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# Clinical characteristics of juvenile systemic lupus erythematosus: Prepubertal and pubertal onset

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## ABSTRACT

**Objective:** Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that affects multiple organ systems and is characterized by periods of flare-ups and remission. In approximately 15-20% of SLE patients, clinical symptoms onset during childhood or adolescence and are defined as juvenile SLE (jSLE). Age at disease onset has been suggested to influence the clinical phenotype, severity of inflammatory activity, and overall disease course in jSLE. The aim of this study was to compare clinical features and disease course between prepubertal (<10 years) and pubertal (≥10 years) jSLE patients.

**Materials and Methods:** This retrospective, single-center, cross-sectional study was conducted on patients diagnosed with jSLE who were followed up at the pediatric rheumatology clinic between January 2015 and September 2025. Patients included in the study had been diagnosed with jSLE according to the 2012 Systemic Lupus International Collaborating Clinics classification criteria.

**Results:** A total of 54 patients with juvenile-onset SLE were included, of whom 88.9% were female. Patients were grouped according to age at diagnosis: prepubertal-onset jSLE (<10 years) included 9 patients (16.7%), and pubertal-onset jSLE (≥10 years) included 45 patients (83.3%). Fever and elevated C-reactive protein levels were significantly more common in jSLE with pre-pubertal onset, whereas mucocutaneous involvement was more prevalent in jSLE with pubertal onset. Renal, hematological, and neurological involvement, autoantibody profiles, and disease activity and damage index at diagnosis were similar across groups. At the last visit, disease activity was significantly lower in jSLE with pre-pubertal onset. No differences in treatment were observed between age groups.

**Conclusion:** In this cohort, prepubertal-onset jSLE tended to present with more prominent inflammatory features, whereas pubertal-onset jSLE more often showed mucocutaneous involvement. Despite these observed phenotypic differences, cumulative organ damage appeared similar between groups.

**Keywords:** Age of onset, puberty, systemic lupus erythematosus

## Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that affects multiple organ systems and is characterized by periods of flare-ups and remission. In approximately 15-20% of SLE patients, clinical symptoms onset during childhood or adolescence and are defined as juvenile SLE (jSLE) (1). The prevalence of jSLE is 1.1–25.7 per 100000 children (2). The median age at diagnosis for jSLE has been reported to range from 11.67 to 13.9 years (3-5).

Juvenile SLE is generally characterized by a more severe disease course and higher disease activity compared with adult-onset SLE (6,7). Beyond the differences between adult and juvenile SLE, current data suggest that jSLE exhibits distinct clinical differences among pediatric age groups. In particular, the age of disease onset has been reported to impact clinical phenotype, severity of inflammatory activity, and disease course (1).

Pre-school children with SLE (<6 years) show an equal gender distribution female-to-male ratio, 1:1. In school-age children and adolescents, the female-to-male ratio is approximately 4-5:1,whereas after adolescence it shifts to a female predominance (9-10:1) characteristic of adult-onset SLE (8). This age-related change in gender distribution, together with increased hormonal activity during adolescence, suggests that sex hormones may play an important role in the pathogenesis of

SLE, in addition to genetic, environmental and infectious factors. Sex hormones are known to affect the regulation of the immune system and the shaping of autoimmune processes (9).

The aim of this study was to compare the clinical characteristics of patients diagnosed with jSLE during the prepubertal (<10 years) and pubertal (≥10 years) periods and to identify age-related differences in clinical features and disease course.

## Materials and Methods

This retrospective, single-center, cross-sectional study was conducted on patients diagnosed with jSLE who were followed up at the Department of Pediatric Rheumatology of Ankara Bilkent City Hospital between January 2015 and September 2025. Patients with a follow-up period of less than 6 months, those with missing data, and those with monogenic lupus confirmed by genetic mutation were excluded.

