

ASSESSMENT OF MORPHOLOGY OF DIABETIC MACULAR EDEMA WITH OPTICAL COHERENCE TOMOGRAPHY AND ITS ASSOCIATION WITH VISUAL ACUITY IN KASHMIR

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ABSTRACT: PURPOSE: This study aimed to assess the severity of Macular Edema in patients with diabetic macular edema using Spectral Domain Optical Coherence Tomography (SD-OCT), a technique for high-resolution cross-sectional imaging of the retina and to describe various morphologic patterns of diabetic macular edema (DME) demonstrated by optical coherence tomography (OCT) and correlate them with visual acuity. **METHODS:** A total of 158 eyes of 100 patients with diabetic retinopathy were studied. Optical coherence tomograms were obtained in a radial spoke pattern centered on the fovea. Macular thickness was reported numerically as averages in each of nine regions. All patients with DME underwent OCT evaluation. The OCT scans were evaluated for the presence of diffuse retinal thickening (DRT), cystoid macular edema (CME), posterior hyaloidal traction (PHT), serous retinal detachment (SRD), and traction retinal detachment (TRD), the retinal thickness was measured and correlated with visual acuity. **RESULTS:** Optical coherence tomography was able to quantify the development of both foveal and extrafoveal macular thickening. The (Mean±SD) Central Macular thickness was (502.8±121.9) in eyes with NPDR and (534.3±152.1) in eyes with PDR. Foveal thickness measured by OCT was highly correlated with visual acuity. Two hundred two OCT scans of 158 eyes of 100 patients were identified. OCT revealed five morphologic patterns of DME: DRT (61.88%); CME (24.75%), SRD without PHT (6.93%); PHT without TRD (5.45%); PHT with TRD (0.99%). Increasing retinal thickness in all patterns was significantly correlated with worse visual acuity (P <0.05). **CONCLUSIONS:** Optical coherence tomography was a useful technique for quantifying macular thickness in patients with diabetic macular edema. DME exhibits five different morphologic patterns on OCT. There is a significant correlation between retinal thickness and visual acuity.

INTRODUCTION: Diabetic retinopathy is the progressive dysfunction of the retinal vasculature caused by hyperglycemia.¹

Diabetic retinopathy is a microangiopathy resulting from the chronic effects of the disease, and shares similarities with the micro vascular alterations that occur in other tissues vulnerable to diabetes mellitus such as the kidneys and the peripheral nerves. The best predictor of diabetic retinopathy is the duration of the disease.¹ The first 5 years of type 1 diabetes has a very low risk of retinopathy. However, 27% of those who have had diabetes for 5–10 years and 71–90% of those who have had diabetes for longer than 10 years have diabetic retinopathy.²

After 20–30 years, the incidence rises to 95%, and about 30–50% of these patients have proliferative diabetic retinopathy (PDR). Wisconsin Epidemiologic Study of Diabetic Retinopathy

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(WESDR) provides valuable information regarding both the prevalence and the risk factors associated with the development of diabetic retinopathy.

In the younger-onset group, which consists of patients whose age at diagnosis of diabetes was less than 30 years and who were taking insulin at the time of the examination (presumably those with type 1 diabetes), retinopathy, either proliferative or non-proliferative, was seen in 13% of patients with less than 5 years duration of diabetes and in 90% of patients with a duration of 10 to 15 years.³ PDR, the most vision-threatening form of the disease, is present in approximately 25% of patients with type 1 diabetes after a 15-year duration of the disease. For patients with an onset of diabetes at 30 years of age or older (those with type 2 diabetes) and a duration of diabetes less than 5 years, 40% of those taking insulin and 24% of those not taking insulin have retinopathy.⁴

These rates increase to 84% and 53%, respectively, with an increased diabetes duration of 15 to 19 years. PDR develops in 2% of patients with type 2 diabetes and duration less than 5 years and 25% of patients with duration of 25 or more years of diabetes. The prevalence of diabetic macular edema did not vary as much by diabetes type. The prevalence of diabetic macular edema is approximately 18% to 20% in patients with either type 1 or type 2 (insulin-taking) diabetes.

