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Circulating anti-phospholipase A2 receptor antibodies as a diagnostic and prognostic marker in Greek patients with idiopathic membranous nephropathy – a retrospective cohort study

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Introduction. Circulating autoantibodies against phospholipase A2 receptor (anti-PLA2R) are recognized as key elements in the pathogenesis of idiopathic membranous nephropathy. In current clinical practice, they are increasingly gaining attention as novel tools for diagnosis and disease monitoring. We investigated the diagnostic and prognostic utility of anti-PLA2R antibody measurements in Greek patients with biopsy-proven membranous nephropathy.

Methods. Anti-PLA2R levels were measured in serum samples from 33 patients at diagnosis using ELISA and were associated with treatment outcome. Moreover, serial anti-PLA2R measurements were performed in 15 patients under different clinical conditions and level alterations were correlated with disease activity.

Results. Positive anti-PLA2R antibodies at diagnosis were found in 16 of 33 patients (48.5%). Anti-PLA2R levels were independently associated with the achievement of complete remission of nephrotic syndrome after immunosuppressive treatment compared to partial remission ($p = 0.02$, $R^2 = 0.265$, 95%CI -0.019 to -0.0003). Higher detectable antibody levels at diagnosis were correlated with higher proteinuria levels ($r = 0.813$, $p = 0.0001$, 95%CI 0.532 to 0.933) and lower eGFR at the end of follow-up ($r = -0.634$, $p = 0.0083$, 95%CI -0.86 to -0.202). Serial antibody measurements during follow-up showed that anti-PLA2R titers were significantly reduced at the end of treatment after complete remission was achieved, remained low under sustained clinical remission, and increased during relapse.

Conclusions. Our findings confirm the usefulness of anti-PLA2R measurements in the diagnosis of idiopathic membranous nephropathy. Low levels of anti-PLA2R antibodies at diagnosis are predictive of complete remission of nephrotic syndrome following immunosuppressive treatment. Serial anti-PLA2R measurements correlate well with clinical status throughout the follow-up period and could be used routinely for monitoring of disease activity and treatment planning.

Key words: autoantibodies, chronic kidney failure, glomerulonephritis, phospholipases A2, proteinuria.

INTRODUCTION

Membranous nephropathy is a leading cause of nephrotic syndrome in adults and one of the most common causes of end-stage renal disease (ESRD) worldwide. Its etiology is mostly idiopathic even though 20-30% may be secondary to malignancy, chronic infections, autoimmune diseases or drugs. In current clinical practice, definite diagnosis can be established only by renal biopsy whereas differentiation between idiopathic and secondary forms is sometimes challenging. The natural course of the disease is longstanding and heterogeneous, with approximately one third of patients exhibiting various levels of persistent proteinuria without disease progression, one third experiencing progressive deterioration of renal function and finally ESRD, and the remaining showing spontaneous remission sustained for many years [1].

The identification of the M-type phosphorlipase A2 receptor (PLA2R) as a key target antigen in idiopathic membranous nephropathy (IMN) almost one decade ago was a landmark discovery which led to a better understanding of the disease pathophysiology [2]. Circulating anti-PLA2R autoantibodies are detected in the majority of IMN patients and correlate with the severity of the disease at presentation, while they are absent in secondary forms of membranous nephropathy [1]. They are strongly associated with concomitant

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PLA2R glomerular deposits in kidney biopsy and the combination of both findings largely increases the sensitivity of diagnosis of IMN [3]. Furthermore, it is considered that anti-PLA2R levels correlate well with long-term disease activity including clinical remission, spontaneous or treatment-induced, and relapse. It has been shown that anti-PLA2R titer alterations precede the correspondent clinical alterations by several months [4, 5]. Therefore, serial measurements of antibody titers could predict outcome or response to treatment [6, 7]. In current clinical practice, anti-PLA2R measurements are gradually being implemented as a guide to diagnosis and treatment planning and it has been proposed that in the near future, they could be able to replace kidney biopsy [8]. Despite the undisputed acknowledgement of their involvement in the pathogenesis of IMN, the exact role of anti-PLA2R as well as of other circulating antibodies [9] in various stages of the disease remains under investigation. At the same time, their expression in different populations is being extensively studied.

This is the first study aiming to examine the presence of anti-PLA2R autoantibodies in Greek patients with newly diagnosed IMN and to evaluate their association with disease clinical activity.

