Characterizing juvenile-onset systemic lupus erythematosus: clinical outcomes, disease progression, and determinants in pediatric populations

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Abstract

Introduction: This study aims to delineate the sociodemographic, clinical, and laboratory characteristics of juvenile-onset systemic lupus erythematosus (jSLE) patients.

Materials and Methods: Retrospective data from jSLE patients treated at Ümraniye Training and Research Hospital's pediatric rheumatology unit between January 2017 and February 2024 were collected. Inclusion criteria comprised meeting at least four of the American College of Rheumatology (ACR) criteria for systemic lupus erythematosus (SLE) classification and being under 18 years old at disease onset.

Results: The study encompassed 69 jSLE patients, with a female-to-male ratio of approximately 3.9:1 and a median diagnosis age of 14.5 (min:2, max:17.5) years. Musculoskeletal symptoms, nephropathy, malar rash, and hematologic abnormalities were predominant clinical features. Thirty-seven patients exhibited renal involvement, 36 presented hematological complications, and 23 had both. Overall, 76.8% of patients demonstrated major organ system involvement. A statistically significant association was observed between renal involvement and initial Anti-double-stranded deoxyribonucleic acid antibody presence (p=0.036) and SLE Disease Activity Index-2000 (SLEDAI-2K) scores (p=0 and p=0.003 at diagnosis and latest visit). Significant associations were observed between follow-up duration, SLEDAI-2K at first visit scores, treatment modalities (pulse methylprednisolone, mycophenolate mofetil and rituximab), and remission subtypes in patients with jSLE. Shorter follow-up periods and lower initial SLEDAI-2K scores were linked to better remission outcomes.

Conclusions: This study found that jSLE mainly affects female patients, with musculoskeletal, renal, and hematologic involvement being the most common manifestations. Renal involvement is associated with initial anti-dsDNA positivity and SLEDAI-2K scores. The study also found that better remission outcomes are linked to lower initial disease activity and longer follow-up periods.

Keywords: Juvenile systemic lupus erythematosus; Clinical characteristics; Disease progression.

Introduction

Juvenile-onset systemic lupus erythematosus (jSLE) stands as a multisystem autoimmune/inflammatory disorder capable of affecting any organ, often leading to profound impairment, disability, or even mortality. Emerging before the age of eighteen, jSLE constitutes approximately 15–20% of all systemic lupus erythematosus (SLE) cases[1–5]. Its incidence varies, ranging from 0.36 to 2.5 cases per 100,000 children, with a prevalence rate spanning from 1.89 to 34.1 per 100,000 [6–10]. In contrast to adult-onset SLE (aSLE), jSLE typically exhibits a more aggressive disease trajectory, frequently accompanied by lupus nephritis (LN), hematologic abnormalities, heightened photosensitivity, neuropsychiatric manifestations, and mucocutaneous lesions[3–5].

Age at onset or diagnosis displays significant heterogeneity across regions[11]. Symptoms typically emerge around 11-12 years of age, with occurrences before age five exceedingly rare[12,13]. Reflecting patterns seen in adult cases, jSLE manifests a distinct female predominance, with female-to-male ratios of 4:3 and 4:1 during the first and second decades of life, respectively[14,15]. Instances of jSLE onset prior to age five often present with atypical symptoms, fewer autoantibodies, and a more aggressive disease course with less favorable outcomes[1,11–13].

jSLE epitomizes a complex, inflammatory autoimmune disorder with diverse clinical manifestations. Its chronic nature encompasses potential involvement of multiple organs and systems, alongside variable disease courses and substantial morbidity and mortality risks[16–20]. Clinical presentation and disease intensity vary widely, influenced by genetic predispositions and socio-economic factors[21]. Complications may entail permanent damage accumulation, compromised health-related quality of life, and shortened lifespan primarily due to infections and recurrent disease flares[22,23].

This study aims to evaluate the clinical presentations, treatment responses, and long-term outcomes of jSLE within a diverse patient cohort. Emphasis is placed on identifying prognostic factors influencing disease progression and health-related quality of life.

