Anti-C1q antibodies as a marker for disease activity in systemic lupus erythematosus and lupus nephritis

Eman A.H. Omran[a], Nadia M. Ismail[a], Eman Mosad[b], Yasmine S. Hussein[a]

[a]Department of Physical Medicine, Rheumatology and Rehabilitation, Assiut University Hospital, Faculty of Medicine, [b]Department of Clinical Pathology, South Egypt Cancer Institute, Assiut University, Assiut, Egypt

Correspondence to Yasmine S. Hussein (MSc), Department of Physical Medicine, Rheumatology and Rehabilitation, Assiut University Hospital, Egypt
Postal/zip code: 71515; Tel: +20 100 292 9015; e-mail: yasmine.saad@aun.edu.eg

Received 01 June 2016
Accepted 14 July 2016

Journal of Current Medical Research and Practice
September-December 2016, 1:47–53

Background
Systemic lupus erythematosus (SLE) is a chronic multisystem inflammatory autoimmune disease that is characterized by a number of immunological abnormalities. Disease onset is triggered by ill-defined environmental factors in genetically susceptible individuals. C1q plays a key role in apoptotic cell and immune complex removal, and hence it is a very important functional molecule in SLE pathogenesis. Investigation of the relationship between peripheral lymphocyte apoptosis and serum levels of anti-C1q autoantibodies in SLE patients suggests that increased serum levels of anti-C1q autoantibodies are responsible for apoptosis and may play a pathogenic role in SLE patients, especially in active disease.

Objectives
The aim of this study was to measure the serum level of anti-C1q in SLE patients, and to evaluate the correlation between anti-C1q and SLE disease activity, especially renal activity.

Patients and methods
Fifty SLE patients diagnosed according to the Systemic Lupus International Collaborating Clinics classification criteria 2012 and 33 healthy volunteers who were age and sex matched were included in the study. SLE activity was assessed using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), and renal activity was assessed using the renal SLEDAI. Anti-C1q was estimated using enzyme-linked immunosorbent assay kit.

Results
Serum anti-C1q was significantly higher in SLE patients (64.86 ± 27.88 U/ml) compared with healthy controls (30.15 ± 13.93 U/ml) ($P < 0.000$). There was a significantly positive correlation between anti-C1q and the SLEDAI ($P = 0.035$, $r = 0.299$) and the renal SLEDAI ($P = 0.025$, $r = 0.316$). Anti-C1q has a sensitivity and specificity of 92.7 and 66.7%, respectively, a positive predictive value of 92.7%, negative predictive value of 66.7%, and 88.0% accuracy for detecting SLE disease activity, whereas for lupus nephritis diagnosis anti-C1q has a sensitivity and specificity of 94.12 and 50.0%, respectively, a positive predictive value of 80.0%, negative predictive value of 80.0%, and 80.0% accuracy.

Conclusion
Our results support the finding that anti-C1q level might be used as a marker for SLE activity and not lupus nephritis in adult SLE patients.

Keywords:
anti-C1q antibodies, SLE, lupus nephritis

J Curr Med Res Pract 1:47–53

2357-0121

Introduction

Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease that is characterized by a number of immunological abnormalities affecting multiple systems [1]. Current theories on the pathogenesis of SLE focus on aberrant apoptosis and/or necrosis resulting in the availability of nuclear antigens to the immune system, and the uptake of nucleic acid-containing immune complexes by plasmacytoid dendritic cells causing the activation of type I interferon overexpression. The resulting inflammatory environment leads to the development of T-cells into the proinflammatory pathways, defective function of regulatory T-cells leading to hyperactivity of Th cells, and the survival and activation of B-cells that produce autoantibodies [2].

The complement system has long been known for its role in combating infections. More recently, the complement system has been appreciated for its role in waste product transport, immune tolerance, and shaping of the adaptive immune response. In the adaptive immune response antibodies represents the humoral part, moreover complement system interacts with antibodies. The complement system can be activated by antibodies, it is also can be the target of auto-antibodies. C1q is targeted by autoantibodies, which are currently considered to play a role in human disease [3]. The first

component of the classical pathway of the complement system (C1q) is considered to have a pivotal role in the clearance of immune complexes and in the removal of waste material originating from apoptotic cells. An autoimmune response can result from prolonged exposure of C1q epitopes to the immune system [4].

