**Uludağ Üniversitesi Tıp Fakültesi Dergisi**
***Journal of Uludağ University Medical Faculty***
**52, 1818835, 2026**
**DOI: https://doi.org/10.32708/uutfd.1818835**

ORIGINAL RESEARCH

# The Role of Survivin in Systemic Lupus Erythematosus: Its Relationship with Diagnosis and Disease Activity

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**ABSTRACT**

Systemic Lupus Erythematosus (SLE) is a chronic connective tissue disease of unclear etiopathogenesis characterized by affecting multiple organs and systems. Survivin, an apoptosis inhibitor protein (IAP) family member is involved in apoptosis, cell division, development and differentiation. In the pathogenesis of SLE, increased apoptosis is thought to play a significant role. Therefore, this study aims to investigate the relationship between survivin levels and disease activity, etiopathogenesis, and biomarkers related to apoptosis and inflammation in patients with SLE. The study included 36 patients with SLE, 17 patients with Sjögren's syndrome (SjS) and 29 healthy controls who applied to the department, met the eligibility criteria and were non-consecutively enrolled between September 2019 and March 2020. Blood and urine samples were collected and analyzed using enzyme-linked immunoassay (ELISA) method. SLE activity was assessed using SLE Disease Activity Index (SLEDAI) and Systemic Lupus International Collaborating Clinics (SLICC)/American College of Rheumatology (ACR) criteria. SjS activity was assessed using EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI). Plasma survivin levels were significantly lower in SLE patients compared to healthy controls ($p<0.001$). A strong positive correlation was found between plasma survivin levels and apoptotic and inflammatory markers in SLE patients ($p<0.001$). No correlation was found between urinary survivin levels, plasma survivin levels and inflammatory, apoptotic markers in SLE ($p>0.05$). No significant correlation was found between SLEDAI scores and either plasma or urinary survivin levels ($p > 0.05$). This study shows that survivin holds significant potential in the diagnosis, disease monitoring, and pathophysiological understanding of SLE, providing foundational data for future research.

**Keywords: Survivin. Systemic lupus erythematosus.**

**Sistemik Lupus Eritematozus'ta Survivinin Rolü: Tanı ve Hastalık Aktivitesi ile İlişkisi**

**ÖZET**

Sistemik Lupus Eritematozus (SLE), etiyopatogenezi tam olarak aydınlatılamamış, birden fazla organ ve sistemi etkileyen kronik bir bağ dokusu hastalığıdır. Apoptoz inhibitörü protein (IAP) ailesinin bir üyesi olan survivin; apoptoz, hücre bölünmesi, gelişim ve farklılaşma süreçlerinde rol almaktadır. SLE patogenezinde artmış apoptozun önemli bir rol oynadığı düşünülmektedir. Bu nedenle bu çalışma, SLE hastalarında survivin düzeyleri ile hastalık aktivitesi, etiyopatogenez ve apoptoz ile inflamasyonla ilişkili biyobelirteçler arasındaki ilişkiyi araştırmayı amaçlamaktadır.

Çalışmaya, Eylül 2019 ile Mart 2020 tarihleri arasında başvuran, uygunluk kriterlerini karşılayan ve ardışık olmayan şekilde çalışmaya dahil edilen 36 SLE hastası, 17 Sjögren sendromu (SjS) hastası ve 29 sağlıklı kontrol dahil edilmiştir. Kan ve idrar örnekleri toplanmış ve enzim bağlantılı immünosorbent analiz (ELISA) yöntemi kullanılarak analiz edilmiştir. SLE hastalık aktivitesi, SLE Hastalık Aktivite İndeksi (SLEDAI) ve Sistemik Lupus Uluslararası İş Birliği Klinikleri (SLICC)/Amerikan Romatoloji Koleji (ACR) kriterleri kullanılarak değerlendirilmiştir. SjS aktivitesi ise EULAR Sjögren Sendromu Hastalık Aktivite İndeksi (ESSDAI) ile değerlendirilmiştir.

