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Original Article

Relation between nailfold capillaroscopic pattern (assessed using a dermoscope) and organ involvement in systemic sclerosis

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ABSTRACT

Objectives: The objectives of the study were: (1) To document the nailfold capillary changes (using a dermoscope) in patients with systemic sclerosis attending a tertiary care center, (2) to study the relation between nailfold capillaroscopic pattern and skin sclerosis assessed by modified Rodnan skin score (mRSS), and (3) to study the relation between nailfold capillaroscopic pattern and organ involvement in systemic sclerosis.

Materials and Methods: A cross-sectional study was conducted among 40 patients with systemic sclerosis who attended the dermatology outpatient department of a tertiary care center from January 1, 2018, to December 31, 2018. Nailfold capillaries were examined with the help of dinolite dermoscope AM4113ZT at 50× and 200× magnification, under polarized light.

Results: Study participants included 34 (85%) females and 6 males (15%). The nailfold capillaroscopy showed "early scleroderma pattern" in 3 (7.5%) "active pattern" in 28 (70%) and "late pattern" in 9 (22.5%) patients. "Late scleroderma pattern" showed a significant association with disease duration, mRSS, and mean number of organs affected.

Limitations: The study participants may be over-representing advanced cases since the study was conducted among patients attending a tertiary referral center.

Conclusion: We found dermoscope to be a useful tool to study the nailfold capillary changes in patients with systemic sclerosis as reported by others. Late scleroderma pattern may serve as an indicator of high mRSS and involvement of more number of organs in systemic sclerosis.

Keywords: Dermoscope, Nailfold capillaroscopy, Systemic sclerosis, Organ involvement, Scleroderma pattern

INTRODUCTION

Microvascular dysfunction plays a crucial role in the pathogenesis of systemic sclerosis.[1] Nailfold capillaroscopy is a simple, non-invasive method for the analysis of microvascular abnormalities [Figure 1].[2] Nailfold video capillaroscopic (NVC) patterns have been defined and correlated with different clinical aspects and manifestations of systemic sclerosis.[3]

Nailfold video capillaroscope, the established tool for nailfold capillaroscopy, is an expensive equipment, not easily available in developing countries. However, recent studies have established the utility of an inexpensive dermoscope in the evaluation of nailfold capillaries in systemic sclerosis.[4,5]

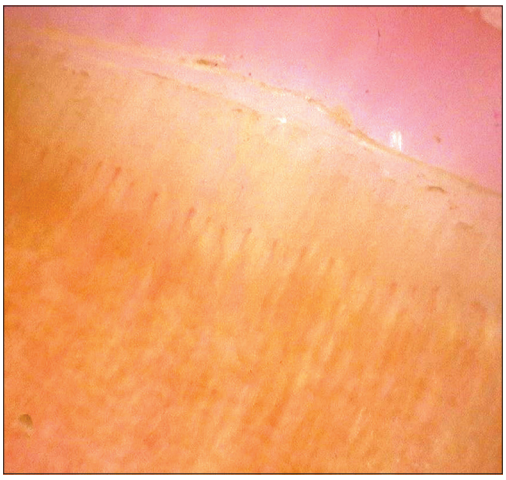

Figure 1: Normal nailfold capillary pattern (Dino-Lite Dermoscope AM4113ZT, polarized light, 50×).

In this setting, using a dermoscope, we studied nailfold capillary changes in systemic sclerosis and tried to understand its relation with skin sclerosis and organ involvement.

MATERIALS AND METHODS

All individuals diagnosed to have systemic sclerosis by American College of Rheumatology (ACR) criteria, and who attended the dermatology outpatient clinic of our institution from January 1, 2018, to December 31, 2018, were included in the study (considering the less common prevalence of systemic sclerosis in general population, instead of recruiting a predetermined sample size of patients, we decided to include all the systemic sclerosis patients who satisfied the inclusion criteria and were willing to participate in the study).[6]

Pregnant patients, patients who also satisfied the ACR criteria for any other collagen vascular disease, patients with diabetes mellitus, hypertension or habit of smoking, patients who were receiving drugs that could affect the peripheral circulation, fingers which had recently sustained trauma, and children below 12 years were excluded from the study.

Institutional Ethics Committee approved the study. Individual study participant gave written informed consent.

We collected data on patient characteristics, duration and evolution of the disease, family history of systemic sclerosis, or other collagen vascular diseases, and the treatment received for systemic sclerosis using a preset proforma.

