Diagnostic Accuracy of Spectral Domain Optical Coherence Tomography in the Diagnosis of Cystoid Macular Edema among Diabetes Mellitus Patients Using Fundus Fluorescein Angiography as Gold Standard

Raheela Naz[1], Hussain Ahmad Khaqan[1], Hasnain Muhammad Buksh[1], Muhammad Ali Haider[1], Ateeq Ur Rehman[1]

Abstract

Objective: To evaluate the diagnostic accuracy of spectral-domain optical coherence tomography (SD-OCT) to detect diabetic macular edema (DME) in diabetic patients using fundus fluorescein angiography (FFA) as gold standard.

Methodology: A cross sectional study was conducted in the Outpatient Department of Ophthalmology, Lahore General Hospital, Lahore from October 1, 2019 to April 1, 2020. A total of 161 patients who fulfilled the inclusion criteria were selected randomly from outpatient department. Informed consent was taken from all patients for taking retinal images and examination. All participants were examined by indirect bio microscopy. Fundus fluorescein angiography and optical coherence tomography were done for the cystoid macular edema. A proforma was designed to collect data. All the collected data was analyzed by SPSS version 25v.

Results: The mean age of patients was 47.47±10.32 year. In our study 133(89.9%) patients were positive in cystoid macular edema in OCT findings while 148(91.9%) patients were detected positive by FFA. Cystoid macular edema was not detected by OCT in 15(10.1%) patients. The sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of presence of cystoid macular edema detected on OCT vs FFA was 89.86%, 38.46%, 94.33%, 25.00% and 85.71% respectively.

Conclusion: The present study showed exhibited the diagnostic potential and efficacy of OCT compared to FFA as is reliable and safe for the detection of diabetic macular edema in diabetic mellitus patients. *Al-Shifa Journal of Ophthalmology 2022; 18(3): 105-111. © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.*

1. Ophthalmology Department, Lahore General Hospital, Lahore

Correspondence to:
Dr. Husnain Muhammad Buksh
AMC, PGMI, Lahore General Hospital, Lahore.
Email: hasnain_md106@hotmail.com

Introduction:

Cystoid macular edema (CME) is defined as retinal thickening of macula secondary to disruption of the normal blood retinal barrier; this disruption causes leakage from the peri-foveal retinal capillaries resulting in accumulation of fluid within the intracellular spaces of the retina, primarily involving the inner nuclear and outer plexiform layer.[1] In the developed world, CME is the leading cause of central vision loss. The common causes of CME are retinal vein occlusion, diabetic retinopathy,

posterior uveitis, post intra ocular surgery.[2,3]

Cystoid macular edema can be diagnosed on Optical coherence tomography (OCT) diagnosis. Each modality has its own strength and weakness.[4,5,6] OCT is a new technology used for cross sectional imaging of retina. It is analogous to ultrasound B-scan but the use of optical waves provides higher resolution of retina that is of the order of less than 5 micron. OCT is non-invasive, comfortable, and safe. It uses 800-840nm wavelength range infrared light. It is based on Michelson interferometry principle.[7]

The normal retinal tissue displays different reflectivity patterns on OCT. The retinal nerve fiber and retinal pigment epithelium (RPE) displays high reflectivity, the plexiform and nuclear layer displays medium reflectivity and photoreceptors display low reflectivity.[8] The advantage of OCT appears to optically dissect and visualize the flow in various layers of retina, the high resolution, and safety of not using an injected dye.

FFA is a technique that is used to examine the circulation of the retina and choroid by using fluorescent dye and a specialized camera. Sodium fluorescein is injected into the circulation, retina is illuminated with blue white light at a wavelength of 490nm, and an angiogram is obtained by photographing the fluorescent green light that is emitted by the dye. This test is basically a dye tracing method.[9,10] FFA provides information regarding the flow and speed of filling and health of the vessels can be assessed by looking for leakage. In FFA a dye is injected which has a small probability of serious complications.[9]

This study is intended to assess the diagnostic accuracy of optical coherence tomography in the diagnosis of cystoid macular edema in diabetic patients taking the fluorescein angiography as a gold standard as the diabetic macular edema is a leading cause of central vision loss in our

and Fundus fluorescein angiography (FFA).[5,6] Both modalities complement each other and, in many situations, both modalities are required to make correct population and fluorescein angiography being invasive, time consuming and not without contraindications and complications. Therefore, the need for reliable, safe and immediate detection of diabetic macular edema is a need for the management of the patients.

