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Original Article

Video-dermoscopic Assessment of Capillaroscopic Pattern in Hansen's Disease

KM Sudhakar Rao[1], SV Smitha[2], MS Aruna[3], R Tanuja[4]

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Leprosy is a chronic granulomatous infectious disease with a proven role of *Mycobacterium lepra*e invasion into endothelial cells. Animal studies have shown evidence of involvement of vasa nervorum in the process of nerve invasion. Capillaries act as the mirror image of vascular involvement in any rheumatic disorder and holds good for leprosy also. Nailfold capillaroscopy (NFC) is a non-invasive, easily reproducible technique to study proximal nailfold capillaries. The aim of this study is to investigate morphological nailfold capillaroscopic alterations in patients with leprosy in its various forms and comparison with the normal individual. Total 20 Leprosy patients and 20 normal age and sex matched individuals recruited for nailfold capillaroscopic examination using video dermoscopye. Among 20 normal individuals, 3(15%) individuals showed tortuous capillaries and microhemorrhages each, 2(10%) showed meandering vessels, 1(5%) each showed megacapillaries, dilated/ectatic capillaries and bizarre vessels. Out of 20 leprosy patients, 11 (55%) patients showed bizarre and meandering capillaries, 10(50%) showed dilated vessels and avascular areas, 9(45%) showed capillary dropouts and neovascularisation, 8(40%) showed tortuous vessels, 6(30%) haemorrhages and 4 (20%) showed megacapillaries. Findings like avascular areas, capillary dropouts, haemorrhages were more noticed in lepromatous and borderline lepromatous leprosy, whereas early capillary abnormalities like dilated, meandering, bizarre vessels and neoangiogenesis were noticed more in borderline tuberculoid leprosy. However, statistical significant difference between clinical and dermoscopic observations was not seen in this study. Further studies with a large sample size are required to find out the same. Morphological changes may denote micro-vascular invasion by *Mycobacterium leprae* and may act as warning signs of fore-coming complications like loss of sensation and trophic ulcers. Follow-up studies are required to understand such correlation, if any.

Keywords : Leprosy, Hansen's Disease, Nailfold-capillaroscopy, Video-dermoscope, Vasa nervorum, Meandering, Bizarre, Avascular areas

Introduction

The disease leprosy is known to mankind since biblical times. It is a chronic granulomatous disease caused by infection of *Mycobacterium leprae*. Leprosy is highly contagious disease, but since most of the population is naturally resistant to infection leading to low morbidity. Skin and peripheral nerves are the main targets of leprosy.

[1] Dr KM Sudhakar Rao, MD, Professor,
[2] Dr Smitha SV, MBBS, Junior Resident
[3] Dr MS Aruna, MD, Assistant Professor, Department of Community Medicine, Kurnool Medical College, Kurnool, Andhra Pradesh-518005, India
[4] Dr Tanuja R, MBBS, Junior Resident
Department of Dermatology, Venereology and Leprosy, SNMC and HSK Hospital Navanagar, Bagalkot, Karnataka- 587102, India
Corresponding Author: Dr Smitha SV, **Email :** smithasv3@gmail.com

Mechanisms that do not directly involve the Schwann cell but may involve the neurovascular endothelium may play major roles in the tropism of *M. leprae* to peripheral nerve. The high prevalence of *M. leprae* infection of epineurial and perineurial endothelial cells has several important implications for the pathogenesis of nerve injury in leprosy (Scollard et al 1999). Nailfold capillaroscopy (NFC) is a reproducible, noninvasive and painless technique for studying proximal nailfold (PNF) capillaries (Shore 2000). Despite the recent advances of dermoscope and videodermoscope in dermatology, there is still discrepancy of their usage in NFC studies of leprosy. To the best of our knowledge, there is only one article in literature which can depict the nailfold capillaroscopic findings in leprosy. Here, we are presenting study on morphological changes in nailfold capillaries of the infected and its comparison with nailfold capillaries of age, sex matched normal individuals.

