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Review

Juvenile Systemic Lupus Erythematosus (JSLE): A Literature Review

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ABSTRACT

Juvenile systemic lupus erythematosus (JSLE) is a rare but clinically impactful autoimmune disease characterized by multisystem inflammation driven by dysregulated autoantibody production. Compared to adult-onset lupus, JSLE follows a more aggressive course, with earlier onset, severe visceral involvement and greater cumulative organ damage. Its pathogenesis involves genetic, epigenetic and environmental factors-most notably type I interferon pathway activation, hormonal alterations and ultraviolet exposure as key immunological triggers. Exaggerated expression of inflammatory cytokines such as TNF-α and IL-6 perpetuates the pathological immune response. Clinically, manifestations include cutaneous lesions, non-erosive arthritis, lupus nephritis (particularly classes III and IV) and hematological and neurological alterations. Lupus nephritis is a leading cause of morbidity, requiring renal biopsy for diagnosis and individualized treatment. Diagnosis relies on the 2019 EULAR/ACR criteria, which combine detailed clinical assessment with serology positive for ANA, anti-dsDNA and anti-Sm; hypocomplementemia serves as an important marker of disease activity. Treatment comprises systemic corticosteroids, immunosuppressants (azathioprine, methotrexate, mycophenolate) and biologics (rituximab, belimumab) in refractory cases. Prolonged corticosteroid exposure, however, can lead to serious adverse effects such as osteopenia and growth retardation, prompting exploration of steroid-sparing strategies. Therapeutic management must be multidisciplinary-integrating rheumatology, nephrology, psychology and rehabilitation-and address psychosocial challenges of adolescence (e.g., body image issues, transition to adult care). Educational programs and psychological support are essential to ensure treatment adherence and efficacy. Future perspectives include targeted therapies (JAK/STAT inhibitors, P2X7 blockers) and personalized medicine approaches based on immunogenetic biomarkers. Advancing understanding of JSLE immunopathogenesis and conducting pediatric-specific multicenter clinical trials are crucial to improve management and prognosis.

Keywords: Systemic lupus erythematosus; Pediatric rheumatology; Autoantibodies; Immunosuppression; Prognosis

Introduction

Juvenile systemic lupus erythematosus (JSLE) is a chronic, multisystem autoimmune disease presenting before 18 years of age. It is characterized by dysregulated production of autoantibodies against nuclear and cytoplasmic components, resulting in widespread inflammation and progressive tissue damage[1-3]. Estimated incidence ranges from 0.3 to 0.9 cases per 100,000 child-years, with a prevalence of 3.3 to 8.8 per 100,000 pediatric population and a female:male ratio of 4:1 to 5:1 after puberty[3,4]. Pathogenesis involves complex interplay among genetic predisposition (HLA variants, complement components, type I interferon receptors), epigenetic modifications and environmental triggers (viral infections, UV exposure, hormonal changes of adolescence) that break self-tolerance[5]. Type I interferon hyperactivation recruits and activates autoreactive B cells, while pro-inflammatory cytokines (TNF-α, IL-6) and T-cell chemokines perpetuate inflammation, leading to cutaneous, articular, renal and neurological injury[6].

Clinically, JSLE features earlier and more severe multisystem involvement than adult-onset lupus. Malar rash and photosensitivity occur in up to 80% of patients, non-erosive arthritis in ~70% and lupus nephritis (classes III/IV) in ~50%, representing the main sources of morbidity and mortality[7]. Hematologic (hemolytic anemia, thrombocytopenia) and neuropsychiatric manifestations (seizures, psychosis) are also common and often more severe in JSLE[8]. Classification per the 2019 EULAR/ACR criteria requires a weighted score ≥ 10 based on clinical and serological parameters[2]. Serology includes ANA (high sensitivity but low specificity), anti-dsDNA and anti-Sm (high specificity and correlation with nephritis activity). Persistent hypocomplementemia complements these markers and is monitored for therapeutic response and early detection of flares[4,6].

Therapeutic goals in JSLE are to control inflammation, prevent organ damage and minimize long-term adverse effects. Systemic corticosteroids administered as pulse therapy or daily dosing form the backbone for severe manifestations, followed by disease-modifying agents (azathioprine, mycophenolate mofetil, methotrexate) for maintenance[9]. In refractory cases, biologics (rituximab, belimumab) reduce autoantibody titers and proteinuria, though pediatric-specific randomized trials remain limited[10].

A multidisciplinary approach rheumatologist, nephrologist, dermatologist, psychologist, rehabilitation team is essential to monitor side effects, optimize adherence and address psychosocial challenges of adolescence[11,12].

Objectives

This literature review synthesizes the main epidemiological, pathogenetic, clinical and therapeutic characteristics of JSLE, highlighting recent advances and knowledge gaps that guide future research.

Materials and Methods

A literature review was conducted using PubMed, SciELO, Google Scholar and ScienceDirect databases.

Discussion

Comparison between JSLE and adult-onset SLE reveals marked differences warranting pediatric-specific protocols. Children and adolescents score higher on instruments like SLEDAI and accumulate early damage per SDI, reflecting heightened immunologic plasticity and immature tolerance mechanisms that favor exaggerated inflammatory responses[13,3]. Elevated interferon-stimulated gene (ISG) expression and high anti-dsDNA titers (70-90% of patients) correlate with nephritis activity and worsen renal prognosis[4,6]. Proliferative lupus nephritis (classes III/IV) poses the greatest therapeutic challenge, affecting half of patients and requiring aggressive induction regimens. Cyclophosphamide pulses and mycophenolate mofetil are primary induction options, followed by maintenance with azathioprine or mycophenolate. Evidence suggests rituximab reduces proteinuria and preserves renal function in refractory cases, though robust pediatric trials are lacking[7,10].

