

Nailfold Capillaroscopic Changes as a Marker of Interstitial Lung Disease in Systemic Sclerosis: A Cross-Sectional Study in a Tertiary Care Hospital in Eastern India

Abstract

Background: Systemic sclerosis (SSc) is an autoimmune connective tissue disorder causing microvascular abnormality leading to Raynaud's phenomenon, skin tightening, and nailfold capillary changes. The patient may have systemic involvement, among them interstitial lung disease (ILD) and pulmonary arterial hypertension are mainly associated with disease-related mortality. **Aims:** To find out an association between nailfold capillaroscopic changes with ILD severity. **Materials and Methods:** An institution based cross-sectional study was performed among the patients of SSc above 18 years. Detailed history was taken. Clinical examinations, nailfold capillaroscopy (NFC) with a dermatoscope and high-resolution computed tomography (HRCT) scan of thorax were done. Data were analyzed in MedCalc statistical software version 20. **Results:** Out of total 43 patients, 74.4% ($n = 32$) were female. Mean age was 35.05 ± 7.24 years and mean duration 4.28 ± 2.81 years. Diffuse SSc was found in 88.37% ($n = 38$). On NFC, early, active, and late patterns were found in 30.2% ($n = 13$), 25.6% ($n = 11$), and 44.2% ($n = 19$) cases, respectively. On HRCT, early, active, and late ILD were present in 18.6% ($n = 8$), 37.2% ($n = 16$), and 30.2% ($n = 13$) cases, respectively. ILD changes were absent in 14% ($n = 6$) though NFC changes were present in them. Respiratory symptoms were absent in 20.93% ($n = 9$) patients though all had features of early NFC and among them 9.3% ($n = 4$) showed early ILD changes on HRCT. Significant associations were found between NFC changes and ILD severity ($P = 0.0003$), NFC changes and respiratory symptoms ($P < 0.0001$) and between ILD changes and respiratory symptoms ($P < 0.0001$). **Discussion:** NFC, an inexpensive procedure, can be performed in all patients of SSc to detect development of early ILD even before appearance of respiratory symptoms to prevent further progression.

Keywords: *Interstitial lung disease, nailfold capillaroscopy, systemic sclerosis*

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Introduction

Systemic sclerosis (SSc) is an autoimmune connective tissue disease characterized by microvascular damage and fibrosis of the skin and internal organs. Endothelial and fibroblast dysfunction with microvascular abnormality leading to tissue hypoxia and altered immune responses play key roles in the pathogenesis. Nailfold capillaroscopy (NFC) is an established method for evaluation of microvasculature abnormalities, which characterize >95% patients with SSc, and these NFC changes may appear even before appearance of systemic manifestations.^[1]

Interstitial lung disease (ILD) and pulmonary artery hypertension are the two main pulmonary manifestations of SSc and cause disease-related mortality.^[2] About

two-third of the patients of SSc develop scleroderma ILD (SILD).^[3] High-resolution computed tomography (HRCT) is more sensitive and accurate investigation than chest radiography in detecting and characterizing diffuse lung disease in SSc. There is dearth of data regarding the impact of NFC in predicting ILD, as well as the association between extent of ILD and the NFC changes in SSc, particularly in Indian population. So, we have conducted this study.

Materials and Methods

An institute-based observational cross-sectional study was carried out in a tertiary care hospital in Eastern India and done over a period of 2 years. The

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study protocol was approved by Institutional ethics committee. Patients above 18 years of age fulfilling the American college of Rheumatology and European League against Rheumatism (ACR-EULAR) criteria for SSc were included in the study after informed consent. Patients with hypertension, diabetes mellitus, history of smoking, thyroid disorder, malignancy, pregnant and lactating mother, and other autoimmune connective disorders like systemic lupus erythematosus, dermatomyositis, overlap syndromes were excluded from the study.

