THE IMMUNOLOGICAL ACTIVITY OF LUPUS NEPHRITIS ASSOCIATES WITH THE CONCURRENT DEFICIENCY OF MANNOSE-BINDING LECTIN AND C1Q

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INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease of unclear etiology that involves almost all organs [1]. Mannan-binding lectin (MBL) and C1q are important molecules in the immunity [2]. Serum MBL levels correlate with the presence of low (O/O and XA/O), intermediate (XA/XA and YA/O) or high producing (YA/YA) *MBL2* genotypes [3]. A more severe SLE course in patients deficient in MBL and C1q is implied [4, 5].

AIM

The aim of our study was to compare the immunological activity of lupus nephritis (LN) in patients with different *MBL2* genotypes in relation to C1q serum levels.

MATERIAL AND METHODS

The study involved **57** patients with LN and **65** healthy controls (C). *MBL2* genotyping on blood DNA was performed by the PCR-RFLP analysis. Serum MBL, C1q and antibodies to C1q (anti-C1q) and double-stranded DNA (anti-dsDNA) were determined by the enzyme-linked immunosorbent assays. The activity of SLE was measured using the SLE Disease Activity Index (SLEDAI-2K). Thirty-nine patients constituted the group with active LN (aLN), whereas 18 patients were in inactive phase of the disease (inLN). Demographic and clinical data of the patients are presented in **Table 1**.

Table 1. Demographic and clinical data of patients arranged according to the *MBL2* genotypes and clinical activity of LN.

	LN – YA/YA			LN – YA/XA			LN – YA/O + XA/XA			LN – O/O + XA/O
	aLN	inLN	p	aLN	inLN	p	aLN	inLN	p	aLN
No. of cases	15	7		9	8		9	3		6
Sex F/M	14/1	7/0	Ns	8/1	8/0	Ns	8/1	3/0	Ns	6/0
Age (years) Mean ± SD	32 ± 9	29 ± 10	Ns	35 ± 12	35 ± 8.5	Ns	32.4 ± 8.4	33.3 ± 9.0	Ns	39.3 ± 14.3
Disease duration (months) Mean Median (range)	36.3 12 (6-30)	91.9 60 (24-132)	0.0172	53.4 36 (17.5-72)	72.5 77 (45-96)	Ns	35.7 12 (6-72)	64 60 (24-108)	Ns	49.3 30 (4.5-87)
SLEDAI-2K score Mean ± SD	20.2 ± 7.4	3.8 ± 2.2	<0.0001	18 ± 6	4.3 ± 1.6	<0.0001	15.1 ± 4.7	4 ± 2	0.0031	19.8 ± 7.5
Proteinuria (g/day) Mean Median (range)	2.5 2.0 (1.4-3.6)	0.4 0.3 (0.13-0.32)	0.0006	3.4 1.9 (0.9-6.4)	0.9 0.6 (0.1-1.31)	0.0274	2.1 1.5 (0.1-3.9)	0.2 0.2 (0.1-0.4)	Ns	5.5 5.0 (0.3-10.2)
Nephrotic No. (%)	5 (33.3)	0 (0)	Ns	4 (44.4)	0 (0)	Ns	3 (33.3)	0 (0)	Ns	4 (66.7)
Erythrocyturia (No. per HPF) Mean Median (range)	22 10 (6-27)	2 2 (1-2)	0.001	25 9 (4-45)	1 1 (1-2)	0.0019	11 10 (6-15)	2 1 (1-3)	0.0159	14 10 (2-26)
eGFR (ml/min/1.73m^2) Mean ± SD	72.5 ± 40.5	91.7 ± 37.5	Ns	75.4 ± 34.3	79.6 ± 30	Ns	87.56 ± 25	106.7 ± 6.4	Ns	56.2 ± 44.9
Hypertension No. (%)	7 (46.7)	5 (71.4)	Ns	6 (66.7)	3 (37,5)	Ns	4 (44.4)	2 (66.7)	Ns	5 (83.3)

RESULTS

In the LN group, the YA/YA, YA/XA, YA/O or XA/XA, and O/O or O/XA genotypes were carried by 38.6%, 29.8%, 21.1%, and 10.5% of patients. The matching values in the C group were 33.8%, 33.8%, 23.2%, and 9.2%. In both groups, the respective genotypes had a significant effect on serum levels of MBL (**Fig. 1A and 1B**). The highest levels of anti-dsDNA and anti-C1q antibodies were observed in aLN patients presenting O/O or O/XA genotypes that concurrently had the lowest concentrations of C1q and MBL in their sera (**Table 2**).

