ORIGINAL ARTICLE

Nailfold Capillaroscopy Using Dermatoscope As a Tool to Assess Correlation of Vasculopathy in Nailfolds with Retinopathy in Diabetes Mellitus Patients

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Abstract

Background: Diabetic retinopathy (DR) is an important long term complication in diabetes patients and if not treated adequately, can lead to permanent visual disturbances. Nail fold capillaroscopy (NFC) can be used as an screening and reliable tool in evaluating the progression of the disease by monitoring the microvascular changes associated with it. **Aims:** We aimed to correlate the capillaroscopic parameters with the severity of DR in diabetes mellitus patients. **Material and Methods:** Cross sectional observational study was conducted on 100 diabetics (50 with diabetic retinopathy and 50 without retinopathy) in outpatient department of dermatology for a period of 1 year. All the participants were subjected to NFC and ophthalmological assessment. **Results:** Four NC parameters showed significant positive correlation with severity of DR i.e age (years), duration of diabetes (years), tortuous capillary and avascular area with correlation coefficient of 0.28, 0.864, 0.364, 0.274 respectively. Significant negative correlation was seen with mean capillary density (capillaries/mm) with correlation coefficient of -0.38. Non-significant mild positive correlation was seen with HbA1c (%), gender, meandering capillary, bushy capillary, neoangiogenesis, capillary dropout and bizarre capillary. **Conclusion:** NFC can be used as a tool in assessing the capillaroscopic alterations in diabetics as an indicator of severity of DR.

Key Words

Nail fold capillaroscopy, Diabetic retinopathy, Diabetes

Introduction

Diabetes mellitus refers to a state of chronic hyperglycemia resulting from defective release of insulin, defect in insulin action or both. It is a serious medical problem affecting 366 million individuals globally [1].

Diabetes-related complications affect many organ systems including skin and are responsible for significant morbidity and mortality rates due to its chronic complications which can be either microvascular or macrovascular. Microvascular complications include retinopathy, neuropathy and nephropathy whereas macrovascular consist of cardiovascular disease, stroke and peripheral arterial disease (PAD)[2].

Diabetic retinopathy (DR) is identified in a third of

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patients with diabetes and is associated with increased risk of systemic vascular complications like stroke, coronary heart disease, and heart failure. DR remains one of the leading cause of visual disability in adults. DR is classified into two stages: non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR). Diabetic macular edema (DME) and PDR specifically carries poor prognosis and can result in permanent visual impairment, despite the availability of newer treatment modalities like vitreous surgeries and lasers. This has led to the increase in number of untreated longstanding patients of DR. Thus, there is a need to establish techniques that can be used in large scale for screening diabetes and its complications, thereby achieving good visual outcomes[1].

Nailfold Capillaroscopy is a rapid, highly specific and reproducible investigation which involves visualisation of nailfold capillaries that can serve as indicators of vascular damage caused by various diseases like diabetes, stroke, autoimmune connective tissue diseases. It has got an established role in distinguishing primary Raynaud's phenomenon from Secondary Raynaud's phenomenon and in diagnosing systemic sclerosis. Its role is increasingly being evaluated in other connective tissue diseases as well like idiopathic inflammatory myopathies, systemic lupus erythematosus, mixed connective tissue disease etc [3].

NFC is still insufficiently applied to diseases other than CTDs, which affect the microvascular circulation. In comparison to retinal microvascular changes in diabetics, little is known regarding the NFC features of diabetics. Worldwide including India, diabetic population is growing fast and there is a need of early diagnosis and management of patients at risk so as to prevent and postpone future microvascular complications and associated morbidity and mortality of this disease [4].

Thus, dermatoscope can serve as a tool for physicians to analyse nailfold capillaroscopic changes in diabetes patients. These findings can then be correlated with severity of other microvascular complications (Diabetic retinopathy in this study). Hence, nailfold capillaroscopy (NFC) examination using dermatoscope can become a screening tool for diabetes associated complications. This study was carried out to assess these nailfold capillaroscopic changes in diabetes patients and to study their correlation with severity of diabetic retinopathy.

Material & Methods

This was a comparative observational study conducted over a period of 12 months in Government Medical College Jammu and associated hospitals after taking Institutional ethical committee clearance vide Number IEC/GMC/2022/801 and informed consent from each participant prior to the start of the study. 2 groups of 100 participants each: diabetics and normal healthy indivduals were studied. Diabetes mellitus patients had 2 subgroups: 50 with diabetic retinopathy (DR) and 50 without diabetic retinopathy (NDR).