Detailed clinical history regarding age, sex, duration, age of onset, progression, family history, systemic complaints, and treatment history were taken. Systemic and cutaneous examinations were done. Baseline investigations, serology, pulmonary function test, and HRCT of thorax were done. On HRCT, early stage of ILD consists of few ground-glass or fibro-reticular opacities in lower lobes with mild subpleural reticulation. Active stage ILD includes ground glass opacities with reticulonodular interstitial thickening in periphery of both lung fields and bulla. Late stage ILD comprises of extensive subpleural reticulation with ground-glass opacities and honey combing.^[4] NFC was done with Dermatoscope (DermLite DL3N) placing immersion oil (Cedarwood oil) on the nailfold bed after proper washing of the fingers for better visualization of the capillaries. On NFC, few enlarged/giant capillaries with relatively well-preserved capillary distribution, no loss of capillaries is defined as early pattern. Active pattern is described as frequent giant capillaries and capillary hemorrhages, moderate loss of capillaries, disorganization of capillary architecture, absent or mild ramified capillaries. Late pattern includes absent giant capillaries and hemorrhages, severe loss of capillaries with extensive avascular areas, disorganization of the normal capillary array, and ramified or bushy capillaries.^[1,5] It was done by a single observer, later the images were stored, processed, and interpreted by two independent observers. All 10 fingernails were examined for any abnormality after making the patient sit comfortably at ambient room temperature for 15 min. Fingers affected by recent local trauma were excluded. All relevant data were recorded in a pretested, predesigned, and semistructured schedule and later imported to Microsoft excel sheet and computed by statistical software MedCalc version 20.

Results

A total 43 patients were selected, out of which 74.4% ($n = 32$) were female. Mean age was 35.05 ± 7.24 years, and mean duration was 4.28 ± 2.81 years. Diffuse and limited cutaneous SSc was found in 88.37% ($n = 38$) and 11.63% ($n = 5$) cases, respectively. On NFC, early patterns (few enlarged/giant capillaries, relatively well-preserved capillary distribution) have been found in 30.2% ($n = 13$) [Figures 1 and 2], active patterns (frequent enlarged capillaries, capillary hemorrhages, disorganization of capillary architecture) seen in 25.6% ($n = 11$)

[Figures 3 and 4], and late patterns (extensive avascular areas, ramified/bushy capillaries) in 44.2% ($n = 19$) of patients [Figures 5 and 6], respectively. Table 1 shows details of NFC changes among study populations. On HRCT, early ILD found in 18.6% ($n = 8$), active and late ILD in 37.2% ($n = 16$), and 30.2% ($n = 13$) patients, respectively. ILD changes were absent in 14% ($n = 6$), though NFC changes were present in them. Respiratory symptoms were absent in 20.93% ($n = 9$) patients, though all had features of early NFC changes and among them 9.3% ($n = 4$) showed early ILD changes on HRCT. Table 2 shows significant associations between NFC changes with ILD severity ($P = 0.0003$, Chi-squared test). Significant associations were also found between NFC changes with respiratory symptoms ($P < 0.0001$, Chi-square test) [Table 3] and between ILD changes with respiratory symptoms ($P < 0.0001$, Chi-square test) [Table 4].

Discussion

Abnormal NFC change has been accepted as part of ACR EULAR classification criteria of SSc, scoring two points out of the nine required for classification.^[6] In 1973, Maricq *et al.*^[7] published the first article in arthritis and rheumatism, describing the specific capillaroscopic patterns in SSc as well as the modification of the capillary

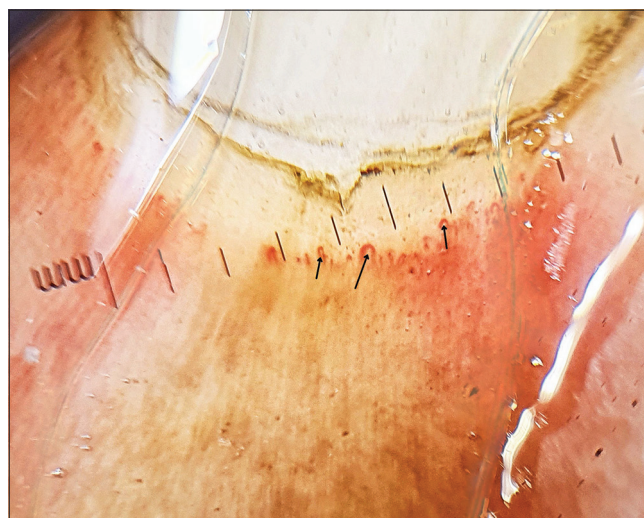


Figure 1: Early pattern of NFC showing few enlarged/giant capillaries (marked by arrow)

