Juvenile- and adult-onset systemic sclerosis: similarities and differences in early disease patterns. A scoping review

N. Vasquez-Canizares[1], M. Twilt[2], Q. McCormick[3], P. Bhave[4], I.A. Dobre[2], S.C. Li[5]

[1]Department of Paediatrics, Division of Paediatric Rheumatology, Children's Hospital at Montefiore, Albert Einstein College of Medicine, Bronx, NY, USA;
[2]Department of Paediatrics, Alberta Children's Hospital, Cumming School of Medicine, University of Calgary, Alberta, Canada;
[3]Department of Anaesthesiology, George Washington School of Medicine, Washington, DC;
[4]Department of Internal Medicine and Paediatrics, Rush University Medical Centre, Chicago, IL;
[5]Department of Paediatrics, Division of Paediatric Rheumatology, Hackensack Meridian School of Medicine, Joseph M. Sanzari Children's Hospital, Hackensack, NJ, USA.

Natalia Vasquez-Canizares, MD, MS
Marinka Twilt, MD, MScE
Quinn McCormick, MD
Priya Bhave, MD, MPH
Ioana A. Dobre MD
Suzanne C. Li, MD, PhD

Please address correspondence to:
Suzanne C. Li
Hackensack Meridian School of Medicine, Joseph M. Sanzari Children's Hospital, 30 Prospect Avenue, WFAN 337, Hackensack, NJ 07601, USA.
E-mail: suzanne.li@hmhn.org

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ABSTRACT

Objective. *Juvenile systemic sclerosis (jSSc) is a rare disease associated with high morbidity and a significant mortality risk. Improving recognition of early disease could enable earlier treatment initiation and a reduced risk for irreversible damage such as lung fibrosis. We conducted a scoping review to understand the early jSSc disease pattern and compared it with the early adult SSc pattern.*

Methods. *A systematic search of PubMed, Embase, MEDLINE, and CENTRAL (January 1946–April 2026) identified studies reporting clinical features of jSSc (≥3 patients) or aSSc (≥500 patients). Included studies were stratified by disease duration into early (≤3 years) and late (≥5 years) strata. Studies requiring fulfilment of the 1980 ACR or 2007 PRES/ACR/EULAR criteria were considered to represent late rather than early disease.*

Results. *Thirty-nine studies (935 jSSc; 15,451 aSSc patients) from 41 countries were included. jSSc demonstrated predominance of diffuse cutaneous disease (~70% vs. ~41% aSSc), higher rates of overlap features including myositis (33% vs. 5%) and arthritis (32.6% vs. 18%), greater early vascular burden with digital ulcers (51% vs. 20%), and notably low rates of scleroderma renal crisis (0% vs. 6%) in early disease. Crude mortality was lower in jSSc (7.7% vs. 20.4%).*

Conclusion. *Early jSSc disease shares many similarities with, but also several differences from, early aSSc disease. Understanding these early clinical patterns should improve diagnostic accuracy, support earlier treatment initiation, and reduce tissue damage, thereby improving long-term outcomes for these children.*

Introduction

Systemic sclerosis (SSc) is a rare autoimmune disease characterised by immune-mediated vasculopathy and progressive fibrosis. It has significant morbidity and one of the highest mortality rates among rheumatic diseases (1). Juvenile onset disease (jSSc) is rarer than adult-onset disease (aSSc), with jSSc estimated to account for <10% of all SSc cases (2, 3). While jSSc and aSSc manifest the same organ manifestations, the pattern of certain features differs between them. Observational studies have reported a predominance of diffuse cutaneous disease (dcSSc), higher rates of overlap syndromes, a low frequency of anticentromere autoantibody (ACA), and a much better survival rate for jSSc than aSSc (4-11). Cardiorespiratory disease remains the main cause of mortality for jSSc as it is for aSSc, while an additional morbidity specific to jSSc is growth impairment (12, 13).

Of the three main pathological processes, most therapies are directed towards controlling inflammation because of the paucity of options for treating fibrosis and vasculopathy. Inflammation occurs early in the disease, so improved recognition of the early stage would allow for earlier treatment initiation and the potential to reduce the development of irreversible damage such as lung fibrosis (14). While considerable effort has focused on defining early aSSc to improve diagnosis and facilitate earlier treatment (15), early disease in jSSc remains poorly characterised despite the potential to similarly improve long-term outcomes.

Current knowledge of jSSc is limited by the predominance of single-centre, cross-sectional studies that report findings on small numbers of patients across broad disease durations. A further challenge is that existing classification crite-

ria may introduce bias toward identifying patients later in their disease course. The 1980 ACR criteria (16) and the 2007 PRES/ACR/EULAR provisional criteria for jSSc (17) are now recognised as being focused toward identifying later rather than early disease, which was a key motivation for the revision of SSc criteria in 2013 (18). The 2013 ACR/EULAR SSc classification criteria demonstrate superior performance, with a sensitivity of 91% and a specificity of 92% for SSc, compared to 75% and 72%, respectively, found with the 1980 ACR classification criteria (18). In other studies, the sensitivity of the 2013 classification criteria for aSSc has been identified as high as 98% (19).