Thus, the study aimed to measure the serum level of anti-C1q in SLE patients, and to evaluate the correlation between anti-C1q and SLE disease activity and lupus nephritis (LN).

Patients and methods

Study population

This case–control study was carried out in the Rheumatology, Rehabilitation and Physical Medicine Department in Assiut University Hospitals during the period from January 2013 to April 2013. This study was conducted on 50 SLE patients diagnosed according to the Systemic Lupus International Collaborating Clinics classification criteria for the classification of SLE [5]. Thirty-three healthy volunteers, age and sex matched with the studied group, were enrolled in the study and served as a control group.

Ethical issues

Ethical approval was obtained from the local authority of Faculty of Medicine.

Informed consent form was prepared in Arabic language to be read by the participating patients or to be read out to them if they were illiterate and then to be signed.

Confidentiality

The participating patients would not be named in any publications from the trials.

Inclusion criteria

(1) SLE patients older than 18 years
(2) Patients suffering from SLE who fulfilled four or more criteria (at least one clinical and one laboratory criterion) or biopsy-proven LN with positive antinuclear antibodies or anti-DNA according to the Systemic Lupus International Collaborating Clinics classification criteria.

Exclusion criteria

(1) Patients with other systemic autoimmune diseases
(2) Patients with urinary tract infection (≥100 000 colony-forming units in urine culture)
(3) LN patients undergoing hemodialysis or those with a history of renal transplantation.

All SLE patients were subjected to the following:

(1) History and full clinical examination
   (a) Full history taking and thorough clinical examination, including age, sex, menstrual history, disease duration, history of present illness, and past and family history
   (b) Demographic, clinical, and anthropometric data for patients and controls through complete medical history, physical examination, and articular examination
   (c) Therapeutic history.

(2) Assessment of SLE activity and renal activity
   (a) Disease activity of SLE was assessed using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). Patients were considered active if SLEDAI score was 8 or more and inactive if SLEDAI score was less than 8 [6]
   (b) Renal involvement was assessed with the renal SLEDAI, which consists of the four kidney-related parameters of the SLEDAI: hematuria, pyuria, proteinuria, and urinary casts. Each item in the renal SLEDAI is assigned four points. Thus, scores for the renal SLEDAI can range from 0 (inactive renal disease) to a maximum of 16; a SLEDAI score of 4 was taken as an indicator of active LN [6]
   (c) SLE patients were classified as follows:
      (i) Active SLE: patients with SLEDAI score of 8 or more (41 patients)
      (ii) Inactive SLE: patients with SLEDAI score less than 8 (nine patients)
      (iii) SLE patients with LN (34 patients)
      (iv) SLE without LN (16 patients).

(3) Laboratory investigations

The following laboratory investigations were carried out for all SLE patients.

(a) *Routine investigations included the following*: first hour erythrocyte sedimentation rate (ESR) using the Westergren technique; C-reactive protein measured quantitatively (N: up to 6 mg/l); complete blood count, including blood hemoglobin (Hb), white blood cells (WBCs) count, and platelet count; liver function test including liver enzymes such as aspartate transaminase and alanine transaminase and serum albumin; muscle enzymes such as creatinine phosphokinase and lactate dehydrogenase; kidney function test; complete urine analysis for hematuria, pyuria, proteinuria, urinary casts, and creatinine clearance; and lipid profile such as serum cholesterol, serum

triglycerides, low-density lipoproteins, and high-density lipoproteins

(b) *Immunological profile included the following*: antinuclear antibodies, anti-dsDNA, and complements (C3, N: 3.7–10.5 μg/ml; C4, N: 2.4–7 μg/ml).

(4) Blood was taken for the assay of the anti-C1q. Levels of anti-C1q were measured using the enzyme-linked immunosorbent assay (ELISA) kits.

Methods of anti-C1q estimation in blood

Anti-C1q estimation

Anti-C1q estimation was carried out using the kit of ORGENTEC Diagnostika GmbH (Mainz, Germany), immunometric enzyme immunoassay, for the quantitative determination of autoantibodies against C1q ORG 549.

