Original Articles

Clinical analysis of Clinically Significant Macular Edema (CSME) by Slitlamp Biomicroscopy with +90D lens, Optical Coherance Tomography (OCT) and Fundus Fluorescein Angiography (FFA) among patients of diabetes mellitus - cross sectional observational study.

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Keywords: Clinically Significant Macular Edema, Optical Coherance Tomography, Fundus Fluorescein Angiography.

ABSTRACT

Introduction : Diabetic Retinopathy is a major cause of blindness in the world. Proper and affordable diagnosis of Clinically Significant Macular Edema (CSME) is very much important for early detection and treatment of this kind of vision loss. Slitlamp biomicroscopy with +90D lens (SLB), Optical Coherance Tomography (OCT) and Fundus Fluorescence (FFA) are the available methods for detection of CSME. Clinical evalution of CSME by all these methods is very much important to know their reliability, repeatability and affordability. **Aim :** To analyse findings of slit lamp biomicroscopy with 90D lens, Optical Coherance Tomography and Fundus Fluorescein Angiography in patient of diabetes with CSME. **Methods :** 33 eyes of 25 patients were analysed for findings of CSME by slitlamp biomicroscopy with +90D lens, Optical Coherence Tomogrphy and Fundus Fluorescence Angiography after general ophthalmic examination. **Results :** CME was found better on OCT (27%) in comparision to SLB (9%) and FFA(18%). ERM (9%) and SRF(18%) was found only on OCT. Hard exudates were found better and equally on OCT and biomicroscopy(85%) compared to FFA(18%). DRT was found by biomicroscopy(88%), OCT(100%), FFA(85%). **Conclusion :** OCT helps in better anatomical characterization of CSME and therefore more relevant while planning management strategies.

INTRODUCTION

A major cause of blindness in working class is Diabetic Retinopathy. According to the World Health Organization, India will become one of the major hubs of Diabetic population during the next two decades.[1] Diabetic eye disease is a leading cause of vision loss in person aged 20 to 74years of which retinopathy is most important.[2] From 1980 to 2014, worldwide age-standardised adult diabetes prevalence increased from 4.3% (95% CrI 2.4-7.0) to 9.0% (7.2-11.1) in men and from 5.0% (2.9-7.9) to 7.9% (6.4-9.7) in women; the posterior probabilities that these were true increases were 0.994 and 0.954, respectively. Over these years, crude adult prevalence increased from 3.6% (2.0-5.9) to 8.8% (7.0-10.8) in men, and from 4.7% (2.7-7.4) to 8.2% (6.6-9.9) in women.[3] Indirect fundoscopy was carried out by an experienced consultant ophthalmologist using slit-lamp biomicroscopy with 78 D lens for the posterior pole and a superfield lens for the periphery. Diabetic retinopathy stage was classified according to the Early Treatment Diabetic Retinopathy Study (ETDRS) criteria as no diabetic retinopathy (no DR), mild nonproliferative DR (NPDR), moderate NPDR, severe NPDR, proliferative DR (PDR) with new vessels at the disc (NVD), PDR with new vessels elsewhere in the retina (NVE), or advanced PDR with vitreous hemorrhage, fibrous tissue, or recent retinal detachment.[4] An important diagnostic tool of DR is fluorescein angiography.[5] The drawbacks of this procedure are venipuncture, anaphylaxis and death related to contrast injection, even though rare. In addition to this, the technique is expensive and requires up to 10 minute for framing acquisition making it time consuming. Howsoever it is considered the gold standard in DR analysis.[6] OCT provides in vivo cross-sectional information of macular structure with micrometre resolution without requiring physical contact with the patient. The 'non-contact' feature makes the technique very useful when examining children and noncompliant patients. Optical Coherence Tomography helps in identifying macular edema which is the most common complication of Diabetic Retinopathy as well as epiretinal membrane, tractional retinal detachment to name a few.[7,8] Present study was done to do clinical analysis of CSME by these three different methods keeping in mind the unpredictable and continuous evolution of DR recent past, aggravation, vision loss and to prevent serious complications of

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disease in diabetics which adds to the burden of social economic status of the country through increased morbidities and deteriorating quality of life.

MATERIALS ANS METHODOLOGY

Diabetic patients coming to Ophthalmology OPD of our hospital were screened for duration of 1 year (from july 2018 to June 2019). Detailed history and examination viz. visual acuity by ETDRS chart, refraction & correction, Best corrected visual acuity, anterior segment examination by Slit lamp biomicroscopy, Intra ocular pressure measurement by Applanation tonometry, Fundus examination with 90D lenses, Fundus Fluorescein Angiography (FFA), Optical Coherence Tomography (OCT) and systemic evaluation were done.