MATERIALS AND METHODS

We retrospectively studied patients with biopsy-proven IMN who were diagnosed, treated and followed-up in two tertiary hospitals in Greece. All patients enrolled in the study had available serum samples routinely collected at diagnosis and/or during their follow-up visits. Patients aged under 18 years and with advanced chronic kidney disease (estimated glomerular filtration rate, eGFR < 30 mL/min/1.73 m^2) were excluded from the study. The study protocol was approved by the local Ethics Committees and a written informed consent was obtained from all patients prior to sample collection.

At diagnosis, exhaustive work-up for exclusion of secondary causes of membranous nephropathy was performed in all patients including hematologic and imaging tests for autoimmune and infectious diseases, malignancies or any toxicity. All patients were treated according to international guidelines [10]. More specifically, they received supportive treatment including renin-angiotensin system blockade for at least 6 months and they were started on immunosuppressive treatment after not showing a spontaneous remission of nephrotic syndrome. The initial immunosuppressive regimen consisted of corticosteroids plus cyclosporine for approximately 6 months followed by gradual dose reduction. The median follow-up time was 48 months (range, 12-208 months). All patients were followed-up every 2 months during treatment and every 3-6 months or upon any change in clinical status onwards. Clinical and laboratory data were recorded in each visit including 24-hour proteinuria, serum creatinine, eGFR calculated using the CKD-EPI formula, and serum albumin.

The achievement of complete or partial clinical remission as well as the appearance of relapse episodes was recorded. Complete clinical remission was defined as reduction of proteinuria below 0.3 g/day in a 24-hour urine collection, partial clinical remission as reduction of proteinuria to a level between 0.3-3.5 g/day and less than 50% from baseline level and no remission as persistent proteinuria above 3.5 g/day. Relapse was defined as increase of proteinuria to more than 3.5 g/day after a complete or partial clinical remission had been achieved. Relapse episodes were treated with reinstitution of the initial immunosuppressive therapy [10].

A total of 59 serum samples was retrieved from our patients, which had been appropriately stored at -80°C until assay after separation from clotted blood by centrifugation for 15 minutes at 1000 x g in room temperature. Circulating anti-PLA2R levels were measured in all serum samples using a commercial ELISA test (EuroImmune AG). According to the manufacturer's instructions, a positive cut-off value was considered for levels > 20 RU/mL and a negative for < 14 RU/mL, whereas levels between 14-20 RU/mL were considered as borderline. In our patient cohort, antibody values < 20 RU/mL were reported as negative.

In the first part of the study, we measured anti-PLA2R levels at diagnosis from 33 patients. All serum samples were obtained at the time of kidney biopsy and prior to initiation of immunosuppressive treatment. We examined the association of baseline antibody levels with demographic parameters, treatment outcome, relapses of nephrotic syndrome and long-term clinical outcome.

In the second part of the study, we investigated alterations of antibody levels between two distinct time points aiming to further address

the potential association of anti-PLA2R with disease clinical activity. We studied three groups of patients under different clinical conditions. The first group consisted of 4 patients with one serum sample obtained at disease presentation and another one at complete remission of nephrotic syndrome after receiving immunosuppressive treatment. Additionally, 11 patients were included with two available anti-PLA2R measurements only during follow-up. The second group comprised 5 patients with two serum samples obtained under sustained clinical remission. The third group consisted of 6 patients with samples available both at remission and during a recorded relapse of nephrotic syndrome. Each set of samples was obtained with a time interval of at least 12 months in order to ensure that any underlying immunological process would have clinically revealed itself within that time. Alterations in antibody positivity as well as titer between the two time points were compared and correlated with corresponding alterations in proteinuria levels.

Statistical analysis

Data are presented as mean ± standard deviation for normally distributed variables and as median (range) for non-normally distributed variables. Continuous variables were compared with Mann-Whitney or Student's t-test. Correlations were examined with Pearson's correlation coefficient for normally distributed data and with Spearman's rank correlation coefficient for nonparametric data. Categorical variables were expressed as percentages and analyzed with chi-square test or Fisher's exact test. Multiple regression analyses were performed to identify the impact of several variables on the achievement of clinical remission. All statistical analysis was done using Graphpad Instat 3.0 (©Graphpad Software Inc.) and p-value < 0.05 was considered statistically significant.