Materials and Methods

This was a cross-sectional pilot study conducted in Department of Dermatology, Venereology and Leprosy, SNMC and HSK Hospital Navanagar, Bagalkot, a tertiary care hospital in South India. The study was conducted from October 2020 to June 2021 for a period of 8 months. Written and informed consents were taken from all the cases and controls. Old cases and newly diagnosed cases (WHO 2016) of leprosy attending dermatology clinics were included. Subjects aged between 20 years to 70 years were recruited. Age and sex matched control subjects who accompanying patients were recruited as controls. The leprosy cases were classified as tuberculoid (TT), borderline tuberculoid (BT), borderline borderline (BB), borderline lepromatous (BL), lepromatous leprosy (LL), histoid and pure neuritic (PN) leprosy according to clinical and histological findings (IAL 1982). Patients with history of pregnancy, lactation, smoking, diabetes, hypertension, auto-immune disorders, connective tissue disorders, trauma, onychotillomania, onychophagia, malignancy and drug history were excluded in both the groups.

Clinical history was noted down and detailed physical examination was done for the patient to look for skin lesions, peripheral nerve involvement and areas of anesthesia. Clinical images and NFC images were taken with the help of Foto Finder videodermoscope (Medicam 1000s, Foto Finder Systems GmbH, Bad Birnbach, Germany) in polarized mode at 20X magnification. The patient was asked to sit at an environmental temperature of 23-25^{0} C for about 15 minutes before undergoing NFC examination and should restrain from smoking and caffeine intake for 4 hours (Chojnowski et al 2016). NFC examination was done under polarized mode in 20X magnification using ultrasound gel as interface medium on PNF. Hands are kept at heart level and pressure was made optimum not to blanch the capillaries. NFC examination was done. Ring and middle fingers of the hands were selected for examination. Alternatively, other fingers were also examined. The NFC images were captured, interpreted and assessed statistically.

Parameters Assessed

Various morphological alterations in the capillary loops were carefully assessed and recorded. The abnormal capillary morphology was taken to be significant in an individual when it was seen in more than two fingers.

Results

Total 20 cases of leprosy and 20 age and sex matched normal control subjects were studied for NFC in this study. Among 40 cases, 26(65%) were males and 14 (35%) were females. The age-group ranged between 21 years to 66 years with average of 47.8 years in both the groups. Among 20 cases

of leprosy, 3 (15%) cases were borderline tuberculoid (BT), 9(45%) cases were borderline leprosy (BL), 6(30%) cases were lepromatous leprosy (LL), 1 (15%) each of histoid and pure neural (PN) leprosy (Fig. 1). Among total 40 subjects, 12 (30%) were skilled workers, 20 (50%) were daily wage manual labourers, 4 (10%) were students and unemployed each.

Among BT, all 3 (100%) patients presented with anesthetic hypopigmented patches with no associated leprosy reaction (Fig. 2). Two of them showed unilateral ulnar nerve enlargement and one showed enlargement bilateral ulnar and left common peroneal nerve enlargement. Among 9 BL patients, 4 (44.4%) patients presented with hypopigmented patches, five (55.5%) with

