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NAILFOLD CAPILLAROSCOPY IN AUTOIMMUNE CONNECTIVE TISSUE DISORDERS: A CROSS-SECTIONAL OBSERVATIONAL STUDY IN WESTERN GUJARAT

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Abstract

Background: Nailfold capillaroscopy (NFC) is a non-invasive technique that allows visualization of the microvascular abnormalities associated with autoimmune connective tissue disorders (ACTDs). This study aimed to evaluate the nailfold capillaroscopic findings in various ACTDs and correlate them with clinical features and disease severity. **Methods:** This cross-sectional observational study enrolled 50 patients clinically diagnosed with systemic sclerosis (SSc), systemic lupus erythematosus (SLE), mixed connective tissue disease (MCTD), and dermatomyositis. Comprehensive medical histories, clinical examinations, and relevant investigations were performed. Nailfold capillaroscopy was conducted using a hand-held dermoscope, and images were analyzed for capillary morphology, density, and patterns. Statistical analysis compared capillaroscopic findings across disease groups and assessed associations with clinical features. **Results:** Among the 50 patients, avascular areas (72%), tortuous capillaries (56%), and dilated capillaries (52%) were the most frequent capillaroscopic findings. Avascular areas were most prevalent in SSc (84%), while dilated capillaries were more common in SLE (85%). The scleroderma pattern was observed in 50% of SSc patients and 15% of SLE patients. Significant associations were found between capillaroscopic patterns and clinical features like Raynaud's phenomenon, digital ulceration, proximal muscle weakness, photosensitivity, and respiratory involvement ($p < 0.05$). **Conclusion:** Nailfold capillaroscopy aids in the evaluation of microvascular abnormalities in ACTDs, potentially improving diagnostic accuracy and guiding therapeutic decisions. Distinct capillaroscopic patterns were associated with specific clinical manifestations, highlighting the utility of this technique in disease management.

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Keywords: Nailfold capillaroscopy, autoimmune connective tissue disorders, systemic sclerosis, systemic lupus erythematosus, mixed connective tissue disease, dermatomyositis.

Introduction

Nailfold capillaroscopy (NFC) is an economical, non-invasive, and painless in-vivo technique for examining the proximal nail fold capillaries which depicts the anatomical and hemodynamic effects of various conditions on cutaneous microvasculature. [1,2]

Capillaries form loops connecting arterial and venous limbs in nail folds, allowing for thorough visualization due to their horizontal orientation, unlike the vertical capillary network in the skin. [3] As compared with capillaries of conjunctiva and retina, nailfold capillaries are acral, easily accessible and provide more reliable correlation with systematic disease and its progression.[4]

In 1663, Sir Johan Christophorus Kolhaus pioneered conducting nailfold capillaroscopy (NFC) using a basic microscope, which was improvised further dramatically over the later centuries. Later on, Maricq and Le Roy identified particular capillaroscopic features associated with systemic sclerosis.[5] Cutolo et al. further classified nailfold video capillaroscopic patterns in patients with systemic sclerosis into six types: Normal, Early SS, Active SS, Late SS, SLE, and Non specific. These patterns range from normal capillary alignment to various levels of capillary loss, disorganization, and abnormal morphological changes.[6]

Over the years, NFC has progressed to be instrumental and mandatory investigation in differentiating among various connective tissue diseases, in their early diagnosis and is also included in diagnostic criteria for Scleroderma and Raynauds phenomenon.[7,8]This technique is gaining recognition not only as a sensitive diagnostic marker but also for its prognostic significance and its usefulness in monitoring the effectiveness of therapy in those with connective tissue disorders. [9]

Vascular changes resulting from functional and structural abnormalities in the microcirculation play a crucial role in the development of collagen vascular disorders. Though a digital video capillaroscope is considered the gold standard for evaluating these capillaries, it requires sophisticated equipment, is relatively costly, time-consuming, and not easily portable. [10] In contrast, a dermoscope is a novel tool that can detect subtle clinical patterns in skin lesions and subsurface structures that are usually not visible to the naked eye.

In this study, NFC patterns were analyzed in patients with systemic sclerosis, systemic lupus erythematosus, dermatomyositis and mixed connective tissue disorder. These patterns were then correlated with the clinical status of the patients.

