Turkish Archives of Pediatrics

ORIGINAL ARTICLE
DOI: 10.5152/TurkArchPediatr.2025.25092

Achievement and Features Associated with Childhood Definition of Remission in Juvenile-Onset Systemic Lupus Erythematosus

Hakan Kisaoglu, Ozge Baba, Mukaddes Kalyoncu

Division of Pediatric Rheumatology, Karadeniz Technical University Faculty of Medicine, Trabzon, Türkiye

What is already known on this topic?

- *Achievement of the adult definition of remission is associated with improved outcomes in children with systemic lupus erythematosus (SLE).*
- *Childhood definition of remission employs a lower glucocorticoid threshold for younger and lighter patients.*

What this study adds on this topic?

- *Childhood definition of remission is achievable in two-thirds of children with SLE.*
- *Childhood and adult definitions display significant concordance, and only a minority of children cannot achieve the childhood definition of remission despite attaining the adult definition.*
- *Serological activity adversely affects remission.*

ABSTRACT

Objective: To identify the feasibility of achieving the childhood definition of remission, investigate factors affecting achievement and determine the concordance rate with adult definition in children with systemic lupus erythematosus (SLE).

Materials and Methods: Medical records of children diagnosed with SLE between 2012 and 2022 were reviewed. The Definitions of Remission in Systemic Lupus Erythematosus (DORIS) definition of remission was used as the adult definition of remission, and a lower glucocorticoid threshold, as proposed, was used for children weighing <50 kg. Cox regression analysis was performed to identify features associated with remission.

Results: Among the 50 included patients, 35 (70%) achieved the adult definition of remission in a median of 16 months. While 33 (66%) patients achieved the childhood definition of remission, 25 (76%) achieved both definitions concomitantly. A lower rate of damage (15.2% vs. 52.9%, P = .008) and flare count (median 1 vs. 2, P = .001) were observed in patients with remission despite significantly longer follow-up duration (median 59 months vs. 32 months, P = .007). Survival analysis revealed that the presence of positive anti-dsDNA antibodies (hazard ratio [HR], 0.47; P = .035) and immunosuppressive usage (HR: 0.45, P = .032) were associated with a higher risk of not achieving remission.

Conclusion: Childhood definition of remission is achievable in two-thirds of children with SLE and displays substantial concordance with the adult definition. Additionally, the higher risk of failure to achieve remission in children using immunosuppressants reflects a milder course in a subgroup of children who achieved remission and signifies the need for more efficacious treatment modalities for severe manifestations.

Keywords: Children, dsDNA, remission, systemic lupus erythematosus, treatment

INTRODUCTION

Systemic lupus erythematosus (SLE) is a prototype autoimmune disease associated with antinuclear antibody development with a relapsing remitting nature.[1] The disease predominantly affects women of childbearing age and displays a high burden among affected individuals.[2] Childhood-onset disease is more severe compared to its adult counterparts and is associated with early damage accrual with more frequent major organ/system involvement.[3,4]

In the last decade, the management of patients with SLE has changed significantly. Despite being effective, the association of moderate to high doses of glucocorticoid treatment with damage leads to the targeting of lower doses of glucocorticoids in the management of patients with SLE.[5] In this context, a treat-to-target approach has emerged using composite outcomes to target well-controlled disease with low glucocorticoid doses.[6] Among these treatment targets, lupus low disease activity state and remission have been shown to be

Corresponding author:
Hakan Kisaoglu
✉ kisaoglu@outlook.com.tr
Received: March 27, 2025
Revision Requested: April 23, 2025
Last Revision Received: May 27, 2025
Accepted: May 31, 2025
Publication Date: July 1, 2025

Cite this article as: Kisaoglu H, Baba O, Kalyoncu M. Achievement and features associated with childhood definition of remission in juvenile-onset systemic lupus erythematosus. *Turk Arch Pediatr.* 2025;60(4):398-403.

protective against damage accrual and flare in both adults and children.[7-11] Recently, a childhood definition of remission was proposed using a lower glucocorticoid threshold for children weighing <50 kg.[12] However, the feasibility of the achievement of childhood-onset remission and differences in attainment compared to the adult definition have not been widely studied.

With this study, the aim was to identify the feasibility of the achievement of childhood definition of remission, investigate factors affecting the achievement and determine the concordance rate with adult definition in children with SLE.

