Original Article

Sight Threatening Diabetic Retinopathy in Type – 2 Diabetes Mellitus

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Purpose: To determine the proportions of Proliferative Diabetic Retinopathy (PDR) and Clinically Significant Macular Edema (CSME) in patients with known type–2 Diabetes Mellitus.

Material and Methods: A prospective study was conducted at Ophthalmology Department, Liaquat University of Medical and Health Sciences, Hyderabad, Pakistan. Duration of study was one year, starting from 1st January 2010 till 31st December 2010. Two hundred consecutive type – 2 diabetics diagnosed with diabetic retinopathy were classified according to the most severe changes in the worse eye into the following three stages based on EDTRS classification. 1) Patients with Non–Proliferative Diabetic Retinopathy (NPDR). 2) Patients with CSME stage (in the presence of NPDR). 3) Patients with PDR stage (irrespective of presence or absence of CSME).

Results: The mean age of patients with diabetic retinopathy was 51.7 ± 9.4 years. 62 (31%) patients had PDR, and another 66 (33%) patients had CSME. 51.6% of patients with PDR were in the age group of 40 – 49 years and 56% of patients with CSME were 50 – 59 years. Patients presented with PDR were significantly younger (P–value < 0.001) than patients with CSME and NPDR. 51% of patients had DM for 15.7 ± 6.1 years; with a mean age of 30.5 ± 4.6 years at diagnosis with type – 2 DM.

Conclusion: 64% of patients had sight – threatening stages of diabetic retinopathy, and 34.4% of them were 40 – 49 years of age.

Diabetes Mellitus (DM) is a chronic, costly and potentially disabling disease due to its severe complications. There are 285 million adults worldwide with DM; having a prevalence of 6.4% among adults aged 20 – 79 years.[1] Pakistan has the 7th largest population of DM with 7.1 million people; having a prevalence of 9% among adults ≥ 25 years of age[1,2].

Diabetic retinopathy is one of the common micro-vascular complications of DM. The risk of developing diabetic retinopathy increases with the duration of DM. [3] The prevalence of diabetic retinopathy among diabetic subjects varies between 15.3% and 28.9% in various studies conducted in Pakistan[4,5].

Diabetic retinopathy progresses from the asymptomatic Non-Proliferative Diabetic Retinopathy (NPDR); characterized by increased vascular permeability and progressive vascular closure, to the sight – threatening Proliferative Diabetic Retinopathy (PDR); characterized by growth of new blood vessels on the retina[3,6].

The new blood vessels in PDR may bleed causing vitreous hemorrhage with sudden loss of vision, or may lead to tractional retinal detachment and neovascular glaucoma. Meanwhile; Clinically Significant Macular Edema (CSME) can develop during any stage of diabetic retinopathy, and it is characterized by retinal thickening from leaky blood vessels causing slow and gradual blurring of vision[3,6].

More than 90% of cases of diabetes worldwide are type – 2 DM. Type – 2 DM occurs at a relatively younger age in the Indian Subcontinent than elsewhere in the world[7]. Basit et al[8] in a study on 2199 type – 2 diabetics had observed that; the age at onset of DM was < 40 years in 46.3% of type – 2 diabetics.

Early onset type – 2 DM may cause diabetic retinopathy to develop at a relatively younger age. The aim of this study was to determine the proportions of Proliferative Diabetic Retinopathy (PDR) and Clinically Significant Macular Edema (CSME) in patients with known type – 2 DM.

MATERIAL AND METHODS

This cross sectional study was carried out at Department of Ophthalmology, Liaquat University of Medical and Health Sciences, Hyderabad, Pakistan, from 1st January 2010 to 31st December 2010. The sample size was calculated using computer software Open Epi Version 2. A sample of 200 diabetics with retinopathy was required for 15.3% prevalence at 95% confidence interval and absolute precision of ± 5% (based on 15.3% prevalence of diabetic retinopathy in the diabetic subjects of the Pakistan National Blindness and Visual Impairment Survey)[4].

Diabetic retinopathy screening was performed in all known as well as newly diagnosed type – 2 diabetics (already on oral hypoglycemic drugs or on insulin) coming to our hospital for routine checkup with or without complain of decreased vision or any other ocular symptom.

Detailed history was taken including name, age, gender, duration of DM and the mode of treatment (oral hypoglycemic drugs or insulin). Detailed ocular examination was performed including best corrected visual acuity (BCVA), anterior segment examination and fundus examination. Patients were excluded if fundus details were not visible due to cataract or corneal opacity.