All patients who were diagnosed with Diabetes mellitus attending Dermatology/Endocrinology OPD of Government Medical College, Jammu were included regardless to age, sex, ethnic origin and occupation. Comparison group comprised healthy individuals without any comorbidities including diabetes mellitus. All the diabetic patients were of Type 2 diabetes mellitus and their latest Hba1c levels were done. Fundoscopy examination of the diabetics was done in coordination of Department of Ophthalmology of our hospital. A predesigned proforma was used to record relevant history and clinical findings in the patients. Patients with Connective tissue diseases, systemic diseases like hypertension which cause retinopathy and vasculopathy in nailfolds, pregnant women, patients with sepsis or organ dysfunction (liver/kidney/heart) ,smokers, patients having history or evidence of other nail disorders, trauma, nail infections and recent manicure were excluded from the study.

Nailfold Capillaroscopy (NFC) Examination

Dermoscopic examination was done using DermLite DL4 (4th generation handheld DermLite dermoscope).

Technique of Nailfoldcapillaroscopy (NFC)[5]:

All patients selected for nailfoldcapillaroscopy examination were made to sit for 15-20 minutes in normal ambient temperature (20-22ºC) room. Both hands were placed over a dull non-refractile surface . Ultrasound Jelly was placed over proximal nailfold. Then the dermoscope with IceCap attached, was placed over it at an appropriate angle but not pressed to avoid blanching of the blood vessels. Proximal Nailfold capillaries of 8 fingers (excluding thumbs) were examined first at 10x and them image zoomed upto 100x for noting qualitative changes if any. At least 1 sharply focused image in JPEG format of each digit's nailfold capillaries was clicked for future analysis.

Quantitative parameter i.e. Mean Capillary Density was calculated by analysis of 4th and 5thfingers of both hands. With the help of 1 mm markings seen in images clicked by DermLite DL4, quantitative analysis was done. Among Qualitative parameters, the various morphological

alterations (like tortuous capillaries, meandering, receding capillaries, neoangiogenesis and avascular areas etc) in capillary loops were carefully visualized and recorded.

Ocular Examination

Fundus examination of both the eyes was done in coordination with Upgraded Department of Ophthalmology, GMC Jammu. Pupils of both the eyes were dilated with tropicamide eye drops to achieve maximum dilatation. Direct ophthalmoscopy, slip lamp biomicroscopy with 90 D lens and indirect ophthalmoscopy with 20 D lens were done and the posterior pole as well as periphery of retina was visualized. Any changes attributed to diabetes were noted and graded as–

1. No signs of Retinopathy
2. Non proliferative Diabetic retinopathy (NPDR)
3. Proliferative Diabetic retinopathy (PDR)

Statistical Analyais

The Categorical variables were presented in the form of number and percentage (%). On the other hand, the quantitative data were depicted as the means ± SD and as median with 25th and 75th percentiles (interquartile range). The following statistical tests were applied for the results:

1. For quantitative variables- Independent t test (for two groups) and ANOVA test (for more than two groups).
2. For qualitative variables- Chi-Square test. If any cell had an expected value of less than 5 then Fisher's exact test was used.
3. Spearman rank correlation coefficient- to find correlation of Age, Mean capillary density, Duration of diabetes and HbA1c with severity of DR.
4. Point biserial correlation coefficient- to find correlation of Gender, Tortuous capillary, Receding capillary, Capillary dilation, Meandering capillary, Bushy capillary, Neoangiogenesis, Avascular area, Capillary dropout, Microhemorrhages, Angulated capillary, Bizarre capillary andSubpapillary plexus visibility with severity of DR.

For statistical significance, p value of less than 0.05 was considered statistically significant.

Results

In our present study distribution of gender was comparable between severity of DR {Proliferative DR, Nonproliferative DR, Patients without DR}. (Female- 20% vs 47.50% vs 56% respectively, Male:- 80% vs 52.50% vs 44% respectively) with p value=0.124. Mean ± SD of age (years) in proliferative DR was 59.3 ± 5.93 which was significantly higher as compared to neoangiogenesis, capillary dropouts, microhemorrhages [Fig 2], angulated capillary, bizarre capillary and subpapillary plexus visibility was comparable between severity of DR {Proliferative DR, Nonproliferative DR, Patients without DR} with p value of 0.80,0.73,0.325, 0.559, 0.244, 0.562 ,1, 1, 0.296, 0.746 respectively. Proportion of patients with avascular area was significantly higher in proliferative DR as compared to nonproliferative DR and patients without DR (60% vs 20%, 14% respectively) [Table 1].

