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ARTICLE

Exploring the Relationship between Serum IL-33 Levels and Clinical Manifestations in Systemic Lupus Erythematosus: A Comprehensive Analysis

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Abstract

Aims/Background Systemic lupus erythematosus (SLE) is a complex autoimmune disorder characterised by an unpredictable disease course and multifaceted clinical presentations. Recent studies have highlighted the potential role of interleukin-33 (IL-33) in autoimmune diseases, but its exact relationship with SLE remains unclear. Therefore, to investigate the role of serum IL-33 levels as a biomarker, we evaluated its correlation with disease activity and organ damage in SLE patients.

Methods This retrospective analysis included 120 SLE patients from the Department of Rheumatology and Immunology, The Fourth Affiliated Hospital of Soochow University between January 2018 and December 2022. For comparative analysis, we recruited 60 healthy controls. Correlations between IL-33 levels and disease metrics were evaluated, and subgroup analyses were performed to explore specific clinical associations.

Results Our findings revealed that SLE patients had significantly higher serum IL-33 levels than the control group (258.7 $\pm$ 103.5 pg/mL vs 78.3 $\pm$ 32.6 pg/mL, $p < 0.001$). Furthermore, IL-33 levels showed a significant association with both disease activity (Systemic Lupus Erythematosus Disease Activity Index (SLEDAI)) (r = 0.68, $p < 0.001$) and cumulative organ damage (Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SLICC/ACR DI)) scores (r = 0.45, $p < 0.01$). Notably, patients with active disease (SLEDAI $\geq$6) exhibited substantially elevated IL-33 levels ($p < 0.001$). Patients with organ damage (SLICC/ACR DI $\geq$1) demonstrated significantly higher IL-33 levels than those without organ damage (289.6 $\pm$ 95.3 pg/mL vs 234.1 $\pm$ 86.2 pg/mL, $p = 0.001$), and those with renal involvement showed higher IL-33 levels ($p < 0.01$). Receiver operating characteristic (ROC) curve analysis revealed better diagnostic potential of serum IL-33 levels for SLE (area under the curve (AUC) = 0.892, 95% confidence interval (CI): 0.845–0.939, sensitivity = 84.2%, specificity = 82.7%) and for identifying active disease (AUC = 0.816, 95% CI: 0.752–0.880, sensitivity = 77.8%, specificity = 75.0%).

Conclusion Our findings suggest that serum IL-33 may serve as a promising biomarker for comprehensive SLE assessment, offering new avenues for monitoring disease progression and guiding therapeutic strategies.

Key words: systemic lupus erythematosus; interleukin-33; biomarker; disease progression; organ damage

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Introduction

Systemic lupus erythematosus (SLE) is a complex autoimmune disorder characterised by diverse clinical manifestations and unpredictable disease progression

(Harley and Sawalha, 2022; Aldakheel et al, 2023). Despite extensive research conducted on SLE, the exact mechanisms underlying its origin and progression remain poorly understood. Current evidence suggests that SLE results from a complex interaction among genetic predisposition, environmental stimuli, and immune system dysregulation (Nedeva, 2021).

Recent advancements in immunology have highlighted the potential roles of various cytokines in SLE pathophysiology. Among these, interleukin-33 (IL-33), a member of the IL-1 cytokine family, has gained significant attention due to its multifunctional role as a signalling molecule (Stojanovic et al, 2023). A recent study has underscored its crucial role in modulating immune responses and mediating inflammatory processes (Guo et al, 2022). IL-33 exhibits pleiotropic effects on the immune system, acting as an alarmin to initiate immediate defense mechanisms and contributing to specialized, targeted immune reactions (Ramezani et al, 2022; Sarrand and Soyfoo, 2022).

Evaluating disease activity and cumulative organ damage in SLE presents significant challenges in clinical practice. While current methods for assessing lupus severity and progression are widely adopted in clinical settings, these approaches face several challenges. One important issue is observer variability, in which different clinicians assign varying scores to the same patient, impacting the consistency of evaluations. For instance, the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), a tool for measuring disease activity, and the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SLICC/ACR DI), the primary tool for quantifying cumulative damage, have been extensively used but are not without their limitations. These limitations underscore the need for more objective and responsive evaluation techniques to enhance SLE management (Cruciani et al, 2023; Lacerda et al, 2021).

Addressing these challenges emphasizes identifying unbiased biological indicators in lupus research. Such markers should precisely detect active disease processes while quantifying the cumulative impact of the condition over time. Moreover, these dual-purpose molecular signatures would significantly improve SLE monitoring and management, enabling greater accuracy and responsiveness (Plevris and Lees, 2022).

