal, economic, or additional variables, there are no potential hazards for research participants. Those who participated were given a thorough explanation of the study goals, methodology, risks, and advantages. The research-eligible participants were provided written informed consent. Our study was conducted in accordance with the Declaration of Helsinki for studies on human subjects. Moreover, the study

has been reviewed and authorized by the ethics committee of the Faculty of Medicine, Aswan University, Egypt.

Statistical Analysis:

The data were collected, revised, coded, and analyzed using the Statistical Package for Social Science (IBM SPSS) version 20. The quantitative data were presented as mean, standard deviations, and ranges when their distribution was parametric, while qualitative data were presented as numbers and percentages. The comparison between two independent groups with quantitative data and parametric distribution was made using an independent t-test. The comparison between two independent groups with quantitative data and non-parametric distribution was performed using the Mann–Whitney Test. While the comparison between the two groups with qualitative data was performed using the Chi-square test and/or Fisher exact test was used instead of the Chi-square test when the expected count in any cell was less than 5. The confidence interval was set to 95%, and the margin of error accepted was set to 5%. Therefore, the p-value was considered significant as the following: $P > 0.05$ = non-significant (NS), $P < 0.05$ = significant (S) and $P < 0.001$ = highly significant (HS).

RESULTS

The current study included 90 participants: 30 healthy controls (HCs) and 60 patients with SLE from Aswan University Hospital. The majority of them were females (80%), with an average age of 27.79 ± 9.16 years, and average body mass index (BMI) of 23.12 ± 2.34 kg/m^2.

The results showed significant differences between patients and control groups in some tested parameters, including hemoglobin (HB), creatinine, urea, serum albumin, ANTI ds DNA, ANA, Alb/creat ratio, e GFR, ESR, SLEDAI score, complement C3, C4, and anti-C1q. Conversely, there were no significant differences regarding white blood cells (WBC) and platelets (PLT), as illustrated in **Table (1)** , **Figures (1) and (2)**.

Table (1): Comparison between Groups 1 (active LN), 2 (absent LN) and 3 (Control) regarding SLEDAI score and laboratory investigations.

		Group 1 No. = 30	Group 2 No. = 30	Group 3 No. = 30	Test value	P-value
SLEDAI score	Mean ± SD	15.97 ± 10.37	6.03 ± 3.87	–	24.141€	0.000**
	Range	2 – 58	2 – 20	–		
HB	Mean ± SD	10.46 ± 1.66	10.61 ± 1.30	12.17 ± 1.70	10.972•	0.000**
	Range	6.7 – 14	8.8 – 13.5	10 – 15		
WBC	Mean ± SD	7.94 ± 4.33	6.37 ± 2.51	6.26 ± 1.41	2.928•	0.059
	Range	2.5 – 22	2.4 – 13	3.5 – 8.6		
PLT	Mean ± SD	268.00 ± 90.03	260.00 ± 84.07	280.30 ± 55.27	0.516•	0.599
	Range	94 – 450	70 – 415	180 – 370		
Creatinine	Mean ± SD	2.29 ± 1.99	1.02 ± 0.19	0.47 ± 0.15	19.471•	0.000**
	Range	0.7 – 9.5	0.7 – 1.3	0.2 – 0.8		
Urea	Mean ± SD	88.43 ± 57.61	34.97 ± 9.59	20.70 ± 2.59	33.577•	0.000**
	Range	26 – 264	18 – 55	17 – 25		
Alb/creat ratio	Mean ± SD	1097.00 ± 1366.89	138.33 ± 53.42	19.77 ± 4.75	16.782•	0.000**
	Range	160 – 6725	40 – 280	10 – 29		
Serum albumin	Mean ± SD	2.91 ± 0.32	3.76 ± 0.35	4.37 ± 0.47	110.407•	0.000**
	Range	2 – 3.5	3 – 4.3	3.6 – 5		
ANTI ds DNA	Negative	1 (3.3%)	2 (6.7%)	30 (100.0%)	77.799*	0.000**
	Positive	29 (96.7%)	28 (93.3%)	0 (0.0%)		
ANA	Negative	1 (3.3%)	0 (0.0%)	30 (100.0%)	85.719*	0.000**
	Positive	29 (96.7%)	30 (100.0%)	0 (0.0%)		
C3	Mean ± SD	67.20 ± 24.05	85.33 ± 19.18	109.40 ± 10.10	38.480•	0.000**

