THE RELATIONSHIP BETWEEN THE MANNAN-BINDING PROTEIN GENOTYPES AND CLINICAL MANIFESTATION OF LUPUS NEPHRITIS

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INTRODUCTION AND AIMS

Mannan-binding lectin (MBL) has been suggested to have a dual mode of action in the development of systemic lupus erythematosus (SLE). Increased MBL leads to enhanced complement activation and tissue damage, while its deficiency results in aggravation of autoimmunity (1-3). Since serum MBL levels correlate with the presence of low (*O/O and XA/O*), intermediate (*XA/XA and YA/XA*) or high producing (*YA/YA*) *MBL2* genotypes (4), we looked for the incidence of these genotypes in patients with lupus nephritis (LN) and tried to relate their occurrence with the clinical features of this disease.

MATERIAL AND METHODS

The study involved 99 patients with LN and 94 healthy controls (C). DNA was extracted from the whole blood and *MBL2* genotyping was performed by the polymerase-chain reaction followed by restriction fragment length polymorphism analysis. Serum level of MBL was determined by an enzyme-linked immunosorbent assay. The activity of SLE was assessed using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI-2K).

RESULTS

The *YA/YA* genotype was carried by 33.0% of patients with LN and 45.4% of C. The *YA/XA* heterozygosity was stated in 34.0% of patients with LN and in 30.3% of C. The *YA/O* or *XA/XA* genotypes were found in 23.4% of patients with LN and in 17.2% of C. The remaining 9.6% of patients with LN and 7.1% of C carried the *O/O* or *XA/O* genotypes. In LN and C, serum levels of MBL differed significantly between the high and low producing *MBL2* genotypes ($p<0.001$), with no differences between the subgroups of these cohorts carrying the corresponding genotypes
However, when the activity of SLE was taken into account, it turned out that in patients with the *YA/YA* genotype, the median MBL level was significantly lower in inactive LN (inLN) compared to the active phase of the disease (aLN) (**Table 1**).

Table 1. *Demographic, immunological and clinical data of patients with LN.*

	LN – YA/YA			LN – YA/XA			LN – YA/0 + XA/XA			LN – 0/0 +XA/0		
	aLN	**inLN**	***p***	**aLN**	**inLN**	***p***	**aLN**	**inLN**	***p***	**aLN**	**inLN**	***p***
No. of cases	26	19		17	13		11	6		6	1	
Sex (F/M)	21/5	17/2	Ns	14/3	13/0	Ns	10/1	6/0	Ns	6/0	1/0	-
Age (years) **Median** (range)	26 (19-50)	31.5 (18-56)	Ns	33 (20-73)	34 (25-55)	Ns	33 (22-62)	32.5 (24-42)	Ns	35.5 26-58	23	-
Disease duration (months) **Median** (range)	14 (1-264)	84 (24-372)	<0.0001	48 (1-192)	34 (25-55)	Ns	60 (3-525)	63.5 (12-120)	Ns	29.5 (3-168)	5	-
MBL (µg/ml) **Median** (range)	2.62 (0.51-5.66)	1.49 (0.37-3.80)	**0.0042**	1.08 (0.09-4.76)	1.43 (0.03-3.56)	Ns	0.27 (0.17-0.63)	0.34 (0.06-0.60)	Ns	0.06 (0.02-0.16)	0.01	-
C3 (g/l) **Median** (range)	0.56 (0.29-1.17)	0.98 (0.69-1.74)	<0.0001	0.79 (0.30-1.39)	1.03 (0.73-1.59)	0.0013	0.67 (0.33-1.38)	1.24 (0.89-1.51)	0.0024	0.56 (0.29-0.80)	0.93	-
C4 (g/l) **Median** (range)	0.07 (0.03-0.39)	0.14 (0.06-0.43)	0.0019	0.13 (0.05-0.32)	0.20 (0.09-0.36)	0.0022	0.07 (0.04-0.29)	0.22 (0.16-0.40)	0.0057	0.06 (0.04-0.34)	0.11	-
A-dsDNA (IU/ml) **Median** (range)	235.6 (7-1010)	50 (9-380)	<0.0001	250.3 (33-1142)	50 (20-800)	0.0089	363.0 (40-853)	92.8 (17-455)	0.0181	964 (391-1331)	40	-
SLEDAI-2K score **Median** (range)	19 (10-38)	5 (0-8)	<0.0001	14 (10-30)	5 (1-8)	<0.0001	16 (10-20)	7 (2-8)	<0.0001	20 (10-32)	5	-
eGFR (ml/min/1.73m^2) **Median** (range)	69.5 (30.8-180)	91 (23-149)	Ns	74 (8-136)	72 (16-155)	Ns	78.0 (15-91)	110.5 (87-154)	0.0032	31 (19-131)	93	-

