Allergy and Immunology

AIMS Allergy and Immunology, 10(3): 209–221.
DOI: 10.3934/Allergy.2026015
Received: 13 January 2026
Revised: 13 September 2026
Accepted: 20 September 2026
Published: 28 September 2026

https://www.aimspress.com/journal/Allergy

Research article

Anti-Pentraxin 3 autoantibodies in systemic lupus erythematosus: A comparative study of patients with and without proteinuria

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Abstract: Background and objectives: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease frequently complicated by renal involvement, known as lupus nephritis (LN). Pentraxin 3 (PTX3) is an acute-phase protein implicated in immune regulation, and autoantibodies against PTX3 (anti-PTX3) have been hypothesized to exert a protective effect against the development of LN in SLE patients. The objective of the current study was to evaluate serum levels of anti-PTX3 IgG and anti-double-stranded DNA (anti-dsDNA) IgG antibodies in SLE patients and to assess their association with disease activity and proteinuria. Methods: This cross-sectional study included 69 participants divided into three groups: SLE patients with proteinuria, SLE patients without proteinuria, and healthy controls. Serum IgG anti-PTX3 and anti-dsDNA levels were measured using enzyme-linked immunosorbent assay (ELISA). Proteinuria was assessed by measuring the albumin-to-creatinine ratio (A/Cr). Associations between antibody levels, proteinuria, and disease activity index were analyzed. Results: Serum anti-PTX3 levels were highest in SLE patients without proteinuria, with a statistically significant difference among the three groups (p = 0.031). Anti-dsDNA antibodies were detected exclusively in SLE patients; however, no significant difference was observed between patients with and without proteinuria (p = 1.00). Anti-PTX3 levels demonstrated a weak negative correlation with A/Cr (r = −0.082) and with disease activity index (r = −0.142). Conclusions: Higher anti-PTX3 levels in SLE patients without proteinuria and their inverse relationship with proteinuria

and disease activity were observed in this cross-sectional sample; however, these correlations were weak and not statistically significant, and a protective or causal role cannot be established from these data. Anti-PTX3 may represent a candidate marker warranting longitudinal validation in patients with SLE.

Keywords: anti-dsDNA antibody; anti-PTX3; ELISA; lupus nephritis; proteinuria; systemic lupus erythematosus

Abbreviations: SLE: Systemic lupus erythematosus; LN: Lupus nephritis; PTX3: Pentraxin 3; anti-PTX3: Anti-pentraxin 3 IgG autoantibody; anti-dsDNA: Anti-double-stranded DNA IgG antibody; ELISA: Enzyme-linked immunosorbent assay; A/Cr: Urinary albumin-to-creatinine ratio; ACR: American College of Rheumatology; SLICC: Systemic Lupus International Collaborating Clinics; SLEDAI-SELENA: Systemic Lupus Erythematosus Disease Activity Index—Safety of Estrogens in Lupus National Assessment; IQR: Interquartile range; IC: Immune complex; Ads: Autoimmune diseases; SPSS: Statistical Package for the Social Sciences

1. Introduction

Autoimmune diseases (ADs) were once considered rare but are now becoming increasingly prevalent. These include many conditions affecting different organs and body systems, and are a major concern due to their high morbidity and mortality. An estimated 2.5%–5% of the world's population suffers from autoimmune diseases [1]. SLE is one such disease with multi-system involvement and heterogeneous manifestations [2]. It is termed as "the cruel mystery" due to its unknown etiology, debilitating and destructive nature, and possibly fatal outcomes. It exhibits a strong female predominance, influenced by hormonal and immunological factors. Estrogen influences immune cell survival and function, resulting in stronger immune responses in females, which confers a survival advantage but also increases the risk of autoimmune diseases [3,4]. SLE is mainly seen in adults, while childhood-onset SLE accounts for about 15%–20% of cases [5]. The most distinct feature of SLE is the loss of tolerance to nuclear autoantigens [6]. LN is a serious and disabling complication of SLE, affecting nearly half of patients and leading to significant suffering and loss of life [7]. As per the guidelines laid down by the American College of Rheumatology (ACR), LN should be suspected in patients with persistent abnormalities in the urinary sediment, such as hematuria and pyuria, urinary casts, or proteinuria >0.5 g/day or increased serum creatinine. The diagnosis is confirmed by renal biopsy [8]. Owing to the invasive nature of biopsy and potential complications, proteinuria is frequently used to monitor disease activity in LN [7].