Materials And Methods

Patient selection

The data of patients diagnosed with jSLE at the pediatric rheumatology unit were collected retrospectively and examined from January 2017 to February 2024 at the Ümraniye Training and

Research Hospital's pediatric rheumatology unit. jSLE patients who met the inclusion criteria at diagnosis were included. The criteria were: (1) meeting at least four American College of Rheumatology (ACR) classification criteria for SLE and (2) disease onset before 18 years of age. Ethical considerations were strictly adhered to in accordance with the principles of the Declaration of Helsinki (2013 revision). The study protocol received the necessary approval from the Research and Ethical Review Board of the hospital where the study was conducted (Document ID: 224909521-354).

Clinical assessment

For each patient in the study, detailed data on clinical variables associated with the risk of permanent damage were systematically collected from medical records. The patterns of organ involvement, clinical manifestations, and laboratory results were cumulatively extracted from patient files, spanning from the disease's onset to their most recent visit. The diagnosis of CNS involvement was determined based on the 1999 American College of Rheumatology criteria and definitions for neuropsychiatric SLE[24]. Lupus-related renal involvement encompasses a range of renal manifestations in SLE, from mild proteinuria to severe renal impairment. The criteria for renal involvement include proteinuria (>0.5 g/d) or the presence of cellular casts in urinalysis or hematuria[25]. LN, a specific form of renal involvement, is defined histopathologically by immune complex-mediated glomerulonephritis. According to the 2003 International Society of Nephrology/Renal Pathology Society classification, LN is divided into six subtypes based on renal biopsy findings, distinguishing normal histology from various degrees of mesangial, proliferative, or membranous glomerular damage[26]. Routine follow-ups are scheduled every two to three months, with intervals adjusted according to the patient's disease activity and individual characteristics.

Laboratory assessments

Clinical tests play a crucial role in diagnosing jSLE, tracking the intensity of ongoing inflammatory reactions attributed to jSLE, and identifying instances of disease flare-ups. A summary of the most effective clinical tests for confirming a jSLE diagnosis is provided.

The analysis encompassed a complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), complement levels and a range of autoantibodies including antinuclear antibodies (ANA), Anti-double-stranded deoxyribonucleic acid antibodies (anti-dsDNA Abs), and anticardiolipin (aCL). Anticardiolipin immunoglobulin (IgG) and IgM were the sole antiphospholipid antibodies tested systematically across all subjects. As the assessment of anti-Smith (anti-Sm), anti-U1RNP, anti-Ro/SSA, anti-La/SSB, anti-beta 2 glycoprotein I (antib2GPI)

antibodies, and lupus anticoagulant (LA) was not uniformly conducted for every patient, the frequency of these autoantibodies is not mentioned. Detection of ANA utilized the indirect immunofluorescence method with HEp-2 cell lines as the base. Anti-dsDNA Abs and additional autoantibodies were evaluated through the enzyme-linked immunosorbent assay (ELISA).

Disease Activity

SLE Disease Activity Index-2000 (SLEDAI-2K) served as the metric for evaluating the disease activity, consistently recorded during each patient encounter. Specifically, SLEDAI-2K scores at the time of diagnosis and during the final assessment were extracted from health records for presentation.

Damage Assessment

The assessment of cumulative damage was conducted using the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI), a comprehensive tool comprising forty-one components across twelve organ systems/domains, with a scoring range of 0–49[27]. Damage is identified as any irreversible alteration unrelated to ongoing inflammation that has been evident since the SLE onset, confirmed through clinical examination and persisting for a minimum of six months. Such damage might result from illness, its treatment, or concurrent health issues.

Defining Prolonged Remission

Remission is categorized into three stages. The first stage, Complete Remission, is characterized by the absence of both clinical and serological disease activity (SLEDAI-2K = 0) without the use of corticosteroids (CS) or immunosuppressants, although antimalarials are permitted. The second stage, Clinical Remission off CS, refers to serologically active but clinically quiescent disease (SACQ) in patients who are not on CS, with the use of immunosuppressants and antimalarials allowed. The third stage, Clinical Remission on CSs, describes SACQ disease in patients receiving a low dose of CS (1–5 mg of prednisone or equivalent), along with immunosuppressants and antimalarials[28].