Materials And Methods

This study was a one-year, cross-sectional, observational study conducted in the Department of Dermatology at a Government Medical College and Hospital in Western Gujarat. The study protocol was approved by the Institutional Ethics Committee.

Study Population: Patients aged 18 years or older, clinically diagnosed with various autoimmune connective tissue disorders (ACTDs) according to respective classification criteria, were enrolled in the study. These included:

1. Systemic Sclerosis (SSc): 2013 ACR/EULAR classification criteria [7,8]
2. Systemic Lupus Erythematosus (SLE): 2012 SLICC criteria [11]
3. Dermatomyositis: 2017 ACR/EULAR criteria [11]
4. Mixed Connective Tissue Disease (MCTD): Defined clinical criteria [11]

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Patients who did not provide written informed consent or had conditions like psoriatic nail changes, onychomycosis, or periungual eczematization that could interfere with nailfold capillaroscopy (NFC) were excluded.

Data Collection:

A comprehensive medical history was obtained, and a thorough clinical examination was performed for all enrolled patients. Routine laboratory investigations were carried out. Additional relevant investigations such as skin biopsy, ANA profile, ultrasonography, HRCT, serology, pulmonary function tests, barium studies, and echocardiography were performed as required. The results were recorded and analyzed concerning nail fold capillaroscopic patterns.

The scleroderma-type capillaroscopic pattern, first described by Maricq et al. in 1980, was found in 83-93% of overt scleroderma cases. [6,12]

Nail fold capillary patterns in scleroderma include early (few dilated capillaries and hemorrhages), active (numerous giant capillaries, moderate capillary loss, and edema), and late (severe capillary loss and avascular areas). [6] Defective neoangiogenesis is indicated by bushy, ramified capillaries, or multiple capillary loops in a dermal papilla. Some of these patterns can also be seen in other scleroderma-related disorders like overlap syndromes, mixed connective tissue disorders, undifferentiated connective tissue disorder, dermatomyositis, etc, and is known as the scleroderma-like capillaroscopic pattern. [12]

NFC was carried out using a Hand-held dermoscope (Dermlite DL-4) attached to an iPhone, with ultrasound gel as linkage fluid for better imaging. This device provides up to 10x magnification and features polarized and white LED lights for clear pictures. Before the procedure, patients sat comfortably for 15 minutes at room temperature, allowing their hands to rest at heart level. [6,12]

Ultrasound gel was applied to the cuticles and nail folds of eight fingers (excluding thumbs), and the dermoscope was used in polarized mode to examine and photograph the nail folds. The images were stored in JPEG/PNG format.

Image Analysis: Two independent observers analyzed the capillaroscopy images in detail, assessing capillary morphology, density, and patterns to identify characteristic abnormalities associated with different ACTDs. The findings were correlated with the clinical and laboratory data of the patients.

Statistical analysis

The statistical analysis was performed using SPSS software (Version 26.1). Descriptive statistics were used to summarize the baseline characteristics of the study population. Continuous variables were presented as mean ± standard deviation and categorical variables were reported as frequencies and percentages.

For the analysis of clinical features across different autoimmune connective tissue disorders, the chi-square test or Fisher's exact test (for small cell counts) was employed to assess the significance of differences in proportions. A p-value < 0.05 was considered statistically significant.

The capillaroscopic findings were analyzed similarly, using the chi-square test or Fisher's exact test to compare the prevalence of various capillary abnormalities (e.g., avascular areas, tortuosity, dilated capillaries, capillary dropouts, giant capillaries, microhemorrhages, neoangiogenesis, bizarre capillaries, scleroderma pattern, and non-specific pattern) among the different disease groups (systemic sclerosis, systemic lupus erythematosus, mixed connective tissue disease, and dermatomyositis). Significant differences were determined using a p-value threshold of 0.05.

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To evaluate the association between clinical features and capillaroscopic patterns, the chi-square test or Fisher's exact test was employed. The proportions of patients exhibiting each clinical feature (e.g., Raynaud's phenomenon, digital ulceration, proximal muscle weakness, photosensitivity, malar rash, respiratory symptoms, and gastrointestinal symptoms) were compared across the different capillaroscopic patterns (early SS pattern, active SS pattern, late SS pattern, SLE pattern, and non-specific pattern). A p-value < 0.05 was considered statistically significant for these associations.

