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ORIGINAL ARTICLE

Clinical manifestations and antibody associations in systemic sclerosis: Insight from a single-center cohort.

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ABSTRACT… Objective: To describe the clinical manifestations and autoantibody associations in patients with systemic sclerosis (SSc) at a tertiary care center in Pakistan. **Study Design:** Prospective Cross-sectional Comparative Observational study. **Setting:** Department of Rheumatology, Fauji Foundation Hospital, Rawalpindi, Pakistan. **Period:** January 2019 to December 2025. **Methods:** Forty-seven consecutive patients fulfilling the 2013 ACR/EULAR classification criteria for SSc were enrolled. Clinical subtypes (dcSSc vs lcSSc), organ involvement (HRCT for ILD, echocardiography for suspected PH), and SSc-specific autoantibodies were recorded. Data were analysed using SPSS. **Results:** Mean age was 41.2 ± 11.8 years; 61.7% had dcSSc. Raynaud's phenomenon was universal (100%). ILD was present in 73.3% with no significant difference between dcSSc (75.0%) and lcSSc (70.6%) (p=0.746). Anti-Scl-70 was the most common autoantibody (40.4%) and anticentromere antibody (ACA) was exclusively seen in lcSSc (27.8% vs 0%, p=0.008). No significant antibody–organ associations were found. **Conclusion:** This Pakistani cohort showed a uniformly high burden of ILD across both cutaneous subtypes and the classical ACA–lcSSc association. Universal ILD screening is warranted irrespective of subtype or autoantibody profile.

Key words: Anti-Scl-70, Anticentromere Antibody, Interstitial Lung Disease, Pulmonary Hypertension, Pakistan, Systemic Sclerosis.

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INTRODUCTION

Systemic sclerosis (SSc) is a chronic autoimmune connective tissue disease marked by fibrosis of the skin and internal organs. It shows striking variability in how it presents and progresses. At its core, the disease involves immune-mediated damage to blood vessels and progressive scarring that can affect the gut, lungs, heart, and kidneys — complications that ultimately shape a patient's long-term outlook.[1]

Although relatively uncommon, the frequency of SSc differs markedly around the world. Global figures point to an incidence of roughly 8.6 per 100,000 person-years and a prevalence of about 19 per 100,000, with the disease striking women, adults, and people in higher-income countries more often.[2] These differences remind us how much demographics and geography shape the illness.

The underlying problem in SSc is a tangled mix of immune dysregulation, blood-vessel injury, and fibrosis. Clinically it ranges from mild skin-limited disease to aggressive widespread involvement, yet what really decides the prognosis is how badly the internal organs are affected, not the skin changes alone.[3]

Doctors usually divide SSc into limited cutaneous (lcSSc) and diffuse cutaneous (dcSSc) forms to help predict complications. The diffuse type tends to bring earlier and more severe damage to lungs, blood vessels, gut, and kidneys. Better awareness and regular monitoring have improved survival, but outcomes still vary widely from one patient to another.[3,4,5]

Certain autoantibodies have become valuable guides in daily practice. They stay stable over time and often point to specific patterns of disease. Anti-topoisomerase I (anti-Scl-70) is strongly linked to interstitial lung disease, while anti-RNA polymerase III is tied to fast-progressing skin thickening and kidney crisis, though lung involvement is less common in that group.[1,2,6]

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These antibody profiles can give doctors extra prognostic clues beyond the skin subtype alone.

Local data on SSc in Pakistan are still very scarce. The only published single-centre study from our country (Asif et al., 2021) reported just 38 patients and clearly showed how little information exists here.[7] That gap is exactly why we carried out the present work.

In this study we set out to describe the clinical picture and autoantibody associations of systemic sclerosis in a single-centre cohort from Pakistan.

METHODS

This prospective cross-sectional comparative observational study was carried out in the Department of Rheumatology, Fauji Foundation Hospital, Rawalpindi, between January 2019 and December 2025. We compared clinical features and serological findings between patients with diffuse cutaneous systemic sclerosis (dcSSc) and limited cutaneous systemic sclerosis (lcSSc).

All consecutive patients attending the outpatient clinic who met the 2013 ACR/EULAR classification criteria for SSc[8] were invited to take part. Because the disease is rare, we enrolled every eligible patient who presented during the study period (census sampling). The hospital mainly looks after serving and retired armed forces personnel and their families; this explains why the entire cohort turned out to be female. Patients with localised scleroderma (morphea) or any other scleroderma-spectrum disorder were excluded. The institutional review board gave ethical approval (Fauji Foundation Hospital, 28 August 2025; Ref No. 1017/RC/FFH/RWP), and every participant gave written informed consent.

