National Journal of Medical and Allied Sciences

[ISSN Online: 2319 – 6335, Print: 2393 – 9192|Original article |Open Access]

Website:-www.njmsonline.org

CORRELATION BETWEEN MACULAR THICKNESS AND VOLUME WITH VISUAL ACUITY IN DIABETIC MACULAR EDEMA BY USING DOMAIN OPTICAL COHERENCE TOMOGRAPHY

Ajnas C.P[1], Muhemmed Swadique[2], J Muthiah[3], Rajesh P[4]

1. Resident in Ophthalmology, Al Salama Eye Hospital, Perinthalmanna 2. Professor of Ophthalmology, MES Medical College, Perinthalmanna. 3. Professor of Ophthalmology, Al Salama Eye Hospital, Perinthalmanna. 4. Consultant in VR services, Al Salama Eye Hospital, Perinthalmanna.

ABSTRACT

Introduction: To investigate the correlation between Macular thickness and Volume with Best-corrected visual acuity (BCVA) in eyes with Diabetic macular edema and Type 2 diabetes.

Materials and Methods: A retrospective study including 60 eyes of 60 patients evaluating Retinal thickness and macular volume measured with Spectral Domain Optical Coherence Tomography and best corrected visual acuity was measured with the Snellens Chart.

Results: There is significant increase in the macular thickness and macular volume with decrease in the best corrected visual acuity.

Conclusion: Diabetic macular edema causes decrease in visual acuity due increase in macular thickness and volume.

Keywords: Diabetic retinopathy, Diabetic macular edema (DME), Optical coherence tomography (OCT), BCVA (Best corrected visual acuity)

Corresponding Author: Dr. Ajnas C.P, Al Salama Eye Hospital, Email: swadique@gmail.com

INTRODUCTION

Diabetic retinopathy is the leading cause of blindness in working aged adults. Diabetic macular edema (DME) has been reported at rates of 10% and occurs more frequently in type 2 diabetes mellitus than in type1. Diabetic patients also have multiple risk factors for retinopathy such as hyperglycemia and hypertension [(1)]. Their visual acuity is often dependent the central foveal involvement, perifoveal capillary blood flow velocity, severity of perifoveal capillary occlusion, and retinal thickness at the central fovea [(2,3)] .The clinical findings of diabetic retinopathy are microaneurysms, soft exudates, accumulation of hard exudates, and neovascularisation. Macular edema can develop at any stage of diabetic retinopathy. Optical coherence tomography (OCT) has been used for detection of macular edema secondary to different pathologies, such as diabetes mellitus, central or branched retinal vein occlusion, uveitis, and age related macular degeneration [(4-10)]. Treatment of diabetic macular edema is readily available and management guidelines of diabetic macular edema have largely evolved around the use of new laser machines, newer pharmacological agents such as antivascular endothelial growth factors (anti-VEGF), and different steroid preparations [(11,12)]. In the past decade, the evaluation of treatment efficacy was mainly based on visual acuity measurements and the detection of structural improvement on optical coherence tomography (OCT) scans. Undoubtedly, the fast, objective, and noninvasive OCT has emerged into a valuable tool, not only in DME, but also in other macular diseases such as age-related macular degeneration (AMD) and central serous chorioretinopathy. However, the correlation between OCT measured