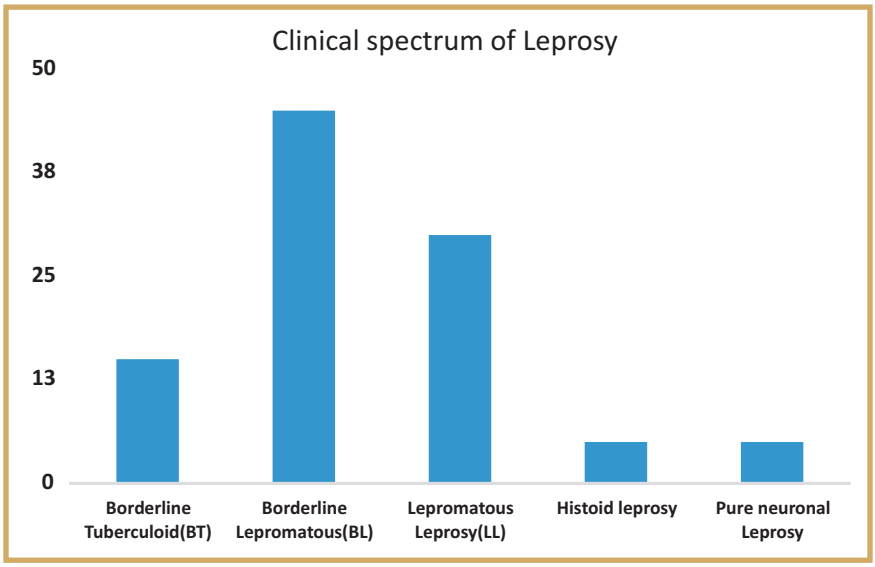

Fig. 1 : Clinical spectrum of leprosy cases studied

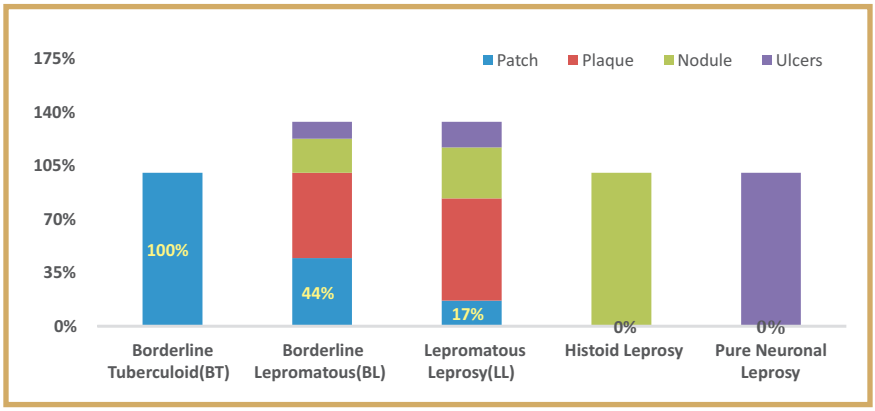

Fig. 2 : Clinical presentation among leprosy patients included in the study

plaques, 2 (22.2%) patients with plaques also had nodules and one (11.1%) patient with plaques had trophic ulcer on left foot (Fig. 2). Two patients (22.2%) had associated type 2 lepra reaction during time of presentation. 5 (55.5%) out of nine patients had bilateral ulnar, radial and common peroneal nerve enlargement among whom one patient had left sided posterior nerve enlargement also. 3 (33.3%) out of nine patients had bilateral ulnar nerve enlargement only.

Among 6 LL patients, four (66.6%) patients presented with plaques in whom one (16.6%) had trophic ulcer on left index finger and one had nodular lesions also. One (16.6%) patient each had patches and nodules on their body (Fig. 2). Two (33.3%) had presented with simultaneous type 2 lepra reaction during presentation. Five (83.3%) out of 6 patients had bilateral greater auricular, ulnar, radial and common peroneal nerve enlargement. One patient had bilateral ulnar and common peroneal nerve enlargement only.

Among 20 normal individuals, 3(15%) individuals showed tortuous capillaries and microhemorrhages each, 2(10%) showed meandering vessles, 1 (5%) (Fig. 3) each showed megacapillaries, dilated/ectatic capillaries and bizarre vessels each. None of the control showed capillary drop-outs, avascular areas and neoangiogenesis. These findings are comparable with a similar study in which NFC study of normal individuals showed tortuous vessels (22%), microhemorrhages (14%), meandering capillaries (14%), and dilated capillaries (6%) and bizarre vessels (2%) (Jakhar et al 2020).

One patient out of 20 cases had histoid and pure neural leprosy each. Histoid leprosy patient presented with nodular lesions all over the body with associated Type 2 lepra reaction. She had enlargement of bilateral, ulcer, median and common peroneal nerves. Pure neural leprosy patient

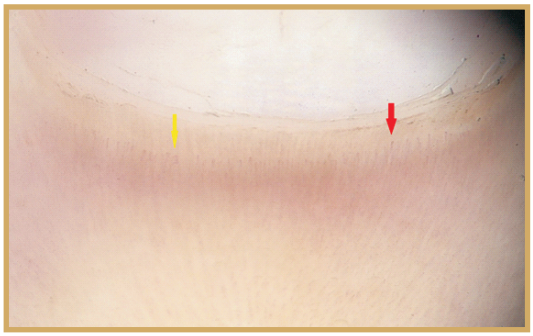

Fig. 3 : Nailfold capillaroscopy (NFC) changes findings in normal individuals showing meandering vessels (red arrows) and neoangiogenesis (yellow arrows) (20x magnification)

presented with glove and stoking anaesthesia pattern with tropic ulcers on bilateral 10 finger tips. He had enlargement of bilateral ulnar and median nerves with atrophy of hypothenar muscles.