The mechanism of renal inflammation in LN is a multistep process, beginning with the development of autoantibodies directed against nuclear and cellular antigens. These antigens are either circulating in the blood or found locally in the renal parenchyma. The binding of antibodies to these antigens leads to immune complex (IC) formation. These ICs are deposited in the glomeruli as blood is filtered [9]. Complement activation by the ICs further aggravates intrarenal inflammation, recruiting inflammatory cells and causing kidney damage [10]. Pentraxin 3 (PTX3) is an acute-phase protein that binds to apoptotic materials. When PTX3 binds to apoptotic debris, it promotes their deposition in organs and tissues. This allows for C1q fixation, complement activation, and resultant tissue destruction by inflammatory mediators [11]. Several studies have reported increased circulating PTX3

levels in patients with SLE compared with healthy controls. High PTX3 levels have been associated with SLE flares and the development of lupus nephritis. These studies indicate serum PTX3 level might be a significant mediator in SLE [11,12]. Anti-PTX3 antibodies are hypothesized to exert a nephroprotective effect by blocking PTX3, thereby preventing kidney damage and the progression of LN in SLE patients [11]. Studies have documented an inverse association between renal PTX3 deposition and circulating anti-PTX3 antibody levels in patients with lupus nephritis, with greater PTX3 deposition associated with renal fibrosis. In animal models, Gatto et al. demonstrated that immunization with PTX3 induced anti-PTX3 antibody production and prevented the progression of lupus nephritis from the subclinical to the clinical stage, likely by blocking renal PTX3 deposition [13,14]. Such studies have highlighted anti-PTX3 antibodies as potential protective factors against renal inflammation. Hence, determining anti-PTX3 antibody levels in SLE patients can help classify them into high- or low-risk groups for developing renal complications.

This study aimed to compare IgG anti-PTX3 and anti-dsDNA antibody levels in SLE patients with and without overt proteinuria and to assess their association with renal involvement and disease activity in SLE. Due to the invasiveness of renal biopsy, the urinary albumin-to-creatinine ratio (A/Cr) was used as a non-invasive measure to classify participants according to the presence or absence of proteinuria.

2. Materials and methods

2.1. Study design, setting, and participants

A cross-sectional comparative study was conducted at the Department of Immunology, University of Health Sciences, Lahore, during 2022 and 2023. Sixty-nine participants were enrolled in the study: 60 (87%) were females, and 9 (13%) were males. The study was conducted as a pilot study.

- Healthy control group, labeled as group I, consisted of 23 healthy individuals, based on normal CBC, urine DRE, and no history of infection in the last two weeks.
- SLE patients were enrolled and further divided into two groups, based on renal involvement. Group II had 23 SLE patients without proteinuria; Group III had 23 SLE patients with proteinuria. Disease duration of the SLE patients ranged from 1 month to 132 months, with a mean of 44 months.

2.2. Sample size calculation

An a priori sample-size calculation was performed prior to data collection, based on anticipated mean serum anti-PTX3 levels in SLE patients versus healthy controls reported in a previously published study [15], using the formula $n = [(Z_{1-\beta} + Z_{1-\alpha/2})^2 \times (\sigma_1^2 + \sigma_2^2)]/(\mu_1 - \mu_2)^2$, where $Z_{1-\beta} = 1.28$ (90% power) and $Z_{1-\alpha/2} = 1.96$ (5% two-sided significance level); $\mu_1 = 0.268$ and $\mu_2 = 0.134$ were the anticipated mean anti-PTX3 levels in SLE patients and healthy controls, respectively, and $\sigma1 = 0.19$ and $\sigma2 = 0.07$ were the corresponding standard deviations reported in that study. This yielded a calculated sample size of approximately 23 participants per group (total N = 69).

2.3. Clinical assessment and disease activity

All the study participants were evaluated by doing a thorough clinical examination. Systemic Lupus International Collaborating Clinics (SLICC 2012) diagnostic criteria were applied; those who

met the criteria were included as SLE patients. Disease activity was assessed according to the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI-SELENA), which is a modified version of the SLEDAI (1985), devised for use in the Safety of Estrogens in Lupus National Assessment (SELENA) study in 2005. Complete urinalysis was performed, as follows:

- In group I, to mark the healthy control.
- In group II, to establish the absence of renal involvement in SLE patients.
- In group III, to mark the renal involvement in SLE patients.