|						
	Range	22 – 100	35 – 125	94 – 124		
C4	Mean ± SD	16.23 ± 5.90	22.44 ± 8.86	31.00 ± 4.78	36.369•	0.000**
	Range	6 – 31	5.2 – 48	24 – 40		
ESR	Mean ± SD	77.90 ± 21.90	64.30 ± 24.42	11.57 ± 1.70	102.388•	0.000**
	Range	35 – 135	30 – 110	8 – 14		
Anti-C1q	Negative	9 (30.0%)	15 (50.0%)	30 (100.0%)	32.500*	0.000**
	Positive	21 (70.0%)	15 (50.0%)	0 (0.0%)		
	Mean ± SD	1.24 ± 0.95	0.28 ± 0.27	–	28.084€	0.000**
	Range	0.0488 – 2.7441	0.037 – 0.9211	–		
e GFR	Mean ± SD	43.03 ± 23.80	79.10 ± 20.87	149.23 ± 20.80	182.949•	0.000**
	Range	4 – 112	46 – 125	107 – 190		

HB (hemoglobin), WBC (white blood count), PLT (platelet), ANA (antinuclear antibody), anti-ds DNA (Anti-double stranded DNA), ESR (Erythrocyte sedimentation rate),e GFR(estimated glomerular filtration rate)
P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value < 0.01: highly significant (HS)**
*: Chi-square test, €: Independent t-test, •: One Way ANOVA Test
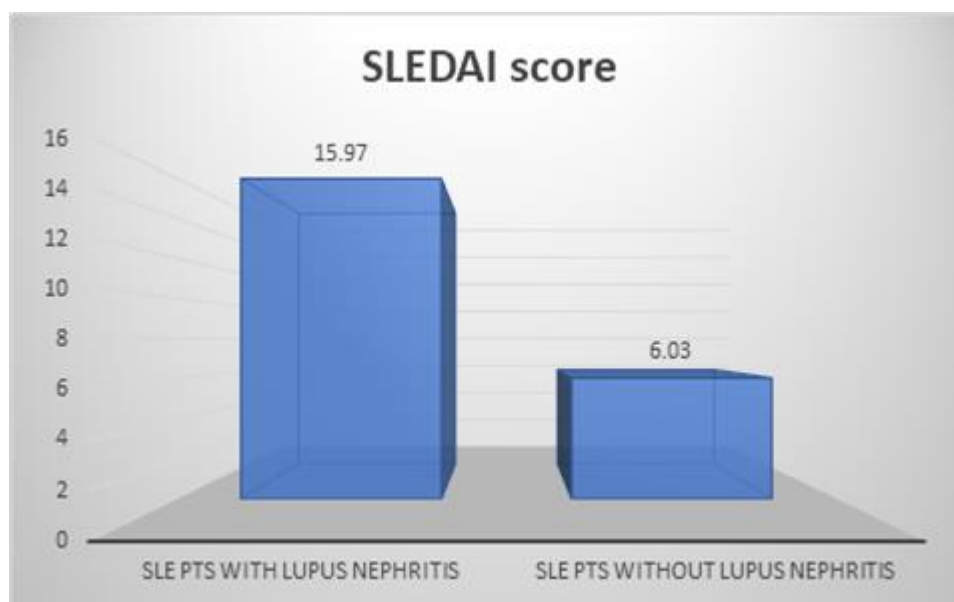
Figure (1): The difference between Group 1 and Group 2 regarding disease activity.
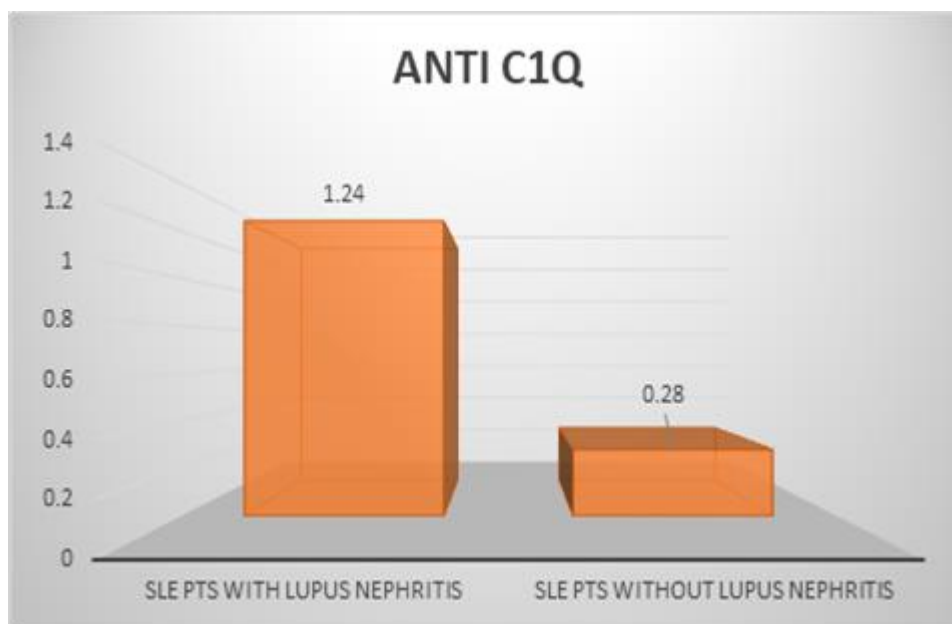
Figure (2): The difference between Group 1 and Group 2 regarding anti-C1q.

