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Research Article

A Study to Assess the Pattern of Diabetic Macular Edema Using Optical Coherence Tomography (OCT) and to Evaluate the Relevant Risk Factors

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Abstract

Purpose: To assess the pattern of diabetic macular edema using optical coherence tomography and to evaluate relevant risk factors.

Design: This was a cross sectional, open labelled observational study.

Setting: Outpatient Department of Ophthalmology, Government Medical College, Patiala.

Materials and Methods: 100 patients above 18 years of age diagnosed with diabetic macular edema (DME) were enrolled in the study. Only one eye of one patient with worse visual acuity was considered in this study. Eye with good visual acuity was excluded from study. After ocular examination, Optical Coherence Tomography was performed on patients. Using the retinal thickness map analysis protocol, macular thickness was determined and compared with normative data.

Statistical Analysis: The data was collected from patients using a proforma. Data was compiled in excel format. Data was subjected to statistical analysis using SPSS version 22 (SPSS Inc., Chicago, Illinois, USA).Pearson Chi Square test and ANOVA Analysis was used for assessment of level of significance. p value of less than 0.05 was taken as significant.

Results: Majority of the patients in our study had spongy DME (47%) followed by cystoid (39%), Serous Macular Detachment (9%), Mixed (5%). Among 9 patients of serous macular detachment (SMD) 7 were males. Maximum mean Cental Macular Thickness (CMT) was observed in Cystoid (523.82 µm) followed by Mixed (496.4 µm, SMD (380.22 µm), and spongy (328.91 µm) variants. Maximum mean Central Macular Volume (CMV) was observed in mixed (0.49 mm^3) followed by cystoid (0.45 mm^3), SMD (0.41 mm^3), and spongy (0.36 mm^3) variants. Low visual acuity was observed in Cystoid macular edema and serous macular detachment while patients having spongy macular edema had relatively good vision. On comparison of mean age, duration of diabetes mellitus, CMV and CMT in different patterns of macular edema a statistically significant difference was found. Highest mean age (77.67 years), highest mean duration of DM (14.56 years), highest FBS level (198.89 mg/dl), highest triglyceride level (257.00 mg/dl) was observed in SMD. Highest mean hba1c level was observed in cystoid (9.32%) followed by SMD (9.22%). Cystoid macular edema was more common in females and spongy macular edema was more common in males. Spongy macular edema (78.12%) was predominantly present in

patients with duration of diabetes mellitus ≤5 years while in patients with duration of diabetes mellitus between 5-10 years cystoid macular edema (53.19%) was predominantly present. Proportion of cystoid macular edema (50.90%) was more in patients having hba1c >8.5% while proportion of spongy macular edema (62.22%) was more in patients having HbA1c <8.5%. Among 9 patients of Serous Macular Detachment 7 patients had hba1c>8.5%. Proportion of cystoid macular edema (44.28%) was more in patients having Fasting Blood Sugar (FBS) >125 mg/dl while spongy macular edema (63.33%) was more in patients having FBS ≤ 125 mg/dl. In patients having triglyceride >200 mg/dl major proportion of patients had cystoid macular edema (49.02%) while in patients having triglyceride level <150 mg/dl major proportion of patients have spongy macular edema (72.22%). Statistically the difference in distribution of macular edema with respect to gender, habit of smoking, duration of diabetes mellitus, treatment of DM, visual acuity, grading of diabetic retinopathy, FBS and HbA_{1c} and Triglyceride was significant with p value = 0.016, 0.02, 0.02, 0.02, 0.01, 0.018, 0.004, 0.01 and 0.03 respectively. A significant negative correlation of visual acuity was present with grading of DR, CMT, CMV, HbA1c, FBS. The correlation between age, alcohol consumption, type of DM, Family history of DM, IOP, SBP, DBP, BMI, statin use, Cerebro Vascular Disease (CVD), LDL, HDL with pattern of DME was not statistically significant (p value = 0.87, 0.95, 0.12, 0.85, 0.17, 0.004, 0.779, 0.243, 0.46, 0.30, 0.179 and 0.21 respectively).

Conclusion: The pathophysiology of DME remains unknown and different patterns of DME can be caused by different ocular or systemic risk factors. The patients with chronic hyperglycemia, hyperlipidemia have more proportion of cystoid macular edema which leads to worsening of visual acuity. The foundation of treatment and prevention of DME progression lies in the strict control of chronic hyperglycemia, hypertension and hyperlipidemia.

