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FUNDUS AUTOFLUORSECNCE IN DIABETIC MACULAR OEDEMA

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ABSTRACT **Introduction:** Diabetic macular oedema accounts for more than half the cases of vision loss in diabetics. With a shifting trend on early diagnosis and treatment of DME, fundus autofluorescence may prove to be valuable. Traditional methods of 90d slit lamp examination and OCT may not detect early DME. **Purpose:** The purpose of this study was to evaluate fundus autofluorescence patterns in diabetic macular oedema and to assess the correlation with the severity of diabetic retinopathy. **Methods:** In this observational study 39 diabetic patients (70 eyes)who reported to the ophthalmology OPD of a tertiary hospital in Maharashtra underwent a detailed ophthalmic evaluation. Patients with a central macular thickness of 212+/-20µm on OCT were included. Fundus picture and fundus autofluorescence images were captured. Poor quality images were discarded, and the remaining were analyzed and classified as various patterns. **Results:** A total 39 diabetic patients were studied. The total number of males in the study were 24 and females were 15.Among the 73 eyes studied 12 Eyes had mild NPDR (16%),38 Eyes moderate NPDR (52%),15 eyes severe NPDR (21%) while 8 eyes had PDR (11%). The most common type of pattern noticed was cystoid increase seen in 35 eyes (48%). 26 eyes had single spot increase (36%) and none of the patients in our study had an irregular decrease pattern. 12 eyes had diabetic macular oedema clinically and on OCT but normal autofluorescence. (16%). Cystoid increase and single spot increase patterns corelated with moderate and severe forms of NPDR. Patients with mild NPDR with DME showed no autoflourscence pattern. **Conclusions:** Diabetes is a debilitating disorder affecting all the organs in the body. The number of individuals with the disorder is on the rise due to sedentary lifestyle and dietary habits.The gold standard for diagnosing DME remains fundus slit lamp bio microscopy. 1 Recently optical coherence tomography (OCT) and fundus autofluorescence have proved valuable in early detection of DME. Lesions can be hyper-autofluorescent, hypo-autofluorescent , or iso-autofluorescent. FAF might reflect the damage of the retina and visualize photoreceptor integrity, which gives an insight into status of the retina in DME. Dynamic FAF monitoring helps to better evaluate the disease progression of DME as well as visual function. Since FAF does not require mydriasis, it is a faster and relatively inexpensive method of detecting DME.

KEYWORDS : diabetes, macular oedema, fundus autofluorescence, autofluorescence patterns in diabetic macular oedema.

INTRODUCTION:

India is the diabetes capital of the world with the second highest number of diabetic cases after China.Currently there are approximately 69.9 million diabetics in the country.

Ocular morbidity due to diabetes in India in 2019 was reported as 16.9% with Diabetic macular edema (DME) responsible for 4.6%. Early detection and treatment of DME would thus be of value.

Slit lamp biomicroscopy with the 90 D lens and optical coherence tomography (OCT)are the usual methods employed to evaluate macular pathology.Fundus autofluorescence (FAF), a relatively new non-invasive imaging modality can be used for evaluation of the metabolism of the RPE in DME.

Autofluorescence (AF) is based on the capacity of molecules (fluorophores)to emit light when they are excited by suitable wavelengths(488nm-514nm).

Lipofuscin which is an oxidative breakdown product of the photoreceptor outer segment located in the RPE, is the dominant fluorophore within the retina.

In a normal fundus, blood vessels appear dark as blood is able to strongly absorb the blue (~488nm) or green (~514nm) light that is used. The optic nerve appears dark due to the absence of RPE or lipofuscin in this region. The fovea is usually visualized as a spot of hypo-autofluorescence due to the high concentration of light-absorbing macular pigments such as Lutein and zeaxanthin in this area. These are usually present in the photoreceptors, and Inner nuclear layer and block the FAF emitted by the Lipofuscin in the RPE.

Based on the distribution of lipofuscin in the retina due to various pathologies, different patterns of FAF have been observed. In macular pathologies there is hyper-autofluorescence due to increased lipofuscin accumulation. This study was undertaken to evaluate patterns of FAF in Diabetic Macular oedema.

MATERIALS AND METHODS:

The study was conducted after approval by the institutional ethics committee. Prior permission was taken from the participants in the form of written informed consent. All the data was captured on a predetermined proforma. Adult diabetic patients visiting the ophthalmology OPD of a tertiary hospital between OCT 2019 to SEPT 2021 were evaluated and those detected to have DME which had not been treated were included in the study. Patients with history of retinal surgery or macular pathology due to any other etiology were excluded. Poor quality FAF images due to significant media opacities were also not analyzed. Patients were subjected to a complete ophthalmic examination, including Best corrected visual acuity, slit lamp evaluation, dilated fundus examination with +90D lens and indirect ophthalmoscope and intra ocular pressure measurement using a non-contact tonometer.