Of interest, in patients with aLN carrying the *O/O+XA/O* genotypes, a significantly higher level of anti-dsDNA antibodies was observed, compared to those with aLN presenting the *YA/YA* and *YA/XA* genotypes (***Fig. 1***). In addition, a significant negative correlation between the levels of MBL and anti-dsDNA antibodies was noted in aLN with the *YA/O+XA/XA* and *O/O+XA/O MBL2* genotypes (***Fig. 2***). Irrespective of *MBL2* genotypes, a positive correlation between the level of MBL and glomerular filtration rate was obtained in inLN (***Fig. 3***).

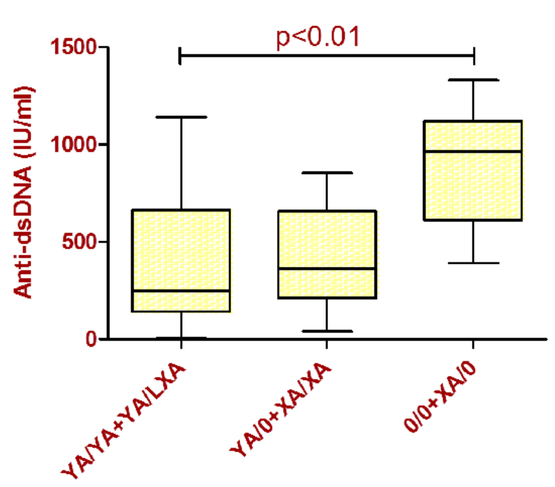

Fig. 1. The comparison of anti-dsDNA Abs in LN patients with MBL-sufficient and MBL-insufficient genotypes.

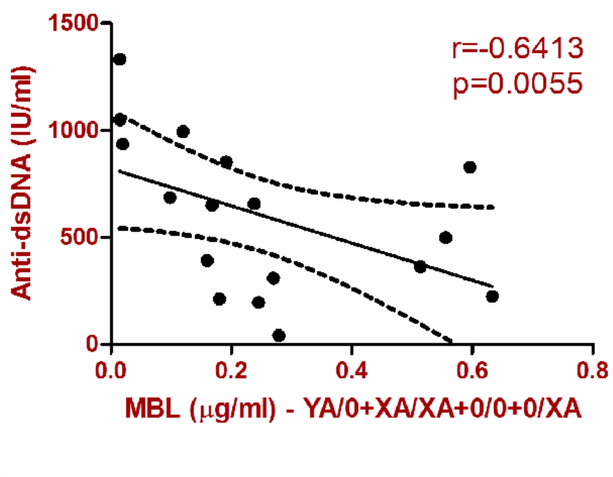

Fig. 2. Correlation between serum levels of anti-dsDNA Abs and MBL in LN patients with MBL-insufficient genotypes.

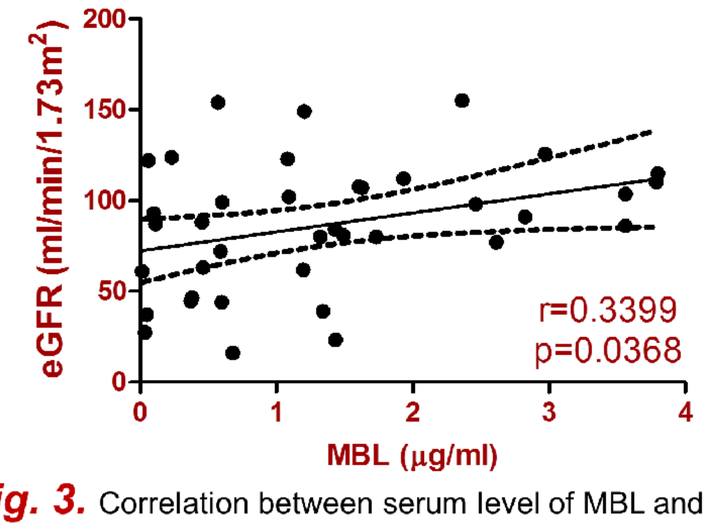

Fig. 3. Correlation between serum level of MBL and eGFR in LN patients with inactive phase of the disease.

CONCLUSIONS

The results of our study seem to point to MBL as to a biomarker protecting from the development of LN. Further studies are required to confirm this suggestion.

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