



Research Article

## FOVEAL SLOPE MEASUREMENT ON OCT TO PREDICT THE DEVELOPMENT OF SIGHT THREATENING DIABETIC RETINOPATHY

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### ABSTRACT

**Aims:** To measure the foveal slope on optical coherence tomography in diabetic retinopathy to predict the development of sight threatening retinopathy. **Materials and Methods:** 154 patients were enrolled and all the subjects underwent comprehensive ophthalmic evaluation including spectral domain optical coherence tomography. Fovea thickness was calculated automatically using an inbuilt topographic mapping software Central subfield thickness (CSFT). Foveal slope in all four quadrants was calculated at a distance of 500  $\mu$ m from the foveal centre. **Results:** Total of 154 patients were taken out of which 94(61%) were male and 60 (39%) were females. There was significant shallowness of average foveal slope of both right and left eye of STDR patients when compared with No diabetes, DR and NSTDR (p=.000). Temporal slope was shallowest for right eye in STDR patients (-2.74 $\pm$ 11...01) whereas Nasal slope was shallowest (-2.42 $\pm$ 10.98) for left eye in STDR patients. **Conclusion:** There was a trend of shallowness of foveal slope in all quadrants with increase in the severity of DR. Thus, sequential OCT with slope measurements may predict progression of DR as well sight threatening DR.

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### INTRODUCTION

Diabetes is a global epidemic and it is estimated that in 2012, the number of people with diabetes worldwide was approximately 366 million. According to the International Diabetes Federation, 61.3 million people in India had diabetes in 2011. That figure is projected to rise to 101.2 million by 2030<sup>1</sup>. Diabetic retinopathy (DR) is a one of the most common micro vascular complication seen in type 1 and type 2 diabetes. Visual functions of the patient are usually impaired when macula of more precisely fovea is involved. Variation in foveal shape is related to the structural alterations of the retinal layers. Various parameters of the foveal structure have been found to be altered in subjects with diabetic retinopathy (DR)<sup>2,3,4</sup> and age-related macular degeneration.<sup>5</sup> Although foveal thickness has been used as marker of structural changes in various retinal diseases, there are evidences of using other foveal parameters such as foveal diameter, foveal slope, and foveal depth to assess the structural integrity of macula.<sup>6</sup> It is known that the foveal avascular zone (FAZ) diameter enlarges in DR and further increases with severity of retinopathy due to the capillary dropout.<sup>3,4</sup> Early neuronal degeneration has also been reported in diabetic subjects even with no retinopathy.<sup>7,8</sup> Dubis *et al.*<sup>9</sup> have shown a strong relationship between FAZ and foveal pit morphology.

Foveal slope measurement has been tried in macular diseases such as macular hole<sup>6</sup> and age-related macular degeneration,<sup>5</sup> and correlated with disease prognosis and macular pigment optical density<sup>10</sup>. This study was to done to assess the foveal slope in subjects with type 2 diabetes in to correlate foveal slope with severity of diabetes.

### MATERIALS AND METHODS

It was a prospective study of diagnosed patients of type 2 Diabetes mellitus attending eye OPD from July 2016 to June 2017. All diabetic patients attending eye OPD meeting the American Diabetes Association (ADA) criteria were examined

And patient having history of previous ocular surgery, macular pathology like AMD, hereditary maculopathy or opaque ocular media were excluded from the study. The patients were subjected to various biochemical investigations and detailed ophthalmological examination. DR was graded clinically using Klein's Classification (modified early treatment DR study (ETDRS) scales)<sup>11</sup> and the subjects were further divided as no DR, as non sight-threatening DR (non-STDR) and as STDR. Non-STDR subjects included cases of mild and moderate nonproliferative DR and those with STDR included severe nonproliferative DR, proliferative DR, and clinically significant macular edema. Retinal photographs were obtained after pupillary dilatation using fundus camera (KOWA'S FUNDUS CAMERA VX-10, Tokyo Japan), Retinal thickness was measured using 3D