Regarding LN activity, renal biopsy was done that revealed 8 (26.7%) patients were in class I, 3 (10.0%) patients in class II, 11 (36.7%) patients in class III and 8 (26.7%) patients in class IV. Also; there was a significant difference between LN activity and Anti C1q (P=0.000) and C3 (P=0.010), but there was no significant difference between LN activity and C4 (P=0.220) and Anti ds DNA (P=0.416), as shown in **Table (2)**.

Table (2) Relation between LN activity and Anti C1q, C3, C4 and Anti ds DNA

Renal biopsy		Diffuse lupus nephritis class IV	Focal lupus nephritis class III	Mesangial proliferative lupus nephritis (class I I)	Minimal mesangial lupus nephritis(class I)	Test value	P-value
		No. = 8	No. = 11	No. = 3	No. = 8		
Anti C1Q	Mean ± SD	2.48 ± 0.12	1.37 ± 0.24	0.56 ± 0.45	0.06 ± 0.01	202.015•	0.000[**]
	Range	2.34 – 2.74	1.03 – 1.80	0.06 – 0.95	0.05 – 0.08		
C3	Mean ± SD	44.88 ± 25.60	71.18 ± 20.88	82.33 ± 15.31	78.38 ± 14.68	4.639•	0.010[*]
	Range	22 – 85	40 – 97	65 – 94	57 – 100		
C4	Mean ± SD	14.00 ± 4.28	15.09 ± 4.54	21.00 ± 9.54	18.25 ± 6.94	1.573•	0.220
	Range	8 – 20	6 – 22	12 – 31	6 – 25		
Anti ds DNA	Negative	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (12.5%)	2.845*	0.416
	Positive	8 (100.0%)	11 (100.0%)	3 (100.0%)	7 (87.5%)		

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value < 0.01: highly significant (HS) **
*: Chi-square test, •: One Way ANOVA Test

As regard the sensitivity and specificity of biomarker of LN , Receiver operating characteristic curve (ROC) was done that showed ; the best cut off point of **Anti C1q** to detect the SLE Patients with lupus nephritis group was found > 0.92 with sensitivity of 66.7%, specificity of 100.0%, PPV of 100.0%, NPV of 75.0% and total accuracy of 78.0%. The best cut off point of **C3** to detect SLE Pts with lupus nephritis group was found ≤ 75 with sensitivity of 56.7%, specificity of 80.0%, PPV of 73.9%, NPV of 64.9% and total accuracy of 72.0%. The best cut off point of **C4** to detect SLE Pts with lupus nephritis group was found ≤ 18 with sensitivity of 66.7%, specificity of 70.0%, PPV of 69.0%, NPV of 67.7% and total accuracy of 73.0%, as shown in **Figures (3).**
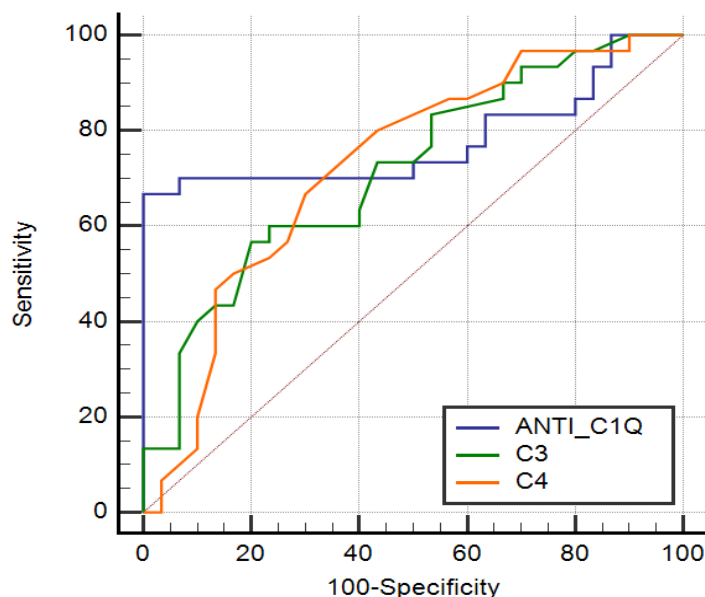
Figure (3) ROC curve regarding Anti C1q, C3 and C4