Results

Table 1 Clinical Features in Various Autoimmune Connective Tissue Disorders

Clinical Features	Total Patients (n=50)	Systemic Sclerosis (n=26)	SLE (n=20)	MCTD (n=3)	DM (n=1)	p-value
Raynaud's phenomenon	38 (76%)	20 (76%)	15 (75%)	3 (100%)	0 (0%)	0.242
Digital ulceration	28 (56%)	19 (73%)	7 (35%)	2 (66%)	0 (0%)	0.043*
Skin tightening	23 (46%)	17 (65%)	4 (20%)	2 (66%)	0 (0%)	0.013*
Photosensitivity	23 (46%)	2 (7%)	18 (90%)	2 (66%)	1 (100%)	0.000*
Malar rash	20 (40%)	1 (3%)	18 (90%)	1 (33%)	0 (0%)	0.000*
Proximal muscle weakness	16 (32%)	7 (26%)	5 (25%)	3 (100%)	1 (100%)	0.001*
Joint involvement	19 (38%)	6 (23%)	9 (45%)	3 (100%)	1 (100%)	0.011*
Oral ulceration	10 (20%)	0 (0%)	8 (40%)	1 (33%)	0 (0%)	0.004*
Respiratory involvement	13 (26%)	9 (34%)	2 (10%)	2 (66%)	0 (0%)	0.027*
Gastrointestinal involvement	7 (14%)	6 (23%)	0 (0%)	1 (33%)	0 (0%)	0.038*

* Significant p-values.

Table-1: Clinical Features in Various Autoimmune Connective Tissue Disorders

This table presents the clinical features observed in patients with various autoimmune connective tissue disorders, including Systemic Sclerosis (SSc), Systemic Lupus Erythematosus (SLE), Mixed Connective Tissue Disease (MCTD), and Dermatomyositis (DM). The total patient cohort consists of 50 individuals.

- **Raynaud's Phenomenon**: Present in 76% of the total patients, this feature is most common in MCTD (100%), followed by SSc (76%) and SLE (75%). However, it is absent in the single DM patient (0%), with a p-value of 0.242, indicating no significant difference among the groups.
- **Digital Ulceration**: Found in 56% of the total patients, digital ulceration is most prevalent in SSc (73%) and MCTD (66%), less so in SLE (35%), and absent in DM (0%). The p-value of 0.043 indicates a significant difference.
- **Skin Tightening**: Observed in 46% of all patients, this feature is notably more frequent in SSc (65%) and MCTD (66%), compared to SLE (20%) and DM (0%), with a significant p-value of 0.013.

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- **Photosensitivity**: Present in 46% overall, but highly associated with SLE (90%) and DM (100%), while rare in SSc (7%) and MCTD (66%). The p-value is 0.000, indicating a highly significant difference.
- **Malar Rash**: This rash is seen in 40% of the total cohort, predominantly in SLE (90%) and less so in MCTD (33%), while almost absent in SSc (3%) and DM (0%). The difference is highly significant with a p-value of 0.000.
- **Proximal Muscle Weakness**: Found in 32% of patients, particularly in MCTD (100%) and DM (100%), and to a lesser extent in SSc (26%) and SLE (25%). The p-value of 0.001 shows a significant difference.
- **Joint Involvement**: Observed in 38% of patients, mostly in MCTD (100%) and DM (100%), compared to SLE (45%) and SSc (23%), with a p-value of 0.011, indicating significance.
- **Oral Ulceration**: Present in 20% of the cohort, mainly in SLE (40%) and MCTD (33%), and absent in SSc and DM. The p-value of 0.004 signifies a significant difference.
- **Respiratory Involvement**: Seen in 26% of patients, most frequently in SSc (34%) and MCTD (66%), less so in SLE (10%), and absent in DM. The p-value is 0.027, indicating significance.
- **Gastrointestinal Involvement**: Found in 14% overall, more common in SSc (23%) and MCTD (33%), absent in SLE and DM. The p-value of 0.038 denotes a significant difference.

