



A SINGLE OBSERVATIONAL CROSS SECTIONAL STUDY OF NAILFOLD CAPILLAROSCOPIC PATTERNS IN CONNECTIVE TISSUE DISORDERS.

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ABSTRACT **Introduction:** Connective tissue diseases (CTD) are progressive, multiorgan system diseases. Nailfold capillaroscopy is a simple, noninvasive technique used to recognize macroangiopathic changes and serves as an evolving technique in the early diagnosis and prognosis of the various connective tissue disorders. Hence with the aim of improving the characterisation of various patterns of nail fold capillaroscopy in different connective tissue diseases, we decided to study the nailfold capillaroscopy in systemic sclerosis, systemic lupus erythematosus and MCTD.

Method: We recruited total 37 patients of CTD coming to department of dermatology and performed nailfold capillaroscopy on them.

Results: We found scleroderoid pattern in all the patients of systemic sclerosis thus highlighting the high negative predictive value of almost 100%. Glomeruloid capillary pattern with loss of architecture was seen in 24% of SLE patients which was a new finding and has not been described in literature. Due to small sample size its significance could not be established and hence further evaluation is needed in large scale studies.

KEYWORDS : Nailfold capillaroscopy, scleroderoid pattern, glomerular capillaries. CTD.

Introduction:

Capillaroscopy is a non-invasive diagnostic technique designed to evaluate small vessels of the microcirculation[1]. Nailfold capillaries were first observed in the 17th century with primitive magnifying equipment, and in the early 19th century the first associations between inflammation and capillary alterations were made. Maurice Raynaud in the first decade of 20th century established a direct link between capillary abnormalities and certain medical conditions.

In a systemic disease in which vascular damage is one of the pathogenetic factors, abnormalities in capillary morphology can be observed long before the onset of clinical symptoms. In patients already diagnosed with a systemic disease, damage to the capillaries may reflect the involvement of internal organs and help determine the stage of the disease. [2] Nailfold capillaroscopy is a method enabling direct assessment of capillaries of the periungual region by means of stereoscopic microscopy. It is a non-invasive and safe technique used to recognize peripheral microangiopathy and it is also reported to have both diagnostic and prognostic value. [3] Microcirculation in capillaries is routinely evaluated within the skin of the nailfold. The entire skin abounds in capillaries; however, they run perpendicular to the skin surface, and only the tip of the loop is visible. In the nailfold, terminal rows of capillaries run parallel to the skin surface and, therefore, all morphological details and the nature of the blood flow can be examined.

Nailfold capillaroscopy (NFC) is an evolving technique in the early diagnosis and prognosis of the various connective tissue disorders including systemic sclerosis, systemic lupus erythematosus, MCTD. There are few studies related to this technique and further research is needed in this field.

Hence with the aim of improving the characterisation of various patterns of nail fold capillaroscopy in different connective tissue diseases, we decided to study the nailfold capillaroscopy in systemic sclerosis, systemic lupus erythematosus and MCTD.

Materials and Methods:

All the patients who were diagnosed either as systemic sclerosis, systemic lupus erythematosus or MCTD were recruited in the study. A written informed consent was taken. The patients who refused to give consent were excluded from the study. A total of 37 patients were recruited in the study in which 17 patients were of SLE, 14 patients of systemic sclerosis and 6 patients of MCTD. The nailfold capillaroscopy was then performed with the OITEZ e-scope [DP-M17 filter e-scope pro] on the right and left ring finger of the selected patients. The images were recorded under polarized light at 20x and 200x. The images of the capillaroscopy were stored and the different

parameters were noted. The data was then analysed. The qualitative variables are depicted in table and bar chart displaying absolute and relative frequencies.

Results:

The frequency of various nailfold capillaroscopy findings in systemic sclerosis, SLE and MCTD is tabulated below. [Table1] The scleroderoid pattern (capillary dilatation, avascular areas, bushy capillaries) was seen in all the patients of systemic sclerosis (n=14). Among the scleroderoid pattern capillary dilatation was the most common finding seen in 71% of patients (n=10), followed by avascular areas (64%, n=9) and bushy capillaries (57%, n=8). No other features other than scleroderoid pattern were seen in systemic sclerosis patients.

In SLE 24% of patients showed features of scleroderoid pattern (n=4) while 76% (n=13) showed features different from the scleroderoid pattern. These features included loss of most distal line of capillaries, subpapillary plexus visualisation, meandering (wavy and curly) of capillaries and glomerular capillaries. Among these features meandering of capillaries was the most frequent finding seen in 41% of SLE patients (n=7). The 82% of SLE patients showed nailfold capillaroscopic abnormalities while 18% showed normal findings.

Among the MCTD patients 83% (n=5) showed the nailfold capillaroscopic abnormalities mainly of scleroderoid type. Microhaemorrhages was the most common finding seen in MCTD patients followed by capillary dilatation.