Keywords: DR; DME; OCT; Cystoid Macular Edema; Spongy Macular Edema; Mixed Macular Edema; Serous Macular Detachment

Introduction

Around 25% of people with diabetes suffer from some form of diabetic retinopathy (DR) and number of cases increase with the duration of the diabetes. Studies have shown that after 10 years the prevalence of retinopathy in diabetic patients is 7%, after 25 years it is more than 90%. As per national institute of health (1995), in developed countries diabetic eye disease is the leading contributor of blindness in adults under the age of 75 years [1,2].

The two main complications of DR causing visual loss are proliferative retinopathy and diabetic macular edema (DME) [3-5]. Proliferative DR is caused by retinal ischemia leading to retinal neovascularization. This may lead to significant visual loss due to intraocular hemorrhage and retinal detachment. Diabetic macular edema is the thickening of the central portion of the retina called the macula. It involves edema and deposition of lipoproteins or hard exudates and this contributes to loss of central vision overtime due to deterioration of function of various retinal cells. Clinically significant macular edema (CSME) is the most severe form of DME. Chances of developing diabetic macular edema increases with the duration of diabetes [6-9].

Diabetic macular edema classification proposed by Otani and Murakami is based on Optical Coherence Tomography (OCT) measurements [10]. Using OCT, DME can be classified into four main types presented as follows:

- **Type 1:** Diffuse spongy macular edema (Figure 1,2)
- **Type 2:** Cystoid macular edema (Figure 3,4)
- **Type 3:** Serous macular detachment (Figure 5,6)
- **Type 4:** Mixed (Figure 7,8)

Traditional methods for evaluating macular edema such as stereoscopic fundus photography and non-contact fundus biomicroscopy are not sensitive enough to determine the details of the involved area. Optical Coherence Tomography (OCT) is a non-invasive modality which produces cross-sectional or three-dimensional, high-resolution images of the retinal layers and quantitative assessment of retinal thickness and other features of macular edema which correlate well with retinal histology as viewed by light microscopy especially with the introduction of Spectral Domain (SD) OCT. Optical Coherence Tomography enables precise measurement of macular thickness and facilitates the detection of macular edema which is the main pathologic feature

of diabetic maculopathy [11,12]. OCT has been widely used as a valuable tool for diagnosis and management of DME during the past two decades. Based on the findings of OCT, various morphologic patterns have been suggested for categorization of DME. In various studies it has been postulated that multiple factors influence the occurrence of diabetic macular edema including Fasting Blood Sugar (FBS), duration of DM, increased HbA_1c level, smoking, family history of DM and increased BP levels [13-15]. In this study, we evaluated the prevalence of OCT patterns of DME. This study was conducted to assess various patterns of diabetic macular edema and their associated relevant risk factors.

Material and Methods

100 patients above 18 years of age diagnosed with diabetic macular edema attending Ophthalmology Outpatient Department of Government Medical College, Patiala and willing to participate were enrolled in the study. A written informed consent was taken from the patient after explaining them the purpose of study, in accordance with declaration of Helsinki. All the study participants were given the option to opt out of the study at any point of time without having to give any reason for doing so. After detailed ocular examination, OCT was performed on patients. Using the retinal thickness map analysis protocol, macular thickness was determined and compared with normative data. The study was also approved by the ethical committee of the institute.

Only one eye of one patient with worse visual acuity was considered in this study. Eye with good visual acuity was excluded from study. The appearance of images on the OCT monitor was the sole criteria for scoring the patterns of DME. Diffuse spongy macular edema was identified by increase in retinal thickness and reduction in intraretinal reflectivity. Cystoid macular edema was identified by cystoid like spaces surrounded by highly reflective septa. SRF was identified by dome like fluid accumulation in the subretinal space. Mixed macular edema was identified by cystoid spaces along with subretinal fluid.

Statistical analysis

The data was collected from patients using a proforma. Data was compiled in excel format. Data was subjected to statistical analysis using SPSS version 22 (SPSS Inc., Chicago, Illinois, USA). Pearson Chi Square test and ANOVA Analysis was used for assessment of level of significance. p value of less than 0.05 was taken as statistically significant.

Figure 1: Fundus picture of right eye showing moderate NPDR.

Figure 2: OCT scan of above patient showing spongy macular edema.