OPTICAL COHERENCE TOMOGRAPHY (OCT): OCT is a modern imaging technique for non-invasive and non-contact “in vivo” examination of the retina and the vitreoretinal interface on cross-section images or on a 3D image reconstruction, and for objective measurement of retinal thickness.⁵

Optical coherence tomographic imaging is analogous to B-scan ultrasound imaging, except that it uses light instead of sound.⁶ The interface between different ocular tissues can be determined by changes in reflective properties between the tissues. Current experimental ophthalmic OCT instruments provide more structural information than any other ophthalmic diagnostic technique.⁷

MATERIAL AND METHODS: This study was conducted in the Post Graduate Department of Ophthalmology, Government Medical College Srinagar, which is the sole referral tertiary care hospital for Kashmir Valley.

Study Design: Observational, Retrospective, Case series.

Study Duration: The Study was conducted from March-2012 to Oct-2013

Inclusion and Exclusion Criteria:

Inclusion Criteria: All patients with diagnosed Diabetic Retinopathy with macular edema except those mentioned in the exclusion criteria underwent Optical Coherence Tomography and topography of diabetic macular edema was assessed with the help of Spectral Domain Optical Coherence Tomography, a technique for high-resolution cross-sectional imaging of the retina.

Optical coherence tomograms were obtained in a radial spoke pattern centered on the fovea. Macular thickness was reported numerically as averages in each of nine regions. All patients with DME underwent line scan also.

Exclusion Criteria: Patients with macular edema due to other causes:

- Retinal vein occlusion.
- Hypertensive retinopathy.
- Radiation retinopathy.

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- Uveitis.
- Scleritis.
- Following cataract extraction.
- Following Nd: YAG Laser capsulotomy.
- Panretinal photocoagulation.
- Retinal dystrophies including retinitis pigmentosa, gyrate atrophy.
- Leukaemia.

Study Size and Data Collection: All the patients visited Department of Ophthalmology, Government Medical College Srinagar from March-2012 to October-2013 with diagnosis of Diabetic Macular Edema were included. The patients were selected as per inclusion and exclusion criteria. The patients were diagnosed on the basis of detailed history, comprehensive eye examination and appropriate investigations were done, which include:

- Visual acuity.
- Torch light examination.
- Slit lamp examination including 90D.
- Direct ophthalmoscopy.
- Indirect ophthalmoscopy.
- Fundus fluorescein angiography.
- Optical Coherence Tomography.

OBSERVATIONS AND RESULTS:

Age (Years)	Males		Females		Total		P-value
	n (48)	%	n (52)	%	n (100)	%	
≤20	1	2.08	4	7.70	5	5.0	0.182 (NS)
21-30	0	0.00	4	7.70	4	4.0	
31-40	2	4.17	4	7.70	6	6.0	
41-50	21	43.75	16	30.76	37	37.0	
51-60	19	39.58	21	40.38	40	40.0	
> 60	5	10.42	3	5.76	8	8.0	
Mean ± SD (Min; Max)	51.10 ±8.8 (18, 65)		46.65 ±12.3 (17, 65)		48.80 ±10.9 (17, 65)		

TABLE 1: Age and Gender Distribution of Study Subjects

Mann-Whitney U-Test

Table-1: Shows that the maximum number of patients in male (43.75%) was in the age group of (41-50) years with range (18-65) years and that in case of female (40.38%) were in the age group of (51-60) years with range (17-65) years. The (Mean ± SD) in case of male subjects was (51.10 ±8.8), in case of female subjects was (46.65 ± 12.3) and overall (Mean ± SD) was 48.80 ±10.9, Using Mann-Whitney U-Test, there was no significant difference as for as the age in male and female subjects is concerned, with p-value=0.182.

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Treatment	Frequency	% age
OHA	30	30.00
Insulin	22	22.00
Both	48	48.00
Total	100	100.00

TABLE 2: Treatment Modalities of Study Subjects

OHA → Oral Hypoglycemic Agents.

Table-2: Shows maximum number of Study Subjects (48 %) were on both (Insulin ± OHA), 30% of Study Subjects on OHA and 22 % on Insulin.

