An Observational Case Control Study of Nailfold Capillary Dermoscopy in a Sample of Iraqi Patients with Connective Tissue Diseases: A Single Center Study

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ABSTRACT:

BACKGROUND:
Connective tissue diseases show certain characteristic morphological changes in their nailfold capillaries. Studies are limited on nailfold capilloroscopic findings using dermoscopy.

OBJECTIVE:
To describe nailfold capillary findings and patterns in patients with connective tissue diseases using dermoscopy.

PAT IENTS AND METHODS:
Demographic variables, nailfold capillary findings and patterns were examined and described using a handheld dermoscope in 40 healthy control subjects and 85 patients with connective tissue diseases including 37 scleroderma patients, 36 systemic lupus erythematosus and 12 dermatomyositis patients.

RESULTS:
Capillary disorganization, giant capillaries, capillary hemorrhage, avascular areas and ramified capillaries were significantly higher in patients than control subjects ($p<0.001$). Giant capillaries, hemorrhages, avascular areas, disorganized and ramified capillaries were observed significantly more in scleroderma and dermatomyositis patients than systemic lupus erythematosus patients, but no single finding differentiated scleroderma from dermatomyositis. The presence of tortuous capillaries was significantly more in systemic lupus erythematosus patients than scleroderma and dermatomyositis ($p<0.001$). The scleroderma-dermatomyositis pattern is observed significantly higher in patients than controls ($p<0.001$). The scleroderma-dermatomyositis pattern was seen significantly more in dermatomyositis and scleroderma than in patients with systemic lupus (100% and 86.5% respectively vs. 11.1%, $p<0.001$). The normal pattern was significantly more seen in systemic lupus than scleroderma and dermatomyosits (66.7% vs 5.4% and 0% respectively, $p<0.001$).

CONCLUSION:
The dermoscope is a very useful tool in detecting scleroderma- dermatomyositis pattern, allowing a confident differentiation among normal subjects and those with underlying connective tissue diseases. The scleroderma-dermatomyositis pattern is seen in scleroderma as well as in dermatomyositis but to a much lesser extent in systemic lupus erythematosus patients. Detecting a normal pattern in a patient with underlying connective tissue disease is more likely to be seen in systemic lupus erythematosus patients rather than other diagnoses.

KEYWORDS Nailfold capillaroscopy, connective tissue diseases, Raynaud's, scleroderma, dermatomyositis, and systemic lupus erythematosus.

INTRODUCTION:

Autoimmune diseases, such as scleroderma (SCD), dermatomyositis (DM), and systemic lupus erythematosus (SLE) are commonly associated with changes of the nailfold capillaries[1,2].

Conventional nailfold capillaroscopy usually requires special equipment that often makes it necessary to send the patient to a specialized center. Some authors have postulated the use of simple devices such as ophthalmoscopes or dermoscopes in the study of nailfold vascular alterations[3–7]. Dermoscopy allows for rapid evaluation of the nailfold for the presence or absence of vascular abnormalities[1].

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The capillaries in the proximal nailfold run parallel to the skin surface. The morphology of these capillaries, therefore, can be visualized well here. Elsewhere, the skin capillaries are generally only seen as red dots as they project up from the upper dermal plexus into the dermal papillae[8,9].

Examination of nailfold capillaries (NFC) gives a good idea about the state of capillaries in connective tissue diseases (CTDs). A number of studies dealt with the examination of FNC using dermoscope and identified certain important findings and grouped such findings into patterns[10, 11, 12, 13]. The scleroderma-dermatomyositis pattern is defined by the presence of two or more of the following abnormalities:

1. Giant capillaries
2. Capillary hemorrhages
3. Capillary Disorganization
4. Avascular areas
5. Tortuous capillaries
6. Twisted capillaries
7. Ramified capillaries.

