

Clinico-pathological profile of Systemic Sclerosis in a tertiary care center

Dilip Kumar SA, Alaka Sahu*

Department of Dermatology, LSLAM Govt. Medical College, Raigarh Chhattisgarh, India

* Department of Pathology, VIMSAR, Burla, India

Abstract

Objective To find out the profile of cutaneous and systemic features of systemic sclerosis (SSc) in people of East-Central part of India.

Methods This was a cross-sectional descriptive study conducted over eight years in a tertiary care center. All the patients of SSc were evaluated for cutaneous and systemic involvement.

Results 54 cases (48 females and 6 males) of SSc were evaluated. Mean age was 31.81 ± 14.52 years. We found microstomia in 88.8%, sclerodactyly 88.8%, Raynaud's phenomenon in 81.4%, salt-and-pepper pigmentation in 70.3%, fingertip ulceration in 66.6%, pinched nose in 61.1%, radial furrows around mouth in 33.3%, diffuse alopecia in 18.5%, nail changes in 18.5%, calcinosis cutis in 7.4% and digital gangrene in 5.6% cases. Among the systemic features, we observed arthralgia in 55.5%, dyspnea on exertion in 55.5%, dysphagia in 51.8%, esophageal reflux in 46.2%, cough in 11.1%, and palpitation in 7.4% cases. Antinuclear antibody (ANA) was positive in 85.1%, abnormal pulmonary function test in 59.2%, abnormal X-ray hand in 33.3% and proteinuria in 7.4% cases.

Conclusion Pulmonary, renal and cardiac involvement were less in our study population as compared to other studies.

Key words

Systemic sclerosis, cutaneous features, systemic features.

Introduction

Systemic sclerosis (SSc) is a chronic disorder of unknown etiology characterized clinically by thickening and stiffening of skin caused by accumulation of connective tissue and by structural and functional abnormalities of visceral organs including gastrointestinal tract, lung, heart, kidney.¹ It is characterized pathologically by vascular abnormalities, sclerosis of connective tissue, epidermal atrophy

and autoantibodies. Patients with systemic sclerosis are classified as limited cutaneous systemic sclerosis and diffuse cutaneous systemic sclerosis.² Based on extent of skin involvement, limited cutaneous systemic sclerosis is defined as skin involvement confined to areas distal to elbows and knees and also face and neck whereas diffuse cutaneous systemic sclerosis as that extending proximal to the elbows and knees, face, neck and trunk. Patients with limited cutaneous systemic sclerosis have long duration of Raynaud's phenomenon, esophageal dysmotility or reflux, gastrointestinal problems, pulmonary fibrosis and pulmonary hypertension late in the course of their disease. They are often positive for anticentromere antibody.² Patients with diffuse cutaneous

Address for correspondence

Dilip Kumar SA

Cutis Skin & LASER Clinic, Gourishankar Mandir

Raod, Raigarh, Chhattisgarh, India PIN Code

496001

Ph: +91-7024449837

Email: dr.dilip.kmc@gmail.com

systemic sclerosis have short duration of Raynaud's phenomenon preceding onset of cutaneous features, fatigue, arthralgia, gastrointestinal manifestations, pulmonary fibrosis, cardiac involvement and renal crisis. They often have antibodies to Scl-70.² SSc mimics many other skin conditions like generalized morphea, scleromyxedema, scleredema of Buschke, primary systemic amyloidosis, chronic graft-versus-host disease, eosinophilic fasciitis etc.³ The criteria for diagnosis of systemic sclerosis have been established by the subcommittee for scleroderma criteria of American Rheumatism Association (now called the American College of Rheumatology).⁴ The single major criterion is presence of sclerodermatous involvement proximal to the digits, affecting limbs, face, neck, or trunk usually in a bilateral and symmetrical pattern.; the minor criteria are sclerodactyly, digital pitted scars or tissue loss of volar pads of fingertips, and bibasilar pulmonary fibrosis.⁴ The diagnosis is based on presence of either the major criterion or at least two of minor criteria. These criteria have 97% sensitivity and 98% specificity. The addition of Raynaud's phenomenon and nail fold capillary microscopy and systemic sclerosis selective antibodies as additional minor criteria improve the sensitivity of these criteria.⁵ This study intended to explore the cutaneous and systemic features of patients of SSc in the East-central part of India.

