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RESEARCH ARTICLE

A STUDY TO CORRELATE OPTICAL COHERENCE TOMOGRAPHY PARAMETERS WITH VISUAL ACUITY IN PATIENTS WITH DIABETIC MACULAR EDEMA

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Abstract

Aims: To correlate various Optical Coherence Tomography (OCT) parameters with Visual Acuity (VA) in patients with Diabetic Macular Edema (DME). To determine which OCT parameter correlates more with Vision.

Design: It is a hospital based cross-sectional prospective study with 150 eyes of 120 patients done for a period of 3yrs.

Methods: Patients with DME were subjected to Spectral Domain (SD) - OCT imaging. Total 7 OCT parameters were analysed. Central Foveal Thickness (CFT), Intra-retinal cystoid spaces, Disorganization of Retinal Inner Layers(DRIL), Hyper-reflective foci(HRF), sub-foveal neuro sensory detachment, Ellipsoid Zone(EZ)disorganization, VitreoRetinal(VR)-interface abnormalities like Epiretinal Membrane(ERM), Vitreo Macular Adhesion(VMA) and Vitreo Macular Traction(VMT).

STATISTICAL ANALYSIS: The data was analyzed using SPSS version 29 statistical software. Pearson coefficient was used to test for correlations.

Results: Out of the 7 parameters measured a statistically significant correlation was found in 4 parameters with visual acuity. They are CFT(P=0.05), DRIL(p<0.001), EZ disruption (p<0.001), and HRF(p<0.001). Among the 7 parameters, DRIL was the most commonly seen but EZ disruption correlated more with a mean VA of logmar 1.45. Whenever HRF was found in outer retinal layers it was associated with EZ disruption(p<0.001).

Conclusion: The presence of CFT, DRIL, EZ disruption and HRF showed a statistical significant correlation with Vision. DRIL was the most commonly seen OCT parameter but the severity EZ disruption correlated more with worsening of VA.

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Introduction:-

Diabetes mellitus is an important concern for healthcare systems in the world. Diabetes is known to cause alterations in retinal microvasculature and retina that progressively lead to visual impairment.¹ The overall prevalence of DME in patients with Diabetic Retinopathy is 29%.² Diabetic Macular Edema results from the hyperglycemia-induced breakdown of the blood-retinal barrier which leads to fluid extravasation from retinal vessels into the surrounding

retinal tissue.³Optical coherence tomography (OCT) is a noncontact, noninvasive, in vivo, high-resolution, cross-sectional imaging of the eye that measures backscattered light. SD-OCT gives a higher axial resolution of $\approx 5\mu\text{m}$ and scans 20,000-40,000 A-scans per second.⁴ It works on the same principle as ultrasound B-mode imaging but uses light instead of sound.⁵Multiple studies have considered single OCT parameter and have established correlations with visual acuity. There are very few studies in literature that have considered all these parameters together and have correlated them with VA. In our study, we will correlate various OCT parameters together with Visual Acuity in DME and see which OCT parameter correlates more and which OCT parameter occurs more frequently, which will help in the future to narrow down the multiple OCT parameters so that one parameter can be used as a standard protocol in many upcoming treatment trials or while prognosticating vision while giving treatment.

Methods:-

It was a hospital-based cross-sectional prospective, an observational study done at a tertiary eye hospital. This study has obtained approval from institutional ethics review board.

Inclusion Criteria:

Patients with type 1 & 2 diabetes with macular edema were considered.

Exclusion Criteria:

Patients with other retinal diseases like Age Related Macular Degeneration(ARMD), Retinal Detachment, concurrent macular diseases, and other causes of macular edema other than Diabetes. Patients with significant media opacities and any associated ocular pathologies like uveitis or vitreous diseases. For all 120 patients, detailed history recording, demographic details, and prior treatments for DME like Panretinal Photocoagulation, Focal laser, intra-vitreous injections like triamcinolone, and anti-vegf were noted. The best corrected visual acuity was assessed initially in Snellen's and then converted to logMAR. Detailed ocular examination using Slit-lamp biomicroscopy, fundus evaluation by indirect ophthalmoscopy were done. Patients who were clinically diagnosed with DME were subjected to SD-OCT imaging.