Region (<500 μm radius)	Group Name	(Mean±SD)	Mean Diff.	95.00% C.I.		Cal.t	P-Value
				Lower Limit	Upper Limit		
CENTRAL	NPDR	(502.8 ± 121.9)	-31.509	-80.80	17.79	-	0.21 (NS)
	PDR	(534.3 ± 152.1)					
Inner ring (1 DD radius)							
SUPERIOR	NPDR	(555.9 ±120.5)	-39.909	-89.25	9.43	-	0.11(NS)
	PDR	(595.8 ±156.9)					
INFERIOR	NPDR	(557.1 ±121.8)	-37.531	-87.27	12.21	-	0.14(NS)
	PDR	(594.7 ±157.0)					
TEMPORAL	NPDR	(553.4 ±119.8)	-45.000	-94.25	4.25	-	0.07(NS)
	PDR	(598.4 ±157.7)					
NASAL	NPDR	(573.8 ±120.2)	-44.648	-93.86	4.56	-	0.07 (NS)
	PDR	(618.5 ±156.3)					
Outer ring (2 DD radius)							
SUPERIOR	NPDR	(532.3 ±121.6)	-33.466	-82.97	16.04	-	0.18 (NS)
	PDR	(565.7 ±155.1)					
INFERIOR	NPDR	(532.1±122.8)	-33.847	-83.73	16.04	-	0.18 (NS)
	PDR	(566.0±155.5)					
TEMPORAL	NPDR	(527.9 ±122.1)	-40.193	-90.17	9.78	-	0.11 (NS)
	PDR	(568.1 ±158.9)					
NASAL	NPDR	(537.4±121.5)	-39.461	-89.09	10.17	-	0.11 (NS)
	PDR	(576.8 ±156.9)					
DD = disc diameter (1.5 mm); NPDR=non-proliferative diabetic retinopathy; PDR= proliferative diabetic retinopathy;							
TABLE 3: Statistical Analysis of Macular Thickness in Diabetic Eyes (NPDR = 124; PDR = 34)							

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Table-3: Shows, The (Mean \pm SD) Central Macular thickness was (502.8 \pm 121.9) in eyes with NPDR and (534.3 \pm 152.1) in eyes with PDR There were no significant differences in average thickness in any region (ETDR Regions) between eyes with NPDR and eyes with PDR, with p-value > 0.05, using independent samples t-test.

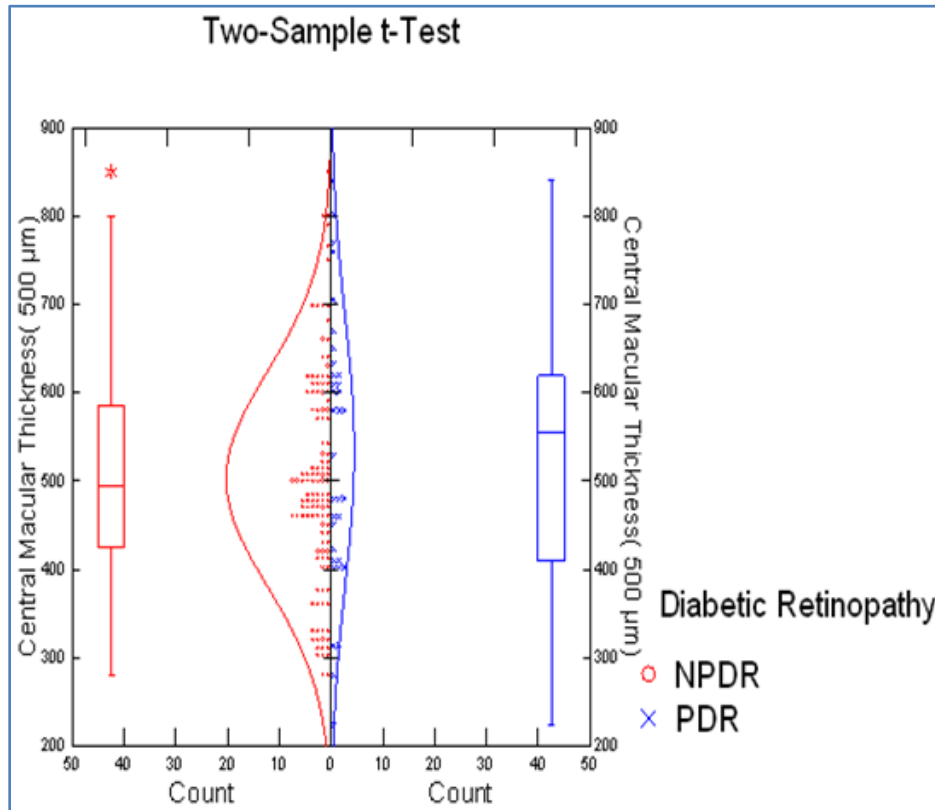


Figure 3

Foveal Thickness (microns)	Mean Visual Acuity (LogMAR)
< 300	0.325
300-400	0.60
400-500	0.80
500-600	0.87
600-700	0.972
700-800	1.11
> 800	2.0

ANALYSIS TABLE 4: Association of Foveal Thickness and Visual Acuity in Diabetic Eyes

Table 4 Shows association of foveal thickness and visual acuity in diabetic eyes, with increasing retinal thickness visual acuity decreases.