The nonspecific pattern lacks the complete scleroderma pattern criteria [13]. This study was designed to describe nailfold capillary findings and patterns in patients with connective tissue diseases using dermoscopy.

PATIENTS AND METHODS:

Study setting and design

This case control study was conducted in the outpatient rheumatology consultation unit in addition to the Ward of Rheumatology in Baghdad Teaching Hospital, from January 2017 to January 2018. Informed consent was taken from patients or their parents before starting examination. The ethical approval was given by the scientific committee of the scientific council of Dermatology and Venereology-Arab Board for medical specialization.

Selection of the study sample

A total number of 85 patients (9 males and 76 females with an age range of 5-59 years and a mean of 35.25 years) diagnosed with CTDs (37 scleroderma, 36 systemic lupus erythematosus, and 12 dermatomyositis) were examined. The cases were selected after the diagnosis was established by a consultant rheumatologist according to the American College of Rheumatology criteria. All clinical diagnoses were verified by reviewing the patients' inpatient and outpatient files at the time of dermoscopic examination.

A total of 40 healthy controls with a negative past history of any chronic illnesses or connective tissue diseases (4 males and 36 females with an age range of 6-56 years and a mean of 36.47 years were examined from the department of dermatology in Baghdad Teaching Hospital, with consideration to be matched for age, gender and to cancel the effect of confounding factors such as smoking.

Examinations

A drop of immersion oil was placed on the proximal aspect of the nailfolds of every finger of each subject[14,15]. A dermoscope (Dermlite Dl4; 3Gen Inc. San Juan Capistrano, CA USA) with a magnification power of 10-fold was then placed on each proximal nail fold and viewed through an iPhone connected to the dermoscope. All examinations were performed by the same investigator (D.M). Representative photographs were taken with an iPhone 6 smartphone.

Data collection

A preformed Questionnaire was used to get information from the studied population. The data included the following: age, gender, occupation, marital status, history of smoking, history of Raynaud's phenomenon, diagnosis, and disease duration.

Statistical analysis

The collected data was organized, tabulated, and statistically analyzed using Statistical Package for Social Sciences (SPSS) version 21. Values were expressed as mean ± SD. A comparison of continuous variables was performed by an unpaired two-tailed Student's t-test, whilst chi-square tests were used for categorical variables. Significance levels were set at P values < 0.05 in all cases.

RESULTS:

Demographic data

Demographic data of patients and controls is shown in table 1. There were no significant differences between patients and controls regarding these data. However, comparing the demographic data of different patients' groups (table 2) showed that the mean age for patients was significantly lower in DM group than SLE and SCD groups (23.17 vs 34.81 and 39.59 years respectively, P=<0.001).

Nailfold capillary findings

The following findings (giant capillaries, hemorrhage, avascular areas, disorganized, ramified and twisted capillaries) were observed significantly more in patients than controls(figure 2-5) (table 3).

Regarding NFC findings in patients' group (table 4), disorganized capillaries were seen significantly more in patients with DM and SCD than in SLE patients (83.3% and 75.5% vs 2.8% respectively). Giant capillaries were seen significantly more in patients with SCD and DM than in SLE patients (64.9% and 66.7% vs 5.6% respectively).

Hemorrhagic nailfold capillaries were significantly more common in SCD and DM than SLE (48.6% and 41.7% vs. 11.1%). Avascular areas were seen significantly more in patients with DM and SCD than in SLE (83.3% and 73% respectively vs. 2.8%).

Ramified capillaries were seen significantly more in patients with DM and SCD than in SLE (83.3% and 64.9% respectively vs. 0.0%).

Tortuous capillaries were only seen in SLE patients (27.8%) but not observed in any of SCD or DM patients. Twisted capillaries were most commonly seen in DM patients (16.7%) followed by SCD patients (8.1%) and last by SLE patients (2.8%), but the observed difference was not statistically significant.