Imaging:

DME was evaluated with SD-OCT(Cirrus™ HD-OCT (Carl Zeiss Meditec, Inc., Dublin, CA) for all 150 eyes. A 5-line HD RASTER scan with a signal strength of >5 was selected, Total of 3 readings from each scan was taken and the average of it was documented for each eye. All OCT parameters were assessed at 500μ on either side of the center of the fovea. Based on the morphology of Central foveal Thickness in OCT, it was categorized into Diffuse, focal, cystoid, with sub-retinal fluid and combined type. Few OCT parameters were sub-categorized and graded/grouped according to their severity.

The OCT parameters which were studied are as follows:-

1. Height of the central foveal thickness
2. Presence of intra-retinal cystoid spaces: group 0 – No cystoid spaces
group 1 – cystoid spaces of $<200\mu\text{m}$ in size
group 2 – cystoid spaces of $>200\mu\text{m}$ in size
3. Presence of Disorganization of retinal inner layers: grade 0 – NO DRIL
grade 1 - $<50\%$ DRIL is present
grade 2 - $>50\%$ DRIL is present
4. Presence of Retinal Hyper-Reflective Foci: group 0 – the absence of Hyper-Reflective Foci
group 1 - Hyper-Reflective Foci in inner retinal layers
group 2 - Hyper-Reflective Foci in outer retinal layers
5. Presence or absence of sub-foveal neurons-sensory detachment
6. Ellipsoid zone disruption:
grade 0 – EZ is intact
grade 1 - $<50\%$ OF EZ disruption
grade 2 - $>50\%$ OF EZ disruption
7. Presence of Vitreo-retinal interface abnormalities:group 0 – ABSENT VR ABNORMALITIES
Group 1 – presence of epiretinal membrane
Group 2 – presence of vitreomacular adhesion
Group 3 – presence of vitreomacular traction

Statistical Analysis:

The BCVA in Snellen measurements were converted to logMAR. The data was analyzed using SPSS version 29 statistical software. the descriptive values were expressed in mean±standard deviation. .We used the Pearson coefficient to test for correlations between Visual Acuity and various OCT parameters (linear variables). A p-value of 0.05 or less was considered statistically significant in the analyses.

Results:-

Descriptive characteristics of the study population are shown in the table. A total of 150 eyes from 120 patients were studied for a period of 3 years, with 68% males and 32% females. The mean age of the study population was 56.5 years with SD – 9yrs. The mean diabetes duration was 9 years with SD – 5.9yrs. All had type 2 diabetes. 36 pts also had hypertension. Mean visual acuity was logMAR 0.94 with SD of log0.4. Our study included a total of 120 patients. out of this, for 30 patients both eyes were considered, which accounted for a total of 60 eyes. For the rest 80 patients single eye was taken into consideration due to other eye having significant media opacities, no significant macular edema, VH, TRD. Diabetic Retinopathy Staging – 23 eyes had MILD NPDR, 68 eyes had MODERATE NPDR, 32 eyes had SEVERE NPDR, and 27 eyes had PDR. Few eyes had taken treatment priorly, 10 eyes had macular laser, 14 eyes had PRP, 1 eye had anti-vegf and 3 eyes had a previous history of intravitreal triamcinolone injection.

Correlation of Visual Acuity With oct Parameters:

1. Central Foveal Thickness showed a modest correlation with VA with a correlation coefficient of 0.272 and $p=0.05$
2. Intra-Retinal Cystoid Spaces showed a correlation of $p=0.14$, it was observed that mean VA decreased from log 0.88 to log 1 as the size of the cystoid spaces increased especially in outer retinal layers indicating photoreceptor damage caused by cystoid spaces.
3. DRIL had a correlation coefficient of 0.502 with $p<0.001$ showing statistical significance. It was observed as the severity of disorganization increases the mean VA decreases. At $<50\%$ DRIL mean VA was log0.89(62eyes) but at $>50\%$ DRIL mean VA was log1.34(23eyes)
4. HyperReflective Foci had a positive correlation coefficient of 0.335 with $p<0.001$ showing statistical significance. The HRF present in the outer retinal layers showed a mean VA of log 1.43(17eyes), indicating high severity even in less number of eyes
5. Sub-foveal Neuro-sensory Retinal Detachment did not show any statistical significant correlation with Visual Acuity ($p=0.929$),
6. Ellipsoid zone disruption showed a positive and strong correlation (0.670) with statistically significant $p<0.001$. As the percentage of EZ disruption increased the mean VA decreased. At $<50\%$ disruption VA was log 0.91 but at $>50\%$ disruption VA was log 1.45. An association with a statistically significant correlation was found between HRF and EZ disruption ($p<0.001$)
7. VR abnormalities did not show statistical significance ($p=0.076$) but the mean VA was less in VMA (log1.14) and VMT (log1.27.) Among the OCT parameters observed, DRIL was most commonly found (85eyes). HRF in 67 eyes, Cystoid spaces were seen in 64 eyes, EZ disruption in 63 eyes Hard exudates in 61 eyes, and VR abnormalities in 32 eyes.