SELECTION CRITERIA

INCLUSION CRITERIA

- Patient giving written and informed consent.
- All adult patients.
- Diabetic patient diagnosed having CSME.

EXCLUSION CRITERIA

- Patients not giving written and informed consent.
- Patient having pre-existing retinopathy other than diabetic retinopathy.
- Patient with any anterior or posterior segment abnormality causing difficulty in visualisation of fundus.
- Patient having allergy to Fluorescein dye.

CONSENT

Participent's conset aged >18 years.

EVALUATION OF PARAMETERS:

➢ Methods of collecting data

- Study as approved by Institutional Review Board (IRB).
- Participants information sheet (PIS) regarding details of study were prepared in english and gujarati languages. PIS was given to the participents and they were explained about the type and purpose of study according to their concerned language. After their consent, they were enrolled in study.
- Patient's rights for the participation in the study were safeguarded. Participation in the study was voluntary and at any point, they were free to go away, without giving reason, without any loss to medical care.
- A detailed history of each patient obtained from either the patient or relative was taken as per the attached performa. Following protocols were under taken in each cases :

The history included- Name, Age, Gender, Locality (urban/rural), General vital examination

OPHTHALMIC EXAMINATION

- Distance visual acuity of each eye was taken by ETDRS chart and after that best corrected visual acuity and pin hole vision will be taken.
- General ophthalmic examination of eyebrow, eyelid, conjunctiva, cornea, sclera, anterior chamber, iris, pupil and lens was done by slitlamp biomicroscopy. Intraocular pressure was measured by goldmann applanation tonometry.
- Patient's pupil was dilated with tropicamide+ phenylephrine eyedrops. Punctual occlusion was explained and done to minimize side effects.
- Slit lamp biomicroscopy was done using +90D Volk lens and findings were noted on CRF.
- Both eyes were selected for analysis of macular region by TOPCON optical coherence tomography 3D OCT-1 MAESTRO having software version 8.42 and finding were noted on CRF.
- Patient will be given subcutaneous test dose of 0.05 ml of sodium fluoresceine. 2 ml 20% Sodium fluoresceine dye will be injected through antecubital vein and FFA was done using TOPCON RETINAL CAMERA TRC-50DX having software version IMAGEnet R4, CAMERA MODEL Nikon D80 SLR camera 10 megapixels | 2.5" screen |APS-C sensor and CAMERA RESOLUTION max 3872 x 2592. Finding of FFA was noted on CRF.

ANALYSIS OF CSME :

➢ Analysis of CSME by slitlamp biomicroscopy with +90D lens was recored as presence or absence of pathology in macular region showen as bellow

(1) Diffuse retinal thickening (DRT), which is seen as altered or absent fovela reflex associated with presence or absence of dot hemorrhages and hard exudates in surrounding area.

(2) Cystoids macular edema (CME), which is seen as flower petal appearance in macular region.

(3) Epiretinal Membrane (ERM), which is fibrous membrane formation over Internal Limitting Membrane.

(4) Vitreomacular Traction (VMT), which is seen as taut elevated retinal layers on binocular vision.

(5) Sub retinal fluid(SRF).

➢ All OCT scans were performed through a dilated pupil and the macula was scanned.

These various patterns of DME were scored based on their unique appearance on

(1) Diffuse retinal thickening (DRT) as increased retinal thickness (defined as greater than 200µm) with reduced intraretinal reflectivity and expanded areas

of lower reflectivity, especially in the outer retinal layers greater than 200 µm in width

(2) Cystoid macular edema (CME) was identified by the localization of intraretinal cystoid-like spaces that appeared as round or oval areas of low reflectivity with highly reflective septa separating the cystoid-like cavities

(3) Epiretinal Membrane (ERM) without retinal detachment was defined as a highly reflective signal arising from the inner retinal surface and extending towards the optic nerve or peripherally.

(4) Sub Retinal Fluid (SRF) was defined as an accumulation of sub retinal fluid (which appeared dark) beneath a highly reflective and elevation, resembling a dome, of the detached retina. The identification of the highly reflective posterior border of detached retina distinguished subretinal from intraretinal fluid.

(5) Vitreomacular Traction (VMT), defined as a peak-shaped detachment of the retina.

(6) Other than this presence or absence of dot hemorrhages and hard exudates were also noted.

