Original Article

Pulmonary involvement in systemic sclerosis: A clinical profile

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ABSTRACT

Background: Systemic sclerosis is a generalized disorder of connective tissue affecting skin and internal organs. Lung involvement accounts for significant morbidity and is a leading cause of mortality in patients. **Objectives:** This study intends to study the frequency of occurrence of pulmonary involvement in progressive systemic sclerosis (PSS) and to describe the clinical and radiological picture of pulmonary involvement in PSS. **Materials and Methods:** This was a descriptive cross-sectional study. A detailed history, modified Rodnan score, clinical examination, routine investigation, antinuclear antibody, immuno biot, chest X-ray (CXR), pulmonary function test (PFT), and 6 min walk test (6MWT) were performed on all patients. High resolution computed tomography was done on those who consented. **Results:** Hundred subjects with PSS were included in the study; 90 were females and 10 were males. Common presenting complaints were skin thickening in 98% and Raynaud's phenomenon in 98%. Skin thickening of digits beyond metacarpo phalangeal was seen in 98%, face and neck in 92%, and hands in 92%. Chest wall thickening was seen in 40 subjects (40%). 90 (90%) of the studied subjects had pulmonary involvement, longer duration of disease was significantly associated with pulmonary involvement ($P < 0.05$). Dyspnea, cough, bilateral crepitations, CXR, Borg score, and Rodnan score was found to be significantly associated with severe pulmonary involvement ($P < 0.05$). **Conclusion:** The prevalence of pulmonary involvement in this cohort study was 90%. Almost 1/3rd of patients, that is 29 (29%) were detected to have pulmonary involvement despite being asymptomatic for respiratory complaints, hence early screening and evaluation is recommended. PFT and 6MWT are noninvasive, cost-effective, and easily available screening tests which can be used in resource-limited settings.

KEY WORDS: Diffusing capacity of the lungs for carbon monoxide (DLCO), forced expiratory volume at 1 s, forced vital capacity, metacarpo phalangeal, mixed connective tissue disorder, systemic sclerosis

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INTRODUCTION

Systemic sclerosis is a systemic autoimmune disease that is characterized by endothelial dysfunction resulting in a small-vessel vasculopathy, fibroblast dysfunction with resultant excessive collagen production and fibrosis, and immunological abnormalities.[1] Systemic sclerosis is an acquired, sporadic disease with worldwide distribution, with peak age incidence of 30–50 years, preferentially affecting women (M: F = 1:3–4).

Lung involvement accounts for significant morbidity and is a leading cause of mortality in patients with systemic sclerosis.[2,3] The exact prevalence of interstitial lung disease (ILD) in systemic sclerosis (SSc) is difficult to estimate because the patient is clinically asymptomatic early in the course.[4] Earlier studies have reported 74–100% prevalence of ILD in SSc patients at autopsy.[5,6] Ninety-one percent of patients had interstitial abnormalities on high resolution computed tomography (HRCT).[6,7]

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Systemic sclerosis has been extensively reported in Western literature, which showed pulmonary involvement of 50–56% in SSc patients.[7] Since there are very few studies available in the Indian population,[8,9] this is of great interest in terms of clinical manifestations, laboratory parameters, survival, and other features.[10,11]

Aims and objectives

This study intends to study the frequency of occurrence of pulmonary involvement in SSc and to describe the clinical and radiological picture of pulmonary involvement in SSc.[12] Statistical analysis also made to study the predictors of severity of pulmonary involvement in SSc.

MATERIALS AND METHODS

This was a descriptive cross-sectional study. SSc patients attending Immunology/Pulmonary medicine outpatient departments of a tertiary care hospital in South India were studied from March 2007 to June 2013. The Institution Review Board of the hospital approved the study. The patients aged more than 18 years with SSc satisfying the American Rheumatism Association criteria who consented for the study were included. Patients with other collagen vascular disease/mixed connective tissue disorder, and overlap syndromes were excluded.

After obtaining an informed consent, basic demographic details were collected, detailed history, and clinical examination was noted. Modified Rodnan skin score was calculated for all the patients.[1] Antinuclear antibody was determined by indirect immunofluorescence in all the patients and its various patterns were noted. Immunoblot was used to determine antigenic specificities by immunodiffusion kits.[13,14]

Pulmonary function test (PFT) and 6 min walk test (6MWT) were performed according to American thoracic society guidelines.[15] Restrictive lung disease was diagnosed if the percentage predicted forced vital capacity (FVC) was <80%.[16] Obstructive lung disease was diagnosed if the forced expiratory volume at 1 s/FVC was <70%. The percent of predicted DLCO was obtained using the single breath technique. Abnormal diffusing capacity was defined by a percent predicted DLCO <80%. All patients underwent a chest radiograph, and HRCT was performed when, indicated.