Grades of DR were classified according to ETDRS classification Macular scan was performed with a TOPCON 3D OCT- 1 MAESTRO using the 3D macula (6.0 x 6.0mm-512 X128) scan program. The thickness of the central 1mm of the ETDRS map was recorded. An average central thickness of 212µm and above was considered as macular oedema., Scans of poor quality (less than 22) were not considered. In patients with macular oedema confirmed on OCT, a fundus picture and fundus autofluorescence were captured using the Topcon TRC-NW8F mydriatic/non-----mydriatic retinal camera . Poor quality images and those with artifacts were discarded. FAF pictures were grouped into four patterns: -Normal, single spot increase, cystoid increase**[Image1-3]**.

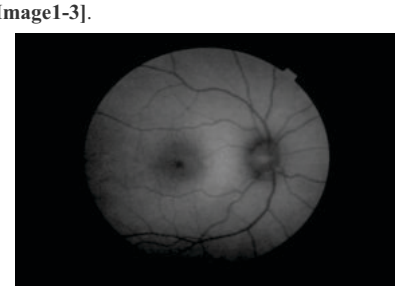

Image 1: Normal Faf

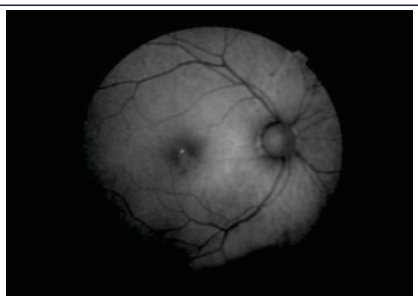

Image 2: Single Spot Increase Faf

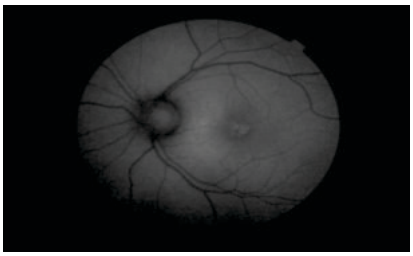

Image 3 : Cystoid Increase Faf

RESULTS :

39 diabetic patients with ages ranging from 40 to 75 years were included in the study. Of these 24 were males and 15 were females. Patients had been under treatment from 1 month to 32 yrs with majority having DM for more than 5yrs.

A total of 73 eyes were evaluated. Mild Non Proliferative Diabetic Retinopathy (NPDR) was present in 12 eyes (16%), moderate NPDR in 38 eyes (52%), severe NPDR in 15 eyes (21%) and Proliferative DR in 8 eyes (11%).

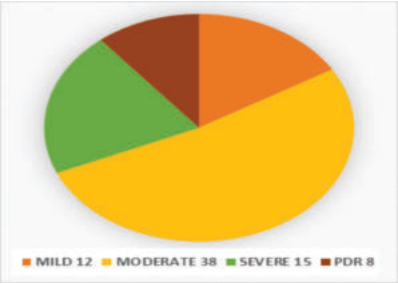

Figure 1: Grades of Diabetic Retinopathy

Macular thickness values ranged from 222µm to 646.8µm.

Table 1: Macular Thickness

GRADE OF DR	MINIMUM (µm)	MAXIMUM (µm)	AVERAGE (µm)
MILD NPDR	222	357	289.5
MODERATE NPDR	250	420	335
SEVERE NPDR	278.6	379.4	329
PDR	310	646.8	478

Of the 73 eyes studied, abnormal FAF was noted in 61 eyes (51%) and normal FAF was seen in 12 eyes (16%).The distribution of FAF was as follows. 35 eyes had cystoid increase (48%), 26 eyes had single spot increase (36%) No eyes showed irregular decrease and 12 eyes had normal autofluorescence. (16%).

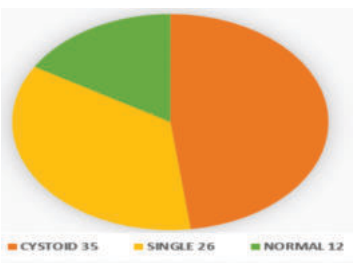

Figure 2: Type of Faf

Patterns of FAF seen in various grades of DR were as shown in Table 2. Irregular decrease was not seen in any eye.

Table 2: Faf Patterns In Various Grades of Dr

PATTERN OF AUTOFLUORSCENCE	NUMBER OF EYES Total n=73	MACULAR THICKNESS	MILD NPDR	MODERATE NPDR	SEVERE NPDR	PDR
CYSTOID INCREASE	35	250µ-420µm	0	13	14	8
SINGLE SPOT INCREASE	26	241µm - 380µm	3	22	1	0
NORMAL	12	222µ - 356µm	9	3	0	0
TOTAL	73		12	38	15	8

DISCUSSION:

This was an observational study where 73 eyes of 39 patients detected to have DME on OCT were evaluated. A central macular thickness of 212 +/-20 µm was considered as DME. .Of 39 patients, 24 were males and 15 females.

Non Proliferative Diabetic Retinopathy was seen in 65 eyes and 8 eyes had proliferative diabetic retinopathy.