There has been only limited evaluation of classification criteria performance in jSSc. An evaluation of the 2007 preliminary jSSc PRES/ACR/EULAR vs 2013 ACR/EULAR SSc classification criteria in an early cohort of jSSc (disease duration of ~1 year after their first non-Raynaud phenomenon symptom) similarly highlighted the poorer performance of the earlier criteria, with identified sensitivities for jSSc of 66% *vs*. 86%, respectively (20). The 2013 ACR/EULAR SSc classification criteria were found to have a similar sensitivity for jSSc in two other cohorts: a French multicentre cohort (18 patients, 83% sensitivity) (21) and the CARRA Legacy Registry (59 patients, 81% sensitivity) (Stevens, Li, unpublished). The lower sensitivity of the 2013 criteria for jSSc than those reported for aSSc suggests there are phenotypic differences between jSSc and aSSc that may limit the performance of the 2013 ACR/EULAR classification criteria for jSSc, underscoring the need for a more detailed understanding of how disease features differ between these populations, particularly in early disease.

To better understand the early jSSc disease pattern and how it differs from early aSSc, we conducted a scoping literature review. By synthesising global cohort data, we sought to identify features consistently associated with jSSc, define characteristics of early disease that may improve earlier recognition and intervention, and work towards improving long-term outcomes for children with jSSc.

Methods

Search strategy and study selection

This scoping review was conducted in accordance with the JBI methodology and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) guidelines (22, 23). A systematic search of PubMed, Embase, MEDLINE, and CENTRAL identified eligible studies published between January 1946 and April 30, 2026. Searches combined controlled vocabulary and free-text terms related to systemic sclerosis and paediatric disease. Additional studies were identified through manual screening of reference lists from eligible articles and relevant reviews, including a manual search from April 2026 to May 2026.

The review aimed to characterise clinical features, geographic distribution, treatment strategies, and similarities and differences between juvenile- and adult-onset disease across early and late disease stages.

All records were imported into Covidence (Veritas Health Innovation, Melbourne, Australia). Two reviewers independently screened titles, abstracts, and full texts, with disagreements resolved by a third reviewer.

Eligibility criteria

Studies were eligible if they: i) included patients with SSc defined according to the authors' reported classification criteria or diagnostic definition; ii) enrolled ≥3 patients with jSSc or ≥500 patients with aSSc; and iii) reported at least one clinical or laboratory feature of interest.

Studies were excluded if they were not published in English, lacked relevant clinical data, reported duplicate or overlapping cohorts (unless providing complementary data), combined paediatric and adult patients without separate analyses, had insufficient disease-duration information for temporal stratification, or, for the early-disease stratum only, required fulfilment of the 1980 ACR or 2007 PRES/ACR/EULAR classification criteria as an inclusion criterion. These studies were retained for the late-disease stratum.

The latter exclusion was intended to minimise ascertainment bias, as both the 1980 ACR and 2007 PRES/ACR/EULAR criteria preferentially identify established rather than early disease and would therefore systematically exclude patients in the inflammatory phase targeted by this review.

Disease duration stratification

Studies were stratified by disease duration into early disease (mean or median duration ≤3 years from symptom onset) and late disease (≥5 years). Given the rarity of jSSc and the limited number of available cohorts, these cut-offs were applied with some flexibility for jSSc studies with disease durations very close to the defined thresholds, to avoid excluding scarce but informative data. For aSSc, where larger and more numerous cohorts are available, the cutoffs were applied more strictly.

Studies with mean or median disease durations between 3 and 5 years were excluded from both strata to create a buffer zone that minimised misclassification and reduced overlap between the early and late disease categories, thereby improving the temporal distinctness of each stratum.

To improve temporal homogeneity, studies were also evaluated for disease-duration dispersion. Early-disease studies were excluded if the reported standard deviation (SD) or interquartile range (IQR) suggested substantial overlap with late disease. Likewise, late-disease studies were generally excluded when the SD or IQR exceeded the mean or median duration, unless most patients clearly had established disease.

These criteria were applied because many jSSc studies are cross-sectional and include patients with widely varying disease durations. Considering disease-duration dispersion reduced overlap between temporal strata and improved comparisons of stage-specific disease features.

Data extraction and synthesis

Data extracted from each study included study design, geographic location, patient number, demographics, disease duration, cutaneous subtype, organ in-

volvement, overlap syndromes, autoantibody profiles, and treatment strategies. When multiple publications reported overlapping cohorts, preference was given to the article containing the greatest number of relevant variables for the appropriate disease-duration stratum, although complementary information was extracted from additional publications when necessary. Data were summarised descriptively by disease duration and age group.