The current study seeks to elucidate the complex relationship between circulating IL-33 levels and established disease metrics in SLE. By evaluating these associations, we aim to assess the viability of IL-33 as a novel and multifaceted molecular indicator for comprehensive lupus evaluation and monitoring. The outcomes of this study could help develop improved disease monitoring strategies and refine patient care approaches in SLE management.

Methods

Patient Selection and Study Design

This retrospective study included 120 SLE patients who underwent treatment at the Department of Rheumatology and Immunology, The Fourth Affiliated Hospital of Soochow University, between January 2018 and December 2022. As detailed

in Fig. 1, 186 SLE patients were initially assessed for eligibility. All study participants met the 2019 European League Against Rheumatism/American College of Rheumatology diagnostic and classification criteria for SLE (Aringer et al, 2019). Inclusion criteria were as follows: (1) individuals aged ≥18 years; (2) individuals meeting the 2019 European League Against Rheumatism and the American College of Rheumatology (EULAR/ACR) classification criteria for SLE; and (3) individuals with availability of complete clinical and laboratory data. However, exclusion criteria were as follows: (1) individuals with concurrent autoimmune disorders (n = 18); (2) severe infections (n = 15); (3) other malignancies (n = 12); (4) pregnancy (n = 11); and (5) those used medications affecting IL-33 levels (e.g., high-dose corticosteroids within the past month) (n = 10).

Furthermore, to establish a baseline comparison, a cohort of 60 healthy volunteers was included. The control group was selected to compare the SLE patients regarding age and gender distribution. Following the predetermined inclusion-exclusion criteria, 120 SLE patients were included in the final analysis.

Quantification of Serum IL-33

Serum IL-33 levels were quantified using a high-sensitivity, validated, commercially available enzyme-linked immunosorbent assay (ELISA) platform (Catalog D3300B, R&D Systems, Minneapolis, MN, USA), specifically designed for the precise detection of human IL-33 in serum. Quantification was performed in strict adherence to standardized laboratory procedures, with rigorous experimental settings and quality control measures integrated throughout the analytical workflow to ensure reliability and reproducibility of IL-33 measurements. Furthermore, to enhance data precision and minimize measurement variability, each sample underwent duplicate analysis. The resulting paired values were then averaged, and the arithmetic mean was used as the final data point for all subsequent statistical interpretations.

Clinical Assessment Tools

To assess the severity of lupus manifestations, we employed the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K), a comprehensive, multi-parameter clinical index widely accepted in rheumatology (Gladman et al, 2002). This tool assigns numerical values to various disease indicators, resulting in a composite score ranging from 0 to 105. Patients with a score of 6 or higher were classified as having active disease (Cruciani et al, 2023).

Moreover, cumulative organ damage was determined using the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SLICC/ACR DI) (Dayal et al, 2002). This index evaluates irreversible damage across 12 organ systems, with scores ranging from 0 to 47. Both assessments were performed by experienced rheumatologists blinded to the IL-33 results, ensuring unbiased evaluation.