Out of three BT patients, two (66.6%) of them on NFC showed dilated vessels with neoangiogenesis, microhemorrhages, where as meandering vessels, dropouts and bizarre vessels are shown by one (33.3%) patient each. None of the BT patients showed megacapillaries or avascular areas (Fig. 4). Among nine BL patients, seven (77.7%) showed capillary dropouts, five (55.5%) patients showed meandering, tortuous and bizarre vessels, avascular areas and neoangiogenesis each (Fig. 5). Four (44.4%) patients showed dilated vessels, 2 (22.2%) showed microhemorrhages and one (11.1%) patient each showed megacapillaries.

Among six LL patients, four (66.6%) patients showed meandering, bizarre vessels and avascularities, three (50%) patients showed dilated vessels and megacapillaries (Figs. 6 and 7), two (33.3%) patients showed tortuous vessels. Hemorrhage, capillary dropout and neoangio-

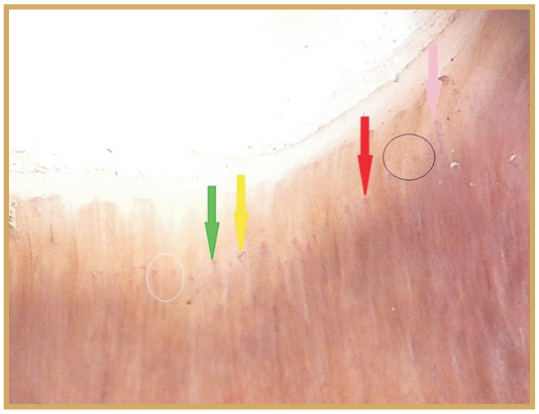

Fig. 4 : Nailfold capillaroscopy (NFC) changes of BT patient showing dilated capillaries (green arrow), meandering capillaries (red arrow), bizarre capillary (pink arrow), neoangiogenesis (yellow arrow), dropouts (white circle) and avascular areas (black circle). (20x magnification)

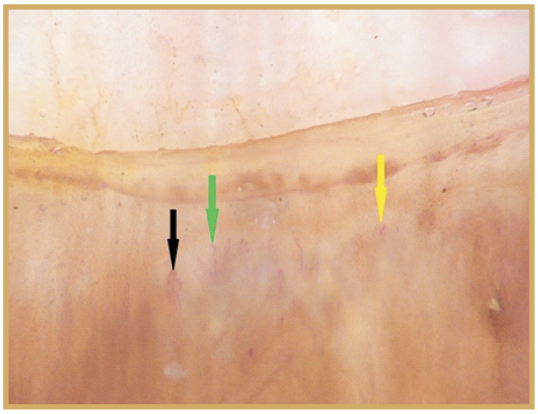

Fig. 6 : Nailfold capillaroscopy (NFC) changes of LL patients showing dilated capillaries (green arrow), neoangiogenesis (yellow arrow) and megacapillaries (black arrow). (20x magnification)

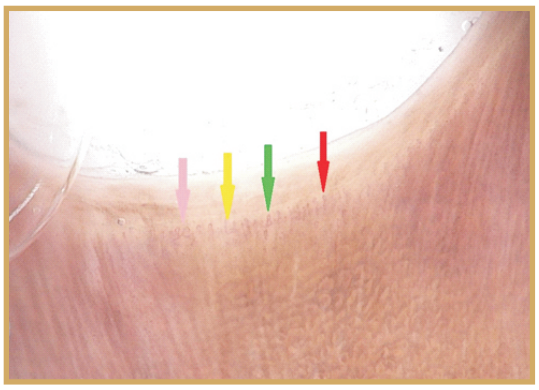

Fig. 5 : Nailfold capillaroscopy (NFC) changes of BL patients showing dilated capillaries (green arrow), meandering capillaries (red arrow), neoangiogenesis (yellow arrow) and bizarre capillaries (pink arrow). (20x magnification)

