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ASSESSMENT OF SOME BIOCHEMICAL AND IMMUNOLOGICAL MARKERS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOUS: A CASE-CONTROL STUDY

Noor Nayyef Oudah 1, *,
Malaa M. Taki 2,
Aymen Radhi Habeeb 3
1* College of Medical and Health Techniques, University of Bilad Alrafidain, Diyala, Iraq.
2Department of Basic Science, College of Nursing, University of Kirkuk, Kirkuk, Iraq
3 Directorate of education of Rasafa , Ministry of education, Iraq
Noor.naief@yahoo.com
malaa.majed@gmail.com
Aymenbash512@gmail.com

Abstract:

Background: Systemic Lupus Erythematosus (SLE) is a complex autoimmune disease frequently involving renal complications, most notably lupus nephritis. Early detection and monitoring of renal involvement are critical for effective disease management. Therefore, the current study designed to evaluate a biochemical (urea, creatinine, uric acid) and immunological (anti-dsDNA, PR3-ANCA) markers in SLE patients to evaluate their potential as diagnostic and prognostic indicators of renal dysfunction. **Methods**: A case-control study was conducted involving 68 participants (33 males, 35 females), divided into patient and healthy control groups. Serum levels of urea, creatinine, uric acid, anti-dsDNA antibodies, and PR3-ANCA were measured using standardized assays. Statistical comparisons were made using unpaired t-tests with a significance threshold of $p < 0.01$. **Results**: SLE patients showed significantly elevated levels of urea (101.1 ± 6.6 vs. 35.4 ± 1.2 mg/dL), creatinine (1.8 ± 0.6 vs. 0.5 ± 0.1 mg/dL), and uric acid (6.9 ± 1.2 vs. 4.5 ± 0.7 mg/dL) compared to controls (all $p < 0.0001$). Similarly, anti-dsDNA (45 ± 6.9 vs. 12.9 ± 1.8 IU/mL) and PR3-ANCA (2.6 ± 0.8 vs. 0.5 ± 0.3 IU/mL) levels were significantly higher in patients, indicating heightened autoimmune and vasculitis activity. **Conclusion**: The concurrent elevation of renal and immunological markers suggests that kidney dysfunction in SLE patients is closely linked to underlying autoimmune mechanisms. Anti-dsDNA and PR3-ANCA may serve as valuable biomarkers for diagnosing and monitoring renal involvement in SLE.

Keywords: SLE, Nephritis, dsDNA, RFTs, PR3-ANCA.

Introduction

Systemic Lupus Erythematosus (SLE) is a chronic, heterogeneous autoimmune disease characterized by a loss of immune tolerance, leading to widespread inflammation and tissue damage across multiple organ systems. As one of the most complex autoimmune disorders, SLE poses significant diagnostic and therapeutic challenges, profoundly impacting patients' quality of life and survival. This study seeks to address critical gaps in understanding SLE's pathogenesis and management, aiming to contribute to improved patient outcomes through innovative research.(Siegel & Sammaritano, 2024)

SLE affects approximately 20–150 individuals per 100,000 globally, with a striking female predominance (9:1 female-to-male ratio), particularly among those of childbearing age. Ethnic disparities are notable, with higher prevalence and severity observed in African American, Hispanic, and Asian populations compared to Caucasians. These demographic variations due to the interaction of genetic, environmental, and socioeconomic factors in disease susceptibility and progression.(Barber et al ., 2021; Duarte-García et al ., 2022)

The etiology of SLE involves multifactorial mechanisms, including genetic predisposition (e.g., polymorphisms in HLA, IRF5), dysregulated immune responses (e.g., hyperactivity of B cells, impaired clearance of apoptotic cells), and environmental triggers (e.g., UV light, infections). Key pathways such as type I interferon signaling and immune complex deposition drive systemic inflammation, leading to organ damage. Autoantibodies like anti-dsDNA and anti-Smith are hallmark biomarkers, though their role in prognosis remains incompletely understood.(Ameer et al., 2022; Akhil et al., 2023)

SLE's clinical presentation is highly variable, ranging from mild cutaneous involvement (e.g., malar rash, photosensitivity) to severe organ-threatening disease (e.g., lupus nephritis, neuropsychiatric lupus). Current diagnostic criteria (ACR/SLICC) emphasize multisystem involvement and serological markers, yet early detection remains elusive in many cases. Despite advances, SLE mortality remains elevated, particularly in refractory cases. (Lerkvaleekul et al., 2022). Therefore, the current study designed to evaluate Anti-dsDNA Abs and PR3-ANCA Abs in SLE patients with kidney involvement as attempt to enhance the diagnostic tools.

