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STUDY OF SKIN CHANGES, HAND ABNORMALITIES AND PULMONARY MANIFESTATIONS IN DIFFUSE SCLERODERMA IN A TERTIARY CARE HOSPITAL OF EASTERN INDIA

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ABSTRACT **Introduction:** Scleroderma is a connective tissue disease characterized by fibrosis affecting the skin and internal organs.Joint involvement has been reported to occur in 46%- 97% of SSc patients. Bone and soft tissues may also be targeted; calcinosis and acro-osteolysis are thought to be the main characteristic findings in SSc. Pulmonary disease in SSc falls into two major categories: interstitial lung disease (ILD) and pulmonary hypertension. Using PFTs, significant pulmonary involvement is detectable in 25% of the patients with SSc within 3 years of initial diagnosis. The gold standard for determination of PAH in patients with SSc is right heart catheterization. The HRCT features of lung disease are ground-glass opacification predominant or admixed with reticular abnormalities in the majority of cases and little or no honeycombing. **Aims and Objectives:** To study the demographic profile, Clinical Manifestations, Radiological abnormalities, Lung involvement and PAH. **Materials and Methods:** 35 newly diagnosed Sclederma patients attending Medicine and Rheumatology OPD of Medical College Kolkata were studied in this Cross-sectional observational study. Clinical Manifestations are noted and Radiological Investigations were recorded in structured Proforma. Data analysed using standard statistical methods. **Results and Analysis:** In our study, the study population had an F: M ratio of 10:1. majority of population (38%) having age group(30-40) yrs followed by less than 30 yrs & 41yrs or more (31% each). In our study clinically hand abnormality was evident in 69% patients & radiologically hand abnormality was evident in 74% patients. In our study population 29% patients have had acroosteolysis, 26% patients had erosion & 19% patients had flexion contracture. In our study we found all the patient with documented ILD had abnormal PFT. In our study group restrictive pattern in PFT was evident in 63% patients & mixed pattern was evident in 23% patients. Twelve patients (35% of the total cohort) had pulmonary hypertension defined as PAs of 30 mm Hg or greater. In our study we found Out of 30 patients with documented ILD in HRCT 20 patients had PAH & 10 patients had no PAH. **Conclusion:** Females are more affected than males. Majority of the patients affected are in the age group of 30-40 years.69% patients had clinically evident hand abnormality and 74% patients had radiologically evident hand abnormality.CXR showed ILD in 63% patients whereas86% patients had documented ILD in HRCT.Restrictive pattern of PFT abnormality is more than mixed pattern.57% patients had documented PAH in echocardiography.HRCT is more sensitive than chest radiography for detection of ILD.

KEYWORDS : Diffuse Sclerodema, skin changes, Hand and Pulmonary Manifestations.

INTRODUCTION:

Scleroderma is a connective tissue disease characterized by fibrosis affecting the skin and internal organs.Skin disease is nearly universal among patients with SSc. Measurement of skin thickness is used as surrogate measure of disease severity and mortality in patients with diffuse SSc; an increase in skin thickening is associated with involvement of internal organs and increased mortality The most important validated method ('gold standard') for measuring the dermal skin thickness is the modified Rodnan skin score (mRSS) [1]. Joint involvement has been reported to occur in 46%- 97% of SSc patients. Many distinct radiographic abnormalities have been recognized. Bone and soft tissues may also be targeted; calcinosis and acro-osteolysis are thought to be the main characteristic findings in SSc,[2] but little is known about their distribution or their association with disease phenotype. Pulmonary disease is now the leading cause of death for patients with SSc[3].Pulmonary disease in SSc falls into two major categories: interstitial lung disease (ILD) and pulmonary hypertension.Abnormalities in results of pulmonary function tests (PFTs) are common in patients with SSc. Although for many patients these are relatively minor. Using PFTs, significant pulmonary involvement is detectable in 25% of the patients with SSc within 3 years of initial diagnosis.

Impaired diffusion capacity for carbon monoxide (DLCO) is an early marker of both ILD and PAH, and correlates with the severity of underlying disease in both instances.[4] The 6-min walk test is a useful non-invasive method for assessing the severity ofdyspnoea in PAH related to CTD[5]The gold standard for determination of PAH in patients with SSc is right heart catheterization, which enables the responses of pulmonary vessels to vasodilators to be quantified, thereby guiding the choice of treatment. The presence of PAH is indicated by an mean pulmonary artery pressure (PAP) ≥25mmHg with a pulmonary capillary wedge pressure ≤15mmHg upon right heart catheterization.[6] Doppler echocardiography is, however, the usual starting point for screening.Findings of ILD on plain radiographs of SSc patients are characterized by predominant ground-glass opacification with a superimposed reticular pattern. Radiographic evidence of traction bronchiectasis may be exhibited by SSc patients with ILD, although in contrast to patients with IPF, there is typically little evidence of obvious honeycombing.The HRCT features of lung disease closely resemble those of patients with NSIP, with ground-glass opacification predominant or admixed with reticular abnormalities in the majority of cases and little or no honeycombing.Early signs of ILD include septal and subpleural line opacities, ground-glass opacities and subpleural cysts.