Significant positive correlation was seen between severity of DR with age (years), duration of diabetes (years), tortuous capillary and avascular area with correlation coefficient of 0.28, 0.864, 0.364, 0.274 respectively [Image1,2,3]. Significant negative correlation was seen between severity of DR with mean capillary density (capillaries/mm) with correlation coefficient of -

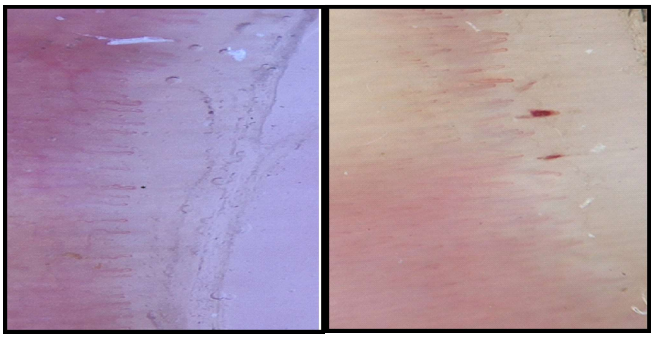

Fig1: Showing Dilated Tortuous Capillary

Fig 2: Microhemorrhages

nonproliferative DR (47.28 ± 8.04) and patients without DR (46.2 ± 9.76) (p value=0.0002).

Mean ± SD of duration of diabetes (years) in proliferative DR was 20.7 ± 4.4 which was higher as compared to nonproliferative DR (12.22 ± 3.85) and patients without DR (3.14 ± 2.54) with p value<0.0001. Mean ± SD of HbA1c (%) in proliferative DR was 9.41 ± 1.6, nonproliferative DR was 9.3 ± 1.89 and patients without DR was 8.85 ± 2.31 with no significant association between them. Mean ± SD of mean capillary density(capillaries/mm) in patients without DR was 6.83 ± 0.33 which was remarkably higher as compared to nonproliferative DR (6.57 ± 0.33) and proliferative DR (6.47 ± 0.45). Proportion of patients with tortuous capillary [Fig 1] was comparatively higher in proliferative DR as compared to nonproliferative DR and patients without DR (100% vs 75%, 48% respectively). Distribution of other variables like receding capillary, capillary dilation, meandering capillary, bushy capillary ,