Additionally, the anti-C1q antibodies studied in all groups revealed a significant positive correlation between anti-C1q and SLEDAI score, creatinine, urea, ANTI ds DNA and Alb/creat ratio. There was a significant negative correlation between anti-C1q and Serum albumin, complement C3, C4, and e GFR. In contrast, there was no significant correlation between anti-C1q and HGB, WBC, PLT, and ESR, as shown in **Table (3)**.
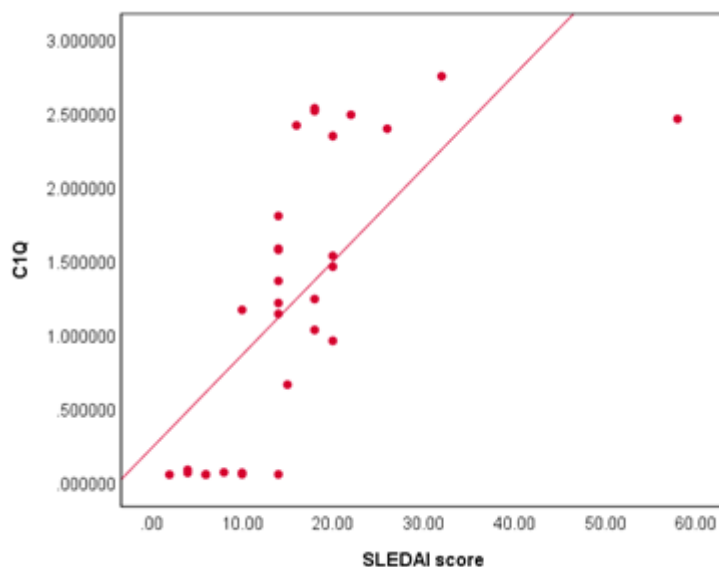
Table (3): The correlation between anti-C1q, disease activity, and lab investigations of all studied groups.

All cases	Anti-C1q	
	R	P-value
SLEDAI score	**0.823****	**0.000****
HB	-0.142	0.281
WBC	0.249	0.055
PLT	0.176	0.178
Creatinine	**0.603****	**0.000****
Urea	**0.521****	**0.000****
Alb/creat ratio	**0.653****	**0.000****

| Serum albumin	-0.615**		0.000**
C3	-0.343**		0.007**
C4	-0.394**		0.002**
ESR	0.042		0.753
e GFR	-0.594**		0.000**
ANTI ds DNA	**Anti-C1q**		0.016*
	Mean ± SD	**Range**	
Negative	0.19 ± 0.23	0.04 – 0.46	
Positive	0.79± 0.86	0.04 – 2.74	

HB (hemoglobin), WBC (white blood cells), PLT (platelet), ESR (Erythrocyte sedimentation rate), e GFR (estimated glomerular filtration rate) anti-ds DNA (Anti-double stranded DNA)