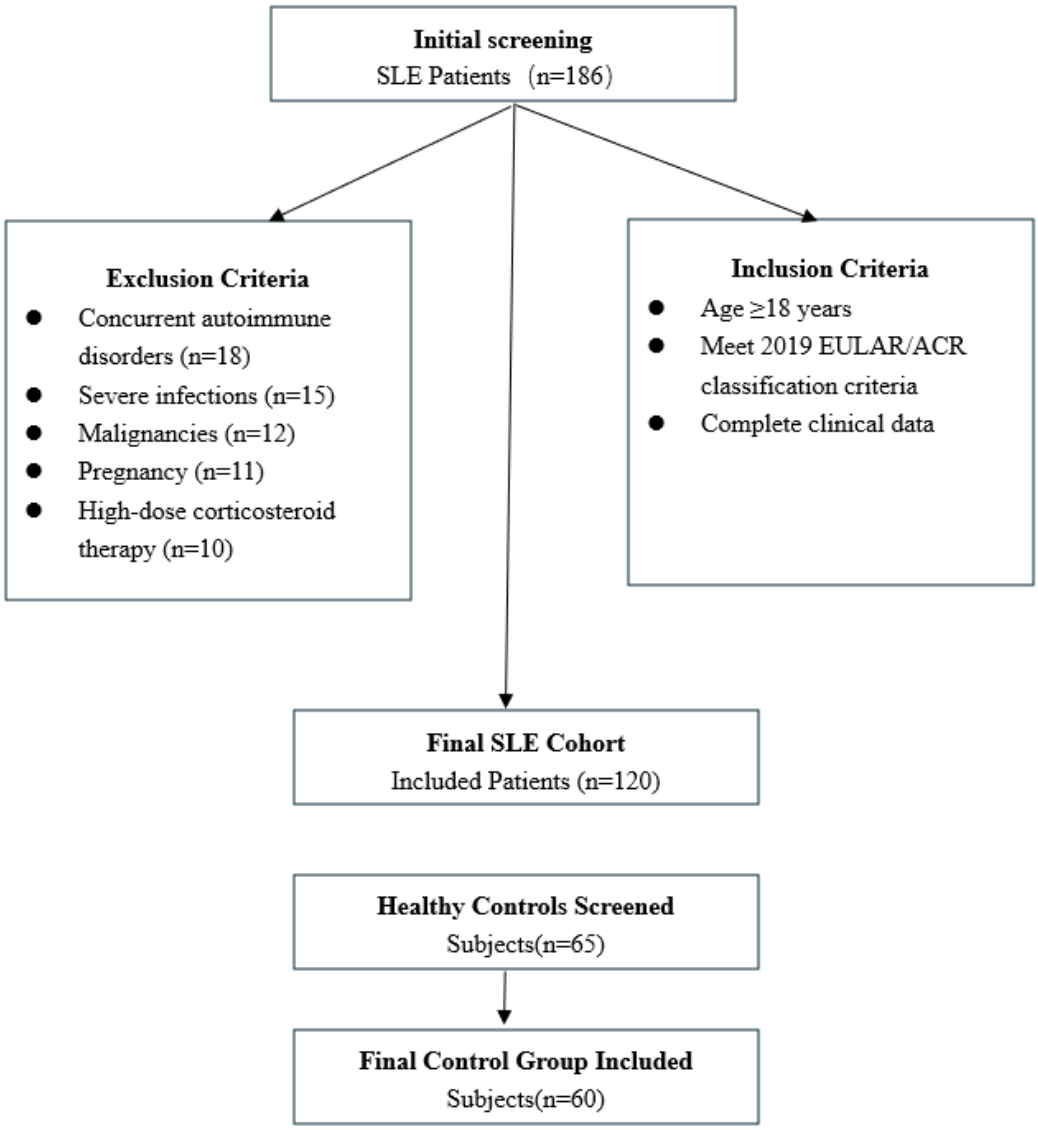

Fig. 1. A flow chart of study subject selection. This flowchart illustrates the patient selection process for a study on systemic lupus erythematosus (SLE). The inclusion criteria mention the 2019 European League Against Rheumatism and the American College of Rheumatology (EULAR/ACR) classification criteria. The initial screening included 186 SLE patients, with various exclusion criteria applied. The final SLE cohort consisted of 120 patients, while 60 subjects were included in the final control group.

Statistical Analysis

Statistical analysis was performed using Statistical Product and Service Solutions (SPSS) version 25.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed using the Shapiro-Wilk test. Normally distributed continuous variables were presented as means and standard deviations, while non-normally distributed variables were described as medians and interquartile ranges. Comparative analyses between groups were conducted using parametric or non-parametric tests, depending on the distribution characteristics of the data. To evaluate the diagnostic potential of serum IL-33, receiver operating characteristic (ROC) curve analysis was performed. The area under the curve (AUC), sensitivity, speci-

Table 1. Comparison of baseline characteristics and serum IL-33 levels between SLE patients and healthy controls.

Characteristic	SLE patients (n = 120)	Normal controls (n = 60)	t/χ^2	p-value
Age (years, $\bar{x} \pm s$)	38.6 ± 12.3	37.9 ± 11.8	0.368	0.713
Gender (female/male)	105/15	52/8	0.022	0.881
Disease duration (years, $\bar{x} \pm s$)	7.2 ± 5.4	-	-	-
Serum IL-33 (pg/mL, $\bar{x} \pm s$)	258.7 ± 103.5	78.3 ± 32.6	13.475	<0.001

SLE, systemic lupus erythematosus; IL-33, interleukin-33.

ficity, and optimal cutoff values were calculated. For discrete data, chi-square tests or Fisher's exact tests were applied as appropriate. The associations between serum IL-33 levels and clinical indices were evaluated using Pearson's correlation coefficient for normally distributed data or Spearman's rank correlation coefficient for non-normally distributed data. To identify independent factors influencing key disease metrics, we constructed multivariate linear regression models by incorporating potential explanatory predictors to account for variations in disease activity and cumulative damage scores. A two-tailed hypothesis with a significance threshold of $p < 0.05$ was implemented throughout the analyses for statistical inference.

