



Prevalence of Diabetic Macular Edema in association with Severity of Diabetic Retinopathy

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Abstract

Introduction: Diabetic eye disease is a leading cause of vision loss in persons aged 20 to 74 years.¹ Diabetic retinopathy is the most common microvascular complication of diabetes², and can be broadly divided into two clinical stages: non proliferative (NPDR) and proliferative diabetic retinopathy (PDR). Diabetic macular edema (DME) is the leading cause of visual loss and legal blindness³ in people with diabetes mellitus affecting up to 15% of patients 15 years after diagnosis. ⁴Despite the significance of this problem, and the rising prevalence of diabetes, notably in emerging Asian countries such as India and China^{5,6} there are few precise contemporary estimates of the worldwide prevalence of DR, particularly severe vision-threatening stages of the disease, including PDR and DME.

Materials and Methods: It was a cross sectional observational study where 300 cases of pre-diagnosed Diabetes with retinopathy, attending the ophthalmology OPD with their informed written consent were included in the study. In all the patients clinical examination included assessment of Visual acuity, slit lamp examination, fundus examination with +90 D lens, applanation tonometry, gonioscopy with three mirror gonioscope, direct and indirect ophthalmoscopy, Stereoscopic 30° macula centered photograph (by Carl Zeiss - fundus camera), Cirrus OCT macula.

Result: Out of 600 eyes, a total of 65 (10.8%) eyes were unaffected, 493 (82.2%) were identified as NPDR - of these 225 (45.6%) were graded as minimal NPDR, 152 (25.3%) were graded as mild NPDR (25.3%), 72 (12%) as moderate NPDR, 34 (5.7%) and 10 (1.6%) as severe and very severe NPDR. A total of 37 (6.2%) were graded as PDR - of these 18 (3%) were mild to moderate PDR, 13 (2.2%) were high risk PDR and remaining 6 (1%) were advanced diabetic disease cases. A total of 5 (0.8%) eyes could not be assessed. A total of (20.1%) of females and (29.5%) males had DME, but this association was not found to be significant statistically ($p=0.062$). Among different age groups prevalence of DME ranged from 11.8% (30-40 years) to 31.9% (40-50 years), but association between age and prevalence of DME was not found to be significant statistically ($p=0.156$). Among different categories, a significant increase in prevalence of DME was observed with increasing severity of NPDR ($p<0.001$) with prevalence rates showing an increase from 10.7% to 70% from minimal to very severe NPDR groups. Out of the 300 patients prevalence of DME was 14.0% and 24.3% in NPDR and PDR types. Statistically, this difference was not significant ($p=0.226$).

Conclusion: The overall prevalence of DME in diabetics with Diabetic Retinopathy is 29%. Prevalence of DME is more in NPDR and increases with severity of NPDR. The prevalence of DME pattern of diffused retinal thickening is most followed by cystoid macular edema and serous retinal detachment among subjects with diabetic retinopathy.

Keywords: Diabetic retinopathy, diabetes, prevalence, DME.

Introduction

Diabetic eye disease is a leading cause of vision loss in persons aged 20 to 74 years.¹ Diabetic retinopathy is the most common microvascular complication of diabetes². It is a progressive disease predominantly affecting the integrity of the microscopic vessels found in the retina and can be broadly divided into two clinical stages: non proliferative (NPDR) and proliferative diabetic retinopathy (PDR). According to the Early Treatment of Diabetic Retinopathy Study (ETDRS report number 7, 1991), Clinically Significant Macular Edema (CSME) is defined as observation of retinal thickness or hard exudates accompanied with retinal thickening within 500µm of the center of the macula or if a zone of one-disc area size of retinal thickness is seen within one-disc diameter of the center of the macula. Diabetic macular edema (DME) is the leading cause of visual loss and legal blindness (Vision in better eye <1/60 to Perception light)³ in people with diabetes mellitus affecting up to 15% of patients 15 years after diagnosis.⁴ It must be noted that of the visually disabling conditions in persons with diabetic eye disease, diabetic macular edema (DME), left untreated, is a common cause of vision loss. DME affects central vision and can lead to decline in vision ranging from slight visual blurring to blindness,

substantially affecting independence and quality of life.^{7,8} There are no comprehensive documentation, in available literature about prevalence, appearance, progression and associated visual loss in diabetic population with specific reference to macular edema.