Nailfold Capillary Patterns

The analysis of NFC patterns showed that scleroderma-dermatomyositis (SCDDM) pattern was not observed in control group while 48(56.5%) of patients demonstrated the SCDDM pattern (table 5). Analysis of NFC patterns in patients' group showed that the SCDDM pattern was seen more significantly in DM and SCD than in patients with SLE (100% and 86.5% respectively vs. 11.1%).

Although the nonspecific pattern was more commonly seen in SLE than SCD and DM (22.25% vs. 8.1% and 0%) respectively, this difference was not statistically significant. The normal pattern (figure 1) was significantly more seen in SLE than SCD and DM (66.7% vs 5.4% and 0% respectively) (table 6)

Table1. Demographic features of patients and healthy controls

Demographic/Study Groups		Patients	Controls	P-Value
Age Mean ± SD (Years)		35.25	36.47	0.557
		11.189	10.148	
Gender N (%)	Male	9 (10.6%)	4(10.0%)	0.920
	Female	76(89.4%)	36(90%)	
Smoking		6(7.1%)	2(5%)	0.661
Total Number		**85**	**40**	

SD:Standard Deviation

Table 2. Demographic features of patients with Connective Tissue diseases

Demographics		SLE	SCD	DM	P-Value
Age Mean ± SD (Years)		34.81	39.59	23.17	<0.001
		9.893	10.084	9.399	
Gender N (%)	Male	3(8.3%)	2(5.4%)	4(33.35)	0.20
	Female	33(91.7%)	35(94.6%)	8(66.7%)	
Smoking N (%)		3(8.3%)	2(5.4%)	1(8.3%)	0.87
Total Number N (%)		**36(42.3%)**	**37(43.5%)**	**12(14.2%)**	

SD: Standard Deviation, SLE: Systemic lupus erythematosus, SCD: Scleroderma, DM: dermatomyositis.

Table 3. Nailfold Capillary findings in patients and controls:

Findings N (%)	Patients	Controls	P-Value
Disorganization	39(45.9%)	0(0%)	<0.001
Giant	34(40%)	0(0%)	<0.001
Hemorrhage	27(31.8%)	2(5%)	0.001
Avascular	38(44.7%)	0(0%)	<0.001
Ramified	34(40%)	0(0%)	<0.001
Tortuous	10(11.8%)	3(7.5%)	0.466
Twisted	**6(7.1%)**	**2(5%)**	**0.661**

Table 4. Nailfold capillary findings in Connective Tissue Diseases

Findings N (%)	SLE	SCD	DM	Total	P-Value
Disorganization	1(2.8%)	28(75.7)	10(83.3)	39(45.9%)	<0.001
Giant	2(5.6%)	24(64.9%)	8(66.7%)	34(40%)	<0.001*
Hemorrhage	4(11.1%)	18(48.6%)	5(41.7%)	27(31.8)	0.002*
Avascular	1(2.8%)	27(73%)	10(83.3%)	38(44.7%)	<0.001
Ramified	0(0%)	24(64.9%)	10(83.3%)	34(40%)	<0.001*
Tortuous	10(27.8%)	0(0%)	0(0%)	10(11.8%)	<0.001*
Twisted	1(2.8%)	3(8.1%)	2(16.7%)	6(7.1%)	0.252*

*Fischer Exact test is used. SLE: Systemic lupus erythematosus, SCD: Scleroderma, DM:dermatomyositis.