Results

Demographic and Clinical Characteristics

The study included 180 participants who were divided into two distinct groups. The primary cohort consisted of 120 individuals diagnosed with SLE, predominantly female (87.5%, n = 105), with a mean age of 38.6 ± 12.3 years. The average disease duration within this group was 7.2 ± 5.4 years, with substantial individual variability. For comparative analysis, 60 healthy volunteers were included, matched to the SLE cohort in age and gender distribution, maintaining a similar female-to-male ratio. Statistical analysis revealed comparable demographic profiles between the SLE and control groups. The mean age of the control group was 37.9 ± 11.8 years ($p > 0.05$) and the ratio of females was 86.7% ($p > 0.05$), with no statistically significant differences observed (Table 1).

Comparison Serum IL-33 Levels in SLE Patients and Healthy Controls

Analysis of serum biomarker concentrations revealed significant differences between the lupus and healthy control groups, as detailed in Table 1. SLE patients had substantially higher circulating IL-33 levels than the healthy control group (258.7 ± 103.5 pg/mL vs 78.3 ± 32.6 pg/mL, $p < 0.001$). Furthermore, lupus patients exhibited, on average, more than a threefold increase in serum IL-33 concentrations.

IL-33 as an Indicator of Disease Intensity

Statistical analysis revealed a strong positive relationship between circulating IL-33 levels and quantitative measures of lupus activity. Serum IL-33 levels showed a significant correlation with SLEDAI scores (r = 0.68, $p < 0.001$), suggest-

ing that higher IL-33 levels closely align with increased disease severity. Further investigation revealed substantial variation in IL-33 levels between patients experiencing active disease flares and those in remission. Patients with active disease (SLEDAI $\geq$6) showed significantly higher IL-33 levels compared to those with inactive disease (312.5 $\pm$ 98.7 pg/mL vs 178.2 $\pm$ 67.4 pg/mL, t = 8.245, $p < 0.001$) (Table 2, Fig. 2A).

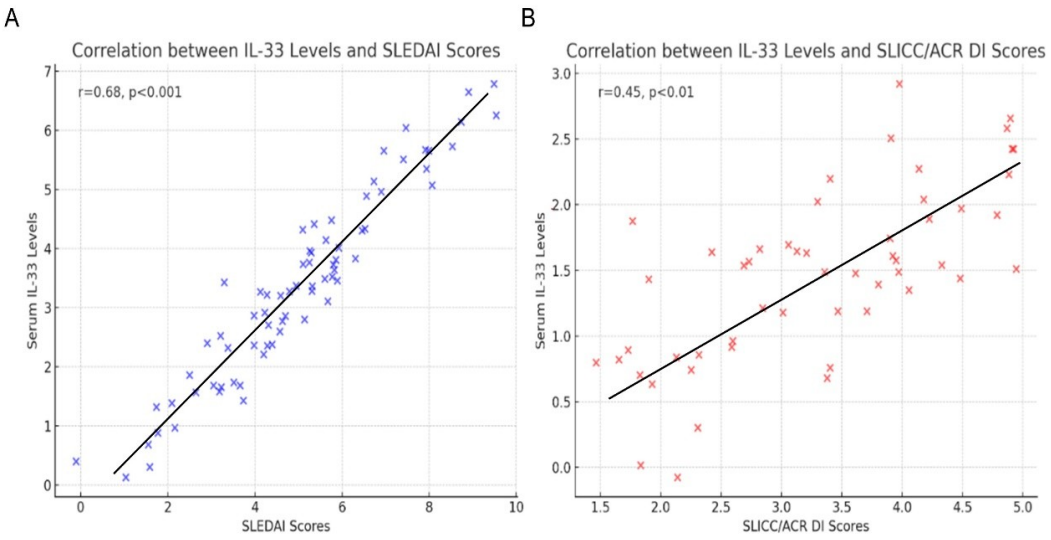

Fig. 2. Analyzing the relationship between circulating IL-33 and key lupus metrics. This figure illustrates the associations between serum IL-33 concentrations and two critical measures of SLE progression. (A) Lupus activity index: Demonstrating how IL-33 levels correspond with standardized disease activity scores. (B) Cumulative organ damage assessment: Depicting the connection between IL-33 and long-term physiological impact quantification.