Specimen collection, storage, and handling

Collect whole blood specimens using acceptable medical techniques to avoid hemolysis. Allow blood to clot and separate the serum by means of centrifugation. The test serum should be clear and nonhemolyzed. Contamination with hemolysis or lipemia is best avoided, but does not interfere with this assay. Specimens may be refrigerated at 2–8°C for up to 5 days or stored at −20°C up to 6 months.

Statistical analyses

Statistical analyses were performed using statistical package for the social sciences (version 20.0, SPSS Inc., Chicago, Illinois, USA). Continuous data were expressed as mean ± SD, whereas categorical data were expressed as numbers and percentages. The differences between groups were determined using the χ^2-test for categorical data or the *t*-test and analysis of variance for continuous data. Correlation between different variables was made. Receiver operating characteristic (ROC) curve was constructed for the calculation of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy. Statistical significance was defined as *P* value less than 0.05.

Results

In total, 50 SLE patients were studied. There were 44 (88%) women and six (12%) men. Their mean age was 28.30 ± 8.9 years. The mean SLE duration was 4.0 ± 3.2 years. Anti-C1q had a mean value of 64.86 ± 27.88, which was significantly higher than that in the control group (30.15 ± 13.93) ($P < 0.000$). There was a very highly significant difference in anti-C1q. Demographic data, clinical data, laboratory data, and medications received are shown in Tables 1–3.

Table 1 Demographic data of the SLE patients

Variables	SLE patients (*n*=50)
Age (years)	28.30±8.9
Sex:female (*n* (%))	44 (88.0)
Disease duration (years)	4.0±3.2

SLE, systemic lupus erythematosus.

Table 2 Clinical and laboratory data in SLE patients

Variables	SLE patients (*n*=50) (*n* (%))
Clinical data	
Fatigue	42 (84.0)
Fever	3 (6.0)
Alopecia	25 (50.0)
Malar rash	12 (24.0)
Nasal or oral ulcers	4 (8.0)
Myositis	10 (20.0)
Arthritis	30 (60.0)
Neuropsychiatric	19 (38.0)
Vasculitis	8 (16.0)
Renal	34 (68.0)
Serositis	5 (10.0)
Laboratory	
ESR (mm/first h)	47.82±30.69
CRP (mg/l)	10.81±3.54
Hemoglobin (g/dl)	10.93±3.55
WBCs (10^3/μl)	5.26±2.34
Platelets (10^3/μl)	281.42±111.22
AST (U/l)	20.46±4.31
ALT (U/l)	23.68±7.40
CPK (U/l)	80.58±26.09
LDH (U/l)	315.64±129.76
Serum albumin (g/dl)	37.98±7.37
Urea (mmol/l)	5.80±2.33
Creatinine (μmol/l)	75.11±28.18
Creatinine clearance (ml/min)	100.33±44.44
24 h protein in urine (mg)	1175.61±660.88
Pus/hpf in urine	22 (44.0)
RBCs/hpf in urine	19 (38.0)
Urinary cast	5 (10.0)
Crystals in urine	7 (14.0)
Albumin in urine	21 (42.0)
Serum uric acid (mg/dl)	4.41±1.62
Serum cholesterol (mg/dl)	168.42±44.65
Triglyceride (mg/dl)	134.74±54.17
HDL (mg/dl)	44.80±15.78
LDL (mg/dl)	96.31±39.96
ANA	43 (86.0)
Anti-dsDNA	2.00±1.57
C3 (μg/ml)	3.39±2.92
C4 (μg/ml)	2.48±1.61

ALT, alanine transaminase; ANA, antinuclear antibodies; AST, aspartate transaminase; C3, complement 3; C4: complement 4; CPK, creatinine phosphokinase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HDL, high-density lipoprotein; hpf, high power field of microscope; LDL, low-density lipoprotein; LDH, lactate dehydrogenase; RBC, red blood cell; WBC, white blood cell.