RESULTS

Anti-PLA2R antibodies at diagnosis

In 33 patients, anti-PLA2R levels were measured at the time of biopsy and before treatment initiation. Basic demographic data are presented in Table 1. Anti-PLA2R antibodies were found positive in 16 patients (48.5%) and negative in 17 (51.5%). Positive antibodies were more frequently found in females (p = 0.01, RR = 0.39, 95%CI 0.187 to 0.812). Antibody levels did not correlate with any clinical parameter at presentation including level of proteinuria (p = 0.44). Similarly, there was no significant correlation between antibody and proteinuria levels in the subgroup of 16 patients with detectable anti-PLA2R antibodies (p = 0.20).

Table 1

Baseline characteristics of patients with anti-PLA2R antibodies measured at diagnosis. Numbers are expressed as mean ± standard deviation or as median [range] (eGFR, estimated glomerular filtration rate; PLA2R, phospholipase A2 receptor)

	Positive anti-PLA2R at diagnosis (n = 16)	**Negative anti-PLA2R at diagnosis (n = 17)**	***p*-value**
Male/Female ratio	6/10	14/3	***p = 0.01***
Age (years)	54.2 ± 12.9	56.2 ± 12.1	*p = 0.64*
Arterial hypertension (n, %)	12 (75%)	8 (47%)	*p = 0.16*
Proteinuria (g/day)	6.0 ± 2.9	6.6 ± 3.4	*p = 0.62*
eGFR (mL/min)	87.6 ± 31.6	72.6 ± 30.1	*p = 0.17*
Serum creatinine (mg/dL)	1.0 ± 0.5	1.4 ± 0.9	*p = 0.20*
Serum albumin (g/dL)	2.8 ± 0.3	2.7 ± 0.6	*p = 0.64*
Total cholesterol (mg/dL)	244.8 ± 78.7	244.6 ± 45.3	*p = 0.99*
Triglycerides (mg/dL)	210.0 ± 84	244.8 ± 48	*p = 0.16*
Anti-PLA2R titer (RU/mL)	150.4 [23.1-1669.2]	0.6 [0.4-12.4]	***p<0.001***

Subsequently, we estimated baseline positivity with cut-off antibody levels other than 20 RU/mL. We used the cut-off level of 14 RU/mL, which was considered borderline negative by the manufacturer, and of 2 RU/mL which is the lowest standard supplied with the ELISA kit. Anti-PLA2R positivity was found to be the same with 14 RU/mL (16 out of 33 patients, 48.5%), whereas it was increased when 2 RU/mL was applied as the cut-off (19 out of 33 patients, 57.6%).

Clinical outcome and correlation with baseline anti-PLA2R antibodies

The mean follow-up period of the 33 patients was 53.9 ± 30.1 months. Complete remission of

nephrotic syndrome as a result of the immunosuppressive treatment was achieved in 13 patients, partial in 17, and no remission in 3 (39%, 52%, and 9% respectively). Relapses of nephrotic syndrome were recorded in 14 of 33 patients (42%). At the end of the follow-up period, renal function had remained stable in the majority of the patients; however, 2 of 33 patients (6%) had developed ESRD and initiated renal replacement therapy whereas 3 patients (9%) had progressed to CKD stage 4. There was no significant difference in patient clinical outcome between anti-PLA2R positive and negative patients (Table 2).

In those patients with detectable anti-PLA2R antibodies at diagnosis, we investigated the association of antibody levels with several outcome parameters. Baseline antibody levels were positively associated with end proteinuria levels (r = 0.813, p = 0.0001, 95%CI 0.532 to 0.933) and negatively with eGFR (r = -0.634, p = 0.0083, 95%CI -0.86 to -0.202) at the end of follow-up (Figure 1). On the contrary, baseline anti-PL2R levels were not associated with the appearance of clinical relapses of nephrotic syndrome during follow-up (p = 0.14).

Patients who achieved complete remission of nephrotic syndrome had significantly higher serum albumin levels (p = 0.04) and lower proteinuria levels (p = 0.03) at diagnosis compared to those who achieved partial remission, indicating less severe disease (Table 3). Accordingly, they had significantly lower baseline anti-PLA2R titers in comparison to those with partial remission (2.3 [0.4-238.7] RU/mL *vs*. 29.4 [0.4-849.8] RU/mL, p = 0.045, 95%CI -285.39 to -3.388). Multiple regression analysis showed that anti-PLA2R titer at diagnosis was the only parameter independently associated with treatment outcome (complete *versus* partial remission of nephrotic syndrome) (R^2 = 0.265, p = 0.02, 95%CI -0.019 to -0.0003).