Plazma survivin düzeyleri, SLE hastalarında sağlıklı kontrollere kıyasla anlamlı derecede daha düşük bulunmuştur ($p<0,001$). SLE hastalarında plazma survivin düzeyleri ile apoptotik ve inflamatuvar belirteçler arasında güçlü bir pozitif korelasyon saptanmıştır ($p<0,001$). SLE hastalarında idrar survivin düzeyleri ile plazma survivin düzeyleri ve inflamatuvar ya da apoptotik belirteçler arasında herhangi bir korelasyon bulunmamıştır ($p>0,05$). SLEDAI skorları ile plazma veya idrar survivin düzeyleri arasında da anlamlı bir ilişki saptanmamıştır ($p>0,05$).

Bu çalışma, survivinin SLE'nin tanısı, hastalık izlemi ve patofizyolojik mekanizmalarının anlaşılmasında önemli bir potansiyele sahip olduğunu göstermekte ve gelecekte yapılacak araştırmalar için temel veriler sunmaktadır.

**Anahtar Kelimeler: Survivin. Sistemik lupus eritematozus.**

**Date Received:** 29.November.2025
**Date Accepted:** 9.March.2026

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SLE is a connective tissue disease with a heterogeneous clinical presentation that can involve multiple organs and manifest with various clinical patterns[1]. This heterogeneous nature of SLE complicates its diagnosis and monitoring. The diagnosis and monitoring of SLE activation are performed using test sets that include numerous clinical and immunological parameters[2,3]. Physiologically, there is a balance between cell proliferation and cell death in the body. As new cells are generated, those that lose their function are eliminated through programmed (apoptosis, autophagy) and pathological (necrosis) cell death pathways[4]. Increased apoptosis plays a significant role in the development and activation of SLE. This condition has been associated with factors that increase apoptosis, such as UV rays and viral infections, as well as with defects in mechanisms that inhibit apoptosis[5–7]. The regulation of apoptosis involves proteins such as bcl-2 and IAP family. Survivin is a member of the IAP family[8,9].

In our study, we aimed to evaluate serum and urinary survivin protein levels in SLE patients to determine their role in disease diagnosis and monitoring of activation. In addition, we aimed to assess the relationship between serum survivin levels and general apoptotic process, as well as the relationship between urinary survivin levels and renal apoptotic process. In order to evaluate whether this process is specifically associated with SLE or with inflammation and autoimmunity, we included Sjögren's Syndrome (SjS) patients as a disease control group, in addition to a healthy control group.

## Materials And Methods

*Study design*

Our study, which aims to investigate the relationship between survivin protein levels, disease clinic and inflammatory markers in SLE and SjS patients, is a cross-sectional study design in the single-center.

The study included 36 patients with SLE and 17 patients with SjS, who were followed at the Rheumatology Division of the Department of Internal Medicine between September 2019 and March 2020. Additionally, 29 age and gender-matched healthy volunteers who applied to the General Internal Medicine outpatient clinic of the same institution were enrolled as the control group. Participants were selected in a nonconsecutive manner. All individuals included in the study were informed about the study and written informed consent was obtained from each participant. Eligible participants were between 18 and 65 years of age and met the SLICC criteria for SLE[10] or the 2016 ACR criteria for SjS[11]. Exclusion criteria included being under 18 or over 65 years of age, pregnancy, the presence of an active infection or a current or past history of malignancy.

*Variables, data sources and measurement*

A detailed medical history was taken from all individuals included in the study and physical examinations were performed. The patients' demographic characteristics, habits, disease duration, treatments they had received and were currently receiving, as well as organ involvement, were obtained from the patients themselves, the center's database, their medical records. On the day of participation in the study, disease activity was calculated using the SLEDAI and SLICC/ACR indices for SLE patients and the ESSDAI activity index for SjS patients. For SLE patients a SLEDAI score of <6 was considered mild, 6-12 moderate, and >12 severe disease[12]. For primary SjS patients an ESSDAI score of <5 was considered low, 5-13 moderate, and ≥14 high activity.

Blood samples were collected from participants after an 8-12 hour fasting period. Routine laboratory tests performed at our hospital, including complete blood count, C3, C4, as well as urea, creatinine, glucose and albumin, were conducted using spectrophotometric methods for biochemical analysis. Erythrocyte sedimentation rate (ESR) was measured by the Westergren method and C-reactive protein (CRP) was assessed using a turbidimetric method. Antinuclear antibody (ANA), anti-Ro, anti-La, rheumatoid factor (RF) and cyclic citrullinated peptide (CCP) levels were obtained from the patients' records and the center's database.