Patients included in the study were diagnosed with jSLE according to the 2012 Systemic Lupus International Collaborating Clinics classification criteria (10). All patients' data were obtained retrospectively from the hospital's electronic medical record system. Patients' demographic characteristics (gender, age at diagnosis, follow-up duration), laboratory parameters [erythrocyte sedimentation rate, C-reactive protein (CRP), antinuclear antibody (ANA), anti-dsDNA, anti-smith antibody, ribonucleoprotein antibody, ribosomal P and low complement, antiphospholipid (aPL) antibodies] clinical findings and organ involvements, and treatments were recorded. If a renal biopsy was performed, the renal biopsy findings were documented according to the 2003 Lupus Nephritis Classification of the International Society of Nephrology/Renal Pathology Society (11). The activity of the disease at the time of diagnosis and during follow-up was assessed using the SLE Disease Activity Index 2000 (SLEDAI-2K) (12). The damage related to the disease itself and medications was asssessed at last outpatient clinic examination based on the pediatric version of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (PedSDI) (13).

Patients were divided into prepubertal (<10 years) and pubertal (≥10 years) groups based on the age at diagnosis, according to the World Health Organisation's definition of adolescence (10–19 years) (14).

### Statistical analysis

IBM Statistical Package for the Social Sciences, version 23.0 (SPSS Inc., Armonk, NY, IBM Corp., USA). In the descriptive statistics section, categorical variables were presented in tables with counts and percentages, while continuous variables that did not follow a normal distribution were presented with median (interquartile range) values. The conformity of continuous variables to normal distribution was evaluated using visual (histogram and probability graphs) and analytical methods (Kolmogorov–Smirnov/Shapiro–Wilk tests). Mann–Whitney U test was used in comparisons of continuous variables that did not conform to normal distribution between two groups. The chi-square test was used in comparisons of categorical variables. Statistical significance level was accepted as $p \leq 0.050$

## Results

During the study period, 65 jSLE patients were followed up in the pediatric rheumatology department. Two patients with a follow-up period of less than 6 months, four patients with missing data, and five patients with monogenic lupus confirmed by genetic mutation were excluded from the study. The remaining 54 jSLE patients were included in the study. Of these patients, 48 (88.9%) were female. The median follow-up duration was 31.5 (12-54) months, and the median age at symptom onset was 12.7 (10.5-14.9) years.

Constitutional symptoms were observed in 42 patients (77.8%), followed by renal involvement in 31 (57.4%), cutaneous involvement in 30 (55.6%), hematological involvement in 29 (53.7%), arthritis in 24 (44.4%) and neurological involvement in 20 (37.0%) (Table I). Among patients with renal involvement (n=31), lupus nephritis was classified as Class I in 3 patients (9.7%), Class II in 11 (35.5%), Class IV in 11 (35.5%), and Class V in one patient (3.2%) based on renal pathology.

Among the immunological parameters, hypocomplementemia was observed in 40 patients (74.1%), ANA positivity in 52 patients (96.3%), anti-dsDNA positivity in 44 patients (81.5%), and antiphospholipid antibody positivity in 12 patients (22.2%). The median SLEDAI score was 14.5 (8–20.3) at diagnosis and 2 (0–4) at the last visit. The baseline demographic and clinical characteristics of all patients are shown in Table I.

### Comparison of clinical characteristics in prepubertal- and pubertal-onset juvenile systemic lupus erythematosus

Patients were grouped according to age at diagnosis: prepubertal-onset jSLE (<10 years) included 9 patients (16.7%), and pubertal-onset jSLE (≥10 years) included 45 patients (83.3%).

Seven patients (77.8%) with prepubertal-onset jSLE and 41 patients (91.1%) with pubertal-onset jSLE were female. There was no statistically significant difference between the groups in terms of gender (p=0.259). The female-to-male ratio was 3.5:1 in the <10 age group and 10.2:1 in the pubertal group. The follow-up period was 35.5 months (31.5–72) in the prepubertal-onset jSLE and 25 months (12–47.5) in the pubertal group, although it was longer in the prepubertal group (p=0.051). The median age at symptom onset was 8.4 (7.2–8.9) years in the prepubertal-onset jSLE and 12.9 (11.8–15.1) years in the pubertal-onset jSLE (p<0.001).

Fever was more common in prepubertal-onset jSLE, occurring in 7 patients (77.8%), whereas it was observed in 17 patients (37.8%) in the pubertal-onset jSLE group (p=0.027). Lymphadenopathy was present in 4 patients (9.1%), alopecia in 6 patients (13.3%), and oral ulceration in 7 patients (15.6%), and was only observed in the pubertal-onset jSLE. Cutaneous involvement was present in 2 patients (22.2%) in the prepubertal onset jSLE and in 28 patients (62.2%) in the pubertal group, and was significantly more prevalent in the pubertal onset jSLE (p=0.027).