The patients were divided according to the most severe diabetic retinopathy changes in the worse eye into the following three groups based on EDTRS classification: a) Patients with NPDR stage b) Patients with CSME stage (in the presence of NPDR) c) Patients with PDR stage (irrespective of presence or absence of CSME). Also; the patients were stratified according to their age into the following five age groups: Below 30 years, 30 – 39 years, 40 – 49 years, 50 – 59 years and above 59 years of age.

The data was analyzed using SPSS version 11 software. The Descriptive Statistics obtained were; the age distribution, the proportion of various stages of diabetic retinopathy, and the distribution of stage of retinopathy by the age of patients. The mean and standard deviation (SD) for the age at presentation with diabetic retinopathy, the duration of DM, and the estimated age at onset of DM were compared; between different stages of diabetic retinopathy using one way ANOVA test. P – Value < 0.05 was taken as significant.

RESULTS

In this study; 200 consecutive type – 2 diabetics diagnosed with diabetic retinopathy were included. 121 (60.5%) patients had presented with an ocular symptom, meanwhile; the remaining 79 (39.5%) patients were referred for diabetic retinopathy screening by physicians.

Over 52% of our patients were females with mean age of 50.4 ± 9.7 years. Males were significantly older with mean age of 53.1 ± 8.8 years (P – value = 0.043). Males also had a significantly longer duration of DM (P – value < 0.001); the duration of DM in males was 14.6 ± 7.4 years, while females had a mean duration of 11.9 ± 4 years.

Table 1 shows the overall demographic features of our patients along with difference in demographics of patients with different stages of diabetic retinopathy.

The difference in the mean duration of DM in patients with different stages of diabetic retinopathy was statistically insignificant (P – value = 0.083). However; patients with PDR were significantly younger at the time of diagnosis with DM than other patients (P – value < 0.001) (Fig. 1).

In 51% of patients the age at diagnosis with DM was < 40 years; and they were considered to have early onset type – 2 DM. 40.2% (41/ 102) of patients with early onset type – 2 DM had already been shifted from oral hypoglycemic drugs to insulin by their physicians to control their DM. Meanwhile; 17.3% (17 / 98) of patients with late onset type – 2 DM were on insulin.

Because of early onset type – 2 DM in our patients; 58.1% (36 / 62) of patients with PDR were < 50 years of age. Table 2 shows an overall comparison between patients with early onset type – 2 DM v/s late onset type – 2 DM. Table 3 shows detailed comparison between patients with early onset type – 2 DM v/s late onset type – 2 DM; presented with different stages of diabetic retinopathy.

DISCUSSION

The prevalence and severity of diabetic retinopathy increases with the duration of DM and age of the patients, along with; poor metabolic control. But

Table 1: Diabetic retinopathy and the demographics (N = 200).

Demographics	N (%)	NDPR (N = 72)	CSME (N = 66)	PDR (N = 62)	P - Value †
Gender	M:F = 1:1.11				
Male	95 (47.5)	27	39	29	
Female	105 (52.5)	45	27	33	
Stage of diabetic retinopathy					
NDPR		72 (36.0)			
CSME			66 (33.0)		
PDR				62 (31.0)	
Age at Presentation (Years)					
Mean + SD	51.7 ± 9.4	54.3 ± 10.4	53.4 ± 8.7	47.0 ± 6.8	
Min - Max	35 - 70	39 - 70	35 - 70	35 - 60	
< 30	00 (00.0)	00	00	00	< 0.001*
30 - 39	15 (07.5)	7 (9.7%)	4 (6.1%)	4 (6.5%)	
40 - 49	66 (33.0)	22 (30.6%)	12 (18.2%)	32 (51.6%)	
50 - 59	70 (35.0)	9 (12.5%)	37 (56.0%)	24 (38.7%)	
> 59	49 (24.5)	34 (47.2%)	13 (19.7%)	2 (3.2%)	
Duration of DM (Years)					
Mean ± SD	13.2 ± 6.0	14.4 ± 5.9	12.3 ± 5.7	12.8 ± 6.2	
Min - Max	02 - 35	06 - 35	02 - 22	05 – 30	
≤ 5	23 (11.5)	00	15 (22.7%)	8 (12.9%)	0.083**
6 - 10	47 (23.5)	19 (26.4%)	8 (12.1%)	20 (32.3%)	
11 - 15	90 (45.0)	35 (48.6%)	31 (47.0%)	24 (38.7%)	
≥ 16	40 (20.0)	18 (25.0%)	12 (18.2%)	10 (16.1%)	
Age at Diagnosis with DM (Years)					
Mean ± SD	38.5 ± 10	39.8 ± 11.2	41.1 ± 11.2	34.2 ± 8.4	
Min - Max	20 - 59	25 - 59	30 - 58	20 - 47	< 0.001*
Early onset DM < 40 Years	102 (51.0)	40	28	34	
Late onset DM ≥ 40 Years	98 (49.0)	32	38	28	

