

## Risk factors associated with diabetic retinopathy among patients with type 2 diabetes mellitus in central India

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### Abstract

**Aim:** To assess the clinical profile and association of various risk factors with severity of diabetic retinopathy (DR) in patients with type 2 diabetes mellitus (DM).

**Materials and Methods:** A prospective observational study included 56 patients (112 eyes) of type 2 DM with DR. All cases underwent ophthalmic examination and severity of diabetic retinopathy was graded according to the modified ETDRS classification. Risk factors like age, gender, duration of DM, hypertension, HbA1C levels, haemoglobin level and serum lipid profile were studied for any association with severity of DR. Data were analyzed using standard statistical technique and a probability value ('p' value) of < 0.05 was considered as statistically significant.

**Results:** The mean age of study group was 52.90±10.60 years. M: F ratio was 2.3:1. 17.86% were in Non -PDR, 28.60% in PDR and 53.60% were in advanced diabetic retinopathy. Severity of diabetic retinopathy was significantly associated with more duration of DM, high HbA1c level, Hypertension, anemia, dyslipidemia, positive family history of DM and low socioeconomic status.

**Conclusion:** Controlling modifiable risk factors like hypertension, dyslipidemia, high HbA1c level and anaemia are helpful in preventing the development and reducing the severity of diabetic retinopathy.

### Introduction

Diabetes mellitus (DM) is gradually becoming major medical problem with increasing prevalence throughout the world. In 2008, almost 347 million people had diabetes mellitus in the world and the prevalence is increasing. India had 69.2 million people having diabetes (8.7%) as per the 2015 data. [WHO]. There are almost 93 million people with diabetic retinopathy, 17 million with proliferative diabetic retinopathy, 21 million with diabetic macular edema, and 28 million with vision threatening DR in the world.<sup>1</sup> Diabetic retinopathy is the cause of blindness in approximately 2.5 million of the estimated 50 million blind people of the world. However, as a cause of blindness, it is less common in India as per population-based studies.<sup>2,3</sup> India is set to emerge as the diabetic capital of the world.<sup>4</sup> According to WHO, 31.7 million people were affected by DM in India in the year 2000. This figure is estimated to rise to 79.4 million by 2030, the largest number in any nation in the world. Diabetic retinopathy is common in adult's age between 20 - 74 in developed country like United States of America and PDR is the main cause of vision loss.<sup>1,5</sup>

Diabetic retinopathy is a progressive micro vascular complication of diabetes, which is characterized by signs of retinal ischemia such as micro aneurysms; cotton wool spots

(CWS), hemorrhages, venous caliber abnormalities, intra retinal micro vascular abnormalities (IRMAs), neovascularization.<sup>6</sup> If it is not controlled properly it leads to advanced diabetic retinopathy which is characterized by proliferative diabetic retinopathy, vitreous hemorrhage, tractional retinal detachment, rubeosis iridis and ultimately leads to irreversible blindness.

As per the available literature various risk factors including duration of diabetes, more age, gender, poor glycemic control, hypertension, deranged lipid profile, anemia, nephropathy, body mass index, smoking, socioeconomic status and family history of DM<sup>7,8</sup> are significantly associated with development and progression of Diabetic retinopathy (DR).

The present study was conducted with the view of adding significantly to the current body of evidence by providing a collective report on associations of various potential risk factors with development and progression of diabetic retinopathy. The aim were to find severity status of DR in type 2 DM patients and to determine association between severity and more age, socioeconomic status, positive family history of DM, duration of DM, HbA1c level, hypertension, dyslipidemia and anemia.

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## Materials and Methods

This prospective observational study was carried out on 56 patients (112 eyes) with diabetic retinopathy for duration of one and half years (August 2016 to September 2018). Diabetes Mellitus patients with diabetic retinopathy attending ophthalmic OPD or vitreo-retina clinic were included in this study and those with any other retinal pathology were excluded. Informed and written consent was obtained from each patient for participation in the study. The study was approved by institutional ethical committee and followed the declaration of helsinki. Data was spread in Microsoft excel sheet and descriptive statistics (mean and SD) were calculated for the variables. Test of significance (chi square and Anova test) wherever applicable, were applied, ( $p < 0.05$ ) was taken significant at 95% confident interval.

The demographic details of patients were recorded. A brief history about presenting complaints, duration of diabetes, family history of DM, hypertension were taken. The ocular examination including Visual acuity on snellens chart, intraocular pressure by applanation tonometry were recorded. Slit-lamp examination of anterior segment to rule out iris neovascularization and cataract, Fundus examination by indirect ophthalmoscopy with volks +20D lens, slit lamp biomicroscopy with +90D lens were done. Fundus findings were recorded and fundus pictures were taken. Then patients

were classified as per modified early treatment diabetic retinopathy study classification. Grading of disease was based on the worst eye findings. Patients having CSME were grouped separately from non CSME. Blood investigations like fasting blood sugar, post prandial blood sugar, glycosylated hemoglobin, renal function test, serum triglycerides, High density lipoprotein (HDL), hemoglobin (Hb) and low density lipoprotein (LDL) were done. Total cholesterol  $>200$ mg/dl or triglyceride  $\geq 150$ mg/dl or low density lipoprotein  $>130$ mg/dl were considered as dislipidemia.