Aims and objectives:

1. To study the demographic profile of Scleroderma patients in this part of Eastern India.
2. To document clinically the skin, hand manifestations of this patients.
3. To Evaluate Radiologically Hand involvement, Lung involvement and Pulmonary Arterial Hypertension(PAH)

MATERIALS AND METHODS

Study area:

Medical college and hospital, Kolkata, West Bengal, India.

Study period: January 2018 to September 2019

Study population: Newly diagnosed patient of diffuse scleroderma attending General Medicine OPD & Rheumatology OPD at Medical College & Hospital, Kolkata.

Sample Size: 35 patients [90% prevalence of interstitial lung disease in diffuse scleroderma.[104] Sample size calculates by using the formula

$z^2 \times p \times q / l^2$ {z-1.96, p-0.9, q-0.1, l(acceptable error)-0.1}= 34.5 rounded off to 35]

Sample Design:
All consecutive patients will be taken till sample size reached 35.

Inclusion Criteria:
All cases diagnosed as diffuse scleroderma according to ACR criteria and not received any immunosuppression therapy.

Exclusion Criteria:
i. Critically ill patient of diffuse scleroderma
ii. Other autoimmune disease with diffuse scleroderma overlap.
iii. Diabetes melitus
iv. hypothyroidism

Study Design: Hospital based cross-sectional,Observational study

Study tools & techniques:
1)Predesigned and pretested proforma
2)Clinical variables**:**
a) Skin changes
b) Hand abnormality
3)Investigation**:**
a) Pulmonary function test
b) Chest X-ray
c) X-ray hand
d) Echocardiography
e) HRCT

Method of data collection:
Informed consent was taken from the study participants after explaining the importance of the study to them in detail. Anonymity and confidentiality was assured to all the participants. All the cases were studied as per study proforma.

Statistical analysis :
The data were tabulated on a master chart. The results were analysed as Number (Percentage/proportion) for categorical Variables and measures of central tendency & dispersion for continuous variables. For categorical variables, Chi Square Test (with Yate's correction if necessary) was done to assess statistical significance between two parameters while for continuous variables, unpaired t-test/ one way ANOVA was done to test of significance considering 'p' value of less than 0.05 as statistically significant with 95% CI. The data after analysis were presented as tables and figures. All the Statistical Analysis was done with Epi Info software.

RESULTS AND ANALYSIS:
In our study, the study population had an F: M ratio of 10:1; 91% % of study population was female and 9% was male. All the patients were native Indians. So in our study we could find only one racial distribution. Jimenez SA and colleagues in their study showed that women are four to nine times more likely to develop scleroderma than men.[7]

In our study group, majority of population (38%) having age group(30-40) years followed by less than 30 yrs& 41yrs or more (31% each). Rula A and colleagues in their study showed that diffuse scleroderma most commonly first presents between the ages of 20 and 50 years, although any age group can be affected.[8] Discussing the distribution of religion, 69% of study subjects were found to be Hindu and 31% belonged to Muslim community. No publication available regarding this communal distribution in India or abroad.

Analyzing the records of residence, we documented that majority of our patients came from Howrah & Malda Districts (14%) followed by Midnapore, Murshidabad&Birbhum District. However we did not treat any patient from the neighboring states.There is no documentation of difference in incidence of diffuse scleroderma between urban and rural area.

Regarding occupation groups in our study, housewives formed the largest group (68%), then student (23%).None of the studies proved any significant association between occupation and development of scleroderma. No reports available on occupational distribution of the disease from India, or abroad. In our study group, majority of the patients are married (77%) & 23% patients are unmarried. No reports available on marital status distribution of the disease from India, or abroad.

In our study clinically hand abnormality was evident in 69% patients according to Modified Rodnan Skin Score & radiologically hand abnormality was evident in 74% patients.

Table 1:- Distribution of study population according to clinical hand changes (n=35)

Hand changes	Frequency	Percent (%)
Yes	24	69
No	11	31
Total	35	100

Erre GL et al in their study found that the skeletal and articular involvement of the hand was frequent in SSc, being clinically evident in 30/41 (73%) and radiologically in 33/41 (80%) of patients. The periarticular pattern (defined as the occurrence of bone resorption of ungual tufts, soft tissue calcifications and/or flexion deformities) was the most frequent pattern detected 14/41 patients(34.1%) and finger flexion contractures and bone resorptions were associated with interstitial lung disease, reduced FVC.[9]

In another study done by Scutellari PN et al [10] radiographs and xerographs of the hands of 35 patients with progressive systemic sclerosis (PSS), as defined by the ACR, were reviewed. Patients with "overlap" syndromes (i.e., mixed connective tissue disease, systemic lupus erythematosus or rheumatoid arthritis) have been excluded. The most common bony change was resorption of distal phalanges; diffuse osteoporosisis also frequent; the distal interphalangeal and first carpometacarpal joints involvement appear as a distinctive feature of this erosive arthritis.

