



Study of Epidemiology of Diabetic Retinopathy in Central India (SEDI)

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Abstract

Background: Diabetic retinopathy (DR), an imperative sequel is posing huge threat of blindness because of substantial prevalence of diabetes in the population of Central India. In depth understanding of its risk factors is relatively unexplored in this region.

Objective: To identify the prevalence and risk predictors of diabetic retinopathy in Central India.

Methods: A cross sectional study was conducted in 300 type 2 diabetic subjects of age ≥ 40 years. Consenting subjects were tested with dilated pupil fundoscopy and categorized into non proliferative (NPDR) and proliferative diabetic retinopathy (PDR) according to ETDRS Classification.

Results: Univariate regression analysis revealed advancing age (≥ 60 years), duration of diabetes (DOD) > 10 years, systolic (> 120 mmHg), obesity, smoking, proteinuria, Hyperlipdemia (total cholesterol > 200 mg/dl), as risk factors. In multivariable logistic regression analysis, age ≥ 60 years, DOD > 10 years, SBP > 120 mmHg, total cholesterol > 200 mg/dl, raised blood sugar level were observed to be substantial risk variables influencing independently the risk of DR in the population of Central India.

Conclusion: Prevalence of Diabetic Retinopathy in Central India is 30.33% with Age of the patient, duration of diabetes, uncontrolled blood sugar, hypertension, hyperlipidemia being important factors for development & progression of DR. The primary prevention intervention for DR is good diabetes management through the control of blood sugar, blood pressure & lipids, maintaining healthy weight & cessation of smoking.

Keywords: prevalence of diabetic retinopathy, risk factors, NPDR, PDR, macular edema.

Introduction

DR is the leading cause of vision loss in working age adults (20 to 65 years) and approximately one

in three people living with diabetes have some degree of DR and one in ten will develop a vision threatening form of the disease.¹ As per the

estimates of the International Association on the Prevention of Blindness (IAPB), 145 million people had some form of DR and 45 million people suffered from vision threatening DR in 2015.³⁻⁵ The prevalence of any retinopathy in persons with diabetes is 35% while proliferative (vision threatening) retinopathy is 7%.⁶. The proportion of moderate and severe vision impairment attributable to DR was 1.3% in 1990 worldwide and this increased to 1.9% in 2010.² The proportion of blindness cases attributable to DR increased from 2.1% in 1990 to 2.6% in 2010.² Diabetic retinopathy develops in nearly all persons with Type I diabetes and in more than 77% of those with Type 2 diabetes who survive over 20 years with the disease¹⁰. Some studies suggest that retinopathy progression is almost inexistent in younger-onset diabetics (less than 13 years-old). There are theories that puberty hormones might be a protection factor¹¹. There is evidence that retinopathy begins to develop at least 7-12 years before the clinical diagnosis of Type 2 diabetes^{12,13}. There exists direct correlation between the duration of diabetes and the prevalence and the severity of diabetic retinopathy. It is very well established that longer the patients have diabetes, the higher the prevalence of diabetic retinopathy^{10,14,15,16}.

Since DR is largely asymptomatic in the early stages, it is essential that people with diabetes have retinal screening on a regular basis in order to detect DR and DME. The methods for DR diagnosis include ophthalmoscopy, optical coherence tomography, retinal photography and fluorescein angiography. Screening for retinopathy should be done regularly after the diagnosis of diabetes.^{1,7} The primary prevention intervention for DR is good diabetes management. This can be achieved through intensive blood glucose self-management via diet with medication if required which can prevent the onset of DR by 76% and its progression by 54% for insulin treated patients.⁸ Moreover, for people with type 2 diabetes more intensive blood glucose control can improve eye health outcomes by 13% compared to

regular care.⁹ Studies of various complications in Indian diabetics is therefore of great interest and very few studies are available on the prevalence of diabetic retinopathy from Central India.