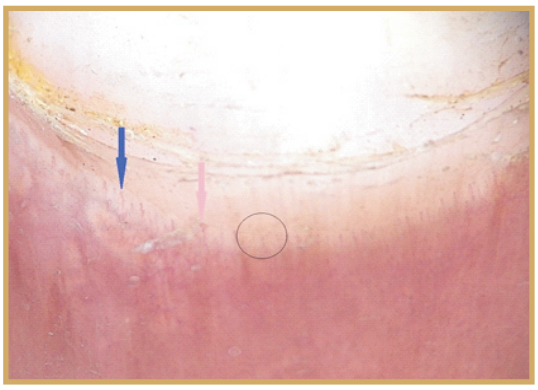

Fig. 7 : Nailfold capillaroscopy (NFC) changes of LL patients showing tortuous capillaries (blue arrow), bizarre capillary (pink arrow) and avascular areas (black circle). (20x magnification)

genesis were shown by one (16.6%) patient each. Single (100%) case of Histoid leprosy on NFC showed dilated, meandering, bizarre vessels, avascular areas (Fig. 8) and neoangiogenesis. Single (100%) case of pure neural leprosy showed microhemorrhages (Fig. 9) with absence of other capillaroscopic findings. Out of three patients with ulcers, two (66.6%) patients showed avas-

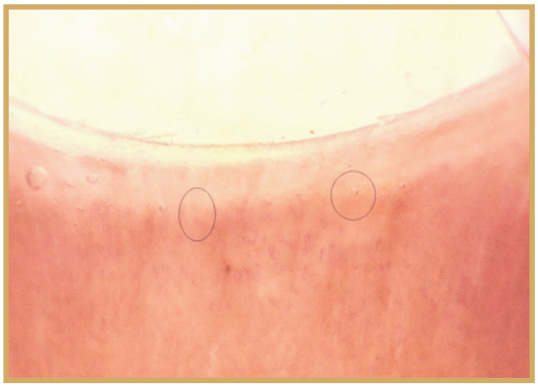

Fig. 8 : Nailfold capillaroscopy (NFC) of Histoid leprosy showing avascular areas (black circle). (20x magnification)

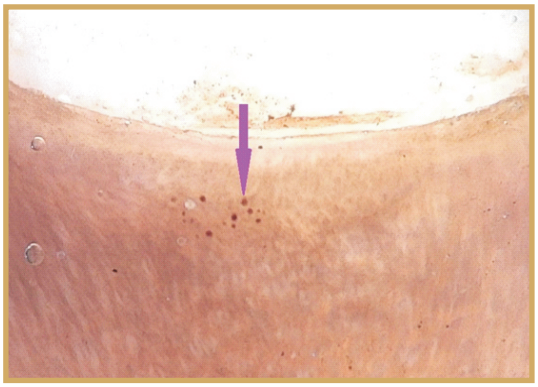

Fig. 9 : Nailfold capillaroscopy (NFC) of Pure neuronal leprosy showing microhemorrhages (purple arrow). (20x magnification)