IL-33 as a Marker of Cumulative Organ Damage

We found a significant association between circulating IL-33 and indices of long-term physiological impairment in lupus patients. A moderate positive correlation was observed between serum IL-33 levels and SLICC/ACR DI scores (r = 0.45, $p < 0.01$), suggesting IL-33's potential role in reflecting cumulative systemic damage. Stratifying patients based on organ involvement yielded intriguing results. Patients with signs of tissue damage (SLICC/ACR DI $\geq$1) demonstrated substantially elevated IL-33 levels compared to those without detectable organ dysfunction (289.6 $\pm$ 95.3 pg/mL vs 234.1 $\pm$ 86.2 pg/mL, t = 3.316, p = 0.001) (Table 2, Fig. 2B).

ROC Curve Analysis for IL-33 in SLE Assessment

To evaluate the diagnostic potential of serum IL-33, ROC curve analysis was performed. Serum IL-33 levels showed an AUC of 0.892 in distinguishing SLE patients from healthy controls, with an optimal cutoff value of 125.6 pg/mL, yielding a sensitivity of 84.2% and a specificity of 82.7%. Furthermore, patients with active disease (SLEDAI $\geq$6) had the AUC of 0.816, with an optimal cutoff value of 245.3 pg/mL, providing a sensitivity of 77.8% and specificity of 75.0% (Fig. 3).

Table 2. IL-33 as a potential indicator of lupus progression and systemic impact.

Characteristic	n	Serum IL-33 (pg/mL, $\bar{x} \pm s$)	*t*-value	*p*-value
SLEDAI score			8.245	<0.001
≥6 (active)	72	312.5 ± 98.7		
<6 (inactive)	48	178.2 ± 67.4		
SLICC/ACR DI score			3.316	0.001
≥1 (with organ damage)	53	289.6 ± 95.3		
0 (without organ damage)	67	234.1 ± 86.2		
Renal involvement			3.697	<0.01
Yes	42	298.3 ± 89.7		
No	78	238.5 ± 78.6		

Note: SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; SLICC/ACR DI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index.

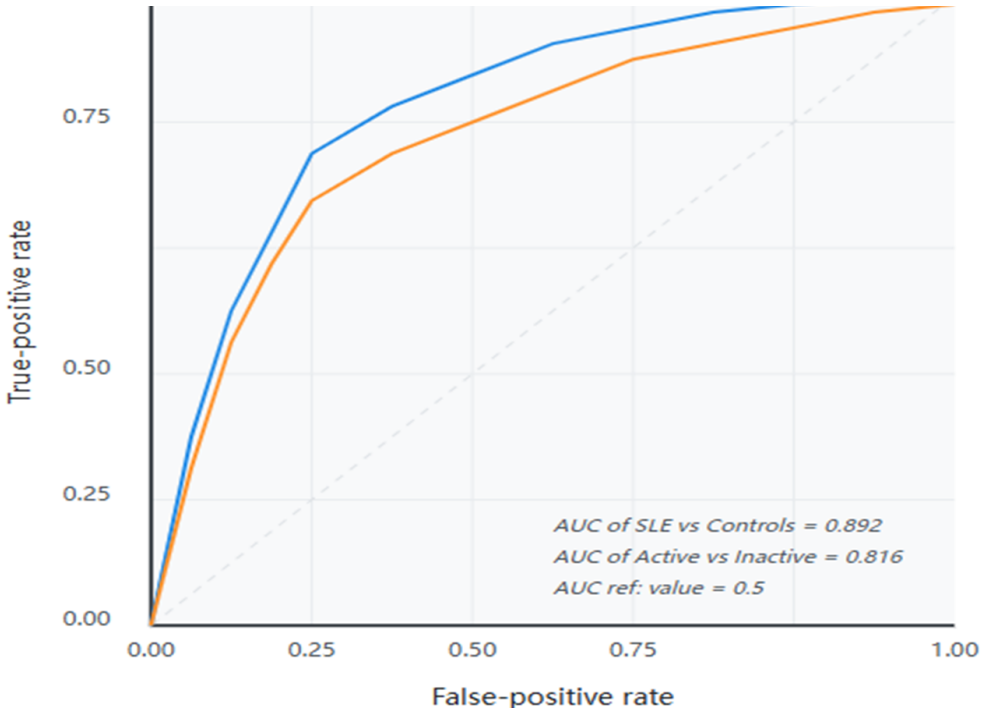

Fig. 3. AUC curve analysis for serum IL-33 in SLE diagnosis and disease activity assessment. The blue line represents the AUC curve for discriminating SLE patients from healthy controls (AUC = 0.892, 95% CI: 0.845–0.939, $p < 0.001$), with an optimal cutoff value of 125.6 pg/mL (sensitivity: 84.2%, specificity: 82.7%). The orange line shows the ROC curve for identifying active disease (SLEDAI ≥6) in SLE patients (AUC = 0.816, 95% CI: 0.752–0.880, $p < 0.001$), with an optimal cutoff value of 245.3 pg/mL (sensitivity: 77.8%, specificity: 75.0%). The diagonal dashed line represents the reference line (AUC = 0.5). AUC, area under the curve; CI, confidence interval; SLEDAI, SLE Disease Activity Index.