Serial anti-PLA2R measurements

Serial measurements of anti-PLA2R antibodies were evaluated in 3 groups of patients (Table 4, Figure 2). The first group consisted of 4 patients who achieved complete remission of nephrotic syndrome after administration of immunosuppressive treatment. Anti-PLA2R measurements were available both at the beginning and at the end of treatment (25 ± 12.9 months, range 14-38 months). In all cases, antibodies were positive at diagnosis and became negative after achievement of complete remission of nephrotic syndrome (from 123.5 [23.4-238.7] RU/mL to 0.8 [0-2.7] RU/mL, p = 0.045).

Table 2

Comparison of patient clinical outcome between anti-PLA2R positive and negative patients (eGFR, estimated glomerular filtration rate)

	Positive anti-PLA2R at diagnosis (n = 16)	**Negative anti-PLA2R at diagnosis (n = 17)**	***p*-value**
Follow-up (months)	50.3 ± 29.5	57.3 ± 31.2	*p = 0.51*
Complete remission (n, %)	5 (31.3%)	8 (47.1%)	*p = 0.48*
Partial remission (n, %)	10 (62.5%)	7 (41.2%)	*p = 0.30*
No remission (n, %)	1 (6.3%)	2 (11.8%)	*p = 1.00*
Relapses (n, %)	7 (43.8%)	7 (41.2%)	*p = 1.00*
eGFR (mL/min)	68.1 ± 20.6	65.7 ± 31.6	*p = 0.80*
Disease progression (n, %)	2 (1.3%)	3 (1.8%)	*P = 1.00*

Table 3

Comparison of patients who achieved complete and partial remission of nephrotic syndrome after initial treatment. Numbers are expressed as mean ± standard deviation or as median [range] (eGFR, estimated glomerular filtration rate; PLA2R, phospholipase A2 receptor)

	Complete remission (n = 13)	**Partial remission (n = 17)**	***p-value***
Total follow-up (months)	60.9 ± 33	46.7 ± 28.3	*p = 0.23*
Male/Female ratio	8/5	10/7	*p = 1.00*
Age (years)	52.5 ± 11.1	57.1 ± 14	*p = 0.32*
Baseline eGFR (mL/min)	84.0 ± 30.8	79.8 ± 32.8	*p = 0.72*
Baseline serum creatinine (mg/dL)	1.1 ± 0.4	1.0 [0.7-4.7]	*p = 0.9*
Baseline serum albumin (g/dL)	2.9 ± 0.5	2.5 [1.9-3.1]	***p = 0.04***
Baseline proteinuria (g/day)	4.9 ± 2.9	7.4 ± 3.1	***p = 0.03***
Baseline anti-PLA2R (RU/mL)	2.3 [0.4-238.7]	29.4 [0.4-849.8]	***p = 0.045***
Baseline anti-PLA2R positivity	5 (38.5%)	10 (62.5%)	*p = 0.46*