MATERIALS AND METHODS

In this descriptive cohort study, children diagnosed with SLE between 2012 and 2022, from a tertiary referral center (Karadeniz Technical University Farabi Hospital), experienced in management of children with SLE in Türkiye, who fulfilled the SLICC 2012 criteria, were included in the study.[13] Patients with irregular visits (>6 months) were excluded.

The study was conducted by reviewing the medical charts of the patients. This study was conducted in accordance with the Declaration of Helsinki and approval was granted by the Ethical Committee of the Karadeniz Technical University Faculty of Medicine (approval no: 2023/114, date: 16.06.2023). Informed consent was obtained from all participants or legal guardians. Clinical and laboratory features, treatments, and disease activity were extracted from the medical files. Disease activity was assessed using the systemic lupus erythematosus disease activity index (SLEDAI) score.[14] Disease associated damage at last visit, number of flares through the course and, attainment and time to first achievement of the adult and childhood definitions of remission was noted.

Flare was defined as new-onset disease activity or worsening of a previous manifestation that required either pulse methylprednisolone, increase of the prednisolone dose, or initiation of a new immunosuppressant or biological drug.[15] Damage was evaluated using the SLICC/ACR damage index at the last visit of patients.[16] The DORIS definition of remission on treatment was used for the adult definition of remission, which requires i) absence of SLEDAI-based clinical activity irrespective of serological activity, ii) a physician global score of <0.5 (range 0-3) for disease activity, iii) stable doses of immunosuppressants and/or biologics, and iv) a prednisolone equivalent dose of ≤5 mg/day.[17] Proposed childhood definition of remission on treatment is same with DORIS definition except requires ≤0.01 mg/kg/day (maximum 5 mg/day) prednisolone equivalent dose that result in a lower dose for children weighting <50 mg.[12] Achievement was accepted as fulfilment of remission criteria in consecutive visits at least 3 months apart.

Descriptive statistics are presented as frequencies with percentages, means with SDs for normally distributed data, or medians with interquartile ranges (IQR) for non-normally distributed data. Normality was assessed using the Kolmogorov-Smirnov test with histograms. Categorical variables were compared using Fisher's exact test, and continuous variables were compared using Student's *t*-test or the Mann–Whitney *U* test, according to the distribution of the data. Cox proportional hazard analysis was used to identify features associated with remission. Features associated with remission were identified using univariate analysis. Even statistically significant associations were identified in univariate analysis a stepwise approach, using variables significant at a *P*-value of <.01, was employed for multivariate analysis, owing to the small sample size of the study. Statistical analysis was performed using the SPSS version 23 (IBM SPSS Corp.; Armonk, NY, USA), with statistical significance set at $P < .05$.

RESULTS

Among 54 patients diagnosed with SLE, 4 were excluded of whom 2 due to irregular visits, 1 due to missing information on disease activity and treatments and 1 due to proceeding treatment in another center shortly after diagnosis. The remaining 50 children with SLE, of whom 42 (84%) were female, were included. The mean age at diagnosis was 13.8 ± 3.1 years and the median follow-up duration was 50 months. The most frequent systemic involvement was musculoskeletal in 35 patients (70%). Kidney involvement was observed in 25 (50%) patients, and 16 (32%) patients displayed proliferative lupus nephritis. While hypocomplementemia was evident in 42 (84%) patients, ever presence of anti-dsDNA antibody was observed in 27 (54%) patients. The clinical and serological features of the patients included in this study are shown in Table 1.

Table 1. Cumulative Clinical and Serological Characteristics of Children Included in the Study

Features	**n:50 (%)**
Age at onset (years), mean±SD	13.8 ± 3.1
Sex (female)	42 (84)
Follow-up duration (months), median (IQR)	50 (35-70)
Clinical characteristics	
SLEDAI at onset, median (IQR)	12 (7-19)
Fever	26 (52)
Cutaneous involvement	26 (52)
Musculoskeletal involvement	35 (70)
Kidney involvement	25 (50)
Proliferative nephritis (Class III/IV)	16 (32)
Leukopenia	21 (42)
Oral/nasal ulcers	10 (20)
Alopecia	10 (20)
AIHA	15 (30)
Thrombocytopenia	14 (28)
Serositis	12 (24)
Neurological involvement	10 (20)
Serological features	
Hypocomplementemia	42 (84)
Positive anti-dsDNA	27 (54)
Positive anti-Sm	24 (48)
Positive anti-RNP	14 (28)
Positive anti-SSA	11 (22)
Positive anti-ribosomal P	9 (18)
Lupus anticoagulant	12 (24)
Positive anti-cardiolipin antibodies	8 (16)
Positive anti-β2glycoprotein1 antibodies	6 (12)