variables and visual acuity has not been well established. Although reports have shown good correlation of OCT measured macular changes with vision, there were also reports that produced contradicting results [13].Ophthalmologists have associated diabetic macular edema (DME) and a reduction in visual acuity for decades [14].It is well established that treatments that reduce DME can improve or stabilize visual acuity ([15-17]. Using optical coherence tomography (OCT), it is now possible to measure objectively macular thickness and investigate quantitatively the relationship of DME and visual acuity The introduction of OCT allows an objective evaluation of DME with effectiveness in both qualitative and quantitative description of this pathology. That is why it becomes a standard tool in the management of patients with DME [18]. More than ten years after ETDRS, OCT greatly enhanced our ability to detect macular thickening and has brought new insights on the morphology of DME and on the presence of vitreo-retinal interface abnormalities. With the precise and useful data given by OCT, we can better diagnose, catalogue and follow DME. OCT also provides quantitative retinal thickness data, which are useful to monitor retinal changes in clinical and research settings. The use of the OCT was incorporated in the work routine of the ophthalmologist after studies demonstrated its collaboration on the detection of the disease. Besides confirming diagnostic impressions, the OCT monitors the pharmacological treatment of the macular edema and follows its progression [19]. The introduction of the spectral domain OCT improved the clinical value of the evaluation of eyes with macular diseases, among them the DR. With advanced technology, the CirrusTM SD-OCT (spectral domain) acquires data 70 times faster (27.000 versus 400 A-scans per second) and with higher resolution (5 μm versus 10 μm of axial resolution in tissue) than previous versions.OCT is a noninvasive imaging technique used to obtain high resolution cross sectional images of the retina. It was not available at the time of the EDTRS study. The macular edema extent was determined by bio-microscopy examination or inspection of stereoscopic photographs and was based only on the area of thickening, and not on the magnitude of the axial thickness. Variations in the amount of stereopsis present in paired stereo photographs or in the threshold for thickening adopted by the observer may further complicate the accurate and reproducible detection of areas of edema. Thus, there is potential for considerable variability and possible lack of sensitivity in prior art methods for identifying macular edema that were used in previous clinical studies

MATERIAL AND METHODS

This is a retrospective trial including 60 eyes of 60 patients was studied in the Department of Retina of Al Salama eye hospital, an associate institution of MES Medical college, Perinthalmanna, Kerala. As the study involved sophisticated and expensive equipment the sample size could not be enhanced. Institutional ethical committee approval was obtained. Retinal thickness and volume measured with spectral domain high-definition optical coherence tomography(Cirrus HD-OCT (Carl Zeiss Meditec, Dublin, California, USA)and best-corrected visual acuity (BCVA) in each eye was assessed using Snellen's Vision chart at 6 m distance. Sixty numbers of eyes taken for the study they classified in to three groups based on macular thickness, macular volume and BCVA .Both males and females are considered. Patients without any other ocular disease/systemic disease/ .All scans of signal strength above 5 and those diagnosed with newly developed macular edema was included. Patients who underwent any intraocular surgery or laser photocoagulation in past 3 months have been excluded. Also those cases with dense media opacities like cataract/corneal opacity and whose scan signal strength less than 5 was also excluded. All patients underwent a complete eye examination including assessment of visual acuity (unaided and best corrected) using Snellens chart, intra ocular pressure by Non Contact Tonometer and Slitlamp and fundus examination with IDO, OCT for macular thickness. OCT scans were performed after dilating the 60 eyes of 60 participants. The measurements were executed 2 times according to a OCT protocol developed at the ophthalmology out patients clinic of Al Salama Eye Hospital in the participants who could cooperate well with a signal strength of 5 or higher were required. In participants where the measurements were more difficult we tried to

have as much good measurements as possible. All measurements were executed by the same persons.

Statistical Methods[20 – 24] **:** Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made, Assumptions: 1.Dependent variables should be normally distributed, 2.Samples drawn from the population should be random, Cases of the samples should be independent

Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients,

Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

Pearson correlation between study variables is performed to find the degree of relationship

Classification of Correlation Co-efficient (r)

Up to 0.1 Trivial Correlations
0.1-0.3 Small Correlation
0.3-0.5 Moderate Correlation
0.5-0.7 Large Correlation
0.7-0.9 V. Large Correlation
0.9- 1.0 Nearly Perfect correlation
1 Perfect correlation

Significant figures

+ Suggestive significance (P value: 0.05<P<0.10)
* Moderately significant (P value: 0.01<P ≤ 0.05)
** Strongly significant (P value: P≤0.01)

Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1 ,Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

RESULTS

In this study for the correlation between best corrected visual acuity and macular thickness and macular volume. Of the total 60 eyes studied, 21 (35%), 29(48.3%), 10(16.7%) of the patients falls in the category of 6/6-6/9, 6/12-6/18 and 6/24-6/60 of BCVA respectively. In comparison to the macular thickness, the highest number of patients with BCVA of 6/6-6/9 was 12(58.3%) and they are having macular thickness of (300-400) with only 2(13.3%) had thickness (>400). In patients with BCVA 6/12-6/18 highest number was 17(51.5%) and they had thickness of (300-400), 5(41.7%) had thickness of (<300) and 7(46.7%) had thickness of (>400). In patients with BCVA of 6/24-6/60 most patients 6(40%) had thickness of (>400), 0(0%) had thickness (<300) and 4(12.1%) had thickness (300-400) (Graph1)

In comparison to macular volume, the highest number of patients with BCVA of 6/6-6/9 was 17(37%) and they are having macular volume of (10-15mm^3), no patients had volume (15-20mm$^{3)}$ (Table 1). In patients with BCVA 6/12-6/18 most patients 23(50%) had volume of (10-15mm^3) and only 2 (33.3%) patients has volume (15-20mm$^{3)}$ (Table 2). In patients with BCVA of 6/24-6/60 most patients 6(66.7%) had volume of (10-15mm^3), 4(13%) had volume (15-20mm$^{3)}$ and no patients had volume (<10mm$^{3)}$ (Graph2). The average thickness found was 317.00±84.29, 376.70±84.96 and 572.67±98.52 in categories of <300, 300-400 and >400 of macular thickness respectively (Table 3). And the correlation with change in BCVA was found to be statistically significant (p <0.001) (Table 4).

The average volume found was 8.93±1.10, 11.42±1.13 and 16.92±1.66 in categories of <10mm^3, 10-15mm^3 and 15-20mm^3 of macular volume respectively. And the correlation with change in BCVA was found to be statistically significant (p <0.001). Fisher Exact test has been used to find the significance of study parameter and Pearson correlation between study variables is performed to find the degree of relationship.

Table 1: Vision distribution in relation to Volume levels

Vision	**Volume**			**Total**
	<10mm3	**10-15mm3**	**15-20mm3**	
6/6-6/9	4(50%)	17(37%)	0(0%)	21(35%)
6/12-6/18	4(50%)	23(50%)	2(33.3%)	29(48.3%)
6/24-6/60	0(0%)	6(13%)	4(66.7%)	10(16.7%)
Total	8(100%)	46(100%)	6(100%)	60(100%)

P=0.023*, Significant, Fisher Exact test

Table 2: Vision distribution in relation to Macular thickness levels

Vision	Macular thickness			Total
	<300	300-400	>400	
6/6-6/9	7(58.3%)	12(36.4%)	2(13.3%)	21(35%)
6/12-6/18	5(41.7%)	17(51.5%)	7(46.7%)	29(48.3%)
6/24-6/60	0(0%)	4(12.1%)	6(40%)	10(16.7%)
Total	12(100%)	33(100%)	15(100%)	60(100%)

P=0.031*, Significant, Fisher Exact test

Table 3: Volume and macular thickness

Variables	Volume			Total	P value
	<10mm3	10-15mm3	15-20 mm3		
Volume	8.93 ±1.10	11.42 ±1.13	16.92 ±1.66	11.64 ±2.28	<0.001**
Macular thickness	317.00 ±84.29	376.70 ±84.96	572.67 ±98.52	388.33 ±106.87	<0.001**