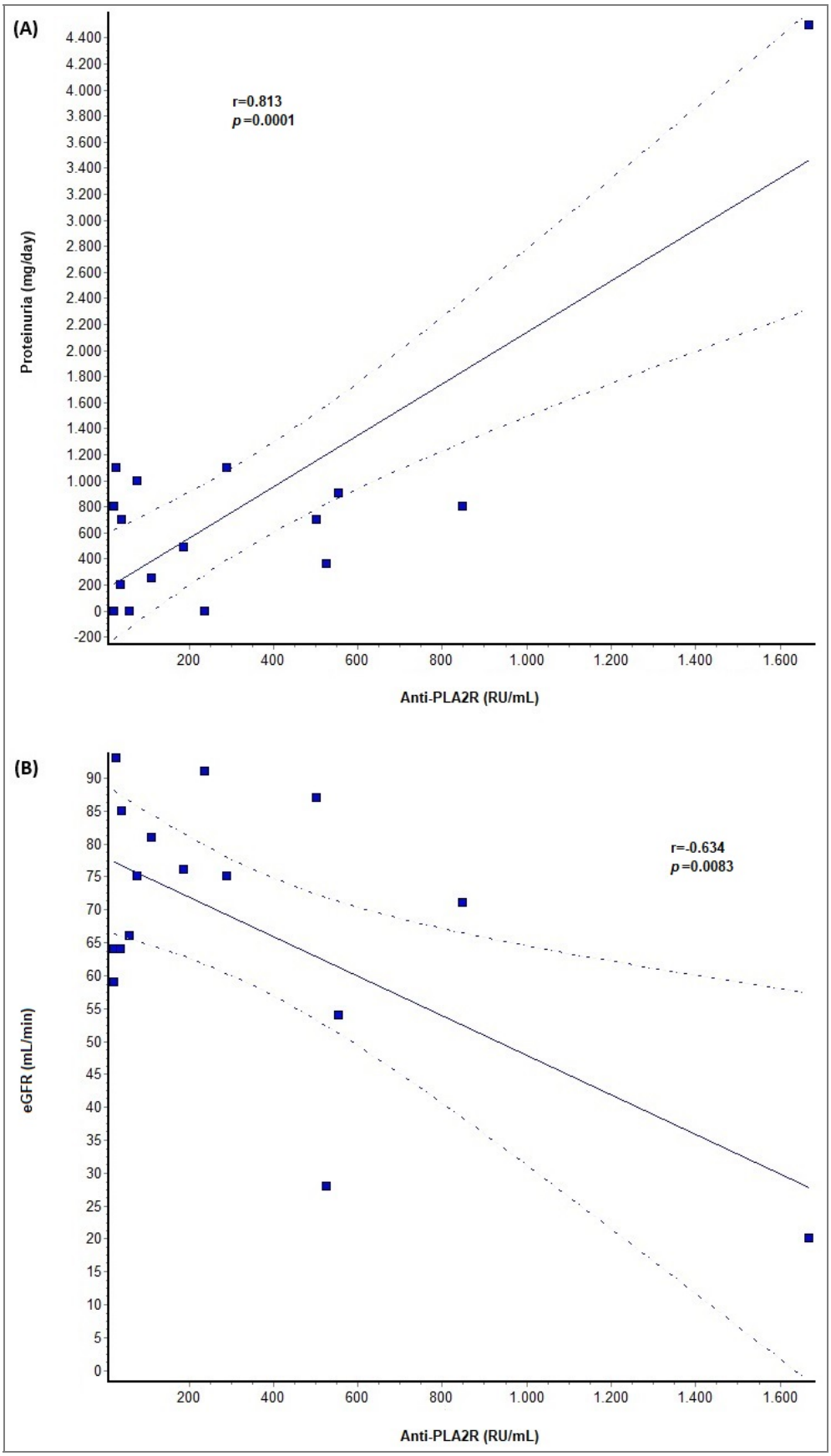

Figure 1. Correlation of anti-PLA2R levels at diagnosis with proteinuria levels (A) and eGFR (B) at the end of follow-up, in 16 patients with detectable anti-PLA2R antibodies.