AIHA, Autoimmune hemolytic anemia; dsDNA, deoxyribonucleic acid; IQR, Interquartile range; n, number; RNP, Ribonucleoprotein; Sm, Smith; SSA, Sjogren's' syndrome associated protein A.

Among treatments, all patients received glucocorticoid treatment and all, but 1, patients used hydroxychloroquine which was due to a severe hydroxychloroquine induced drug reaction. Immunosuppressive use was observed in 32 (64%) patients. While cyclophosphamide and mycophenolate mofetil were the most frequently used immunosuppressives in 19 (38%) and 12 (24%) patients, respectively, azathioprine, methotrexate, and tacrolimus were used in 11 (22%), 8 (16%), and 4 (8%) patients, respectively. Also, 5 (10%) received rituximab treatment for refractory manifestations.

During follow-up, 35 (70%) patients achieved the adult definition of remission in a median of 16 months. The childhood definition of remission was achieved in 33 (66%) patients, and among patients who achieved adult definition of remission, 26 (74%) achieved adult and childhood definitions contemporary. The remaining 7 patients achieved childhood definition within a median of 3 months. Only 2 patients achieved adult definition without attainment of childhood definition owing to the glucocorticoid (GC) threshold due to the absence of actively attempting to achieve GC threshold of childhood definition in clinical practice. Furthermore, the weight of these 2 patients was in the 45-50 kg range, indicating that some patients close to the weight threshold of childhood definition may not attain childhood definition owing to the lack of tapering toward the lower glucocorticoid threshold. Also, specific withdrawal strategies for attainment of remission dosage have not been actively implemented and driven by the clinical judgement. Achievement of adult and childhood definitions are shown in Table 2.

When compared, patients who achieved the childhood definition of remission displayed a significantly longer follow-up duration [median months (IQR): 59 (47-72) vs. 32 (20-60), *P* = .007]. Interestingly, the prevalence of kidney activity or proliferative nephritis did not differ according to the achievement of remission. However, autoimmune anemia (15.2% vs. 58.2%, *P* = .03), positive anti-dsDNA (36.4% vs. 88.2%, *P* = .001), and anti-phospholipid antibodies (12.1% vs. 58.8%, *P* = .001) were significantly less frequent in patients who achieved remission. In addition, patients with remission displayed a lower flare count [median (IQR): 1 (0-1.5) vs. 2 (1-3.5), *P* = .001] and less frequent damage (15.2% vs. 52.9%, *P* = .008) despite a longer follow-up duration. Comparison of features according to the achievement of the childhood definition of remission is shown in Table 3.

Table 2. Achievement of Adult and Childhood Definitions of Remission

	n:50 (%)
Patients achieved adult definition of remission	35 (70)
Time to adult definition of remission definition (months) median (IQR) (n:35)	16 (10-21)
Patients achieved childhood definition of remission	33 (66)
Contemporary achievement of both definitions (n:35)	26 (74)
Time to subsequent achievement of both definitios after attainment of adult definition (months) median (IQR) (n:7)	3 (3-4)

IQR, interquartile range; n, number.

Cox regression analysis was performed to identify the features associated with remission. Univariate analysis revealed that autoimmune anemia (hazard ratio [HR], 0.37; *P* = .02), leukopenia (HR, 0.47; *P* = .04), immunosuppressive requirement (HR: 0.37, *P* = .005), positive anti-dsDNA (HR: 0.37, *P* = .006), and positive anti-Sm (HR: 0.46, *P* = .03) were associated with a higher risk of not achieving remission. The features selected in the regression analysis are listed in Table 4. Among these variables, only positive anti-dsDNA and immunosuppressive use were associated with a higher risk with a *P*-value <.01 and were thus included in the multivariate analysis. Multivariate analysis showed that both anti-dsDNA positivity and immunosuppressive use were associated with a higher risk of not achieving remission. Kaplan–Maier curves by the achievement of remission are given in Figure 1.