Methods

A cross-sectional, descriptive study was conducted over a period of eight years in a tertiary care center in East-central part of India. All the patients of systemic sclerosis giving written consent for the study and fulfilling the criteria laid down by the subcommittee for scleroderma criteria of the American College of Rheumatology were recruited for the study.⁴

Patients with overlap syndrome and mixed connective tissue disorders were excluded from the study. Detailed history, clinical examination and necessary investigations were undertaken. Special investigations like high resolution CT scan, skin biopsy, echocardiography etc. were performed in a subset of patients. Data analysis was done using Microsoft Office Excel 2007 and SPSS

Results

A total of 54 cases of SSc were evaluated; of which 36 (66.7%) belonged to diffuse cutaneous and 18 (33.3%) to limited cutaneous variety. Female to male ratio was 8:1 (48 females and 6 males). The mean age of our patients was 31.81 ± 14.52 years with a range of 12 to 65 years. By occupation 38 (70.3%) were housewives, 10 (18.5%) were students, 4 (7.4%) were farmers, 1 (1.8%) was industrial worker and 1 (1.8%) was businessman.

Duration of disease varied from 2 months to 10 years with a mean of 3.2 ± 2.96 years. Raynaud's phenomenon was present in 44 (81.4%) cases. Duration of Raynaud's varied from 1 month to 10 years with mean of 4 ± 3.03 years. Raynaud's phenomenon preceded skin tightening in 49 (90.7%) cases whereas both occurred simultaneously in 5 (9.3%) cases.

Among the cutaneous features (**Table 1**), fingertip ulceration was found in 36 (66.7%), sclerodactyly in 48 (88.8%) (**Figure 1**), digital pitted scars in 30 (55.5%) (**Figure 2**), digital gangrene in 3 (5.6%), calcinosis cutis in 4 (7.4%), microstomia in 48 (88.8%) (**Figure 3**), radial furrows around mouth in 18 (33.3%) (**Figure 4**), pinched nose in 33 (61.1%), diffuse alopecia in 10 (18.5%) and nail changes in 10 (18.5%) cases. We noticed pigmentary changes in 50 (92.6%) cases, of which 30 (55.5%) had



Figure 1 Sclerodactyly in a case of diffuse cutaneous systemic sclerosis.



Figure 2 Digital pitted scars in a case of limited cutaneous systemic sclerosis



Figure 3 Microstomia in a case of Systemic Sclerosis



Figure 4 Radial furrows around the mouth in a case of systemic sclerosis

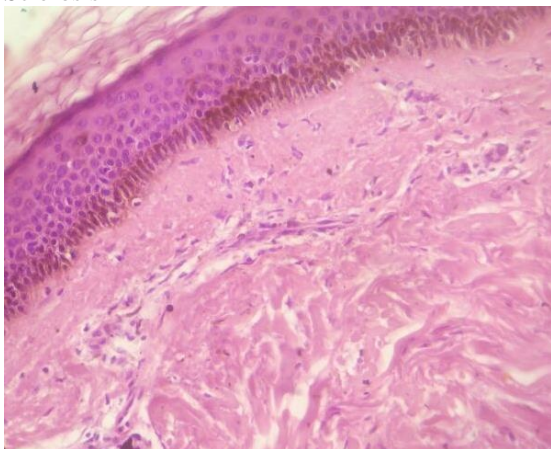


Figure 5 Thinning of epidermis, effacement of rete ridges, thickening of collagen bundles in a case of systemic sclerosis (H&E, 100X)

Table1 Cutaneous findings, systemic features and laboratory parameters in Systemic Sclerosis (n=54)