Table 1: Details of nailfold capillaroscopic changes among study populations

Nailfold capillaroscopic changes parameters	Number of patients
Dilated capillaries	30 (69.76%)
Abnormal capillary morphology	43 (100%)
Presence of capillary hemorrhages	8 (18.6%)
Capillary drop outs	30 (69.76%)
Presence of avascular areas	19 (44.18%)
Bushy-ramified capillaries	6 (13.95%)

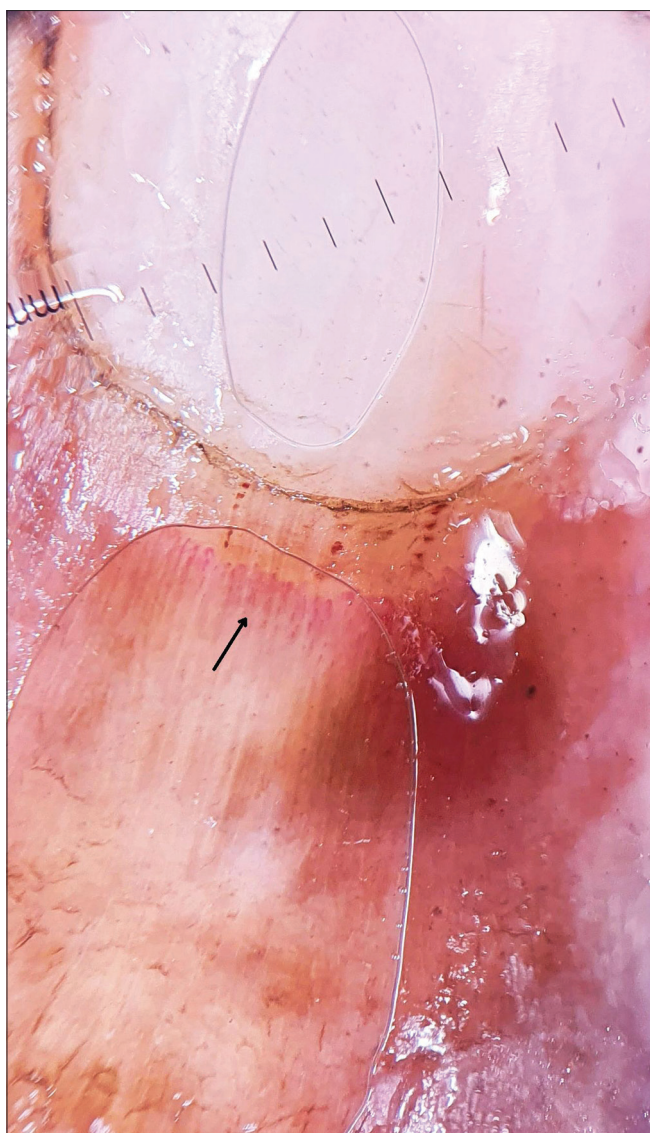


Figure 2: Few dilated capillaries with a well-preserved capillary architecture (marked by arrow) – early NFC changes

blood flow during cold exposure, both in primary and secondary Raynaud’s phenomenon. Nailfold capillaroscope is an expensive, nonportable device that require technical skills and training. So, we preferred dermoscopy which is portable, inexpensive simple but an effective tool to assess the capillary network of nail folds. Three defined major NFC patterns “early,” “active,” and “late” have been considered useful in determining the appearance and progression of the sclerodermic microangiopathy. In our study, the mean age was 35.05 ± 7.24 years, mean duration was 4.28 ± 2.81 years, and male: female ratio was 11:32, whereas Caetano *et al.*^[8] found a male to female ratio of 5:43, mean age 52 ± 26 years, and age of onset was 43.5 ± 27 years. Jakhar *et al.*^[9] found male to female ratio (0.125:1) with the mean age being 33.40 ± 9.78 years and mean disease duration was 5.8 ± 4.94 years. In our study, diffuse (dSSc) and limited (lSSc) cutaneous SSc was found in 88.37% ($n = 38$) and 11.63% ($n = 5$)