In a study done by Baron M et al [11] the articular manifestations of progressive systemic sclerosis (PSS) were studied in 38 patients. Of these, 66% experienced joint pain and 61% had signs of joint inflammation. Limitation of joint movement was seen in 45%. Radiological abnormalities included periarticular osteoporosis (42%), joint space narrowing (34%), and erosions (40%).

In our study population 29% patients have had acroosteolysis, 26% patients had erosion & 19% patients had flexion contracture.

Table 2:- Distribution of study population according to radiological hand changes (n=35)

Radiological hand changes	Frequency	Percent(%)
Acro-osteolysis	10	29
Erosion	9	26
Flexion contracture	7	19
Normal	9	26
Total	35	100

Piorunek T et al in their study of 37 scleroderma patients showed sex ratio F/M-31/6 . High resolution computed tomography (HRCT), spirometry, body plethysmography, and lung diffusion examinations (DLco) were performed. The HRCT showed septal and subpleural lines in 70%, ground-glass opacities in 51%, and honeycomb lungs in 30% of the cases. The DLco values were decreased in 92% of the patients. Total lung capacity (TLC) showed a restrictive pattern in 74% of the patients, and only in 11% of them obstruction predominated.[12]

Steen VD and colleagues in their study showed that 40-75% patients of diffuse scleroderma had abnormal PFT.[13] In our study we found all the the patients with documented ILD had abnormal PFT. This observation was statistically significant..

In our study group restrictive pattern in PFT was evident in 63% patients & mixed pattern was evident in 23% patients This higher percentage of abnormal PFT may be due to patient attended this institution in late stage as this institution is a tertiary care unit.

Table 3:- Distribution of study population according to pulmonary function test (n=35)

Pulmonary function test	Frequency	Percent(%)
Normal	5	14
Restrictive	22	63
Restrictive + Obstructive	8	23
Total	35	100

In our study group 57% population had pulmonary arterial hypertension in echocardiography.

In one study thirty-four patients with scleroderma studied. All patients had 12-lead ECGs and two-dimensional and Doppler echocardiograms. The pulmonary artery systolic pressure (PAs) was calculated. Twelve patients (35% of the total cohort) had pulmonary hypertension defined as PAs of 30 mm Hg or greater.

In our study out of 30 patients with documented ILD in HRCT, 20 patients had PAH & 10 patients had no PAH. 5 patient without ILD in HRCT also did not have PAH.

Table 4: Distribution of study subjects according to chest X-ray & HRCT changes for detection of ILD (n=35)

	HRCT		Total
Chest X-ray	ILD	No ILD	
ILD	22	0	22
No ILD	8	5	13
Total	30	5	35

Using skin score data from patients entered in The University of Pittsburgh Scleroderma Databank, Steen and Medsger.have found that skin thickening, as measured by mRss, provides a surrogate measure of disease severity and has prognostic value, especially in dcSSc. In their study, Steen and Medsger examined the relationship between changes in skin thickening over a 2-year period and outcome in 278 patients with early-stage (duration <3 years) dcSSc. They found that patients with an improvement in skin thickening of >25% of their peak skin score and a rate of improvement of at least 5 U/year had a significantly better outcome than patients who experienced further skin thickening or no improvement. Survival rates at 5 and 10 years were 90 and 80%, respectively, for the 'improved skin group' compared with 77 and 60%, respectively, for the 'no improvement group' ($P < 0.0001$). Patients with the highest peak skin scores were those least likely to improve, and patients with no improvement experienced significantly more severe organ involvement, which likely contributed to their poorer outcome.

In one study high-resolution computed tomographic (HRCT) scans and chest radiographs were obtained in 23 patients with progressive systemic sclerosis (PSS) to assess the diagnostic merits of HRCT compared with chest radiography in detecting interstitial lung involvement in these patients. HRCT scans showed interstitial disease in 21 patients (91%). Chest radiographs, on the other hand, showed interstitial opacification patterns in 15 patients (65%) while eight patients (35%) had normal chest radiographs.

In our study HRCT scans showed ILD in 86% patients and chest radiograph showed ILD in 63% patients. Thus, HRCT is much more sensitive than chest radiography when assessing minimal interstitial lung involvement in patients with diffuse scleroderma.

CONCLUSION:

1. Females are more affected than males.
2. Majority of the patients affected are in the age group of 30-40 years.
3. 69% patients had clinically evident hand abnormality and 74% patients had radiologically evident hand abnormality.
4. CXR showed ILD in 63% patients whereas86% patients had documented ILD in HRCT.
5. Restrictive pattern of PFT abnormality is more than mixed pattern.
6. 57% patients had documented PAH in echocardiography.
7. HRCT is more sensitive than chest radiography for detection of ILD.

Limitations of the study:

Study population was small. Future studies on a large population sample are welcome. It was a single institution based study (Medical College & Hospital, Kolkata).Confirmation of the diagnosis of pulmonary arterial hypertension requires right heart catheterization .

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Conflict of interest: None.

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