Patterns observed on FAF were grouped as cystoid increase, single spot increase and normal autofluorescence.

A cystoid increase pattern was found in 35 eyes (56%). No patient with mild DR showed this pattern. Central macular thickness in these eyes ranged from 250µ-420µm. The OCT images revealed the presence of large intraretinal cysts.(group E2B)13 It is known that in severe cases of macular oedema, accumulation of intraretinal fluid occurs in well-defined spaces of the outer plexiform layer. The arrangement of the cysts is determined by the Müller fibres. Intraretinal cysts in DME unmask the underlying RPE by displacing the luteal pigment in the fovea centralis. This prevents the normal blockage of foveal FAF signal from the RPE at the level of intraretinal cysts. Increased FAF has been said to correspond to areas of decreased retinal sensitivity. This increase may be associated with a greater central macular thickness, reduced outer nuclear layer thickness as well as defects in the IS/OS as detected on OCT.

Studies on FAF in DME have found a Cystoid pattern in roughly half of the cases studied (57% and 53% respectively), Stela Vujosevic et al in Italy with a sample size of 116 eyes, detected a high incidence of this patten (45%) Saurabh et al. studied 112 eyes of diabetics with DME in Eastern India and found cystoid increase in FAF in 96 eyes. (86.6%)8 However this study did not include any eyes with normal FAF pattern, leading to this higher percentage.

Single spot increase pattern was seen in 26 eyes(36%). Most of these patients had moderate NPDR and few mild NPDR. No case with PDR showed this pattern. The macular thickness in these cases ranged from 241µm to 380µm. OCT showed the presence of small cystic spaces.(group E2A)13 Similar findings were found in the study by Vujosevic et al in 48 eyes(32%).

Early stages of DR lead to increased retinal thickness and distortion of the IS/OS junction with little or no fluid collection/ cysts.The damage to the photoreceptors and increased lipofuscin in the RPE is responsible for this FAF pattern.This may explain why patients with a single spot increase pattern belonged to mild and moderate grades of DR.

Saurabh Kumar et al found an increased spot autofluorescence in only 8% of all eyes with abnormal FAF. They attributed this to the presence of highly reflective hard exudates at the fovea thereby giving raise to pseudo-autofluorescence.

We found that in 12(16%) eyes in patients with mild or moderate diabetic retinopathy FAF showed a normal pattern despite recording macular thickness values >212µm. The OCT of these patients showed no evidence of cysts or RPE disruption. They may be classified as DME group E1 viz Simple thickening of macula without any cystic changes. A study carried out in Italy by Vujovsvic et al using a confocal

scanning laser ophthalmoscope found 35 (23%) eyes with normal FAF. They concluded that decreased FAF was the result of the blockage produced by macular pigments, and thus they considered it to be normal. Shen et al also reported 4(13%) eyes with normal pattern which was attributed to the relatively normal distribution of pigments in the RPE.

A fourth pattern of an irregular decrease in FAF has also been described by some authors. A study conducted by Shen et al, showed this pattern in 4 of 26 (13%) eyes. The reason for this was attributed to the presence of large hard exudates in the subfoveal region obscuring the underlying lipofuscin. Saurabh et al also observed this pattern in the peri and para foveal areas in a small percentage of eyes(5%). They also found these patients had damaged photoreceptor layers indicating a loss of photoreceptor cells and hence reduced lipofuscin production. Since the RPE functions is disrupted by diabetes, phagocytosis of the photoreceptor outer segments reduces with concomitant lower amounts of fluorophore debris, including lipofuscin In our study we did not obtain an irregular decrease patten in any of the 73 eyes since we considered only the central 1mm of the macula.

A recent study carried out in Mexico by Sergio Hernández,Lima-Gómez et al in 2020 have described a fifth pattern of autofluorescence known as plaque pattern.however we did not observe this pattern in any of the eyes studied.

CONCLUSION:

Diabetes mellitus is aVisual morbidity due to diabetes is a major lifestyle challenge. Approximately 14% of all diabetics are affected by Diabetic macular oedema (DME).

optical coherence tomography (OCT) remains the gold standard imagining modality for diagnosing DME. Recently, fundus autofluorescence has is also being considered as another valuable modality in early detection of D ME. The signal intensity on FAF images depends on the concentration of lipofuscin, and various patterns of autofluorescence are seen the various patterns observed can direct us to the structural and functional damage at the macula. We found that 84% of our DME cases had abnormal pattern FAF. Cystoid pattern was the most was most frequently documented in our study.

OCT provides detailed analysis of various macular abnormalities, however availability and cost may be limiting factors. Newer digital fundus cameras are equipped with non-infrared FAF and could prove to be a relatively inexpensive method of detecting DME. Routine screening of diabetic patients by using FAF along with coloured fundus photography can help the clinician in early detection and aid in treatment of DME.

Limitations of the study are a small sample size and a single point analysis of FAF. A longitudinal study would define any FAF changes with treatment and duration of diabetes.

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