We did a detailed clinical examination for evaluating the dermatology and systemic involvement. The extent of skin sclerosis was assessed using modified Rodnan skin score (mRSS).[7]

We classified patients into those with limited cutaneous systemic sclerosis (when skin sclerosis was limited to face, chin, and distal extremities below elbows and knees) and diffuse cutaneous systemic sclerosis (when sclerosis affected trunk and limbs proximal to knees and elbows).[1,8]

Complete hemogram, urine microscopic examination, peripheral smear analysis, serum uric acid, renal and liver function tests, and random blood sugar estimation were done in each patient at the time of recruitment to the study. Urine protein-creatinine ratio was determined in those who showed microscopic albuminuria. Those who had joint symptoms were advised serology for rheumatoid factor and those who tested positive for the same, received a rheumatology referral. Patients with coexisting rheumatoid arthritis were excluded from the study. Results of antinuclear antibody (ANA) and ANA profile were noted in each case. Patients who had not undergone the tests were advised the same and the results were recorded. We did a skin biopsy from the representative lesion in patients who had not received a histopathology confirmation.

We sought a detailed gastroenterology evaluation in all cases. Esophagoscopy and ultrasonogram of abdomen were done in each study participant. Barium studies and colonoscopy were performed as and when advised by the gastroenterologist. We did chest radiography for all patients. All the study participants received a detailed pulmonology evaluation including pulmonary function test (PFT). High-resolution computed tomography (HRCT) of chest was performed whenever advised by the pulmonologist. Cardiology evaluation and electrocardiogram were performed in all and echocardiogram was carried out when advised by the cardiologist. Patients who showed abnormalities in urine microscopy and/or renal function test received further evaluation in the nephrology department. Ultrasonogram of kidney and urinary bladder and renal Doppler study was performed as and when advised by the nephrologist. Systemic involvement was diagnosed when a study participant showed clinical and/or investigation findings suggestive of involvement of an internal organ [Table 1].

Nailfold capillaroscopy

As pre-examination preparation, patients washed hands with soap and water and sat for 15–20 minutes at room temperature before examination. Patients' hands were examined at heart level. A single observer (first author) performed nailfold capillaroscopy using Dino-Lite Dermoscope AM4113ZT first at 50× to study the overall arrangement of capillaries and then at 200× to study the morphology of individual capillary. The whole proximal nailfold region including the edges was examined in all fingers except thumbs. Images were subsequently coded and stored. Capillaries with width >10 times that of surrounding normal capillaries were considered as giant capillaries.[9] Disappearance of contiguous capillaries was considered as evidence of loss of capillaries. Any extravasation of blood outside capillaries was considered as hemorrhages. Distortion of the normal regular

Table 1: Features of systemic involvement as per clinical evaluation and by investigations in patients with systemic sclerosis.

Organ system	Symptom	Investigation finding
Gastrointestinal system	Dysphagia Gastroesophageal reflux	Endoscopy – Delayed emptying and/or motility disorder, esophagitis, gastric antral vascular ectasia
Pulmonary system	Dyspnea Cough Tachypnea or cyanosis	*Chest X-ray – Reticular/reticulonodular shadows in the lower zone *Pulmonary function test – mild-to-moderate or severe restrictive pattern High-resolution ultrasonogram of thorax – reticulations, tiny cystic spaces representing honey combing, and patchy ground-glass opacities suggestive of interstitial lung disease
Renal system	Periorbital edema Reduced urine output	*Urine microscopy – Albuminuria *Elevated 24 hour urine protein
Cardiovascular system	Palpitation	*Electrocardiogram – arrhythmia, conduction blocks Echocardiogram – pulmonary artery hypertension
Musculoskeletal system	Proximal muscle weakness Arthralgia Resorption/ shortening of phalanges Contractures of interphalangeal joints	*Elevated serum lactate dehydrogenase – myositis *Electromyography – myopathic pattern

*After excluding other causes for the same

capillary pattern was documented as disorganization of capillary pattern. Curved capillary limbs, when observed, were noted as tortuous capillaries.[9,10]

The nailfold capillary changes were categorized as follows: [3]

1. Early scleroderma pattern: Few giant capillaries, few hemorrhages, and well-preserved capillary distribution.
2. Active scleroderma pattern: Frequent giant capillaries, frequent hemorrhages, moderate loss of capillaries, and mild disorganization of capillary architecture.
3. Late scleroderma pattern: Irregular enlargement of capillaries, few or absent giant capillaries and hemorrhages, severe loss of capillaries with extensive avascular areas, and disorganized capillary architecture.