Figure 3: Frequent enlarged capillaries with disorganization of a capillary architecture (marked by arrow) – characteristics of an active NFC pattern

Table 2: Associations between nailfold capillaroscopic changes and interstitial lung disease severity

Interstitial lung disease severity	Nailfold capillaroscopic changes			Total	P
	Early	Active	Late		
No	5	1	0	6 (14%)	0.0003
Early	5	3	0	8 (18.6%)	
Active	3	5	8	16 (37.2%)	
Late	0	2	11	13 (30.2%)	
	13	11	19	43	

cases, respectively, whereas Jakhar *et al.*^[9] found dSSc in 73.34% ($n = 33/45$) cases. In our study, we found that NFC changes were present in all patients of SSc. Similar results were also observed by Piotto *et al.*^[10] and Corrado *et al.*^[11] Though Jakhar *et al.*^[9] found abnormality in 97.8% ($n = 44$) and normal capillary morphology in 2.2% ($n = 1$) patients. Early, active, late NFC patterns of 30.2%, 25.6%, and 44.2%, respectively, were found in our study, whereas Cutolo *et al.*^[1] found it 33%, 37%, and 29%, respectively, and Caetano *et al.*^[8] demonstrated it 51.2%, 30.2%, and 18.6%, respectively. In our study, active stage of ILD was found highest in 37.2% ($n = 16$) followed by late and early stage. ILD changes were absent in 14% ($n = 6$), though NFC changes were present in all of them. Recently, Corrado *et al.*^[11] pointed out differences in the nailfold pattern between ILD in SSc (SILD) patients and idiopathic pulmonary fibrosis (IPF), i.e., SILD patients have typical capillary loop changes even in the very early stages of disease, whereas IPF patients present only minimal capillary alterations.

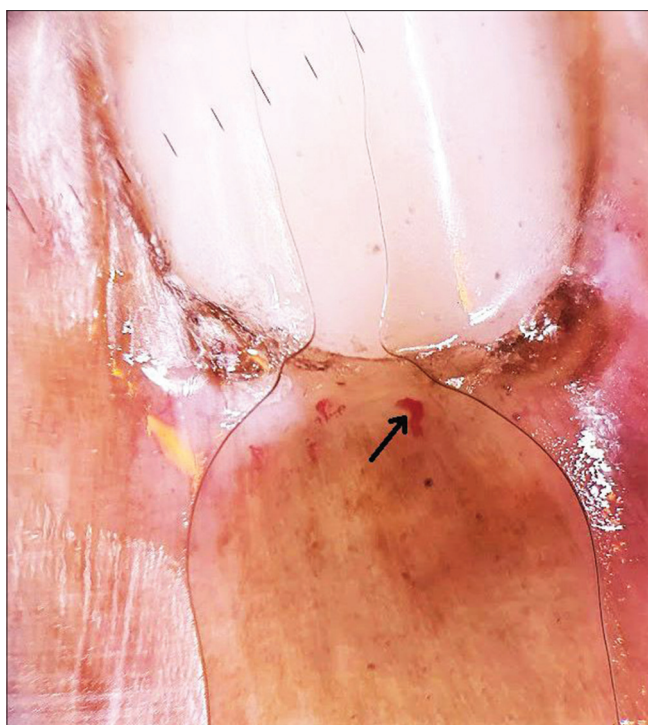
In our study, significant associations were found between NFC changes and ILD severity, NFC changes and respiratory symptoms, and ILD changes and respiratory symptoms. Respiratory symptoms were absent in 20.93% ($n = 9$) patients, though all had features of early NFC changes, and among them

Table 3: Associations between nailfold capillaroscopic changes and respiratory symptoms

Respiratory symptoms	Nailfold capillaroscopic changes			Total	P
	Early	Active	Late		
Absent	9	0	0	9 (20.9%)	<0.0001
Present	4	11	19	34 (79.1%)	
	13 (30.2%)	11 (25.6%)	19 (44.2%)	43	