Figure 3: Fundus picture of left eye showing PDR and CME.

Figure 4: OCT scan of above patient showing cystoid macular edema.

Figure 5: Fundus picture of left eye showing CSME.

Figure 6: OCT scan of above patient showing serous macular detachment.

Figure 7: Fundus picture of left eye showing moderate NPDR with CSME.

Figure 8: OCT scan of above patient showing mixed macular detachment.

Results

The mean age was found to be 61.29 ± 12.54 years with 58% males and 42% females. 88% patients had type 2 DM and 12% had type 1 DM. In age group ≤40 years, 41-50 years and 71-80 years cystoid macular edema was more common. (66.66%, 56.25%, and 53.33% respectively). In age group 51-60 years and 61-70 years spongy macular edema was more common (66.67% and 62.50% respectively). In age group >80 years most of the patients had serous macular detachment (55.56%) followed by cystoid (22.22%).

Maximum mean CMT was observed in Cystoid (523.82 µm) followed by Mixed (496.4 µm), SMD (380.22 µm), and spongiform (328.91 µm) variants. Maximum mean CMV was observed in mixed (0.49 mm^3) followed by cystoid (0.45 mm^3), SMD (0.41 mm^3), and spongy (0.36 mm^3) types (Figure10).

In females cystoid macular edema (54.7%) was more common. In males spongy macular edema (55.17%) was more common, Serous Macular Detachment (SMD) was more common in males as compared to females. Among 9 patients of SMD 7 were males. Statistically the difference in distribution of macular edema with respect to gender was significant (p value = 0.016) (Figure 13).

Cystoid macular edema (50%) was more common in smokers and spongy macular edema (50%) was more common in non-smokers. Statistically the difference in distribution of macular edema with respect to habit of smoking was significant (p value = 0.02) (Figure 14).

Most of the patients were suffering from DM since 5-10 years (47%) followed by 11-20 years (21%) and <5 years (32%). Spongy macular edema (78.12%) was most common pattern observed in patients with duration of DM ≤5 years. In patients with duration of DM 5-10 years cystoid macular edema (53.19%) was most common pattern observed. In patients with duration of DM 11-20 years cystoid macular edema (38.09%) and SMD (38.09%) was predominantly present. Statistically the difference in distribution of macular edema with respect to duration of DM was significant (p value = 0.02) (Figure 15).

Amongst 88 patients of type 2 diabetes 60 patients were on OHA, 25 were on Insulin and 3 were on both insulin and OHA. All patients of type1 DM were on insulin. In patients taking insulin as treatment cystoid macular edema (51.35%) was most common pattern observed while in patients taking OHA spongy macular edema (53.33%) was most common pattern observed. Among 9 patients of SMD 7 were on oral hypoglycemics. Statistically the difference in distribution of macular edema with respect to treatment of diabetes mellitus was significant (p value = 0.028) (Figure 16).

Most patients had visual acuity as 6/18-6/36 (41%), followed by worse than 3/60 (29%) followed by 6/60-4/60 (28%) and only 2% had presenting visual acuity between 6/6-6/12 (Figure

12). 40% patients in our study had severe NPDR followed by PDR (28%), moderate NPDR (26%) and mild NPDR (6%) (Figure 11). 47% patients had spongy DME followed by cystoid (39%), SMD (9%), mixed (5%) ME (Figure 9). Patients having visual acuity in range worse than 3/60 had major proportion of cystoid macular edema (55.17%). Patients having visual acuity between 6/60-4/60 had equal proportion of cystoid and spongy macular edema (35.71%). Patients having visual acuity in between 6/18-6/36 had major proportion of spongy macular edema (68.29%). Patients having visual acuity in between 6/6-6/12 had major proportion of spongy macular edema (100%).Out of 9 patients of SMD all cases belong to low visual acuity range. Statistically the difference in distribution of macular edema with respect to Visual acuity was significant (p value = 0.01) (Figure 17).

In patients having mild, moderate, severe NPDR; spongy macular edema (100%, 65.38%, 47.50% respectively) was most common pattern. In patients with PDR cystoid macular edema (57.14%) was most common pattern. Statistically the difference in distribution of macular edema with respect to diabetic retinopathy was significant (p value = 0.018) (Figure 18).

