THE RELATIONSHIP BETWEEN SERUM C1Q AND ANTI-C1Q ANTIBODIES IN PATIENTS WITH LUPUS NEPHRITIS

Smykal-Jankowiak Katarzyna, Niemir I. Zofia, Polcyn-Adamczak Magdalena

Department of Nephrology, Transplantology and Internal Medicine, University of Medical Sciences, Poznan, Poland

INTRODUCTION

Systemic lupus erythematosus (SLE) is a multi-organ disease with still unclear pathogenesis. The production of variety autoantibodies, defective clearance and accumulation of immune complexes, altered apoptosis, and lymphocyte B dysfunction seem to be the basic immunological disorders in patients with SLE [1]. The most important predisposing factor for the development of SLE is the congenital C1q deficiency [2]. However, a close relationship between the serum levels of C1q and the occurrence of anti-C1q Abs has been suggested, particularly in patients with lupus nephritis (LN) [3,4]. Anti-C1q Abs seem to be a non-invasive serological marker of renal involvement in course of SLE [4-6].

AIM

The aim of this study was to determine the serum concentrations of C1q and anti-C1q Abs in patients with LN and to compare these results with those obtained in healthy controls (C). We examined the relationship between C1q, anti-C1q Abs and activity of LN, SLE-related clinical, biochemical and immunological features.

MATERIAL AND METHODS

The study involved **63** patients with **LN** and **79** healthy controls (**C**).
The SLE activity was scored using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI-2K). Forty-one patients presented with active LN (**aLN**), whereas the remaining 22 patients were in inactive phase of the disease (**inLN**).
Serum levels of C1q and anti-C1q were determined by standardized enzyme-linked immunosorbent assays.

RESULTS

The median values of serum C1q were 279.6 (134.2 - 442.7) ng/ml in LN and 270.9 (151.9 - 570.2) ng/ml in C. Anti-C1q Abs were detected in 66.7% of patients with LN and in 8.9% of C ($p<0.0001$). The prevalence of anti-C1q Abs was significantly higher in aLN than inLN ***(Figure 1)***. It was also true for serum concentrations of anti-C1q Abs ***(Figure 2)***.
In LN, a significant negative correlation between the C1q and anti-C1q levels was observed ***(Figure 3)***. In addition, positive correlations between both anti-C1q and anti-dsDNA Abs and the SLEDAI-2K score were found ***(Figures 4 and 5)***. Apart from this, haematuria and the nephrotic syndrome occurred significantly more often in the anti-C1q positive LN ***(Table 2)***.
After all patients' arrangement into C1q quartiles, 27% of them were allocated to the first quartile, 20.6% to the second quartile, 38.1% to the third quartile and only 14.3% to the fourth quartile ($p<0.05$). The prevalence of anti-C1q Abs detection was the highest in patients allocated to the first quartile and the lowest in those from the fourth quartile (***Figure 6***). Interestingly, a decrease in GFR below 60 ml/min/1.73m2 in the last month was observed almost only in patients from the first and second quartile (***Figure 7***). Among systemic symptoms of SLE, the relationship between low serum concentration of C1q and skin lesions was observed ***(Figure 8).***

TABLE 1. Morphological, clinical and biochemical data of patients with LN.

Histological type	*Number of patients*	*SLEDAI-2K score (median) [interquartile range]*	*Age (years) [mean±SD]*	*Serum creatinine level (mg/dl) [mean±SD]*	*eGFR - MDRD (ml/min/1.73m2) [mean±SD]*	*Proteinuria (g/24h) [mean±SD]*
Class II	6	8 (4.5-10)	29±9	0.7±0.2	118.7±41.5	0.7±0.6
Class III	13	13 (10-16)	33±10	1.0±0.4	81.5±33.1	1.8±1.8
Class IV	29	18 (12-21)	34±11	1.5±1.3	64.9±35.8	3.2±3.1
Class V	3	20 (13-20)	33±10	1.1±0.5	70.7±31.8	2.7±2.2
Without biopsy	12	5.5 (4.8-10.5)	34±9	1.2±0.8	66.8±29.5	0.9±1.9

TABLE 2. Associations between SLE-related clinical and laboratory parameters and the prevalence of anti-C1q Abs in patients with LN.