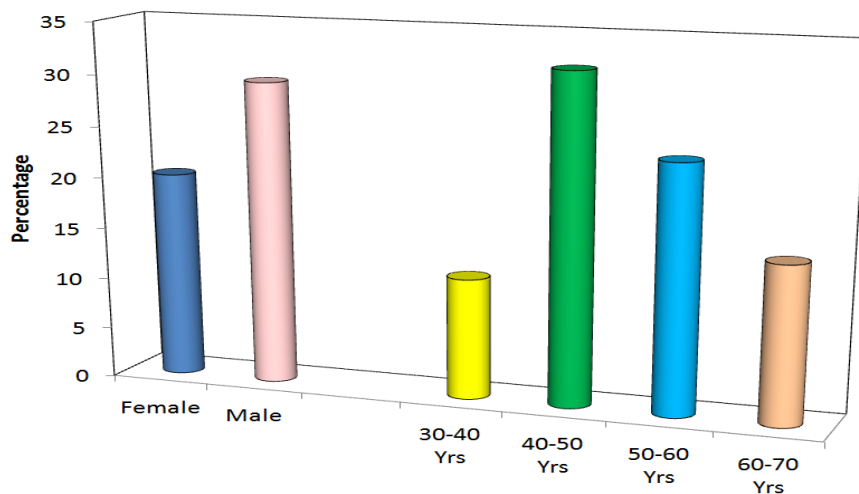
Materials and Methods

It was a cross sectional observational study. 300 cases of pre-diagnosed Diabetes with retinopathy, attending the ophthalmology OPD with their informed written consent were included in the study. In all the patients clinical examination included assessment of Visual acuity, slit lamp examination, fundus examination with +90 D lens, applanation tonometry, gonioscopy by three mirrored gonioscope, direct and indirect ophthalmoscopy, Stereoscopic 30⁰ macula centered photograph (by Carl Zeiss - fundus camera), Cirrus OCT macula. The data was analyzed using Statistical Package for Social Sciences, version 15.0. For, categorical data Chi-square test was used whereas continuous data was analyzed using ANOVA and student "t"-test. Multivariate assessment was done using logistic regression. The confidence level of the study was kept at 95% and hence a "p" value less than 0.05 indicated a statistically significant association.

Observation

Table 1: Association of DME with Age and Gender Profile of Patients (n=300)

SN	Characteristic	Total No.	With DME		Without DME		Statistical significance
			No.	%	No.	%	
1.	Gender						
	Female	144	29	20.1	115	79.9	$\chi^2=3.490$; p=0.062
	Male	156	46	29.5	110	70.5	
2.	Age						
	30-40 Yrs	17	2	11.8	15	88.2	$\chi^2=5.232$; p=0.156 (NS)
	40-50 Yrs	91	28	31.9	63	68.1	
	50-60 Yrs	166	40	24.1	126	75.9	
	60-70 Yrs	26	4	15.4	22	84.6	



A total of (20.1%) of females and (29.5%) males had DME. Although, proportion of patients with DME was higher among males as compared to females yet this association was not found to be significant ($p=0.062$).

Among different age groups prevalence of DME ranged from 11.8% (30-40 years) to 31.9% (40-50 years). This association between age and prevalence of DME was also found to be insignificant statistically ($p=0.156$).

Table 2: Distribution of patients according to Patterns of DME (EDTR) (n=87)

SN	Characteristic	No. of Eyes	Percentage
1.	Diffuse retinal thickening	52	59.8
2.	Cystoid macular edema	19	21.8
3.	Serous retinal detachment	16	18.4

A total of 87 eyes were diagnosed as diabetic macular edema. Out of these, majority (59.8%) had diffuse retinal thickening. Cystoid macular

edema was seen in 19 (21.8%) and serous retinal detachment in 16 (18.4%).