Amongst 100 patients 55% had Hba1c >8.5%. Most patients with HbA1c >8.5% had cystoid macular edema (50.90%) followed by spongy macular edema (34.54%). Proportion of spongy macular edema (62.22%) was more in patients having HbA1c <8.5%. Among 9 patients of SMD 7 patients had HbA1c >8.5%. Statistically the difference in distribution of macular edema with respect to HbA1c was significant (p value = 0.01) (Figure 19).

Most patients with FBS >125 mg/dl had cystoid macular edema (44.28%). In patient with FBS ≤ 125 mg/dl most patient had spongy macular edema (63.33%). Out of 39 patients of cystoid macular edema, 31 were having FBS >125 mg/dl. Statistically the difference in distribution of macular edema with respect to FBS was significant (p value = 0.004) (Figure 20).

In patients having triglyceride <150 mg/dl major proportion of patients had spongy macular edema (72.22%) while in patients having triglyceride >200 mg/dl major proportion of patients had cystoid macular edema (41.94%). Out of 9 patients of serous macular detachment 7 were having triglyceride level >200 mg/dl. Statistically the difference in distribution of macular edema with respect to triglyceride was significant (p value = 0.031) (Figure 21).

On comparison of mean values of age, duration of diabetes mellitus, CMV and CMT in different patterns of macular edema a statistically significant difference was found. Highest mean age (77.67 years), highest mean duration of DM (14.56 years), highest FBS level (198.89 mg/dl), highest triglyceride level (257.00 mg/dl) was observed in SMD. Highest mean HbA1c level was observed in cystoid (9.32%) followed by SMD (9.22%) (Table 1).

Statistically the difference in distribution of macular edema with respect to gender, habit of smoking, duration of diabetes mellitus (diabetic age), treatment of DM, visual acuity, diabetic retinopathy, FBS and HbA_{1c} and Triglyceride was significant with p value = 0.016, 0.02, 0.02, 0.02, 0.01, 0.018, 0.004, 0.01 and 0.03 respectively.

A significant negative correlation of visual acuity was present with grading of DR, CMT, CMV, HbA1c, FBS. A non-significant negative correlation of visual acuity was present with pattern of BMI, age and duration of DM. In our study, correlation between age, alcohol, type of DM, Family history of DM, IOP, SBP, DBP, BMI, history of hypertension, statin use, cerebro-vascular disease (CVD), LDL, HDL with pattern of DME was not statistically significant. (p value = 0.87, 0.95, 0.12, 0.85, 0.17, 0.92, 0.14, 0.779, 0.243, 0.40, 0.46, 0.30, and 0.259 respectively).

		N	Mean	Std. Deviation	F value	p value
Age	Cystoid	39	60.33	13.20	7.503	0.001
	Mixed	5	66.20	16.66		
	Spongy	47	58.43	10.01		
	Serous Macular Detachment	9	77.67	5.81		
	Total	100	61.29	12.54		

Duration of DM	Cystoid	39	7.77	3.63	16.095	0.0021
	Mixed	5	10.20	7.12		
	Spongy	47	5.36	3.37		
	Serous Macular Detachment	9	14.56	4.56		
	Total	100	7.37	4.60		
HbA1c	Cystoid	39	9.32	1.19	1.843	0.145
	Mixed	5	8.88	0.83		
	Spongy	47	8.73	1.27		
	Serous Macular Detachment	9	9.22	0.96		
	Total	100	9.01	1.21		
FBS	Cystoid	39	193.69	71.43	0.319	0.812
	Mixed	5	176.20	76.02		
	Spongy	47	182.23	69.29		
	Serous Macular Detachment	9	198.89	53.01		
	Total	100	187.90	68.53		
Cholesterol	Cystoid	39	189.33	59.34	0.208	0.890
	Mixed	5	181.40	84.83		
	Spongy	47	199.30	73.41		
	Serous Macular Detachment	9	192.22	77.89		
	Total	100	193.88	68.31		
LDL	Cystoid	39	102.04	34.64	1.669	0.179
	Mixed	5	144.00	110.05		
	Spongy	47	106.74	33.69		
	Serous Macular Detachment	9	101.33	31.62		
	Total	100	106.29	40.49		
HDL	Cystoid	39	47.36	8.78	5.277	0.21
	Mixed	5	41.60	10.92		
	Spongy	47	40.15	8.88		
	Serous Macular Detachment	9	39.22	8.80		
	Total	100	42.95	9.49		
Trig	Cystoid	39	198.46	73.29	5.886	0.001
	Mixed	5	206.80	47.18		
	Spongy	47	164.53	59.71		
	Serous Macular Detachment	9	257.00	60.69		
	Total	100	188.20	69.72		