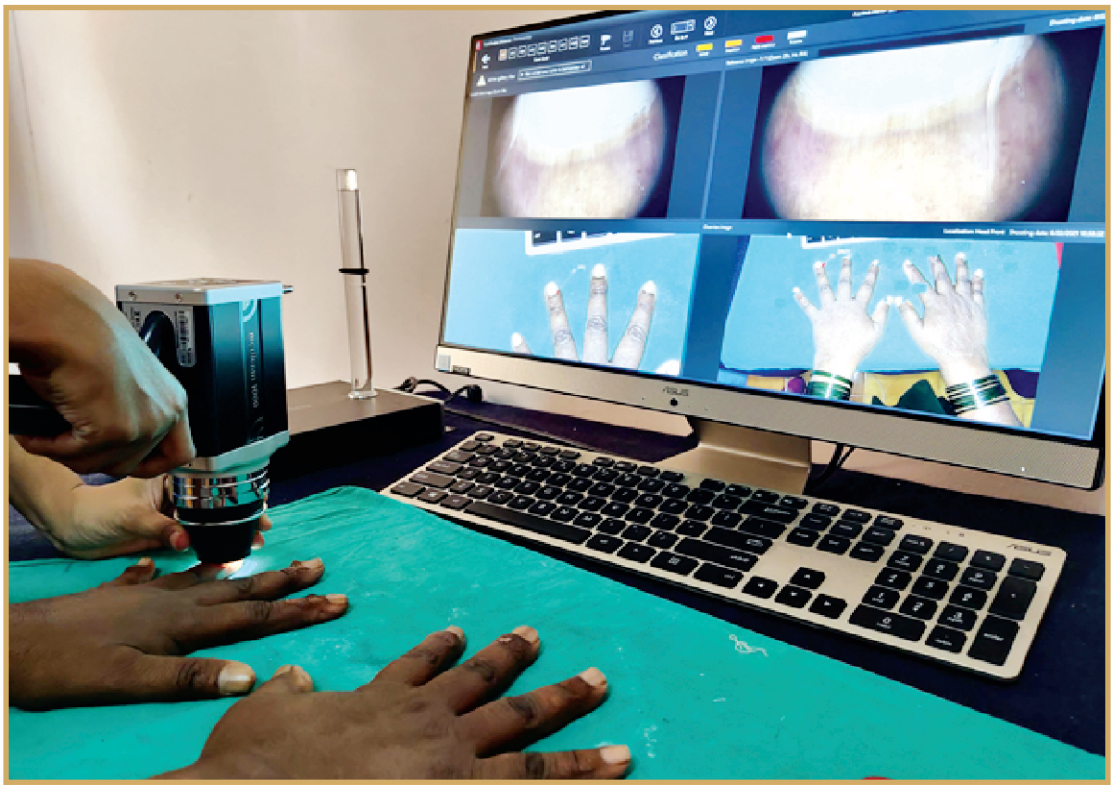

Fig. 10 : Image of nailfold capillaroscopy (NFC) examination of leprosy patient with FotoFinder videodermoscope.

Table 1 : Percentage distribution of NFC changes in clinical spectrum of leprosy

Clinical type	Capillaro-scopy of normal individuals (n=20)	Borderline tuberculoid (n=3)	Borderline Lepro-matous (n=9)	Lepro-matous leprosy (n=6)	Histoid leprosy (n=1)	Pure neural leprosy (n=1)	Total (n=40)
Nerve involvement	Nil	3(100%)	9 (100%)	6 (100%)	1(100 %)	1 (100%)	20(50%)
Mega capillaries	1(5%)	0	1 (11.1%)	3 (50%)	0	0	5(12.5%)
Tortuous capillaries	3(15%)	1(33.3%)	5 (55.6%)	2 (33.3%)	0	0	11 (27.5%)
Dilated/ectatic vessles	1(5%)	2 (66.7%)	4 (44.4%)	5 (50%)	1 (100%)	0	13 (32.5%)
Meandering vessels	2(10%)	1(33.3%)	5 (55.6%)	4 (66.7%)	1 (100%)	0	13 (32.5%)
Microhemo-rrhages	3(15%)	2 (66.7%)	2 (22.2%)	1 (16.7%)	0	1 (100%)	9 (22.5%)
Capillary dropouts	nil	1 (33.4%)	7 (77.8%)	1 (16.7%)	0	0	9 (22.5%)
Avascular areas	nil	0	5 (55.6%)	4 (66.7%)	1 (100%)	0	10 (25%)
Bizarre vessels	1(5%)	1(33.4%)	5 (55.6%)	4 (66.7%)	1 (100%)	0	12 (30%)
Neoangio-genesis	nil	2 (66.7%)	5 (55.6%)	1 (16.7%)	1 (100%)	0	9 (22.5%)

Table 2 : Sensitivity and specificity of meandering and tortuous capillaries with Hansen disease

S.No.	Capillary morphology	Sensitivity	Specificity
1.	Meandering capillaries	55%	90%
2.	Tortous capillaries	30%	85%

cular areas and capillary dropouts.