## Results

The present study included 56 patients (112 eyes) of type 2 DM with DR. Mean age in study participates was  $52.90 \pm 10.60$  years. Maximum patients 44.6% were in the age group between 50-59 years. Out of total 56 cases, 39 (69.6%) were males and 17 (30.4%) were females with Male: Female ratio 2.3:1. With reference to grade of severity in study participants 17.9% were in non proliferative diabetic retinopathy (NPDR), 28.6% were proliferative diabetic retinopathy and 53.6% were in advanced diabetic eye disease.

The mean duration of diabetes was  $12.30 \pm 8.8$  years. Duration of DM was found to be a significant risk factor for severity of DM ( $p$  value 0.017334) (Table 1).

**Table 1:** Association of various risk factors with severity of Diabetic Retinopathy

		NPDR	PDR	ADR	P value
Duration of DM (years)	$\leq 5$ years	4	1	1	0.017334
	6-10 years	3	3	4	
	11-15 years	2	4	6	
	$\geq 16$ years	1	8	19	
HbA1c	$< 7\%$	8	1	1	0.00001
	7-9%	1	2	1	
	$> 9\%$	1	13	28	
Hypertension	Present	3	13	24	0.0059579
	Absent	7	3	6	
Dyslipidemia	Yes	6	15	29	0.004072
	No	4	1	1	
Hemoglobin	$\leq 12$ g/dl	3	13	27	0.000453
	$> 12$ g/dl	7	3	3	
Family history of diabetes mellitus	Yes	2	9	25	0.001042
	No	8	7	5	
Type of Diet	Vegetarians	6	7	10	0.321421
	Non vegetarians	4	9	20	

**Table 2:** Association between CSME and Risk factors

S. No	Factors Mean $\pm$ SD	With CSME	Without CSME	P -value
1	Duration of DM (Yrs)	11.91 $\pm$ 7.80	12.84 $\pm$ 10.24	0.5870
3	HbA1c (%)	10.55 $\pm$ 2.0	9.03 $\pm$ 2.83	<b>0.0012</b>
4	Hemoglobin (g %)	10.94 $\pm$ 1.30	11.10 $\pm$ 1.60	0.5621
5	Total Cholesterol (mg %)	226.13 $\pm$ 39.0	210.82 $\pm$ 43.0	0.0532
6	LDL (mg %)	142.75 $\pm$ 6.33	124.04 $\pm$ 18.40	<b>0.0001</b>
7	HDL (mg %)	41.70 $\pm$ 4.63	43.81 $\pm$ 7.44	0.0669

In present study the mean HbA1C was  $10.0 \pm 2.52\%$ . The level of HbA1C was higher in patients with severe PDR than in patients with Non-PDR. High Glycosylated hemoglobin is significantly associated with more severe diabetic retinopathy with chi-square statistic 34.8044 and p value 0.00001 ( $<0.05$ ) (Table 1). Among Non proliferative diabetic retinopathy patients 3 were hypertensive and 7 were not. While among proliferative diabetic retinopathy 13 were hypertensive and 3 were not. Among advanced diabetic retinopathy patients 24 were hypertensive and 6 were not. On applying chi square test the statistic was 10.2462. The p value was 0.0059579 ( $<0.05$ ) (Table 1). Hence hypertension was found to be a significant risk factor for severe diabetic retinopathy. Deranged lipid profile was also significant risk factor for severe diabetic retinopathy with p value was 0.004072 (Table 1). Anemia also associated with severe diabetic retinopathy with p value 0.000453 (Table 1). Positive family history of DM is a significant risk factor for severity of diabetic retinopathy (p value 0.001042) (Table 1). Patients of lower socioeconomic status had severe diabetic retinopathy (p value 0.035919 ( $<0.05$ )). Age and diet were not risk factor for severity of DR in our study.

On comparing the CSME and non CSME group, the serum LDL level among the CSME group was  $142.75 \pm 6.33 \text{ mg\%}$  which was significantly higher than the non CSME group  $124.04 \pm 18.40 \text{ mg\%}$  (p value 0.0001) (Table 2). Glycosylated Haemoglobin (HbA1c) level among the CSME group ( $10.55 \pm 2.0$ ) was also significantly higher than the non CSME group ( $9.03 \pm 2.83$ ) with p value 0.0012 (Table 2).

## Discussion

DM is a major cause of avoidable blindness. Diabetes is a multi-factorial disease. Knowledge of factors affecting the incidence and the severity of diabetic retinopathy are useful for preventing blindness as well as other micro-vascular complications of DM. Proper screening of diabetic patients and advising to control these factors will be useful for managing diabetic retinopathy.