Subgroup Analysis

Further stratification of the study cohort based on renal involvement yielded compelling results. A subset of participants diagnosed with lupus-associated kid-

Table 3. Multifactorial analysis of IL-33's predictive capability for lupus severity indices.

Dependent variable	Independent variable	Standardized β	SE	95% CI	*t*-value	*p*-value
SLEDAI score	Serum IL-33 level	0.68	0.076	0.531–0.829	8.952	<0.001
SLICC/ACRDI score	Serum IL-33 level	0.45	0.085	0.283–0.617	5.287	0.0015

SE, standard error; CI, confidence interval.

ney complications demonstrated substantially elevated circulating IL-33 levels. Patients with renal involvement showed significantly higher IL-33 levels than those without apparent renal manifestations (298.3 ± 89.7 pg/mL vs 238.5 ± 78.6 pg/mL, $p < 0.01$, Table 2). Such a disparity in cytokine profiles between these two subgroups indicates a possible mechanistic link between IL-33 and lupus-induced nephropathy.

Multifactorial Predictive Modeling of Disease Parameters

Advanced statistical modelling, accounting for demographic variables and disease chronicity, revealed the independent influence of IL-33 on key lupus indices. Multivariate linear regression analysis showed that serum IL-33 levels were independently associated with SLEDAI scores (standardized $\beta = 0.68$, $p < 0.001$) and SLICC/ACR DI scores (standardized $\beta = 0.45$, $p = 0.0015$), even after adjusting for age, gender, and disease duration (Table 3).

Discussion

Our in-depth analysis provides compelling evidence supporting the role of IL-33 as an innovative indicator of lupus assessment. This study revealed a significant variation in circulating IL-33 levels between the SLE and healthy control groups. Furthermore, a robust association was found between IL-33 levels and established metrics of lupus severity. Notably, IL-33 levels exhibited strong correlations with both measures of active disease and indicators of long-term physiological alterations. These findings underscore the versatility of IL-33 as a potential biomarker, capable of detecting both acute disease states and cumulative impacts in SLE.

The increased IL-33 levels observed in lupus patients resonate with a growing body of evidence implicating this cytokine in autoimmune dysregulation. It is important to note that while IL-33 is elevated in various inflammatory conditions, including skin inflammatory diseases, ROC analysis demonstrates its significant discriminative ability for SLE (AUC = 0.892). These observations suggest that IL-33 could be a potential component of a comprehensive diagnostic approach for SLE. This concordance with the existing scientific landscape reinforces the notion of IL-33's pivotal role in the complex network of immune-mediated disorders. Such alignment not only validates our results but also contributes to the broader understanding of IL-33's significance in autoimmune pathobiology (Cayrol, 2021; Cayrol and Girard, 2022). Importantly, our study extends beyond establishing an association, revealing robust correlations between IL-33 levels and both SLEDAI and SLICC/ACR DI scores. The robustness of the association between IL-33 levels and lupus manifestations, even after adjusting for confounding factors, highlights its

potential as an independent biomarker in SLE. This statistical robustness suggests that IL-33 might offer unique insights into lupus pathology, serving as a reliable indicator of both disease severity and progression over time, independent of other clinical or demographic factors (Yi et al, 2022). Furthermore, the strong association between IL-33 and SLEDAI scores is particularly crucial. Current approaches for evaluating SLE disease activity, such as LEDAI, rely heavily on composite indices which, while effective, have inherent limitations including subjectivity and delayed responsiveness to disease changes. IL-33, as a potentially more objective and responsive biomarker, could address these limitations, offering improved disease monitoring and informing treatment decisions in clinical practice (Guimarães et al, 2022).

Moreover, the association between IL-33 and SLICC/ACR DI scores ($r = 0.45$, $p < 0.01$) suggests that this cytokine may serve as a biomarker of both active disease and cumulative organ damage. This dual capability makes IL-33 an exceptionally valuable indicator in the long-term management of SLE patients, offering potential benefits for acute care decisions and long-term prognostication. The ROC analysis further supports this utility, indicating strong discriminative performance for identifying active disease (AUC = 0.816).