In addition, 10 mL of blood was collected for the analysis of survivin, caspase-3, caspase-9, TNF-α, IL-2, IL-6, INF-α, NF-κB, BAFF and APRIL parameters. The samples were centrifuged at 3000 rpm for 5 minutes. The obtained serum were stored at -20°C until the day of the study. Commercial ELISA test (Sunred Brand) ELISA test kits were used to determine survivin, caspase-3, caspase-9, TNF-α, IL-2, IL-6, INF-α, NF-κB, BAFF and APRIL parameters. Furthermore, urine samples were collected from participants as the first morning void. Complete urinalysis and spectrophotometric analysis of micrototal protein and creatinine in spot urine were performed. For the analysis of survivin in urine, 2 mL of urine was collected and centrifuged at 2000 rpm for 5 minutes.

The samples obtained were stored at -20°C until the day of the study. Since the ELISA test protocol is the same for all parameters, only the survivin test protocol is explained. The study was carried out in accordance with the user manual using Sunred brand human ELISA kits in the research laboratory of the Physiology Department of Inonu University Faculty of Medicine. For each test well, 40 µl of sample was

added, followed by 10 µl of Surv-antibody and 50 µl of Streptavidin-HRP. The membrane was sealed and gently shaken, then incubated at 37°C for 60 minutes. The washing solution was diluted 30 times with distilled water and set aside. The membrane was removed, the liquid was discarded and any remaining liquid was shaken off. To each test well, 50 µl of Chromogen solution A and B were added. The mixture was incubated at 37°C, protected from light for 10 minutes. Subsequently, 50 µl of stop solution was added to each well. Optical density (OD) was measured at a wavelength of 450 nm within 15 minutes of adding the stop solution. Based on the concentration of the standards and their corresponding OD values, the standard curve's linear regression equation was used for calculation. The OD values of the samples were then applied to this regression equation to determine the corresponding concentrations of the samples.

*Procedures*

Before starting our study, ethical approval (decision no: 2019/163) was obtained from the İnönü University Clinical Research Ethics Committee and financial support (Project code: TTU-2020-1986) was received from the İnönü University Scientific Research Projects Coordination Unit.

*Statistical analyses*

The minimum sample size required to detect a significant difference using this test was calculated, with a Type I error rate (alpha) of 0.05, a power (1-beta) of 0.9, and an effect size of 0.39.

The data analyses obtaine d from the research were performed using IBM SPSS Statistics 25.0. The data were presented as median (minimum-maximum), mean (standard deviation), and frequency (percentage). Normality of distribution was assessed using the Shapiro-Wilk test. Statistical analyses included the Mann-Whitney U test, independent t-test, Kruskal-Wallis test, one-way analysis of variance (ANOVA), Pearson chi-square test, Fisher's exact chi-square test, and Spearman's correlation coefficient, depending on the suitability of the data. For multiple comparisons, the Tukey test was used for one-way ANOVA, while Bonferroni-corrected Mann-Whitney U tests were used for Kruskal-Wallis test. A p-value $<0.05$ was considered statistically significant in the analysis results.

*Patient consent statement*

All patients provided informed consent prior to participation in the study. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki, all personal data were handled confidentially and anonymized to protect patient privacy.

## Results

The demographic characteristics and laboratory data of the study groups are summarized in (Table I)

When evaluating organ involvement in SLE patients, the most common involvement is observed in joint is most common at % 63 and pulmonary involvement is at least %13.9.

Plasma and urine survivin levels were compared between the SLE and control groups. Urinary survivin levels did not show a significant difference between the groups ($p=0.08$). However, plasma survivin levels exhibited a significant difference between the groups ($p<0.001$) (Table II).

No significant correlation was found between plasma and urinary survivin levels and organ/system involvement (kidney, joint, skin, lung, heart and nervous system) in SLE patients (for all parameters, $p>0.05$). A strong positive correlation ($p<0.001$) was identified between inflammatory markers and plasma survivin levels, while no correlation was found with urinary survivin levels ($p>0.05$). The relationship between plasma and urinary survivin levels was also investigated, but no significant correlation was found between these two parameters ($p=0.95$) (Table III). Similar results were obtained for the evaluated parameters in the SLE patient group (Table IV).

