AMERICAN JOURNAL OF MULTIDISCIPLINARY BULLETIN
ISSN: 2996-511X (online) | ResearchBib (IF) = 9.512 IMPACT FACTOR
Volume-4| Issue-4| 2026 Published: |30-04-2026|

MODERN EVIDENCE-BASED APPROACHES TO THE TREATMENT OF SYSTEMIC SCLERODERMA IN CHILDREN

https://doi.org/10.5281/zenodo.19638156

Kurbanova Dilbar Raximovna
Tashkent State Medical University

Abstract

Systemic scleroderma (systemic sclerosis, SSc) is a rare, chronic autoimmune connective tissue disorder characterized by immune dysregulation, widespread vasculopathy, and progressive fibrosis of the skin and internal organs. Pediatric systemic sclerosis (pSSc) represents a particularly challenging subset due to its early onset, heterogeneous clinical presentation, and potential for severe organ involvement. Over the past decade, advances in understanding disease pathogenesis have led to the development of targeted therapeutic strategies. This article provides a comprehensive overview of modern, evidence-based approaches to the treatment of systemic scleroderma in children, including immunosuppressive therapy, biologic agents, antifibrotic treatments, vascular management, and hematopoietic stem cell transplantation. Emphasis is placed on individualized, multidisciplinary care and emerging therapeutic directions.

Introduction. Systemic sclerosis in children is a rare but severe autoimmune disease, with an estimated incidence significantly lower than in adults. It is characterized by progressive fibrosis of the skin and internal organs, immune system activation, and microvascular damage. Pediatric cases often present with more aggressive disease progression, requiring early diagnosis and prompt initiation of therapy. The pathogenesis involves a complex interplay between endothelial injury, immune activation, and fibroblast dysfunction. Advances in molecular biology have identified key pathways, including transforming growth factor-beta (TGF-β), interleukin-6 (IL-6), and B-cell-mediated autoimmunity, which serve as targets for modern therapeutic interventions.

Pathophysiology. The pathophysiological mechanisms of systemic sclerosis can be divided into three major processes:

1. **Vascular injury and dysfunction**. Endothelial cell damage leads to vasoconstriction, impaired angiogenesis, and tissue ischemia. This results in clinical manifestations such as Raynaud's phenomenon and digital ulcers.

AMERICAN JOURNAL OF MULTIDISCIPLINARY BULLETIN
ISSN: 2996-511X (online) | ResearchBib (IF) = 9.512 IMPACT FACTOR
Volume-4| Issue-4| 2026 Published: |30-04-2026|

2. **Immune system activation**. Both innate and adaptive immune responses are involved. Autoantibodies (e.g., anti-centromere, anti-Scl-70) and cytokines such as IL-6 and TGF-β contribute to disease progression.

3. **Fibrosis**. Activated fibroblasts produce excessive extracellular matrix components, leading to skin thickening and organ fibrosis, particularly in the lungs, heart, and gastrointestinal tract.

Clinical Manifestations in Children

Pediatric systemic sclerosis may present with:

- Skin induration and thickening (often diffuse type)
- Raynaud's phenomenon (early and common symptom)
- Digital ulcers and ischemic lesions
- Interstitial lung disease (ILD)
- Pulmonary arterial hypertension (PAH)
- Gastrointestinal dysmotility (reflux, malabsorption)
- Cardiac involvement (arrhythmias, cardiomyopathy)
- Musculoskeletal symptoms (arthritis, myopathy)

Disease severity varies, but early organ involvement is associated with poorer prognosis.

Modern Therapeutic Approaches

1. Immunosuppressive Therapy. Immunosuppressive agents remain the cornerstone of treatment, particularly in early and inflammatory stages of the disease.

Methotrexate

Methotrexate is widely used for skin involvement and early diffuse disease. It inhibits dihydrofolate reductase, reducing lymphocyte proliferation and inflammatory cytokine production. Clinical studies have demonstrated improvement in skin scores and stabilization of disease progression.

Mycophenolate Mofetil (MMF). MMF is increasingly preferred, especially in children with interstitial lung disease. It inhibits inosine monophosphate dehydrogenase, suppressing lymphocyte proliferation. Compared to cyclophosphamide, MMF has a more favorable safety profile and is suitable for long-term use.

Cyclophosphamide. Cyclophosphamide is reserved for severe organ involvement, particularly progressive ILD. It has demonstrated efficacy in improving lung function and reducing fibrosis but is associated with significant toxicity, including bone marrow suppression and infertility risk.

2. Biologic Therapy. Biologic agents target specific components of the immune system and are increasingly used in refractory or severe cases.

Tocilizumab. An IL-6 receptor antagonist, tocilizumab has shown efficacy in reducing skin fibrosis and stabilizing lung function. It is particularly useful in patients with elevated inflammatory markers.

Rituximab. Rituximab targets CD20-positive B cells, reducing autoantibody production. Studies suggest improvement in skin thickness and lung involvement, making it a promising option in pediatric patients.

Abatacept. Abatacept modulates T-cell activation by inhibiting co-stimulation. Early evidence indicates potential benefits in reducing disease activity and improving functional outcomes.

3. Antifibrotic Therapy

Fibrosis is central to disease progression, and antifibrotic agents represent a major advancement.

Nintedanib

Nintedanib is a tyrosine kinase inhibitor that targets pathways involved in fibrosis. It has been shown to slow the decline in lung function in patients with systemic sclerosis-associated ILD.