Variables	N (%)
<i>Cutaneous</i>	
Pigmentary changes	50 (92.6)
Sclerodactyly	48 (88.8)
Microstomia	48 (88.8)
Raynaud's phenomenon	44 (81.4)
Fingertip ulceration	36 (66.6)
Pinched nose	33 (61.1)
Radial furrows around mouth	18 (33.3)
Diffuse alopecia	10 (18.5)
Nail changes	10 (18.5)
Calcinosis cutis	4 (7.4)
Digital gangrene	3 (5.55)
<i>Systemic</i>	
Arthralgia	30 (55.5)
Dyspnea on exertion	30 (55.5)
Dysphagia	28 (51.8)
Esophageal reflux	25 (46.2)
Cough	6 (11.1)
Palpitation	4 (7.4)
<i>Laboratory parameters</i>	
Anemia	51 (94.4)
Raised ESR	46 (85.1)
ANA positivity	46 (85.1)
Proteinuria	4 (7.4)
Abnormality in X-ray hands	18 (33.3)
Abnormality in chest X-ray	10 (18.5)
Abnormal pulmonary function tests	32 (59.2)
Abnormality in ECG	3 (5.6)

diffuse hyperpigmentation and 38 (70.3%) had salt-and-pepper pigmentation (mottled pigmentation).

Among the systemic presentations, arthralgia was present in 30 (55.5%) cases, dyspnea on exertion in 30 (55.5%), dysphagia in 28 (51.8%), esophageal reflux in 25 (46.2%), cough in 6 (11.1%) and palpitation in 4 (7.4%) cases.

Hemoglobin level in our patients ranged from 7.6 to 12.6gm/dl with a mean of 10.35±1.52 gm/dl. Anemia was noted in 51 (94.4%) cases. ESR level was raised in 46 (85.1%) patients with a mean ESR of 27.13± 16.31mm first hour (range was 3 to 76). ANA was positive in 46 (85.1%) and proteinuria in 4 (7.4%) patients. Abnormality in X-ray hands was found in 18

(33.3%) cases, of which 8 (14.8%) cases showed acro-osteolysis, 5 (9.3%) cases showed contracture and another 5 (9.3%) cases showed both these features. Abnormality in chest X-ray was found in 10 (18.5%) cases. Pulmonary function test showed restrictive pattern of ventilatory defect in 32 (59.2%) cases. Abnormal ECG was noted in 3 (5.6%) cases. We performed skin biopsy in a subset of patients and observed features like epidermal atrophy, flattening of rete ridges, thickening and hyalinization of collagen bundles, encroachment of fat by collagen bundles and perivascular inflammatory infiltrate (**Figure 5**).

Discussion

The mean age of presentation in our study was 31.81±14.52 years which is in concordance with Sharma *et al.*⁶ (32.75± 11.62years), Ghosh *et al.*⁷ (29.6±12.3 years) and Basel *et al.*⁸ (36.17±13.9 years). However, the mean age was higher in a study conducted at Sarawak General hospital by Teh *et al.*⁹ We found female preponderance in our study with female to male ratio of 8:1. Most of the studies in literature also noted female preponderance with female to male ratio varying from 3.9:1 to 8.37:1.^{6,7,10-12} Occupational history is important in SSc as scleroderma like lesions occur in workers exposed to chemicals like vinyl chloride, perchlorethylene, trichlorethylene, organic solvents, pesticides, epoxy resins etc.³ None of our patients had exposure to these chemicals. By occupation majority of our patients were housewives followed by students.

Mean duration of disease in our study was 3.2±2.9 years which is shorter than a North Indian study.⁶ Raynaud's phenomenon was found in 81.4% patients which is similar to Sharma *et al.*⁶, Ghosh *et al.*⁷ and Teh *et al.*⁹ However, Krishnamurthy *et al.*¹⁰ noted Raynaud's phenomenon in only 28.2% cases. In

majority of cases Raynaud's phenomenon precedes cutaneous changes; this is much shorter in males than in females. In our study, 90.7% cases gave the history of Raynaud's phenomenon prior to onset of cutaneous changes. Fingertip ulceration was observed in 66.6% patients as compared to 58.6% by Sharma *et al.*⁶, and 52% by Teh *et al.*⁹ We observed diffuse hyperpigmentation in 55.5% whereas Sharma *et al.*⁶ found this in a higher proportion of cases (88.1%). Salt-and-pepper pigmentation was found in 70.3% cases as compared to 51.2% cases by Sharma *et al.*⁶ and 70% by Dia *et al.*¹¹ Calcinosis cutis most commonly found in fingers and is more common in female than in males. It may lead to ulceration with discharge of chalky materials.³ We noticed calcinosis cutis in relatively higher proportion of cases compared to Ghosh *et al.*⁷ and Al-Adhath *et al.*¹² Sclerodactyly and digital pitted scars are included as minor criteria by subcommittee for scleroderma criteria.⁴ Sclerodactyly was also found in a higher proportion in our study compared to Sharma *et al.*⁶ (64.6%) and Teh *et al.*⁹ (65%). We noticed digital pitted scars in 55.5% cases. Microstomia was found in 88.8% as compared to 55.5% in a North Indian study.⁶ Microstomia may interfere with speaking, eating and maintenance of oral hygiene.³ Radial furrows around the mouth were found in about one-third of our cases and diffuse alopecia in 21.7% cases.