In the SLE patient group, no significant correlation were found between plasma and urinary survivin levels and demographic characteristics disease activity indices and routine laboratory tests ($p>0.05$). Additionally, no significant difference was observed in plasma survivin levels between patients using or not using medications such as cyclophosphamide, hydroxychloroquine, mycophenolate mofetil, azathioprine, corticosteroids and angiotensin converting enzyme inhibitors/angiotens in II receptor blockers ($p>0.05$ for each medication).

## Discussion and Conclusion

In this cross-sectional study, the role of survivin, an anti-apoptotic protein in the pathogenesis of SLE and the pathways it affects were investigated. The relationship between serum and urinary levels of survivin and apoptotic and inflammatory markers was compared in SLE, SjS (patient control), and healthy control groups. Plasma survivin levels in the SLE (89.3±34.5 pg/ml) and SjS (107.8±72.4 pg/ml) patient groups were found to be significantly lower compared to the healthy control group (186.9±100 pg/ml). In the SLE group, a strong positive correlation was found between plasma survivin levels and apoptotic and inflammatory markers ($p<0.001$).

**Table I.** Demographic characteristics of the participants, average values of routine blood tests, and intergroup comparisons

| | SLE (a) n: 36 | SjS (b) n: 17 | Control (c) n: 29 | p |
|---|---|---|---|---|
| **Gender (M/F), n (%)** | 2/34 (5.6/94.4) | 1/16 (5.9/16) | 2/27 (6.9/93,1) | 0.974 |
| **Age (years), mean ± SD** | 37.1±10.6 | 51.5±8.0 | 35.8±9.9 | **<0.001** |
| **BMI (kg/m²), [median (min/max)]** | 24.5 (17/46.6) | 27.9 (19.8/39) | 25 (19.2/32) | 0.050 |
| **Disease duration (years), [median (min/max)]** | 6 (1/32) | 3 (1/7) | - | 0.068 |
| **Smoking status, n (%)** | 6 (16.7) | 2 (11.8) | - | 1.000 |
| **WBC ($10^6$/L), mean ± SD** | 6886.2±2496.5 | 6168±1530 | 7380±1518 | 0.19 |
| **Neutrophils ($10^6$/L), mean ± SD** | 4334±2168 | 3508.8±13.3 | 4225.3±1203.3 | 0.13 |
| **Lymphocytes ($10^6$/L), mean ± SD** | 1783.9±853.4 | 1974.7±429 | 2458.2±652.7 | **0.02 a-c,b-c** |
| **Hemoglobin (g/dL), mean ± SD** | 11.7±1.8 | 13.4±1.0 | 13.4±1.0 | **<0.001 a-c, a-b** |
| **Platelets ($10^9$/L), mean ± SD** | 265.6±85.4 | 268.8±68.7 | 277.8±73.5 | 0.81 |
| **GFR (mL/min/1.73 m²), mean ± SD** | 107.6±17.6 | 97.5±11.7 | - | **0.03** |
| **ESR (mm/hour), mean ± SD** | 19.4±12.2 | 12±9.3 | 8.6±6 | **<0.001 a-b, a-c** |
| **CRP (mg/dL), mean ± SD** | 0.5±0.6 | 0.5+0.4 | 0.4±0.3 | 0.97 |

*a-b: comparison between SLE and SjS, a-c: comparison between SLE and Control, b-c: comparison between SjS and Control.*
*BMI: Body Mass Index CRP: C-Reactive Protein, ESR: Erythrocyte Sedimentation Rate, F: Female, GFR:* ***Glomerular Filtration Rate,*** *M:Male WBC: White Blood Cell*

**Table II.** Comparison of Plasma and Urinary Survivin Levels in SLE, SjS and Healthy Control Groups

| | SLE (a) n:36 | SjS (b) n:17 | Control (c) n:29 | p |
|---|---|---|---|---|
| **Plasma survivin (pg/ml), median (min/max)** | 80 (0/375.1) | 75.9 (65.9/206) | 163 (65.1/383) | **p<0.001 a-c, b-c** |
| **Urine survivin (pg/ml), median (min/max)** | 127 (127/584) | 121.9 (91/148) | 114.4(84/155) | p=0.08 |