Serologically, persistent hypocomplementemia and high anti-dsDNA titers are activity indicators and relapse predictors, monitored to guide early therapeutic adjustments. Emerging biomarkers type I interferon signatures in monocytes, free nucleosome levels show potential for anticipating flares but require validation in prospective pediatric cohorts[14]. Adverse effects of therapy are of particular concern in pediatric patients. Cumulative high-dose corticosteroids associate with osteopenia, growth retardation, metabolic dysfunctions and reduced quality of life[9,11]. Steroid-reduction protocols and early introduction of steroid-sparing agents seek to mitigate these complications, demanding close monitoring to prevent disease flares.

Psychosocial management is essential in JSLE: adolescents face body image concerns, social stigma and complexities of transitioning from pediatric to adult care. Health education programs, individual and group psychological support and structured transition plans reduce treatment dropout and hospitalizations, improving adherence and long-term outcomes[12,11]. Therapeutic prospects include oral JAK/STAT inhibitors modulating pro-inflammatory cytokine signaling and P2X7 receptor blockers targeting ATP-mediated inflammation[6]. Personalized medicine strategies, guided by genetic and epigenetic profiles, may optimize therapy selection, enhancing efficacy while minimizing toxicity. However, the paucity of pediatric multicenter trials limits formal incorporation of these approaches into guidelines.

Conclusion

JSLE differs from adult-onset lupus by its earlier onset, more aggressive clinical course and greater organ damage accumulation particularly renal and neuropsychiatric[1,8]. Complex interplay of genetic predisposition, type I interferon hyperactivation and environmental exposures yields a multisystem disease requiring prompt diagnosis and intervention. The 2019 EULAR/ACR criteria offer a robust classification tool using weighted clinical and serological scores, enabling high diagnostic sensitivity and specificity[2,4]. Current treatment combines corticosteroids, conventional immunosuppressants and biologics in protocols balancing disease control against adverse effects on growth, bone health and psychosocial well-being[9]. Challenges remain in therapy personalization and predicting individual response. Emerging biomarkers interferon signatures, nucleosome fragments hold promise for flare prediction and therapeutic guidance but await validation in pediatric trials. JAK/STAT inhibitors and P2X7 blockers are promising but require evidence from prospective studies.

Effective transition between pediatric and adult care teams, along with continued psychological support, is critical for maintaining adherence and quality of life during adolescence[11,12]. Structured education programs and individualized transition plans reduce dropout and hospitalizations, improving outcomes. Finally, progress in JSLE management depends on international multicenter collaboration, creation of national patient registries and conduction of controlled clinical trials including pediatric populations. Such initiatives will consolidate evidence, establish pediatric-specific guidelines and enable precision medicine in JSLE, fostering increasingly individualized and effective care[15].

References

1. Alarcón GS, et al. Systemic lupus erythematosus in childhood. Arthritis & Rheumatism 1997;40(10):1729-1737.
2. Aringer M, Costenbader K, Daikh D, et al. European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. Arthritis Rheumatol 2019;71(9):1400-1412.
3. Brunner HI, Gladman DD, Ibañez D, et al. Differences in disease features between childhood-onset and adult-onset systemic lupus erythematosus. Arthritis Rheum 2010;62(2):556-566.
4. Petri M orbai AM, Alarcon 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.
5. Lu R, et al. Genome-wide association study identifies new susceptibility loci for systemic lupus erythematosus in the Chinese population. Nat Commun 2019;10:2628.
6. Fanouriakis A, Kostopoulou M, Cheema K, et al. 2019 update of the joint European League Against Rheumatism and European Renal Association-European Dialysis and Transplant Association recommendations for the management of lupus nephritis. Ann Rheum Dis 2020;79(6):713-723.
7. Scott D, Forger F. Pediatric-onset lupus nephritis: Pathogenesis and management. Clin Kidney J 2018;11(1):58-67.
8. Hanly JG, Mc Curdy G, Fougere L, et al. Neuropsychiatric events in systemic lupus erythematosus: attribution and clinical significance. J Rheumatol 2016;43(2):168-178.
9. Hahn BH, McMahon MA, Wilkinson A, et al. American College of Rheumatology guidelines for screening, treatment and management of lupus nephritis. Arthritis Care Res 2012;64(6):797-808.
10. Merrill JT, Neuwelt CM, Wallace DJ, et al. Efficacy and safety of rituximab in systemic lupus erythematosus: results from the randomized, placebo-controlled EXPLORER trial. Arthritis Rheumatol 2016;68(2):428-438.
11. Lai N, et al. Transition of care in adolescents with pediatric-onset systemic lupus erythematosus. Pediatr Rheumatol Online J 2021;19(1):7.
12. Galeazzi M, Accardo S. Psychosocial aspects of pediatric systemic lupus erythematosus. Pediatr Rheumatol. Online J 2022;20(1):45.
13. Tilliker J, et al. Damage accrual in pediatric-onset systemic lupus erythematosus: comparison with adult-onset disease. Arthritis Care Res 2012;64(11):1620-1627.
14. Crow MK. Type I interferon in organ-targeted autoimmune and inflammatory diseases. Arthritis Res Ther 2014;16: 1.
15. Mok CC, Ying KY, Ng WL, et al. Outcome of diffuse proliferative lupus glomerulonephritis: a long-term observational study. Clin J Am Soc Nephrol 2010;5(1):35-41.