CLINICAL CHARACTERISTICS AND PROGNOSIS OF PATIENTS WITH PRIMARY MEMBRANOUS NEPHROPATHY REGARDING PRESENCE OF PLA2R ANTIBODIES – A CROATIAN MULTICENTER STUDY

Mario Laganović [1], Ivica Horvatić[2], Ivan Bubić[3], Mario Ilić[4], Bojana Maksimović[5], Ana Kozmar[6], Ema Ivandić[1], Matija Crnogorac[2], Tajana Željković Vrkić[1], Marijana Živko[1], Margareta Fištrek[1], Željka Jureković[5], Danica Galešić Ljubanović[7], Marijana Ćorić[8], Stela Bulimbašić[8], Krešimir Galešić[2], Mladen Knotek[5], Bojan Jelaković[1]

[1] Department of Nephrology, Hypertension, Dialysis and Transplantation, University Hospital Center Zagreb, School of Medicine University of Zagreb, Croatia,
[2] Department of Nephrology and Dialysis, Clinical Hospital Dubrava, School of Medicine University of Zagreb, Croatia
[3]Department of Nephrology and Dialysis, University Hospital Center Rijeka, School of Medicine University of Rijeka, Croatia
[4]Department of Nephrology and Dialysis, General Hospital Dubrovnik, Croatia
[5] Department of Nephrology, Clinical Hospital Merkur, School of Medicine University of Zagreb, Croatia
[6]Department of laboratory diagnostics, University Hospital Center Zagreb, Croatia
[7]Department for Pathology, Clinical Hospital Dubrava, School of Medicine University of Zagreb, Croatia
[8]Clinical Department of Pathology and Cytology, University Hospital Centre Zagreb, School of Medicine University of Zagreb, Croatia

Introduction

Idiopathic membranous nephropathy (iMN) is one of the most common causes of nephrotic syndrome in adult population. As natural course of iMN varies it is important to determine clinical and laboratory parameters reliable for prediction of clinical outcome and decision on immunosuppressive treatment. Antibodies against M-type phospolipase A2 receptor (anti PLA2R) are considered highly specific for iMN in which autoantibodies can be found in about 70% of patients.

Objective: In this first Croatian multicenter retrospective study we evaluate the clinical course and prognosis of patients with iMN regarding anti PLA2R status.