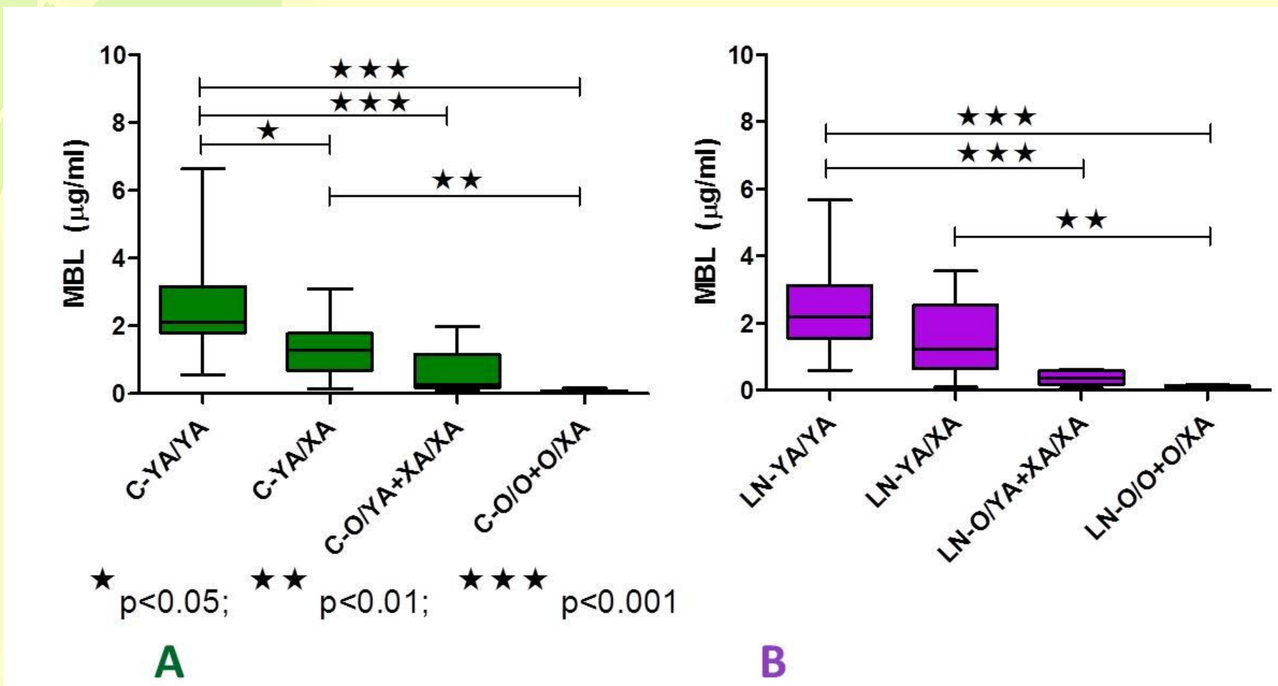

Fig. 1. **The comparison of serum MBL concentrations in controls (A) and LN patients (B) arranged according to *MBL2* genotypes.**

Table 2. Levels of MBL, C1q, anti-dsDNA, and anti-C1q antibodies in LN patients with different *MBL2* genotypes.

	LN – A/A			LN – A/XA			LN – A/O + XA/XA			LN – O/O + XA/O
	aLN	inLN	p	aLN	inLN	p	aLN	inLN	p	aLN
MBL (µg/ml) Mean ± SD	3.01 ± 1.38	1.52 ± 0.68	0.0142	1.38 ± 1.12	1.66 ± 1.12	Ns	0.35 ± 0.22	0.39 ± 0.25	Ns	0.07 ± 0.06
C1q (ng/ml) Mean Median (range)	480 343 (178-645)	456 342 (99-402)	Ns	269 177 (138-419)	515 497 (194-795)	Ns	211 206 (166-273)	276 240 (182-404)	Ns	150 74 (57-280)
C3 (g/l) Mean ± SD	0.55 ± 0.23	1.09 ± 0.38	0.0017	0.58 ± 0.27	1.11 ± 0.29	0.0016	0.77 ± 0.41	0.97 ± 0.10	Ns	0.52 ± 0.19
C4 (g/l) Mean ± SD	0.09 ± 0.06	0.23 ± 0.13	0.024	0.10 ± 0.04	0.19 ± 0.09	0.0160	0.11 ± 0.08	0.19 ± 0.03	Ns	0.11 ± 0.10
Anti-dsDNA (IU/ml) Mean Median (range)	517 642 (215-794)	107 54 (24-120)	0.0015	376 392 (89-488)	141 75 (25-288)	0.0745	452 363 (182-739)	200 129 (17-455)	Ns	848 964 (538-1120)
Anti-C1q (IU/ml) Mean ± SD	153 ± 140	58 ± 55	Ns	210 ± 149	33 ± 23	0.0016	198 ± 178	17 ± 7	0.0364	298 ± 230