Table 3 Medications received by SLE patients and their SLEDAI and renal SLEDAI

Variables	SLE patients (*n*=50) (*n* (%))
Medications	
Systemic steroids	42 (84.0)
Antimalarial	44 (88.0)
Azathioprine	38 (76.0)
Methotrexate	11 (22.0)
Cyclophosphamide	8 (16.0)
Mycophenolate mofetil	0 (0)
SLEDAI	
Score ≤ 8	9 (18.0)
Score>8	41 (82.0)
Renal SLEDAI	
Score 0	16 (32.0)
Score ≥ 4	34 (68.0)

Correlation of serum level of anti-C1q with clinical and laboratory data showed a significant correlation with alopecia (P = 0.004) and serositis (P = 0.05) for clinical data and for laboratory data. Anti-C1q was significantly correlated with Hb (P = 0.03), WBCs (P = 0.05), serum albumin (P = 0.04), urea (P = 0.002), serum uric acid (P = 0.004), pus/hpf in urine (P = 0.05), and with the SLEDAI (P = 0.035) and the renal SLEDAI (P 0.025), as shown in Table 4.

To quantify the use of anti-C1q and anti-dsDNA using ELISA in SLE patients in detecting the activity of SLE disease, a ROC curve was constructed. The area under the curves for anti-C1q and anti-dsDNA were 0.809 and 0.684, respectively. For anti-C1q at cutoff point more than 41, the sensitivity and specificity were 92.7 and 66.7%, respectively, with a PPV of 92.7%, NPV of 66.7, and 88.0% accuracy. For anti-dsDNA at cutoff point more than 1, the sensitivity and specificity were 68.3 and 66.7%, respectively, PPV and NPV were 90.3 and 31.6%, respectively, and accuracy was 68.0% (Table 5). To quantify the use of anti-C1q and anti-dsDNA using ELISA in SLE patients in diagnosing LN, a ROC curve was constructed. The area under the curves for anti-C1q and anti-dsDNA were 0.656 and 0.641, respectively. For anti-C1q at cutoff point more than 44, the sensitivity and specificity were 94.12 and 50.0%, respectively, with a PPV of 80.0%, NPV of 80.0%, and 80.0% accuracy. For anti-dsDNA at cutoff point more than 0.8, the sensitivity and specificity were 79.4 and 56.3%, respectively, PPV and NPV were 79.4 and 56.2%, respectively, and accuracy was 72.0%, as shown in Table 6.

Table 4 Correlation of anti-C1q with clinical and laboratory data in SLE patients

Variables	Anti-C1q in SLE patients	
	R	*P*
Fatigue	0.019	0.87
Fever	0.175	0.15
Alopecia	0.344	0.004**
Malar rash	0.178	0.139
Ulcer	0.181	0.13
Myositis	−0.022	0.855
Arthritis	−0.158	0.19
Neuropsychiatric	0.141	0.24
Vasculitis	0.129	0.28
Serositis	0.235	0.05*
ESR (mm/first h)	0.173	0.23
CRP (mg/l)	−0.117	0.42
Hemoglobin (g/dl)	−0.308	0.03*
WBCs (10^3/μl)	0.272	0.05*
Platelets (10^3/μl)	−0.027	0.85
AST (U/l)	−0.083	0.56
ALT (U/l)	−0.170	0.24
CPK (U/l)	−0.260	0.68
LDH (U/l)	−0.184	0.2
Serum albumin (g/dl)	−0.291	0.04*
Urea (mmol/l)	0.427	0.002**
Creatinine (μmol/l)	0.130	0.37
Creatinine clearance (ml/min)	−0.053	0.71
24 h protein in urine (mg)	0.136	0.35
Pus/hpf in urine	0.233	0.05*
RBCs/hpf in urine	0.179	0.14
Urinary cast	0.185	0.12
Crystals in urine	−0.151	0.21
Albumin in urine	0.168	0.16
Serum uric acid (mg/dl)	0.403	0.004**
Serum cholesterol (mg/dl)	0.172	0.23
Triglyceride (mg/dl)	0.248	0.08
HDL (mg/dl)	−0.090	0.53
LDL (mg/dl)	0.118	0.41
ANA	−0.113	0.35
Anti-dsDNA	0.258	0.07
C3 (μg/ml)	−0.166	0.249
C4 (μg/ml)	−0.267	0.061
SLEDAI	0.299	0.035*
Renal SLEDAI	0.316	0.025*

**Moderately statisitcally significant. ALT, alanine transaminase; ANA, antinuclear antibodies; AST, aspartate transaminase; C3, complement 3; C4, complement 4; CPK, creatinine phosphokinase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HDL, high-density lipoprotein; hpf, high power field of microscope; LDH, lactate dehydrogenase; LDL, low-density lipoprotein; RBC, red blood cell; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; WBC, white blood cell. *Statistically significant.