Materials and Methods

Study Design and Participants

This case-control study compared biochemical and immunological markers between patient and control groups. A total of 68 participants (33 males and 35 females) were enrolled. The patient group comprised individuals exhibiting clinical features suggestive of renal or autoimmune dysfunction, while the control group consisted of age- and sex-matched healthy individuals.

The samples were collected after written consent optioned from all participates who visited the private clinicals in Diyala province.

Inclusion criteria for patients were based on clinical suspicion of renal impairment or autoimmune disorders, while controls were excluded if they had a history of chronic diseases or recent infections.

Sample Collection and Biochemical Assays

All participants had venous blood drawn while they were fasting. Centrifugation (3000 rpm for 10 minutes) was used to separate the serum, which was then kept at -80°C until analysis. The following biochemical parameters were measured:

Urea, creatinine levels and uric acid (mg/dL) were quantified using standardized colorimetric assays (automated analyzer, Roche Diagnostics).

Immunological Marker Analysis

Using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (EUROIMMUN, Germany), anti-dsDNA and PR3-ANCA antibodies (IU/mL) were quantified in accordance with manufacturer's in instructions.

Statistical Analysis

The mean ± standard deviation is used to display the data. For normally distribution continuous variables, unpaired student's t-tests were used to compare groups (patient vs. control). P-values less than 0.01 were regarded as statistically significant. To do statistical studies, GraphPad Prism 8.0.1 was utilized, and figures were generated to visualize group differences (bar graphs for sex distribution and biomarker levels).

Results

The study compared biochemical and immunological markers between control and patient groups, with results visualized in Figures 1 to 5. The current study included 33 males and 35 females without significant difference, p value >0.01as shown in figure 1.

Urea levels (mg/dL) were assessed in both control and patient groups. The patient group exhibited significantly higher urea concentrations (35.4±1.2) mg/dl compared to the control group (101.1±6.6) mg/dl, p value <0.0001. Elevated urea levels are often indicative of impaired kidney function, suggesting potential renal dysfunction in the patient cohort. As shown in Figure 2.

According to creatinine levels (mg/dL), a key marker of renal health, were markedly elevated in the patient group relative to controls. The current study found the level of creatinine in patients' group (1.8± 0.6) was significantly higher than control group (0.5±0.1), p value <0.0001.

This increase aligns with the urea findings, further supporting the likelihood of compromised kidney filtration or chronic kidney disease in the patient population. Figure 3 illustrates a clear separation between the two groups, emphasizing the clinical relevance of this parameter.

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Uric acid concentrations (mg/dL) were higher in the patient group compared to controls. The level in patients' group was (6.9±1.2), while in control group was (4.5±0.7), and this refer to significant difference found between them, p value <0.0001 as shown in figure 4.

Elevated uric acid is commonly associated with conditions such as gout, metabolic syndrome, or inflammatory disorders. The data presented in Figure 4 suggest a potential link between the patient cohort's pathology and purine metabolism dysregulation.

Anti-double-stranded DNA (Anti-dsDNA) antibodies (IU/mL), a hallmark of systemic lupus erythematosus (SLE), were significantly elevated in the patient group (45±6.9) when compare with control group (12.9±1.8), p value <0.0001. as shown in figure 5.

Figure 4 demonstrates a stark contrast between the two groups, underscoring the autoimmune activity characteristic of SLE or related autoimmune conditions in the patients. These antibodies are critical for diagnosis and monitoring disease progression.

Proteinase 3 anti-neutrophil cytoplasmic antibodies (PR3-ANCA) was notably higher significantly in the patient group(2.6±0.8) when compare with control group(0.5±0.3). The pronounced difference shown in Figure 6 suggests active vasculitis processes, reinforcing the need for targeted immunological interventions in these patients.

Collectively, the results indicating a significant metabolic and immunological disturbances in the patient group. Elevated urea and creatinine levels point to renal impairment, while increased uric acid may reflect metabolic or inflammatory dysregulation. The pronounced presence of Anti-dsDNA Abs and PR3-ANCA highlights autoimmune and vasculitis pathologies, respectively.