Our subgroup analysis revealed that patients with lupus-associated renal complications had significantly elevated IL-33 levels. This distinctive cytokine profile among patients with kidney involvement suggests exciting avenues for future research. The observed association between increased IL-33 levels and lupus nephritis highlights the significance of this cytokine in organ-specific manifestations of SLE. These observations not only signify the tissue-specific roles of IL-33 but also raise compelling questions about its mechanistic contributions to renal pathology in lupus (Lee and Song, 2023; Sarrand and Soyfoo, 2022).

Interpreting our results from a mechanistic perspective supports the notion that IL-33 is crucial in lupus pathogenesis. The multifaceted immunomodulatory capabilities of IL-33, including both the innate and adaptive immune pathways, position it as a potential driver of the sustained inflammatory milieu characteristic of SLE. The correlation between higher IL-33 levels, elevated disease severity, and increased organ involvement suggests that this cytokine actively contributes to lupus progression. Rather than a passive indicator, IL-33 emerges as a crucial mediator in the cascade of events leading to tissue injury in SLE.

This study presents several strengths, including the use of standardized assessment protocols, comprehensive statistical analyses such as ROC curve analysis, and careful consideration of confounding factors. Our findings are supported by robust statistical correlations between IL-33 levels and established disease metrics. Additionally, our rigorous statistical analysis, including multivariate regression, supports the validity of our findings. However, certain limitations must be addressed. The cross-sectional design precludes assessment of temporal relationships between IL-33 levels and disease progression. While we adjusted for several confounding factors, unmeasured variables may affect the observed associations. Although our sample size was sufficient for detecting major associations, it may lack the power to observe subtle relationships or allow extensive subgroup analyses. Furthermore,

the study population, with a mean disease duration exceeding 7 years, may not sufficiently represent early-stage SLE cases.

Future investigations should focus on longitudinal studies to evaluate variations in IL-33 levels over time with respect to disease activity, treatment responses, and the prediction of disease flares. Further investigation of IL-33's role in organ-specific manifestations, especially renal involvement, would provide valuable insights. Additionally, exploring IL-33's interactions with other inflammatory mediators could enhance our understanding of SLE pathogenesis. These research efforts could offer valuable insights into the potential therapeutic approaches targeting IL-33, ultimately enhancing SLE disease management and treatment outcomes.

Conclusion

In conclusion, this study presents compelling evidence supporting the role of serum IL-33 as a promising biomarker in SLE, as indicated by comprehensive statistical analyses, including correlation studies and ROC curve analysis (AUC = 0.892). The strong associations of IL-33 with both SLEDAI ($r = 0.68$, $p < 0.001$) and SLICC/ACR DI scores ($r = 0.45$, $p < 0.01$) suggest its versatility as a potential indicator of disease activity and cumulative organ damage. These findings underscore the significance of IL-33 as an integrative biomarker, offering insights into multiple facets of lupus pathology.

Beyond academic significance, our findings bridge the gap between basic science and clinical applications in lupus management. By elucidating the intricate molecular mechanisms underlying SLE, this study improves the prospect of using IL-33 as a promising tool for disease surveillance. This biomarker promises to offer clinicians a more nuanced and responsive approach for monitoring lupus progression and tailoring treatment strategies more effectively. As our understanding of the intricate mechanisms of SLE evolves, biomarkers such as IL-33 are likely to play a crucial role in tailoring patient care. This advancement offers enhanced outcomes for those affected by this complex disease, offering a new era of precision therapy in lust management.

Key Points

- Serum IL-33 levels are significantly higher in SLE patients than in healthy controls (258.7 ± 103.5 pg/mL vs 78.3 ± 32.6 pg/mL, $p < 0.001$).
- IL-33 demonstrates strong diagnostic potential for SLE (ROC curve AUC = 0.892) and active disease identification (AUC = 0.816).
- IL-33 levels positively correlate with both disease activity (SLEDAI, $r = 0.68$) and cumulative organ damage (SLICC/ACR DI, $r = 0.45$).
- Patients with active SLE and renal involvement show significantly higher IL-33 levels.
- Serum IL-33 is an independent indicator of SLE disease activity and organ damage.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

XL conceived and designed the study. XL and SY developed the methodology. XL conducted the formal analysis of the data. SY and YX carried out the investigation and data collection. XL and SY were responsible for data curation. The original draft of the manuscript was written by XL and SY. All authors contributed to the important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Fourth Affiliated Hospital of Soochow University prior to commencement (No. 2024-240615). Written informed consent was obtained from all participants before their enrollment in the study.

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Conflict of Interest

The authors declare no conflict of interest.