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OPTICAL COHERENCE TOMOGRAPHY 3D OCT-1 PC SOFTWARE EDITION Version 8.1X. Retinal thickness was calculated automatically using an inbuilt topographic mapping software .Central subfield thickness (CSFT) was noted. The temporal, superior, inferior, and nasal subfield thicknesses were noted at 3 mm radius. Foveal slope in all four quadrants was calculated at a distance of 500 μm from the foveal center (figure-1). For example, foveal slope in nasal quadrant was calculated as the difference between nasal quadrant thickness in the 3 mm radius and CSFT divided by 500 μm, which is the distance of nasal quadrant thickness from foveal centre. Normally the thickness of any quadrant at 3mm is more than the CFT but as the CFT value increases with severity of Diabetes the slope value will decrease and angle will have the negative value or in other way increase the shallowness of slope. The patient at the time of registration filled out a standard consent form. The study adhered to the Declaration of Helsinki and was approved by the institutional ethics committee.

**Statistical Analysis:** Data collected during the study was tabulated and analysed by using Chi-square test and Anova test. Continuous variables are presented as a mean ± standard deviation, and categorical variables were presented as absolute numbers and percentage. The p-value was calculated and a value of < 0.05 was implied to be statistically significant at 95% confidence interval.

**RESULTS**

Total 154 patients were enrolled, out of which 94(61%) were male and 60(39%) were females. Table -1 showed age and category wise distribution of patients. In first category of 40 years of age and below showed 0 ( 0%) patients of No Diabetes, 1(100%) patient of No DR ,0(0%) patients of NSTDR and 0(0%) patients of STDR. Between 40-49yrs there were 12(42.9%) patients of No Diabetes, 6 (21.4 %) patients of No DR, 6(21.4 %) patients of NSTDR and 4(14.3%) patients of STDR. Between 50-59yrs there were 14 (23.7%) patients of No Diabetes, 13 (22 %) patients of No DR, 16 (27.1%) patients of NSTDR and 16(27.1%) patients of STDR . Between 60 -69 yrs there were 11(20.8%) patients of No diabetes, 11 (20.8%) patients of No DR, 11(20.8%) patients of NSTDR and 20(37.7%) patients of STDR. Age 70years and above, there were 1 (7.7%) patients of No Diabetes, 3 (23.1%) patients of No DR, 2(15.4%) patients of NSTDR and 7(53.8%) patients of STDR. There were 23 (14.9%) patients who had duration of diabetes equal to or less than 5yrs and 93(60.4%) patients who had duration of diabetes greater than 5yrs. Table -2 showed comparison of STDR patients with other groups ( No diabetes, No DR and NSTDR) in respect to duration of diabetes. It was found statistically significant (p=.000).

Table -3 and Figure-2 shows average mean foveal slope value of all four quadrants (superior, nasal, inferior, temporal) of right eyes for different categories. It was seen that patients with No Diabetes had the mean value of 9.67±3.55, No DR patients had the mean value of 7.98±1.98, patients with NSTDR had the mean value of 5.98±2.11 and average foveal slope of patients with STDR had the with mean value of -2.22±9.99.

4 Table -3 and Figure-2 shows average mean foveal slope value of all four quadrants (superior, nasal, inferior, temporal) of right eyes for different categories. It was seen that patients with No Diabetes had the mean value of 9.67±3.55, No DR patients had the mean value of 7.98±1.98, patients with NSTDR had the mean value of 5.98±2.11 and average foveal slope of patients with STDR had the with mean value of -2.22±9.99.

Table - 4 and Figure-3 shows average mean foveal slope value of all four quadrants (superior, nasal, inferior, temporal) of left eyes for different categories. Patients with No Diabetes had the mean value of 9.12±2.46, No DR patients had the mean value of 7.85±2.11, patients with NSTDR had the mean value of 6.38±3.20 and average foveal slope of patients with STDR had the mean value of -1.88±8.84.

Table 5,6 shows comparison of average mean foveal slope of all quadrants (superior, nasal, inferior ,temporal ) of Right eyes and left eyes in patients of STDR group with other categories(No Diabetes, NO DR and NSTDR). It was found to be significant (p=.000).