DISCUSSION

Results of this study showed that the childhood definition of remission is feasible and achieved by two-thirds of patients. Additionally, only 4% of children did not achieve the childhood definition of remission despite achieving the adult definition. Furthermore, childhood and adult definitions display significant concordance, and the duration from the achievement of the adult definition of remission to the childhood definition is not significantly long.

To date, only a recent study has investigated the feasibility of achieving the childhood definition of remission in children with SLE.[18] Similar to these results, adult and childhood definitions displayed significant concordance and showed similar performance in their ability to reduce severe flares and new damage development. Furthermore, they showed that remission on treatment was achieved in 60% of patients with a time difference between adult and childhood targets not strikingly different.[18] It should be noted that neither in this study nor in the study by Sarker et al,[18] glucocorticoid doses actively attempted for attainment of these doses. Thus, these patients may represent those who responded well to treatment rather than cases in which tapering was intentionally pursued. Since further tapering of glucocorticoids after achieving remission is associated with an increased risk of flare in adults,[19] widespread implementation of the childhood definition of remission might require the determination of safety for flares by tapering toward attainment of these glucocorticoid doses in children with low body weight. In adults, the absence of major organ system involvement and lower baseline disease activity has been shown to be associated with remission. Furthermore, the presence of anti-dsDNA adversely influences the achievement of remission in adults.[20,21] While low C3 levels have an adverse effect on spending most of the time for the adult definition of remission in children with SLE, positive dsDNA is associated with a lower duration of attainment for the childhood definition of remission in children.[9,18] This study reached similar conclusions, with anti-dsDNA antibody positivity being associated with an increased risk of not achieving remission. Anti-dsDNA antibodies are well known for their close relationship with disease activity and certain manifestations, such as nephritis and

Table 3. Comparison of Features According to the Achievement of Childhood Definition of Remission

	Patients with Remission, n: 33 (%)	Patients Without Remission, n: 17 (%)	*P*
Age (years), mean ± SD	14.0 ± 3.0	13.4 ± 2.2	.34
Sex (female)	26 (78.8)	16 (94.1)	.24
Follow-up duration (months), median (IQR)	59 (47-72)	32 (20-60)	.007
Cutaneous involvement	16 (48.5)	10 (58.8)	.56
Musculoskeletal involvement	20 (60.6)	15 (88.2)	.06
Kidney involvement	19 (57.6)	9 (52.9)	.77
Proliferative nephritis	9 (27.3)	7 (41.2)	.35
Leukopenia	11 (33.3)	10 (58.8)	.13
AIHA	5 (15.2)	10 (58.8)	.030
Thrombocytopenia	8 (24.2)	6 (35.3)	.51
SLEDAI score, median (IQR)	11 (7-17)	18 (8-24)	.13
Immunosuppressive usage	18 (54.5)	14 (84.2)	.07
HCQ dose (mg/kg/day) mean ± SD	6.1 ± 0.9	5.4 ± 1.7	.07
Flare count, median (IQR)	1 (0-1.5)	2 (1-3.5)	.001
SDI (IQR)	0 (0-0)	1 (0-2)	.004
Patients with damage *	5 (15.2)	9 (52.9)	.008
Positive APLA	4 (12.1)	10 (58.8)	.001
Positive anti-dsDNA	12 (36.4)	15 (88.2)	.001
Hypocomplementemia	28 (84.8)	14 (82.4)	>.99
Positive anti-Sm	13 (39.4)	11 (64.7)	.14
Positive anti-RNP	6 (18.2)	8 (47.1)	.047

AIHA, autoimmune hemolytic anemia; APLA, anti-phospholipid antibodies; dsDNA, double-stranded deoxyribonucleic acid; GC, glucocorticoid; HCQ, hydroxychloroquine; IQR, interquartile range; n, number; RNP, ribonucleoprotein; SDI, systemic lupus erythematosus damage index; SLEDAI, systemic lupus erythematosus disease activity index; Sm, Smith.
* Evaluated at the last visit.