Discussion

SLE is a chronic, autoimmune disease, associated with an inflammatory status and multisystemic damage, due to interaction between genetic, immunological, endocrine, and environmental factors [7]. Although the incidence of SLE has increased, there has been a significant improvement in the long-time survival, inducing a higher incidence of complications and comorbidities [8,9].

C1q is the first component of the classical pathway of complement activation. Together with the enzymatically active components C1r and C1s, C1q forms the C1

complex. Binding of C1 to immunoglobulins in the form of immune complexes leads to the activation of proteases C1r and C1s and a further activation of the classical pathway of complement [10]. C1q plays a key role in apoptotic cell and immune complex removal, and hence it is a very important functional molecule in SLE pathogenesis [11]. Investigation of the relationship between peripheral lymphocyte apoptosis and serum levels of anti-C1q autoantibodies in SLE patients suggest that increased serum levels of anti-C1q autoantibodies are responsible for apoptosis and may play a pathogenic role in SLE patients, especially in active disease. A high occurrence of in-vitro apoptosis of lymphocytes induced by serum from SLE patients is associated with increased serum levels of anti-C1q autoantibodies [12].

In our study, anti-C1q level was significantly higher in SLE patients (64.86 ± 27.88) compared with normal controls (30.15 ± 13.93) (P < 0.000). Among SLE patients, anti-C1q was positively significantly correlated with the SLEDAI and the renal SLEDAI (r = 0.299, P = 0.035, and r = 0.316, P = 0.025, respectively). To quantify the use of anti-C1q using ELISA in SLE patients for diagnosing the activity of SLE disease, a ROC curve was constructed. The area under the curve for anti-C1q was 0.809. At a cutoff point more than 41, the sensitivity and specificity were 92.7 and 66.7%, respectively, with a PPV of 92.7%, NPV of 66.7%, and accuracy of 88.0%. For diagnosing LN, anti-C1q had an area under the curve of 0.656 at cutoff point more than 44; the sensitivity and specificity were 94.12 and 50.0%, respectively, with a PPV of 80.0%, NPV of 80.0%, and 80.0% accuracy.

Table 5 Comparison of the mean levels of anti-C1q between SLE patients and controls and between the SLEDAI and renal SLEDAI groups

		P
SLE patients	64.86±27.88 U/ml	0.000***
Control	30.15±13.93 U/ml	
Active SLE patients with SLEDAI score≤8 (41 patients)	43.67±16.46 U/ml	0.010*
Inactive SLE patients with SLEDAI score>8 (9 patients)	69.51±27.84 U/ml	
SLE patients without lupus nephritis (16 patients)	58.69±32.64 U/ml	0.207
SLE patients with lupus nephritis (34 patients)	67.76±25.36 U/ml	

*Statistically significant, ***Highly statistically significant. SLE, Systemic Lupus Erythematosus; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index.

On comparing our results with other studies, they were consistent with other results [13–16] as regards the presence of a significant increase in anti-C1q levels in SLE patients compared with the control group (P = 0.000).

In the current study, the mean level of anti-C1q in the group of patients with LN (68.0%) was not significantly different from the mean level in patients without LN (32.0%) (P = 0.207). Our results were compatible with those of Zhang *et al.* [15], who found a nonsignificant difference in levels of anti-C1q antibodies in the SLE group between LN patients and non-LN patients (57.14 vs. 41.46%, P > 0.05). Moreover, Oelzner *et al.* [17] who conducted a study on 79 SLE patients, found that the presence of anti-C1q Ab was not different between patients with and those without nephritis. This is compatible with the findings of Bernstein *et al.* [18], who worked on sera obtained from 60 SLE patients. They found that patients with nephritis exhibited nonsignificant mean values for anti-C1q compared with patients in other groups (P = 0.23) [18].

However, in a study conducted by Smykal-Jankowiak *et al.* [19] on 48 patients with LN and 66 healthy controls, they found that anti-C1q was detected in 60% of the patients with LN and the prevalence and mean levels of anti-C1q were significantly higher in patients with active LN than in those with inactive LN or controls [19]. Many other studies found that anti-C1q was significantly higher in patients with LN than in patients without LN [13,20–26].