SBP	Cystoid	39	142.00	16.98	0.156	0.925
	Mixed	5	142.40	14.52		
	Spongy	47	143.36	16.60		
	Serous Macular Detachment	9	139.56	8.59		
	Total	100	142.44	15.95		
DBP	Cystoid	39	84.31	8.84	0.365	0.779
	Mixed	5	87.20	9.96		
	Spongy	47	85.51	13.26		
	Serous Macular Detachment	9	88.22	6.89		
	Total	100	85.37	11.00		
BMI	Cystoid	39	27.77	3.05	1.416	0.243
	Mixed	5	30.40	4.98		
	Spongy	47	28.19	2.86		
	Serous Macular Detachment	9	29.22	3.42		
	Total	100	28.23	3.12		
IOP	Cystoid	39	16.69	1.72	1.704	0.171
	Mixed	5	16.80	1.10		
	Spongy	47	16.85	1.81		
	Serous Macular Detachment	9	18.33	3.77		
	Total	100	16.92	2.01		
CMT	Cystoid	39	523.82	130.24	31.260	0.001
	Mixed	5	496.40	123.96		
	Spongy	47	328.91	55.51		
	Serous Macular Detachment	9	380.33	56.73		
	Total	100	417.82	132.07		
CMV	Cystoid	39	0.45	0.14	4.810	0.004
	Mixed	5	0.49	0.13		
	Spongy	47	0.36	0.09		
	Serous Macular Detachment	9	0.41	0.12		
	Total	100	0.41	0.12		

Table 1: Distribution of various parameters according to pattern of DME.

Figure 9: Pattern of diabetic macular edema.

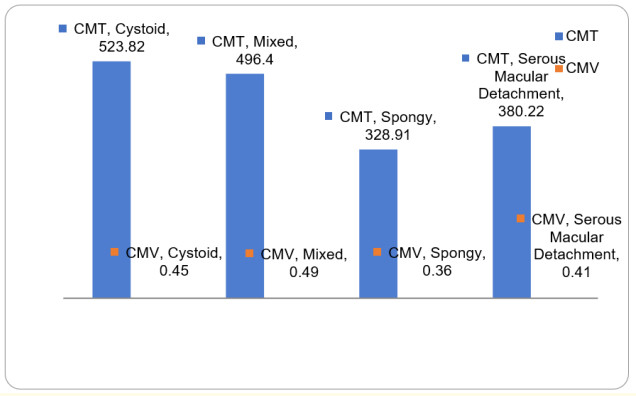

Figure 10: Central macular thickness and central macular volume.

Figure 11: Grading of diabetic retinopathy.

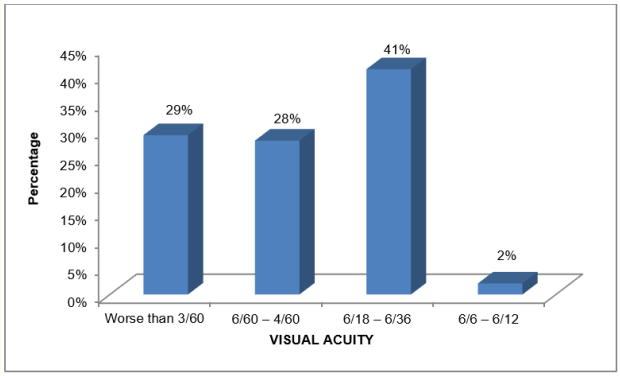

Figure 12: Visual acuity distribution in DME.

Figure 13: Correlation between gender and pattern of diabetic macular edema.

Figure 14: Correlation between smoking and pattern of diabetic macular edema.

Figure 15: Correlation between duration of diabetes mellitus and pattern of macular edema.

Figure 16: Correlation between treatment of diabetes mellitus and pattern of diabetic macular edema.

Figure 17: Correlation between visual acuity and patterns of diabetic macular edema.

Figure 18: Correlations between grading of diabetic retinopathy and pattern of diabetic macular edema.

Figure 19: Correlations between hba1c and pattern of diabetic macular edema.

Figure 20: Correlations between fbs and pattern of diabetic macular edema.

Figure 21: Correlations between serum triglyceride and pattern of diabetic macular edema.