Statistics

All statistical analyses were conducted using SPSS version 26.0 (IBM Corp., Released 2019. IBM SPSS Statistics for Windows, Version 26.0, Armonk, NY: IBM Corp.). Descriptive measures were calculated, with means ± standard deviations used for normally distributed quantitative variables and medians with ranges reported for non-normally distributed data. Absolute

frequencies and percentages were presented with qualitative variables. Normality was assessed using the Shapiro-Wilk test. Group comparisons were performed using the Student's t-test for normally distributed continuous variables and the Mann-Whitney U test for non-normally distributed variables. The chi-square test was applied for proportional data analysis. A p-value of less than 0.05 was considered statistically significant. Demographic and clinical data were presented as the number of cases (n).

Results

Demographic Data

This study was composed of ninety-two patients diagnosed with jSLE. The absence of data on 23 patients was attributed to various reasons: 11 were followed for less than three months, 4 had neonatal SLE, 2 had discoid lupus, 2 had chilblain lupus, 2 were associated with drug-induced lupus, and 2 had monogenic lupus, leaving 69 patients with jSLE eligible for inclusion in the study. Among these sixty-nine patients, fifty-five were female and fourteen were male, presenting a gender ratio of 3.9:1. The median age at the time of diagnosis was 14.5 years (min:2, max:17.5). The mean duration of follow-up for these patients was 3.56 ± 1.82 years (Table I). The survey, which covered a 5-year period, indicated a 100% survival rate

Clinical Characteristics

At the initial consultation, musculoskeletal symptoms, specifically arthralgia, were the most frequently reported. The predominant clinical signs included renal disease, malar rash, and hematological involvement. A significant portion of the patient group exhibited critical organ involvement, either through renal (n=37) or hematological involvement (n=36); notably, 23 patients (33%) presented with complications in both renal and hematological domains. In total, fifty-three patients (76.8%) showed involvement in at least one major organ system, be it CNS, renal, or hematological. Throughout the study, renal complications were observed in 37 (53.6%) participants, with thirty-one undergoing renal biopsies. Biopsy-confirmed LN was identified in twenty-six individuals (37.7%), with histopathological classification revealing 20.3% (n=14) as class IV, 13% (n=9) as class II, 2.9% (n=2) as class V, and 1.5% (n=1) as class III. Neuropsychiatric conditions, categorized according to the ACR 1999 standards for neuropsychiatric lupus, most frequently manifested as headaches in 20.3% (n=14). Hematological symptoms predominantly included anemia in 49.3% (n=34), lymphopenia in 42% (n=29), and thrombocytopenia in 33.3% (n=23). Clinical data of jSLE patients is listed in Table II.

Laboratory data

Among the study's sixty-nine patients, 67 patients (97.1%) tested positive for antinuclear antibodies (ANA). The most frequently encountered specific autoantibody was anti-ds DNA Abs, present in 46.4% of the cohort, with anti-Sm antibodies detected in 17.4% of cases. Other observed autoantibodies included anti-RNP, anti-Ribosomal P, and anti-Histone antibodies.

Of those with positive autoantibody tests, 36% had isolated ANA positivity. Concurrent positivity for two antibodies was found in 19 patients (27%), with ANA and anti-dsDNA Abs being the most common combination, found in 19 and 15 patients, respectively. The simultaneous presence of anti-Sm and anti-RNP antibodies were noted in five patients (7.2%). Three patients (4.3%) were positive for both anti-SSA and anti-SSB antibodies without overlapping conditions. Additionally, seven patients (10.1%) were exclusively positive for anti-Ro antibodies, with no cases of anti-La positivity without concurrent anti-Ro antibodies.

Antiphospholipid antibodies were found in eighteen patients, with four of these cases classified as antiphospholipid syndrome (APS). Positive tests for anti-cardiolipin IgM were seen in seven patients, anti-beta2 IgM in ten patients, and lupus anticoagulant in ten patients. Two individuals had only anti-cardiolipin IgM, four had only anti-beta2 IgM, and six had only lupus anticoagulant positivity, while three had both lupus anticoagulant and anti-cardiolipin IgM positivity.