There was no significant difference between the prepubertal and pubertal onset jSLE patients regarding renal involvement (66.7% vs 55.5%, p=0.680), haematological involvement (77.8% vs 48.9% p=0.153) or neurological involvement (22.2% vs 40.0%, p=0.458).

**Table I: Clinical characteristics of prepubertal- and pubertal-onset jSLE**

| | Total | Prepubertal-onset jSLE | Pubertal-onset jSLE | p |
|---|---|---|---|---|
| Number of patients | 54 | 9 | 45 | - |
| Gender, female* | 48 (88.9) | 7 (77.8) | 41 (91.1) | 0.259‡ |
| Age at symptom onset, years† | 12.7 (10.5-14.9) | 8.4 (7.2-8.9) | 12.9 (11.8-15.1) | <0.001§ |
| Time elapsed until diagnosis, months† | 2 (1-6) | 2 (1.5-4) | 2.5 (1-6) | 0.720§ |
| Follow-up duration, months† | 31.5 (12.0-54.0) | 35 (31.5-72.0) | 25 (12.0-47.5) | 0.051§ |
| Clinical manifestation* | | | | |
| Constitutional symptom | 42 (77.8) | 8 (88.9) | 34 (75.6) | 0.665‡ |
| Fever | 24 (44.4) | 7 (77.8) | 17 (37.8) | 0.027‡ |
| Weakness | 37 (69.8) | 7 (77.8) | 30 (68.2) | 0.706‡ |
| Weight loss | 14 (26.4) | 1 (11.1) | 13 (29.5) | 0.416‡ |
| Lymphadenopathy | 4 (7.5) | 0 (0.0) | 4 (9.1) | N/A |
| Arthritis | 24 (44.4) | 2 (22.2) | 22 (48.9) | 0.270‡ |
| Serositis | 19 (35.2) | 5 (55.6) | 14 (31.1) | 0.251‡ |
| Cutaneous involvement | 30 (55.6) | 2 (22.2) | 28 (62.2) | 0.027‡ |
| Oral ulcers | 7 (13,0) | 0 (0.0) | 7 (15.6) | N/A |
| Alopecia | 6 (11.1) | 0 (0.0) | 6 (13.3) | N/A |
| Renal involvement | 31 (57.4) | 6 (66.7) | 25 (55.5) | 0.717‡ |
| Neurological involvement | 20 (37.0) | 2 (22.2) | 18 (40.0) | 0.458‡ |
| Hematological involvement | 29(53.7) | 7 (77.8) | 22 (48.9) | 0.153‡ |
| Anemia | 19 (35.2) | 5 (55.6) | 14 (31.1) | 0.251‡ |
| Thrombocytopenia | 15 (27.8) | 4 (44.4) | 11 (24.4) | 0.244‡ |
| Lymphopenia | 17 (31.5) | 3 (33.3) | 14 (31.1) | >0.999‡ |
| Laboratory findings* | | | | |
| Elevated erythrocyte sedimentation rate | 30 (55.6) | 5 (55.6) | 25 (55.6) | >0.999‡ |
| Elevated CRP | 19 (35.8) | 7 (77.8) | 12 (27.3) | 0.007‡ |
| ANA positivity | 52 (96.3) | 8 (88.9) | 44 (97.8) | 0.308‡ |
| Anti-dsDNA positivity | 44 (81.5) | 9 (100.0) | 35 (77.8) | N/A |
| Hypocomplementemia | 40 (74.1) | 8 (88.9) | 32 (71.1) | 0.418‡ |
| Direct coombs positivity | 34 (69.4) | 8 (88.9) | 26 (65.0) | 0.242‡ |
| Anti-Sm | 11 (35.5) | 3 (50.0) | 8 (32.0) | 0.638‡ |
| Anti-ribosomal P | 10 (33.3) | 2 (33.3) | 8 (33.3) | >0.999‡ |
| Anti-RNP | 7 (29.2) | 3 (50.0) | 4 (22.2) | 0.307‡ |
| aPL positivity | 12 (23.1) | 2 (22.2) | 10 (23.3) | >0.999‡ |
| SLEDAI-2K score at SLE diagnosis† | 14.5 (8.0-20.3) | 16 (6.0-19.0) | 13 (8.5-22.5) | 0.609§ |
| SLEDAI-2K score at last visit† | 2 (0.0-4.0) | 0 (0.0-0.5) | 2 (0.0-4.0) | 0.015§ |
| PedSDI score† | 0 (0-1) | 1 (0-1) | 0 (0-1) | 0.103§ |
| Remission status* | 33 (67.3) | 6 (66.7) | 27 (67.5) | >0.999‡ |
| Treatmen* | | | | |
| Methylprednisolone | 51 (94.4) | 9 (100.0) | 42 (93.3) | N/A |
| Hydroxychloroquine | 49 (90.7) | 9 (100.0) | 40 (88.9) | N/A |
| Mycophenolate mofetil | 22 (40.7) | 5 (55.6) | 17 (37.8) | 0.461‡ |
| Azathioprine | 3 (5.6) | 1 (11.1) | 2 (4.4) | 0.428‡ |
| Methotrexate | 5 (9.3) | 1 (11.1) | 4 (8.9) | >0.999‡ |
| Cyclophosphamide | 24 (44.4) | 6 (66.7) | 18 (40.0) | 0.165‡ |
| IVIG | 14 (25.9) | 2 (22.2) | 12 (26.7) | >0.999‡ |
| Rituximab | 8 (14.8) | 1 (11.1) | 7 (15.6) | >0.999‡ |