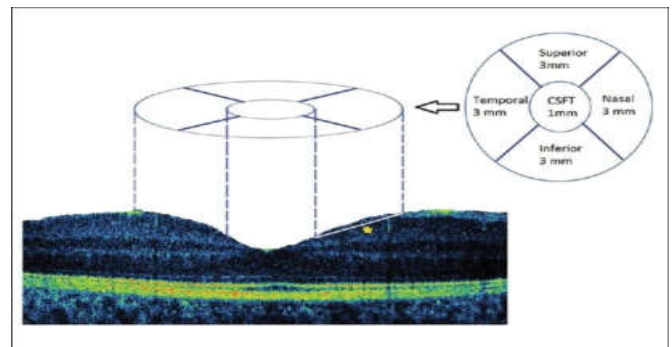


Figure 1 shows how to calculate the slope angle.

Slope angle = Difference in thickness/horizontal distance  
 Slope (°) = tan<sup>-1</sup> (slope angle).

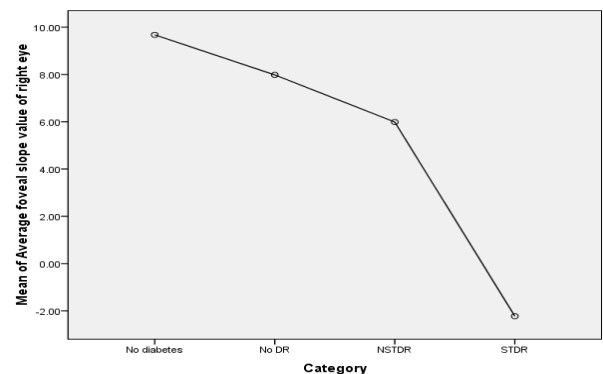


Figure 2 shows trend of mean average foveal slope value of right eyes

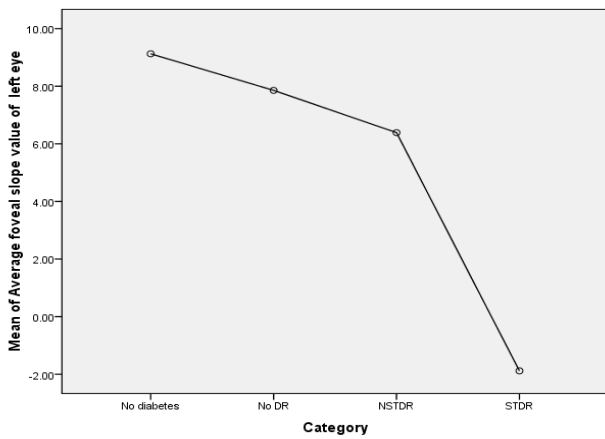


Figure 3 shows trend of mean average foveal slope value of left eyes.

Table 1 shows age and category wise distribution of patients.

	Category	Category				Total
		No diabetes	No DR	NSTDR	STDR	
<40	Count	0	1	0	0	1
	% within Age	.0%	100.0%	.0%	.0%	100.0%
	% within Category	.0%	2.9%	.0%	.0%	.6%
40-49	Count	12	6	6	4	28
	% within Age	42.9%	21.4%	21.4%	14.3%	100.0%
	% within Category	31.6%	17.6%	17.1%	8.5%	18.2%
Age 50-59	Count	14	13	16	16	59
	% within Age	23.7%	22.0%	27.1%	27.1%	100.0%
	% within Category	36.8%	38.2%	45.7%	34.0%	38.3%
60-69	Count	11	11	11	20	53
	% within Age	20.8%	20.8%	20.8%	37.7%	100.0%
	% within Category	28.9%	32.4%	31.4%	42.6%	34.4%
>=70	Count	1	3	2	7	13
	% within Age	7.7%	23.1%	15.4%	53.8%	100.0%
	% within Category	2.6%	8.8%	5.7%	14.9%	8.4%
Total	Count	38	34	35	47	154
	% within Age	24.7%	22.1%	22.7%	30.5%	100.0%
	% within Category	100.0%	100.0%	100.0%	100.0%	100.0%

Table 2 shows comparison of STDR patients with other groups (No diabetes, No DR and NSTDR) in respect to duration of diabetes (p=.000).