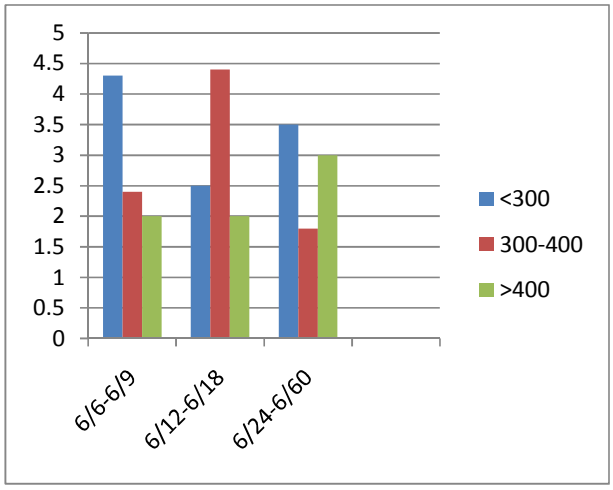
Table 4: Pearson correlation

pair	r value	P value
Age in years **vs** Volume	-0.085	0.517
Age in years **vs** Macular Thickness	-0.034	0.799
Volume **vs** Macular Thickness	0.685	<0.001**

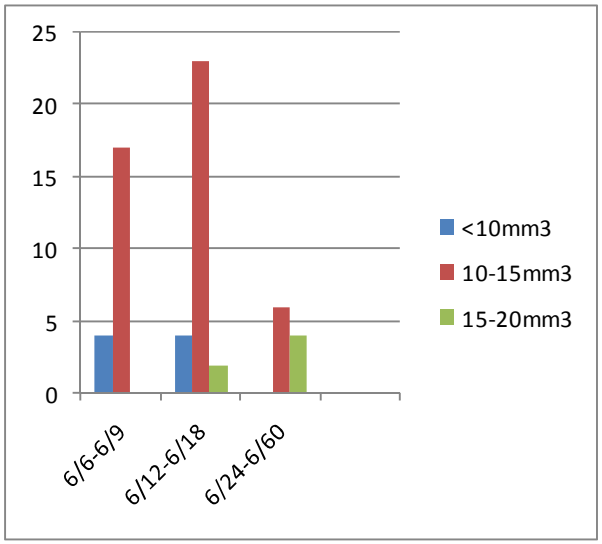
Pearson correlation

Table 5: Volume and macular thickness according to vision

Variables	Vision			Total	P value
	6/6-6/9	6/12-6/18	6/24-6/60		
Volume	10.64±1.47	11.44±1.86	14.30±2.88	11.64±2.28	<0.001**
Macular thickness	328.62±60.40	389.14±92.64	511.40±122.13	388.33±106.87	<0.001**



Graph1: Vision distribution in relation to Macular thickness levels



Graph 2: Vision distribution in relation to Macular volume levels

DISCUSSION

Diabetic macular edema (DME), being a complication of diabetes, is an important cause of visual loss in developed countries. There are different treatments that can delay this impairment. The most commonly accepted pathophysiological theory for DR is the microvascular dysfunction. Changes in the glucose metabolism lead to alterations in the retinal capillaries and to the hematoretinal barrier break, resulting in microaneurysms, hemorrhages and exudates, which in turn lead to detectable retinal thickening in the OCT.A comprehensive understanding of the various OCT measured parameters in DME and its clinical implications is