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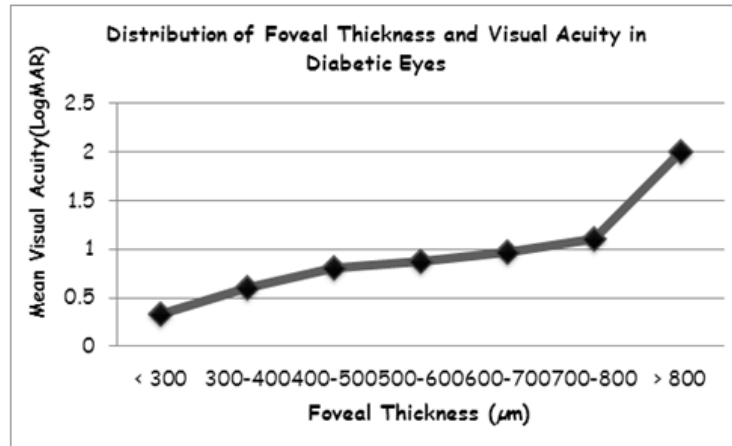


Figure 4

Variables	Means	Pearson Correlation Matrix	
		Foveal Thickness (µm)	VA_LogMAR
Fovial Thickness (µm)	518.99	1.00	
VA_LogMAR	0.872	0.81	1.00

ANALYSIS TABLE 5: Association of foveal thickness and visual acuity in diabetic eyes

Table-5: Shows relationship of optical coherence tomography measurements of Foveal thickness with Visual Acuity, using Pearson Product Moment Correlation Method in 158 eyes with NPDR and PDR. There is a Significant (Strong) Correlation between Foveal Thickness and Visual Acuity with coefficient of correlation ($r = 0.81$)

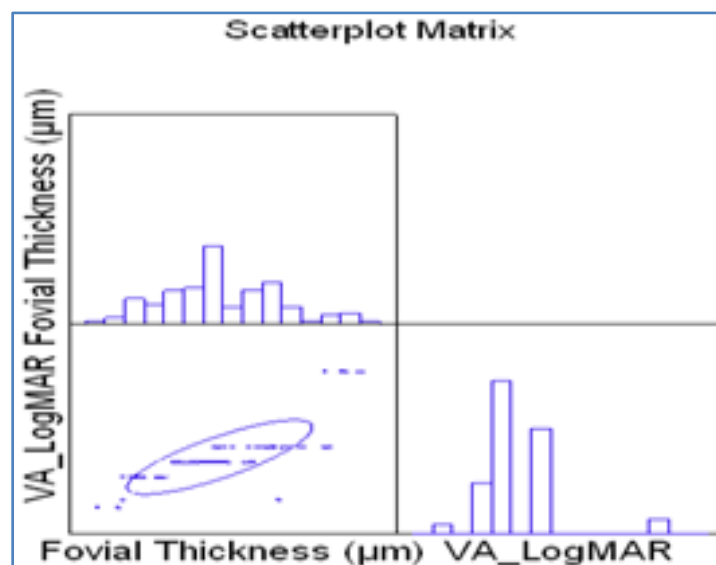


Figure 5

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Dependent Variable		n	Multiple R		Squared Multiple R	
Foveal Thickness (μm)		158	0.809		0.70	
Regression Coefficients $B = (X'X)^{-1}X'Y$						
Effect	Coefficient	S.E	Std. Coefficient	Tolerance	t	p-Value
CONSTANT	203.257	19.40	0.000	.	10.48	< 0.001
VA_LogMAR	362.013	21.10	0.809	1.00	17.16	< 0.001

ANALYSIS TABLE 6: Linear Regression Analysis

Linear Regression Analysis was used to explain the variation in the dependent variable (Foveal Thickness (μm)) and to see linear relation between Foveal Thickness and Visual Acuity.