Outcome

Pulmonary involvement was defined as either Pulmonary fibrosis (bilateral reticular nodular on chest X-ray [CXR], interstitial pneumonitis/ground glass opacities/fibrosis on HRCT), or FVC <70% of predicted.[17]

Statistical analysis

Descriptive statistical analysis has been carried out results on continuous measurements are presented on (mean ± standard deviation), and results on categorical measurements are presented in number (%). Student's *t*-test and Chi-square/Fisher's exact test were used to find the significance of study parameters on continuous and categorical scale.

RESULTS

The baseline characteristics of the study subjects are tabulated in Table 1. Common presenting complaints and their duration such as skin thickening, Raynaud's phenomenon, dyspnea, heart burn, and cough are also described in Table 1.

Skin changes namely, digital tip pitting was noted in 87 subjects, sclerodactyly in 56 patients, nail capillary loop abnormality in 52, nail fold infarct in 42, flexor deformity in 37, and digital gangrene in 14 subjects.

In skin thickening, digit beyond metacarpo phalangeal was involved in 98 subjects, face and neck was involved in 92 subjects, and hands were involved in 92 subjects. Anterior chest wall thickening was seen in 40 subjects. Among systemic findings, 48 subjects had bilateral crepitations and 23 subjects had loud P2.

Blood investigations showed Hb <10 g % in 15 subjects, peripheral smear performed in 40 subjects showed predominantly normocytic normochromic picture in 23 (57%). Erythrocyte sedimentation rate >30 mmHg was seen in 41 subjects, 4 subjects had creatinine >1.2 mg. Antinuclear antibody was present in 98 subjects. On analysis of the immunoblotting for antinuclear antibodies, anti-Scl-70 (84 subjects) was the most common followed by antiro-52 in 27, and anti-RNP in 21 subjects [Table 2].

Among radiological features, 40% subjects had reticulonodular shadows on CXR and 60% subjects had normal CXR. Among 100 subjects, 87 underwent HRCT, basal sub pleural honey

Table 1: The baseline characteristics of the study subjects

Characteristics	Mean±SD or median (range) or *n* (%) *n*=100
Male:Female	10:90
Age (years)	39.25±11.99
Skin thickening/Raynaud phenomenon (months)	24.00 (1.00-180.00)
Dyspnea (months)	6.00 (1.00-120.00)
GERD (months)	12.00 (1.00-120.00)
Skin (%)	
Digit tip pitting	87 (87)
Sclerodactyly	56 (56)
Nail capillary loop abnormality	52 (5)
Digital gangrene	14 (14)
Skin thickening (%)	
Digit beyond MCP	98 (98)
Hand	92 (92)
Face and neck	92 (92)
Forearm	75 (75)
Anterior chest wall	40 (40)

SD: Standard deviation, MCP: Metacarpo phalangeal, GERD: Gastroesophageal reflux disease

combing was the predominant finding in 32.1% followed by fibrosing alveolitis seen in 19.5% of subjects.

Pulmonary involvement was defined as either radiological involvement (CXR/HRCT) or by Spirometry.[18] Using this criteria, 90% of the studied subjects had pulmonary involvement. Among 90 subjects with pulmonary involvement, all of them had skin thickening and Raynaud's phenomenon. Among 90 subjects, 29 were asymptomatic for respiratory complaints, in whom 12 subjects had FVC <70%, 17 subjects had desaturation >4%, 6 had reticular shadows on CXR, and 24 had parenchymal involvement on HRCT. Either dyspnea or cough was not significantly associated with pulmonary involvement ($P > 0.05$).

Predictors of pulmonary involvement was studied

Duration of disease was significantly associated with pulmonary involvement ($P = 0.04$). Other factors such as anterior chest thickening, anti Scl-70 positivity, abnormal echocardiogram (ECHO), and 6 min walk distance was not significantly associated with pulmonary involvement ($P > 0.05$) [Table 3].

Predictors of severity of pulmonary involvement in systemic sclerosis was studied

Severe pulmonary involvement was defined as FVC <50% in patients who had pulmonary involvement.[19] Using this criteria, 20 had severe pulmonary involvement. Various parameters were studied to see significant association with severe pulmonary involvement. Among all dyspnea, cough, bilateral crepts, CXR, Borg score, and Rodnan score was found to be significantly associated with severe pulmonary involvement ($P < 0.05$) [Table 4].

DISCUSSION

In earlier studies, it has been shown that organ damage occurs early in SSc. Renal crisis occurs within the first 4 years of disease and pulmonary fibrosis occurs in the first 2 years of disease, even though patients are often asymptomatic.[20-22] As the patients with organ damage have poor prognosis, all the patients should be carefully evaluated and followed-up in the initial 3 years for organ involvement.[19,22] This facilitates the early identification and initiation of appropriate therapy .

The present study was designed to evaluate the prevalence, clinical features, and predictors of pulmonary involvement in SSc. Majority, 90/100 (90%), of study subjects were females. The common presenting complaints were Raynaud's phenomenon, skin thickening, joint pain, dyspnea, and heart burn. The median duration of disease was 2 years (1 month – 13 years), increased disease duration was significantly associated with pulmonary involvement ($P = 0.04$).