According to the American College of Rheumatology (ACR) clinical and laboratory criteria, in the absence of renal biopsy, lupus nephritis is indicated by urinary protein excretion >0.5 g/day or ≥3+ on dipstick, or increased serum creatinine when urinary sediment data are excluded due to low sensitivity and poor predictive value [8,16].

2.4. Sample collection and storage

After taking written informed consent, in compliance with the Helsinki Declaration, the patient was given a urine container and instructed to collect clean-catch midstream urine (5 mL). The samples were centrifuged and stored in labeled aliquots at −20 °C until analysis was performed.

Three milliliters of whole blood was collected from SLE patients from the antecubital vein aseptically in a disposable syringe and transferred to a serum separator tube. The samples were centrifuged at 3,500 rpm for 3 min, and serum was collected in labeled serum cups and stored at −20 °C until analysis.

2.5. Laboratory and serological assays

- Urinary albumin to creatinine ratio, UA/Cr, was calculated to establish the degree of proteinuria [17]. Urine albumin levels were measured via immunoturbidometric assay using the spectrophotometer kit; urine creatinine levels were measured using the Jaffe method and kit by Tarasco AG, Switzerland (not conducted in the healthy control). Hepatitis B, C, and HIV status were checked in all three groups; positive subjects were excluded.
- Serum levels of IgG anti-PTX3 were measured using a commercially available ELISA kit (Bioassay Technology Laboratory, Birmingham, England), according to the manufacturer's instructions. Serum levels of IgG autoantibodies against dsDNA were detected using the commercially available ELISA kit (QUANTA LITE dsDNA SC ELISA, 704650), according to the manufacturer's instructions (positive >75 IU/mL). These kits followed the indirect ELISA method: Diluted patient serum is added to wells and incubated. Antibodies in patient samples bind to the antigen coated on the wells during the first incubation. All unbound materials are then washed away, and an enzyme conjugate is added, which bonds to the antibody antigen complex. Excess enzyme conjugate is washed off, and the chromogenic substrate is added, resulting in a blue reaction product. The enzyme conjugate catalytic reaction is stopped by adding acid stop solution. This produces a yellow endpoint color. The intensity of the color generated is thus proportional to the amount of bound target antibody. The results were read by a Bio-Rad microplate reader 680 (USA) set at 450 nm.

3. Statistical analysis

Data were tabulated and analyzed using IBM SPSS (Statistical Package for Social Sciences)

software version 25. Median and interquartile range (IQR) were given for quantitative variables, including age and biochemical parameters, whereas qualitative variables were expressed as frequencies and graphs. Kolmogorov–Smirnov and Shapiro–Wilk tests were applied to check the distribution of the data in each group. For comparison of data within the two disease groups, Mann Whitney–U and Kruskal–Wallis H tests were applied. For the correlation study, Spearman's correlation (non-parametric) and Pearson correlation (parametric test) were used. Spearman's rank correlation was used as the primary measure of association, given the non-normal distribution of some variables. Pearson correlation coefficients were additionally calculated for comparison. Multiple comparison correction was applied for correlation analysis. A p-value ≤ 0.05 was considered statistically significant.

4. Results

4.1. Demographic characteristics

The three study groups were predominantly female, consistent with the expected sex distribution of SLE (Figure 1). Age did not differ significantly among the groups ($p = 0.35$), whereas weight did ($p = 0.02$); full demographic values are presented in Table 1.