Table-6: Shows comparison of optical coherence tomography measurements of Foveal thickness with Visual Acuity, using Linear Regression Method in 158 eyes with NPDR and PDR. There is a Significant linear relation between Foveal Thickness and Visual Acuity with ($R^2 = 0.70$) and P-Value < 0.001.

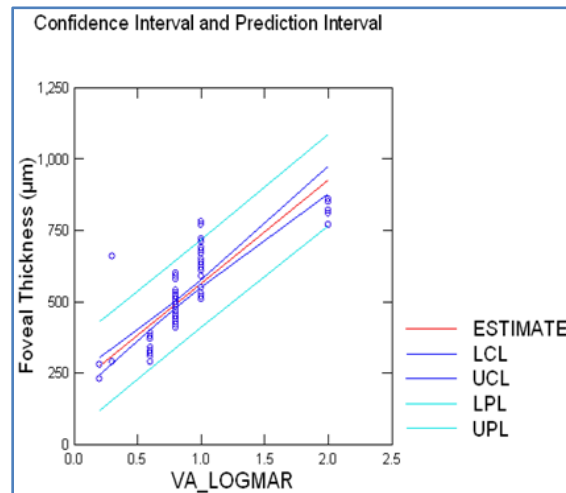


Figure 6

Morphological Sub-types	No of Scans (%age)	Mean Thickness (microns)	Range (microns)
DRT	125 (61.88)	526.32	(230 - 860)
CME	50 (24.75)	519.20	(310 - 820)
SRD Without PHT	14 (6.93)	570.71	(430 - 690)
PHT Without TRD	11 (5.45)	430.91	(290 - 660)
PHT With TRD	02 (0.99)	445.00	(420 - 470)

ANALYSIS TABLE 7: Association of Morphological Sub-types of Diabetic Macular Edema on Optical Coherence Tomographic Imaging With Macular Thickness

DRT→ Diffuse Retinal Thickness; CME→ Cystoid Macular Edema; SRD→Serous Retinal Detachment; PHT → Posterior HyaloidTraction; TRD→Tractional Retinal Detachment.

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Table-7: Shows that out of 202 scans, the most common morphological sub-type was DRT (61.88%) followed by CME (24.75%), SRD without PHT (6.93%) PHT without TRD (5.45%) PHT with TRD (0.99%). Maximum Mean Thickness was seen in SRD without PHT (570.71) microns.

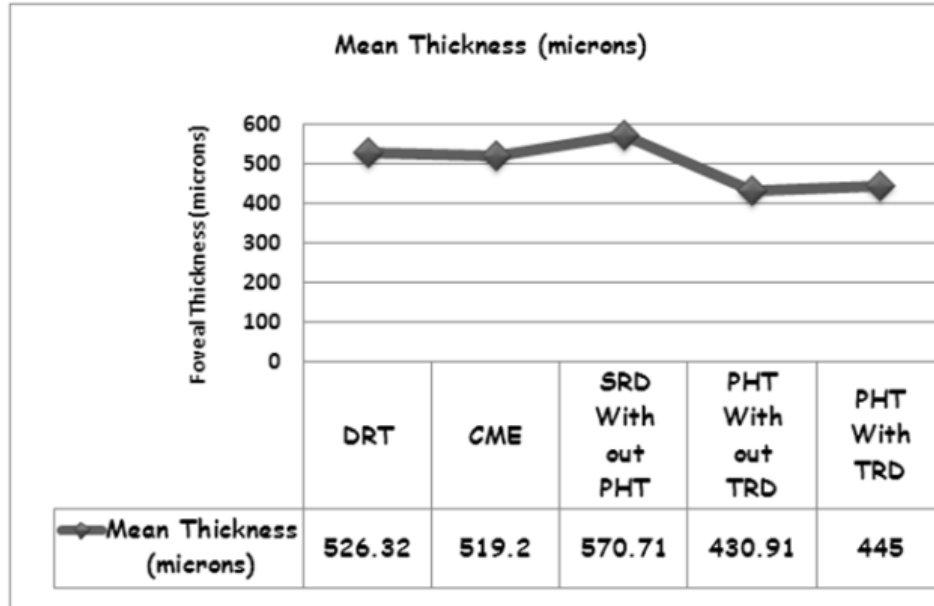


Figure 7

Morphological Sub-types	No. of Scans (%age)	Mean Visual Acuity (LogMAR)	Range (microns)
DRT	125 (61.88)	0.886	(0.2 - 2.0)
CME	50 (24.75)	0.844	(0.6 - 2.0)
SRD Without PHT	14 (6.93)	0.914	(0.8 - 1.0)
PHT Without TRD	11 (5.45)	0.673	(0.3 - 1.0)
PHT With TRD	02 (0.99)	0.800	(0.8- 0.8)