hematological features.[22] Furthermore, positive anti-dsDNA antibodies increase the odds of subsequent nephritis.[23] Thus, a positive anti-dsDNA antibody might be an indicator of an active/relapsing course regarding the attainment of remission, and serologically active children might benefit from a more rigorous treatment strategy. In this study, immunosuppressants were associated with a higher risk of failure to achieve remission. Since survival analysis assesses risk over time, this result does not imply decreased odds for the attainment of remission directly related to immunosuppressives. Instead, it signifies a subgroup of patients where immunosuppressives were not required either due to mild manifestations or glucocorticoid-responsive disease activity, and these patients' risk of not achieving remission over time was lower than children who required immunosuppressives. Which also highlights that more efficacious treatments are required for a significant proportion of patients with manifestations that are refractory to standard treatments. However, comparisons among different immunosuppressives could not be conducted because of the limited sample size.

Hematological system and kidney involvement negatively affect the achievement of remission in adults with SLE.[20,21] Similarly, these results showed that features of hematological system involvement were significantly associated with the hazard of remission in univariate analysis. However, owing

Table 4. Cox Regression Analysis of Features Associated with Remission

Features	Univariable			*P*	Multivariable			*P*
	HR	95% CI			HR	95% CI		
		Lower	Upper			Lower	Upper	
Age	1.02	0.90	1.15	.80				
Sex	1.01	0.44	2.32	.99				
SLEDAI	0.99	0.90	0,99	.027				
AIHA	0.37	0.16	0.85	.020				
Leukopenia	0.47	0.23	0.96	.039				
Proliferative nephritis	0.50	0.23	1.01	.08				
Immunosuppressive usage	0.37	0.19	0.75	.005	0.47	0.23	0.95	.035
Positive anti-dsDNA	0.37	0.19	0.75	.006	0.45	0.22	0.93	.032
Positive APLA	0.50	0.21	1.20	.12				
Positive anti-Sm	0.46	0.23	0.94	.032				

AIHA, autoimmune hemolytic anemia; APLA, anti-phospholipid antibodies; CI, confidence interval; dsDNA, double-stranded deoxyribonucleic acid; HR, hazard ratio; SLEDAI, systemic lupus erythematosus disease activity index; Sm, Smith.

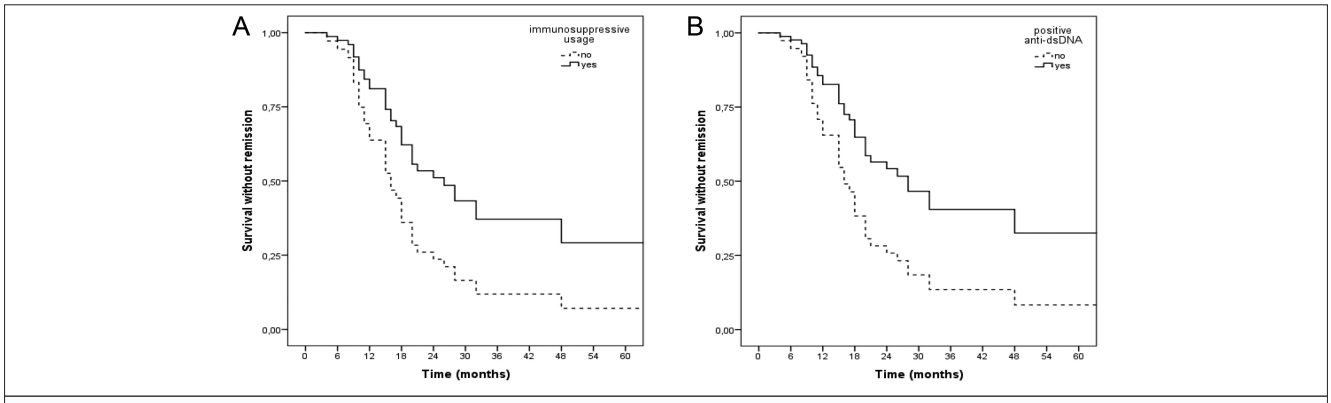

Figure 1. Kaplan–Meier survival curves of patients by the achievement of remission. Ã. According to the positive dsDNA antibody. B. according to the immunosuppressive usage.