Hematological manifestations were predominantly anemia (n=34, 49.3%), lymphopenia (n=29, 42%), and thrombocytopenia (n=23, 33.3%), with eleven patients (16%) having Evans syndrome. The median erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels at diagnosis were 16 mm/hour (range: 0-94) and 0.2 mg/dl (range: 0.1–33), respectively. Reduced complement levels (C3 and/or C4) were noted in 62.3% (43 patients): low C3 in 24 patients (38%), low C4 in 39 patients (56.5%), and both C3 and C4 levels were low in twenty-two patients (32%). The SLEDAI-2K scores at the onset and at the last visit were 11.43(± 5.62) and 3.84(± 3.71), respectively (Table III).

Correlations of clinical manifestations and autoantibody profile

A statistically significant association was observed between anti-dsDNA antibody positivity and renal involvement ($p = 0.036$). Patients with anti-dsDNA antibody positivity at disease onset were more frequently observed to have renal involvement during follow-up.

Subsequent statistical examinations of the correlation between neurological involvement and various factors, including complement levels (C3 and C4), complement deficiencies, and antibody presence (ANA, anti-dsDNA, Sm, RNP, SSA, SSB, Scl70, Ribosomal P, Centromere), as

well as anti-histone antibody positivity, did not demonstrate any statistically significant connections ($p < 0.05$).

This finding suggests that within the scope of the dataset and analyses conducted, there is no substantiated evidence to indicate a statistically significant correlation between these predictors and neurological complications in lupus patients.

In this research, the therapeutic approach for managing patients was notably comprehensive, with an overwhelming 98.6% receiving hydroxychloroquine as a fundamental element of their treatment regimen. A substantial number of patients, 39 (56.5%), received pulse methylprednisolone treatments, providing a substantial anti-inflammatory benefit. Mycophenolate mofetil was prescribed to twenty-eight patients (40.6%), underscoring its increasing importance in controlling disease activity. Azathioprine was part of the treatment for twenty-nine individuals (42%), demonstrating its continued relevance as an immunosuppressant in SLE care. For those with more severe symptoms, particularly affecting the renal and CNS systems, cyclophosphamide was given to twelve patients (17.4%). The use of rituximab in eleven patients (15.9%) indicates the growing incorporation of biologic treatments in SLE therapy. Both intravenous immunoglobulin (IVIG) and methotrexate were utilized by twenty patients (29%), pointing to their applicability in certain SLE patient groups. Tacrolimus was less commonly used, at a rate of 1.4%, highlighting the customized approach required in SLE management strategies. The varied treatment modalities underscore the intricate nature of SLE management and the necessity of personalized treatment plans for each patient's specific conditions.

Disease activity

The discovery of a strong link between renal involvement and SLE Disease Activity Index (SLEDAI) scores at both the time of diagnosis ($p=0$) and during the most recent visit ($p= 0.0038$) indicate a distinct difference in SLEDAI-2K scores among lupus patients with and without renal complications. This correlation suggests that individuals with heightened disease activity face a heightened susceptibility to developing renal complications, a well-established severe outcome of SLE. The relevance of the SLEDAI scores at the latest evaluation further indicates that disease activity levels at the most recent examination differ markedly based on renal involvement, with patients experiencing renal complications typically demonstrating elevated disease activity. This understanding is pivotal for monitoring disease progression and optimizing therapeutic approaches, as consistently elevated SLEDAI scores may necessitate intensified or tailored interventions to manage renal complications and prevent additional damage.

No significant associations were observed between neurological or hematological presentations and SLEDAI-2K scores, either at the onset of diagnosis or at the final follow-up within the scrutinized dataset.

Among the patients diagnosed with jSLE, the most common accompanying conditions were Immune Thrombocytopenic Purpura (ITP), followed by Raynaud's phenomenon, Henoch-Schoenlein purpura (HSP), and APS.