**Table III.** Relationship between plasma and urinary survivin levels and inflammatory and apoptotic markers in all participants

| | | APRIL | BAFF | CASPAS 3 | CASPAS 9 | IFN- α | Nf-KB | TNF-α | IL-2 | IL-6 | XIAP |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Plasma survivin** | **r** | 0.940 | 0.934 | 0.947 | 0.955 | 0.926 | 0.926 | 0.934 | 0.907 | 0.908 | 0.916 |
| | **p** | **<0.001** | **<0.001** | **<0.001** | **<0.001** | **<0.001** | **<0.001** | **<0.001** | **<0.001** | **<0.001** | **<0.001** |
| **Urinary survivin** | **r** | 0.057 | 0.020 | 0.039 | 0.013 | -0.034 | 0.002 | -0.019 | -0.005 | -0.038 | 0.030 |
| | **p** | 0.613 | 0.857 | 0.729 | 0.906 | 0.765 | 0.988 | 0.867 | 0.967 | 0.737 | 0.790 |

*APRIL: A Proliferation-Inducing Ligand, BAFF: B-cell Activating Factor Interferon-alpha, TNF:* ***Tumor Necrosis Factor,*** *IL:* ***Interleukin,*** *Nf-κB:* ***Nuclear Factor kappa-light-chain-enhancer of activated B cells,*** *XIAP: X-linked Inhibitor of Apoptosis Protein*

**Table IV.** Relationship between plasma and urinary survivin levels and inflammatory and apoptotic markers in SLE patients

| | | APRIL | BAFF | CASPAS 3 | CASPAS 9 | IFN- α | Nf-KB | TNF-α | IL-2 | IL-6 | XIAP |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Plasma survivin** | r | 0.91 | 0.96 | 0.93 | 0.90 | 0.89 | 0.94 | 0.92 | 0.87 | 0.92 | 0.94 |
| | p | **<0.001** | **<0.001** | **<0.001** | **<0.001** | **<0.001** | **<0.001** | **<0.001** | **<0.001** | **<0.001** | **<0.001** |
| **Urinary survivin** | r | 0.28 | 0.22 | 0.28 | 0.21 | 0.13 | 0.16 | 0.16 | 0.16 | 0.15 | 0.27 |
| | p | 0.08 | 0.18 | 0.09 | 0.21 | 0.43 | 0.32 | 0.33 | 0.33 | 0.36 | 0.10 |

*APRIL: A Proliferation-Inducing Ligand, BAFF: B-cell Activating Factor Interferon-alpha, TNF:* ***Tumor Necrosis Factor,*** *IL:* ***Interleukin,*** *Nf-κB:* ***Nuclear Factor kappa-light-chain-enhancer of activated B cells,*** *XIAP: X-linked Inhibitor of Apoptosis Protein*

A notable finding in our study was the lack of correlation between urinary survivin levels and renal involvement or other inflammatory markers in SLE patients. This discrepancy c ould be attributed to several factors. First, the molecular weight and stability of survivin in the urinary environment, alongside the influence of systemic treatments on urinary excretion, may affect its detectability during active inflammation. Second, the absence of a significant association might indicate that survivin-mediated apoptotic pathways in the kidney are regulated through distinct intra-renal mechanisms that are not adequately reflected in spot urine samples. Consequently, further longitudinal studies with biopsy-proven nephritis cases are necessitated to fully elucidate the role of urinary survivin.

In a study conducted with 26 SLE patients (F/M: 23/3) and 32 healthy volunteers (F/M: 10/22), the relationship between survivin mRNA expression levels extracted from peripheral blood mononuclear cells of the participants and anti-dsDNA antibodies, C3 and C4 levels was analyzed. The study found that in the SLE group, survivin expression was 1.7 times higher compared to the healthy control group and a positive correlation with anti-dsDNA antibodies ($p<0.01$, $r=0.62$). A negative correlation with C3 levels ($p<0.05$, $r=-0.41$). However, no significant relationship was found between C4 levels and survivin gene expression[11]. In contrast, in our study, serum survivin levels in the SLE group were found to be significantly lower than those in the healthy control group, and no correlation was observed with C3, C4, or anti-dsDNA antibody levels ($p>0.05$). This suggests that increased apoptosis in SLE may affect anti-apoptotic mechanisms due to autoantibody and immune complex formation. The differences between the studies may be attributed to factors such as the average age of the participants (our participants were older), inclusion criteria, methodologies used to measure survivin [mRNA (more short-lived, more sensitive) and protein (active form/demonstrates direct cellular function) based measurements] and the effects of posttranslational modifications