†By one way ANOVA, *Significant difference, **Insignificant difference
NDPR = Non-Proliferative Diabetic Retinopathy, CSME = Clinically Significant Macular Edema
PDR = Proliferative Diabetic Retinopathy

traditionally; the age has been coupled to the duration of DM and was not regarded as an independent risk factor[3]. Niazi et al[9] and Chaudhary[5] reported that only the longer duration of DM was proved to be an independent risk factor for both type and progression of diabetic retinopathy. Al – Maskari and El – Sadig[10] observed an increase in the prevalence of diabetic retinopathy with increasing age (P = 0.004) and disease duration (P = 0.0001). Similar results were reported in several studies[11,12].

In this study; the mean age of patients presenting with diabetic retinopathy was 51.7 ± 9.4 years, which is consistent with other national[5,13–15], and

Table 2: Dempgraphics of early onset type - 2 DM v/s late onset DM

	Early Onset Type - 2 DM at Age < 40 Years (N = 102)	Late Onset Type - 2 DM at Age ≥ 40 Years (N = 98)	P-value †
Age at Presentation with Retinopathy (Years)			
Mean ± SD	46.2 ± 7.9	57.4 ± 7.2	< 0.001*
Min - Mix	35 - 68	45 - 70	
Duration of DM (Years)			
Mean ± SD	15.7 ± 6.1	10.6 ± 4.6	< 0.001*
Min - Mix	5 - 35	2 - 20	
Age at Diagnosis with DM (Years)			
Mean ± SD	30.5 ± 4.6	46.8 ± 6.8	< 0.001*
Min - Mix	20 - 39	40 - 59	

† By one way ANOVA, *Significant difference

Table 3: Diabetic retinopathy in early onset type - 2 DM v/s late onset DM

	Early Onset Type - 2 DM at Age < 40 Years				Late Onset Type - 2 DM at Age ≥ 40 Years			
	NPDR N = 40	CSME N = 28	PDR N = 34	P-value †	NPDR N = 32	CSME N = 38	PDR N = 28	P-value †
Age at Presentation with Retinopathy (Years)								
Mean ± SD	47.3 ± 8.4	48.0 ± 8.3	43.5 ± 6.4	0.045*	63.0 ± 4.6	57.3 ± 6.8	51.1 ± 4.6	< 0.001*
Duration of DM (Years)								
Mean ± SD	16.0 ± 6.2	14.7 ± 6.3	16.2 ± 6.1	0.591**	12.5 ± 4.9	10.5 ± 4.6	8.7 ± 3.2	0.005*
Age at Diagnosis with DM (Years)								
Mean ± SD	31.3 ± 4.3	33.3 ± 3.0	27.3 ± 4.3	< 0.0001*	50.5 ± 7.2	46.8 ± 6.8	42.5 ± 2.5	< 0.001*

† By one way ANOVA, *Significant difference, **Insignificant difference
NPDR = Non-Proliferative Diabetic Retinopathy, CSME = Clinically Significant Macular Edema
PDR = Proliferative Diabetic Retinopathy

international studies[11,16–18]. Thirty one percent of our patients had the sight - threatening PDR, and similar results were reported in literature[2,13,14,16–18]. Meanwhile, other studies had reported lower prevalence of PDR among patients with any type of diabetic retinopathy, i.e. 11.7% (111 / 946) was reported by Chaudhary GM[5], 20.9% (163 / 780) by Khan AJ[15], and 14.6% (172 / 1176) was reported by Agrawal et al[11]. This lower prevalence of PDR might be related to the difference in the duration of DM. The short duration of ≤10 years of DM; was observed in 60.5% by Chaudhary GM[5], in 52.2% by Khan AJ [15], and in 42.4% by Agrawal et al[11]. Whereas in this study, only 35% of patients had DM for ≤10 years.