Long-term outcomes

In our study, the relationship between demographic data, laboratory clinical findings, treatment practices and remission status of jSLE patients was analyzed. Significant differences were detected between follow-up period, SLEDAI-at first visit and pulse methylprednisolone (PMP), Mycophenolate Mofetil (MMF), Rituximab (RTX) data and remission subtypes (Table IV).

In our study, 64 patients (92.7%) achieved complete remission, while 5 patients (7.3%) did not achieve remission. Patients in the complete remission group had a significantly shorter follow-up duration compared to those without remission ($p < 0.05$).

The SLEDAI at first visit score is an important marker of initial disease severity and is closely associated with remission outcomes. Patients with lower scores are more likely to achieve complete remission, while those with higher scores are more likely to remain unremitted or dependent on CSs.

The use of PMP and MMF appears to be strong indicators of disease severity and activity, with significant differences observed across remission categories. Patients in complete remission are less likely to require aggressive CS therapy, indicating better disease control and a favorable prognosis. Patients in clinical remission—particularly those off CSs—often have a history of significant disease activity that required PMP and MMF. Overall, the data suggests that the need for these medications can serve as a marker of past or present severe disease activity and may predict disease course and remission outcomes. Rituximab treatment likely helped stabilize disease for the patient group but was not always sufficient to achieve complete steroid-free remission. Rituximab use serves as a marker of disease severity and resistance to treatment in patients with lupus, particularly in those who are harder to treat or stabilize with conventional therapies. It plays a role in controlling disease activity in some cases, but its use is limited in achieving full remission, especially in more severe or resistant forms of the disease.

Discussion

SLE is a chronic autoimmune disorder that affects individuals of all ages, with about 20% of cases beginning in childhood. Despite significant attention to aSLE, there have been fewer than fifteen studies in the past decade examining jSLE, especially lacking large, single-center cohorts[28–33].

Our most notable finding concerned disease outcomes. Although SLE is a chronic autoimmune disease, we observed that it can generally be well-controlled with appropriate treatment strategies. The remission rates in our study were significantly higher compared to aSLE outcomes reported by Zen et al.[28], with complete remission and clinical remission off corticosteroids (CS) being 3 to 4 times higher (Complete remission: 20% vs. 7.1%; Clinical remission off CS: 56.5% vs. 14.5%).

While aSLE typically shows a female-to-male ratio of around 10:1, our study found a lower ratio of 4:1, consistent with most jSLE studies[34–37]. Female predominance in jSLE, while slightly less pronounced than in adult cases (80%-90.9%), was found to be 80% in our cohort[12,21,25,38–45]. The average age at disease onset and diagnosis aligns with previous jSLE research[7,45–50].

The association between shorter follow-up duration and complete remission likely reflects earlier disease stabilization, with remission criteria being met earlier in the disease course. In this context, follow-up duration represents a time-dependent outcome rather than a true independent predictor of remission. Shorter follow-up periods are known to be particularly susceptible to reverse causality, whereby the observed association is driven by the timing of disease stabilization rather than a causal effect of follow-up itself [51].

Among our jSLE cohort, musculoskeletal symptoms, fatigue, renal, and hematological issues were the most prevalent, reflecting the primary causes of morbidity and mortality in SLE, particularly renal and CNS complications. These findings are consistent with previous research, which also emphasizes the prevalence of nephritis and CNS involvement in jSLE. However, they underscore the relatively benign nature of arthritis in pediatric cases, aligning with the observation that major organ involvement poses a greater risk for morbidity and mortality[52,53].

Our research found a somewhat lower incidence of renal involvement and overt nephritis compared to earlier jSLE studies, adopting a conservative approach towards renal biopsies in cases of mild or asymptomatic proteinuria and hematuria[16,25,40,41,54–56].

While European studies have reported nephritis rates between 43% and 62.5%, our figures were lower, even compared to studies from Europe, Asia, Africa, and Canada, which showed higher frequencies of renal complications[6,39–48]. Class II and IV nephritis were the most prevalent among our cases with confirmed renal involvement, consistent with previous findings[6,38,47].