Table 2: Capillaroscopic Findings in Various Autoimmune Connective Tissue Disorders

Parameter	Systemic Sclerosis (n=26)	SLE (n=20)	MCTD (n=3)	DM (n=1)	p-value
Avascular area	22 (84%)	12 (60%)	2 (66%)	0 (0%)	0.045*
Tortuosity	11 (42%)	15 (75%)	1 (33%)	1 (100%)	0.023*
Dilated capillaries	8 (30%)	17 (85%)	0 (0%)	1 (100%)	0.000*
Capillary dropouts	11 (42%)	6 (30%)	1 (33%)	0 (0%)	0.485
Giant capillaries	7 (26%)	3 (15%)	0 (0%)	0 (0%)	0.379
Microhemorrhage	4 (15%)	7 (35%)	0 (0%)	1 (100%)	0.025*
Neoangiogenesis	11 (42%)	5 (25%)	1 (33%)	0 (0%)	0.426
Bizarre capillaries	10 (38%)	2 (10%)	1 (33%)	0 (0%)	0.114
Scleroderma pattern	13 (50%)	3 (15%)	0 (0%)	0 (0%)	0.002*
Non-specific pattern	6 (23%)	3 (15%)	2 (66%)	1 (100%)	0.007*

* Significant p-values.

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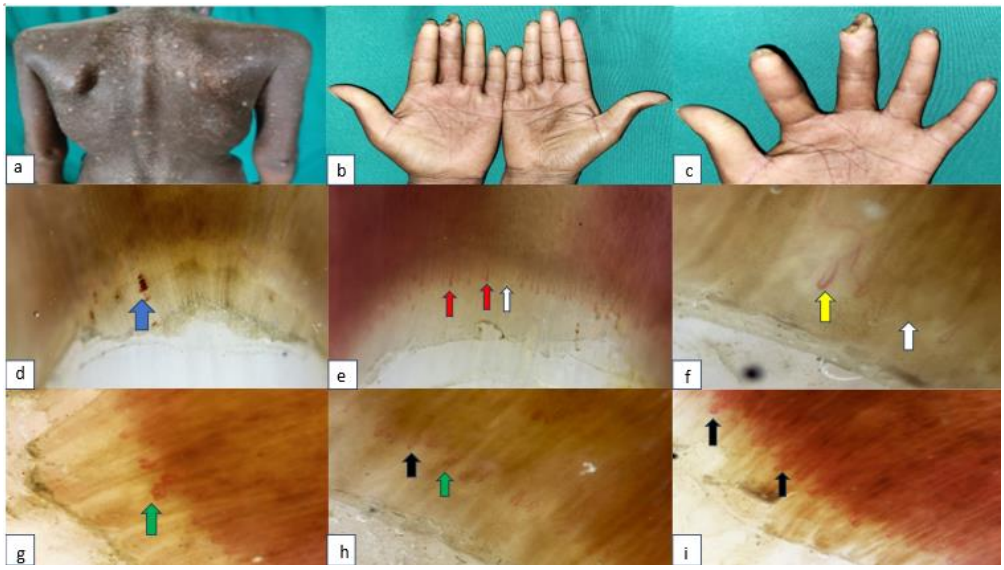

Figure 1: (a, b, c) Systemic sclerosis showing salt and pepper hyperpigmentation, resorption of phalanges, digital ulceration. (d, e, f) NFC showing microhemorrhage (blue arrow), dilated capillaries (red arrow), avascular areas (white arrow), giant capillary (yellow arrow). (g, h, i) NFC showing neoangiogenesis (green arrow), tortuosity (black arrow)