➢ Finding of FFA were noted as leakage of dye in central Foveal avascular zone and the as per appearance of it.

(1) Diffuse Retinal Thickning (DRT), which is seen as the accumulation of fluorescein in the retina or choroid. At the beginning of the angiogram, the fluid in the space contains no fluorescein and is not visible. As fluorescein leaks into the space, the thickening appear distinct.

(2) Hard Exudates, which is easily seen on fundus photography but hard to appreciate in FFA. It is see as area of hyperfluorescence near macula arranged in circular manner.

(3) Cystoid Macular Edema (CME), which is seen as well defined area of hyperfluorescence in macular area in late photograph of FFA.

OBSERVATION

All 33 eyes of 25 patients enrolled in the study were studied. From demography data to general examination and ophthalmic examination including fundus findings were assessed.

CONCLUSION

From the given set of samples detecting 7 items on these three tests, OCT is best method to detect all findings. SLB is equally effective as OCT in detecting Hard exudates. These all observations are based on average method. (Percentage calculation)

Total number of samples = 33

Expected result in numbers = 33 (Assuming that BIOMICROSCOPY and OCT and FFA proves to be perfect.

Fig. I. Gender distribution among patients having CSME shows that out of 25 Patients 15 were male and 10 were female. This Male to Female proportion can be because of low sample size.

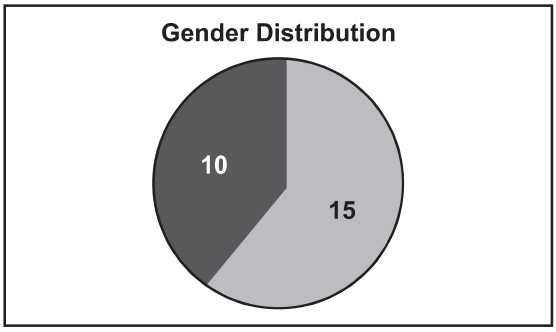


Fig. II. Among 25 patients having CSME, 8 Patients had bilateral CSME while 17 patients had unilateral CSME.

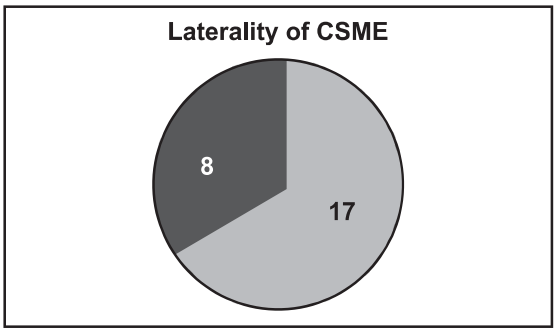


Fig. III. As per demographic data showen above maximum number of patients having CSME were having diabetes for duration of 5-10 years and 10-15 years with 9 patients in each group. 4 patients were having duration >20 years, 2 were having 16-20 years and 1 was having duration <5 years. This distribution is not clinically significant because of low sample size.

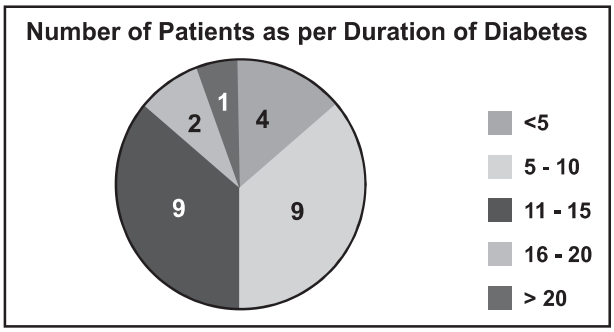


Fig. IV. As per demographic data showen above maximum number of patients having CSME were from age group 65-70 years and >70 years with 8 patients in each, followed by 5 patients in age group 60-65 years, 2 patients in age group 50-55 years and 1 patient in age group 55-60 years and <50 years each. This distribution is not clinically significant because of low sample size.

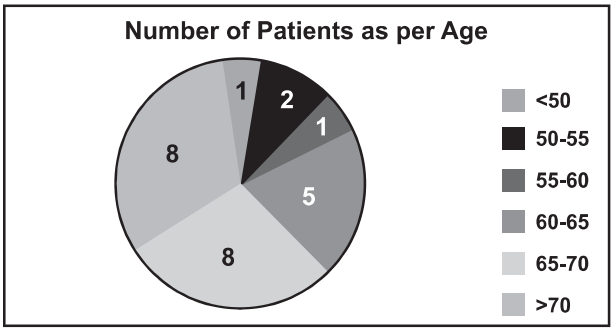


Table I : P value of different fundus findings.