yet to be determined. The advancement in optical coherence tomography (OCT) technologies including the increase in speed of scanning and higher axial resolution (up to ~3 microns for certain OCT machines) has made visualization of the retinal microstructures possible [24, 25]. Reports have looked into the morphological changes happening in the outer retinal hyperreflective bands in subjects with various retinal diseases. The integrity of the inner segment/outer segment (IS/OS) junction has been found to correlate well with visual acuity in subjects with retinal conditions such as retinitis pigmentosa and post macular hole operation [26,27]. Otani et al. investigated the correlation of best-corrected visual acuity with foveal microstructural changes of the external limiting membrane and the junction between the inner and outer segments (IS/OS) of the photoreceptors in DME. It is not possible to know if the average photoreceptor outer segment length shortening observed in DME is caused by multiple points of localized breakdown of the IS/OS junction or from generalized thinning of the photoreceptor outer segment. The reasons can be explained based on what is known about the pathophysiology of this disease, such as tissue ischemia, lipid and fluid exudation and accumulation of toxic metabolic waste products and inflammatory mediators in DME. The visual acuity not always is improved after treatments of the macular edema, which suggests that macular thickness is only one of the factors that worsen the visual function. That means that quantitative measurements may not explain all variations in visual acuity, therefore, other factors including macular ischemia and retinal cell function might be important as well. Study by Tomohirotani et al. explained that the best-corrected visual acuity was strongly associated with the external limiting membrane and inner and outer segments of the photoreceptor. Also study by K Okada, S Yamamoto, et al conducted on study on correlation of retinal sensitivity measured with fundus-related micro perimetry to visual acuity and retinal thickness in eyes with diabetic macular edema. The mean sensitivities in the central 2° and 10° were significantly lower in patients with DME than in normal subjects

CONCLUSION

This study proved that there is significant correlation between increase in the macular thickness and macular volume with decrease in the best corrected visual acuity in patients with diabetic macular edema

ACKNOWLEDGEMENT

The authors would like to thank Dr.K.P.Suresh, Scientist (Biostatistics), National Institute of Veterinary Epidemiology and Disease Informatics (NIVEDI), Bangalore for his contributions to the statistical methods and guiding analysis.

REFERENCES

1.Girach A, Lund-Andersen H. Diabetic macular oedema: a clinical overview. International Journal of Clinical Practice. 2007;61(1):88-97.

2.Gardner T, Larsen M, Girach A, Zhi X. Diabetic macular oedema and visual loss: relationship to location, severity and duration. Acta Ophthalmologica. 2009;87(7):709-713.

3.Sakata K, Funatsu H, Harino S, Noma H, Hori S. Relationship of Macular Microcirculation and Retinal Thickness with Visual Acuity in Diabetic Macular Edema. Ophthalmology. 2007;114(11):2061-2069.

4.Yahia S, Kahloun R, Jelliti B, Khairallah M. Branch Retinal Artery Occlusion Associated with BehÃ§et Disease. Ocular Immunology and Inflammation. 2011;19(4):293-295.

5.Ogino K, Tsujikawa A, Nakamura H, Miyamoto K, Murakami T, Muraoka Y et al. Focal Macular Electroretinogram in Macular Edema Secondary to Central Retinal Vein Occlusion. Investigative Opthalmology & Visual Science. 2011;52(6):3514.

6.Browning D. Comparison of the clinical diagnosis of diabetic macular edema with diagnosis by optical coherence tomography*1. Ophthalmology. 2004;111(4):712-715.

7.Ibrahim M, Sepah Y, Symons R, Channa R, Hatef E, Khwaja A et al. Spectral- and time-domain optical coherence tomography measurements of macular thickness in normal eyes and in eyes with diabetic macular edema. Eye. 2011;26(3):454-462.

8.Medina F, CallÃ©n C, Rebolleda G, MuÃ±oz-Negrete F, CallÃ©n M, del Valle F. Use of Nonmydriatic Spectral-Domain Optical Coherence Tomography for Diagnosing