Emerging Therapies

New agents targeting TGF-β signaling and fibroblast activation are under investigation, offering potential for more effective control of fibrosis.

4. Vascular and Symptomatic Therapy

Management of vascular complications is essential.

- **Calcium channel blockers (e.g., nifedipine)** – first-line treatment for Raynaud's phenomenon
- **Endothelin receptor antagonists (bosentan)** – prevent digital ulcers and treat PAH
- **Phosphodiesterase-5 inhibitors (sildenafil)** – improve pulmonary hemodynamics
- **Prostacyclin analogues (iloprost)** – used in severe ischemia

5. Hematopoietic Stem Cell Transplantation (HSCT)

Autologous HSCT is considered in severe, treatment-resistant cases. It aims to "reset" the immune system. Clinical trials have demonstrated improved survival and disease control; however, the procedure carries significant risks, including infection and treatment-related mortality.

6. Supportive and Multidisciplinary Management

Optimal care requires a multidisciplinary approach involving:

- Pediatric rheumatologists
- Pulmonologists
- Cardiologists

- Gastroenterologists
- Physical and occupational therapists

Supportive care includes:

- Physiotherapy to prevent contractures
- Nutritional support
- Psychological counseling
- Regular monitoring of organ function

Emerging Directions

Future therapeutic strategies focus on:

- Personalized medicine based on genetic and biomarker profiling
- Early aggressive treatment protocols
- Combination targeted therapies
- Gene and cell-based therapies

Ongoing clinical trials are expected to further refine treatment algorithms.

Conclusion

The management of systemic scleroderma in children has evolved significantly with the introduction of targeted therapies and improved understanding of disease mechanisms. Early diagnosis, timely initiation of treatment, and individualized multidisciplinary care are essential for improving outcomes. While current therapies can slow disease progression and improve quality of life, further research is needed to develop curative strategies and reduce long-term complications.

REFERENCES (VANCOUVER STYLE):

1. Martini G, Foeldvari I, Russo R, et al. Systemic sclerosis in childhood: clinical and immunologic features of 153 patients in an international database. *Arthritis Rheum*. 2006;54(12):3971–3978.
2. Zulian F. Systemic sclerosis in childhood. *Autoimmun Rev*. 2013;12(4):558–562.
3. Denton CP, Khanna D. Systemic sclerosis. *Lancet*. 2017;390(10103):1685–1699.
4. Kowal-Bielecka O, et al. Update of EULAR recommendations for the treatment of systemic sclerosis. *Ann Rheum Dis*. 2017;76(8):1327–1339.
5. Tyndall AJ, Bannert B, Vonk M, et al. Causes and risk factors for death in systemic sclerosis. *Ann Rheum Dis*. 2010;69(10):1809–1815.
6. Elhai M, Meune C, Avouac J, et al. Trends in mortality in patients with systemic sclerosis. *Ann Rheum Dis*. 2012;71(7):1183–1189.

7. Distler O, Highland KB, Gahlemann M, et al. Nintedanib for systemic sclerosis-associated interstitial lung disease. *N Engl J Med*. 2019;380(26):2518–2528.

8. Khanna D, Lin CJF, Goldin J, et al. Tocilizumab in systemic sclerosis. *Lancet Respir Med*. 2020;8(10):963–974.

9. Daoussis D, Liossis SNC, Tsamandas AC, et al. Experience with rituximab in scleroderma. *Arthritis Rheum*. 2010;62(1):163–169.

10. Sullivan KM, Goldmuntz EA, Keyes-Elstein L, et al. Myeloablative autologous stem-cell transplantation for severe scleroderma. *N Engl J Med*. 2018;378(1):35–47.

11. Herrick AL. Management of Raynaud's phenomenon and digital ischemia. *Curr Rheumatol Rep*. 2013;15(1):303.

12. Миррахимова, М. Х., and Н. Ю. Нишанбаева. "РОЛЬ TOLL-ПОДОБНЫХ РЕЦЕПТОРОВ В ПАТОГЕНЕЗЕ АТОПИЧЕСКОГО ДЕРМАТИТА." *AMERICAN JOURNAL OF EDUCATION AND LEARNING* 2.5 (2024): 234-236.

13. Mirraximova, Maktuba, and Nilufar Nishonboeva. "Genining polimorfizmi atopik dermatitda." Scientific journal of the Fergana State University 1 (2023): 137-137.

14. 10. Nishanbayeva N. Y. et al. CAUSES OF ATOPIC DERMATITIS AND MEASURES FOR ITS PREVENTION //AMERICAN JOURNAL OF EDUCATION AND LEARNING. – 2025. – Т. 3. – №. 2. – С. 566-573.

15. Wigley FM, Flavahan NA. Raynaud's phenomenon. *N Engl J Med*. 2016;375(6):556–565.

16. Hachulla E, et al. Early detection of pulmonary arterial hypertension in systemic sclerosis. *Eur Respir J*. 2005;25(5):743–749.

17. Foeldvari I, Zhavania M, Birdi N, et al. Favourable outcome in 135 children with juvenile systemic sclerosis. *Rheumatology*. 2000;39(5):556–561.

18. Bruni C, et al. One year in review 2022: systemic sclerosis. *Clin Exp Rheumatol*. 2022;40(1):3–14.