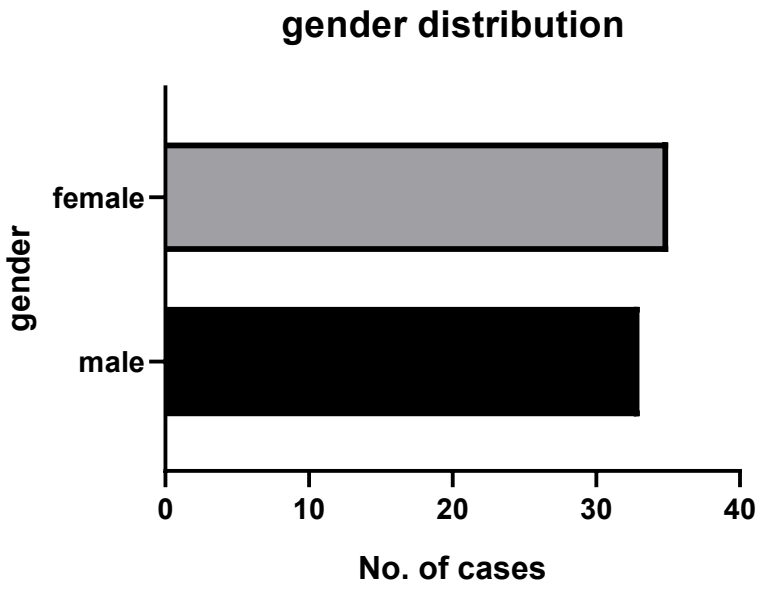

Figure 1: shown distribution of cases according the sex.

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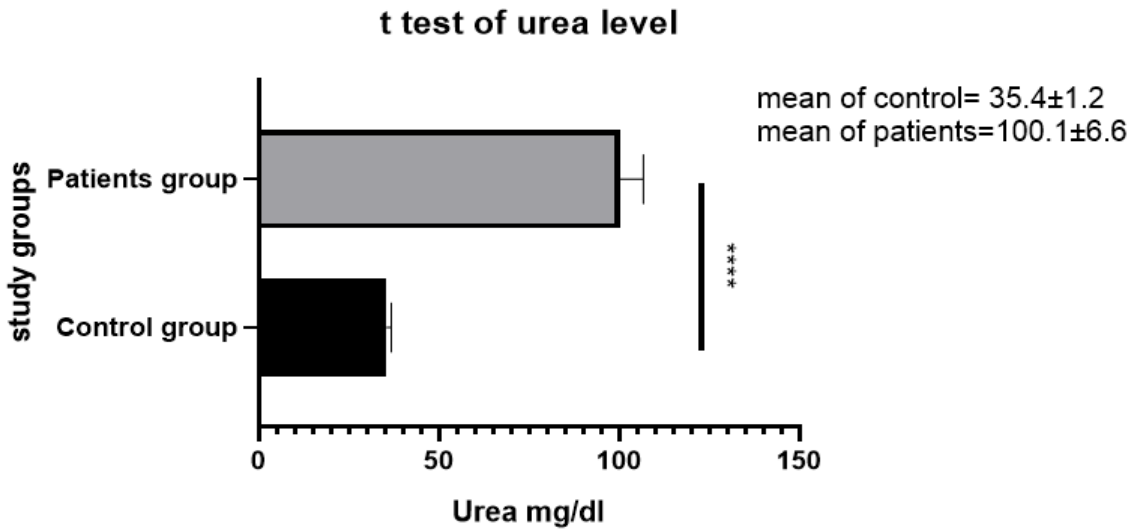

Figure 2. shows the level of urea mg/dl in control and patients' group.