Descriptive Characteristics of The Study Population

Total number of study participants	n=120
Total number of eyes	150
Age - mean(SD)	56.5(9 years)
Gender	82 males(68%) 38 females(32%)
Diabetes Mellitus duration - mean(Standard Deviation)	9(5.9 years)
Hypertension	36 pts(30%)
Diabetic Retinopathy Staging	
MILD NPDR	23eyes
MODERATE NPDR	68 eyes
SEVERE NPDR	32 eyes
PDR	27 eyes
Previous Laser/ Surgery	
Macular laser	12 eyes
PRP	15 eyes
S/P Anti-VEGF	3 eyes
S/P IVTA injection	6 eyes
VA - mean log (SD)	Log 0.94 (SD log 0.4)

Statistical Analysis Of Oct Parameters And Their Correlation With Visual Acuity

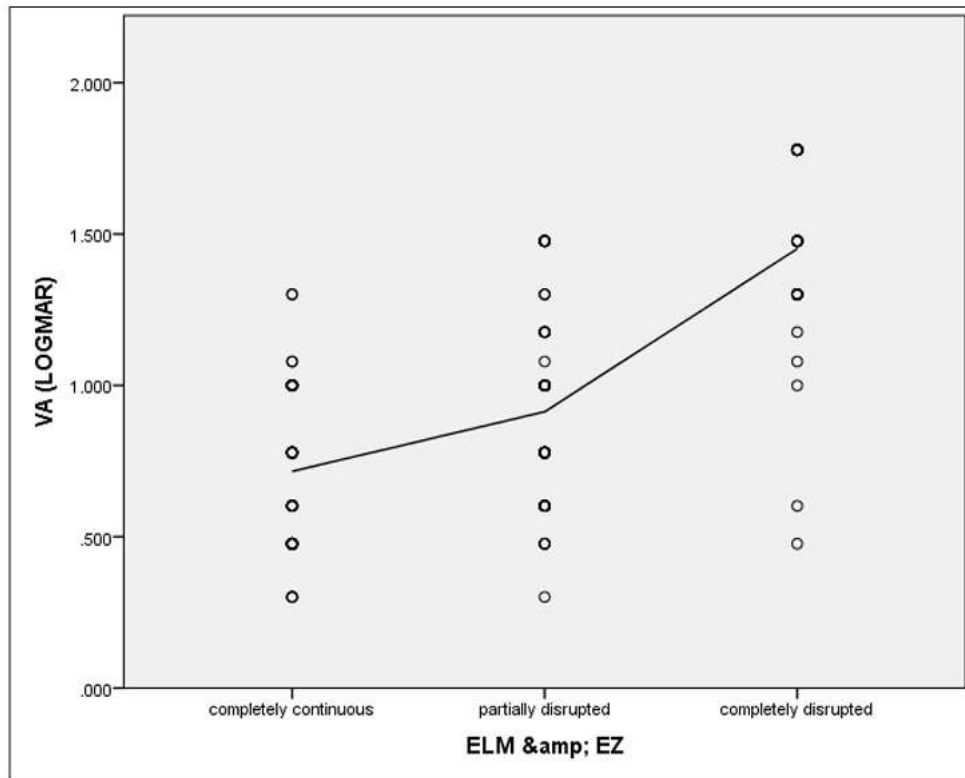
SL NO	OCT parameters	Mean VA (SD)	Correlation Coefficient	P value
1.	CENTRAL FOVEAL THICKNESS PATTERN OF DME COMBINED CYSTOID DIFFUSE FOCAL SUBFOVEAL NSRD	log 0.94(0.4) log 1.04 log 0.94 log 0.94 log 0.81 log 0.80	0.272	P=0.05
2.	INTRA-RETINAL CYSTOID SPACES Absent <200µm >200µm	log 0.88 log 0.98 log 1.00	0.120	P=0.143
3.	DRIL Absent <50% DRIL >50% DRIL	log 0.73 log 0.89 log 1.34	0.502	P<0.001
4.	HYPERREFLECTIVE FOCI Absent HRF in Inner Retinal Layers HRF in Outer Retinal Layers	log 0.83 log 0.88 log 1.43	0.335	P<0.001
5.	SUB-FOVEAL NEUROSENSORY DETACHMENT Absent Present	Log 0.95 Log0.94	0.007	P=0.929
6.	Ellipsoid Zone disruption Absent <50% disruption >50% disruption	log 0.71 log 0.91 log 1.45	0.670	P<0.001
7.	Vitreo-Retinal Abnormalities Absent ERM VMA VMT	log 0.85 log 0.93 log 1.14 log 1.27	0.145	P=0.76