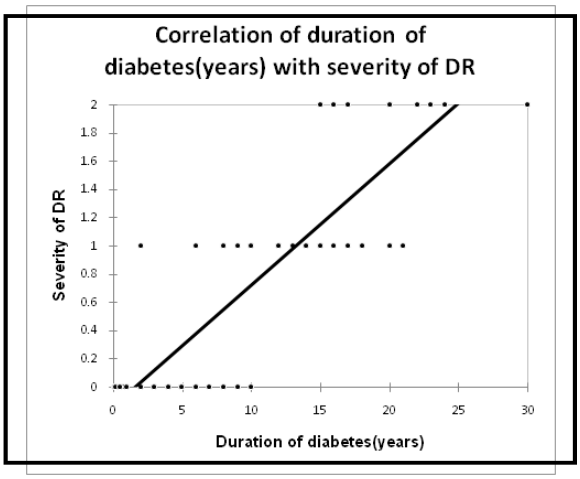

Image 1: Correlation of Duration of Diabetes (years) With Severity of DR

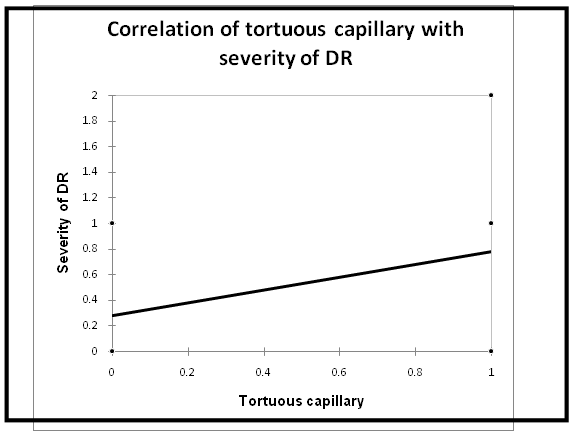

Image 2: Correlation of Tortuous Capillary with Severity of DR

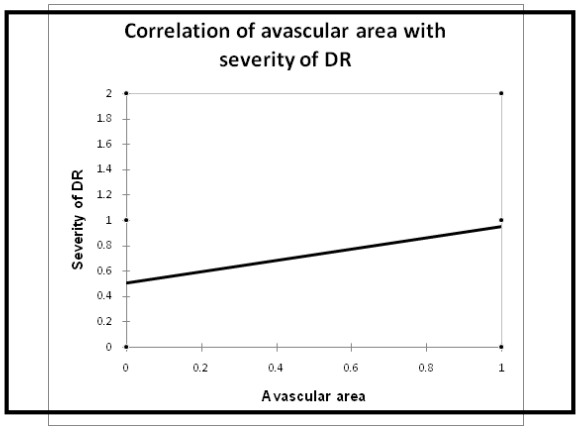

Image 3: Correlation of Avascular Area with Severity of DR

0.38. Non-significant mild positive correlation was seen between variables like severity of DR with HbA1c (%), gender, meandering capillary, bushy capillary, neoangiogenesis, capillary dropout, bizarre capillary with correlation coefficient of 0.178, 0.193, 0.099, 0.089, 0.163, 0.099, 0.14 respectively. No correlation was seen between severity of DR with receding capillary, capillary dilation, microhemorrhages, angulated capillary, subpapillary plexus visibility with correlation coefficient of 0.066, 0.073, 0.027, 0.023, 0.07 respectively [Table 2].

Discussion

Diabetes mellitus is one of the oldest diseases known to man and one of the leading cause of morbidity and mortality with prevalence increasing every year [6] .Microvascular involvement in many systemic diseases including diabetes has been documented in visualised microvascular beds like retina [7]. Periodical dilated fundoscopy is the gold standard screening approach for detecting diabetic retinopathy. But referral to an ophthalmologist is poor due to reasons like ignorance, financial constraints, feasibility and negligence[8]. Thus, there is a need to develop new screening tools which are easy to use and cost effective for early detection of diabetes mellitus and its complications[9].

In the current study, nailfold capillaroscopy was done using dermatoscope in 100 diabetics (50 DR AND 50 NDR) and 100 healthy normal individuals were taken in the comparison group. Among 50 diabetic retinopathy patients, 40 had Non-proliferative diabetic retinopathy (NPDR) and 10 had Proliferative diabetic retinopathy (PDR). Studies conducted in the past like in study by Uyar *et al* [10] 216 Type 2 diabetes mellitus patients (93 had retinopathy, 62 had PDR and 31 had NPDR) and 101 healthy controls were included and in study by Jakhar *et al* [4] 96 diabetics (46 with microvascular complications and 50 without) and 40 healthy controls were studied.

NFC and Severity of Retinopathy

In our current study Mean ± SD of mean capillary density (capillaries/mm) in patients without DR was significantly higher as compared to NPDR and PDR. Also, significant results were reported by Lima *et al* [11] in the past in which there was statistically significant reduction of mean capillary density with increasing severity of retinopathy. Our study also showed significant negative correlation between severity of DR with mean capillary density(capillaries/mm) with correlation coefficient of -0.38.However on literature search, there are limited studies if at all any correlating these two variables. In our present study, Mean ± SD of duration of

Table 1: NFC Variables in Each Group of Patients with Diabetes.

Severity of DR	NDR	NPDR	PDR	P-value
Number of patients	50	40	10	
Gender (M/F)	22/28	21/19	8/2	0.124
Age (years)	46.2 ± 9.76	47.28 ± 8.04	59.3 ± 5.93	**0.0002**
HbA1c	8.85 ± 2.31	9.3 ± 1.89	9.41 ± 1.6	0.525
Duration of Diabetes (years)	3.14 ± 2.54	12.22 ± 3.85	20.7 ± 4.4	**0.0001**
Mean Capillary Density	6.83 ± 0.33	6.57 ± 0.33	6.47 ± 0.45	**0.0003**
Tortuous capillary (present/absent)*	24/50	30/40	10/10	**0.0008**
Receding capillary*	23/27	19/21	6/4	0.803
Capillary dilation*	21/29	20/20	5/5	0.734
Meandering capillary*	18/32	14/26	6/4	0.325
Bushy capillary*	2/48	3/37	1/9	0.559
Neoangiogenesis*	10/40	13/27	4/6	0.244
Avascular areas*	7/43	8/32	6/4	**0.008**
Capillary Dropouts*	13/37	13/27	4/6	0.562
Microhemorrhages*	13/37	11/29	3/7	1
Angulated capillary*	9/41	8/32	2/8	1
Bizarre capillary*	6/44	7/33	3/7	0.296
Subpapillary plexus visibility*	11/39	11/29	3/7	0.746

Table 2: Correlation of Capillaroscopic variables with severity of DR.