ANALYSIS TABLE 8: Association of Morphological Sub-types of Diabetic Macular Edema on Optical Coherence Tomographic Imaging With Visual Acuity

DRT→Diffuse Retinal Thickness; CME→ Cystoid Macular Edema; SRD→Serous Retinal Detachment; PHT→ Posterior Hyaloid Traction; TRD→Tractional Retinal Detachment

Table-8: Shows association of Morphological Sub-types of Diabetic Macular Edema on OCT Imaging with Visual Acuity (LogMAR).

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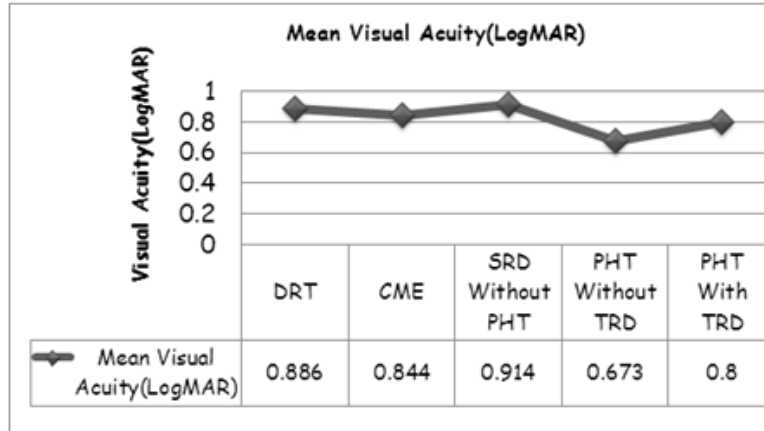


Figure 8

Dependent Variable		n	Multiple R		Squared Multiple R	
Central Macular Thickness (500 µm)		158	0.81		0.70	
Regression Coefficients $B = (X'X)^{-1}X'Y$						
Effect	Coefficient	S.E.	Std. Coef	Tolerance	t	p-Value
CONSTANT	198.01	19.10	0.00	.	10.37	< 0.001
VA_LogMAR	357.26	20.77	0.81	1.00	17.20	< 0.001

Table 9: Linear Regression Analysis

Linear Regression Analysis was used to explain the variation in the dependent variable (Central Macular Thickness (500µm)) and to see linear relation between Central Macular Thickness and Visual Acuity.

Table-9: Shows comparison of optical coherence tomography measurements of Central Macular thickness with Visual Acuity, using Linear Regression Method in 158 eyes with NPDR and PDR. There is a Significant linear relation between Central Macular Thickness and Visual Acuity with ($R^2 = 0.70$) and P-Value < 0.001.

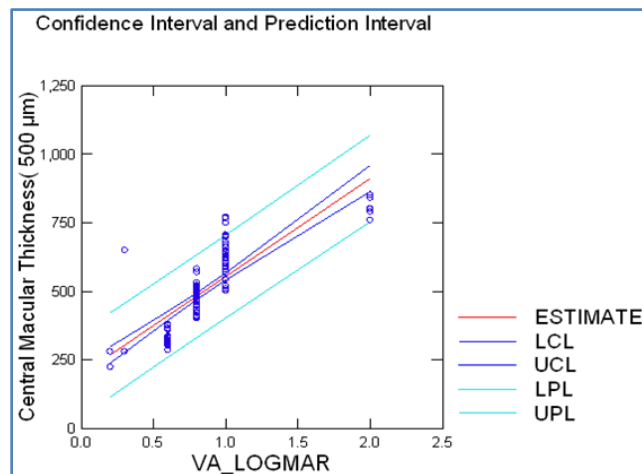


Figure 9

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DISCUSSION: Diabetic macular edema (DME) is one of the main causes of visual impairment in patients with diabetic retinopathy (Williams et al., 2004)⁸. The common diagnostic tools for assessing macular edema are stereo-ophthalmoscopy and fluorescein angiography. Fluorescein angiography is a complementary method for further detecting vascular leakage. However, these methods are subjective and seem to be insensitive for small changes in retinal thickness (Hee et al., 1995; Shahidi et al., 1991).⁹ In 1991 a revolutionary device was introduced in ophthalmology – optical coherence tomography (OCT) – and it dramatically improved the diagnosis of macular pathology (Huang et al., 1991).¹⁰