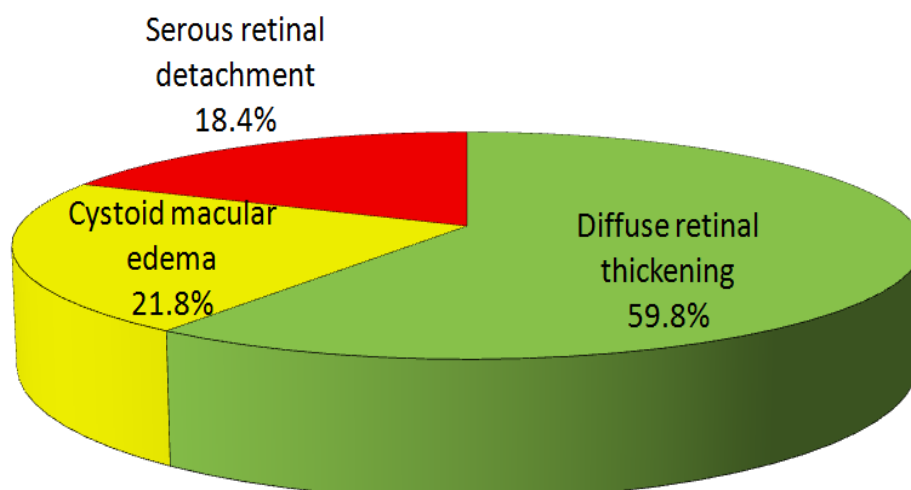
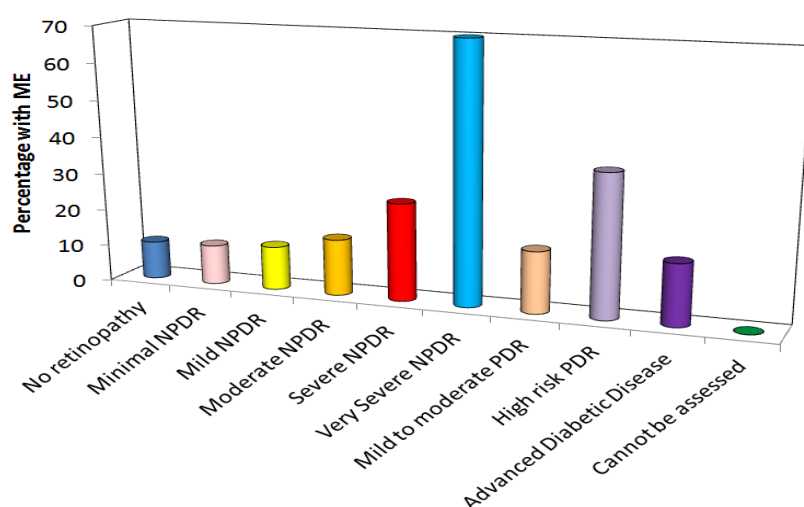


Table 3. Association of Diabetic retinopathy severity (ETDRS) with Diabetic Macular Edema

SN	DR	Total No.	With DME (n=87)		Without DME (n=513)		Statistical Significance	
			No.	%	No.	%	χ^2	'p'
1.	No retinopathy	65	9	10.3	56	89.7	0.025	0.874
2.	NPDR	493	69	14.0	424	86.0	0.567	0.452
	Minimal NPDR	225	24	10.7	201	89.3	33.2	<0.001
	Mild NPDR	152	18	11.8	134	88.2		
	Moderate NPDR	72	11	15.3	61	84.7		
	Severe NPDR	34	9	26.5	25	73.5		
	Very Severe NPDR	10	7	70.0	3	30.0		
3.	PDR	37	9	24.3	28	75.7	3.07	0.08
	Mild to moderate PDR	18	3	16.7	15	83.3	2.18	0.337
	High risk PDR	13	5	38.5	8	61.5		
	Advanced Diabetic Disease	6	1	16.7	5	83.3		
4.	Cannot be assessed	5	0	0	5	100	0.855	0.355

$\chi^2=2.98$ (df=2); p=0.226 (No retinopathy, NPDR and PDR)



Prevalence of DME ranged from 10.3% (No retinopathy) to 70% (very severe NPDR). In major categories, prevalence of DME was 14.0% and 24.3% in NPDR and PDR types. Statistically, this difference was not significant (p=0.226). Among different categories, a significant increase in prevalence of DME was observed with increasing severity of NPDR (p<0.001) with prevalence rates showing an increase from 10.7% to 70% from minimal to very severe NPDR groups.

Result

Out of 600 eyes, a total of 65 (10.8%) eyes were unaffected, 493 (82.2%) were identified as NPDR - of these 225 (45.6%) were graded as minimal NPDR, 152 (25.3%) were graded as mild NPDR (25.3%), 72 (12%) as moderate NPDR, 34 (5.7%) and 10 (1.6%) as severe and very severe NPDR. A total of 37 (6.2%) were graded as PDR - of these