Of interest, in active LN patients with the YA/O or XA/XA, and O/O or O/XA *MBL2* genotypes median serum C1q concentration was lower compared to those carrying the high alleles (**Fig. 2**). In the C group, an opposite trend was observed and subjects presenting the above genotypes had a significantly higher median level of C1q than the patients with corresponding genotypes did (**Fig. 3**).

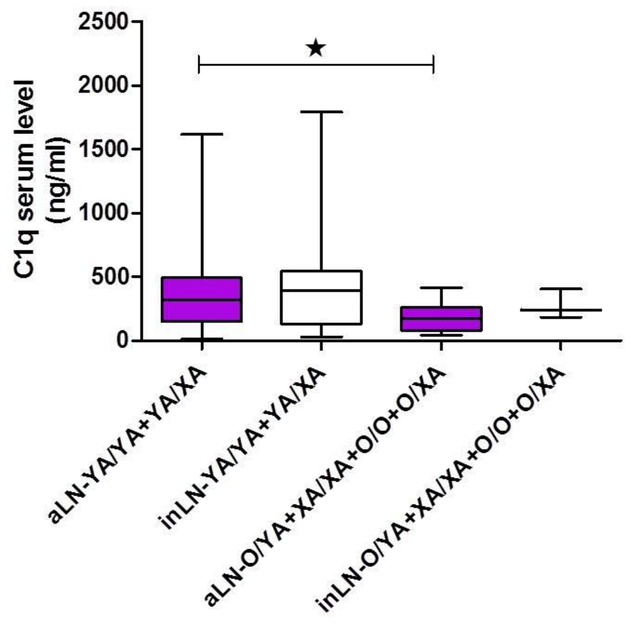

Fig. 2. **The comparison of serum C1q concentrations in LN patients arranged according to *MBL2* genotypes and LN activity.**

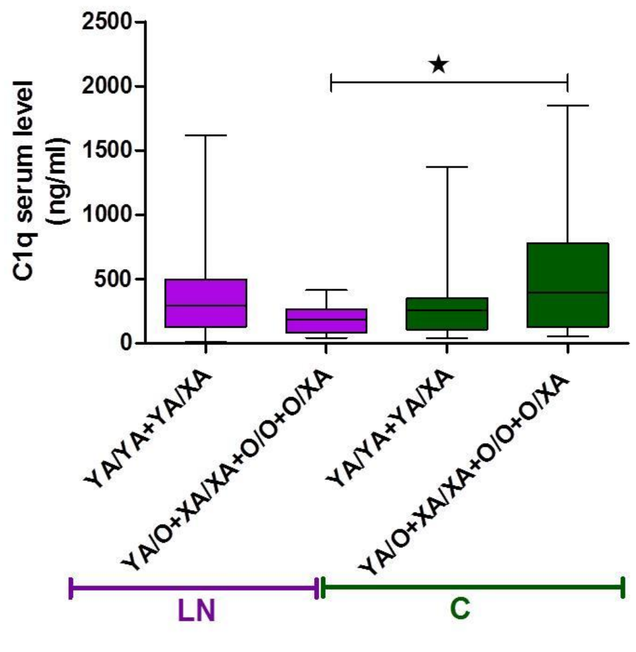

Fig. 3. **The comparison of serum C1q concentrations in LN patients and controls with MBL-sufficient and MBL-deficient genotypes.**

CONCLUSIONS

- Our results show that in LN MBL deficiency associates with that of C1q and they both contribute to the immunological activity of the disease.
- Further studies are required to confirm this idea.

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