In our study most of the patients (44.64%) with diabetic retinopathy were in the age group between 50-59 years. The mean age of presentation in our study was  $52.90 \pm 10.60$  years. Diagnosed diabetes is most prevalent in middle aged and elderly population.<sup>9</sup> Similar types of results were shown by Senthilvel et al (2017)<sup>10</sup> in their study. The mean age in their study was  $53.16 \pm 10.81$  years. Present study included predominantly male patients with Male: Female ratio 2.3:1. The probable reason was that males have easy access to health facility and awareness regarding complications of diabetes as compare to females. Similar observations were made by Senthilvel et al (2017)<sup>10</sup> in their study. Present study had majority of patients (82.14%) with proliferative diabetic retinopathy (PDR). The probable reason was that patients included in our study were predominantly from rural area and low socioeconomic status so they had limited access of advanced health facilities, and lack of awareness regarding the complications of DM and irreversible visual

loss due to it. Similar results were obtained by Senthilvel et al (2017)<sup>10</sup> in their study.

Age was not a significant risk factor for the severity of diabetic retinopathy in our study. Similar results were shown by Senthilvel et al (2017)<sup>10</sup> in their study. However age was a significant risk factor for the severity of diabetic retinopathy in Sannapaneni Krishnaiah et al (2007)<sup>11</sup> study.

Duration of DM was a significant risk factor in our study. CURES (Chennai Urban Rural Epidemiology Eye Study) (2008)<sup>12</sup> and Irini P Chatziralli et al (2010)<sup>13</sup> found similar results in their study. In our study we found that patients with poor glycemic control (HbA1c  $\geq 7\%$ ) had more severe diabetic retinopathy than patients with good glycemic control (HbA1c  $< 7\%$ ). This coincides with the findings of CURES Eye Study (2008),<sup>12</sup> DCCT (The Diabetes Control and Complications Trial) (1993),<sup>14</sup> UKPDS (United Kingdom Prospective Diabetes Study) (1998),<sup>15</sup> and Ramachandran Rajalakshmi et al (2016).<sup>16</sup>

On comparing patients with hypertension or without hypertension, we found that there was a statistically significant difference between the severities of diabetic retinopathy. Patients with hypertension had severe DR than patients without hypertension. Similar type of result was shown by Senthilvel Vasudevan et al (2017),<sup>10</sup> Ramachandran Rajalakshmi et al (2016),<sup>16</sup> UKPDS (1998)<sup>17</sup> and Gallego et al (2008)<sup>18</sup> in their studies.

The severity of diabetic retinopathy between patients with normal lipid profile and patients with deranged lipid profile was compared in our study and found a statistically significant difference between these two. Diabetic retinopathy was severe in the later. This coincides with the findings of Ramachandran Rajalakshmi et al (2016),<sup>16</sup> The Wisconsin Epidemiologic Study of DR XIII study (1991),<sup>19</sup> ETDRS (1996)<sup>20</sup> and CURES eye study (2006)<sup>21</sup> studies.

We also found a positive statistically significant association between low density lipoprotein level and clinically significant macular edema as high level of low density lipoprotein is associated with more number of hard exudates. Das et al (2015)<sup>22</sup> study revealed same results in their study. The total cholesterol of patients with CSME was higher than patients without CSME in our study but the difference was not quite statistically significant. However there was a statistically significant association of raised total cholesterol with CSME in Das et al (2015)<sup>22</sup> study.

Waqas Sami et al (2017)<sup>23</sup> concluded in their study that DM disease is almost confined to rich people who consumed oil, flour and sugar and they found diet rich in oil and sugar is significantly associated with severity of DM. However in present study baseline population belongs to rural area and low socioeconomic status so type of diet (vegetarian or non vegetarian) did not have any significant influence on severity of diabetic retinopathy.

Study conducted by Rand et al (1985),<sup>24</sup> DCCT research group (1997),<sup>25</sup> Ko BC et al (1995)<sup>26</sup> found that positive family history for DM was associated with more incidence and the severity of diabetic retinopathy. In our study as we included patients with diabetic retinopathy, there was a statistically significant association between

positive family history and severity of DM. Senthilvel Vasudevan et al (2017)<sup>10</sup> also found the similar results.

In our study low socioeconomic status was associated with more severe diabetic retinopathy and the difference was statistically significant. Because people were not aware of complications of DM, majority of them came after developing complications. And also their compliance as well as affordability for treatment was not good. This coincides with the findings of Ronald Klein et al (1994)<sup>27</sup> and Mitsuhiro Funakoshi et al (2017).<sup>28</sup>

### Conclusion

Diabetes is a multi-factorial disease. Duration of DM, HbA1C levels, hypertension, anaemia, dyslipidemia, family history of DM, low socioeconomic status, were significant risk factors in our study. Age and diet was not a significant risk factor in this study. Knowledge of factors affecting the incidence and severity of diabetic retinopathy are to be useful for preventing blindness as well as other micro-vascular complications of DM.

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