Data were entered into Microsoft Excel and analyzed using Inc IBM company version 18 Chicago, SPSS Inc. (United States of America).

Relation between duration of disease and presence of internal organ involvement was assessed by Pearson's Chi-square test. Relation between duration of disease and mRSS and between duration of disease and mean number of organs affected was assessed by ANOVA. Relation of nailfold capillaroscopic pattern with presence of Raynaud's phenomenon and organ involvement was assessed by Pearson's Chi-square test. Relation of nailfold capillaroscopic pattern with duration of disease, duration of Raynaud's phenomenon, mean mRSS, and mean number of organs involved was assessed by *t*-test. $P < 0.05$ was considered statistically significant.

RESULTS

We studied 34 females (85%) and 6 males (15%). Age of the study participants ranged 26–67 years (mean 46.9 ± 11.1 years). Majority of the patients belonged to the age group of 41–60 years (23, 57.5%) followed by 21–40 years (12, 30%). Five patients (12.5%) were above 60 years.

Age of onset of disease ranged 21–66 years (Mean 40 ± 11.2 years). Duration of disease ranged 2 months–25 years among the study participants (mean 6.9 ± 6.1 years). Duration of disease was <5 years in 17 (42.5%), 5–9 years in 10 (25%), and 10 years or more in 13 (32.5%) cases.

At the time of recruitment to the study, 21 patients (52.5%) had not received any specific treatment for the disease. Eighteen patients (45%) were on vasodilators, 8 patients (20%) on proton-pump blockers, and 10 patients (25%) were on hydroxychloroquine. Fifteen patients (37.5%) had received or were on cyclophosphamide pulse therapy for interstitial lung disease. The number of cyclophosphamide pulses received by the study participants at the time of recruitment to the study varied from 3 to 12. Three patients (7.5%) had received or were on azathioprine. One patient (2.5%) was on mycophenolate mofetil.

Twenty-three (57.5%) and 17 (42.5%) patients had limited cutaneous and diffuse cutaneous systemic sclerosis, respectively. Diffuse cutaneous sclerosis was the predominant type among males (4/6, 66.7%).

Twenty-six patients (65%) had Raynaud's phenomenon. Thirteen of the 23 patients (56.5%) with limited cutaneous sclerosis and 13 of the 17 (76.5%) with diffuse cutaneous systemic sclerosis had Raynaud's phenomenon. The difference was not significant. The duration of Raynaud's phenomenon ranged from 1 month to 15 years in the study participants (mean – 3.8 ± 4.4 years). The mean duration of the disease was 7.5 ± 5.1 years and 5.7 ± 7.7 years, respectively, in those

with and without Raynaud's phenomenon. The difference was not significant.

The mean mRSS observed in our cases was 16.1 ± 7.6 (range 3–36). The mean mRSS was 13.1 ± 6.6, 17.4 ± 5.6, and 18.9 ± 9.2 in patients with duration of disease <5 years, 5–9 years, and 10 years or more, respectively. The difference was not significant ($P = 0.09$ on ANOVA).

The most commonly affected organ systems [Table 2] were gastrointestinal (34, 85%) and pulmonary systems (34, 85%).

Nineteen patients (47.5%) had symptoms of involvement of gastrointestinal system (retrosternal chest pain after a meal) without any abnormality on investigation. Two patients (5%) had abnormalities on endoscopy evaluation without any symptoms pertaining to the system.

Four patients (10%) who complained of exertional dyspnea had no abnormalities on investigations. Six patients (15%) who showed interstitial pneumonia pattern in HRCT had no clinical symptoms of pulmonary involvement.

Three patients (7.5%) had symptoms suggestive of probable cardiovascular system involvement (palpitation) without any abnormality on investigations and 3 (7.5%) others had abnormal investigations without any clinical symptoms of cardiovascular involvement.

Sixteen patients (40%) had symptoms of musculoskeletal system involvement without any abnormality on investigations, while 1 patient (2.5%) showed abnormal investigation results without any symptoms pertaining to the system.

On Chi-square analysis, significant association was noted between duration of disease and involvement of musculoskeletal system [Table 3] diagnosed by clinical and/or laboratory evaluation ($P = 0.04$). No significant association was noted between duration of disease and mean number of organs affected.