Discussion

Using OCT we classified diabetic macular edema into four types namely diffuse spongy macular edema, cystoid macular edema, serous macular detachment, mixed based on classification proposed by Otani and Murakami.[10] In study conducted by Ghosh S., *et al*. [16]. OCT features were categorized into sponge like retinal swelling, cystoid macular edema, and serous retinal detachment. Ahmadpour-Baghdadabad M., *et al*. [17] categorized diabetic macular edema into Sponge like retinal swelling (SLRS), SRF, CME, posterior hyaloid traction (PHT) based on OCT imaging.

In the present study most of the patients had spongy DME (47%) followed by cystoid (39%), Serous Macular Detachment (9%) and Mixed(5%). In the study done by Al- Sharkawy [18] diffuse retinal thickening (DRT) was found alone in 65% of the eyes, CME in 16%, SRD in 13%, and CME and SRD in 6%. Alkuraya H., *et al*. [19] in their study reported SLRS as most common pattern (45.4%) followed by CME (29.0%) followed by serous retinal detachment (21.8%) and vitreofoveal traction (3.6%).

Ahmadpour-baghdadabad., *et al*. [17] in their study reported SLRS as most common pattern (64%) followed by SRF (47.7%) followed by CME (27.9%) followed by PHT (5.8%). Luxmi S., *et al*. [15] in their study reported Diffuse retinal thickening (DRT) as most common pattern (59.80%) followed by Cystoid macular edema (21.80%) and serous retinal detachment (SRD) (18.4%).

In the present study in age group ≤40 years cystoid macular edema (66.66%) was more common followed by spongy macular edema (33.33%) and in age group 41-50 years cystoid macular edema (56.25%) was more common followed by spongy macular edema (37.50%). In age group 51-60 years spongy macular edema (66.67%) was more common followed by cystoid macular edema (30.30%). In age group 61-70 years spongy macular edema (62.50%) was more common followed by cystoid macular edema (33.33%). In age group 71-80 years, cystoid macular edema (53.33%) was more common followed by serous macular detachment (20%). In age group >80 years most of the patients had serous macular detachment (55.56%) followed by cystoid (22.22%). Statistically the difference in distribution of macular edema with respect to age was not significant (p value = 0.87). Maalej A., *et al*. [20] in their study reported the age of patients ranged from 26 to 83 years. In their study the mean age of the patients was 59 years. The findings of our study are in concordance with the study done by Luxmi S., *et al*. [15] who found that in the age group of 40-50 years, 47.4% were in the group of cystoid macular edema. Among patients of 50-60 years, 59.8% showed diffuse retinal thickening and 18.4% had serous retinal detachment. They also found no significant difference in distribution of macular edema with respect to age.

In the present study male predominance was seen with 58% males and 42% females. In females cystoid macular edema (54.70%) was more common followed by spongy macular edema (35.70%), mixed macular edema (4.76%) and Serous Macular Detachment (4.76%). In males spongy macular edema (55.17%) was more common followed by cystoid macular edema (27.58%) followed by serous macular detachment (12.06%) and mixed pattern (5.17%). Statistically the difference in distribution of macular edema with respect to gender was significant (p value = 0.016). Similar to our study Maalej A., *et al*. [20] reported male predominance with men (54.6%) and women (45.4%). Acan D., *et al*. [14] too, reported DME was more prevelant in males than females. In the study done by Luxmi S., *et al*. [15] 42.3% of males and 57.7% of females showed diffuse retinal thickening. 100% of females showed cystoid macular edema, while no males in their study showed cystoid macular edema. 43.8% of males and 56.3% of females showed serous retinal detachment. They also found statistically significant difference in distribution of macular edema with respect to gender.

Among 9 patients in our study having Serous Macular Detachment (SMD), 7 were males. In study conducted by Ahmadpour-baghdadabad., *et al*. [17] they found subretinal fluid pattern was more common in males. Amongst 88 patients of type 2 diabetes 60 patients were on OHA, 25 were on insulin and 3 were on both. In study conducted by Ahmadpour- baghdadabad., *et al*. [17] 67.4% patients were on oral antidiabetic drug, 21.7% on insulin, 10.9% on both.