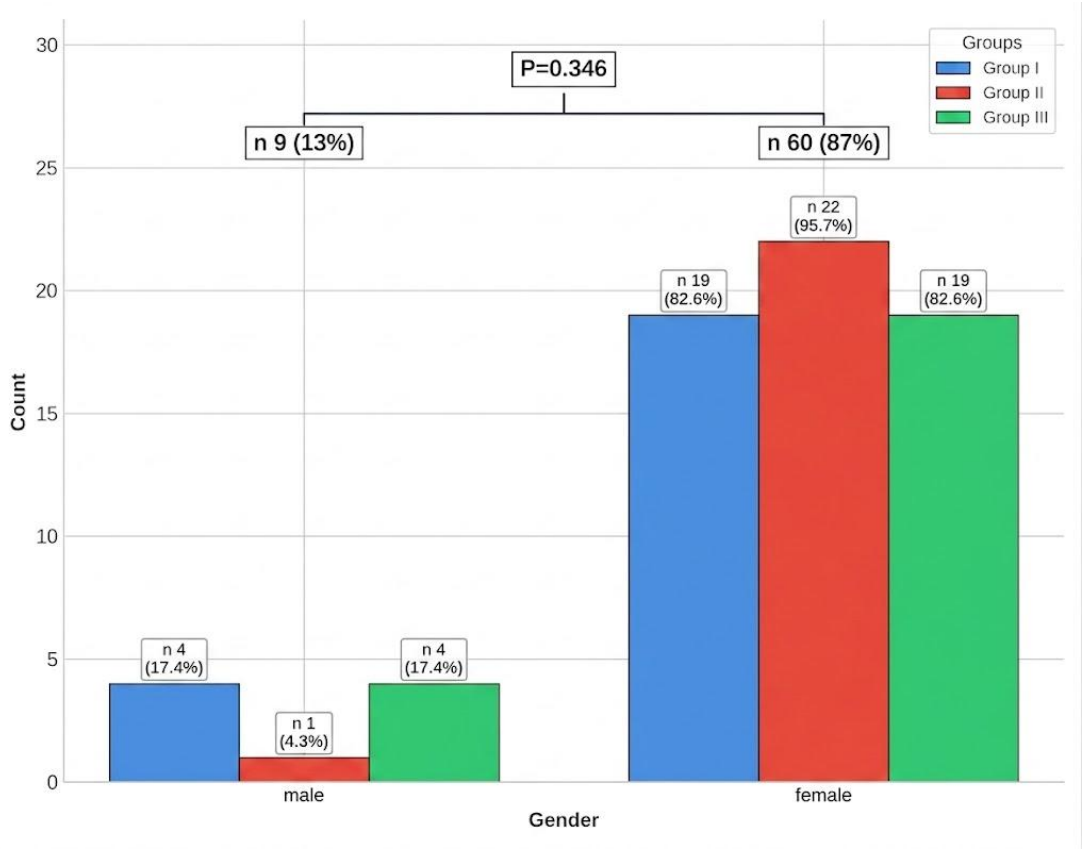


Figure 1. Gender distribution: number, percentage, and comparison between the studied groups.

Table 1. Demographic comparison (age, weight) of SLE patients with and without proteinuria versus healthy controls.

Groups	Healthy controls Group I median (IQR)	SLE without proteinuria Group II median (IQR)	SLE with proteinuria Group III median (IQR)	*p*-value
Age (years)	26 (22.5–31.5)	30 (24–38)	28 (22–36)	0.35
Weight (kg)	54 (50.5–68.5)	52 (45–63.25)	64 (54–70.75)	0.02*

Values are expressed as median (interquartile range); *p-value ≤ 0.05 considered as statistically significant.

4.2. Levels and comparison of anti-PTX3, anti-dsDNA, and urinary albumin-to-creatinine ratio (A/Cr)

Anti-PTX3 autoantibodies were detected in all three groups, with the highest level in group II (Table 2). This difference was statistically significant overall (p = 0.031) and specifically when comparing the healthy control and Group II (p = 0.028) (Table 2).

Table 2. Median levels and comparison of anti-PTX3, anti-dsDNA, and urinary albumin-to-creatinine ratio (A/Cr) among the studied groups.

Variables	Comparison	Group I (n = 23) median (IQR)	Group II (n = 23) median (IQR)	Group III (n = 23) median (IQR)	*p*-value
Anti-PTX3 (ng/L)	*Overall (a)*	500 (350–699)	670 (557–1042)	590 (419–703)	0.03*
	Group I vs Group II (b)				0.02*
	Group II vs Group III (c)				0.31
	Group I vs Group III (d)				0.98
Anti-dsDNA (IU/mL)	*Overall (a)*	12 (6–19)	713 (19.4–1916)	856 (165–2121)	< 0.001*
	Group I vs Group II (b)				< 0.001*
	Group II vs Group III (c)				1.000
	Group I vs Group III (d)				< 0.001*
A/Cr (mg/g)	*Overall (a)*	6.6 (2.40–11.7)	53 (9.0–100)	200 (101–1757)	< 0.001*
	Group I vs Group II (b)				*Not required*
	Group II vs Group III (c)				*Not required*
	Group I vs Group III (d)				0.003*

Group I = Healthy controls; Group II = SLE patients without proteinuria; Group III = SLE patients with proteinuria; Values are presented as median (interquartile range). a = Overall comparison among the three groups performed using the Kruskal–Wallis test; b = Pairwise comparison between Group I and Group II; c = Pairwise comparison between Group II and Group III; d = Pairwise comparison between Group I and Group III; $p \leq 0.05$ considered statistically significant (*); ns = not significant; "Not required" indicates pairwise comparison not applicable for that parameter; n = number of individuals in each group.