In a study involving 62 SLE patients and 92 healthy volunteers, the SLE patients were classified into active and inactive groups based on SLEDAI criteria. It was found that serum survivin levels in SLE patients were significantly lower compared to the healthy control group, but no significant difference was observed between the active and inactive groups. Similarly, in our study no significant difference was found between the clinical characteristics of SLE patients, the medications used and serum survivin levels. In contrast to our study, a negative correlation was found between age and survivin levels[12]. The obtained results suggest that they may be a consequence of the limited number of patients and the diversity in the drug combinations administered.

In a cross-sectional study, unlike our study, four groups were formed, including active SLE, inactive SLE, active lupus nephritis (LN), and inactive lupus nephritis (LN), and serum survivin protein levels were compared with a healthy control group. Similar to the findings in our study, serum survivin protein levels were found to be lower in all groups compared to the healthy control group. This may suggest that survivin proteins **could play a role** in the pathogenesis of SLE. However, when evaluating survivin protein levels in patients with active lupus nephritis before and after treatment, no significant difference was observed[13].

In a study comparing drug-free patients with systemic sclerosis (SSc) and SLE to healthy controls, serum survivin levels in SSc patients (177±75 pg/ml) were found to be significantly higher compared to the control group ($p<0.001$). However, in SLE patients (114±29 pg/ml) serum survivin levels were significantly lower compared to healthy controls (138±42 pg/ml) ($p<0.05$)[14]. Similarly, in our study a significant decrease in plasma survivin levels (186.9±100 pg/ml) was observed in the SLE group, but no significant correlation with disease clinical characteristics was found. In SSc patients an increase in fibroblast number, survival, and function in target tissues occurs. This may be associated with suppressed apoptosis in the related cells. It is believed that excessively activated apoptotic mechanisms play a role in the development of SLE, particularly in the skin. In our study, a decrease in survivin levels was also observed in the SjS group compared to the healthy control group. This suggests that in SjS, the cellular damage in exocrine glands may be associated with a disturbance in apoptosis regulatory mechanisms[15] and that the reduced survivin levels may have played a role in this process. The results of our study support the potential role of anti-apoptotic treatments, including survivin, as a therapeutic option in SLE and other autoimmune diseases. However, the fact that SLE and SjS are inflammatory diseases, along with the positive correlation of survivin with inflammatory markers, suggests that this molecule may also have an acute phase effect. The positive correlation between survivin with pro-inflammatory and inflammatory markers may indicate its impact on the suppression of these pathways. This may be part of a process regulated to control inflammation and cell death. In our study, high correlation coefficients ($r=0.90–0.96$) were observed between plasma survivin and several inflammatory biomarkers. While these strong associations may suggest closely linked pathogenic pathways, they could also partially reflect methodological or assay-related factors. All statistical outputs were re-verified to ensure data integrity and the accuracy of these robust correlations. To fully

comprehend these findings, additional cross-sectional analyses are required, along with an investigation into the behavior of these molecules at various stages of the disease.

Our study had several limitations. The predominance of a female population in our study restricts the evaluation of results in male patients. Additionally, the small sample size limits the assessment of SLE subgroups and disease stages. Furthermore, the age discrepancy between the study groups could be a potential confounding factor that may have influenced biomarker levels, as no age-adjusted analysis was performed. In addition, the lack of evaluation of survivin levels before and after treatment, the unexamined effect of medications on survivin expression, the absence of a group of patients not receiving drug treatment in our study populations, and the fact that most patients were on polypharmacy represent significant limitations.

There is no study in the literature investigating survivin protein levels in blood and urine in relation to the pathogenesis, subgroups, activity of the disease, and its association with apoptotic and inflammatory markers involved in disease pathogenesis. In this respect, our study is original. In our study, plasma survivin levels were found to be lower in the SLE and SjS patient groups compared to the control group and showed a positive correlation with apoptotic and inflammatory markers. These results suggest that survivin may be associated with multiple stages of SLE pathogenesis; however, correlation findings only indicate an association. To establish causality, prospective and multicenter studies with large sample sizes are needed. Based on these findings, serum survivin protein levels may provide supportive information for diagnosis and disease monitoring.