The prevalence of the sight – threatening CSME among our patients with NPDR was 47.8% (66/138), this is consistent with literature[12,14,18,19]. However

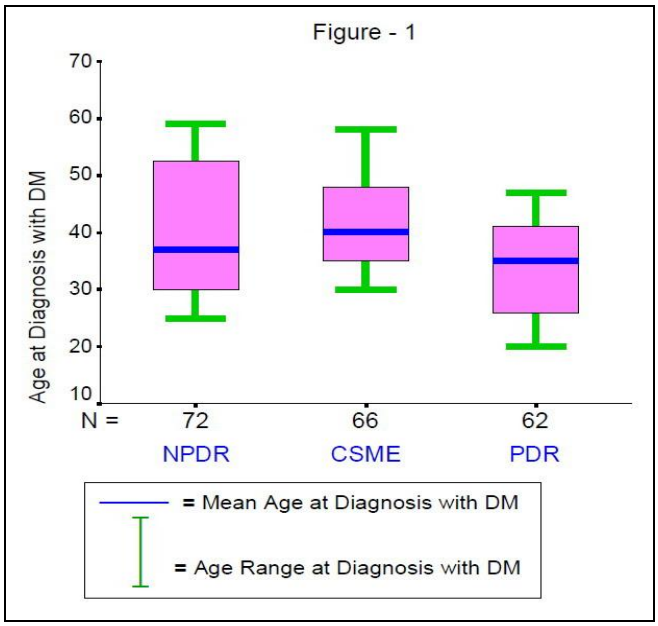

Fig. 1: Diabetic retinopathy and age at diagnosis with diabetes mellitus

lower prevalence of CSME (15-22%)[16,20] has been reported among patients with NPDR, which could be related to the difference in the duration of DM. In the aforementioned studies 53.7%[20] and 49.6%[16] patients had ≥ 11 years duration of DM, while 65% of our patients had that much duration, which might explain the higher prevalence of CSME with NPDR. The sight–threatening diabetic retinopathy (either PDR or CSME) was observed in 64% (128/200) of our patients. This high prevalence may be due to the selection bias, and; it is one of the disadvantages of a tertiary hospital – based study like ours.

The mean age of our patients with CSME was 53.4 ± 8.7 years, and; 56.0% of them were 50 – 59 years, while; 18.2% were 40 – 49 years. Similarly; Aziz-ur-Rahman et al [21] had reported that; 41.5% (34/82) of patients with diabetic maculopathy were 51 – 60 years and 30.5% (25/82) were 41 – 50 years of age. Meanwhile; the mean age of our patients with PDR was 47.0 ± 8.8 years with 58.1% being < 50 years of age, which is younger age comparatively[15].

We observed that, 51% of our patients with diabetic retinopathy had early onset type – 2 DM (< 40 years of age at diagnosis with DM), and among them; 33.3% had presented with PDR, and another 27.5% had CSME. The trend of early onset type – 2 DM in Pakistan had been reported previously[2,8,22].

There is an evidence suggesting that microvas-cular complications may develop and progress more rapidly in patients with early onset type – 2 DM, and that is due to an increased tissue susceptibility to the damaging effects of hyperglycemia at a younger age[23]. Similarly it has been reported that patients with DM diagnosed at < 45 years of age had a higher prevalence and more severe grades of diabetic retinopathy than those diagnosed later, despite matched duration of DM and glycemic control[24]. The younger age at onset of type – 2 DM is an independent risk factor for the development of diabetic retinopathy (the odds ratio for diabetic retinopathy was 1.9, 1.1, and 1; when age at onset of DM was < 45, 45 – 55 and > 55 years respectively)[24].

Early detection of diabetic retinopathy in diabetic patients should be planned in liaison with local general medical practioners. Arranging screening programs for all ages especially between 40-60 years at the time of diagnosis and thereafter annually.

CONCLUSION

Over 51% patients in our study had diabetic retinopathy on diagnosis with a mean age of 30.5± 4.6 years. Majority of the patients with type-2 DM (64%) had sight threatening proliferative diabetic retinopathy with or without CSME on presentation ranging mostly in < 50 years age group. There is a higher prevalence of sight threatening DR (PDR or CSME) in our patients with earlier presentation. Early onset of type-2 DM is related to greater prevalence of sight threatening DR.