Anti-dsDNA levels were elevated in both SLE groups but were within normal limits in the healthy controls. The difference was statistically significant among the three groups overall ($p < 0.001$) and between healthy controls and each SLE group. Anti-dsDNA did not differ significantly between the two SLE groups (Table 2).

A/Cr values for the three groups are summarized in Table 2 and differed significantly between the two SLE groups (p = 0.003). Correlations between A/Cr and the other study parameters are presented in Section 4.3 and Table 3.

Table 3. Interparameter correlations among anti-PTX3, anti-dsDNA, urinary A/Cr ratio, and SELENA-SLEDAI score in patients with SLE with and without proteinuria.

Parameter		$r(p_1)^{ab}$	$r(p_2)^{ab}$	$r(p_3)^{ab}$	$r(p_4)^{ab}$
1. Anti-PTX3 ng/L					
2. Anti-dsDNA (IU/mL)	A	0.17 (0.16)			
	B	0.01 (0.87)			
3. A/Cr (mg/g)	A	0.13 (0.26)	0.50 (<0.001)*		
	B	−0.08 (0.50)	0.21 (0.07)		
4. SELENA-SLEDAI	A	0.01 (0.93)	0.36 (0.01)*	0.42 (0.00)*	
	B	−0.14 (0.34)	0.36 (0.01)*	0.25 (0.08)	

Row A = Spearman's rank correlation coefficient (non-parametric test); Row B = Pearson's correlation coefficient (parametric test); r = correlation coefficient; p = probability value (significance level) where p_1 = correlation of parameter 1 (anti-PTX3) with parameters 2, 3, and 4; p_2 = correlation of parameter 2 (anti-dsDNA) with parameters 3 and 4; p_3 = correlation of parameter 3 (A/Cr ratio) with parameter 4; correlation is considered statistically significant at $p \leq 0.05$. Diagonal cells are not applicable because they represent correlations of each parameter with itself.

4.3. Correlation analyses

Anti-PTX3 levels showed only weak, statistically nonsignificant negative correlations with A/Cr and disease-activity scores, with the negative association between anti-PTX3 and A/Cr illustrated by the Pearson correlation analysis in Figure 2. A nonsignificant positive correlation was observed between anti-PTX3 and anti-dsDNA (Table 3), suggesting that anti-PTX3 may not be a sensitive indicator of short-term disease activity or renal involvement in this cohort. In contrast, anti-dsDNA showed significant positive correlations with both A/Cr and disease activity, and A/Cr itself correlated positively with disease activity (Table 3, Figure 3), indicating that, unlike anti-PTX3, elevated anti-dsDNA and A/Cr were associated with greater disease activity in this cohort.