to the small sample size of the study, these features did not progress into the multivariable analysis to avoid overfitting of the model. Despite being considered among the most severe manifestations of SLE and associated with unfavorable outcomes, these results did not show any effect of proliferative nephritis on the achievement of remission. This result is most likely due to the use of intermittent pulse glucocorticoid treatment in the management of children with proliferative nephritis at the center. Adult studies have shown that increased exposure to glucocorticoids, especially pulse treatment, is associated with increased kidney response in patients with proliferative nephritis.[24] Furthermore, intermittent mini-pulse treatments have been shown to be associated with lower prednisolone doses through follow-up of patients with lupus nephritis.[25]

The retrospective nature and small sample size are the most notable limitations of this study. The absence of actively attempting to achieve these treatment goals, specifically tapering toward the target glucocorticoid dose of remission, could be considered a limitation of this study. However, at the center, glucocorticoids were tapered toward the lowest possible dose as a treatment target, even before the proposal of these outcome measures. Furthermore, even prospective validation studies of these treatment targets in adults have not actively attempted to achieve these targets. Additionally, the absence of a longitudinal evaluation of disease activity and comparison according to indications and usage of different immunosuppressants might be regarded as a limitation. Despite the small sample size, the results provide significant insight into the implementation of a treat-to-target approach in children and show similar connections compared to adult and childhood studies.

Conclusion

In conclusion, the childhood definition of remission is associated with improved outcomes and is comparable to that used for adults. Adult and childhood definitions display significant overlap, and only a minority of patients can achieve the adult definition without attaining the childhood definition. However, the lower risk of remission with immunosuppressants might signify a milder course of disease and highlight the need for more efficacious treatments for children. Since adult and childhood definitions were similar in terms of attainment and protective value, further implementation of remission in the management of children with SLE would require determination of the flare risk with tapering toward the lower glucocorticoid threshold in children with low body weight.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: This study was approved by Ethics Committee of Karadeniz Technical University Faculty of Medicine (approval no: 2023/114, date: 16.06.2023).

Informed Consent: Informed consent was obtained from the participants or their legal guardians who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – H.K., O.B.; Design – H.K., O.B.; Supervision – M.K.; Data Collection and/or Processing – H.K., O.B.; Analysis and/or Interpretation – H.K., O.B., M.K.; Literature Search – H.K., O.B.; Writing – H.K.; Critical Review – H.K., O.B., M.K.

Declaration of Interests: The authors have no conflicts of interest to declare.

Funding: The authors declare that this study received no financial support.

REFERENCES

1. Pisetsky DS, Lipsky PE. New insights into the role of antinuclear antibodies in systemic lupus erythematosus. *Nat Rev Rheumatol.* 2020;16(10):565-579. [CrossRef]
2. Hoi A, Igel T, Mok CC, Arnaud L. Systemic lupus erythematosus. *Lancet.* 2024;403(10441):2326-2338. [CrossRef]
3. Kamphuis S, Silverman ED. Prevalence and burden of pediatric-onset systemic lupus erythematosus. *Nat Rev Rheumatol.* 2010;6(9):538-546. [CrossRef]
4. Avar-Aydın PÖ, Brunner HI. Revisiting childhood-onset systemic lupus erythematosus. *Turk Arch Pediatr.* 2024;59(4):336-344. [CrossRef]
5. Bertsias G, Askanase A, Doria A, Saxena A, Vital EM. A path to glucocorticoid Stewardship: a critical review of clinical recommendations for the treatment of systemic lupus erythematosus. *Rheumatology (Oxford).* 2024;63(7):1837-1849. [CrossRef]
6. Golder V, Tsang-A-Sjoe MWP. Treatment targets in SLE: remission and low disease activity state. *Rheumatology (Oxford).* 2020;59(suppl 5):v19-v28. [CrossRef]