Table 4: Associations between interstitial lung disease and respiratory symptoms

Respiratory symptoms	Interstitial lung disease				Total	P
	No ILD	Early	Active	Late		
Absent	5	4	0	0	9 (20.9%)	<0.0001
Present	0	4	16	14	34 (79.1%)	
	5 (11.63%)	8 (18.6%)	16 (37.2%)	14 (32.56%)	43	

**Figure 4: Active NFC pattern with hemorrhage (marked by arrow)**

9.3% ($n = 4$) showed early ILD changes on HRCT. Similarly, Lovy *et al.*^[12] and Sato *et al.*^[13] have shown a correlation between NFC abnormalities and cutaneous and pulmonary involvement (interstitial fibrosis) in SSc patients. Caetano *et al.*^[8] also found that capillary loss and avascular area showed a significant association with the presence of ILD. Smith *et al.*^[14] demonstrated that late patterns of NFC were mostly associated with severe pulmonary involvement, which is concordant with our study. Castellvi *et al.*^[15] showed that the patients with capillaroscopic findings had slightly worse pulmonary function test values compared to those without, but the difference was not significant. However, no previous study has compared NFC changes with ILD severity grading like we did in this study.

**Figure 5: Absent giant capillaries and hemorrhages, extensive avascular areas – late NFC pattern**

Conclusion

NFC, an inexpensive simple procedure, can be performed in all patients of SSc to detect development of early ILD even before appearance of respiratory symptoms to prevent further progression. It might provide a window of opportunity for initiation and escalation of treatment in SSc individuals who are more likely to get benefit from the earlier administration of immune suppressants or vasodilators. It can be used as a basic screening tool for the assessment of disease severity in the patients of SSc. Our study opens up a scientific window for future research in larger population.

Limitation

Small sample size, limited time duration, and absence of control population are the main pitfalls of the study. Additional studies like prospective longitudinal analysis of NFC changes and HRCT along with serial measurements

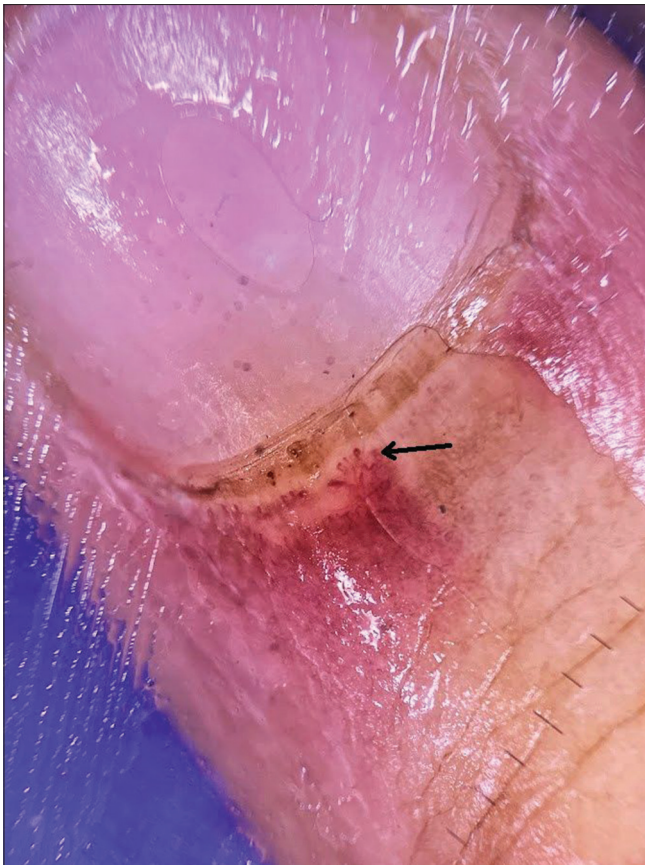


Figure 6: Ramified/bushy capillaries (marked by arrow) – characteristics of a late NFC pattern

of pulmonary function tests can help to better define the role of NFC in diagnosis of ILD in SSc.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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