Table1: Nailfold capillaroscopic findings in connective tissue diseases

	Syste- mic sclerosis	SLE	MCTD
Capillary dilatation	71%	29%	5%
Bushy capillaries	57%	11%	0%
Microhaemorrhages	43%	29%	33%
Avascular areas	64%	0%	0%
Loss of architecture	36%	24%	0%
Ragged cuticle	7%	11%	0%
Loss of most distal line line of capillaries	0%	24%	0%
Subpapillary plexus visualisation	0%	11%	0%
Meandering	0%	41%	0%
Glomerular capillaries	0%	24%	0%
Normal	0%	18%	0.17%

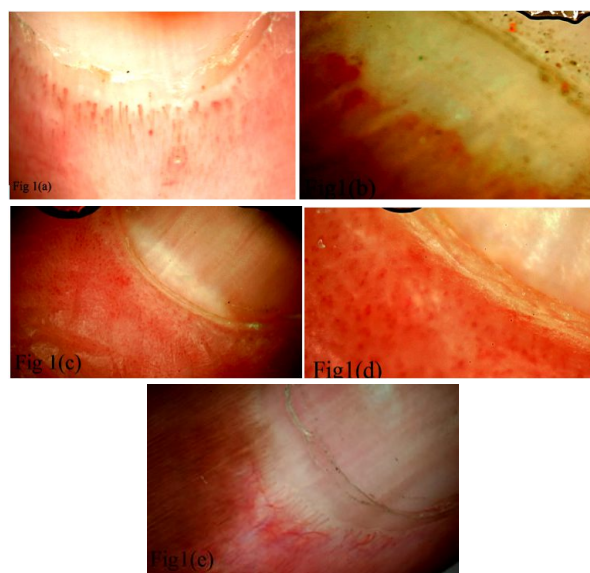
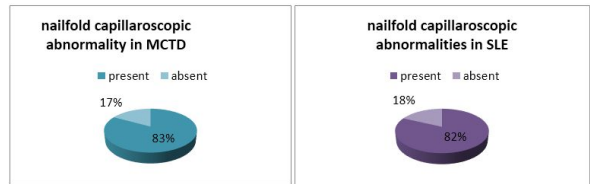
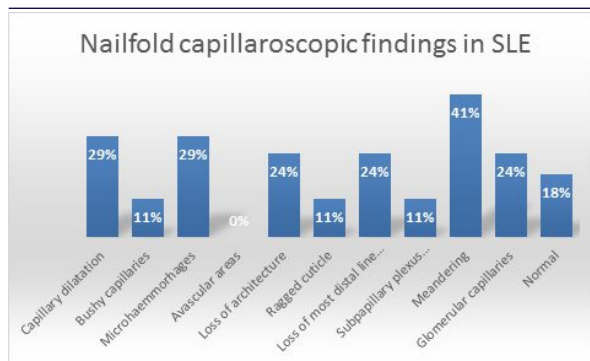


Fig 1: Nail capillaroscopic findings in SLE. (a) meandering of capillaries (b) loss of most distal line of capillaries (c) and (d) glomeruloid capillaries with loss of architecture (e) Elongation of capillaries with subpapillary plexus visualization

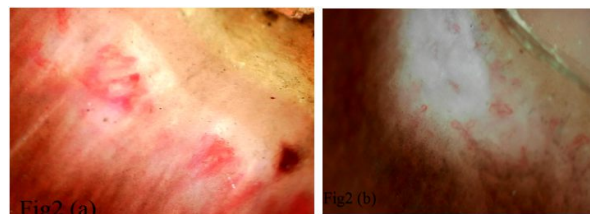


Figure 2: Sclerodermoid pattern: (a) Dilatation of capillaries with microhaemorrhage. (b) Avascular areas with neoangiogenesis (bushy capillaries) with loss of architecture.

Discussion: Nailfold capillaroscopy has become a relevant diagnostic tool in connective tissue diseases. Many investigators have analysed pictures of the periungual bed, seeking patterns in the capillaries that could distinguish different connective tissue diseases.

[4,5] Capillary changes observed by NFC have been well documented in several rheumatic disorders, particularly in RP, SSc, and SSc-like diseases. Meli et al. reported 308 RP patients without serological findings or clinical signs of connective tissue disease (CTD) but with pathological NFC features indicating CTD. [6]

In 1981, H. R. Maricq first described Sclerodermoid pattern as enlargement of capillary loops, loss of capillaries, disruption of capillary bed and distortion and budding of capillary or hemorrhage[7]. Later, giant capillaries and loss of capillaries were included as sclerodermoid patterns, which exhibited 80% and 89% diagnostic sensitivity and specificity, respectively. [8] Although the sensitivity of the capillaroscopic method is lower in SLE patients in respect to the so-called scleroderma-related diseases, it can provide a valid support for the diagnosis [9]

This work aimed to study the prevalence of nailfold capillaroscopy changes in patients with SLE, systemic sclerosis and MCTD and find out the different patterns in each disease.