Results

The study selection process is summarised in Figure 1. The search identified 7,854 records (2,626 jSSc and 5,228 aSSc). After removal of 1,422 duplicates, 6,436 records underwent title and abstract screening, leaving 260 articles for full-text review. Thirty-nine studies met inclusion criteria, including 27 jSSc and 12 aSSc cohorts (Supplementary Table S1).

The included studies comprised 935 patients with jSSc and 15,451 with aSSc (Table I) from 41 countries across Europe (24 countries), Asia and the Middle East (7 countries), North America and the Caribbean (3 countries), South America (2 countries), Oceania (2 countries), and Africa (2 countries) (data not shown). Among the 27 unique jSSc studies, 5 provided data exclusively for early disease (≤3 years), 17 provided data exclusively for late disease (≥5 years), and 5 provided data across both disease strata. For the 12 unique aSSc studies, four cohorts were classified as early and eight as late disease. Disease duration ranged from 1.3–3.1 years in early jSSc and 4.1–18.6 years in late jSSc. Female predominance was similar in both populations (78.4% jSSc *vs.* 83% aSSc), and in most studies the mean age at first non-Raynaud manifestation in jSSc ranged from 7.2–14.9 years.

Mortality data were available for 791/935 (84.6%) patients with jSSc and 7,593/15,451 (49%) patients with aSSc, corresponding to crude mortality rates of 7.7% and 20.4%, respectively.

Most studies were retrospective (97% of jSSc and 77% of aSSc). Classification criteria varied across studies, including the 2013 ACR/EULAR (n=13), 2007 PRES/ACR/EULAR (n=7), 1980 ACR (n=11), and physician diagnosis or other definitions (n=10) (Supplementary Table S1).

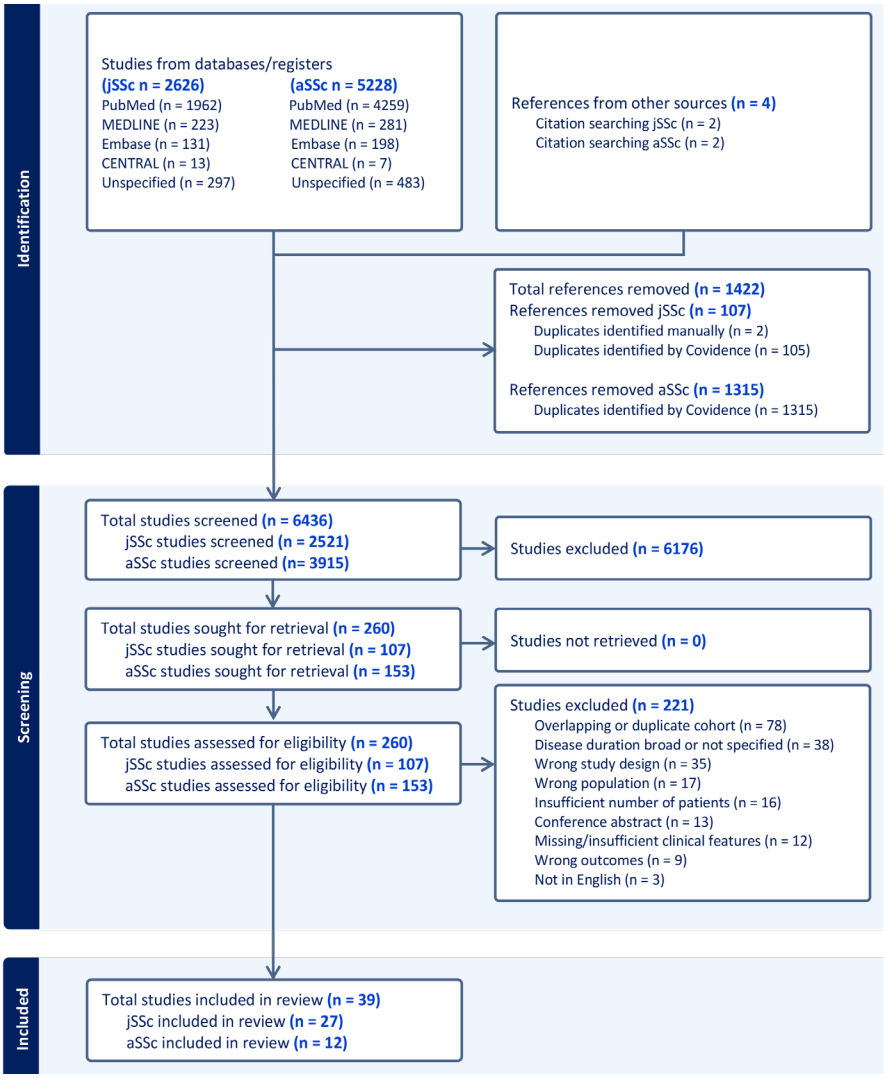

Fig. 1. PRISMA flow diagram. jSSc : juvenile onset disease; aSSc: adult systemic sclerosis

Table I. Characteristics of included studies and cohorts.