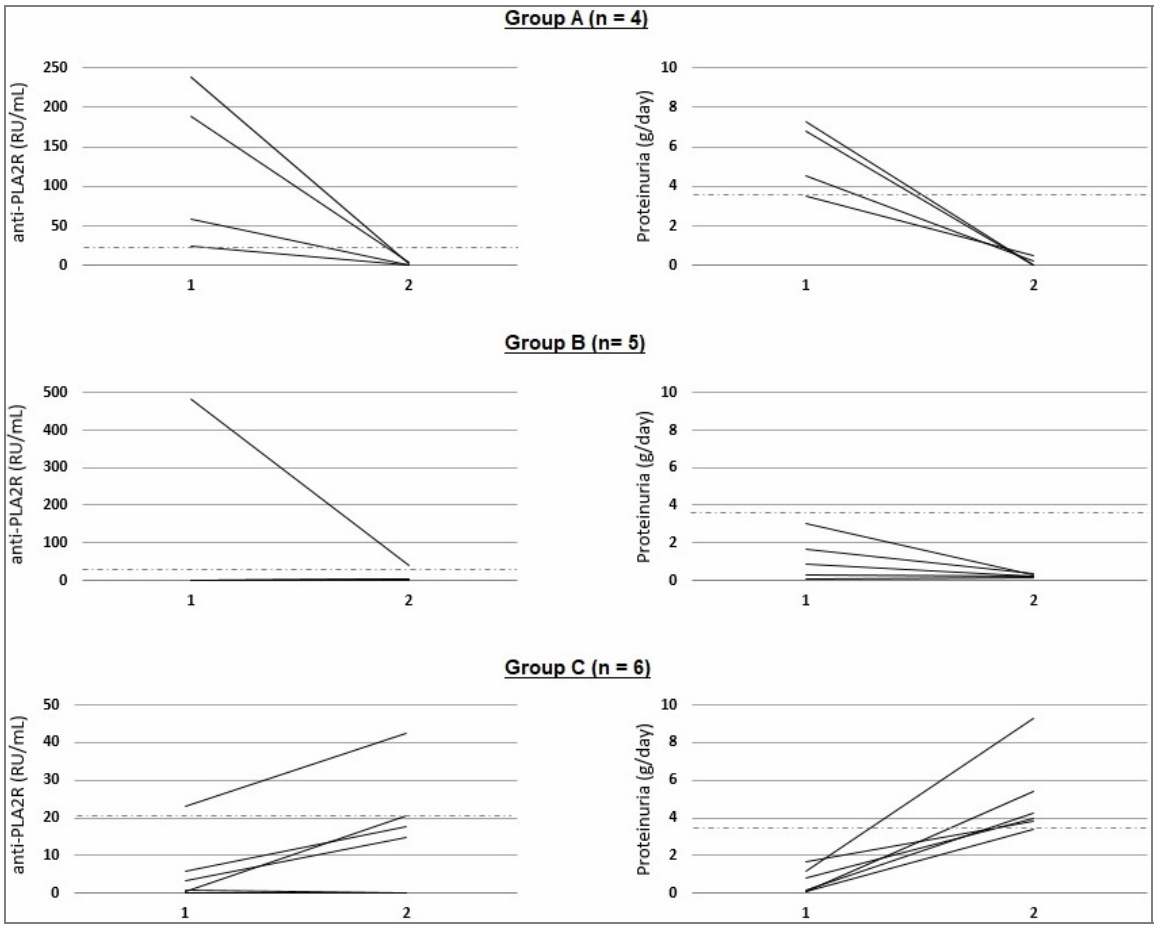

Figure 2. Alterations in anti-PLA2R levels (first column) and proteinuria levels (second column) between two time points, in three different groups of patients. Group A, Anti-PLA2R measured at diagnosis and at the end of treatment. Group B, Anti-PLA2R measured at sustained clinical remission. Group C, Anti-PLA2R measured at clinical remission and during relapse. The dashed lines represent the positivity level of 20 RU/mL for anti-PLA2R and the level of 3.5 g/day for nephrotic range proteinuria, respectively.

Table 4

Serial measurements of anti-PLA2R antibodies in three different clinical conditions. Numbers are expressed as mean ± standard deviation or as median [range] (PLA2R, phospholipase A2 receptor)

	1st time point	**2nd time point**	***p*-value**
Group A (n = 4)			
Time from biopsy (months)	0	26 [12-36]	
Proteinuria (g/day]	6.5 ± 1.0	0.1 ± 0.1	$p = 0.001$
Anti-PL2AR titer (RU/mL)	123.5 [23.4-238.7]	0.8 [0-2.7]	$\mathbf{p = 0.045}$
Group B (n = 5)			
Time from biopsy (months)	16.2 ± 8.8	39.8 ± 14.9	
Proteinuria (g/day]	1.2 ± 1.2	0.2 ± 0.1	$p = 0.14$
Anti-PLA2R titer (RU/mL)	0.3 [0.0-482.7]	1.4 [0.0-37.6]	$p = 0.38$
Group C (n = 6)			
Time from biopsy (months)	79 ± 56.4	116.8 ± 59.0	
Proteinuria (g/day]	0.7 ± 0.6	5.0 ± 2.2	$p = 0.004$
Anti-PLA2R titer (RU/mL)	2.0 [0-23.1]	16.3 [0-42.5]	$\mathbf{p = 0.038}$

The second group consisted of 5 patients with available serum samples after treatment initiation and during follow-up. All of them were at sustained clinical remission in both measurements. Antibody status remained unchanged in all patients with 1 in 5 anti-PLA2R-positive patients (20%). Alterations in antibody titers were not considered significant between the two measurements (from 0.33 [0.0-482.7] RU/mL to 1.43 [0.0-37.6] RU/mL, p = 0.38).

The third group included 6 patients with a recorded relapse episode after remission. All these

patients had completed immunosuppressive treatment and were evaluated at regular follow-up visits. The first serum sample was obtained while in clinical remission (mean proteinuria 0.7 ± 0.6 g/day) and the second within 3 months of the relapse (mean proteinuria 5.0 ± 2.2 g/day). Median anti-PLA2R levels increased significantly during relapse (from 2.03 [0-23.1] RU/mL to 16.3 [0-42.5] RU/mL, p = 0.038). Antibody titers were positive in one patient during remission (16.7%) and in 2 patients during relapse (33.3%). However, when the cut-off point for positivity was set to 14 RU/mL, antibody positivity during relapse was increased to 4 out of 6 patients (66.7%).