In the present study spongy macular edema (78.12%) was predominantly present in patients with duration of diabetes mellitus ≤5 years. In patients with duration of diabetes mellitus 5-10 years cystoid macular edema (53.19%) was predominantly present. In patients with duration of diabetes mellitus 11-20 years both cystoid macular edema (38.09%) and serous macular detachment (38.09%) were predominantly present. Statistically the difference in distribution of macular edema with respect to duration of diabetes mellitus was significant (p = 0.02) in our study. In study conducted by Luxmi S., *et al*. [15] those cases where the disease duration was between 10-20 years, 63.5% showed diffuse retinal thickening. Further, patients with disease duration of 21-40 years 47.4% had cystoid macular edema and 31.3% had SMD (p value = 0.367).

In the present study among patients taking insulin as treatment cystoid macular edema (51.35%) was in major proportion while in patients taking OHA spongy macular edema (53.33%) was the major proportion. Among 9 patients of Serous Macular Detachment 7 were on oral hypoglycemics. Statistically the difference in distribution of macular edema with respect to treatment of diabetes mellitus was significant (p value = 0.028).

In the study done by Luxmi S., *et al*. [15] A total of 145 patients (48.3%) were on Oral Hypoglycemic Agents (OHAs), 120 (40%) were on insulin. Amongst the cases on oral hypoglycemic agents 75% showed serous retinal detachment. Amongst the cases on insulin, 63.2% had a positive correlation with cystoid macular edema. Raman., *et al*. [21] also observed that those taking OHAs comprised the maximum proportion of their DR population.

Statistically the difference in distribution of macular edema with respect to FBS in our study was significant (p value = 0.004). In the study done by Luxmi S., *et al*. [15] they observed FBS levels of >125 mg/dl in 59.6% patients of diffuse retinal thickening, 89.5% patients of cystoid macular edema and 81.3% patients of serous retinal detachment (p value = 0.029).

Amongst 100 patients in our series, 55% had HbA1c>8.5%. In the study done by Luxmi S., *et al*. [15]. The proportion of those with uncontrolled diabetes was relatively much higher with 84.3% patients having HbA1c levels >8.5%.

Most patients in our study with HbA1c >8.5% had cystoid macular edema (50.90%) followed by spongy macular edema (34.54%). Proportion of spongy macular edema (62.22%) was more in patients having HbA1c <8.5%. Among 9 patients of SMD 7 patients had HbA1c>8.5%. Statistically the difference in distribution of macular edema with respect to HbA1c was significant (p value = 0.01).

Similar to our study, the series conducted by Raman., *et al*. [21] reported that higher HbA1c levels were associated with a higher risk of DR. In this study HbA1c levels >8.5%, 52.6% had cystoid macular edema. While levels between 7.1% to 8.5% had positive correlation to diffuse retinal thickening 46.2% and serous retinal detachment 56.3% (p value = 0.441).

In patents having triglyceride <150 mg/dl major proportion of patients had spongy macular edema (72.22%) while In patients having triglyceride >200 mg/dl major proportion of patients had cystoid macular edema (49.02%). Out of 9 patients of serous macular detachment 7 were having triglyceride level >200 mg/dL. Statistically the difference in distribution of macular edema with respect to triglyceride was significant (p value = 0.031). Ahmadpour-Baghdadabad M., *et al*. [17] in their study reported that Sub- retinal fluid pattern was more common in patients with serum TG > 200 mg/dl.

No statistically significant result was found by correlating HDL, LDL, total cholesterol with pattern of DME and to best of our knowledge no study has so far been conducted correlating these factors with pattern of DME.

Benarous R [22] assessed the association of serum lipids with diabetic retinopathy (DR), diabetic macular edema (DME), and macular thickness in adults with diabetes and found that Serum lipids were independently associated with the CSME, but not with DR, mild or moderate DME, or macular thickness.

In the present study patients having visual acuity in range 3/60, 2/60, 1/60, FC and HM had major proportion of cystoid macular edema (55.17%). Patients having visual acuity between 4/60,5/60,6/60 had equal proportion of cystoid and spongy macular edema (35.71%). Patients having visual acuity in between 6/18, 6/24, 6/36 had major proportion of spongy macular edema (68.29%). Patients having visual acuity in between 6/6,6/9,6/12 had major proportion of spongy macular edema (100%). Out of 9 patients of serous macular detachment all cases belonged to low visual acuity range. Statistically the difference in distribution of macular edema with respect to Visual acuity was significant. (p value = 0.01).