Facina et al. [10] reported the prevalence of SLE patients having capillaroscopic abnormalities to be 76.7%. Percentage of patients of SLE with capillaroscopic abnormalities in a study by Ragab.O was found to be 75%. [11] Our study showed a slightly higher percentage of capillaroscopic abnormalities in SLE patients of about 82%. Kuryliszyn-Moskal et al. reported the prevalence of nailfold capillary abnormalities to be 95.5% in their SLE patients. [12] In a study by Ragab.O the abnormal capillaroscopic patterns in the patients were as follows: 18 patients (45%) were found to have tortuous capillaries, 20 patients (50%) had meandering capillaries, 6 patients (15%) had corkscrew capillaries, 3 patients (7.5%) had bushy capillaries, 9 patients (22.5%) had capillary enlargement and 4 patients (10%) had capillary hemorrhage. Nagy and Czirja chose the meandering capillary pattern as a predictive variable for SLE in patients having the manifestations of connective tissue disease. Meandering capillary pattern which is the commonest usually found in SLE patients may provide a support for diagnosis of SLE as does the megacapillaries pattern in scleroderma. [13] Ragab.O found a statistically significant positive correlation ($P < 0.05$) between presence of meandering capillaries and 24 hours urinary proteins. He also found a statistical significant positive correlation ($P < 0.05$) between the presence of meandering capillaries and Systemic Lupus Erythematosus Disease Activity Index (SLEDI) score. [11]

Similarly in our study meandering capillaries was the most common nailfold finding in SLE patients and more specific as none of the patient in systemic sclerosis group and MCTD showed the similar finding.

Regarding enlarged capillaries, they were found in 22.5% of patients in a study by Ragab.O [11] Quite similar results were found by Nagy and Czirjak [13], who reported that enlarged capillaries were found in 24.2% of patients. In our study enlarged capillaries were seen in 29% of patients.

Our study found a glomeruloid pattern capillaries with loss of architecture in 24% of SLE patients (n=4). This finding is not described in literature and is a new finding which we have discovered in SLE patients. As our sample size was small and clinical and laboratory data was not correlated, the significance of this finding in SLE patients could not be established. Further studies with larger sample size and clinical and laboratory correlation are required.

The presence of megacapillaries and a decreased capillary density are the hallmarks of the SSc capillary pattern. In a recent study, microvascular alterations as detected by NVC in patients with SSc have been re-classified in three different patterns [14]. The patterns identified within the 'SSc pattern' include: (i) 'Early' NVC pattern: few enlarged/giant capillaries, few capillary haemorrhages, relatively well-preserved capillary distribution, no evident loss of capillaries (Fig. 1); (ii) 'Active' NVC pattern: frequent giant capillaries, frequent capillary haemorrhages, moderate loss of capillaries, mild disorganization of the capillary architecture, absent or mild ramified capillaries (Fig. 2A); and (iii) 'Late' NVC pattern: irregular enlargement of the capillaries, few or absent giant capillaries and haemorrhages, severe loss of capillaries with extensive avascular areas, disorganization of the normal capillary array, ramified/bushy capillaries. According to study by Bissell, detection of a SSc NFC pattern had a sensitivity of 71 %, specificity 95 %, positive predictive value 84 % and negative predictive value 90 %.[15]

Our study demonstrated the scleroderma pattern in all the enrolled systemic sclerosis patients thus demonstrating a high negative predictive value of about 100%.

In a study by Granier F. of the 22 patients with MCTD, 63.6% had an Sclerodermoid pattern, 22.7% had an SLE pattern, 13.6% had nonspecific abnormalities, and 72.7% had bushy capillary formations. The presence of bushy capillaries was suggestive of MCTD. For

diagnostic purposes, bushy capillaries displayed 72% sensitivity, 80% specificity, and 87.2% negative predictive value. [16] In previous 2 studies by Maricq and Minkin discussing nailfold capillaroscopy in MCTD, capillaroscopic pattern specific for MCTD have not been individualised. [17,18] In our study, there was a slight variation with microhaemorrhages the most common finding (33%) followed by capillary dilatation in about 5%. No other abnormality was seen in patients with MCTD.

Conclusion:

Although NFC lacks specificity, it is a noninvasive, easy, repeatable, safe, and inexpensive method of evaluating microvascular abnormalities in connective tissue diseases. Although this method is indicated for distinguishing between primary and secondary Raynauds phenomenon, in recent years it is also used for diagnosis of other connective tissue diseases. We concluded that patients with SLE had abnormal NFC changes with the meandering capillaries the most frequent pattern to occur. Also we found the new pattern of glomeruloid capillaries with loss of architecture in SLE patients which need further evaluation in large scale studies. The negative predictive value of the sclerodermoid pattern is 100% in systemic sclerosis patients according to our study. Hence the nail fold capillaroscopy serves as a useful noninvasive diagnostic tool for early diagnosis of systemic sclerosis.

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