	Anti-C1q Abs positive (n=42)	Anti-C1q Abs negative (n=21)	P value
systemic signs and symptoms, n (%)			
neurological disorders	8 (19.4%)	1 (4.8%)	0.25
vasculitis	1 (2.4%)	0	1.00
arthritis	1 (2.4%)	1 (4.8%)	1.00
skin lesions	7 (16.7%)	3 (14.3%)	1.00
mucosal ulcers	1 (2.4%)	0	1.00
serositis	3 (7.1%)	1 (4.8%)	1.00
fever	5 (11.9%)	1 (4.8%)	0.65
hematological disorders (decreased PLT and/or WBC and/or Hb)	8 (19.4%)	3 (14.3%)	0.74
renal abnormalities, n (%)			
urinary casts (heme-granular or RBC casts)	16 (38.1%)	3 (14.3%)	0.08
hematuria (>5 RBC/high power field)	**29 (69.0%)**	**6 (28.6%)**	**0.003**
proteinuria (>0.5 g/24h)	28 (66.7%)	13 (61.9%)	0.78
nephrotic syndrome	**15 (35.7%)**	**2 (9.5%)**	**0.04**
leukocyturia (>5 WBC/ high power field)	**22 (52.4%)**	**5 (23.8%)**	**0.04**
decrease in GFR below 60 ml/min/1.73m2 in the last month	6 (14.3%)	1 (4.8%)	0.41
immunological parameters, n (%)			
ANA	**41 (97.6%)**	**14 (66.7%)**	**0.001**
anti-dsDNA Abs	**35 (83.3%)**	**12 (57.1%)**	**0.03**
anti-nucleosome Abs	14 (33.3%)	3 (14.3%)	0.14
anti-Ro (SSA) Abs	13 (31.0%)	6 (28.6%)	1.00
anti-La (SSB) Abs	4 (9.5%)	3 (14.3%)	0.68
anti-Sm Abs	5 (11.9%)	1 (4.8%)	0.65
anti-RNP Abs	6 (14.3%)	1 (4.8%)	0.41
anti-ribosomal P Abs	3 (7.1%)	0	0.54
anti-histone Abs	12 (28.6%)	2 (9.5%)	0.11
anti-PCNA Abs	4 (9.5%)	0	0.29
anti-centromere Abs	1 (2.4%)	0	1.00
anti-AMA-M2 Abs	4 (9.5%)	0	0.29
anti-cardiolipin Abs	5 (11.9%)	2 (9.5%)	1.00
anti-β2 glikoprotein 1 Abs	5 (11.9%)	2 (9.5%)	1.00

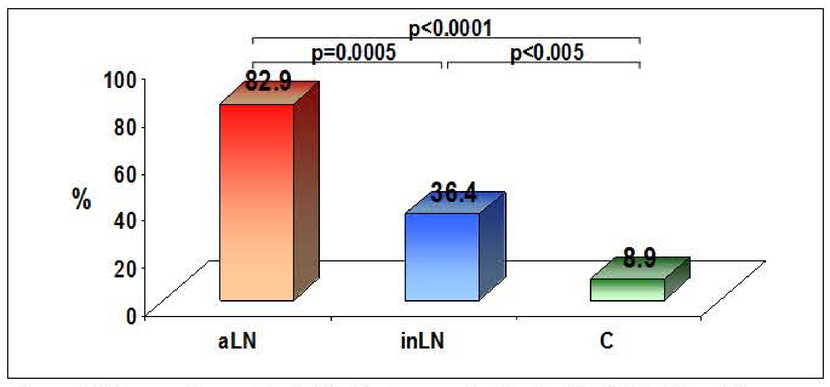

Figure 1. The prevalence of anti-C1q Abs in sera of patients with aLN, inLN and C group.