In the study done by Alkuraya H., *et al*. [19], serous retinal detachment patterns were accompanied by a higher central retinal thickness and a worse visual acuity. In the series of Yamamoto S., *et al*. [23], the CME pattern was associated with a lower visual acuity. Also in another study by Kim BY., *et al*. [24], the CME and posterior hyaloidal traction (PHT) without tractional retinal detachment were related to a worse visual acuity. Ahmadpour-Baghdadabad M., *et al*. [17] in their study showed that worst visual acuity pertain to the CME pattern.

The process begins as diffuse retinal thickening with sponge like appearance of the retinal layers because of increase in the extracellular spaces and then advancing to the typical image of cystoid spaces. In newly developed CME cystoid spaces are primarily located in the plexiform layer, while in well established CME, cystoid spaces become confluent and large cystoid cavities appear. Increase thickening of retina may also appear as an accumulation of serous fluid under the neurosensory retina, leading to a serous retinal detachment [18].

DME develops when fluid leaks from incompetent vascular bed and accumulates in the retina. Diabetic retinopathy progresses through a series of stages: mild, moderate, severe non-proliferative diabetic retinopathy (NPDR), proliferative diabetic retinopathy (PDR), to high risk PDR [25].

Most of our patients, 40% had severe NPDR followed by 28% PDR, 26% were having moderate NPDR and 6% were mild NPDR. In study conducted by by Acan D., *et al*. [14] DME prevelance rate was 28.6% in patients with mild- moderate NPDR while it was 72.6% in patients with severe NPDR to PDR. We enrolled only patients suffering from diabetic macular edema and in our study no follow up was done. However Acan D., *et al*. [14] enrolled diabetic patients and followed them unlike our study. In patients having cystoid macular edema most of their patients had PDR. In patients with mixed macular edema most of the patients had severe NPDR followed by PDR. In patients with mild and moderate and severe NPDR spongy macular edema was common. Statistically the difference in distribution of macular edema with respect to diabetic retinopathy was significant (p value = 0.018).

A significant negative correlation of visual acuity (recorded by Snellen chart) was present with grading of DR, CMT, CMV, HbA1c, FBS. Similar study was done by Sharkawy HT [18] who investigated the correlation between different features of optical coherence tomography, macular thickness, and visual acuity (VA) in patients with diabetic macular edema. Thus concluding CME had worst visual outcome and greatest central point thickness (CPT) and Average Macular Thickness (AMT). In diffuse retinal thickening (DRT), worse VA correlated more with CPT than with AMT, whereas in CME and SRD, correlation of VA was more with AMT than with CPT. VA correlated with height of lesion in eyes with SRD but not with CME. The height of cystoid space correlated with CPT but not with AMT, whereas the height of SRD correlated with both CPT and AMT. A non significant negative correlation of visual acuity was present with pattern of BMI, age and duration of diabetes mellitus.

Our study had several limitations some of which included

Cross sectional design and a limited sample size. No serial follow ups were done on such patients. Vitreoretinal interface abnormalities such as incomplete PVD and epiretinal membrane can be coexistent with DME and can contribute to vision loss in DME patients. Though not readily visible on ophthalmoscopy they can be easily detected by OCT. Posterior hyaloid traction, tractional macular edema are considered distinct entity in many DR classification systems but were not included in our study.

Conclusion

To conclude, the pathophysiology of DME remains unknown and different patterns of DME could be caused by different ocular or systemic risk factors. DME is the major cause of progressive vision loss and blindness in patient suffering from diabetes. At the moment OCT seems to be the technique of choice for the diagnosis

of macular edema as early stages of DME can be missed on slit lamp examination. OCT provides quantitative assessment and macular thickness mapping. It can provide thickness at any point of macular area. Fortunately, early detection and treatment of DME can avoid permanent vision loss. The control of DME risk factors may help to prevent or restrict the development of DME, as well as improve treatment response. The foundation of treatment and prevention of DME progression lies in the strict control of chronic hyperglycemia, hypertension and hyperlipidemia. Given recent therapy breakthroughs in minimising vision loss and preserving vision in people with DME, all people with diabetes should get screened early; this suggestion is even more critical for people who are at higher risk for DME.

Conflict of Interest

The authors declared no conflict of interest.

Availability of Data

The information regarding any resources and data availability that support the findings of this study should be directed to the corresponding author and will be considered upon reasonable request.

Consent for Participation

A written informed consent was taken from the patient after

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