18 (3%) were mild to moderate PDR, 13 (2.2%) were high risk PDR and remaining 6 (1%) were advanced diabetic disease cases. A total of 5 (0.8%) eyes could not be assessed. A total of (20.1%) of females and (29.5%) males had DME. Although, proportion of patients with DME was higher among males as compared to females yet this association was not found to be significant statistically (p=0.062). Among different age groups prevalence of DME ranged from 11.8% (30-40 years) to 31.9% (40-50 years). However, the association between age and prevalence of DME was not found to be significant statistically (p=0.156). The pattern distribution of DME in Diabetic Retinopathy cases is that; macular edema in majority cases 59.8% occurs as diffused retinal thickening followed by cystoid macular edema in 21.8% and serous retinal detachment in 18.4%. Among different categories, a significant

increase in prevalence of DME was observed with increasing severity of NPDR ($p < 0.001$) with prevalence rates showing an increase from 10.7% to 70% from minimal to very severe NPDR groups. Out of the 300 patients prevalence of DME was 14.0% and 24.3% in NPDR and PDR types. Statistically, this difference was not significant ($p = 0.226$).

Discussion

Diabetic macular edema (DME) is one of the leading causes of blindness and is a known progressive complication among patients with diabetic retinopathy. Prevalence has been reported to increase from 3% within 5 yrs of diagnosis to 28% after 20 yrs duration.⁹ Owing to severe vision threatening consequences associated with diabetic macular edema, it is a major cause of concern.

For this purpose, a cross-sectional study was carried out in which a total of 300 patients (600 eyes) prediagnosed cases of diabetes with diabetic retinopathy in age group 30-70 year were enrolled. Cases of diabetic retinopathy having any confounders viz. other macular pathology, opaque/hazy ocular media preventing fundus visualization and co-existing ocular disorders likely to mask the findings of diabetic retinopathy were not included in the assessment.

With respect to type of diabetic retinopathy, NPDR (82.2%) was more common than PDR (6.2%). 65 (10.8%) patients had only unilateral retinopathy. These findings are in agreement with global estimates of prevalence of different types of diabetic retinopathy. In a recent metaanalysis,¹⁰ proliferative retinopathy comprised nearly 20% of total burden of diabetic retinopathy, thus indicating that as far as prevalence is concerned, proliferative type plays a dormant role while NPDR is dominating.

In present study, no significant association of age and gender was observed with occurrence of macular edema. Macular edema was seen in 87 eyes (14.5%).

Considering the pattern of DME amongst DR patients; in present study of all the DME patients,

majority (59.8%) had diffuse retinal thickening. Cystoid macular edema was seen in 19 (21.8%) and serous retinal detachment in 16 (18.4%). Similar to results of present study, diffuse retinal thickening was found to be the major finding in other studies too^{11,12,13,14}. The prevalence of serous retinal detachment in present study was also in accordance with other series^{11,14} where it varies from 15% to 31%, depending on the series. However, prevalence of cystoid macular edema was slightly lower in present study as compared to the finding of Otani *et al.* (1999)¹⁵ who reported it to be the prevalent in 47% of patients. One of the reason for this differences in pattern findings of present study to that of others could be attributed to the fact that in present study we assigned only one pattern to an eye whereas in some other studies¹⁵ more than one patterns were identified and reported from a single eye. However, in present study we considered only the dominating pattern.

In their study, Yau *et al.* (2012)¹⁰ reported the prevalence of diabetic macular edema among diabetic retinopathy patients to be much lower at 7.48%. However, Wong *et al.* (2008) reported DME in nearly 16.3% of diabetic retinopathy patients. In a recent metaanalysis, Lee *et al.* (2015)¹⁶ found prevalence of DME to range from 1.4% to 33.3% in different studies. Ding and Wong (2012)¹⁷ reported that nearly 29% of US adults with diabetes have diabetic retinopathy and of these nearly 10% have diabetic macular edema. In a study from rural China, the prevalence of DME in DR patients was found to be 12%.¹⁸ Unlike present study which was specifically targeted to see the prevalence of macular edema in diabetics having retinopathy, most of the other studies have targeted on the prevalence of diabetic macular edema among diabetic patients in general and have considered diabetic macular edema as an extended complication in diabetic retinopathy patients.

The present study failed to show any significant association of DME with different ETDRS categories of DR. However, within NPDR subtype

a significant association between severity of NPDR and DME was observed. The findings in general endorse that diabetic macular edema does not fit the regular course of diabetic retinopathy progression and may occur at any stage of diabetic retinopathy, whether nonproliferative, moderate, or severe, or even at the more advanced stages of the retinopathy.

CONCLUSION

The overall prevalence of DME in diabetics with Diabetic Retinopathy is 29%. Prevalence of DME is more in NPDR and increases with severity of NPDR. The prevalence of DME pattern of diffused retinal thickening is most followed by cystoid macular edema and serous retinal detachment among subjects with diabetic retinopathy.

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