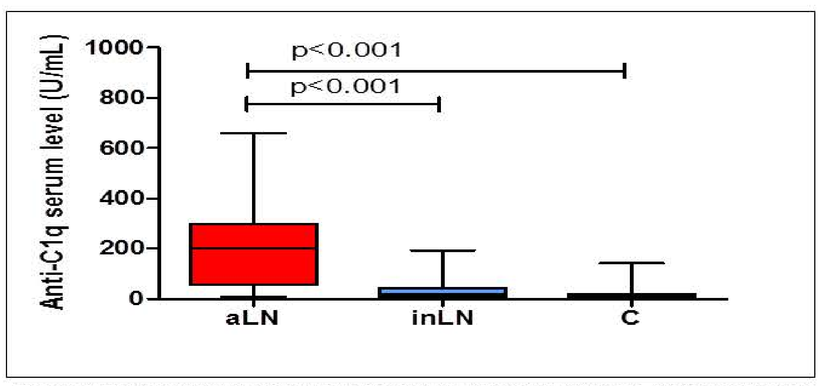

Figure 2. The mean levels of anti-C1q Abs in sera of patients with aLN, inLN and C group.

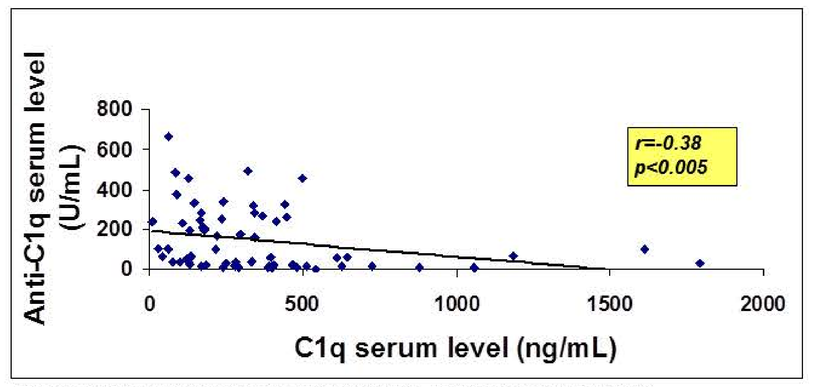

Figure 3. Correlation between concentrations of C1q and anti-C1q Abs in sera of patients with LN.

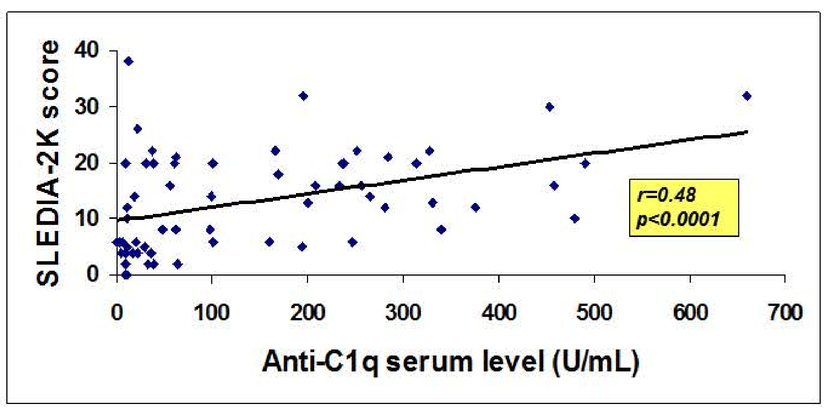

Figure 4. Correlation between serum concentration of anti-C1q Abs and SLEDAI-2K score in patients with LN.

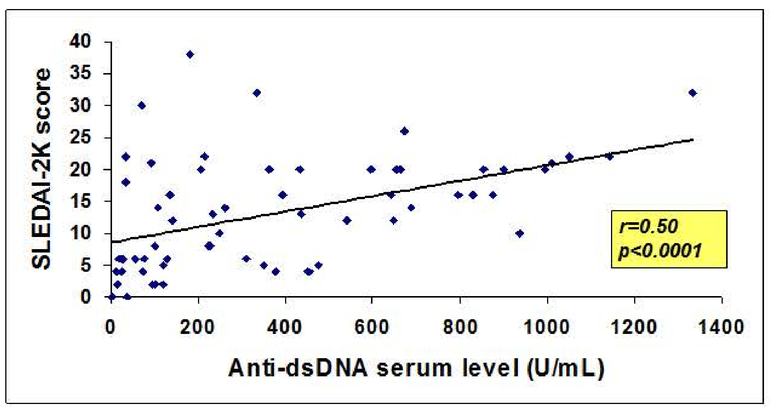

Figure 5. Correlation between serum concentration of anti-dsDNA Abs and SLEDAI-2K score in patients with LN.