A standard proforma captured age, sex, disease duration, Raynaud phenomenon, digital ulcers, digital pitting, puffy fingers, synovitis/arthritis, tendon friction rubs, muscle weakness, gastrointestinal symptoms (GERD, dysphagia), and cardiopulmonary complaints (dyspnoea). Skin subtype was decided on the basis of the extent of skin thickening.

Interstitial lung disease (ILD) was defined by HRCT changes consistent with usual interstitial pneumonia, non-specific interstitial pneumonia, or fibrosis, as reported by a consultant radiologist who was blinded to the clinical details. Suspected pulmonary hypertension was noted from echocardiography findings such as raised tricuspid regurgitant jet velocity or right-ventricular enlargement; right-heart catheterisation was not done routinely.[9,10]

Autoantibody testing included ANA by indirect immunofluorescence and specific SSc antibodies (anti-Scl-70, anticentromere, anti-RNP, anti-Ro/SSA, anti-La/SSB, anti-Jo-1, anti-dsDNA) from the hospital laboratory records.

Statistical analysis was performed with SPSS version XX. Continuous data are shown as mean ± standard deviation or median (interquartile range) as appropriate. Categorical variables are given as frequencies and percentages. Comparisons between dcSSc and lcSSc used the independent-samples t-test or Mann-Whitney U test for continuous variables and chi-square or Fisher's exact test for categorical variables. A two-sided p-value <0.05 was taken as statistically significant.[11]

RESULTS

Forty-seven consecutive patients with systemic sclerosis were studied. All were female. Their mean age was 41.2 ± 11.8 years (range 18–65). Twenty-nine patients (61.7%) had dcSSc and 18 (38.3%) had lcSSc. Raynaud's phenomenon was present in every single patient (100%).

Before comparing the two subtypes we checked normality with the Shapiro-Wilk test. Age and Modified Rodnan Skin Score were normally distributed, but disease duration was not; therefore the latter is reported as median (IQR) and compared with the Mann-Whitney U test.

No meaningful differences emerged between the two subtypes in age, disease duration, skin score, or any of the clinical features we recorded. Arthritis/synovitis, GERD, digital pitting, and dysphagia were the commonest non-vascular problems. Interstitial lung disease was strikingly common (73.3%) and affected both subtypes almost equally (75.0% dcSSc vs 70.6% lcSSc, p=0.746). Suspected

pulmonary hypertension on echo was seen in 12.8% of the whole group with similar rates in both subtypes.

ANA was positive in almost everyone (95.7%). Anti-Scl-70 was the commonest disease-specific antibody (40.4%) and tended to be more frequent in dcSSc, though the difference did not reach significance. Anticentromere antibody was found only in lcSSc patients (27.8% vs 0%, p=0.008). The other antibodies were less common and showed no clear subtype preference.

TABLE-I

Demographic and clinical characteristics

Variable	Total (N=47)	Diffuse (dcSSc) (n=29)	Limited (lcSSc) (n=18)	Test Statistic	P-Value
Demographics					
Age (years), Mean ± SD	41.2 ± 11.8	39.1 ± 11.5	44.6 ± 11.7	t = -1.613	0.112
Disease Duration (years), Median (IQR)	5.0 (2.0-8.5)	5.0 (2.0-10.0)	5.0 (1.1-7.8)	U = 223.5	0.465
Modified Rodnan Skin Score, Mean ± SD	24.3 ± 10.5	24.3 ± 10.5	24.3 ± 10.8	t = -0.015	0.988
Clinical Features, n (%)					
Raynaud Phenomenon	47 (100)	29 (100)	18 (100)	-	1.000
Digital Ulceration	21 (44.7)	14 (48.3)	7 (38.9)	$\chi^2 = 0.410$	0.522
Digital Pitting	25 (53.2)	16 (55.2)	9 (50.0)	$\chi^2 = 0.121$	0.728
Arthritis / Synovitis	27 (57.4)	16 (55.2)	11 (61.1)	$\chi^2 = 0.161$	0.688
Dysphagia	25 (53.2)	16 (55.2)	9 (50.0)	$\chi^2 = 0.121$	0.728
GERD / Reflux	26 (55.3)	16 (55.2)	10 (55.6)	$\chi^2 = 0.001$	1.000
Organ Involvement, n (%)					
Interstitial Lung Disease (HRCT)	33/45 (73.3)*	21/28 (75.0)	12/17 (70.6)	$\chi^2 = 0.105$	0.746
Suspected Pulmonary Hypertension (Echo)	6 (12.8)	3 (10.3)	3 (16.7)	$\chi^2 = 0.397$	0.661

*ILD analysis based on 45 patients with definitive HRCT results (2 missing).