Characteristic n (%)	Juvenile-onset systemic sclerosis (jSSc)	Adult-onset systemic sclerosis (aSSc)
n. of included studies*	27	12
Studies providing only early disease data	5 (18.5)	4 (33)
Studies providing only late disease data	17 (63)	8 (67)
Studies providing both early and late data	5 (18.5)	-
Total number of patients	935	15451
Early disease	525 (56)	5542 (35.9)
Late disease	630 (67.4)	9909 (64.1)
Female sex	669/868 (78.4)	12796/15447(83)
Male sex	186/866 (21.5)	2651/15447 (17)
Reported deaths	61/791 (7.7)	1546/7593 (20.4)
Study design		
Prospective	1 (3)	3 (33)
Retrospective	29 (97)	10 (77)
Single centre	24 (75)	2 (15)
Multicentre	8 (25)	11 (85)

*5 jSSc studies provided data for both early and late disease stages.

The frequency of clinical manifestations across early and late disease strata for both jSSc and aSSc is presented in Table II.

Table II. Disease characteristics and clinical manifestations according to disease duration.

Disease characteristics	Early jSSc (n=525)	Early aSSc (n=5542)	Late jSSc (n=630)	Late aSSc (n=9909)
Cutaneous subtype				
Diffuse cutaneous	339/478 (70.9)	1243/2994 (41.5)	302/433 (69.7)	2653/9862 (27)
Limited cutaneous	117/478 (24.5)	1752/2994 (58.5)	112/433 (25.9)	6312/9862 (64)
Sine scleroderma	0/478 (0)	0/2994 (0)	12/433 (2.8)	691/9862 (7)
Overlap syndrome	35/478 (7.3)	0/2994 (0)	63/433 (14.5)	470/9862 (4.7)
Autoantibodies				
ANA	368/427 (86)	1218/1275 (95.5)	289/338 (85.5)	4841/5063 (95.6)
Anti-topoisomerase I	129/363 (35.5)	649/2442 (26.6)	108/361 (30)	2381/9415 (25)
Anticentromere	52/338 (15)	686/2495 (27.5)	34/284 (12)	3666/9451 (38.8)
Anti-RNA polymerase III	5/137 (3.6)	398/2193 (18)	6 /141 (4.2)	451/5661 (8)
Anti-U1RNP	15/90 (16.6)	63/1617 (4)	25/182 (13.7)	180/3956 (4.5)
Anti-PM/Scl	27/156 (17)	37/1473 (2.5)	25/141 (17.7)	212/3922 (5.4)
Vascular manifestations				
Raynaud's Phenomenon	417/498 (83.7)	1445/1930 (75)	349/405 (86)	4094/4229 (97)
Nailfold capillary abnormalities	231/393 (58.7)	771/938 (82)	189/229 (82.5)	2792/3612 (77)
Digital pitting scars	85/221 (38.5)	129/938 (13.7)	124/280 (44)	1505/2813 (53.5)
Digital ulcers	169/328 (51)	537/2670 (20)	143/269 (53)	3330/9276 (36)
Telangiectasia	65/172 (38)	675/1316 (51)	31/99 (31)	3374/5457 (61.8)
Skin manifestations				
Skin involvement	-	-	227/232 (98)	2746/2883 (95)
Skin thickening	156/211 (74)	-	157/194 (81)	-
Sclerodactyly	246/389 (63)	-	164/227 (72)	943/1005 (94)
Calcinosis	50/405 (12)	64/549 (11.6)	73/335 (22)	978/5452 (18)
MSK manifestations				
Joint involvement	148/262 (56.5)	291/598 (48.6)	52/99 (52.5)	-
Arthritis	131/402 (32.6)	202/1102 (18)	106/251 (42)	1454/7516 (19)
Arthralgia	153/338 (45)	84/938 (9)	134/244 (55)	-
Contractures	129/289 (44.6)	581/1377 (42)	59/129 (46)	383/2338 (16.4)
Myositis	29/87 (33)	37/698 (5)	4/30 (13)	433/4159 (10)
Tendon friction rubs	20/306 (6.5)	194/1377 (14)	20/217 (9)	249/2733 (9)
Pulmonary manifestations				
Interstitial lung disease	121/445 (27)	493/1323 (37)	176/420 (42)	4524/7919 (57)
Reduced FVC <80%	98/420 (23)	82/475 (17)	116/239 (48.5)	360/1393 (26)
Reduced DLCO <80%	84/322 (26)	249/471 (53)	73/163 (44.8)	-
Pulmonary arterial hypertension	23/499 (4.6)	133/3765 (3.5)	32/457 (7)	1100/8216 (13)
Cardiac manifestations				
Cardiac involvement	29/279 (10.4)	-	35/203 (17)	238/662 (36)
Arrhythmia	8/159 (5)	94/3297 (3)	19/260 (7)	447/3829 (11.7)
Heart failure	5/175 (3)	174/3293 (5)	19/219 (8.7)	562/4417 (12.7)
GI manifestations				
GI involvement	159/329 (48)	467/1987 (23.5)	75/143 (52.4)	1689/2512 (67)
Oesophageal involvement	109/371 (29)	-	54/198 (27)	2255/2822 (80)
Dysphagia	48/261 (18)	-	64 /242 (26)	-
GERD	61/323 (19)	56/1376 (4)	74 /210 (35)	507/662 (76.6)
Weight loss	49/236 (21)	-	49/180 (27)	-
Renal manifestations				
Scleroderma renal crisis	0/366 (0)	82/1348 (6)	5/326 (1.5)	260/8850 (3)
Hypertension	3/348 (0.9)	867/2778 (31)	8/201 (4)	-
Neurological manifestations				
Neurological involvement	10/256 (4)	-	2/89 (2.2)	-
Peripheral neuropathy	1/153 (0.65)	27/1376 (2)	7/205 (3.4)	562/1922 (29)