Dependent Variable	(I) Category	(J) Category	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Duration	No diabetes	No DR	-6.971*	.696	.000	-8.78	-5.16
		NSTDR	-9.257*	.691	.000	-11.05	-7.46
		STDR	-12.298*	.644	.000	-13.97	-10.63
	No DR	No diabetes	6.971*	.696	.000	5.16	8.78
		NSTDR	-2.287*	.710	.008	-4.13	-.44
		STDR	-5.327*	.664	.000	-7.05	-3.60
	NSTDR	No diabetes	9.257*	.691	.000	7.46	11.05
		No DR	2.287*	.710	.008	.44	4.13
		STDR	-3.041*	.659	.000	-4.75	-1.33
	STDR	No diabetes	12.298*	.644	.000	10.63	13.97
		No DR	5.327*	.664	.000	3.60	7.05
		NSTDR	3.041*	.659	.000	1.33	4.75

Table 3 shows average foveal slope all four quadrants (superior, nasal, inferior, temporal) of right eyes for different categories.

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum	
					Lower Bound	Upper Bound			
Average foveal slope value of right eye	No diabetes	38	9.6740	3.55337	.57643	8.5060	10.8420	4.56	20.69
	No DR	34	7.9806	1.98216	.33994	7.2890	8.6722	4.40	14.34
	NSTDR	35	5.9866	2.11792	.35799	5.2590	6.7141	2.01	11.88
	STDR	47	-2.2252	9.98753	1.45683	-5.1577	.7072	-24.42	20.31
Total	154	4.8305	7.64973	61643	3.6127	6.0483	-24.42	20.69	

Table 4 shows average foveal slope all four quadrants (superior, nasal, inferior, temporal) of left eyes for different categories.

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum	
					Lower Bound	Upper Bound			
Average foveal slope value of left eye	No diabetes	38	9.1241	2.46584	.40001	8.3136	9.9346	4.78	16.69
	No DR	34	7.8554	2.11582	.36286	7.1171	8.5936	2.66	12.71
	NSTDR	35	6.3877	3.20954	.54251	5.2852	7.4902	-2.72	14.86
	STDR	47	-1.8820	8.84695	1.29046	-4.4795	.7156	-20.75	11.92
Total	154	4.8631	7.01880	.56559	3.7457	5.9805	-20.75	16.69	

Table 5 shows on comparison of average foveal slope of all quadrants (superior, nasal, inferior, temporal) of right eye patients of STDR with other categories (No Diabetes, No DR and NSTDR)(p=.000).

Dependent Variable	(I) Category	(J) Category	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Average foveal slope value of right eye	No diabetes	No DR	1.69342	1.40823	.626	-1.9652	5.3521
		NSTDR	3.68746*	1.39757	.045	.0565	7.3184
		STDR	11.89923*	1.30139	.000	8.5181	15.2803
	No DR	No diabetes	-1.69342	1.40823	.626	-5.3521	1.9652
		NSTDR	1.99403	1.43645	.509	-1.7380	5.7260
		STDR	10.20581*	1.34305	.000	6.7165	13.6951
	NSTDR	No diabetes	-3.68746*	1.39757	.045	-7.3184	-.0565
		No DR	-1.99403	1.43645	.509	-5.7260	1.7380
		STDR	8.21178*	1.33187	.000	4.7515	11.6721
	STDR	No diabetes	-11.89923*	1.30139	.000	-15.2803	-8.5181
		No DR	-10.20581*	1.34305	.000	-13.6951	-6.7165
		NSTDR	-8.21178*	1.33187	.000	-11.6721	-4.7515

Table 6 shows comparison of average foveal slope of all quadrants (superior, nasal, inferior, temporal) of left eye patients of STDR with other categories (No Diabetes, No DR and NSTDR)(p=.000).

Dependent Variable	(I) Category	(J) Category	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Average foveal slope value of left eye	No diabetes	No DR	1.26871	1.26735	.749	-2.0239	4.5614
		NSTDR	2.73636	1.25776	.135	-.5314	6.0041
		STDR	11.00605*	1.17120	.000	7.9632	14.0489
	No DR	No diabetes	-1.26871	1.26735	.749	-4.5614	2.0239
		NSTDR	1.46765	1.29275	.668	-1.8910	4.8263
		STDR	9.73734*	1.20869	.000	6.5971	12.8776
	NSTDR	No diabetes	-2.73636	1.25776	.135	-6.0041	.5314
		No DR	-1.46765	1.29275	.668	-4.8263	1.8910
		STDR	8.26969*	1.19863	.000	5.1556	11.3838
	STDR	No diabetes	11.00605*	1.17120	.000	-14.0489	-7.9632
		No DR	-9.73734*	1.20869	.000	-12.8776	-6.5971
		NSTDR	-8.26969*	1.19863	.000	-11.3838	-5.1556