OCT provides detailed information about retinal microstructure and measures retinal thickness with high precision and reproducibility (Diabetic Retinopathy Clinical Research Network [DRCRN], 2007¹¹; Paunescu et al., 2004; Polito et al., 2005¹²Puliafito et al., 1995). The recently introduced spectral-domain OCT (SD OCT) machines have numerous improvements that enhance our ability to examine retinal microstructure and obtain more reliable measurements. The introduction of optical coherence tomography (OCT) further allows for objective evaluation of DME.¹³⁻¹⁶In addition, OCT produces cross-sectional images of the retina that have been found to correlate well with retinal histology as demonstrated by light microscopy.¹⁷

Our study was conducted on 100 patients diagnosed as Non Proliferative Diabetic Retinopathy (NPDR) and Proliferative Diabetic Retinopathy (PDR) on Fundus Fluorescein Angiography (FFA) and all the patients underwent Optical Coherence Tomography (OCT).

Our study highlights several important findings. In this study, maximum number of patients was aged above 50 years. The maximum number of patients in male (43.75%) was in the age-group of (41-50) years with range (18-65) years and that in case of female (40.38%) were in the age group of (51-60) years with range (17-65) years. The (Mean \pm SD) in case of male subjects was (51.10 \pm 8.8), in case of female subjects was (46.65 \pm 12.3) and overall (Mean \pm SD) was 48.80 \pm 10.9, Using Mann-Whitney U-Test, there was no significant difference as for as the age in male and female subjects is concerned, with p-value=0.182(Table-1).Maximum number of Study Subjects (48%) were on both (Insulin \pm OHA), 30% of Study Subjects on OHA and 22 % on Insulin (Table-2).

The (Mean \pm SD) Central Macular thickness was (502.8 \pm 121.9) in eyes with NPDR and (534.3 \pm 152.1) in eyes with PDR. There were no significant differences in average thickness in any region (ETDR Regions) between eyes with NPDR and eyes with PDR, with p-value >0.05, using independent samples t-test. (Table-3: fig: 3).Our finding is similar to the one reported by Michael R. Hee, et al.²⁰

Our study shows relationship of optical coherence tomography measurements of Foveal thickness with Visual Acuity in 158 eyes with NPDR and PDR. There is a Significant (Strong) Correlation between Foveal Thickness and Visual Acuity with coefficient of correlation ($r = 0.81$), using Pearson Product Moment Correlation Method (Table-5; fig: 5).

Our study shows out of 202 scans, the most common morphological sub-type was DRT (61.88%) followed by CME (24.75%), SRD without PHT (6.93%) PHT without TRD (5.45%) PHT with TRD (0.99%).Maximum Mean Thickness was seen in SRD without PHT (570.71) microns. (Table-7; fig: 7) Similar to the reports by Otani and Yamamoto,¹⁸⁻¹⁹ the most common subtype seen in our study was diffuse retinal thickening, being present in (61.88%) of the scans, compared with 88% in Otani's paper, and 60% in Yamamoto's study. CME in the setting of DME was also present in (24.75%) of eyes in our study compared with 47% CME rate noted by Otani, and 40% by Yamamoto.

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Malta Shahtn MD, Amal El-Bendary MD and Salah El-Bayed Mady MD found the most frequent pattern was DRT seen in 38 eyes (59.4%) followed by CME seen in 36 eyes (56.3%). Both DRT and CME were seen in 10 eyes (15.6%). SRD was seen in 18 eyes (28.1%). PHT was seen in 11 eyes (17.1%). PVD was seen in 14 eyes (21.9%).

Kim BY, Smith SD, Kaiser PK, described various morphologic patterns of diabetic macular edema (DME) demonstrated by optical coherence tomography (OCT) and correlate them with visual acuity. The OCT scans were evaluated for the presence of diffuse retinal thickening (DRT), cystoid macular edema (CME), posterior hyaloidal traction (PHT), serous retinal detachment (SRD), and traction retinal detachment (TRD). Additionally, the retinal thickness was measured and visual acuity evaluated. Two hundred seventy-six OCT scans of 164 eyes of 119 patients were identified.