Table 5: Nailfold Capillary patterns in patients and controls

Patterns		Study Sample		P-value
		Patients	Control	
Nailfold Pattern	SCDDM Pattern	48(56.5%)	0(0%)	<0.001
	Non-Specific	11(12.9%)	7(17.5%)	0.49
	Normal	26(30.6%)	33(82.5%)	<0.001

SCDDM: Scleroderma-dermatomyositis pattern

Table 6: Nailfold Capillary Patterns in Connective Tissue Diseases

Pattern N (%)		SLE	SCD	DM	Total	P-Value
Pattern	SCDDM	4(11.1%)	32(86.5%)	12(100%)	48(56.5%)	<0.001*
	Nonspecific	8(22.25%)	3(8.1%)	0(0%)	11(12.9%)	
	Normal	24(66.7%)	2(5.4%)	0(0%)	26(30.6)	

*Fischer Exact test is used. SCDDM: Scleroderma-dermatomyositis pattern. SLE: Systemic lupus erythematosus, SCD: Scleroderma, DM: dermatomyositis

Figure 1. Normal nailfold capillary pattern. Regularly distributed hairpin capillaries with normal density and no morphological alterations.

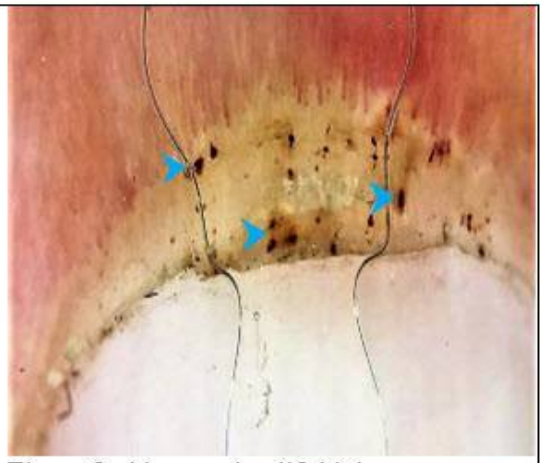

Figure 2. Abnormal nailfold dermoscopy. Mildly enlarged capillaries with multiple capillary hemorrhages (arrowheads).

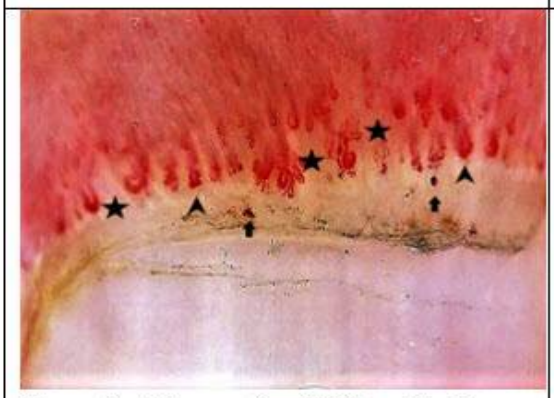

Figure 3. Abnormal nailfold capillaries.: giant capillaries(Arrow heads); capillary hemorrhages(Arrows) ; avascular areas and disorganization of capillary distribution (stars).

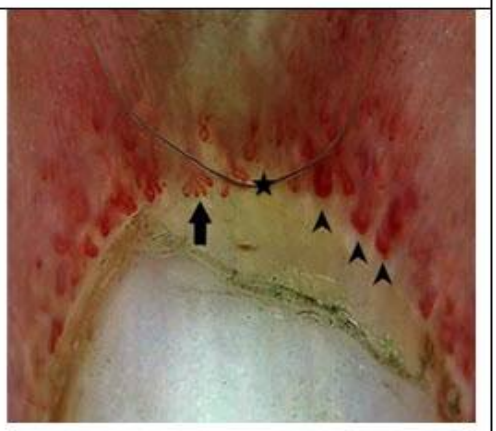

Figure 4: Abnormal nailfold capillaries demonstrating ramified capillaries (black arrow), giant capillaries (arrow heads), avascular areas (stars)