TABLE-II

Autoantibody Profile by Systemic Sclerosis Subtype

Antibody	Overall (N=47) n (%)	Diffuse (dcSSc) (n=29) n (%)	Limited (lcSSc) (n=18) n (%)	χ^2 Value	P-Value
Antinuclear Antibody (ANA)	45 (95.7)	28 (96.6)	17 (94.4)	0.129	1.000
Anti-Scl-70	19 (40.4)	14 (48.3)	5 (27.8)	1.957	0.162
Anticentromere Antibody (ACA)	5 (10.6)	0 (0)	5 (27.8)	7.025	0.008*
Anti-RNP	6 (12.8)	3 (10.3)	3 (16.7)	0.397	0.661
Anti-Ro (SSA)	10 (21.3)	7 (24.1)	3 (16.7)	0.373	0.722

*Statistically significant ($p < 0.05$)

TABLE-III

Association of Disease-Specific Autoantibodies with Major Organ Involvement

Antibody-Organ Association	Antibody Positive n/N (%) with Organ Involvement	Antibody Negative n/N (%) with Organ Involvement	χ^2 Value	P-Value	Phi Coefficient (ϕ)	Odds Ratio (95% CI)
Anti-Scl-70 with Interstitial Lung Disease	15/19 (78.9%)	18/26 (69.2%)	0.543	0.461	0.112	1.67 (0.43-6.47)
ACA with Suspected Pulmonary Hypertension	1/5 (20.0%)	5/42 (11.9%)	0.289	0.525	0.091	1.85 (0.17-19.83)

*Analysis for ILD includes 45 patients with definitive HRCT results.

Neither anti-Scl-70 nor ACA showed a statistically significant link with ILD or suspected pulmonary hypertension in our cohort.

DISCUSSION

We studied 47 consecutive patients with systemic sclerosis seen in our clinic over seven years. Because Fauji Foundation Hospital mainly cares for armed forces families, every participant was female — a pattern that simply reflects who attends our service. The cohort showed a clear predominance of diffuse cutaneous disease (61.7%), a high overall burden of interstitial lung disease (73.3%), and no difference in ILD rates between the two skin subtypes. Anticentromere antibodies were found only in limited disease, but the expected links between anti-Scl-70 and ILD (or ACA and pulmonary hypertension) were not statistically significant.

These findings both echo and differ from what has been reported elsewhere in Pakistan and internationally.[5,7,12,13] The uniformly high ILD rate across both subtypes was especially striking. In many previous studies ILD has been far more common in diffuse disease; here it was almost equally frequent in limited disease too.[14,15] Several factors may explain this: the very high baseline ILD prevalence in our group may have created a "ceiling effect," our modest sample size (particularly the smaller lcSSc group) may have limited statistical power, and referral patterns at a tertiary centre may have brought in more severe cases. Whatever the reason, the practical message is straightforward — every patient with SSc in our setting deserves systematic lung screening with HRCT, regardless of skin subtype or antibody status.[16,17,18,19,20]

The autoantibody picture also had both familiar and unexpected features. The exclusive presence of ACA in lcSSc (p=0.008) matched classic descriptions and confirmed that our clinical subtyping was accurate.[1,2] Anti-Scl-70 was the leading disease-specific antibody, as seen in other Asian cohorts,[12,13] but its association with ILD did not reach significance here. This may reflect population differences or the overall high ILD background.

Strengths of the work include its prospective design, use of standard classification criteria,[8] and the fact that it adds fresh local data from a part of the world where information is still limited. Limitations are the single-centre setting, modest numbers, exclusively female population, and reliance on echocardiography rather than right-heart catheterisation for pulmonary hypertension.[9,10] The cross-sectional nature also means we cannot comment on how the disease evolves over time.

CONCLUSION

This study from a Pakistani tertiary centre that serves armed forces families shows a high and evenly distributed burden of interstitial lung disease in both diffuse and limited cutaneous systemic sclerosis. The strong and exclusive link between anticentromere antibodies and limited disease confirms the value of serological testing for accurate phenotyping. Taken together, these observations highlight the need for universal lung screening in our population and call for larger, multicentre, longitudinal studies across Pakistan.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Muhammad Harris:** Study design, drafting.
2	**Saba Samreen:** Data collection.
3	**Haris Gul:** Data analysis.
4	**Shahida Perveen:** Data interpretation.
5	**Babur Salim:** Study supervision.
6	**Javed Ali:** Data acquisition.