Nailfold capillaroscopy showed early scleroderma pattern [Figure 2] in 3 patients (7.5%), active scleroderma pattern [Figure 3] in 28 patients (70%), and late scleroderma pattern [Figure 4] in 9 patients (22.5%). Mean duration of the disease was 1, 5.8, and 12.1 years in patients showing early, active, and late scleroderma patterns, respectively. By classifying patients showing early and active scleroderma pattern as one group (mean duration of the disease 5.3 ± 5.1 years) and those showing late scleroderma pattern (mean duration of the disease 12.1 ± 6.5 years) as another group, a significantly longer duration of disease was noted among those showing the late pattern ($P = 0.002$).

None of the patients showing early pattern had Raynaud's phenomenon while 67.9% and 77.8% of cases showing active and late patterns, respectively, had Raynaud's phenomenon. The mean duration of Raynaud's phenomenon in patients with active and late NVC patterns was 5.2 years and 7.8 years, respectively. The difference was not significant.

The comparison of mRSS documented in those with late pattern (21.2 ± 6.3) as against those with early or active pattern (14.6 ± 7.4) showed a statistically significant difference between the two groups ($P = 0.02$).

No significant association was noted between involvement of any specific internal organ and nailfold capillaroscopic pattern [Table 4].

Mean number of internal organs affected by clinical and/or laboratory evaluation in patients showing early or active scleroderma pattern was 2.2 ± 0.9. Mean number of internal organs affected by clinical and/or laboratory evaluation in patients showing late scleroderma pattern

Table 2: Clinical and investigation findings indicating internal organ involvement in patients with systemic sclerosis.

Systemic involvement	Clinical symptoms, *n*=40	Investigation findings, *n*=40
Gastrointestinal system	Gastroesophageal reflux – 26 (65%) Dysphagia – 15 (37.5%)	Erosive esophagitis – 10 (25%) Esophageal dilatation – 6 (15%) Lax gastroesophageal junction – 3 (7.5%) Antral gastritis – 3 (7.5%) Hiatus hernia – 2 (5%) Gastric antral vascular ectasia – 1 (2.5%)
Pulmonary system	Dyspnea on exertion – 27 (67.5%) Cough – 3 (7.5%)	Interstitial lung disease – 18 (45%) Restrictive pattern on pulmonary function test – 13 (32.5%) Reticular/reticulonodular shadows on chest X-ray – 5 (12.5%)
Cardiovascular system	Palpitation – 4 (10%)	Pulmonary artery hypertension – 3 (7.5%) *Aortic valve sclerosis – 1 (2.5%)
Musculoskeletal system	Arthralgia – 13 (32.5%) Muscle weakness – 7 (17.5%)	Elevated serum lactate dehydrogenase – 3 (7.5%) Myopathic pattern in electromyogram – 1 (2.5%)

*Other causes of aortic valve sclerosis ruled out by evaluation

Table 3: Association between duration of disease and internal organ involvement.

Organ involvement	Duration of disease			*P*-value
	Less than 5 years (*n*=17)	5–9 years (*n*=10)	10 years or more (*n*=13)	
Gastrointestinal system				
No	5 (29.4%)	1 (10%)	0 (0%)	0.07
Yes	12 (70.6%)	9 (90%)	13(100%)	
Pulmonary system				
No	4 (23.5%)	1 (10%)	1 (7.7%)	0.4
Yes	13 (76.5%)	9 (90%)	12 (92.3%)	
Cardiovascular system				
No	15 (88.2%)	8 (80%)	10 (76.9%)	0.7
Yes	2 (11.8%)	2 (20%)	3 (23.1%)	
Musculoskeletal system				
No	12 (70.6%)	2 (20%)	6 (46.2%)	0.04
Yes	5 (29.4%)	8 (80%)	7 (53.8%)	
Mean number of internal organs affected	1.9±0.78	2.8±0.63	2.7±0.85	0.107