DISCUSSION

This is the first study assessing anti-PLA2R antibodies in Greek patients with IMN. The percentage of patients with positive antibodies at diagnosis in our cohort was 48.5% and lower than that reported in most studies. It has been estimated that 52-82% of IMN patients from several ethnic populations have positive baseline antibodies measured with different techniques [11], whereas in European patients this percentage reaches 72% with the use of ELISA [12]. There are several potential explanations for this discrepancy, such as our small sample size or a delay between kidney biopsy and serum sampling during which an immunological remission could already have started [3, 11]. It has also been suggested that originally PLA2R antigen expression may be present only in glomerular deposits [13], or that seronegative patients can subsequently become seropositive [14]. The inability to perform PLA2R staining in kidney tissue simultaneously is a significant restraint, as it would be expected to increase the diagnostic accuracy of serum testing in our patients. Another possible reason for the low percentage of positive anti-PLA2R at diagnosis is the misclassification of anti-PLA2R negative patients as idiopathic with a secondary cause of MN revealed years later [3, 15, 16]. However, this does not apply to any of our patients. More recently it was supported that negative baseline antibodies may reflect the presence of different podocyte antigens such as THSD7A [9, 15]. Whether this is the case in our population remains to be investigated.

In our study, anti-PLA2R antibodies at diagnosis were more frequently found in females. This has not been reported in other studies and might be related to the small number of women included in the study. No correlation of anti-PLA2R levels with baseline proteinuria levels was observed in our patients, which could also be attributed to the small sample size. Some studies have shown significant correlations between baseline proteinuria and anti-PLA2R levels [12, 15-17] but they included both nephrotic and non-nephrotic patients. On the other hand, studies similar to ours that examined mostly patients with nephrotic range proteinuria also found no association [18, 19]. Furthermore, the degree of proteinuria may reflect the impact of other factors such as patient compliance with renin-angiotensin system inhibitors or secondary glomerular changes associated with prolonged disease [4, 7, 20].

An interesting finding of our study was the correlation of baseline anti-PLA2R levels with patient outcomes. More specifically, antibody levels were strongly and independently associated with the achievement of complete remission, compared to partial remission of nephrotic syndrome at the end of immunosuppressive treatment. We also found that higher positive anti-PLA2R levels at baseline were strongly associated with higher proteinuria level and lower eGFR at the end of a follow-up period of nearly 5 years. These results are in accordance with recent studies, in which undetectable or very low anti-PLA2R levels at presentation strongly predicted a higher remission rate and a shorter time to remission [20, 21]. Furthermore, among patients with detectable serum anti-PLA2R antibodies, high baseline titers were repeatedly found to correlate with worse long-term outcomes and higher risk to develop ESRD [6, 22, 23].

In our study, serial anti-PLA2R alterations during different clinical conditions confirmed the correlation of anti-PLA2R antibodies with disease activity. Both in achievement of clinical remission following initial treatment and in clinical relapse, anti-PLA2R levels changed respectively. Conversely, there were no significant anti-PLA2R level alterations in patients who remained at sustained clinical remission. Potentially confounding factors are that the initial anti-PLA2 status of these patients was unknown and that serial antibody measurements were not conducted in prespecified time points in order to confirm the sequential pattern of immunological expression followed by delayed clinical expression. Despite these restraints, the association between anti-PLA2R alterations and clinical activity in our patients is evident. Other studies have also reported that anti-PLA2R level alterations correspond with proteinuria levels and precede clinical remission

as well as relapse of proteinuria [1, 4, 5, 24, 25]. Serial anti-PLA2R measurements have been proposed by many researchers as predictors of clinical response to treatment [4, 5, 7, 19, 21]. It is considered that serial monitoring of anti-PLA2R antibodies during immunosuppression could be useful in the prediction of long-term response to treatment and risk of relapse [21, 26]. More importantly, it could lead to a more personalized approach in patient management that would ensure maximum benefit while minimizing the side effects associated with treatment [13, 21].