Our study also identified less severe disease activity with favorable initial SLEDAI-2K scores compared to those documented elsewhere, aligning only with a Canadian study's findings[6]. The rate of neurological involvement in our cohort was consistent with the broad range reported internationally, which could be attributed to the diversity in CNS disorder definitions and disease duration differences[16,25,39–41]. Neuropsychiatric involvement in our cohort was predominantly mild, with headache being the most frequent manifestation. Consistent with this generally mild disease profile, damage development after a mean disease duration of 4.4 years was observed in 26.1% of patients and was characterized by a lower incidence and severity compared with reports from certain Canadian and South African cohorts[6,47]. Our analysis also confirmed comparable rates of ANA, anti-dsDNA Abs positivity, and decreased complement levels to previous research, but a lower prevalence of anticardiolipin (aCL) positivity, with only three patients meeting the criteria for APS. Renal involvement in this study primarily refers to clinically detected renal manifestations based on laboratory and urinary findings, whereas biopsy-proven lupus nephritis represents a histopathologically confirmed subset. Associations observed with anti-dsDNA antibody positivity and higher SLEDAI-2K scores should therefore be interpreted in the context of clinical renal activity rather than biopsy-confirmed nephritis. As renal domains within the SLEDAI-2K are derived from clinical and laboratory parameters, these measures reflect active renal involvement but do not necessarily correspond to histological classification. In the study by Zen et al.[28], 1 out of 16 patients in remission had renal disease, whereas in our cohort, 4 out of 34 patients in remission had renal disease. Consistent with the findings of Zen et al.[28], patients who achieved remission in our study were treated with PMP, MMF and RTX less frequently than those who did not achieve remission during the disease course (Table 4). This pattern likely reflects differences in baseline disease severity, as patients requiring more intensive immunosuppressive regimens typically represent those with higher disease activity or organ-threatening involvement. Accordingly, the observed association between remission status and intensive therapies should be interpreted with caution and not as evidence of a causal treatment effect.

Conclusion

Our study offers significant insights into jSLE, highlighting its distinct clinical and laboratory features compared to SLE. Our findings underscore the importance of age-specific demographic patterns, with a lower female-to-male ratio observed in jSLE.

The predominance of musculoskeletal, renal, and hematological manifestations in our jSLE cohort mirrors the primary causes of morbidity and mortality in SLE. Despite a relatively lower incidence of renal involvement compared to previous studies; the prevalence of nephritis remains consistent. Our analysis also reveals less severe disease activity and neurological involvement compared to other cohorts, suggesting the complexity and variability of jSLE.

Overall, our study contributes valuable insights into the understanding and management of jSLE, emphasizing the need for tailored approaches to diagnosis and treatment in pediatric populations. Further research is warranted to validate these findings and improve outcomes for children and adolescents with this challenging autoimmune disorder.

Tables and Figures

Table I – Demographic data of juvenile systemic lupus erythematosus patients

Parameters	Patients (n=69)
Sex {Female} [n, (%)]	55 (80)
Sex {Male} [n, (%)]	14 (20)
Age at diagnosis, months (median)(min-max)	174 (24-210)
Disease follow up duration, months (median)(min-max)	41 (3-85)

Table II – Clinical data of Juvenile Systemic Lupus Erythematosus patients

Parameters	Patients [n (%)]
Constitutional symptoms	
Fever	12 (17.3)
Anorexia	4(5.8)
Weight Loss	6(8.7)
Fatigue	44 (63.7)
Cutaneous symptoms	
Malar Rash	27 (39.1)
Photosensitivity	21 (30.4)
Oral Aphthous Lesions	24(34.7)
Discoid Rash	5(7.2)
Alopecia	20(28.9)
Musculoskeltal symptoms	
Arthralgia	50(72.5)
Arthritis	29 (42)
Hematological symptoms	36(52.2)
Anaemia	34(49.3)
Leukopenia	11(15.9)
Lymphopenia	29(42)
Thrombocytopenia	23(33.3)
Renal Symptoms	
Renal Involvement	37(53.6)
Lupus Nephritis	26 (37.6)
Proteinuria	37 (53.6)
Vascular	
Raynaud Phenomenon	16 (23.2)
Cardiopulmonary - Serositis	9 (13)
Pericarditis	5(7.2)
Pleuritis	4(5.7)
Neuropsychiatric Symptoms	
Headache	14 (20.2)