**Researcher Contribution Statement:**
Idea and design: Z.Y., S.Y., C.U., S.Y.; Data collection and processing**:** Z.Y., S.Y., C.U., S.Y.; Analysis and interpretation of data: Z.Y., S.Y., C.U., S.Y.; Writing of significant parts of the article: Z.Y.;
**Support and Acknowledgement Statement:**
Financial support (Project code: TTU-2020-1986) was received from the İnönü University Scientific Research Projects Coordination Unit.
**Conflict of Interest Statement:**
All of authors declare that they have no competing interests. The authors have no financial interests.
**Ethics Committee Approval Information:**
Approving Committee: İnönü University Clinical Research Ethics Committee
Approval Date: 2019
Decision No: 2019/163

## References

1. Colglazier CL, Sutej PG, Morris C. Laboratory testing in the rheumatic diseases: A practical review. South Med J. 2005;98:185–91.
2. Yargucu Zihni F, Keser G. Sistemik Lupus Eritematozus Epidemiyolojisi. Türkiye Klin. 2018;1–5.
3. Fava A, Petri M. Systemic lupus erythematosus: Diagnosis and clinical management. J Autoimmun. 2019;1–13.
4. Coşkun G, Özgür H. Apoptoz ve Nekrozun Moleküler Mekanizması. Arşiv Kaynak Tarama Derg. 2014;20:145–58.
5. Pan L, Lu MP, Wang JH, Xu M, Yang SR. Immunological pathogenesis and treatment of systemic lupus erythematosus. World J Pediatr. 2020;16:19–30.
6. Pan Q, Chen J, Guo L, Lu X, Liao S, Zhao C, et al. Mechanistic insights into environmental and genetic risk factors for systemic lupus erythematosus. Am J Transl Res. 2019;11:1241–54.
7. Bertsias GK, Salmon JE, Boumpas DT. Therapeutic opportunities in systemic lupus erythematosus: State of the art and prospects for the new decade. Ann Rheum Dis. 2010 Sep;69:1603–11.
8. Ebrahimiyan H, Aslani S, Rezaei N, Jamshidi A, Mahmoudi M. Survivin and autoimmunity; the ins and outs. Immunol Lett. 2018;193:14–24.
9. Eröz R, Bircan D, Yüce H, Özmerdivenli R. Survivin Hakkında Bilinenler : Survivin ile İlgili Türkiye ' de Yapılmış Olan Çalışmalar. 2015;5:39–58.
10. Vitali C, Bootsma H, Bowman SJ, Dorner T, Gottenberg JE, Mariette X, et al. Classification criteria for Sjögren's syndrome: We actually need to definitively resolve the long debate on the issue [Internet]. Vol. 72, Annals of the Rheumatic Diseases. BMJ Publishing Group Ltd; 2013 [cited 2020 Jul 18]. p. 476–8. Available from: https://ard.bmj.com/content/72/4/476
11. Yin Z hua, Ye Z zhong, Luo X xia. The Abnormal Expression of Survivin Gene in SLE Patients. Prog Mod Biomed. 2007;7:1033–8.
12. Ebrahimian S, Rashtchizadeh N, Ghorbanihaghjo A, Mahdavi AM, Hajialilo M, Khabbazi A. Association between serum levels of survivin and systemic lupus erythematosus. Int J Clin Pract [Internet]. 2021 Mar 1 [cited 2021 Aug 22];75(3):e13706. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/ijcp.13706
13. Lisboa RV, de Oliveira FR, Quaresma TO, de Almeida RM, Ribeiro Oliveira RD, Junior PL. The Behaviour of Serum Survivin in Patients With Lupus Nephritis. Biomark Insights [Internet]. 2022 [cited 2025 Mar 24];17:11772719221131470. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC9597205/
14. Koike Y, Muroi E, Yoshizaki A, Ogawa F, Yanaba K, Takenaka M, et al. Autoantibody against survivin in patients with systemic sclerosis. J Rheumatol [Internet]. 2010 Sep 1 [cited 2020 Aug 28];37(9):1864–70. Available from: www.jrheum.org
15. Ramos-Casals M, Font J. Primary Sjögren's syndrome: Current and emergent aetiopathogenic concepts. Rheumatology. 2005;44:1354–67.