		Number of eyes having positive findings			
		SLB	OCT	FFA	P value
Fundus Findings	DRT	29	33	28	0.0768
	Dot hemorrhages	7	10	-	0.3984
	Hard Exudates	28	28	6	<0.0001
	CME	3	9	6	0.1599
	VMT	2	5	-	0.2304

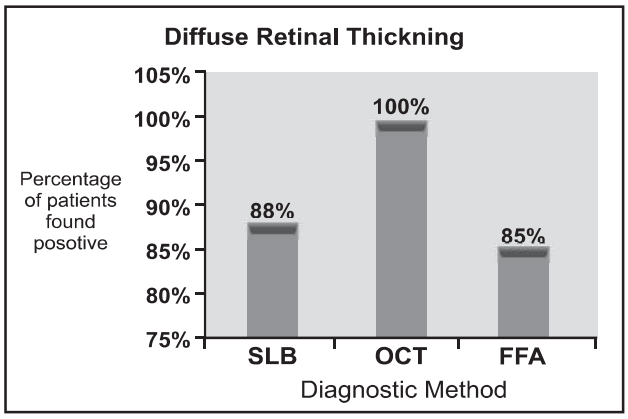
***P value is statistically significant**

All P value is calculated by chi square test

Table II : Number of positive fundus findings by all three methods

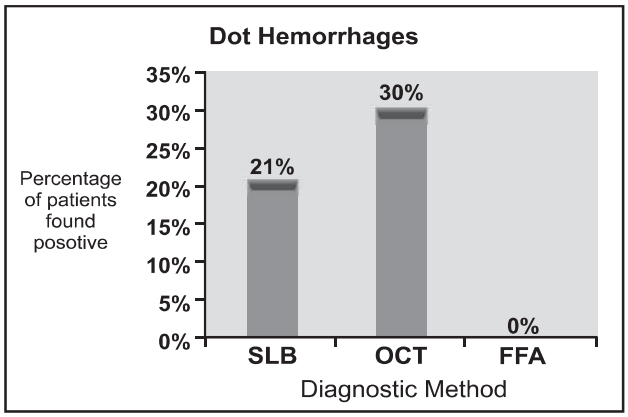
	SLB	OCT	FFA
DRT	29	33	28
Dot Hemorrhages	7	10	0
Hard exudates	28	28	6
CME	3	9	6
ERM	0	3	0
VMT	2	5	0
SRF	0	6	0

Fig. V. Result : By statistical analysis OCT proved the best among three but difference between these methods is statistically insignificant.



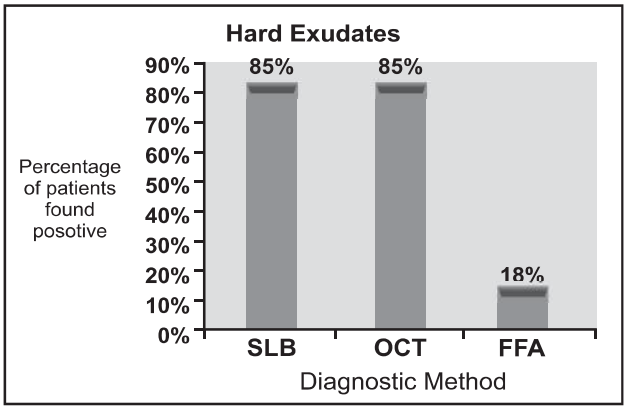
Inference : SLB, OCT and FFA- any method can be adopted.

Fig. VI. Result : By SLB, 21% of the total observations proved to be Valid, by OCT 30% and by FFA 0%.



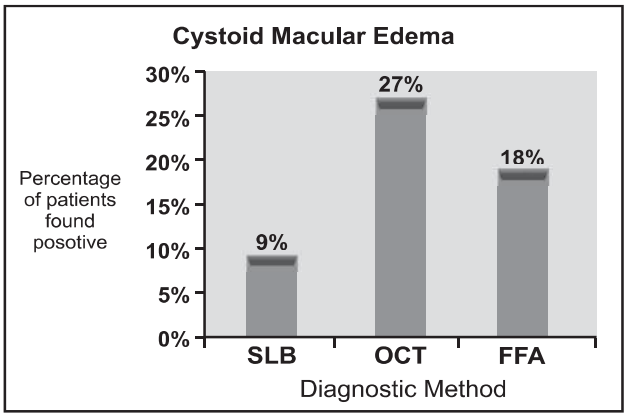
Inference : OCT is found to be more perfect compared to SLB and FFA.