In the present study, correlation between the level of anti-C1q and some clinical parameters showed a significant positive correlation with alopecia (r = 0.344, P < 0.004) and with serositis (r = 0.235, P < 0.05), but there was a nonsignificant correlation with other clinical data. Furthermore, there was a positive significant correlation of anti-C1q with the SLEDAI (r = 0.299, P < 0.035) and the renal SLEDAI (r = 0.316, P < 0.025),

Table 6 The sensitivity and specificity of anti-C1q and anti-dsDNA in detecting SLE disease activity and lupus nephritis

Variable	AUC	Cutoff	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
SLEDAI							
Anti-C1q	0.809	>41	92.7	66.7	92.7	66.75	88.0
Anti-dsDNA	0.684	>1	68.3	66.7	90.3	31.6	68.0
Renal SLEDAI							
Anti-C1q	0.656	>44	94.12	50.0	80.0	80.0	80.0
Anti-dsDNA	0.641	>0.8	79.4	56.3	79.4	56.2	72.0

AUC, area under the curve; NPV, negative predictive value; PPV, positive predictive value; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index.

and when we performed a correlation of anti-C1q with different laboratory findings there was a significant positive correlation with pus in urine/hpf (r = 0.233, P < 0.05), WBCs (r = 0.272, P < 0.05), urea (r = 0.427, P < 0.002), and serum uric acid (r = 0.403, P < 0.004). There was an inverse significant correlation with Hb (r=–0.308, P < 0.03), serum albumin (r=–0.291, P < 0.04), and 25(OH) D (r=–0.314, P < 0.027), with a nonsignificant correlation with other laboratory parameters, including C3, C4, anti-dsDNA, protein in urine in 24 h, and creatinine clearance.

We compared our results with other studies as regards the correlation of anti-C1q with different clinical and laboratory data. Gargiulomde *et al.* [27] found that anti-C1q was found in SLE patients with active renal involvement or with lupus skin disease. Akhter *et al.* [25] found that anti-C1q had the highest association with proteinuria (P = 0.079). Moreover, Moura *et al.* [28] found that the presence of anti-C1q antibodies was associated with proteinuria (P = 0.028) but not with other laboratory or clinical features, such as antinucleosome or anti-dsDNA antibodies, hematuria, urinary casts or renal failure, leukopenia, pericarditis, pleuritis, malar rash, seizures, and psychosis.

In our study, there was a significant correlation between anti-C1q and the SLEDAI (r = 0.299, P < 0.035) and the renal SLEDAI (r = 0.316, P < 0.025). This is compatible with the study by Thanei *et al.* [29], who found that anti-C1q strongly correlates with the occurrence of LN in SLE patients. Moreover, Zhang *et al.* [15] found that anti-C1q antibody levels were positively correlated with levels of SLEDAI scores (P < 0.05). This was compatible with the studies by Katsumata *et al.* [14], Mok *et al.* [30], Moura *et al.* [28], Oelzner *et al.* [17], who found that anti-C1q antibody titers were significantly correlated with SLEDAI scores (P < 0.0001; P < 0.001; r = 0.370, P = 0.001; P < 0.01, respectively). This was also compatible with the study done by Tan *et al.* [23] who found that the levels of both SLEDAI and renal biopsy activity index of patients were correlated with the levels of anti-C1q antibodies (r = 0.520, P < 0.001; r = 0.321, P = 0.003, respectively). This is contradictory to the findings of Meyer *et al.* [22], who found that anti-C1q did not correlate with the SLEDAI. Multiple studies found a positive correlation between anti-C1q and anti-dsDNA [14,15,17].

As regards the sensitivity and specificity of anti-C1q for detecting SLE disease activity and LN, we concluded that for anti-C1q at cutoff point more than 41 the sensitivity and specificity were 92.7 and 66.7%, respectively, with a PPV of 92.7%, NPV of 66.7%, and 88.0% accuracy for detecting SLE disease activity, and that for LN at cutoff point more than 44 the sensitivity and specificity were 94.12 and 50.0%, respectively, with a PPV of 80.0%, NPV of 80.0%, and 80.0% accuracy.