jSSc, juvenile systemic sclerosis; aSSc, adult systemic sclerosis; MSK: musculoskeletal; FVC, forced vital capacity, DLCO, diffusing capacity of the lungs for carbon monoxide; GI: gastrointestinal, GERD: gastroesophageal reflux

Cutaneous subtype and autoantibodies

Diffuse cutaneous SSc (dcSSc) predominated in jSSc (approximately 70%) across both disease stages, whereas limited cutaneous SSc predominated in aSSc (59–64%). Overlap syndromes were more frequent in jSSc than aSSc, with higher frequencies found in the late disease cohorts for both populations. No cases of sine scleroderma were reported in the early jSSc or early aSSc cohorts.

Antinuclear antibody (ANA) positivity exceeded 85% in both populations but was higher in aSSc than jSSc at both early and late timepoints. In early disease, anti-topoisomerase I antibody (ATA) was more common in jSSc than aSSc (35% *vs.* 26.6%), whereas ACA was less common (15% *vs.* 27.5%). In

late disease, ATA frequencies were similar between jSSc and aSSc (30% *vs.* 25%), but the lower frequency of ACA in jSSc persisted (12% *vs.* 38.8%).
Despite a high prevalence of the dcSSc subtype, anti-RNA polymerase III was rare in early jSSc compared to early aSSc (3.6% *vs.* 18%), a pattern that held true in late disease. In contrast, the overlap syndrome-associated antibodies anti-U1-RNP and anti-PM/Scl were substantially more common in jSSc than aSSc during both early disease (U1-RNP: 16.6% *vs.* 4%; PM/Scl: 17% *vs.* 2.5%) and late disease (U1-RNP: 13.7% *vs.* 4.5%; PM/Scl: 17.7% *vs.* 5.4%).

Vascular manifestations
Vascular manifestations varied between early jSSc and early aSSc. Raynaud's phenomenon (RP) was slightly more common in early jSSc than early aSSc (83.7% *vs.* 75%), whereas nailfold capillary abnormalities were less frequent (58.7% vs. 82%). Digital pitting scars (38.5% *vs.* 13.7%) and digital ulcers (51% *vs.* 20%) were more prevalent in early jSSc, while telangiectasias were less common (38% *vs.* 51%).
When comparing early to late jSSc, the frequencies of RP, digital pitting scars, digital ulcers, and telangiectasias remained similar, though nailfold capillary abnormalities increased substantially over time (58.7% early *vs.* 82.5% late). Finally, in late disease, RP (86% *vs.* 97%), digital pitting scars (44% *vs.* 53.5%), and telangiectasias (31% *vs.* 61.8%) were less common in jSSc than aSSc, whereas digital ulcers remained more prevalent in late jSSc (53% *vs.* 36%).

Skin manifestations
Skin thickening and sclerodactyly were reported in 74% and 63% of early jSSc, respectively, while data for early aSSc was not systematically reported for these two features. In late disease, sclerodactyly was observed more commonly in aSSc than jSSc (94% *vs.* 72%, respectively). Calcinosis was similarly prevalent in early disease across both populations, reported in 12% of early jSSc *versus* 11.6% of early aSSc cohorts. In late disease, calcinosis was more common in both groups, somewhat more frequent in jSSc (22%) than aSSc (18%).