Fig VII Result : By SLB, 85% of the total observations proved to beValid, by OCT 85% and by FFA 18%.



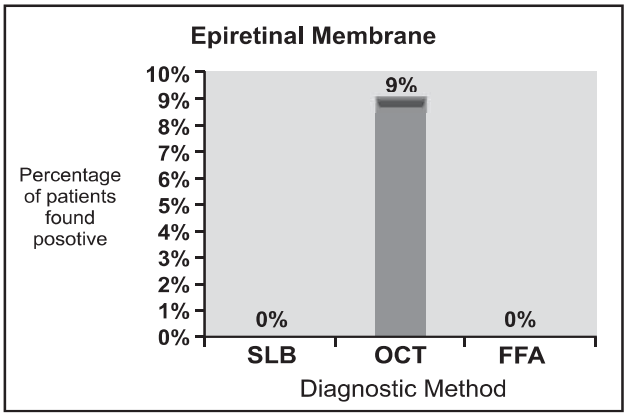
Inference : SLB and OCT is found equally effective compared to FFA. The difference between these methods is statiscally significant.

Fig VIII Result: By SLB 9%, by OCT 27% and by FFA 18% of the total observations proved to be Valid.



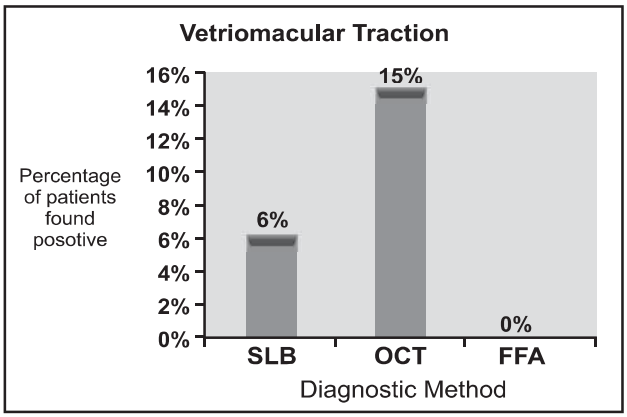
Inference : OCT is found to be more perfect compared to SLB and FFA. OCT can be adopted for CME.

Fig. IX. Result : By SLB 0%, by OCT 9% and by FFA 0% of the total observations proved to be Valid.



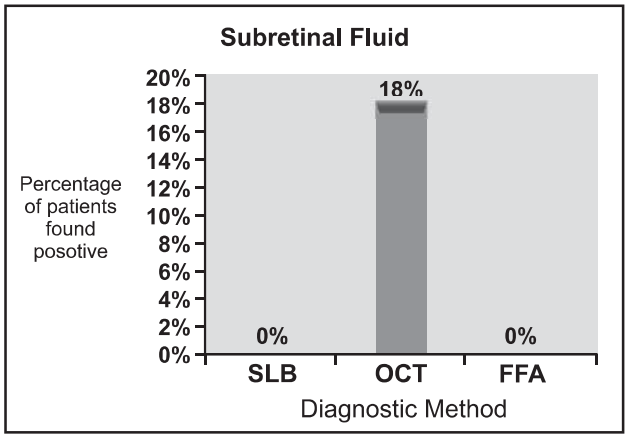
Inference : OCT is found to be more perfect compared to SLB and FFA.OCT can be adopted for ERM.

Fig. X. Result : By SLB 6%, by OCT 15% and by FFA 0% of the total observations proved to be Valid.



Inference : OCT is found to be more perfect compared to SLB and FFA. OCT method can be adopted for VMT.

Fig. XI. Result : By SLB 0%, by OCT 18% and by FFA 0% of the total observations proved to be Valid.



Inference : OCT is found to be more perfect compared to SLB and FFA. OCT method can be adopted for ERM.

DISCUSSION

Yang et al[9] have suggested that OCT may be more sensitive than a clinical examination in assessing diabetic macular edema and is a better tool for documenting changes in macular thickening. OCT-identified diffuse retinal thickning and / or CME was seen in 58% of eyes without CSME in that series. In our series, we found DRT in all the eyes and CME in 27 % with macular edema. Schaudig[10] et al also found similar observations.