Total out of 20 patients, 11 (55%) patients showed bizarre and meandering capillaries, 10 (50%) showed dilated vessels and avascular areas, 9(45%) showed capillary drop-outs and neovascularisation, 8 (40%) showed tortuous vessels, 6(30%) hemorrhages and 4(20%) showed megacapillaries (Table 1). In this study, statistical significance between clinical and dermoscopic observations was not seen.

Discussion

Nailfold capillaroscopy is a non-invasive method, which is an in vivo evaluation of the nailfold microvascular network. Nailfold capillaries were first observed in 17th century with the help of primitive magnifying lens and first association between inflammation and capillary alteration were made in 19th century (Chojnowski et al 2016). The current generation of dermatoscopes and videocapillaroscopes provide high magnification (~200×) and polarization and has sophisticated software simplifying the study of capillary morphology (de Lima et al 2016).

Microvasculature of the human's body consists of capillaries, arterioles and venules. Capillaries are made-up of arterial limb, capillary loop and venous limb. Their major function is exchange of nutrients and gases. Abnormalities in capillary morphology will be reflected way long before clinical presentation of systemic disease which has vascular damage as their pathology. NFC often helps to determine the stages of various systemic diseases (Chojnowski et al 2016). In contrast to the entire skin where capillaries run perpendicular to the skin surface and only tip of loop is visible, nail folds have terminal row of capillaries running parallel to the skin surface. Hence, detailed morphology of capillaries can be examined (Lin et al 2009).

Videocapillaroscope which is considered as the gold standard instrument for NFC has 100–140 magnification with a monitor attachment allowing the dermatologist to store the image and provide detailed observations of individual capillaries (Herrick & Cutolo 2010). Videodermoscope allows panoramic view of panoramic vision of the whole nailfold microvascular network (Fig. 10). This is found to be very useful for the prompt localization of isolated morphological abnormalities and to analyse the architectural characteristics of the nailfold microvascular network (Grassi & De Angelis 2007).

Capillaroscopy in children differ from that of the adults by lower number of loops per millimeter, a higher plexus visualization score and a higher frequency of atypical loops (Herrick et al 2000). In people above seventy years, there will be enlargement and congestion of sub papillary venous plexus and capillaries because of the permanent opening of arterio-venous anastomoses which leads to senile microangiopathy (Merlen 1985). NFC study gained importance after its significant application in prognostic evaluation rheumatic and connective tissue disorders.

According to the study done by de Lima et al (2016) which includes 30% of the patients of Virchow's leprosy; 20%, dimorphic leprosy; 40%, tuberculoid leprosy; and 10% the indeterminate leprosy, 60% of the patients presented some capillaroscopic change, such as micro-hemorrhages, ectatic and corkscrew capillaries. The most frequent changes found were ectatic capillaries and micro-hemorrhages, in 40% of the patients. Greater capillary ectasies (megacapillaries) or capillary dropout areas were not found. Among the patients with detectable capillaroscopic changes, 66.7% presented nail alterations; in patients without capillaroscopic changes, 33% presented some nail alteration detectable at the physical examination. Nail alterations; in patients without capillaroscopic changes, 33% presented some nail alteration detectable at the physical examination. The involvement of endothelial cells by the bacillus could justify changes in cutaneous capillaries, which are analyzed during capillaroscopy. Yet, in their study, specific capillaroscopic patterns of leprosy were not detected in the cases.

As stated in recent studies (Treu et al 2017), lepromatous leprosy causes severe microvascular

dysfunction and significant alterations in capillary structure. They say that structural and functional changes are probably induced by exposure of the microvascular bed to chronic inflammation evoked by the *Mycobacterium leprae*.

In our study, we noticed capillary morphological abnormalities like dilated, meandering, bizarre vessels and neoangiogenesis were more common in BT Hansen patients. Ischemic precursors like avascular areas were found more in LL cases and single case of histoid leprosy (Table 2). There are seen in 66.6% patients with trophic ulcers in this study.

Conclusions

Though statistical significance between clinical and dermoscopic observations was not seen, morphological changes denote micro-vascular invasion by *Mycobacterium leprae*. They may act as warning signs of fore-coming complications like loss of sensation and trophic ulcers in lepromatous patients. Further case-control studies with larger number of sample size are required.

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