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REFERENCES

1. **Shaw JE, Sicree RA, Zimmet PZ.** Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin Pract. 2010; 87: 4-14.
2. **Mahar PS, Awan Z, Manzar N, Memon S.** Prevalence of type-2 diabetes mellitus and diabetic retinopathy: the Gaddap study. J Coll Physicians Surg Pak. 2010; 20: 528–32.
3. **Shaya FT, Aljawadi M.** Diabetic retinopathy. Clin Ophthalmol 2007; 1: 259–65.
4. **Shaikh A, Shaikh F, Shaikh ZA, Ahmed J.** Prevalence of Diabetic Retinopathy and influence factors among newly diagnosed Diabetics in Rural and Urban Areas of Pakistan: Data analysis from the Pakistan National Blindness & Visual Impairment Survey 2003. Pak J Med Sci. 2008; 24: 774–9.
5. **Chaudhary GM.** Retinopathy in diabetic patients. Pak J Med Res. 2005; 44: 82-7.
6. **Shah CA.** Diabetic retinopathy: A comprehensive review. Indian J Med Sci. 2008; 62: 500-19.
7. **Mohan V, Sandeep S, Deepa R, Shah B, Varghese C.** Epidemiology of type 2 diabetes: Indian scenario. Indian J Med Res. 2007; 125: 217–30.
8. **Basit A, Hydrie MZI, Hakeem R, Ahmedani MY, Masood Q.** Frequency of chronic complications of type – 2 diabetes. J Coll Physicians Surg Pak. 2004; 14: 79–83.
9. **Niazi MK, Akram A, Naz MA, Awan S.** Duration of Diabetes as a Significant Factor for Retinopathy. Pak J Ophthalmol. 2010; 26: 182-6.
10. **Al–Maskari F, El–Sadig M.** Prevalence of diabetic retinopathy in the United Arab Emirates: a cross – sectional survey. BMC Ophthalmol. 2007; 7: 11.
11. **Agrawal RP, Ranka M, Beniwal R, Gothwal SR, Jain GC, Kochar DK, et al.** Prevalence of Diabetic Retinopathy in Type 2 Diabetes in Relation to Risk Factors: Hospital Based Study. Int J Diab Dev Ctries. 2003; 23: 16-9.
12. **Khandekar R, Al Lawatii J, Mohammed AJ, Al Raisi A.** Diabetic retinopathy in Oman: a hospital based study. Br J Ophthalmol. 2003; 87: 1061-4.
13. **Kayani H, Rehan N, Ullah N.** Frequency of Retinopathy among diabetics admitted in a teaching hospital of Lahore. J Ayub Med Coll Abottabad. 2003; 15: 53-6.
14. **Siddiqui SJ, Shah SIA, Shaikh AQ, Depar MY, Abbassi SA.** Study of 189 cases of diabetic retinopathy at CMC Larkana. Pak J Ophthalmol. 2007; 23: 92-6.
15. **Khan AJ.** Age, Sex and Duration Relationships and Prevalence of Diabetic Retinopathy in Pakistani Population. Pak J Ophthalmol. 1990; 6: 6-8.
16. **Javadi MA, Katibeh M, Rafati N, Dehghan MH, Zayeri F, Yaseri M et al.** Prevalence of diabetic retinopathy in Tehran province: a population – based study. BMC Ophthalmol. 2009; 9: 12.
17. **El Haddad OA, Saad MK.** Prevalence and risk factors for diabetic retinopathy among Omani diabetics. Br J Ophthalmol. 1998; 82: 901-6.
18. **Bamashmus MA, Gunaid AA, Khandekar RB.** Diabetic retinopathy, visual impairment and ocular status among patients with diabetes mellitus in Yemen: a hospital-based study. Indian J Ophthalmol. 2009; 57: 293-8.
19. **Narendran V, John RK, Raghuram A, Ravindran RD, Nirmalan PK, Thulasiraj RD.** Diabetic retinopathy among self reported diabetics in southern India: a population based assessment. Br J Ophthalmol. 2002; 86: 1014-8.
20. **Ishaque N, Rahman N.** Prevention of significant Visual Loss in Diabetic Macular edema by early Laser Photocoagulation. Pak J Ophthalmol. 1998; 14: 73-6.
21. **Aziz-ur-Rahman, Aziz TM, Niazi JH.** Use of Diode Laser in Diabetic Maculopathy. Pak J Ophthalmol. 2001; 17: 43-7.
22. **Iqbal F, Naz R.** Patterns of diabetes mellitus in Pakistan: An overview of the problem. Pak J Med Res. 2005; 44: 59-64.
23. **Song SH, Hardisty CA.** Early onset type 2 diabetes mellitus: a harbinger for complications in later years--clinical observation from a secondary care cohort. QJM. 2009; 102: 799-806.
24. **Wong J, Molyneaux L, Constantino M, Twigg SM, Yue DK.** Timing is everything: age of onset influences long-term retinopathy risk in type 2 diabetes, independent of traditional risk factors. Diabetes Care. 2008; 31: 1985-90.