References

Aldakheel FM, Alshanqiti MA, Alduraywish SA, Alshammary AF, Dabwan KH, Syed R. Clinical Assessment of Cytokine Profiles and Haematological Parameters in Patients with Systemic Lupus Erythematosus: A Cross-Sectional Study from Saudi Arabia. Frontiers in Bioscience (Landmark Edition). 2023; 28: 358. https://doi.org/10.31083/j.fbl2812358

Aringer M, Costenbader K, Daikh D, Brinks R, Mosca M, Ramsey-Goldman R, et al. 2019 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Systemic Lupus Erythematosus. Arthritis & Rheumatology. 2019; 71: 1400–1412. https://doi.org/10.1002/art.40930

Cayrol C, Girard JP. Interleukin-33 (IL-33): A critical review of its biology and the mechanisms involved in its release as a potent extracellular cytokine. Cytokine. 2022; 156: 155891. https://doi.org/10.1016/j.cyto.2022.155891

Cayrol C. IL-33, an Alarmin of the IL-1 Family Involved in Allergic and Non Allergic Inflammation: Focus on the Mechanisms of Regulation of Its Activity. Cells. 2021; 11: 107. https://doi.org/10.3390/cells11010107

Cruciani C, Zen M, Gatto M, Morand E, Doria A. Assessment of disease activity and damage in SLE: Are we there yet? Best Practice & Research. Clinical Rheumatology. 2023; 37: 101896. https://doi.org/10.1016/j.berh.2023.101896

Dayal NA, Gordon C, Tucker L, Isenberg DA. The SLICC damage index: past, present and future. Lupus. 2002; 11: 261–265. https://doi.org/10.1191/0961203302lu190sa

Gladman DD, Ibañez D, Urowitz MB. Systemic lupus erythematosus disease activity index 2000. The Journal of Rheumatology. 2002; 29: 288–291.

Guimarães JDAR, Furtado SDC, Lucas ACDS, Mori B, Barcellos JFM. Diagnostic test accuracy of novel biomarkers for lupus nephritis-An overview of systematic reviews. PLoS ONE. 2022; 17: e0275016. https://doi.org/10.1371/journal.pone.0275016

Guo H, Bossila EA, Ma X, Zhao C, Zhao Y. Dual Immune Regulatory Roles of Interleukin-33 in Pathological Conditions. Cells. 2022; 11: 3237. https://doi.org/10.3390/cells11203237

Harley ITW, Sawalha AH. Systemic lupus erythematosus as a genetic disease. Clinical Immunology. 2022; 236: 108953. https://doi.org/10.1016/j.clim.2022.108953

Lacerda MI, de Jesús GRR, Dos Santos FC, de Jesús NR, Levy RA, Klumb EM. The SLICC/ACR Damage Index (SDI) may predict adverse obstetric events in patients with systemic lupus erythematosus. Lupus. 2021; 30: 1966–1972. https://doi.org/10.1177/09612033211045061

Lee YH, Song GG. Associations between blood IL-33 levels and IL-33 gene polymorphisms with susceptibility to systemic lupus erythematosus: A meta-analysis. Lupus. 2023; 32: 1179–1187. https://doi.org/10.1177/09612033231193788

Nedeva C. Inflammation and Cell Death of the Innate and Adaptive Immune System during Sepsis. Biomolecules. 2021; 11: 1011. https://doi.org/10.3390/biom11071011

Plevris N, Lees CW. Disease Monitoring in Inflammatory Bowel Disease: Evolving Principles and Possibilities. Gastroenterology. 2022; 162: 1456–1475.e1. https://doi.org/10.1053/j.gastro.2022.01.024

Ramezani F, Babaie F, Aslani S, Hemmatzadeh M, Mohammadi FS, Gowhari-Shabgah A, et al. The Role of the IL-33/ST2 Immune Pathway in Autoimmunity: New Insights and Perspectives. Immunological Investigations. 2022; 51: 1060–1086. https://doi.org/10.1080/08820139.2021.1878212

Sarrand J, Soyfoo M. Involvement of IL-33 in the Pathophysiology of Systemic Lupus Erythematosus: Review. International Journal of Molecular Sciences. 2022; 23: 3138. https://doi.org/10.3390/ijms23063138

Stojanovic B, Gajovic N, Jurisevic M, Stojanovic MD, Jovanovic M, Jovanovic I, et al. Decoding the IL-33/ST2 Axis: Its Impact on the Immune Landscape of Breast Cancer. International Journal of Molecular Sciences. 2023; 24: 14026. https://doi.org/10.3390/ijms241814026

Yi XM, Lian H, Li S. Signaling and functions of interleukin-33 in immune regulation and diseases. Cell Insight. 2022; 1: 100042. https://doi.org/10.1016/j.cellin.2022.100042