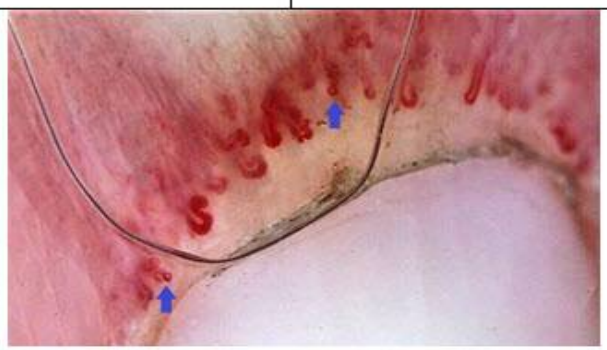

Figure 5. Abnormal nailfold capillaries. twisted capillaries (blue arrows)

DISCUSSION:

The study of NFC findings and patterns is an important step in evaluating patients with CTDs. In the present study the following findings (giant loops, hemorrhage, avascular areas, disorganized & ramified capillaries) were observed significantly more in patients than controls, while tortuous and twisted capillaries were seen in both groups & the difference was not statistically significant (p=0.4, p=0.6 respectively).

Ohtsuka et al (2011) studied a total of 100 patients with CTDs & 18 controls & found that dilated capillaries & capillary hemorrhages were significantly higher in patients with SCD & DM than control group[16]. Bergman et al (2003) evaluated 106 patients with CTDs & 170 controls & has shown that the major findings among controls in his study were capillary hemorrhages and twisted capillaries[12].

Our results show that apart from tortuous and twisted capillaries other findings should prompt further evaluation of an underlying CTD.

In the present study the commonest abnormality seen in SCD patients is capillary disorganization (75.5%) while the commonest abnormalities in DM patients were capillary disorganization, avascular areas & ramified capillaries (equally present in 83% of DM patients). In SLE patients the commonest abnormalities were tortuous capillaries (27.8%) followed by capillary hemorrhages (11.1%). Its noteworthy that most of SLE patients 66.7% had a normal NFC pattern. Ohtsuka et al had shown that dilated capillaries & hemorrhages were the commonest abnormalities in SCD & DM patients respectively, and similar to our study most patients with SLE had normal examination[16].

Analysis of NFC patterns has shown that the normal pattern & the SCDDM pattern significantly differentiated between patients & control groups as 82.5% of the controls had normal pattern & none of them had the SCDDM pattern.

Regarding the SCDDM pattern among the patients in our study, it was observed significantly more in patients with DM & SCD (100% and 86.5%, respectively) than SLE patients (11.1%), and this is consistent with the results of previous studies.

Bergman et al in 2003 using dermoscopy found that the SCDDM pattern was observed in 70% of scleroderma, 63% of DM, and 4.5% of SLE patients[12]. While Beltrn et al in 2006 using dermoscopy demonstrated SCDDM pattern in 77.5% of scleroderma patients[17]. In the same year Cutolo et al using capillaroscopy found that the SCDDM pattern was observed in 74.5% of scleroderma, 26.9% of DM, and in 8.5% of SLE patients[18]. Few years later Muggi et al in 2011 using capillaroscopy found that the SCDDM pattern was observed in 74% of DM patients[19]. Finally Shenvandeh et al in 2015 using capillaroscopy found that the SCDDM pattern was observed in 88.9% of DM patients[20], and in 2017 using capillaroscopy Shenvandeh et al also demonstrated that the SCDDM pattern was observed in 8.3% of SLE patients[21].

One of the standouts is that in our study the detection of SCDDM pattern in DM was even higher than SCD, and although this might seem counter intuitive and even higher than what other studies have shown, but this can be explained by the limited number of DM patients in our study (12 cases).

We can conclude that the dermoscope is a very useful tool in detecting SCDDM pattern with comparable results to the formal capillaroscopy, allowing a confident differentiation among normal subjects and those with underlying connective tissue diseases. Having said that it is important to realize that detecting a SCDDM pattern is not enough to differentiate amongst connective tissue diseases. The SCDDM pattern is seen in SCD as well as in DM but to a much less extent in SLE patients. Detecting a normal pattern in a patient with underlying connective tissue disease is more likely to be seen in SLE patients rather than other diagnoses.

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