Moura *et al.* [26] concluded that anti-C1q was associated with a sensitivity of 86.66%, a specificity of 74.47%, a NPV of 94.59%, and a PPV of 52% for the diagnosis of LN. Mok *et al.* [31] found that the sensitivity and specificity of anti-C1q for detecting concurrent renal lupus activity was 59 and 82%, respectively, PPV and NPV were 48 and 88%, respectively, whereas the sensitivity and specificity of anti-C1q for detecting concurrent extrarenal activity were 45 and 82%, respectively, and PPV and NPV were 0.52 and 0.77%, respectively.

In this study, we found a higher level of anti-C1q in SLE patients and correlated with SLEDAI score, and hence we concluded that anti-C1q levels can be used as a marker for SLE activity but not renal activity.

Recommendations

(1) Inclusion of a larger sample size in the following studies
(2) Analysis of the relationship of anti-C1q levels with histopathological changes in active nephritis by performing renal biopsy for patients and investigation of the correlation between histopathological findings and anti-C1q levels
(3) Patient follow-up to prove the actual role of anti-C1q levels in SLE and LN activity and their relation with damage index.

Conclusion

This study concluded that Anti-C1q antibodies level can be used as a marker for SLE activity but not for lupus nephritis.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1 Rahman A, Isenberg DA. Systemic lupus erythematosus. N Engl J Med 2008; 358:929–939.

2 Liu Z, Davidson A. Taming lupus-a new understanding of pathogenesis is leading to clinical advances. Nat Med 2012; 18:871–882.

3 Beurskens FJ, van Schaarenburg RA, Trouw LA. C1q, antibodies and anti-C1q autoantibodies. Mol Immunol 2015; 68: 6–13

4 Tsirogianni A, Pipi E, Soufleros K. Relevance of anti-C1q autoantibodies

to lupus nephritis. Ann N Y Acad Sci 2009; 1173:243–251.

5 Petri M, Orbai AM, Alarcon GS, Gordon C, Merrill JT, Fortin PR, *et al*. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum 2012; 64:2677–2686.

6 Bombardier C, Gladman DD, Urowitz MB, Caron D, Chang CH. Derivation of the SLEDAI. A disease activity index for lupus patients. The Committee on prognosis Studies in SLE. Arthritis Rheum 1992; 35:630–640.

7 Garcia-Carrasco M, Mendoza-Pinto C, Escarcega RO, Jimenez-Hernandez M, Etchegaray Morales I, Munguia Realpozo P, *et al*. Osteoporosis in patients with systemic lupus erythematosus. Isr Med Assoc J 2009; 11:486–491.

8 Bultink IE. Osteoporosis and fractures in systemic lupus erythematosus. Arthritis Care Res (Hoboken) 2012; 64:2–8.

9 Barbulescu A, FA Vreju, Criveanu C, Rosu A, Ciurea P. Osteoporosis in systemic lupus erythematosus – correlations with disease activity and organ damage. Curr Health Sci J 2015; 41:109–114.

10 Potlukova E, Kralikova P. Complement component c1q and anti-c1q antibodies in theory and in clinical practice. Scand J Immunol 2008; 67:423–430.

11 Pang, Y, Yang, XW, Song, Y, Yu, F, Zhao, MH. Anti-C1q autoantibodies from active lupus nephritis patients could inhibit the clearance of apoptotic cells and complement classical pathway activation mediated by C1q in vitro. Immunobiology 2014; 219:980–989.

12 Hasan, SI, Mohd Ashari, NS, Mohd Daud, K, Che Husin, CM. High occurrence of in vitro apoptosis of lymphocytes induced by serum from systemic lupus erythematosus patients is associated with increased serum levels of anti-C1q autoantibodies. Int J Rheum Dis 2013; 16:430–436.

13 Fang QY, Yu F, Tan Y, Xu LX, Wu LH, Liu G, *et al.* Anti-C1q antibodies and IgG subclass distribution in sera from Chinese patients with lupus nephritis. Nephrol Dial Transplant 2009; 24:172–178.

14 Katsumata Y, Miyake K, Kawaguchi Y, Okamoto Y, Kawamoto M, Gono T, *et al*. Anti-C1q antibodies are associated with systemic lupus erythematosus global activity but not specifically with nephritis: a controlled study of 126 consecutive patients. Arthritis Rheum 2011; 63:2436–2444.

15 Zhang CQ, Ren L, Gao F, Mu FY, You YQ, Liu YH. Anti-C1q antibodies are associated with systemic lupus erythematosus disease activity and lupus nephritis in northeast of China. Clin Rheumatol 2011; 30:967–973.