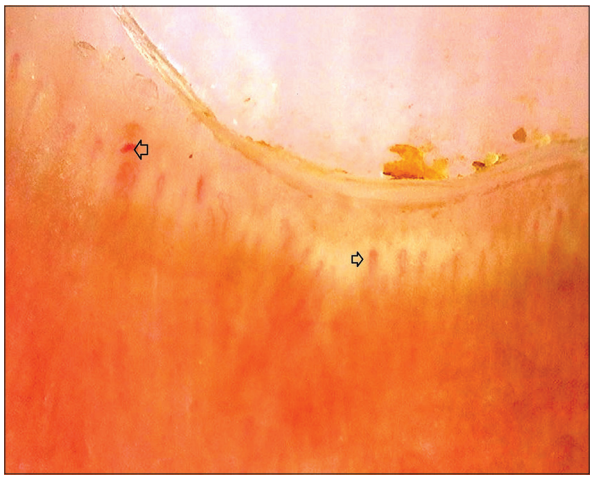

Figure 2: Nailfold capillaroscopy showing a few enlarged capillaries (right arrow), a few capillary hemorrhages (left arrow), relatively well-preserved capillary distribution, no evident loss of capillaries – early scleroderma pattern (Dino-Lite Dermoscope AM4113ZT, polarized light, 50×).

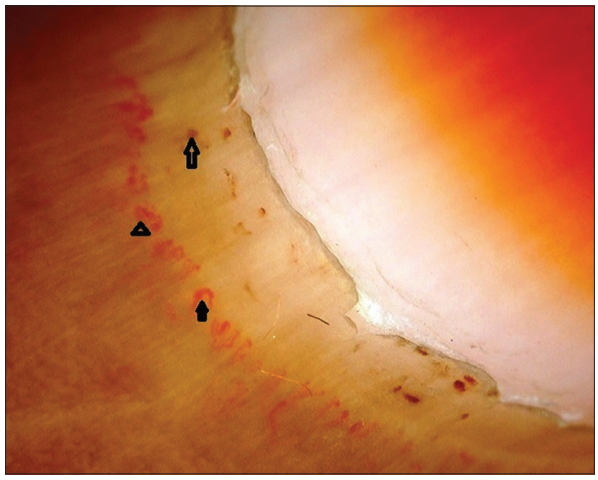

Figure 3: Nailfold capillaroscopy showing frequent giant capillaries (solid black arrow), frequent capillary hemorrhages (black arrow), and mild disorganization of the capillary architecture (arrow head) – active scleroderma pattern (Dino-Lite Dermoscope AM4113ZT, polarized light, 50×).

was 2.9 ± 0.6, respectively. The difference was statistically significant ($P = 0.04$).

DISCUSSION

We found dermoscope to be a useful tool to study the nailfold capillary changes in patients with systemic sclerosis as reported by others.[4]

Age and gender profile, average age of onset of the disease, and predominance of limited cutaneous disease in comparison to the diffuse cutaneous form as observed by us were comparable to literature.[11-15] The distribution of nailfold capillaroscopic patterns noted by us (active [70%], followed by late [22.5%] and early [7.5%] scleroderma pattern) was consistent with the findings of others.[16,17] However, in one of the two cohorts assessed by Avouac *et al*., the late pattern predominated.[14]

For analyzing the association of nailfold capillaroscopic patterns with the duration of the disease and the involvement of organs, we considered early and active scleroderma patterns as one group and late scleroderma pattern as another. Our finding of mean duration of disease having a positive association with late pattern was comparable to certain studies; but another study noted active pattern to be associated with longer disease duration.[16,14]

Raynaud's phenomenon being a feature of late and active patterns alone as noted by us was contradictory to the findings of Sulli *et al*. who recorded Raynaud's phenomenon in all the

Table 4: Relation between internal organ involvement and nailfold capillaroscopic pattern in patients with systemic sclerosis.

Internal organ involvement	Nailfold capillaroscopic pattern		*P*-value
	Early or active scleroderma pattern, *n*=31	Late scleroderma pattern, *n*=9	
Gastrointestinal system			
No	6 (19.4%)	0 (0%)	0.15
Yes	25 (80.6%)	9 (100%)	
Lungs			
No	6 (19.4%)	0 (0%)	0.15
Yes	25 (80.6%)	9 (100%)	
Cardiovascular system			
No	25 (80.6%)	8 (88.9%)	0.57
Yes	6 (19.4%)	1 (11.1%)	
Musculoskeletal system			
No	18 (58.1%)	2 (22.2%)	0.058
Yes	13 (41.9%)	7 (77.8%)	
Mean number of organs affected	2.2±0.9	2.9±0.6	0.04