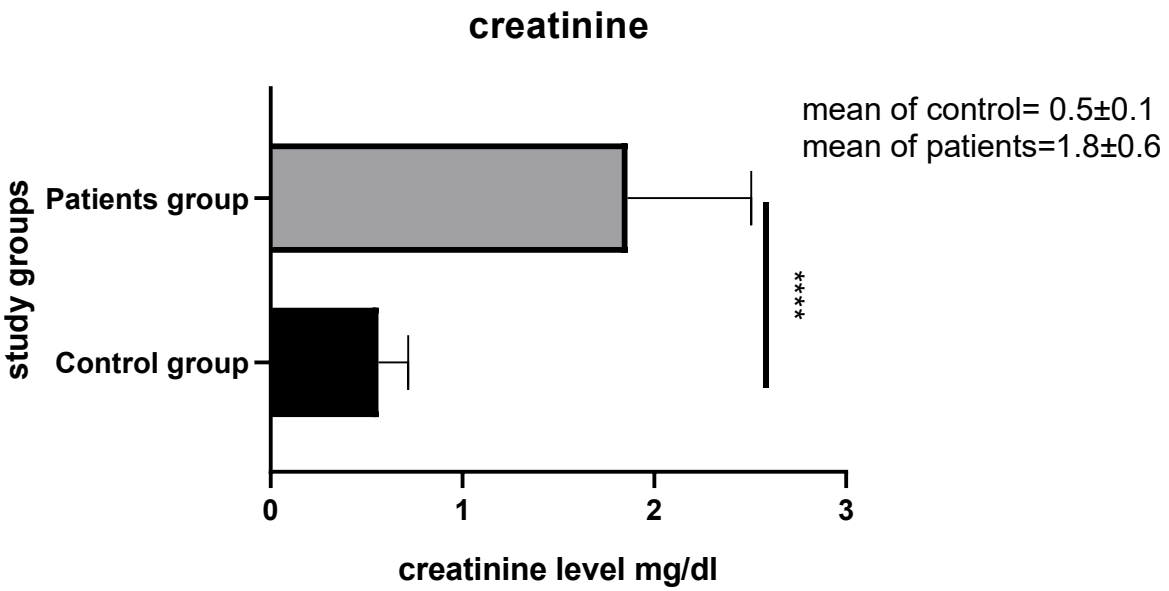

Figure 3. shows the level of creatinine mg/dl in control and patients' group.

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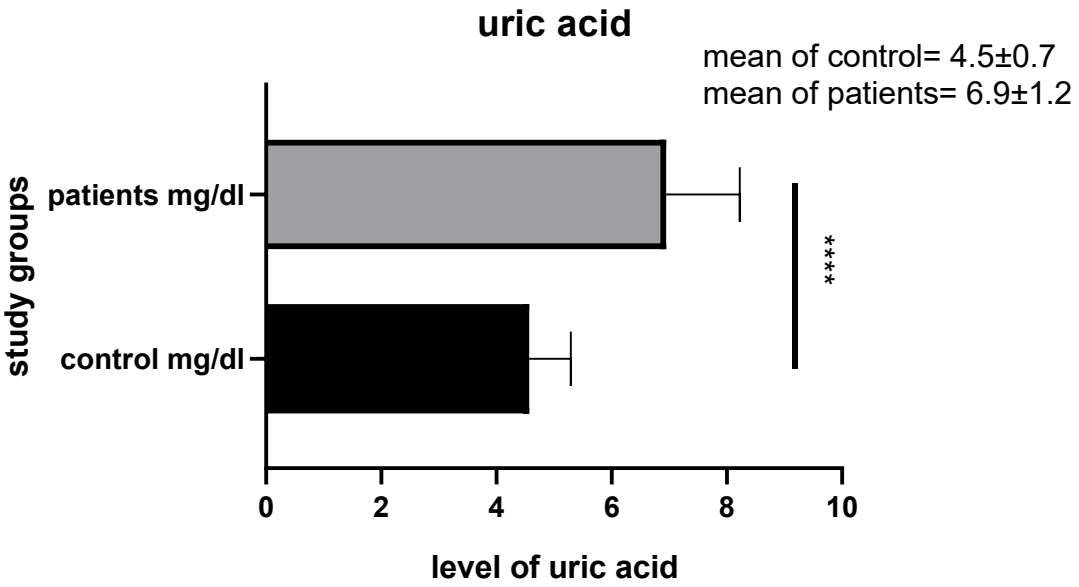

Figure 4. shows the level of uric acid mg/dl in control and patients' group.