16 Orbai AM, Truedsson L, Sturfelt G, Nived O, Fang H, Alarcon GS, *et al*. Anti-C1q antibodies in systemic lupus erythematosus. Lupus 2015; 24:42–49.

17 Oelzner P, Deliyska B, Funfstuck R, Hein G, Herrmann D, Stein G. Anti-C1q antibodies and antiendothelial cell antibodies in systemic lupus erythematosus – relationship with disease activity and renal involvement. Clin Rheumatol 2003; 22:271–278.

18 Bernstein KA, Kahl LE, Balow JE, Lefkowith JB. Serologic markers of lupus nephritis in patients: use of a tissue-based ELISA and evidence for immunopathogenic heterogeneity. Clin Exp Immunol 1994; 98:60–65.

19 Smykal-Jankowiak K, Niemir ZI, Polcyn-Adamczak M. Do circulating antibodies against C1q reflect the activity of lupus nephritis? Pol Arch Med Wewn 2011; 121:287–295.

20 Sinico RA, Radice A, Ikehata M, Giammarresi G, Corace C, Arrigo G, *et al*. Anti-C1q autoantibodies in lupus nephritis: prevalence and clinical significance. Ann N Y Acad Sci 2005; 1050:193–200.

21 Trendelenburg M, Lopez-Trascasa M, Potlukova E, Moll S, Regenass S, Fremeaux-Bacchi V, *et al*. High prevalence of anti-C1q antibodies in biopsy-proven active lupus nephritis. Nephrol Dial Transplant 2006; 21:3115–3121.

22 Meyer OC, Nicaise-Roland P, Cadoudal N, Grootenboer-Mignot S, Palazzo E, Hayem G, *et al.* Anti-C1q antibodies antedate patent active glomerulonephritis in patients with systemic lupus erythematosus. Arthritis Res Ther 2009; 11:R87.

23 Tan, Y, Zhou, W, Yu, F, Fang, Q, Yang, HZ, Zhao, MH. Detection of anti-C1q antibodies and anti-C1q globular head domain antibodies in sera from Chinese patients with lupus nephritis. Mol Immunol 2009; 46:2178–2182.

24 Pradhan V, Patwardhan M, Nadkarni A, Ghosh K. Fc gamma RIIA genotypes and its association with anti-C1q autoantibodies in lupus nephritis (LN) patients from Western India. Autoimmune Dis 2010; 2010:470695.

25 Akhter E, Burlingame RW, Seaman AL, Magder L, Petri M. Anti-C1q antibodies have higher correlation with flares of lupus nephritis than other serum markers. Lupus 2011; 20:1267–1274.

26 Moura CG, Mangueira CL, Cruz LA, Cruz CM. Negative anti-C1q antibody titers may influence therapeutic decisions and reduce the number of renal biopsies in systemic lupus erythematosus. Nephron Clin pract 2011; 118:c355–c360.

27 Gargiulomde, L, Gomez, G, Khoury, M, Collado, MV, Suarez, L, Alvarez, C, Sarano, J. Association between the presence of anti-C1q antibodies and active nephritis in patients with systemic lupus erythematosus. Medicina (B Aires) 2015; 75:23–28.

28 Moura CG, Lima I, Barbosa L, Athanazio D, Reis E, Reis M, *et al.* Anti-C1q antibodies: association with nephritis and disease activity in systemic lupus erythematosus. J Clin Lab Anal 2009; 23:19–23.

29 Thanei S, Vanhecke D, Trendelenburg M. Anti-C1q autoantibodies from systemic lupus erythematosus patients activate the complement system via both the classical and lectin pathways. Clin Immunol 2015; 160:180–187.

30 Mok CC, Ho LY, Leung HW, Wong LG. Performance of anti-C1q, antinucleosome, and anti-dsDNA antibodies for detecting concurrent disease activity of systemic lupus erythematosus. Transl Res 2010; 156:320–325.

31 Mok CC, Birmingham DJ, Ho LY, Hebert LA, Song H, Rovin BH. Vitamin D deficiency as marker for disease activity and damage in systemic lupus erythematosus: a comparison with anti-dsDNA and anti-C1q. Lupus 2012; 21:36–42.