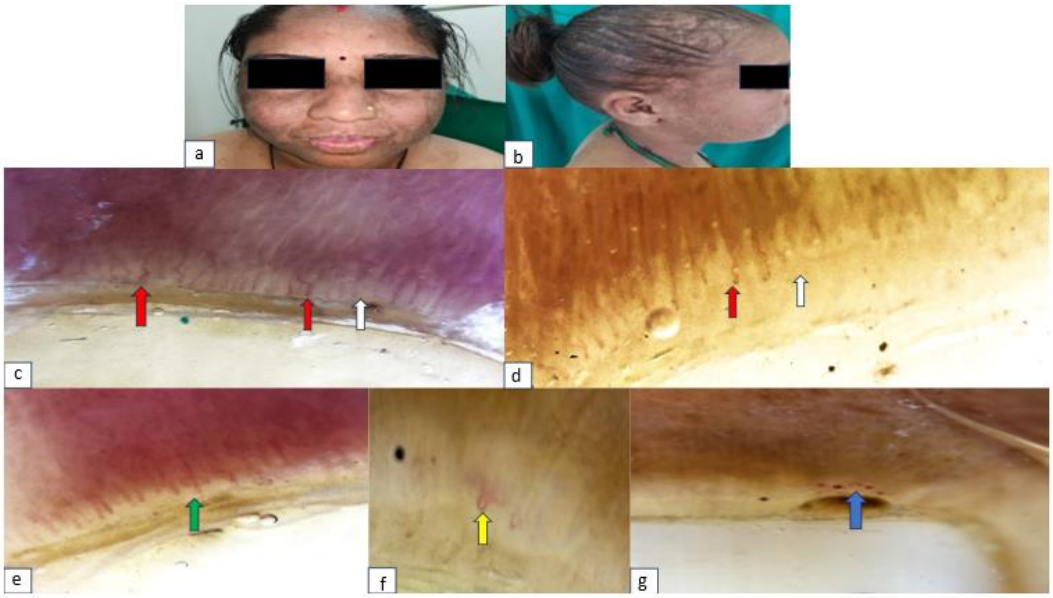

Figure 2: (a, b) Systemic lupus erythematosus with dle (lips), malar rash, diffuse alopecia. (c, d) NFC showing dilated and tortuous capillaries (red arrow), avascular areas (white arrow). (e, f, g) NFC showing neoangiogenesis (green arrow), giant capillary (yellow arrow), microhemorrhage (blue arrow).

Table-2: Capillaroscopic Findings in Various Autoimmune Connective Tissue Disorders
This table details capillaroscopic findings across different autoimmune connective tissue disorders.

- Avascular Area: Observed in 84% of SSc patients, 60% of SLE patients, 66% of MCTD patients, and absent in DM. The p-value of 0.045 indicates a significant difference.

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- Tortuosity: Found in 42% of SSc patients, 75% of SLE patients, 33% of MCTD patients, and in the single DM patient (100%), with a significant p-value of 0.023.
- Dilated Capillaries: This feature is seen in 30% of SSc patients and 85% of SLE patients, absent in MCTD but present in the DM patient (100%), with a highly significant p-value of 0.000.
- Capillary Dropouts: Observed in 42% of SSc patients, 30% of SLE patients, 33% of MCTD patients, and absent in DM, with a p-value of 0.485, indicating no significant difference.
- Giant Capillaries: Found in 26% of SSc patients, 15% of SLE patients, and absent in both MCTD and DM, with a p-value of 0.379, showing no significant difference.
- Microhemorrhage: Present in 15% of SSc patients, 35% of SLE patients, and the single DM patient (100%), absent in MCTD, with a significant p-value of 0.025.
- Neoangiogenesis: Seen in 42% of SSc patients, 25% of SLE patients, 33% of MCTD patients, and absent in DM, with a p-value of 0.426, indicating no significant difference.
- Bizarre Capillaries: Found in 38% of SSc patients, 10% of SLE patients, 33% of MCTD patients, and absent in DM, with a p-value of 0.114, showing no significant difference.
- Scleroderma Pattern: Observed in 50% of SSc patients, 15% of SLE patients, and absent in both MCTD and DM, with a significant p-value of 0.002.
- Non-Specific Pattern: Present in 23% of SSc patients, 15% of SLE patients, 66% of MCTD patients, and the single DM patient (100%), with a significant p-value of 0.007.

Table 3: Association of Capillaroscopic Examination with Cutaneous and Systemic Involvement

Clinical Feature	Early SS Pattern	Active SS Pattern	Late SS Pattern	SLE Pattern	Non-Specific Pattern	Total	p-value
Raynaud's phenomenon	7 (18%)	15 (39%)	11 (28%)	2 (5%)	3 (7%)	38	0.035*
Digital ulceration	4 (14%)	10 (35%)	7 (25%)	1 (3%)	6 (21%)	28	0.047*
Proximal muscle weakness	4 (25%)	2 (12%)	6 (37%)	0 (0%)	4 (25%)	16	0.021*
Photosensitivity	3 (13%)	1 (4%)	2 (8%)	14 (60%)	3 (13%)	23	0.000*
Malar rash	2 (10%)	0 (0%)	3 (15%)	11 (55%)	4 (20%)	20	0.001*
Respiratory symptoms	1 (7%)	2 (15%)	7 (53%)	1 (7%)	2 (15%)	13	0.014*
Gastrointestinal symptoms	0 (0%)	1 (14%)	3 (42%)	0 (0%)	2 (28%)	7	0.039*

*** Significant p-values.**

Table-3 correlates capillaroscopic patterns with cutaneous and systemic involvement in patients.