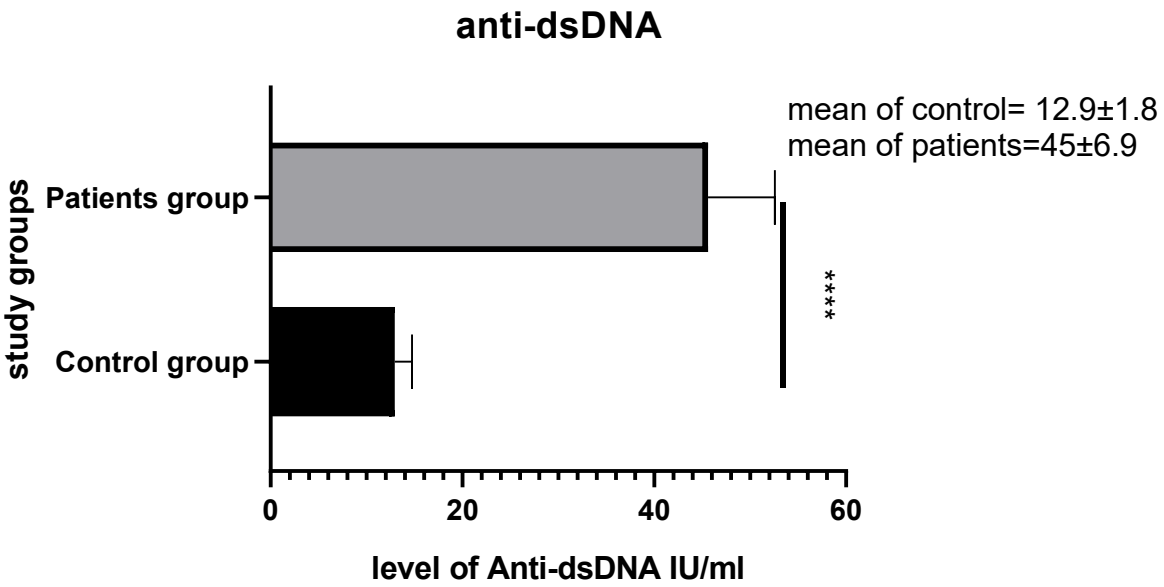

Figure 5. shows the level of Anti-dsDNA Abs IU/ml in control and patients' group.

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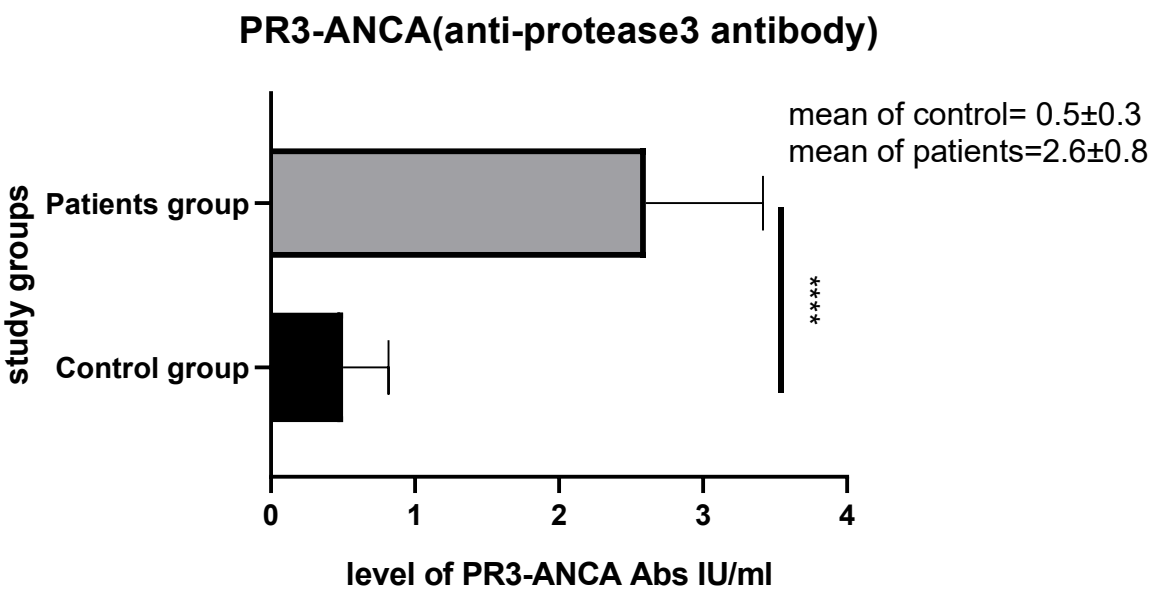

Figure 6. shows the level of PR3-ANCA in control and patients' group.