Esophagus is the most common part of gastrointestinal tract (GIT) to be involved in SSc and gastroesophageal reflux and dysphagia are common gastrointestinal symptoms.³ Dysphagia was found in 51.8% cases in the present study. Gupta *et al.*¹³ noted dysphagia in 82.6% cases of limited cutaneous and 60.7% cases of diffuse cutaneous SSc. Gastroesophageal reflux was found in 46.2% cases compared to 38.7% observed by an Egyptian study.⁸ Pulmonary involvement occurs in about 40% to 90% cases

in SSc.³ Pulmonary fibrosis is usually associated with diffuse cutaneous SSc and pulmonary hypertension with limited cutaneous SSc.¹⁴ Dyspnea on exertion and cough are common pulmonary symptom in SSc.³ Dyspnea on exertion was observed in 55.5% cases in our study. This is consistent with the findings by Arakkal *et al.*¹⁵ (64.3%) and North Indian study⁶ (51.1%). Arakkal *et al.*¹⁵ noted cough in a higher proportion of patients (32%) compared to our findings. Arthralgia was noted in 55.5% cases which is little higher than the result of North Indian study⁶ and lower than the finding of Krishnamurthy *et al.*¹⁰ Malignant hypertension secondary to renal involvement develops in about 8% patients.¹⁶ None of our patients had malignant hypertension. Cardiac involvement in SSc includes myocardial disease, conduction system abnormalities, arrhythmia and pericardial disease. Resting ECG is abnormal in about 50% cases and includes bifid P waves and T wave changes.¹⁷ Only 5.6% of our patients had abnormal ECG which is very less as compared to observations by Arakkal *et al.*¹⁵

We noted raised ESR in about 85% which is consistent with the result of Sharma *et al.*⁶ However, Arakkal *et al.*¹⁵ found raised ESR in a lower proportion (53.6%) of patients. Mean hemoglobin level in our study was found to be 10.35±1.52 gm/dl and 94.4% of our patients were anemic. Hemoglobin less than 10gm/dl was found in 42.9% cases by Arakkal *et al.*¹⁵ whereas Al-Adhath *et al.*¹² observed anemia in only 31% patients. ANA level was raised in 85.1% in our study which is comparable to other studies like Sharma *et al.*⁶ (89.1%), Ghosh *et al.*⁷ (78.2%) and Pradhan *et al.*¹⁸ (87.01%). However, Krishnamurthy *et al.*¹⁰ found ANA positivity in only 56.8% cases. We observed abnormalities in chest X-ray like ground-glass appearance, reticular shadows and honey combing. Abnormal chest X-ray was noted in only 18.5% cases. This finding was higher in

other studies like Sharma *et al.*⁶, Teh *et al.*⁹, Dia *et al.*¹¹ and Arakkal *et al.*¹⁵ Pulmonary function tests are a very useful investigation in SSc and it shows restrictive changes with a decreased forced vital capacity and total lung capacity.³ About 59% of our patients showed restrictive changes in PFT. This finding is consistent with Krishnamurthy *et al.*¹⁰ and Dia *et al.*¹¹ However, Sharma *et al.*⁶ and Arakkal *et al.*¹⁵ noted restrictive pattern of ventilatory defect in a higher proportion of cases. HRCT shows ground glass appearance in areas of active alveolitis or septal fibrosis and honey combing in areas of interstitial fibrosis. We performed HRCT only in selected cases and found the features of interstitial fibrosis in lungs. Mild proteinuria is the most common renal manifestation, often early in the disease. Proteinuria was noted in 7.4% cases which is comparable to results of North Indian⁶ and Egyptian studies.⁸ X-ray hand showed changes like acro-osteolysis, contracture, calcinosis, erosive arthropathy etc.