Musculoskeletal manifestations
Musculoskeletal involvement was notably more frequent in early jSSc than early aSSc. Arthritis was reported in 32.6% of the early jSSc cohort *versus* 18% of early aSSc, while arthralgia was more prevalent in the paediatric population (45% *vs.* 9%). Similarly, myositis was reported in 33% of early jSSc versus only 5% of early aSSc. No difference was found between early jSSc and early aSSc for joint contractures (44.6% *vs.* 42%), whereas tendon friction rubs (TFR) were less frequent in early jSSc than early aSSc (6.5% *vs.* 14%).

Pulmonary manifestations
The frequency of interstitial lung disease (ILD) was lower in the early jSSc cohort than the early aSSc cohort (27% *vs.* 37%). Similarly, decreased DLCO was less common in early jSSc (26% *vs.* 53%), whereas decreased FVC was slightly higher (23% *vs.* 17%).
When comparing early *versus* late cohorts, the frequency of ILD was higher in the late cohorts than the early cohorts for both populations (jSSc: 42% *vs.* 27%; aSSc: 47% *vs.* 37%). For jSSc, the late cohort also exhibited higher frequencies of reduced FVC (48.5% *vs.* 23%) and reduced DLCO (44% *vs.* 26%) compared to the early cohort. For aSSc, a higher frequency of reduced FVC was noted in the late *versus* early cohort (26% *vs.* 17%), while late-cohort DLCO data were not systematically reported.
Pulmonary arterial hypertension (PAH) frequencies were comparable between the early cohorts (jSSc: 4.6% *vs.* aSSc: 3.5%). In the late disease categories, PAH frequency was 7% in jSSc and 13% in aSSc.

Cardiac manifestations
General cardiac involvement was reported in 10% of early jSSc cohorts, while data for early aSSc was not systematically reported. Arrhythmias were present in 5% of early jSSc *versus* 3% of early aSSc, and heart failure was reported in 3% of early jSSc compared to 5% of early aSSc cohorts. Of major clinical importance, cardiac involvement was substantially more common in late *versus* early disease for both populations. In jSSc, general cardiac involvement was 17% in late *versus* 10% in early disease, and heart failure was 8.7% *versus* 3%, respectively.

Gastrointestinal manifestations
Gastrointestinal (GI) manifestations were notably more common in the early jSSc cohort than the early aSSc cohort (48% *vs.* 23.5%). Specific early jSSc manifestations included oesophageal involvement (29%), weight loss (21%), gastroesophageal reflux disease (GERD) (19%), and dysphagia (18%). Apart from GERD, which was observed in only 4% of early aSSc, these specific parameters were not reported for the early aSSc cohort.
When comparing early *versus* late disease, certain GI manifestations were more frequent in the late jSSc cohort than the early jSSc cohort, including overall GI involvement (52.4%), GERD (35%), weight loss (27%), and dysphagia (26%), while oesophageal involvement frequencies were similar. The late aSSc cohort also demonstrated high frequencies of GI manifestations, with overall GI involvement reported at 67%, oesophageal involvement at 80%, and GERD at 76.6%.
Data evaluating lower intestinal involvement, such as small intestinal bacterial overgrowth (SIBO), were extremely limited across the included studies and could not be systematically reported.

Renal manifestations
Renal involvement, including scleroderma renal crisis (SRC), was rare in jSSc, contrasting with adult cohorts. No SRC episodes were reported for early jSSc *versus* a 6% frequency for early aSSc. The frequency of SRC remained low over time for jSSc, with a 1.5% frequency of SRC reported for late jSSc. The frequency of SRC was lower in late aSSc than early aSSc (3% *vs.* 6%, respectively). This overall low renal burden in the paediatric population was further supported by the prevalence of hypertension, which affected only 0.9% of early jSSc and 4% of late jSSc cohorts, whereas it was a prominent early feature in adults, affecting 31% of the early aSSc population.

Table III. Therapeutic management strategies across juvenile and adult systemic sclerosis cohorts.

	Juvenile systemic sclerosis (n=935)	Adult systemic sclerosis (n=15,451)
Any immunosuppressive treatment recorded	282/324 (87)	404/1405 (29)
Corticosteroids	248/467 (53)	379/2778 (13.6)
Cyclophosphamide	48/340 (14)	N/A
Mycophenolate mofetil	37/147 (25)	N/A
Methotrexate	205/372 (55)	N/A
Tocilizumab	7/103 (7)	N/A
Rituximab	8/136 (6)	N/A
Stem cell transplant	4/52 (7.7)	N/A

Neurologic manifestations

Neurological manifestations were generally infrequent, with general neurological involvement reported in 4% of early jSSc cohorts; comparable data for early aSSc were not systematically reported. Peripheral neuropathy was rare in early disease, affecting only 0.65% of early jSSc and 2% of early aSSc populations. The frequency of peripheral neuropathy was higher in late disease, with a greater increase in frequency observed for aSSc than jSSc (adult 2% to 29% *vs.* jSSc 0.65% to 3.4%, respectively).