Discussion

This case-control study aimed to evaluate biochemical and immunological markers indicative of renal and autoimmune dysfunction. The statistically significant differences observed between patient and control groups.

with advances occurred in technologies, SLE mortality still elevated. Renal involvement, termed lupus nephritis (LN), is a severe and common complication of SLE, affecting approximately 40–60% of patients during their disease course. Immune complex deposition in the glomeruli, driven by autoantibodies such as anti-dsDNA and anti-C1q, triggers inflammation, leading to glomerulonephritis, tubular injury, and interstitial fibrosis. **(Gasparotto et al., 2020)**

The markedly elevated levels of urea and creatinine in the patient group ($p < 0.0001$) are strong indicators of compromised renal function. Urea levels (35.4 ± 1.2 mg/dL in patients vs. 101.1 ± 6.6 mg/dL in controls) and creatinine (1.8 ± 0.6 vs. 0.5 ± 0.1 mg/dL) reflect a substantial decline in glomerular filtration rate (GFR), a hallmark of chronic kidney disease (CKD) or acute kidney injury. These findings support the hypothesis that renal dysfunction is a major clinical feature among the studied patient cohort. Elevated creatinine, in particular, reinforces the presence of glomerular damage or impaired filtration, potentially associated with inflammatory or autoimmune nephropathies.

Significantly higher uric acid levels in the patient group (6.9 ± 1.2 vs. 4.5 ± 0.7 mg/dL, $p < 0.0001$) may signal metabolic disturbances. Hyperuricemia is known to be both a cause and consequence of renal dysfunction and is also implicated in inflammatory conditions such as gout and metabolic syndrome. In the context of autoimmune disorders, increased uric acid could reflect enhanced cellular turnover and oxidative stress. Therefore, its elevation in this

study aligns well with systemic involvement, whether metabolic or immunologically mediated. These finding agrees with previous studies (Reátegui-Sokolova et al., 2017; Elera-Fitzcarrald et al., 2020)

Immunological Markers

The robust elevation of anti-dsDNA antibodies (45 ± 6.9 vs. 12.9 ± 1.8 IU/mL, $p < 0.0001$) is highly suggestive of systemic lupus erythematosus (SLE) or lupus-like syndromes. Anti-dsDNA is a highly specific marker for SLE and correlates with disease activity and renal involvement (lupus nephritis). The observed antibody levels in patients may therefore support a diagnosis of autoimmune disease with systemic manifestations. Several previous studies consistent with current finding (Arbuckle et al.,2001; Alba et al., 2003; Enocsson et al., 2015) Similarly, the significantly increased PR3-ANCA levels (2.6 ± 0.8 vs. 0.5 ± 0.3, $p < 0.0001$) are indicative of ANCA-associated vasculitis (AAV), particularly granulomatosis with polyangiitis (GPA). PR3-ANCA is not only diagnostic but also prognostic in such conditions. Its presence in the patient group may denote active vasculitis contributing to renal injury and systemic inflammation. These results agrees with several previous study found PR3-ANCA levels elevated in patients with SLE when compared with healthy people.(Manolova et al., 2001; Kallenberg , 2008;Li et al., 2019)

In general, these results reveal a coherent pathophysiological picture: a combination of renal impairment and autoimmune activity. The simultaneous elevation of renal markers and specific autoantibodies (anti-dsDNA and PR3-ANCA) implies that the renal dysfunction observed may be immune-mediated, as seen in lupus nephritis or ANCA-associated glomerulonephritis. Furthermore, elevated uric acid may serve as a secondary biomarker reflecting both renal and systemic inflammatory burden.

Conclusion

This study highlights the diagnostic utility of integrating biochemical and immunological markers in patients with systemic lupus erythematosus. The significant elevations in urea, creatinine, and uric acid levels reflect underlying renal impairment, consistent with lupus nephritis. Concurrently, elevated anti-dsDNA and PR3-ANCA antibodies point toward active autoimmune and vasculitic processes. These findings collectively underscore the role of immune-mediated damage in SLE-related renal dysfunction. The combined use of these markers can enhance early diagnosis, disease monitoring, and personalized treatment strategies in SLE patients, particularly those at risk for nephritis.

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