Almost all the patients had skin involvement, but its extent and severity was not significantly associated with pulmonary involvement. Four percent had creatinine >1.2 indicating the

Table 2: Investigation

Characteristics	Number (percentage) or Mean±SD
ANA	
Positive (%)	98 (98)
Immunoline	
Anti-Scl-70 (%)	84 (84)
Anti-RNP (%)	21 (21)
Anti-centromere B antibody (%)	5 (5)
CXR	
Reticulo nodular shadows (%)	40 (40)
HRCT	
Total	87
Involved (%)	85 (97.7)
FVC (L/min)	1.81±0.63
FEV$_1$/FVC (percentage of predicted)	89.81±8.52
PASP >25 mmHg (%)	48 (48)

ANA: Antinuclear antibody, HRCT: High resolution computed tomography, FVC: Forced vital capacity, FEV$_1$: Forced expiratory volume at 1 s, CXR: Chest X-ray, PASP: Pulmonary artery systolic pressure

Table 3: Pulmonary involvement

	Pulmonary involvement		*P*
	No	Yes	
Duration of disease	36.00 (12.00-180.00)	24.00 (0.00-180.00)	0.049
Anterior chest wall thickening			
Absent	6 (60.00)	54 (60.00)	1.000
Present	4 (40.00)	36 (40.00)	
Anti-Scl-70 antibody			
Absent	1 (10.00)	15 (16.67)	1.000
Present	9 (90.00)	75 (83.33)	
ECHO			
Abnormal	3 (30.00)	45 (50.00)	0.322
Normal	7 (70.00)	45 (50.00)	
CXR			
Abnormal	10 (10.00)	50 (55.56)	0.005
Normal	0	40 (44.44)	
Difference SaO$_2$%			
<4.0	3 (30.00)	15 (17.24)	0.388
4 and above	7 (70.00)	72 (82.76)	

CXR: Chest X-ray, ECHO: Echocardiogram

Table 4: Predictors of severity of pulmonary involvement in systemic sclerosis

	Severe pulmonary involvement		*P*
	No (55)	Yes (20)	
Age	37.78±12.19	41.65±11.27	0.219
Skin thickening	18.00 (0.00-120.00)	27.00 (6.00-180.00)	0.127
Raynaud's phenomenon	24.00 (1.00-120.00)	27.00 (3.00-120.00)	0.187
Digital tip pitting	47 (85.45)	19 (95.00)	0.430
Nail fold infarct	23 (41.82)	13 (65.00)	0.076
Sclerodactyly	34 (61.82)	13 (65.00)	0.801
Gangrene	6 (10.91)	6 (10.91)	0.693
Anterior chest wall thickening	20 (36.36)	11 (55.00)	0.147
Bilateral crepts	23 (41.82)	14 (70.00)	0.031
Borg scale	1.41±1.26	2.45±1.28	0.002
Rodnan score	25.84±7.07	29.90±7.13	0.031

incidence of renal involvement was low compared to western studies which showed incidence of 19%. Loud P2 was seen in 28% of subjects and ECHO showed pulmonary artery systolic pressure >25 mmHg in 48% of subjects, incidence was higher compared to the western and other Indian studies.

One third of patients were asymptomatic, FVC was <70% predicted in 13.3%, desaturation >4% was seen in 18.8% and 26.6% had pulmonary involvement on HRCT. HRCT was very sensitive in detecting pulmonary involvement even though patients were asymptomatic for respiratory complaints. Hence we should consider PFT, 6MWT, and HRCT in all patients to facilitate early detection.

Various factors predicting the severity of pulmonary involvement was studied which showed respiratory symptoms, Rodnan score, Borg score, and CXR were significantly associated with severe organ damage. 6MWT is a simple, easy, and cost-effective test, and can be easily performed on all patients.

Although PFT and HRCT were not done in all patients, it together increased the early detection. Recent update also recommends follow-up of PFT and 6MWT every 6 months for monitoring disease progression, so that appropriate treatment can start early.[23] This study examined only predictors of lung involvement at one point, further follow-up regarding disease progression, management, and response would help to plan better management protocol.

CONCLUSION

The study was conducted on 100 patients with SSc. Skin thickening and Raynaud's phenomenon was observed in all study subjects. Twenty-nine subjects were asymptomatic for respiratory complaints. Hypothyroidism as a co-existing illness was noted in 14 (46%) of all subjects. The prevalence of pulmonary involvement in this study was 90%. Duration of disease and abnormal CXR were significantly associated to be predictors of pulmonary involvement. 26.6% of them had severe pulmonary involvement. Respiratory symptoms, Rodnan score, bilateral crepts, and abnormal CXR were a predictor of severe pulmonary involvement. Almost 1/3rd of patients were detected to have pulmonary involvement despite being asymptomatic for respiratory complaints, hence early screening and evaluation is recommended. PFT and 6MWT are noninvasive, cost effective, easily available screening tests which can be used in resource limited settings.

Conflicts of interest
There are no conflicts of interest.

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