Treatment strategies

Therapeutic management strategies varied substantially between the two populations, although data regarding specific immunosuppressive agents were reported for <20% of aSSc cohorts compared to 37–50% of jSSc cohorts, limiting direct comparisons between groups. Overall, any form of immunosuppressive treatment was recorded significantly more frequently in the paediatric population, utilised in 87% of jSSc patients compared to just 29% of aSSc patients (Table III). Systemic corticosteroids were also far more prevalent in the jSSc cohort, prescribed to over half of the population (53%), whereas only 13.6% of adult patients received them.

Due to a lack of systematic reporting across the included adult literature, comparative data for individual therapies was unavailable for the aSSc cohorts. Within the jSSc population, methotrexate was the most frequently utilised disease-modifying antirheumatic drug (DMARD), prescribed to 55% of patients, followed by mycophenolate mofetil (MMF) at 25%, and cyclophosphamide at 14%. Biologic therapies were rarely used in the paediatric cohorts, with tocilizumab and rituximab recorded in only 7% and 6% of cases, respectively. Autologous haematopoietic stem cell transplantation (HSCT), typically reserved as an advanced intervention for severe disease, demonstrated a comparable utilisation rate of 7.7% among these recorded jSSc patients.

Discussion

This scoping review synthesised data from 39 studies including 935 patients with jSSc and 15,451 patients with aSSc from 41 countries to characterise the early disease phenotype of jSSc and compare it with early aSSc. Although the two populations shared many fundamental disease features, including female predominance, RP, autoantibody positivity, and early multi-organ involvement, several important differences consistently distinguished early jSSc from adult disease. Compared with early aSSc, early jSSc demonstrated a predominance of diffuse cutaneous disease, higher frequencies of overlap features including arthritis and myositis, greater digital vasculopathy with more digital ulcers and pitting scars, a distinct autoantibody profile characterised by higher frequencies of anti-U1-RNP and anti-PM/Scl antibodies and lower frequencies of ACA and anti-RNA polymerase III antibodies, lower frequencies of ILD, reduced DLCO, telangiectasias, and SRC, and substantially greater use of immunosuppressive therapy. Together, these findings suggest that early jSSc represents a distinct inflammatory phenotype rather than simply an earlier presentation of adult SSc.

The predominance of diffuse cutaneous disease together with frequent arthritis, myositis, overlap syndromes, and overlap-associated autoantibodies supports the concept that inflammation plays a particularly prominent role during early paediatric disease. Although diffuse cutaneous disease predominated in jSSc, anti-RNA polymerase III antibodies, which in adults are strongly associated with diffuse disease, rapid skin progression, and SRC (24), remained uncommon. Conversely, anti-U1-RNP and anti-PM/Scl antibodies were substantially more common than in adults. Together with the lower frequencies of ANA and ACA, these findings suggest that paediatric diffuse disease may arise through immunologic pathways that differ from those in aSSc and are consistent with previous reports describing distinct juvenile and adult phenotypes (4, 5, 6, 10).

Differences in vascular involvement further support the concept that disease evolution differs between children and adults. Digital ulcers and digital pitting scars were more frequent in early jSSc than early aSSc, with the higher prevalence of digital ulcers persisting into late disease. In contrast, telangiectasias and nailfold capillary abnormalities were less common in early jSSc. While nailfold capillary abnormalities increased over time to frequencies comparable with adult disease, telangiectasias remained less common, suggesting that although clinically significant peripheral vasculopathy is prominent early in jSSc, some chronic microvascular changes may develop more gradually than in adults. Similarly, the lower frequencies of ILD, reduced DLCO, and SRC suggest that irreversible fibrotic and vasculopathic damage accumulates later in paediatric disease. However, clinically significant organ involvement is already present during the early disease course, emphasising that early jSSc remains a severe multisystem disease requiring prompt recognition and management.

A major strength of this review is the stratification of cohorts according to disease duration, allowing characterisation of early disease patterns that have

not been previously defined in jSSc. In aSSc, increasing evidence supports a therapeutic "window of opportunity" during the early inflammatory phase, during which timely immunomodulatory therapy may prevent irreversible organ damage (25). Consistent with this concept, we observed higher frequencies of ILD, reduced FVC, reduced DLCO, nailfold capillary abnormalities, and cardiac involvement in late compared with early jSSc, suggesting progressive accumulation of organ damage over time. Together, these findings support the existence of a similar therapeutic window in paediatric disease and underscore the importance of recognising jSSc before irreversible fibrosis and vasculopathy become established.