***:** *n (%),* **†:** *median (IQR),* **‡:** *Chi-square test,* **§:** *Mann-Whitney U test,* ***N/A:*** *Not Applicable,* ***CRP:*** *C-reactive protein,* ***ANA:*** *Antinuclear antibody,* ***anti-dsDNA****: Anti–double-stranded DNA antibody,* ***anti-Sm:*** *Anti-Smith antibody,* ***aPL:*** *Antiphospholipid antibodies,* ***anti-RNP:*** *Anti–ribonucleoprotein antibody,* ***SLEDAI-2K:*** *Systemic Lupus Erythematosus Disease Activity Index 2000,* ***IVIG:*** *Intravenous Immunoglobulin,* ***PedSDI:*** *Pediatric SLICC/ACR Damage Index*

Elevated CRP levels were more frequently observed in the pre-pubertal onset jSLE (7 patients, 77.8%) compared to the pubertal-onset jSLE (12 patients, 27.3%) (p=0.007). Autoantibody profiles, including ANA, anti-dsDNA, and aPL positivity, were similar in both groups. At diagnosis, the SLEDAI score was 16 (6–19) in the <10 age group and 13 (8.5–22.5) in the ≥10 age group, with no significant difference between the two groups (p=0.609). At the last visit, the SLEDAI score was 0 (0–0.5) in the prepubertal onset jSLE and 2 (0–4) in the pubertal onset jSLE. It was significantly higher in the pubertal onset jSLE (p=0.015). Regarding treatment and pedSDI no difference was observed between the two age groups. Comparisons of clinical characteristics between prepubertal- and pubertal-onset jSLE patients are presented in Table I.

## Discussion

Juvenile SLE is a multisystem inflammatory disease characterised by a highly variable presentation and clinical course compared to SLE seen in adults (3). Given the impact of major organ involvement on morbidity and mortality, early diagnosis and age-specific clinical awareness are of crucial importance in pediatric patients. In this retrospective study, the clinical characteristics of jSLE patients were evaluated according to their age at diagnosis. Fever and elevated CRP were observed more frequently in patients diagnosed prepuberally, while cutaneous involvement was more common in patients diagnosed during puberty. Furthermore, lymphadenopathy, oral ulcers, and alopecia were only detected in patients diagnosed during puberty.

Age at diagnosis in the SLE UK cohort was reported to be 12.8 years on average, while a Turkish series reported this age to be 13 years (15,16). In our study, the median age at diagnosis of jSLE was 12.7 years, and 88.9% of patients were female. Murine lupus models have demonstrated that oestrogen accelerates disease development, supporting a key role for sex hormones in lupus pathogenesis (17,18). In our study, the female-to-male ratio was 3.5:1 in pre-pubertal onset jSLE and 10.2:1 in pubertal onset SLE, clearly indicating a predominance in females. This age-related change in gender distribution appears consistent with previous data suggesting a potential role for sex hormones in lupus pathogenesis.