The above table shows all the seven parameters, their sub-classification and their correlation with the vision in logmar which is represented as statistical significance using p value .

Most Common Oct Parameters Observed

OCT PARAMETER	FREQUENCY (NO OF EYES)
INTRA-RETINAL CYSTOID SPACES	82
DISORGANIZATION OF RETINAL INNER LAYERS	108
RETINAL HYPERREFLECTIVE FOCI	85
SUB-FOVEAL NEUROSENSORY DETACHMENT	31
ELLIPSOID ZONE DISRUPTION	90
VITREO RETINAL ABNORMALITIES	46

Table shows frequency of occurrence of OCT parameters in the total number of Eyes studied.



Graph -1 , Scatter plot showing correlation between visual acuity and ellipsoid zone disruption, as the severity of disruption increases- the vision worsening is seen

Discussion:-

Studies have shown a modest correlation with Central foveal Thickness^{6,7} and not a true reliable marker for prognosticating visual acuity in DME. In our study there was only moderate correlation with CFT and VA(p=0.005). Other parameters like cystoid spaces, sub-foveal neurosensory detachment, VitreoRetinal abnormalities did not show any statistical significant correlation with Visual Acuity. Some of the other parameters like DRIL^{8,9} have shown significant correlation. It has been hypothesized that disorganization of the inner retina occurs when bipolar axons snap when their elasticity limit has been exceeded because of edema. It has also been suggested that DRIL represents a loss of bipolar, amacrine, or horizontal cells within the inner retinal layers.⁹ In our study we noted in the center involving DME, DRIL showed statistical significance with VA (p<0.001) which is comparable with previous

studies^{8,9}. We observed that as the severity of DRIL increased, the mean Visual Acuity decreased(log 1.34) and DRIL was the most commonly found OCT parameter.

Studies have shown significant correlation of VA with Ellipsoid zone disruption^{10,11}. We noted that Ellipsoid zone disruption was also associated with poor VA, and our findings are consistent with those from previous studies.¹¹ Ellipsoid Zone represents photoreceptor integrity. The External Limiting Membrane separates the layers of rods and cones from the overlying outer nuclear layer and is a linear confluence of junctional complexes between Muller cells and photoreceptors(EZ).¹² EZ disruption showed a statistically significant correlation with VA($p < 0.001$). It also showed the strongest correlation to VA among all the OCT parameters. As the severity increased the mean VA decreased (log1.45)

Some studies have quantified the disruption¹⁰ and have measured PROS length¹¹. Few studies have shown the presence of hyperreflective foci as a predictor of poor VA.^{13, 14} HyperReflectiveFoci are inflammatory biomarkers representing extravasated protein and/or lipid deposits, precursors of hard exudates, or may represent activated microglial cells. This showed a statistically significant correlation with VA($p < 0.001$). HRF present in the outer retinal layers showed a mean VA of log 1.43 indicating and also an association between EZ disruption and HRF in Outer Retinal Layers was found indicating that HRF, as it migrates from inner to outer retinal layers causes damage to the photoreceptor layer as shown by Uji et al in his study. Among the various OCT parameters studied, DRIL, HRF IN ORL, and EZ disruption correlated more with VA. Hence, these parameters should be considered in the future for clinical decision-making, the timing of therapeutic intervention, and for prognosticating the disease. Since DRIL was more common it would ideal to use DRIL as a standard parameter in any future large clinical trials but since the strongest correlation was found with EZ disruption, this would be ideal for experimental studies. Our study had an advantage of being prospective in nature.

Conclusion:-

Hence, according to our study, the presence of DRIL, presence of hyper-reflective foci especially in the outer-retinal layers and External Limiting Membrane and Ellipsoid Zone disintegrity correlated more with worsening of visual acuity. DRIL was most commonly seen OCT parameter, EZ disruption correlated more when compared to other parameters

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