Patients and Methods:

After taking ethical consent from hospital committee, a cross sectional study was conducted in the Outpatient Department of Ophthalmology, Lahore General Hospital, Lahore from October 1, 2019 to April 1, 2020. Patients, known diabetics, of both genders between aged 30 to 65 years with clear ocular media were included in the study. Patients with nystagmus, claustrophobia or extreme anxiety regarding the procedure, allergy to fluorescein, impaired renal function (serum creatinine >1.2mgdl), significant cardiac disease, moderate asthma, uveitis, central and branch retinal vein occlusion, post intraocular surgery within last 3 months and pregnancy were excluded form from the study.

A total of 161 patients who fulfilled the inclusion criteria were selected randomly from Outpatient Department. Non-probability consecutive sampling technique was used. Informed consent was taken from all patients for taking retinal images and examination. Distant visual acuity was recorded by using Snellen's acuity chart while near vision was used to take 45 degree retinal images.

All participants were examined by indirect bio microscopy. Fundus fluorescein angiography and optical coherence tomography were done for the cystoid macular edema. A proforma was designed to collect data including name, age, gender, registration number, address, visual acuity, indirect bio microscopic examination

findings, OCT and FFA findings and diagnosis.

The data were entered and analyzed by SPSS v25.0. Numeric data like age was presented as mean and S.D, whereas the qualitative data like gender was presented in frequency and percentages. Data were stratified for gender, age and duration of diabetes mellitus. Post-stratification, 2x2 contingency tables was used. A p-value ≤0.05 was considered significant.

Results:

In this study, the results of gender showed that 85(52.8%) were male and 76(47.2%) were female. Male patients were more than female in our study.

The mean age of patients was 47.47±10.32 years. The results of age groups showed that 71(44.1%) patients were from 30-45 years age group and 90(55.9%) patients were from >45 years age group.

The mean value of duration of diabetes mellitus in our study was 5.38±5.37 years.

The results of duration of diabetes mellitus showed that 82(50.9%) patients had 1-5 years duration of diabetes mellitus and 79(49. 1%) patients had >5 years duration of diabetes mellitus.

The frequency distribution results of cystoid macular edema detected on FFA (fluorescein angiography) showed that 148(91.9%) patients detected by FFA (fluorescein angiography).

The frequency distribution results of cystoid macular edema detected on OCT (optical coherence tomography) showed that 141(87.6%) patients detected by OCT (optical coherence tomography).Cystoid macular edema was not detected by OCT in 15(10.1%) patients.

The sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of presence of cystoid macular edema detected on OCT vs. FFA was 89.86%, 38.46%, 94.33%, 25.00% and 85.71% respectively. (Table 2,3 and 4)

Table-1: Cross-tabulation results of cystoid macular edema detected on OCT with FFA

Cystoid Macular edema detected on OCT	Cystoid Macular edema detected on FFA		Total	Sn= 89.86%, Sp= 38.46% PPV= 4.33%, NPV= 25.00% DA= 85.71%
	Present	Absent		
Positive	133	8	141	
Negative	15	5	20	
Total	148	13	161	

Table-2: Stratification of cystoid macular edema detected on OCT and FFA with gender

Gender	Cystoid Macular edema detected on OCT	Cystoid Macular edema detected on FFA		Total	
		Present	Absent		
Male	Positive	70	4	74	Sn= 88.61%, Sp= 33.33% PPV= 94.59%, NPV= 18.18% DA= 84.71%
	Negative	9	2	11	
	Total	79	6	85	
Female	Positive	63	4	67	Sn= 91.30%, Sp= 42.86% PPV= 94.03%, NPV= 33.33% DA= 86.84%
	Negative	6	3	9	
	Total	69	7	76	

Table-3: Stratification of cystoid macular edema detected on OCT and FFA with age groups

Age groups	Cystoid Macular edema detected on OCT	Cystoid Macular edema detected on FFA		Total	
		Present	Absent		
30-45 years	Positive	54	8	62	Sn= 91.53%, Sp= 33.33% PPV= 87.10%, NPV= 44.44% DA= 81.69%
	Negative	5	4	9	
	Total	59	12	71	
>45 years	Positive	79	0	79	Sn= 88.76%, Sp= 100% PPV= 100%, NPV= 9.09% DA= 88.89%
	Negative	10	1	11	
	Total	89	1	90	