- Raynaud's Phenomenon: Found in 76% of patients, primarily associated with the active SS pattern (39%) and early SS pattern (18%), less so with late SS (28%), SLE (5%), and non-specific patterns (7%). The p-value of 0.035 indicates a significant correlation.

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- Digital Ulceration: Observed in 56% of patients, most common in the active SS pattern (35%) and early SS pattern (14%), with less frequency in late SS (25%), SLE (3%), and non-specific patterns (21%). The p-value of 0.047 denotes a significant correlation.
- Proximal Muscle Weakness: Present in 32% of patients, primarily associated with the late SS pattern (37%), early SS pattern (25%), and non-specific patterns (25%), less so with the active SS pattern (12%) and absent in SLE. The p-value of 0.021 signifies a significant correlation.
- Photosensitivity: Found in 46% of patients, predominantly associated with the SLE pattern (60%), and less frequent in early SS (13%), non-specific (13%), and active SS (4%) patterns, with a significant p-value of 0.000.
- Malar Rash: Observed in 40% of patients, mainly in the SLE pattern (55%), with lower frequencies in non-specific (20%), late SS (15%), early SS (10%), and absent in the active SS pattern. The p-value of 0.001 indicates a significant correlation.
- Respiratory Symptoms: Present in 26% of patients, primarily associated with the late SS pattern (53%), active SS (15%), and non-specific patterns (15%), less so with early SS (7%) and SLE (7%). The p-value of 0.014 denotes a significant correlation.
- Gastrointestinal Symptoms: Found in 14% of patients, primarily associated with the late SS pattern (42%) and non-specific patterns (28%), less so with active SS (14%) and absent in early SS and SLE patterns. The p-value of 0.039 indicates a significant correlation.

Discussion

In this study, nailfold capillaroscopy (NFC) was utilized to observe the unique morphological characteristic of proximal nailfold capillaries, where the dermal papillae are aligned parallel to the nail surface, enabling clear visualization of the capillaries along their entire length. (21,22) NFC is recognized for its diagnostic and prognostic value in scleroderma and is now considered an essential tool endorsed by EULAR and ACR guidelines. Research by Lonzetti et al. demonstrated that NFC significantly improves the sensitivity of systemic sclerosis diagnosis from 67% to 99%. (9,11)

In a normal nailfold, the capillaries are arranged in a parallel, hairpin-shaped pattern, with a density of 9 to 14 capillaries per millimeter on NFC. (23) However, there is notable variability among individuals. In some cases, particularly among individuals with darker skin, like Indians, a range of 6 to 9 capillaries per millimeter is considered normal. (24)

In the present study, systemic sclerosis (SSc) accounted for 52% of the cases. The most prevalent NFC findings in SSc patients were avascular areas (84%), tortuous capillaries (42%), and neoangiogenesis (42%). The percentage of avascular areas among diffuse cutaneous SSc patients in other Indian studies was within a similar range (81%-94%) (24,25), in contrast to Shenavandeh et al.'s study (26), where avascular areas were less prevalent (46.7% in diffuse cutaneous SSc), while the incidence of neoangiogenesis (42%) matched the findings by Shenavandeh et al. (26)

In our study, giant capillaries (26%) and microhemorrhages (15%) were less frequent compared to prior studies in India. (24,25) Variations in NFC findings across studies may stem from differences in sample size, skin color, disease duration, and the equipment used.

In mixed connective tissue disease (MCTD), NFC reveals diverse capillary manifestations, recognized as a dynamic process. (20)

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Limitation and recommendation

The smaller sample size and single-center design of this particular study could lead to potential bias in patient selection. Furthermore, the study did not evaluate the course of capillary alterations or the effectiveness of treatment. Nevertheless, larger multi-center investigations are necessary to validate and generalize the findings of this study.

Conclusion

Our study contributes to the clinical understanding of nailfold capillaroscopy's utility as a portable, non-invasive tool for examining microcirculation in autoimmune connective tissue disorders like systemic sclerosis. It aids in early diagnosis, assessing disease severity, and differentiating between diseases, guiding treatment decisions**.** Overall, its utility lies in its ability to provide valuable insights into the pathophysiology and clinical course of autoimmune connective tissue disorders.

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Ethical Approval: Approved

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