Variables	Severity of DR	
	Correlation coefficient	P value
Gender{1 Female, 2-Male}	0.193	0.0544
Tortuous capillary	0.364	0.0002
Receding capillary	0.066	0.5117
Capillary dilation	0.073	0.4729
Meandering capillary	0.099	0.3252
Bushy capillary	0.089	0.3792
Neoangiogenesis	0.163	0.1052
Avascular area	0.274	0.0058
Capillary dropout	0.099	0.3286
Microhemorrhages	0.027	0.7885
Angulated capillary	0.023	0.8199
Bizarre capillary	0.14	0.1653
Subpapillary plexus visibility	0.07	0.4912

Point biserial correlation coefficient

diabetes (years) in PDR was remarkably higher as compared to NPDR and patients without DR but Mean ± SD of duration of diabetes (years) in NPDR was comparatively higher as compared to patients without retinopathy (pvalue<0.0001). These results are comparable to study done in by Mohanty *et al* [8] in past in which mean duration of diabetes was 5.5 ±3.2 years in patients with no DR, 10.4 ± 3.4 years in patients with NPDR and 12.8 ± 4.8 years in patients with PDR.

Significant positive correlation was seen between severity of DR with age and duration of diabetes (years) with correlation coefficients of 0.28 and0.864 respectively in our study. Shrotes [12] showed positive correlation between age and DR however it was not statistically significant in his study. Similar statistically significant correlation between diabetes duration and severity of DR was reported by Bagzai [13] in their study.

Proportion of patients with tortuous capillary and avascular areas was significantly higher in PDR as compared to NPDR and patients without DR in our study.

Capillaroscopic parameters like receding capillary ,capillary dilation, meandering capillary , bushy capillary, neoangiogenesis , capillary dropouts , microhemorrhages , angulated capillary , bizarre capillary and subpapillary plexus visibility were not significantly higher in diabetic patients with PDR as compared to NPDR and patients without DR signifying that they are not associated with severity of retinopathy in our study. These results are near similar to the study by Mohanty *et al* [8] in which tortuosity, neoangiogenesis, microhemorrhages, abnormal forms and avascular areas were seen more frequently in

PDR than NPDR and patients without DR (p value 0.00). However in our study, neongiogenesis, microhemorrhages and abnormal/aberrant forms were not significantly higher. In the study by Uyar *et al* [10] in past tortuosity, bushy capillary, neoformation and capillary ectasia were significantly higher in patients with PDR than NPDR and patients without DR. However, avascular areas were not significantly higher in their study. These typical capillaroscopic findings seen can be attributed to advanced glycation end products (AGEs) which are known to be associated with the complications associated with Diabetes mellitus. This is believed to affect function of pericytes and endothelial cells resulting in impaired angiogenesis [4]. Kowluru [14] suggested that path mechanism of diabetic retinopathy involves apoptosis of pericytes and endothelial cells in retinal capillaries. The NFC changes of T2DM can be explained by same mechanism.

In our present study, significant positive correlation was seen between severity of DR with tortuous capillary and avascular area with correlation coefficients of 0.364 and 0.274 respectively. These findings were also significantly associated with severity of DR as mentioned above. Study by Uyar *et al* [10] also showed significant correlation of capillaroscopy findings with DR. Jakhar *et al* [4] in his study showed that NFC revealed more regressional changes as compared to the retinal changes which were more proliferative in nature. Similar observations were made by Pazos-Moura *et al* [15] in their study in the past. Our observations are comparable as avascular areas correlated but not proliferative changes like neoangiogenesis and bushy capillaries with severity of DR.

Conclusion

Nail fold capillaroscopy using dermatoscope is a quick, non-invasive and reliable technique to detect changes in the microvascular bed which can be used to assess severity of vascular damage in diabetes mellitus. Our results suggest that it could possibly become a useful tool in diabetics to diagnose as well as monitor microvascular complications like retinopathy in future. Further studies with larger sample sizes can help refine its clinical utility.

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