In our study we found that out of 25 patients, 15 were male and 10 were female (Fig I); 17 were having unilateral CSME while 8 were having bilateral CSME (Fig II). Maximum number of patients having CSME were having diabetes for duration of 5-10 years and 10-15 years with 9 patients in each group. 4 patients were having duration >20 years, 2 were having 16-20 years and 1 was having duration <5 years (Fig III). maximum number of patients having CSME were from age group 65-70 years and >70 years with 8 patients in each, followed by 5 patients in age group 60-65 years, 2 patients in age group 50-55 years and 1 patient in age group 55-60 years and <50 years each (Fig IV).

Structural changes in OCT in our series correlate with other data from literature. Otani[11] et al found DRT in 88%, CME in 47% and SRF in 15% of eyes with CSME. Kim[12] et al found DRT in 97%, CME in 55%, SRF in 7%, VMT in 13% of eyes with CSME. Ozdek13 et al had reported DRT in 66%, CME in 16% and SRF in 10% of eyes with diabetic macular edema. In our study, we found DRT in100%, CME in 27%, SRF in 18% and VMT in 15%. Along with this we also found Dot hemorrhages in 30%, Hard exudates in 85% and ERM in 9% patients (Table I).

On comparing OCT, biomicroscopy and FFA, 27% of the eyes had CME on OCT, compared to 9% detected on biomicroscopy and 18% detected on FFA (Fig V). 18% of eyes had SRF with subfoveal detachment on OCT and

was not identified neither on biomicroscopy nor on FFA (Fig VI). 15% of eyes had VMT on OCT compared to 6% on biomicroscopy and no detection on FFA (Fig VII). 9% of eyes had ERM identified by OCT compared to none on biomicroscopy and FFA (Fig VIII) . 85% of eyes had hard exudates on OCT and biomicroscopy compared to 18% on FFA (Fig IX). 30% of eyes had dot hemorrhages on OCT compared to 21% on biomicroscopy and no detection on FFA (Fig X) . DRT was found positive in 88% eyes by SLB, 100% eyes by OCT and 85% of eyes by FFA (Fig XI) Browning et al[14] had also compared stereoscopic slit lamp examination and OCT in the study of CSME and concluded that stereoscopic slit lamp examination of the macula was less sensitive than OCT for detection of diabetic macular edema. Strom[15] et al had found an agreement of 89% on the exact location and 84% agreement on the exact area of CSME when he compared biomicroscopy with OCT and found the latter to be more superior. Ozdek[13] et al did comparision of optical coherence tomographic (OCT) features with clinical and fluorescein angiographic (FA) findings in patients with diabetic retinopathy, In which they found that CME was detected with OCT in 15.4% of eyes, 40% of which was not detected with slit-lamp biomicroscopy and 63.3% of which was not evident in FFA.

In our study, 27% of the eyes had CME on OCT, compared to 9% detected on biomicroscopy. Ozdek13 et al also found that 40% of CME detected on OCT were not detected by biomicroscopy and 63% were not detected even on fluorescein angiography. OCT is thus a better diagnostic tool to diagnose CME in patients with diabetic retinopathy than biomicroscopy or FFA. In our study, 18% of the eyes had SRF, which could not be detected on biomicroscopy or FFA. Most series have found SRF in 8-12% of eyes with CSME.

In our study we try to do find statistically significant difference between OCT, biomicroscopy and FFA for different fundus findings. We use chi square test to calculate it. For Hard Exudates P Value is <0.0001, which shows there is statistically significant difference between these methods in finding hard exudates and OCT as well as biomicroscopy is superior to FFA for this. P Value for DRT, Dot Hemorrhages, CME and VMT is 0.0768, 0.3984, 0.1599 and 0.2304 respectivelly, which is >0.05 so clinically insignificant (Table II). However clinical findings shows that OCT is better compared to other two methods for all these fundus findings, especially CME and VMT. So this clinically insignificant P Value can be because of low sample size.

CONCLUSION

We found that OCT is a useful technique for quantitative measurement and helps in better anatomical characterization of CSME than biomicroscopy and FFA, and thereby more relevant while planning management strategies, followup, prognosis and predicting visual outcome.

We found that OCT is better compared with biomicroscopy and FFA to diagnose CME, to detect subretinal fluid with subfoveal detachment and to study the vitreoretinal interface changes like vitreomacular traction & epiretinal membrane.

Though biomicroscopy is economically affordable and considered as gold standard for macular evalulation, as OCT can reproduce and compare the fundus findings, it is considered superior to biomicroscopy for CSME evaluation and follow up.

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