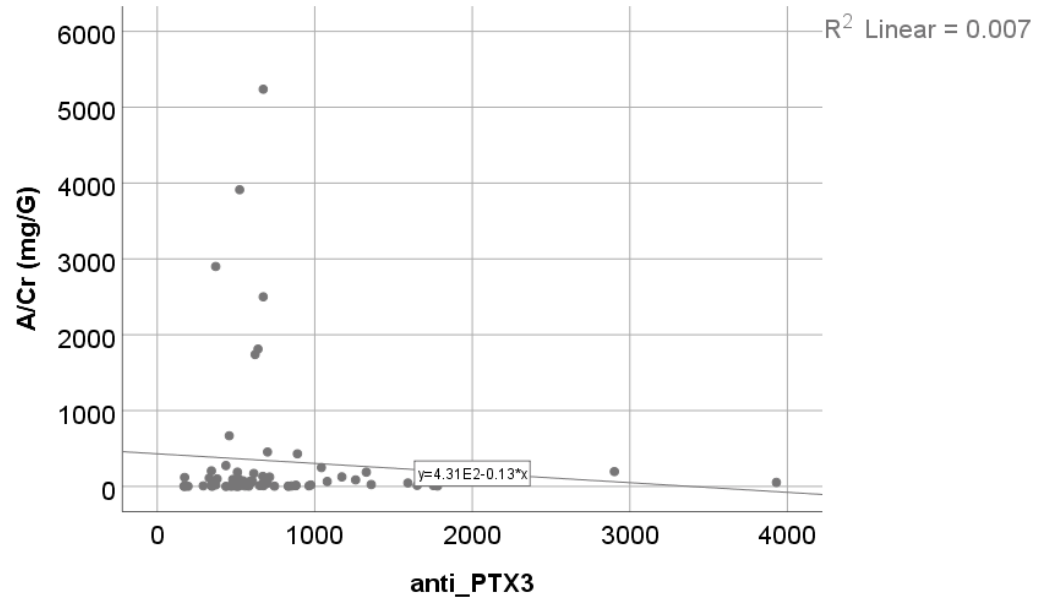


Figure 2. Correlation observed between serum anti-PTX3 levels and proteinuria, expressed as the albumin-to-creatinine ratio (A/Cr). The line indicates the linear regression curve. The Pearson's correlation coefficient is shown.

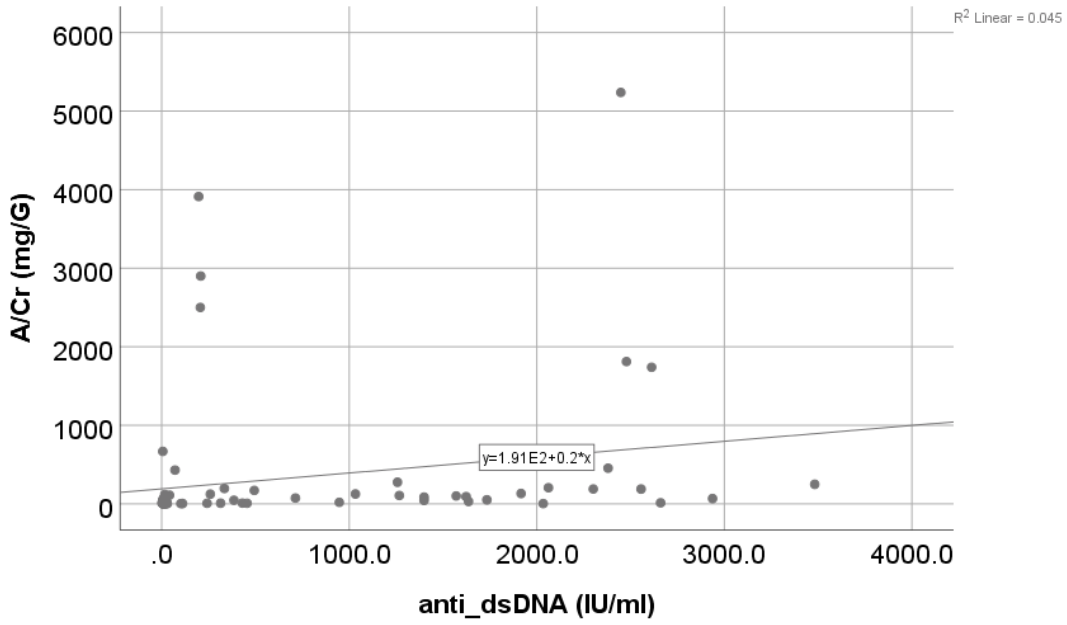


Figure 3. Correlation observed between serum anti-dsDNA levels and proteinuria, expressed as the albumin-to-creatinine ratio (A/Cr). The line indicates the linear regression curve. Spearman's correlation coefficient is shown.

5. Discussion

SLE is a chronic disease with multiple systemic complications and a prolonged course. Consistent

with global trends reporting a female-to-male (F:M) ratio of approximately 9:1 [4], our study observed 22 (95%) females in Group II (F:M 9.6:0.4) and 19 (82%) females in Group III (F:M 8.3:1.7). Among the organs affected in SLE, renal involvement is one of the most severe and debilitating complications, occurring in nearly half of patients, with at least 10% progressing to end-stage renal disease requiring dialysis [9,18].

This autoimmune disease exhibits the most complex and diverse spectrum of autoantibody specificities described in autoimmune diseases, with more than 200 autoantibodies identified [10]. Rapid extracellular antigen profiling (REAP) studies alone have detected at least 84 distinct antibodies directed against extracellular proteins [19]. Autoantibody profiles also vary according to the age at disease onset [20]. With advances in diagnostic technologies, a growing range of novel biomarkers has been identified, some demonstrating performance comparable to or exceeding that of traditional markers [21].