Interestingly, not all inflammatory manifestations followed the same temporal pattern. Arthritis and arthralgia remained common in late jSSc, and overlap syndromes became more frequent, suggesting that inflammatory activity may persist beyond the earliest stages of disease in many children. In contrast, myositis was substantially less common in late than early jSSc, indicating that some inflammatory manifestations may be transient while others persist. Although these observations should be interpreted cautiously given the cross-sectional nature of the included studies, they raise the possibility that the inflammatory therapeutic window in jSSc may be longer or differ qualitatively from that described in aSSc. Longitudinal paediatric studies will be needed to determine the duration of this window and whether it can be leveraged to further improve long-term outcomes.

GI involvement also emerged as an important feature of early jSSc. Nearly half of children had GI manifestations during early disease, while approximately one in five experienced weight loss, with both frequencies increasing in late disease. Unlike adults, these findings have implications beyond organ-specific morbidity because chronic GI disease and poor nutritional status may impair normal growth and pubertal development. Growth impairment is recognised as a unique dimension of disease burden in jSSc and is incorporated into the Juvenile Systemic Sclerosis Severity Score (J4S) alongside skin and internal organ involvement (26). However, growth-related outcomes and pubertal delay were not systematically reported across the included studies, precluding meaningful comparisons between disease stages. Recent international consensus efforts have similarly identified growth and development as priority research domains for future jSSc clinical trials (27). Future paediatric cohort studies should include standardised assessment of growth and pubertal outcomes.

The clinical implications of these findings have important implications for clinical management. Because randomised therapeutic trials in jSSc remain scarce, current paediatric treatment recommendations are largely extrapolated from aSSc. However, our findings suggest that early paediatric disease is not simply a younger form of adult disease. The predominance of inflammatory manifestations together with the lower burden of established fibrosis and chronic vasculopathy suggests that treatment strategies developed for adults may require modification to better address the paediatric disease phenotype. Earlier recognition and prompt initiation of immunomodulatory therapy may provide greater opportunity to prevent irreversible organ damage and preserve normal growth and development in children.

The treatment patterns identified in this review support this concept. Immunosuppressive therapy was reported far more frequently in jSSc than in aSSc (87% *vs*. 29%), although comparisons were limited by incomplete treatment reporting in adult cohorts. Methotrexate was the most prescribed DMARD in children, consistent with current paediatric recommendations (28), followed by MMF. Biologic therapies were used infrequently, likely reflecting both the rarity of the disease and the limited evidence base, though tocilizumab is now FDA-approved for SSc-ILD in adults and emerging paediatric data suggest potential benefit (29, 30). These findings emphasise the need for prospective paediatric clinical trials evaluating treatment strategies specifically designed for the inflammatory phenotype of early jSSc rather than continued reliance on extrapolation from adult studies.

Our findings also highlight an important challenge for future research. Although the 2013 ACR/EULAR classification criteria substantially improved sensitivity for aSSc, published paediatric studies demonstrate lower sensitivity in jSSc, potentially leaving approximately 15–20% of affected children unclassified. Failure to identify these patients may delay diagnosis, postpone initiation of treatment during the early inflammatory phase, and limit enrolment into future clinical trials. The distinct clinical and serologic phenotype identified in this review provides further support for ongoing efforts to develop paediatric-specific classification criteria that better capture early disease.

This review has several limitations. Restriction to English-language publications may have excluded relevant studies. Consistent with scoping review methodology, formal assessment of study quality was not performed, and heterogeneity among included studies precluded quantitative meta-analysis. The inclusion thresholds differed between jSSc (≥3 patients) and aSSc (≥500 patients) cohorts. This asymmetry was a pragmatic decision necessitated by the rarity of jSSc, but it means that the jSSc data are drawn from smaller, potentially less representative cohorts, while the aSSc data reflect larger, more precisely estimated frequencies. Comparisons between the two populations should be interpreted with this imbalance in mind. Although stratification by disease duration improved evaluation of disease evolution, disease progression is continuous rather than discrete, and some overlap between temporal categories was unavoidable. In addition, incomplete reporting of clinical manifestations, autoantibodies, and treatment strategies limited direct comparisons for several variables, particularly within the adult literature. Finally, although some overlap of patients among registry-based publications cannot be entirely excluded, this review represents the most comprehensive synthesis to date of early disease characteristics in jSSc across diverse geographic regions.

Conclusions

This scoping review demonstrates that juvenile- and adult-onset SSc show similar organ manifestations while exhibiting important age-specific differences that are evident early in the disease course. The predominance of diffuse cutaneous disease, inflammatory musculoskeletal involvement, overlap-associated autoantibodies, and low rates of SRC distinguish jSSc from adult disease. These findings emphasize the need for earlier recognition of jSSc and the development of paediatric-specific classification criteria and treatment studies.

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