The SLE patients with active LN (group 1) were tested for anti-C1q antibodies and the results were correlated with other parameters for the same group, revealing a significant positive correlation between anti-C1q and SLEDAI score, creatinine, urea, and Alb/creat ratio. In addition, a significant negative correlation between anti-C1q and serum albumin and e GFR was found, as illustrated in, **Figures (4)**, **(5) and (6)**.
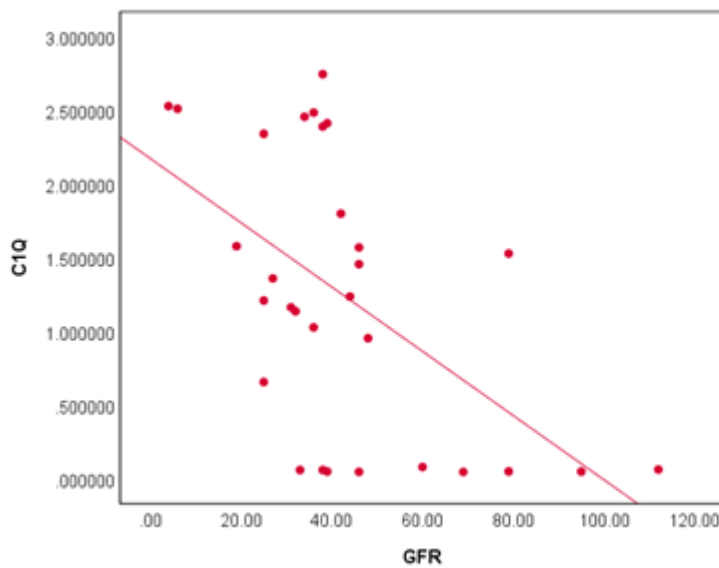

Figure (4): Positive correlation between anti-C1q and SLEDAI score.
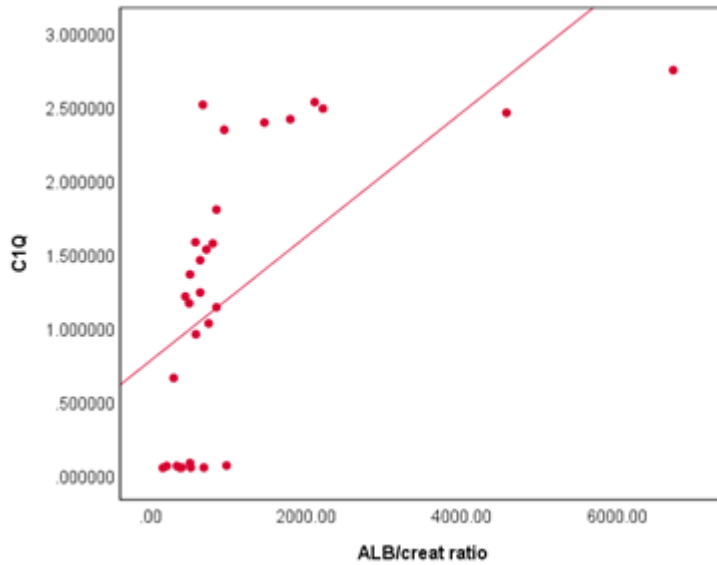
Figure (5): Positive correlation between anti-C1q and Alb/creat ratio.

Figure (6): Negative correlation between anti-C1q and e GFR.

DISCUSSION

   SLE, an autoimmune illness that may influence many systems and essential organs, Lupus nephritis is a frequent main organ presentation and an important contributor to morbidity and mortality[13]. Consequently, LN influences 40-80% of those diagnosed with SIE, and immunosuppressive therapy for LN may negatively affect the kidney function and result in chronic renal failure, thereby increasing morbidity and mortality. As a result, among the most significant prognostic indicators for an individual with SLE is the presence of renal disease activity, and

identifying SLE patients with LN have significant clinical implications for directing the therapy of SLE in clinical settings[14].

In fact, renal problems manifested frequently in SLE patients with both anti-ds DNA and anti-C1q antibodies, and these patients frequently had poor renal outcomes. This is because SLE patients with anti-C1q antibodies had more active renal disease than those without circulating anti-C1q antibodies. Thus, circulating autoantibodies against C1q are proposed to be a marker of LN and a predictor of renal damage and disease activity in SLE patients [15].

Our study included 90 participants: 30 healthy controls (HCs) and 60 patients with SLE; most of them were females (80%) and with a mean age of 27.79±9.16 years. This agrees with the findings of *Abu Al-Fadl et al.*[16], who found that 92% of the cases were females and only 8% were males.

The current results detected significant differences in anti-ds DNA, C3, and C4 levels amongst SLE patients with and without LN and the controls. The findings corroborated those reported by *Troldborg et al.*[17], who claimed that complements consumption and decreases in C3 and C4 concentrations are associated with disease activity. Additionally, *Qu et al.*[18] demonstrated that hypocomplementemia and elevated anti-ds DNA antibodies levels are serological indicators of SLE activity. *Chi et al.*[19] showed that anti-C1q and complement C3 and C4 are more reliable indicators for LN activity than anti-ds DNA antibodies; however, anti-ds DNA antibodies and serum levels of C3 and C4 are superior to anti-C1q for assessing the overall and non-LN SLE activity.