Table III – Laboratory data of Juvenile Systemic Lupus Erythematosus patients

Parameters	**Patients (n=69)**
Complete Blood Count (CBC) Parameters median (min-max)	
Leucocyte /mm3	6.68 (0.33-17.5)
Neutrophil/ mm3	4.22 (0.28-16.1)
Lymphocyte/mm3	1.60 (0.05-6.2)
Haemoglobin gr/dL	11.5 (6.8-14.9)
Platelet/mm3	237 (3-551)
Biochemical Parameters median (min-max)	
BUN	24 (11.3-145)
Creatinine	0.6 (0.2-3.9)
ALT	15 (6-192)
AST	18 (6-102)
Acute Phase Reactants median (min-max)	
CRP mg/L	0.2 (0.1-33)
ESR (mm/h)	16 (0-94)
Serology (Positivity n [%])	
ANA	67(97.1)
Anti-dsDNA	32(46.4)
Anti-SM	12(17.4)
Anti-RNP	7(10.1)
Anti-SSA	10(14.5)
Anti-SSB	3(4.3)
Anti-SCL70	2(2.9)
Anti-Ribosomal P	12(17.4)
Anti-Centromere	3(4.3)
Anti Histon	12(17.4)
Anti-Phospholipid Antibodies (Positivity n [%])	
Anti-Beta 2 Glycoprotein IgM	10(14.5)
Anti-Beta 2 Glycoprotein IgG	6(8.7)
Lupus Anti-coagulant	10(14.5)
Anti-Cardiolipin IgM	7(10.1)
Anti-Cardiolipin IgG	7(10.1)
Direct Coombs (Positivity n [%])	
Direct Coombs	36(52.2)
Complement Levels (n [%])	
Low C3	26(37.7)
Low C4	41(59.4)
Low complement levels	45(65.2)
***Disease Activity (mean score* ± SD)**	
SLEDAI-2K at Diagnosis	11.43(± 5.62)
SLEDAI-2K at Last Visit	3.84(± 3.71)
Damage Index [median score; (min-max)]	
SLE Damage Index (At Last Visit)	0 (0-5)

CBC: Complete Blood Count; BUN: Blood Urea Nitrogen; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; CRP: C-Reactive Protein; ESR: Erythrocyte Sedimentation Rate; ANA: Anti-Nuclear Antibody; ANTI-DsDNA: Anti-Double-Stranded DNA; SM: Smith Antibody; RNP: Ribonucleoprotein; SSA: Sjögren Syndrome-Related Antigen A; SSB: Sjögren Syndrome-Related Antigen B; SCL70: Anti-Topoisomerase I; Anti-Histon: Antibodies against histones; Beta 2 Glycoprotein IgM: Antibodies to beta-2 glycoprotein (IgM subtype); Beta 2 Glycoprotein IgG: Antibodies to beta-2 glycoprotein (IgG subtype); C3: Complement 3; C4: Complement 4; SLEDAI: Systemic Lupus Erythematosus Disease Activity Index 2000.

Table IV – Clinical, laboratory and treatment characteristics according to remission status