## DISCUSSION

We measured the structural variability of the fovea in terms of foveal slope in patients with type 2 diabetes. Total of 154 patients were taken of which 61% were male and 39% were females. Maximum patients were seen in age group ranges from 50-59years (38.3%). Patients were grouped according to the modified ETDRS classification and there were 38 (25%) patients with No diabetes, 34 (22%) patients of No DR, 35

(23% ) patients of NSTDR and 47 (30% ) of STDR. Maximum patients presented to us were in sight threatening group (47patients).Patients were divided into two groups in relation to duration of the disease. In present study 60.4% of patients had duration of diabetes greater than 5 yrs. Jenchitr W et<sup>12</sup> al studied prevalence of diabetic retinopathy in relation to duration of diabetes mellitus in community hospitals of Lampang. They found that in NPDR, the retinopathy varied from 13.11 to 22.91% in persons having diabetes for less than 10 years and up to 42.86% in those with diabetes for up to 20 years. In the PDR group, the prevalence was 2.15 to 2.42% in persons with diabetes for less than 10 years and up to 10.20% for those with diabetes for up to 20 years .In our study severity of diabetic retinopathy increases with duration of diabetes and maximum patents were in the group having duration of disease more than 5 years. On comparison of STDR with other groups (No diabetes, No DR and NSTDR) in respect to duration of diabetes shows significant co-relationship between duration of diabetes (>5 years) and severity of diabetic retinopathy (p=.000).

Foveal thickness has been used as marker of structural changes in various retinal diseases, foveal slope is a important parameter to assess the structural integrity of macula. Average foveal slope of right eye and left were measured for different categories. Average foveal slopes of all four quadrants (nasal,superior inferior and temporal) of right eye of all patients were calculated. Patients with No Diabetes had the mean value of 9.67±3.55, No DR patients had the mean value of 7.98±1.98, patients with NSTDR had the mean value of 5.98±2.11 and average foveal slope of patients with STDR had the mean value of -2.22±9.99. It was found that there was significant shallowness of average foveal slope value of right eye with increase of severity of diabetes. The foveal slope found to be decreased with the increase of severity of diabetes. Average foveal slope for left eyes with No Diabetes had the mean value of 9.12±2.46, No DR patients had the value of 7.85±2.11, with NSTDR had the mean value of 6.38±3.20 and average foveal slope of patients with STDR had the mean value of -1.88±8.84.This was same as seen in right eye with increase in severity of diabetes, shallowness of slopes increased. There was significant shallowness of average foveal slope of both right and left eye of STDR patients when compared with patients of No Diabetes, DR and NSTDR (p=.000). Laxmi Gella et el<sup>13</sup> studied foveal slope configuration in subjects with type 2 diabetes. They found average foveal slope in No DR was 8.5±2.25, in NON-STDR was 8.09±2.23 and in STDR was 7.26±4.46.They found that the shallowness of slope increased with the severity of diabetes. It was in concordance with our study. On comparison of average foveal slope value of all quadrants (superior, nasal, inferior and temporal quadrant) of STDR patients with other category (No Diabetes , No DR,NSTDR) there was a significant shallowness of foveal slopes for both eyes and it was found to be significant.(p=.000).

When individual foveal slopes were compared with in different category patients, it was seen that the Temporal slope was shallowest as compared to other quadrants (-2.74±11) in the patients of STDR for right eye. In Left Eye, Nasal slope was

found to be shallowest (-2.42±10.98) in our study. We did not find any justification for the above finding.

## CONCLUSION

In general, there was a trend of shallowness of foveal slope in all quadrants with increase in the severity as well duration of DR. This was true for both right and left eye. Thus, sequential OCT with slope measurements may predict progression of DR as well sight threatening DR. We suggest that the multicentre trial by various centres who are dealing diabetic retinopathy patients shall prove and strengthen our observations.

### Declaration of patient consent

All authors certify that they have obtained all appropriate patient consent forms. Patients had given their consent in written for images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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