Diabetic Macular Edema. American Journal of Ophthalmology. 2012;153(3):536-543.e1.
9. Suzuma K, Yamada Y, Liu M, Tsuiki E, Fujikawa A, Kitaoka T. Comparing central retinal thickness in diabetic macular edema measured by two different spectral-domain optical coherence tomography devices. Japanese Journal of Ophthalmology. 2011;55(6):620-624.
10. Kwon S, Hwang D, Seo J, Park I. Evaluation of Changes of Macular Thickness in Diabetic Retinopathy after Cataract Surgery. Korean Journal of Ophthalmology. 2011;25(4):238.
11. K. Luttrull J, Dorin G. Subthreshold Diode Micropulse Laser Photocoagulation (SDM) as Invisible Retinal Phototherapy for Diabetic Macular Edema: A Review. Current Diabetes Reviews. 2012;8(4):274-284.
12. Elman M, Bressler N, Qin H, Beck R, Ferris F, Friedman S et al. Expanded 2-Year Follow-up of Ranibizumab Plus Prompt or Deferred Laser or Triamcinolone Plus Prompt Laser for Diabetic Macular Edema. Ophthalmology. 2011;118(4):609-614.
13. Relationship between Optical Coherence Tomographyâ€"Measured Central Retinal Thickness and Visual Acuity in Diabetic Macular Edema. Ophthalmology. 2007;114(3):525-536.
14. Meyer-Schwickerath G, Schott K. Diabetic Retinopathy and Photocoagulation. American Journal of Ophthalmology. 1968;66(4):597-603.
15. Photocoagulation for Diabetic Macular Edema. Archives of Ophthalmology. 1985;103(12):1796.
16. Patelli F, Fasolino G, Radice P, Russo S, Zumbo G, Di Tizio F Et Al. Time Course Of Changes In Retinal Thickness And Visual Acuity After Intravitreal Triamcinolone Acetonide For Diffuse Diabetic Macular Edema With And Without Previous Macular Laser Treatment. Retina. 2005;25(7):840-845.
17. Knudsen L. Retrobulbar Injection Of Methylprednisolone In Diffuse Diabetic Macular Edema. Retina. 2004;24(6):905-909.
18. Massin P, Girach A, Erginay A, Gaudric A. Optical coherence tomography: a key to the future management of patients with diabetic macular oedema. Acta Ophthalmologica Scandinavica. 2006;84(4):466-474.
19. Browning D, Fraser C. The Predictive Value of Patient and Eye Characteristics on the Course of Subclinical Diabetic Macular Edema. American Journal of Ophthalmology. 2008; 145(1):149-154.e3.
20. Bernard Rosner (2000), Fundamentals of Biostatistics, 5th Edition, Duxbury, page 80-240
21. Robert H Riffenburg (2005) , Statistics in Medicine , second edition, Academic press. 85- 125.
22. Sunder Rao P S S , Richard J(2006) : An Introduction to Biostatistics, A manual for students in health sciences , New Delhi: Prentice hall of India. 4th edition, 86-160
23. Suresh K.P. and Chandrasekhar S (2012). Sample Size estimation and Power analysis for Clinical research studies. Journal Human Reproduction Science,5(1), 7-13.
24. Srinivasan V, Monson B, Wojtkowski M, Bilonick R, Gorczynska I, Chen R et al. Characterization of Outer Retinal Morphology with High-Speed, Ultrahigh-Resolution Optical Coherence Tomography. Investigative Opthalmology & Visual Science. 2008;49(4):1571.
25. Shahidi M, Wang Z, Zelkha R. Quantitative Thickness Measurement of Retinal Layers Imaged by Optical Coherence Tomography. American Journal of Ophthalmology. 2005;139(6):1056-1061.
26. Aizawa S, Mitamura Y, Baba T, Hagiwara A, Ogata K, Yamamoto S. Correlation between visual function and photoreceptor inner/outer segment junction in patients with retinitis pigmentosa. Eye. 2008;23(2):304-308.
27. Baba T, Yamamoto S, Arai M, Arai E, Sugawara T, Mitamura Y Et Al. Correlation Of Visual Recovery And Presence Of Photoreceptor Inner/Outer Segment Junction In Optical Coherence Images After Successful Macular Hole Repair. Retina. 2008;28(3):453-458.

Citation: Ajnas C.P, Dr. Swadique M, Muthiah J, Rajesh P. Correlation Between Macular Thickness And Volume With Visual Acuity In Diabetic Macular Edema By Using Domain Optical Coherence Tomography. National Journal of Medical and Allied Sciences 2016; 5(2):30-35.