Table-4: Stratification of cystoid macular edema detected on OCT and FFA with duration of diabetes mellitus

Duration of diabetes mellitus	Cystoid Macular edema detected on OCT	Cystoid Macular edema detected on FFA		Total	
		Present	Absent		
1-5 years	Positive	63	7	70	Sn= 90.0%, Sp= 41.67% PPV= 90.0%, NPV= 41.67% DA= 82.93%
	Negative	7	5	12	
	Total	70	12	82	
>5 years	Positive	70	1	71	Sn= 89.74%, Sp= 0.00% PPV= 98.59%, NPV= 0.00% DA= 88.61%
	Negative	8	0	8	
	Total	78	1	79	

Discussion:

The prevalence of diabetic macular edema (DME) increases with age as in our study it was 55.9% in patients more than 45 years of age which correlate to previous studies.[10-13]

Antcliff et al. in 2000 have conducted a study on "compare optical coherence tomography (OCT) with fundus fluorescein angiography (FFA) for the detection of cystoids macular edema (CME) in patients with Uveitis" and found that OCT performs better compared to FFA in terms of detection of cystoid macular edema. They have also mentioned that sensitivity for detecting CME was 96% (including the eyes with sub-retinal fluid) and the OCT specificity was 100%.[14] While the sensitivity (Se) and specificity (Sp)of OCT in our study was 89.86% and 38.46%respectively.

The incidence of CME was found as 5.5% by OCT and 3.2% by FFA in a study conducted to diagnose post-phacoemulsification macular edema.[15]

Another study highlights the role of FA in imaging macular edema, and suggests that in some cases, even with SD-OCT, fluorescein angiography is a more sensitive determinant of macular edema. Results showed that 3.73% of eyes with FA leakage had no abnormality on SD-OCT.[16]

In a study, subretinal fluid was detected with OCT for 15 eyes whereas, FFA could not detected the same for the same pool of patients13. A similar finding was observed by Antcliff et al. 200014.While in our study cystoid macular edema was not detected by OCT in 15(10.1%) patients.

In 2002, Strom et al. have reported that the degree of agreement between subjectively and objectively assessed retinal thickenings was very good implying that changes in diabetic macular edema can be detected accurately with OCT [17].This strengthens the diagnostic potential of the OCT as it quantifies the macula edema and there is no observer biased error.

In 2012, Maalej et al. have reported about the importance of OCT in routine clinical assessment of diabetic macular oedema. They have also stated that identifying the structural changes in eyes with DME using OCT may allow more effective management of DME patients[18].This noninvasive and fast test not only helps in diagnosis but also in the monitoring of the diabetic macular edema to look for its progression or regression.

Shoughy et al. 2016, have done a study on "selective and complementary use of optical coherence tomography and fluorescein angiography in retinal practice" and stated that the OCT provides detailed imaging of anatomical retinal layers, allows detection of micro-structural changes and helps perform quantitative assessment during follow up and FFA is used to evaluate retinal vascular perfusion and integrity of the inner blood-retinal barrier[19]. FFA is known to be a sensitive method for qualitative assessment of fluid leakage in diabetic macular edema; FFA is an invasive procedure, with side effects ranging from nausea to its rare complication of anaphylaxis and death. While, OCT is non-invasive, comfortable, safe, and fast and can be repeated as often as is required and offers an alternative to FFA in situations where FFA is contraindicated.

References:

1. Murakami T, Nishijima K, Akagi T, Uji A, Horii T, Ueda-Arakawa N, et al. Optical coherence tomographic reflectivity of photoreceptors beneath cystoid spaces in diabetic macular edema. Investigative Ophthalmology & Visual Science. 2012;53(3):1506-11.
2. Jaulim A, Ahmed B, Khanam T, Chatziralli IP. Branch retinal vein occlusion: epidemiology, pathogenesis, risk factors, clinical features, diagnosis, and complications. An update of the literature. Retina. 2013;33(5):901-10.
3. Pielen A, Feltgen N, Isserstedt C, Callizo J, Junker B, Schmucker C.

Efficacy and safety of intravitreal therapy in macular edema due to branch and central retinal vein occlusion: a systematic review. PLoS One. 2013;8(10):e78538.