OCT revealed five morphologic patterns of DME: DRT (269, 97%), CME (152, 55%), SRD without PHT (19, 7.0%), PHT without TRD (35, 12.7%), and PHT with TRD (8, 2.9%). Increasing retinal thickness in all patterns was significantly correlated with worse visual acuity ($P < .005$). DME exhibits at least five different morphologic patterns on OCT. There is a significant correlation between retinal thickness and visual acuity.

Tomohiro Otani, Shoji Kishi, Yasuhiro Maruyama (1999) showed three OCT patterns of diabetic macular edema: sponge-like retinal swelling (52 [88%] of 59 eyes), cystoid macular edema (28 [47%] of 59 eyes), and serous retinal detachment (9 [15%] of 59 eyes). Visual acuity with best correction moderately correlated with retinal thickness regardless of the different tomographic features.

Cho HY, Lee JH .analyzed the correlation between degree of visual acuity and macular thickening as well as the patterns of diabetic macular edema in OCT images. Cystoid macular edema (30 eyes, 54.5%), sponge-like retinal swelling (14 eyes, 25.5%), serous macular detachment (9 eyes, 16.4%), and macular edema with posterior hyaloid traction (2 eyes, 3.6%) were found in OCT. Combined finding were observed in 5 eyes. The foveal thickness and the log MAR scale of best corrected visual acuity showed a significantly positive correlation (correlation coefficient: 0.818, $p=0.01$).

There was no significant difference of visual acuity according to the patterns of diabetic macular edema. OCT appears useful for objectively monitoring of retinal thickness and tomographic changes in patients with diabetic macular edema and there is no correlation between the patterns in OCT images and best corrected visual acuity.

The OCT topographic map of retinal thickness generally correlated with conventional clinical examination. Retinal thickening or hard exudate observed on slit-lamp biomicroscopic analysis almost always correlated with increased thickness on OCT, but there were some occasions in which OCT detected thickening in the absence of any abnormality on slit-lamp examination. Both measurements of central macular thickness and measurements of foveal thickness averaged over a central disk of 500- μm radius appeared to be more sensitive than slit-lamp examination for evaluating clinically significant macular edema.

Edema was difficult to detect clinically when there was no hard exudate in the central macula. Optical coherence tomography retinal thickness also generally correlated with regions of fluorescein leakage; however, increased macular thickness occasionally was evident on OCT in the absence of leakage. Both single measurements of central foveal thickness and measurements averaged over the 500- μm central disc essentially were equivalent in detecting clinically significant thickening.

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Linear Regression Analysis was used to explain the variation in the dependent variable (Central Macular Thickness (500 μ m)) and to see linear relation between Central Macular Thickness and Visual Acuity. Comparison of optical coherence tomography measurements of Central Macular thickness with Visual Acuity, using Linear Regression Method in 158 eyes with NPDR and PDR was done. There is a Significant linear relation between Central Macular Thickness and Visual Acuity with ($R^2 = 0.70$) and P-Value < 0.001 (Table-9: fig: 9). Our finding is similar to the one reported by Michael R. Hee, et al.²⁰

Whatever the cause, identifying the structural changes in patients with DME using OCT may allow more effective management of these patients. We have identified at least five different morphologic patterns of DME using OCT including: DRT, CME, SRD without PHT, PHT without TRD, and PHT with TRD. Each of these morphologic subtypes may represent distinct entities that require specific treatment regimens to achieve the best final result. In addition to identifying each of these patterns, OCT may be useful not only in determining which treatment should be applied, but also in following the progress of this process over time.

CONCLUSION: Our Study shows that OCT has potential to screen patients with early NPDR for the development of macular thickness. Optical coherence tomography is an excellent tool for quantifying macular thickness in patients with diabetic macular edema. The (Mean \pm SD) Central Macular thickness was (502.8 \pm 121.9) in eyes with NPDR and (534.3 \pm 152.1) in eyes with PDR. There were no significant differences in average thickness in any region (ETDR Regions) between eyes with NPDR and eyes with PDR. Foveal thickness measured by OCT was highly correlated with visual acuity. DME exhibits five different morphologic patterns on OCT. There is a significant correlation between retinal thickness and visual acuity.

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