PTX3, a long pentraxin involved in innate immunity and the clearance of apoptotic material, has been proposed to modulate complement activation and induce tissue injury. A study documented more PTX3 deposition with renal fibrosis on renal biopsies of LN patients with anti-PTX3 below cutoff limits [15]. Notably, some studies reported that elevated PTX3 levels correlate positively with disease activity and renal injury indices in lupus nephritis, highlighting the complexity of this immunological pathway [12]. Consequently, the presence of anti-PTX3 autoantibodies may reflect a counter-regulatory immune response that mitigates excessive inflammatory damage within renal tissues. Supporting these anti-inflammatory effects of anti-PTX3, a study in ANCA-associated vasculitis by Padoan et al. demonstrated a significantly higher prevalence of anti-PTX3 antibodies in patients without active disease ($p = 0.015$), suggesting an association with disease quiescence [22]. Elevated levels of PTX3 have been linked to vasculitic disease activity in childhood-onset SLE [23], underscoring that the PTX3/anti-PTX3 axis may be relevant beyond the renal compartment, including in pediatric-onset disease [5].

The present study revealed distinct correlation patterns among the measured biomarkers and disease severity indices in patients with SLE. Although the correlations between anti-PTX3 levels and both the urinary A/Cr ratio ($r = -0.08$, $p = 0.50$) and the SELENA-SLEDAI score ($r = -0.14$, $p = 0.34$) were weak and did not reach statistical significance, the negative direction of these associations is noteworthy. This inverse trend suggests that higher anti-PTX3 antibody levels may be associated with lower disease activity and reduced renal involvement. The findings are in accordance with a recent study by Karlsson et al. documenting higher levels of anti-PTX3 in active SLE patients compared to those in remission ($n = 161$, $p < 0.01$), along with a weak inverse correlation between anti-PTX3 levels and disease activity scores ($rho = -0.17$, $p < 0.05$) [24]. Comparable results were reported by an Italian study by Bassi et al., who displayed a statistically significant negative association between anti-PTX3 and LN (OR = 0.163, 95% CI: 0.074–0.360, $p < 0.0001$), indicating lower odds of LGLN with higher anti-PTX3 levels and ECLAM disease severity score in SLE patients ($r = -0.350$, $p < 0.0001$) [15]. A study conducted in China in 2017 also reported that anti-PTX3 autoantibodies were less prevalent in active LN than in SLE patients without renal involvement (19.4% vs. 40.7%, $p < 0.001$), with a significant inverse correlation ($r = -0.143$, $p = 0.047$) between anti-PTX3 levels and proteinuria [11]. Gatto et al. found circulating PTX3-specific B cells to be markedly reduced in lupus nephritis compared with non-renal SLE, suggesting a loss of PTX3-specific autoreactivity in renal disease [25]. Experimental murine studies by the same team further support a protective role. They demonstrated that immunization with PTX3 induced anti-PTX3 antibodies, delayed the onset of lupus-like nephritis,

reduced proteinuria, and improved survival [13,14]. Several possible reasons may explain this discordance between the weak, nonsignificant inverse correlation found in the present work and previous reports of significant inverse correlations. Our study had a smaller sample size and was cross-sectional rather than longitudinal, limiting statistical power to detect modest correlations. Differences in patient population (ethnicity, disease duration, and treatment exposure), the ELISA kits and cutoff values used, and the reliance on proteinuria rather than biopsy-confirmed lupus nephritis to classify renal involvement may also have contributed to the weaker, nonsignificant associations observed here.

Anti-dsDNA antibodies remain a cornerstone biomarker for assessing disease activity in SLE. These autoantibodies showed a strong positive correlation with both the A/Cr ratio and SELENA-SLEDAI scores in the current study ($p < 0.001$ and $p = 0.01$, respectively), consistent with their already established role in lupus nephritis [26]. Comparison between the two SLE groups showed higher anti-dsDNA levels in the proteinuria group than in the non-proteinuria group; however, this difference was not statistically significant (p = 1.000). While some studies have reported no significant difference in anti-dsDNA levels between renal and non-renal SLE [27], others have demonstrated significantly higher levels in active lupus nephritis [28,29]. These discrepancies may be explained by the inability to definitively exclude subclinical renal involvement in the non-proteinuria group in the absence of renal biopsy [18].