Conclusion

Demographic profile and cutaneous features in our patients were almost similar to many other studies, however, pulmonary, renal and cardiac involvement was relatively less in our study population.

References

1. Gilliland BC. Systemic Sclerosis and related disorders. In: Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL. *Harrisons Principles of Internal Medicine, 16th ed.* New York: McGraw-Hill; 2005. P. 1979-90.
2. LeRoy EC, Black C, Fleischmajer R, Jablonska S, Krieg T, Medsger TA Jr *et al.* Scleroderma (systemic sclerosis): classification, subsets and pathogenesis. *J Rheumatol.* 1988;**15**:202-5.
3. Goodfield MJD, Jones SK, Veale DJ. The Connective Tissue Diseases. In: Burns T, Breathnach S, Cox N, Griffiths C eds. *Rook's Textbook of Dermatology, 8th ed.* Oxford: Wiley-Blackwell; 2010. 51. P. 64-110.
4. Subcommittee for Scleroderma criteria of the American Rheumatism Association Diagnostic and Therapeutic Criteria Committee. Preliminary criteria for the classification of systemic sclerosis. *Arthritis Rheum.* 1980;**23**:581-90.
5. Lonzetti LS, Joyal F, Raynauld JP, Roussin A, Goulet JR, Rich E *et al.* Updating the American college of Rheumatology preliminary classification criteria for systemic sclerosis: addition of severe nail fold capillaroscopy abnormalities markedly increases the sensitivity for limited scleroderma. *Arthritis Rheum.* 2001;**44**:735-6.
6. Sharma VK, Trilokraj T, Khaitan BK, Krishna SM. Profile of systemic sclerosis in a tertiary care center in North India. *Indian J Dermatol Venereol Leprol.* 2006;**72**:416-20.
7. Ghosh SK, Bandyopadhyay D, Saha I, Barua JK. Mucocutaneous and demographic features of systemic sclerosis: A profile of 46 patients from Eastern India. *Indian J Dermatol.* 2012;**57**:201-5.
8. Basel ME, Khalil N. Disease characteristics of systemic sclerosis among Egyptian patients. *Kasr Al Ainy Med J.* 2015;**21**:41-6.
9. Teh CL, Kuan YC, Wong JS. Systemic Sclerosis in Sarawak: a profile of patients treated in the Sarawak General Hospital. *Rheumatol Int.* 2009;**29**:1243-5.
10. Krishnamurthy V, Porkodi R, Ramakrishnan S, Rajendran CP, Madhavan R, Achuthan K *et al.* Progressive systemic sclerosis in south India. *J Assoc Physicians India.* 1991;**39**:254-7.
11. Dia D, Dieng MT, Sy TN, Diallo M, Fall S, Ndongo S *et al.* Systemic scleroderma: 92 cases in Dakar. *Dakar Med.* 2003;**48**(2):82-6.
12. Al-Adhadh RN, Al-Sayed TA. Clinical features of systemic sclerosis. *Saudi Med J.* 2001;**22**:333-6.
13. Gupta R, Bammigatti C, Dinda AK, Marwaha V, Gupta S. Prevalence of renal involvement in Indian patients with systemic sclerosis. *Indian J Dermatol Venereol Leprol.* 2007;**61**:91-6.
14. Antoniou KM, Wells AU. Scleroderma lung disease: evolving understanding in light of newer studies. *Curr Opin Rheumatol.* 2008;**20**:686-91.

15. Arakkal G, Chintagunta SR, Chandrika V, Damarla SV, Manchala S, Kumar BU. Cardiopulmonary involvement in systemic sclerosis: A study in a tertiary care center. *Indian J Dermatol Venereol Leprol*. 2017;**83**:677-82.
16. Steen VD, Constantino JP, Shapiro AP, Medsger TA Jr. Long term outcomes of renal crisis in systemic sclerosis: relation to availability of ACE inhibitors. *Ann Intern Med*. 1990;113:352-7.
17. Champion HC. The heart in scleroderma. *Rheum Dis Clin North Am*. 2008;**34**:181-90.
18. Pradhan V, Rajadhyaksha A, Nandkar M, Pandit P, Surve P, Lecerf M *et al*. Clinical and Autoimmune Profile of Scleroderma Patients from Western India. *Int J Rheumatol*. 2014;**2014**:983781.