7. Golder V, Kandane-Rathnayake R, Huq M, et al. Lupus low disease activity state as a treatment endpoint for systemic lupus erythematosus: a prospective validation study. *Lancet Rheumatol*. 2019;1(2):e95-e102. [CrossRef]
8. Cody EM, Wilson BE, Ogbu EA, et al. Usefulness of the lupus low disease activity state as a treatment target in childhood-onset SLE. *Lupus Sci Med*. 2023;10(1):e000884. [CrossRef]
9. Smith EMD, Tharmaratnam K, Al-Abadi E, et al. Attainment of low disease activity and remission targets reduces the risk of severe flare and new damage in childhood lupus. *Rheumatology (Oxford)*. 2022;61(8):3378-3389. [CrossRef]
10. Ugarte-Gil MF, Mendoza-Pinto C, Reátegui-Sokolova C, et al. Achieving remission or low disease activity is associated with better outcomes in patients with systemic lupus erythematosus: a systematic literature review. *Lupus Sci Med*. 2021;8(1):e000542. [CrossRef]
11. Kisaoglu H, Baba O, Kalyoncu M. Lupus low disease activity state as a treatment target for pediatric patients with lupus nephritis. *Pediatr Nephrol*. 2023;38(4):1167-1175. [CrossRef]
12. Smith EMD, Aggarwal A, Ainsworth J, et al. Defining remission in childhood-onset lupus: PReS-endorsed consensus definitions by an international task force. *Clin Immunol*. 2024;263:110214. [CrossRef]
13. Petri M, Orbai AM, Alarcón GS, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. *Arthritis Rheum*. 2012;64(8):2677-2686. [CrossRef]
14. Gladman DD, Ibañez D, Urowitz MB. Systemic lupus erythematosus disease activity index 2000. *J Rheumatol*. 2002;29(2):288-291.
15. Ruperto N, Hanrahan LM, Alarcón GS, et al. International consensus for a definition of disease flare in lupus. *Lupus*. 2011;20(5):453-462. [CrossRef]
16. Gladman D, Ginzler E, Goldsmith C, et al. The development and initial validation of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index for systemic lupus erythematosus. *Arthritis Rheum*. 1996;39(3):363-369. [CrossRef]
17. van Vollenhoven RF, Bertsias G, Doria A, et al. 2021 DORIS definition of remission in SLE: final recommendations from an international task force. *Lupus Sci Med*. 2021;8(1):e000538. [CrossRef]
18. Sarker C, Jorgensen AL, Tharmaratnam K, et al. Validation of childhood lupus specific targets: ensuring accurate assessment of disease control in younger, lighter paediatric patients. *Rheumatology (Oxford)*. 2025;64(6):3587-3597. [CrossRef]
19. Cho J, Shen L, Huq M, et al. Impact of low disease activity, remission, and complete remission on flares following tapering of corticosteroids and immunosuppressive therapy in patients with systemic lupus erythematous: a multinational cohort study. *Lancet Rheumatol*. 2023;5(10):e584-e593. [CrossRef]
20. Yang Z, Cheng C, Wang Z, et al. Prevalence, predictors, and prognostic benefits of remission achievement in patients with systemic lupus erythematosus: A systematic review. *Arthritis Care Res (Hoboken)*. 2022;74(2):208-218. [CrossRef]
21. Gao D, Hao Y, Mu L, et al. Frequencies and predictors of the lupus low disease activity state and remission in treatment-naïve patients with systemic lupus erythematosus. *Rheumatology (Oxford)*. 2020;59(11):3400-3407. [CrossRef]
22. Lou H, Ling GS, Cao X. Autoantibodies in systemic lupus erythematosus: from immunopathology to therapeutic target. *J Autoimmun*. 2022;132:102861. [CrossRef]
23. Hsu TC, Yang YH, Wang LC, et al. Risk factors for subsequent lupus nephritis in patients with juvenile-onset systemic lupus erythematosus: a retrospective cohort study. *Pediatr Rheumatol Online J*. 2023;21(1):28. [CrossRef]
24. Figueroa-Parra G, Cuéllar-Gutiérrez MC, González-Treviño M, et al. Impact of glucocorticoid dose on complete response, serious infections, and mortality during the initial therapy of lupus nephritis: A systematic review and meta-analysis of the control arms of randomized controlled trials. *Arthritis Rheumatol* [published online first: 28 June 2024]. 2024;76(9):1408-1418. [CrossRef]
25. Ruiz-Irastorza G, Ugarte A, Saint-Pastou Terrier CS-P, et al. Repeated pulses of methyl-prednisolone with reduced doses of prednisone improve the outcome of class III, IV and V lupus nephritis: an observational comparative study of the Lupus-Cruces and lupus-Bordeaux cohorts. *Autoimmun Rev*. 2017;16(8):826-832. [CrossRef]