In the current study, there was highly significant increase in serum creatinine and e GFR among SLE patients with and without LN and the control group. Moreover, *Yang et al .*[20] found those LN patients had elevated serum creatinine levels compared to the normal group. Furthermore, they reported a 2-fold increase in the serum creatinine levels of eight patients, while three patients developed ESRD. According to *Farid et al.* [21], serum creatinine level was higher in patients with active LN than in patients with inactive LN. Additionally, *Yang et al.* [20] observed that patients with LN had decreased e GFRs than those in the normal group.

The present research revealed that SLE patients with LN had higher levels of anti-C1q antibodies than SLE individuals without LN. Autoantibodies targeting Clq (anti-Clq) may be found in around one-third of unselected SLE patients as well as more than 90% of individuals with proliferative lupus nephritis, as reported by *Irure-Ventura and Lopez-Hoyos*[22]. According to *Angeletti et al*[23], 44% of SLE patients had anti-C1q antibodies, 60% had LN, and only 14% without a renal flare, suggesting a correlation between LN and circulating anti-C1q antibodies. This is in accordance with the findings of *Dumestre-Pérard et al.* [24], who demonstrated that patients with active SLE and LN had anti-C1q levels that were significantly higher than those with inactive SLE, absent LN, and healthy persons.

Our study showed a strong positive association between Anti C1q and SLED Al score in SLE patients. Our finding was supported by a recent study demonstrated by **Pang et al.** [25] stated that anti-C1q antibodies were associated with the disease activity of SLE and LN. The authors utilized a large number of LN cohorts and demonstrated a correlation between anti-C1q antibodies and disease activity of SLE and LN. **Irure-Ventura and Lopez-Hoyos**[22] reported a substantial correlation between anti-C1q, hypocomplementemia and SLE activity. Additionally, according to **Dumestre-Perard et al.**[24], there was a positive correlation between the levels of anti-C1q

antibodies and SLEDAl scores. On the other hand, **Ferdian et al.**[26] demonstrated an insignificant correlation between the levels of anti-C1q antibodies and the activity of SLE, as determined by the SELENA-SLEDAI score.

The present study revealed a significant negative correlation between anti-C1q, C3, and C4.These findings are in harmony with *Dumestre-Pérard et al.* [24], who reported an inverse correlation between levels of anti-C1q antibodies and C3 & C4 in patients with SLE.

Regarding the grades of LN, our study showed a highly significant difference between the grades of LN as determined by renal biopsy and the presence of anti-C1q antibodies. According to *Kianmehr et al.*[27,] a significant positive correlation was observed between anti-C1q and the incidence of active proliferative LN in approximately 97% of cases. Research indicates that only one-third of individuals suffering from SLE with inactive or absent LN had anti-C1q antibodies. In addition to an elevated level of anti-C1q in patients with biopsy-proven active LN, anti-C1q titers significantly decreased with effective therapy.

We acknowledge that the present study has some limitations; as we missed to follow the anti-C1q titers after management to detect it is reliability for monitoring the effectiveness of therapy.

CONCLUSION

Anti-C1q antibodies might be a reliable serological biomarker for identification of SLE patients with active LN and active SLE disease because they were substantially strongly associated with LN and SLE activity.

Availability of data and materials
The datasets used during the current study may be made available from the corresponding author upon reasonable request.
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Contributions

Aml Ahmed Sayed, writing the main manuscript text, Aml Ahmed Sayed , and Omaima Mohamed Ali responsible for analysis and interpretation of data, Sahar Abd Elgaber Hassan responsible for collection of data, Islam Fathy Mohamed responsible for technical support and analysis of biomarker ,All authors reviewed the manuscript.
Conflict of interest

All authors declare they have no conflicts of interest to this study.

Abbreviations
SLE: Systemic lupus erythematosus
LN: lupus nephritis
HCs: healthy controls
SLEDAl: SLE Disease Activity Index

e GFR: estimated glomerular filtration rate

ACR: American College of Rheumatology

KDIGO: Kidney Disease Improving Global Outcomes

CKD: chronic kidney disease

BMI: Body Mass Index

CBC: complete blood count

Alb/creat: Albumin/Creatinine

ESR: erythrocyte sedimentation rate

ANA: antinuclear antibody

Anti- ds DNA: anti-double stranded DNA

NS: non-significant

S: significant

HS: highly significant

HB: hemoglobin

WBC: white blood count

PLT: platelets

Lab: laboratory

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