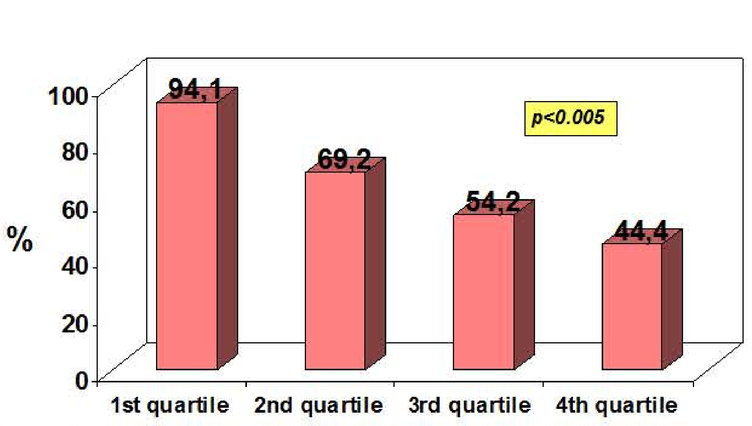

Figure 6. Anti-C1q Abs detection in patients arranged according to the C1q quartiles.

CONCLUSIONS

1. The occurrence of the anti-C1q Abs in sera of patients with LN indicates active phase of disease.
2. The low concentration of C1q in sera of patients with LN is associated with the worsening of renal function and occurrence of skin lesions.
3. Our results confirmed the suggested link between the C1q usage and anti-C1q Abs formation in LN.

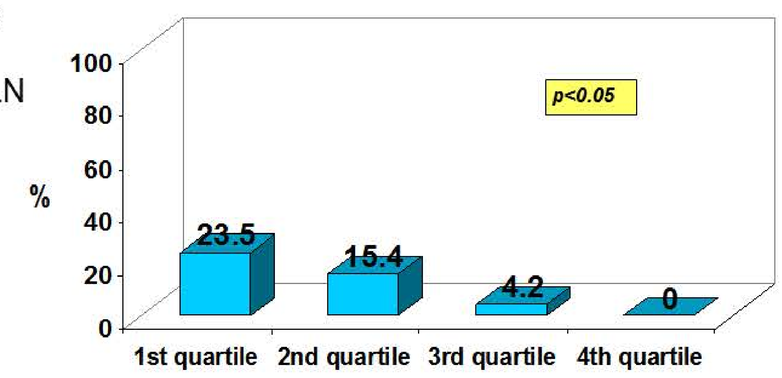

Figure 7. Decrease in GFR below 60 ml/min/1,73m2 in the last month in patients arranged according to the C1q quartiles.

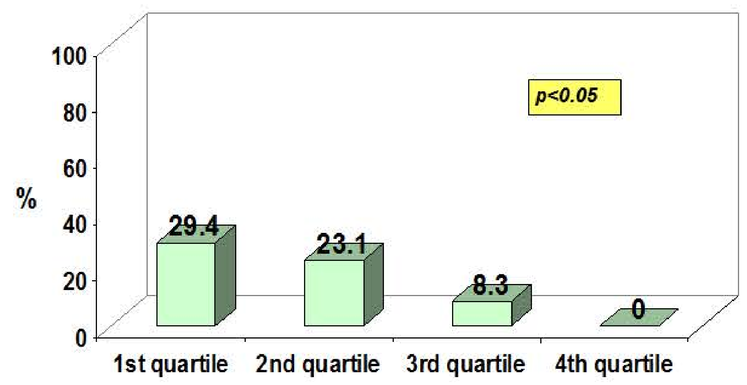

Figure 8. The prevalence of skin lesions in patients arranged according to the C1q quartiles.

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51ERA-EDTA
326-MP
K) Clinical Nephrology, primary and secondary glomerulonephritis.
Katarzyna Smykal-Jankowiak
DOI: 10.3252/pso.eu.51era.2014
Poster presented at: 51 ERA-EDTA CONGRESS AMSTERDAM 2014
PosterSessionOnline.com