			REMISSION STATUS				
		Overall	Complete Remission	Clinical Remission (OFF CS)	Clinical Remission (ON CS)	Unremitted	p-value
CLINICAL CHARACTERISTICS							
Gender	Female, n (%)	55 (79.7)	12 (85.7)	30 (76.9)	8 (72.7)	5 (100)	0.55
	Male, n (%)	14 (20.3)	2 (14.3)	9 (23.1)	3 (27.3)	0 (0)	
Age at diagnosis, months (median, min–max)		174 (24–210)	171.5 (95–210)	177 (33–209)	149 (24–206)	164 (42–199)	0.57
Follow-up duration, months (mean ± SD)		42.76 ± 21.81	27.35 ± 18.51	49.12 ± 20.41	34.72 ± 21.64	54 ± 8.74	**<0.001**
Time period before diagnosis, months (median, min–max)		1 (0–96)	0 (0–60)	1 (0–96)	0 (0–87)	1 (0–80)	0.67
ORGAN INVOLVEMENT							
Lupus nephritis, n (%)		26 (37.7)	1 (3.8)	13 (50.0)	9 (34.6)	3 (11.5)	1.00
Renal involvement, n (%)		37 (53.6)	4 (10.8)	22 (59.4)	8 (21.6)	3 (8.1)	0.15
Neurological involvement, n (%)		14 (20.3)	2 (14.3)	8 (57.1)	2 (14.3)	2 (14.3)	0.67
Hematological involvement, n (%)		36 (52.2)	5 (13.9)	19 (52.8)	9 (25.0)	3 (8.3)	0.13
LABORATORY FINDINGS							
Leukopenia, n (%)		11 (15.9)	1 (9.1)	7 (63.6)	2 (18.2)	1 (9.1)	0.79
Lymphopenia, n (%)		29 (42.0)	4 (13.8)	15 (51.7)	7 (24.1)	3 (10.3)	0.26
Anaemia, n (%)		34 (49.3)	7 (20.6)	16 (47.1)	8 (23.5)	3 (8.8)	0.29
Thrombocytopenia, n (%)		23 (33.3)	3 (13.0)	13 (56.5)	5 (21.7)	2 (8.7)	0.63
Low C3, n (%)		24 (34.7)	3 (12.5)	13 (54.2)	5 (20.8)	3 (12.5)	0.38
Low C4, n (%)		39 (56.5)	5 (12.8)	22 (56.4)	8 (20.5)	4 (10.3)	0.19
ANA positivity, n (%)		67 (97.1)	13 (19.4)	38 (56.7)	11 (16.4)	5 (7.5)	0.71
Anti-dsDNA positivity, n (%)		32 (46.4)	2 (6.3)	19 (59.4)	7 (21.9)	4 (12.5)	0.06
Lupus anticoagulant, n (%)		10 (14.5)	1 (10.0)	6 (60.0)	1 (10.0)	2 (20.0)	0.32

		REMISSION STATUS				
	Overall	Complete Remission	Clinical Remission (OFF CS)	Clinical Remission (ON CS)	Unremitted	p-value
SLEDAI-2K at first visit (median, min–max)	12 (2–28)	6 (2–14)	12 (2–28)	15 (2–19)	12 (10–22)	0.02
SLEDAI-2K at last visit (median, min–max)	4 (0–16)	0 (0–2)	4 (0–16)	4 (2–16)	10 (6–12)	0.73
TREATMENT						
Pulse methylprednisolone, n (%)	39 (56.5)	3 (7.7)	22 (56.4)	10 (25.6)	4 (10.3)	**<0.001**
Hydroxychloroquine, n (%)	68 (98.6)	13 (19.1)	39 (57.4)	11 (16.2)	5 (7.4)	0.26
Cyclophosphamide, n (%)	12 (17.4)	0 (0)	6 (50.0)	4 (33.3)	2 (16.7)	0.06
Mycophenolate mofetil, n (%)	28 (40.6)	2 (7.1)	14 (50.0)	7 (25.0)	5 (17.9)	**<0.001**
Azathioprine, n (%)	29 (42.0)	5 (17.2)	17 (58.6)	4 (13.8)	3 (10.3)	0.78
Tacrolimus, n (%)	1 (1.4)	0 (0)	0 (0)	1 (100)	0 (0)	0.15
Rituximab, n (%)	11 (15.9)	0 (0)	4 (36.4)	4 (36.4)	3 (27.3)	**<0.001**
IVIG, n (%)	20 (29.0)	3 (15.0)	8 (40.0)	6 (30.0)	3 (15.0)	0.06
Methotrexate, n (%)	20 (29.0)	5 (25.0)	12 (60.0)	3 (15.0)	0 (0)	0.49

jSLE: Juvenile Systemic Lupus Erythematosus; LN: Lupus Nephritis; C3: Complement 3; C4: Complement 4; ANA: Anti-Nuclear Antibody; dsDNA: Double-Stranded DNA; SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index 2000; IVIG: Intravenous Immunoglobulin; CS: Corticosteroid.

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