Fever has been reported in 20.4–68.4% of jSLE patients and in 15.4–64.9% of adult-onset SLE patients (19). In a large jSLE cohort, fever was reported as the most common initial symptom of the disease (57.6%) (20). A multicentre study conducted in Brazil demonstrated that fever was significantly more frequent in jSLE patients under 6 years of age compared to older age groups (21). Our data support the observation that younger patients are more prone to febrile episodes, similar to reports of jSLE patients under age six. Interestingly, this age-related trend extended to CRP levels in our study. In jSLE, it is known that elevated CRP levels may reflect accompanying inflammatory conditions such as infection rather than disease activity (22). Approximately 41.9% of newly diagnosed SLE patients were reported to have an infection, and CRP levels were shown to be higher in these cases compared to patients without infection (23). This suggests that elevated CRP levels in the pre-adolescent group may be related to accompanying inflammatory processes, primarily infections, rather than disease activity.

According to data from the UK jSLE study group, more active mucocutaneous, musculoskeletal, renal, and cardiorespiratory involvement, as well as higher overall disease activity, were observed at diagnosis in patients diagnosed during puberty (24). Li et al. (20) have shown that alopecia is more common in adolescents than in other age groups. In contrast, another study found that the frequency of cutaneous findings was more common in those under 10 years of age and that disease activity was higher in the pubertal group (25). In our study, cutaneous involvement was more common in pubertal-onset SLE than in pre-pubertal-onset jSLE, but major organ involvement was similar in both age groups. Furthermore, oral ulcers and alopecia were observed only in the pubertal age group. Disease activity was also similar in both age groups. All these findings indicate that jSLE has a heterogeneous clinical course and severity depending on age, but also suggest that pubertal-onset jSLE presents a more 'classic' phenotype with more pronounced mucocutaneous findings, similar to adult SLE. Furthermore, the observation that some clinical findings were limited to the adolescent group may be related to differences in group size between the two groups. These findings should be confirmed in further studies with larger cohorts.

Although the literature reports a wide range of disease activity scores at diagnosis in patients with SLE, our study found that SLEDAI-2K scores at diagnosis were similar between pubertal and prepubertal groups (24,25). However, higher SLEDAI-2K scores at the last visit among patients in the pubertal period suggest that disease control is more difficult to achieve in this age group. The management of juvenile SLE may be further complicated by the physiological and psychosocial changes of adolescence, as shown in a study (26). These factors may limit optimal disease control during adolescence and may be associated with ongoing disease activity.

In the present study, no significant difference was found between the prepubertal and pubertal groups in terms of cumulative organ damage assessed by pedSDI. This result is consistent with previous jSLE studies reporting similar damage accumulation between groups based on disease onset age (27, 28). All these data suggest that age at disease onset alone may not be a sufficient predictor of cumulative organ damage.

## Limitations

There are some limitations to our study; due to its retrospective design and single-centre setting, the number of patients is limited. In addition, the relatively small size of the prepubertal-onset group may have limited the detection of age-related differences between groups.The inability to evaluate patients under six years of age as a separate group has restricted a more detailed analysis of the clinical phenotype specific to early childhood.

## Conclusion

In conclusion, our results demonstrate that prepubertal-onset jSLE is characterized by a more prominent inflammatory presentation, including higher frequencies of fever and elevated CRP, whereas pubertal-onset jSLE more often presents with mucocutaneous manifestations. Despite these age-related differences in clinical phenotype, cumulative organ damage assessed by pedSDI was similar across groups. Further large-scale studies are needed to comprehensively define age-specific clinical characteristics in patients with jSLE.

### Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by Ankara Bilkent City Hospital (10.12.2025, reference number: TABED 2-25-1715). ).

### Contribution of the authors

Conceptualization: EÖ, BÇA; Methodology: EÖ, BÇA, EÇ, ZET, CK, EET, ŞE, Formal analysis and investigation: EÖ, MIE, SNY, DÖ, YUE, ŞET, USB, BPZ, ÖAB; Writing - original draft preparation: EÖ, ZET;

Writing - review and editing: EÖ, BÇA ; Funding acquisition: None ; Resources: None; Supervision: BÇA

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**Conflict of interest**

The authors declare that there is no conflict of interest.

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