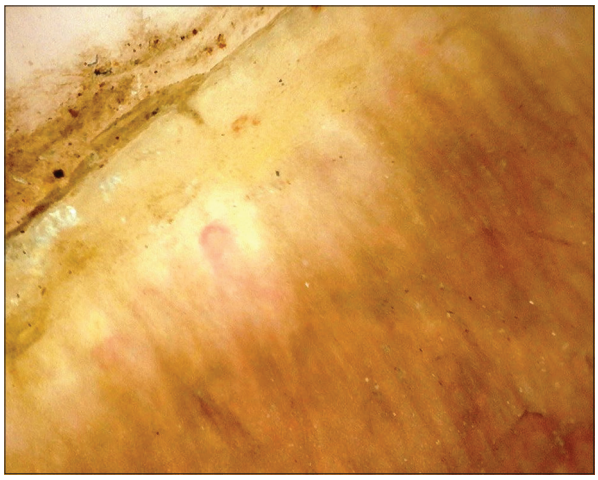

Figure 4: Nailfold capillaroscopy showing a few giant capillaries and severe loss of capillaries with extensive avascular areas – late scleroderma pattern (Dino-Lite Dermoscope AM4113ZT, polarized light, 50×).

cases irrespective of the nailfold capillaroscopic pattern.[18] The previous authors have noted the usefulness of nailfold capillaroscopic pattern to differentiate primary Raynaud's disease from secondary Raynaud's phenomenon.[19] Raynaud's disease shows normal nailfold capillaroscopic pattern. The nailfold capillary changes noted in patients who did not manifest Raynaud's phenomenon by us reiterates the usefulness of nailfold capillaroscopy in the diagnosis of systemic sclerosis even before the appearance of Raynaud's phenomenon.

The overall mean mRSS noted by us (16.1 ± 7.6) was consistent with a previous large study of 3656 patients.[20] Our observation of high mean mRSS in late scleroderma pattern was concordant with the findings of others.[16,14]

Gastrointestinal and pulmonary systems being the most common organ systems affected due to scleroderma as found by us were consistent with literature.[11,15] Patients manifesting clinical symptoms without abnormalities in investigations and vice versa (as noted in some of our patients) were reported earlier.[20-22]

Six patients (two with late and four with active scleroderma pattern in nailfold capillaroscopy) who had no clinical symptoms of pulmonary involvement showed interstitial pneumonia pattern (documented as one of the earliest features of interstitial lung disease) in HRCT. A reduction in the diffusing capacity for carbon monoxide (DLCO) detected on PFT led to HRCT evaluation in these cases. It is suggested that many patients with scleroderma become less physically active due to the fatiguing nature of the disease itself or the accompanying musculoskeletal complaints. This lack of physical activity may lead to a delay in detecting the lung involvement that usually presents with shortness of breath on activity.[23] In a study by Smith *et al*., significant association was noted between future severe organ involvement (joint, muscle, gastrointestinal tract, lung, heart, and kidney) and nailfold capillaroscopy pattern, with maximum correlation for late pattern and least for early pattern.[24] Sulli *et al*. after a 12-year follow-up in systemic sclerosis patients concluded that progression of nailfold capillaroscopic pattern correlated with organ involvement.[25] Markusse *et al*. reported a positive association between cardiopulmonary involvement and scleroderma pattern (active and late).[17] However, no association was noted between pulmonary arterial hypertension and nailfold capillaroscopic pattern in another study.[26] No significant association was noted between specific internal organ involvement and the nailfold capillaroscopic pattern in our study. However, we noted a significant association between late scleroderma pattern and the mean number of organs affected (clinical and/or laboratory evaluation). The association between organ involvement and late scleroderma pattern may be

attributed to the common pathogenic mechanisms, involving microvasculature at different levels.[1] A confounding role for the duration of the disease (which showed a positive association with late scleroderma pattern) was unlikely in our study since no association was noted either between the duration of disease and mRSS or between the duration of disease and mean number of internal organs affected.

Limitations

The major limitations of the study are the small number of early scleroderma cases (which probably affected the significance of this study as far as early disease is concerned) and the cross-sectional design. Moreover, we cannot rule out the possibility of treatment induced alteration of nailfold capillaroscopic pattern in some of our cases.

CONCLUSION

We found dermoscope as an useful tool to study the nailfold capillary changes in patients with systemic sclerosis as reported by others. Late scleroderma pattern may serve as an indicator of high mRSS and involvement of more number of organs in systemic sclerosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

Dr. Sarita Sasidharanpillai, Dr Keerankulangara Devi, Dr. Koyakutty Abdul Samad and Dr. Biju George are on the editorial board of the Journal.

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