4. Wu L, Fernandez-Loaiza P, Sauma J, Hernandez-Bogantes E, Masis M. Classification of diabetic retinopathy and diabetic macular edema. World journal of diabetes. 2013;4(6):290.

5. Adán A, Mesquida M, Llorenç V, Espinosa G, Molins B, Hernández MV, et al. Tocilizumab treatment for refractory uveitis-related cystoid macular edema. Graefe's Archive for Clinical and Experimental Ophthalmology. 2013;251(11):2627-32.

6. Coscas F, Glacet-Bernard A, Miere A, Caillaux V, Uzzan J, Lupidi M, et al. Optical coherence tomography angiography in retinal vein occlusion: evaluation of superficial and deep capillary plexa. American journal of ophthalmology. 2016;161:160-71. e2.

7. Jayadev C, Jain N, Sachdev S, Mohan A, Yadav NK. Utility of noninvasive imaging modalities in a retina practice. Indian journal of ophthalmology. 2016;64(12):940.

8. Trichonas G, Kaiser PK. Optical coherence tomography imaging of macular oedema. British Journal of Ophthalmology. 2014;98(Suppl 2):ii24-ii9.

9. Lommatzsch C, Rothaus K, Koch J, Heinz C, Grisanti S. Vessel Density in Glaucoma of Different Entities as Measured with Optical Coherence Tomography Angiography. Clinical Ophthalmology (Auckland, NZ). 2019;13:2527.

10. Lee R, Wong TY, Sabanayagam C. Epidemiology of diabetic retinopathy, diabetic macular edema and related vision loss. Eye Vis(Lond). 2015;2:17.doi:10.1186/s40662-015-0026-2. eCollection 2015.

11. Varma R, Bressler NM, Doan QV, Gleeson M, Danese M, Bower JK, Selvin E, Dolan C, Fine J, Colman S, Turpcu A. Prevalence of and Risk Factors for Diabetic Macular Edema in the United States. JAMA Ophthalmol.2014;132(11):1334–1340.

12. Kaveeshwar SA, Cornwall J. The current state of diabetes mellitus in India. The Australasian Medical Journal.2014;7(1):45-48. doi:10.4066/AMJ.2013.1979.

13. Madan V, Magdum R, Ghosh S. Efficacy of optical coherence tomography and fundus fluorescein angiography in detection of diabetic macular edema. Indian Journal of Clinical and Experimental Ophthalmology. 2018 Apr;4(2):164-7.

14. Antcliff RJ, Stanford MR, Chauhan DS, Graham EM, Spalton DJ, Shilling JS, fytche TJ, Marshall J. Comparison between optical coherence tomography andfundus fluorescein angiography for the detection ofcystoid macular edema in patients with uveitis. Ophthalmology.2000;107(3):593-9.

15. Kusbeci T, Eryigit L, Yavas G, Inan UU. Evaluation of cystoid macular edema using optical coherence tomography and fundus fluorescein angiography after uncomplicated phacoemulsification surgery. Current eye research. 2012 Apr 1;37(4):327-33.

16. Brar M, Yuson R, Kozak I, Mojana F, Cheng L, Bartsch DU, Oster SF, Freeman WR. Correlation between morphological features on spectral domain optical coherence tomography and angiographic leakage patterns in macular edema. Retina (Philadelphia, Pa.). 2010 Mar;30(3):383.

17. Strøm C, Sander B, Larsen N, Larsen M, Lund-Andersen H. Diabetic macular edema assessed with optical coherence tomography and stereo fundus photography.Invest Ophthalmol Vis Sci. 2002;43(1):241-5.

18. Maalej A, Cheima W, Asma K, Riadh R, Salem G (2012) Optical Coherence Tomography for Diabetic Macular Edema: Early Diagnosis, Classification

and Quantitative Assessment. J Clinic Experiment Ophthalmol S2:004. doi:10.4172/2155-9570.S2-004.

19. Shoughy SS, Kozak I. Selective and complementary use of Optical Coherence Tomography and Fluorescein Angiography in retinal practice. Eye Vis (Lond).2016;3:26. doi:10.1186/s40662-016-0058-2.

Authors Contribution
Concept and Design: Raheela Naz , Hussain Ahmad Khaqan
Data Collection / Assembly: Hasnain Muhammad Buksh
Drafting: Muhammad Ali Haider
Statistical expertise: Ateeq Ur Rehman
Critical Revision: Hussain Ahmad Khaqan