It should be noted that antibody positivity alone was not considered a significant diagnostic or prognostic factor in our patients. This finding has also been described in other studies [17, 21, 26]. Moreover, several studies applied different methods for the evaluation of anti-PLA2R titers, such as additional dilutions in the serum samples [16, 20], or patient classification other than anti-PLA2R-positive or negative [6, 22]. Interestingly, different cut-off levels of positivity have been associated with variable diagnostic efficacy of anti-PLA2R, such as 89% with 2 RU/mL [22], 64% with 14 RU/mL [23], and 71% when 40 RU/mL was used as a cut-off level with an in-house ELISA test [26]. Two recent studies examined the optimal diagnostic sensitivity of anti-PLA2R that did not affect specificity, in Chinese [27] and Italian IMN patients [28]. They recommended use of 2.6 RU/mL and 2.7 RU/mL as cut-off values, which provided a sensitivity of 78.9% and 88.1%, respectively. In our patient cohort, the selection of a lower cut-off value of 2 RU/mL resulted in a higher diagnostic sensitivity of 57%. These observations suggest that assessment of anti-PLA2R positivity requires further investigation and antibody status should be interpreted with caution. Thus, it would probably be more prudent to rely on level alterations rather than positivity for routine measurements.

The main limitations of this study are associated with its small patient size and retrospective nature. Serum samples were not routinely collected at specified time points and antibody measurements at diagnosis were not available in all patients. Moreover, PLA2R staining in renal biopsies and correlation with serum antibody levels was not available. Finally, we were not able to investigate the concomitant presence of anti-THSD7A antibodies in the same population and especially in anti-PLA2R negative patients. However, the present study is the only currently available report of anti-PLA2R autoantibodies in Greek IMN patients and its findings are in accordance with the current literature.

In conclusion, in Greek IMN patients, lower baseline anti-PLA2R levels are associated with the achievement of complete *versus* partial remission of nephrotic syndrome. Among patients with initially detectable antibodies, higher titers are predictive of worse long-term clinical outcomes. Furthermore, alterations of antibody titers during serial measurements correlate with response to treatment and disease clinical activity during follow-up. Larger prospective studies are needed to confirm the aforementioned findings and to investigate the utility of routine anti-PLA2R measurements in the prediction of clinical outcome in IMN patients.

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Declaration of Interest: The authors declare that there are not conflicts of interest.

Introducere. *Anticorpii circulanți anti receptorul fosfolipazei A2 (anti-PLA2R) sunt cunoscuți a avea rol cheie în patogeneza nefropatiei membranoase idiopatice. În practica clinică curentă aceşti anticorpi sunt consideraţi noi biomarkeri pentru diagnosticul şi monitorizarea bolii. Scopul studiului a fost de a investiga utilitatea prognostică şi diagnostică a anticorpilor anti-PLA2R la pacienții greci cu nefropatie membranoasă dovedită histologic.*

Materiale şi metode. *Au fost analizați anticorpii anti-PLA2R din probele serologice a 33 de pacienți folosind ELISA. Nivelurile acestora au fost associate cu răspunsul terapeutic. Au fost realizate măsurători seriate la 15 pacienți iar modificările nivelului anticorpilor au fost asociate cu activitatea bolii.*

Rezultate. *Prevalența anticorpilor anti PLA2R a fost de 48.5% (16 din 33 pacienți au fost pozitivi). Nivelurile anti PLA-2R au fost associate independent cu remisia completă a sindromului nefrotic după tratamentul imunosupresor comparat cu remisia parțială ((p = 0.02, R^2 = 0.265, 95%CI -0.019 – -0.0003).*

Niveluri mai mari ale anticorpilor la diagnostic s-au corelat cu proteinuria (r = 0.813, p = 0.0001, 95%CI 0.532 – 0.933) şi cu niveluri mai mici ale eGFR la finalul follow-up (r = -0.634, p = 0.0083, 95%CI -0.86 – -0.202). Analiza seriată a anticorpilor a arătat că nivelul circulant al anti PLA2R a fost redus semnificativ statistic la finalul tratamentului după ce a apărut remisia completă au rămas la niveluri scăzute pe tot parcursul remisiei şi au crescut în momentul recăderii.

Concluzii. *Rezultatele confirmă utilitatea anticorpilor anti-PLA2R în diagnosticul nefropatiei membranoase idiopatice. Nivelurile scăzute ale anticorpilor la diagnostic sunt prognostice pentru o remisie completă a sindromului nefrotic după terapia imunosupresivă. Măsurătorile seriate se corelează bine cu statusul clinic şi ar putea fi utile pentru monitorizarea activității bolii şi planificarea tratamentului.*

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