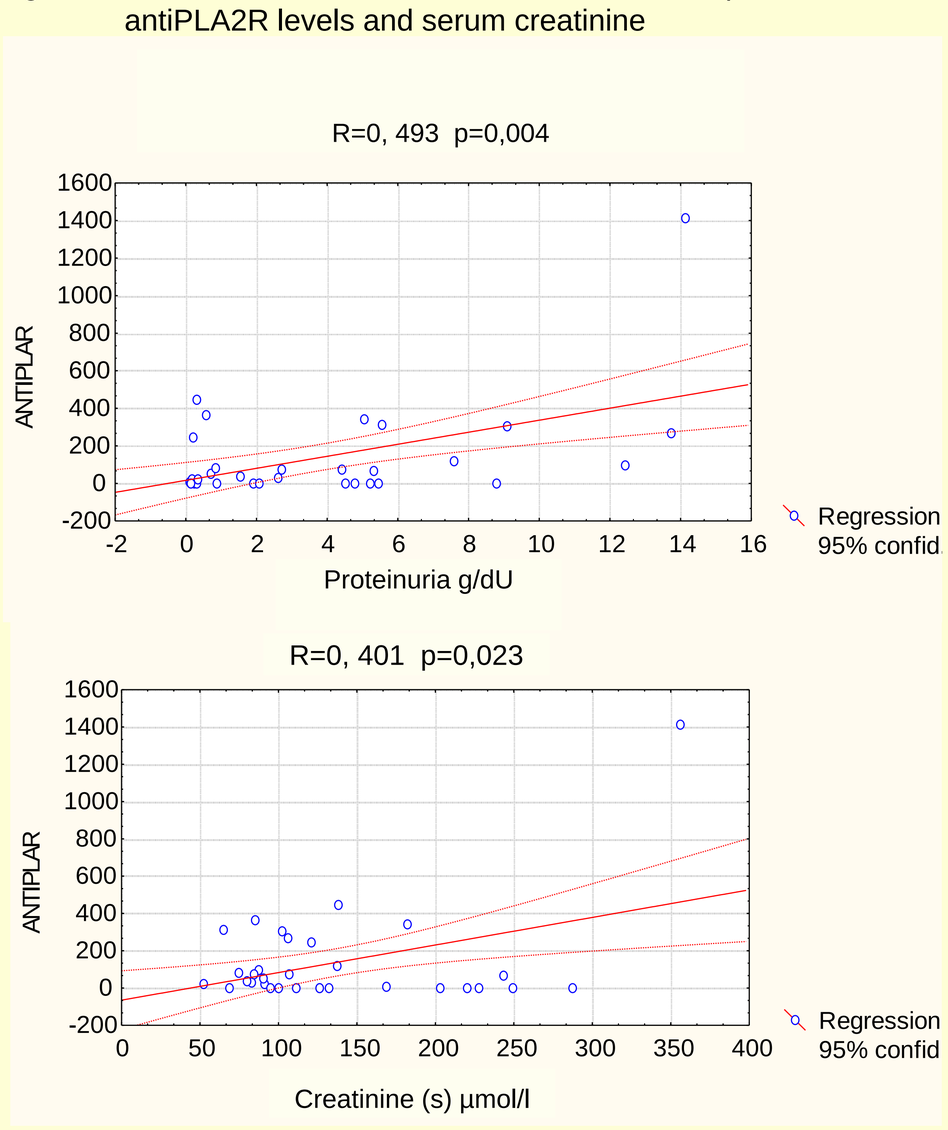
Subjects and methods

We included 32 consecutive patients (21 M, 11 F), median age 55 (20-81) years with biopsy proven iMN and follow-up of at least 6 months. Anthropometric characteristics, blood pressure (BP), hemoglobin (Hb), serum creatinine (sCr), eGFR, 24 proteinuria , serum albumine (sAlb) and atiPLA2R levels (ELISA) were determined in all patients at the time of renal biopsy and during follow-up. All patients were treated with combinations of corticosteroids, cyclophosphamide, cyclosporine and mycophenolate mophetil according to KDIGO guidelines. We defined complete remission as persistent proteinuria < 0.3 g/du and normal serum creatinine (cCr) and partial remission as persistent proteinuria < 3.5 g/du or decrease > 50% from baseline with stable sCr.

Table 1. Baseline patients characteristics and at the end of follow up

	TIME OF BIOPSY			END OF FOLLOW-UP		
	Median	Min.	Maks	Median	Min.	Maks
RR systolic (mmHg)	142	110	190	130	50	180
RR diastolic (mmHg)	90	82	120	80	70	105
Creatinine (µmol/l)	98	55	318	109	52	356
eGFR (ml/min(1,73m^2)	76	17	129	61	14	127
Proteinuria (g/dU)	6,73	1,72	20,7	2,33	0,1	14,14
Albumin (s) (g/l)	28,5	17,9	41	38,15	22	45

Figure 1. Correlations between antiPLA2R levels and proteinuria and antiPLA2R levels and serum creatinine



Results

Baseline patients characteristics are shown on table 1. 19 patients had positive antiPLA2R (> 20 RU/ml) (59,3%), median 97 (21-1418) RU/ml. There were no significant differences in basal values of BP, Hb, sCr, eGFR, proteinuria, sAlb or time to remission between antiPLA2R positive and negative group as well as according to gender. Median follow-up was 18 (range 6-84) months. When we analyse patients regarding lower (< 200 RU/ml) and higher levels (>200 RU/ml) of antiPLAR significant difeference in remision rate was observed (90 vs 50%, $\chi 2$ 4.0, p=0.045) (table 2). Highest antiPLA2R values were found in group without remission (88 vs 265 RU/ml p=0.093). Significant positive correlations were found between antiPLA2R levels and sCr and proteinuria (Figure1). Multiple regression analysis indicate basal sCr and antiPLA2R as key determinants of renal function at the end of follow-up and antiPLA2R levels as key determinant of proteinuria (table 3)

Table 2. Patients characteristics regarding antiPLA2R level

	antiPLA2R <200 RU/ml N=11	antiPLA2R >200 RU/ml N=8	**P**
Creatinine (s) µmol/l	96,7 (33,5)	103,1 (39,2)	0,715
eGFR (ml/min/1,73 m^2)	77,1 (25,7)	78,1 (30,5)	0,945
Proteinuria (g/dU)	8,41 (4,31)	8,72 (4,21)	0,881
RR systolic (mmHg)	140 (12,7)	147 (19,7)	0,348
RR diastolic (mmHg)	84 (11,1)	95 (9,90)	0,041
Albumin (s) (g/l)	28,4 (7,1)	24,6 (5,4)	0,311
Remission (N/%)	10/90	4/50	**0,045**
Time to remission (months)	7,4 (6,2)	7,5 (6,9)	0,937
Follow-UP			
Creatinine (s) µmol/l	102,6 (51,0)	144,3 (92,4)	0,223
eGFR (ml/min/1,73 m2)	73,1 826,9)	57,5 (27,5)	0,233
Proteinuria (g/dU)	3,51 (3,76)	6,07 (5,76)	0,255
RR systolic (mmHg)	135 (13,8)	148 (25,0)	0,153
RR diastolic (mmHg)	81 (9,7)	88 (13,3)	0,201

All values are mean (± SD) Continuous variables were compared using Student-t test or Mann-Whitney U test

Table 3. Multiple regression analysis of influence of different variables on serum creatinine and proteinuria at the end of follow-up

	ß	SE	p
RR systolic	-0,219	0,131	0,105
antiPLAR	0,527	0,124	**<0.001**
Creatinine	0,682	0,133	**<0.001**
Proteinuria	0,110	0,126	0,391

	ß	SE	p
RR systolic	-0,207	0,169	0,232
antiPLAR	0,544	0,161	**0,002**
Creatinine	0,097	0,173	0,580
Proteinuria	0,104	0,163	0,5299

Conclusion

Higher levels of antiPLA2R were associated with worse renal function and higher proteinuria in patients with iMN. Assesment of antiPLA2R could be reliable tool for guidance of theraputic plan.

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Topic: 37 – Glomerulonephritis II **ABSTRACT CODE MP201**

54 ERA 201--MP
Glomerulonephritis II
Mario Laganovic
DOI: 10.3252/pso.eu.54ERA.2017
ePosters supported by F. Hoffmann- La Roche Ltd.