The correlation between anti-PTX3 and anti-dsDNA was positive but not statistically significant (r = 0.02, $p = 0.83$). A previous study by Augusto et al. demonstrated a significant positive correlation between anti-PTX3 and anti-dsDNA levels in patients with SLE (r = 0.218, $p < 0.02$) [30]. In contrast, animal model studies by Gatto et al. reported significantly lower anti-dsDNA levels in lupus-prone mice with higher anti-PTX3 levels and vice versa ($p < 0.001$) [13]. The A/Cr ratio also correlated positively with disease severity, reinforcing its utility as a marker of lupus nephritis and overall disease burden.

In conclusion, these findings suggest a dual immunological pattern: while anti-dsDNA reflects pathogenic disease activity, the role of anti-PTX3 remains less clear. In the present study, the observed negative correlations between anti-PTX3 levels and markers of proteinuria and systemic disease activity were weak and did not reach statistical significance. While the direction of these associations is consistent with a possible regulatory role for anti-PTX3, a protective or causal relationship cannot be established from these cross-sectional data, and this observation should be regarded as hypothesis-generating pending confirmation in larger, longitudinal studies.

6. Conclusions and future perspectives

This study reinforces anti-dsDNA as a marker of disease activity in SLE. The higher anti-PTX3 levels observed in patients without proteinuria are a preliminary, hypothesis-generating finding; given the weak and nonsignificant correlations with proteinuria and disease activity observed here, a protective or causal role for anti-PTX3 cannot be established from these cross-sectional data. Longitudinal, biopsy-confirmed studies with paired measurements of circulating PTX3 are warranted to determine whether anti-PTX3 has genuine mechanistic or prognostic significance in lupus nephritis before any therapeutic implications can be considered. A/Cr remains a valuable non-invasive marker of proteinuria and, in the absence of renal biopsy, is a practical tool for monitoring renal status in SLE patients.

7. Limitations

This study has several limitations that should be considered when interpreting these findings. First, renal involvement was classified using proteinuria alone, without renal biopsy confirmation or use of supplementary renal markers (serum creatinine, eGFR, C3/C4, anti-C1q, urine sediment). Proteinuria may not fully capture subclinical lupus nephritis, nor is it specific to LN. Second, the cross-sectional design and simultaneous measurement of antibody levels and renal status preclude any conclusions about temporal sequence or causality. Third, although the study was based on an a priori sample size calculation with a planned power of 90%, the sample size was primarily intended for the initial assessment of anti-PTX3 levels. The secondary three-group comparisons and correlation analyses were not specifically powered and should consequently be considered exploratory. The relatively small sample size may have reduced the ability to detect smaller or potentially clinically relevant effects and increased the possibility of type II error. Accordingly, nonsignificant findings should be interpreted cautiously and require confirmation in larger, adequately powered studies. Fourth, circulating PTX3 protein itself was not measured, so it could not be determined whether higher anti-PTX3 antibody levels correspond to lower bioactive PTX3. Finally, this was a single-center study, which may limit generalizability. Future prospective, longitudinal, multicenter studies with renal biopsy confirmation and paired PTX3/anti-PTX3 measurements are warranted to validate these observations.

Use of AI tools declaration

No AI tools were used for preparing this manuscript. All scientific content was prepared, reviewed, and validated by the authors, who take full responsibility for the manuscript.

Author contributions

Maria Noor: Study planning, synopsis preparation, data and sample collection, laboratory investigations, data analysis, interpretation of findings, manuscript drafting, revision, and finalization. Khursheed Javaid: Supervision, academic guidance, and critical review of the manuscript. Nadeem Afzal: Supervision, academic guidance, and critical review of the manuscript. Sana Mahmood: Sample collection, laboratory investigations. Ayesha Nadeem: Sample collection, laboratory investigations. Saima Pervaiz: Data collection, and data analysis. Faheem Shahzad: Study design, sample size calculation, and statistical analysis. Muhammad Kashif: Manuscript writing support and assistance with the publication process.

Conflicts of interest

The authors declare no conflict of interest.

Ethical approval

The study was approved by both the University of Health Sciences vide letter no UHS/REG-21/ERC/3923 (Dated 23 Aug 2021) and Sheikh Zayed Hospital Lahore vide letter noSZMC/IRB/External/M. Phil/369 /2021 (Dated 30 Sep 2021), Institutional Review Boards. All the patients provided written, informed consent for study participation and analysis of their data.

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