Material & Methods

The present cross sectional study was conducted from August 2016 to July 2018 on type 2 diabetes mellitus (T2DM) subjects attending Diabetes specialty clinic at a Tertiary Care center in Central India.

A total of 349 self reported Type 2 Diabetes Mellitus subjects were screened. Out of these, 49 subjects were excluded depending upon the exclusion criteria. Finally, 300 subjects were qualified & agreed to participate in the study. Information regarding demographic variables such as age, education status, marital status, tobacco smoking and alcohol drinking was collected by detailed interview with the subjects. Duration of diabetes, medication use, self-reported diseases and previous medical history were recorded from the medical records of the subjects. In all the patients detailed history was followed by clinical examination that included assessment of Visual acuity, slit lamp examination, fundus examination with +90D lens, direct and indirect ophthalmoscopy. Optical Coherence Tomography & fluorescein Angiography were done on as & when required basis. All the patients were subjected to estimation of Blood Pressure, Body Mass Index & blood investigations viz. Random blood sugar, Urine albumin, Lipid Profile, haemoglobin. All the participants gave their written consent. The study protocol was approved by Institutional Ethical Committee and strictly adhered to Helsinki Declaration.

Statistical Analysis

The demographic and clinical information was gathered and was entered into Microsoft excel spreadsheet. Continuous variables were presented as Mean \pm Standard Deviation. Categorical variables were expressed in frequency and

percentages. Continuous variables were compared between with and without diabetic retinopathy by performing independent t-test. Categorical variables were compared by performing chi-square test. For small numbers, Fisher exact test was used wherever applicable. Multiple logistic regression analysis was performed to determine independent predictors of diabetic retinopathy. $P < 0.05$ was considered as statistical significance. Statistical software STATA Version 14.0 was used for data analysis. Prevalence rate of Diabetic retinopathy in Type 2 diabetes patients was determined as the percentage of the total patients examined.

Results

Out of the total study population of 300 cases, 157 cases were males (52.33%) while 143 cases (47.66%) were females. Mean age was 58.14 ± 8.60 years. (Males: 58.28 ± 8.75 years and females: 57.99 ± 8.45 years). The Difference in the mean ages among males and females was not statistically significant ($P = 0.7683$). Out of 300 patients, a total of 201 (69.67%) were unaffected, 72 (23.99%) were identified as NPDR of these 30 (10%) were graded as mild NPDR, 31 (10.33%) as moderate NPDR, 7 (2.33%) and 4 (1.33%) as severe and very severe NPDR. A total of 19 (6.33%) were graded as PDR. Diabetic macular edema was present in 18 (19.78%) out of 91 patients with DR. Majority of the patients with D.M.E were PDR (38.88%) followed by Moderate NPDR (33.33%), Severe NPDR (16.66) & Very Severe NPDR (11.11%). Among patients having diabetic retinopathy, 54 cases were males (59.34%) while 37 cases (40.65%) were females, showing male preponderance. Thus Prevalence of Diabetic Retinopathy in our study was 30.33% (34.4% among males and 25.8% among females). Among different age groups prevalence of DR ranged from 9.3% (41-50 years) to 93.3% (71-80 years). The odds ratio of having diabetic retinopathy in this study population was 6.77 in patients above 60 years as compared to patient below 60 years of age (CI :3.77-12.30, $P < 0.001$).

The association between age and prevalence of DR was found to be significant statistically ($p < 0.001$). The mean duration of diabetes was 9.97 ± 3.62 in patients with diabetic retinopathy & 3.37 ± 2.48 in patients without diabetic retinopathy. In our study the duration of Diabetes was the strongest predictor for development and progression of Diabetic Retinopathy ($P < 0.001$). The mean Systolic Blood pressure among males in our study was 132.29 ± 16.28 mmHg and the mean Systolic Blood pressure among females was 132.93 ± 17.19 mmHg. This difference in mean Systolic Blood pressure among males and females, in our study, had no statistical Significance ($P = 0.7392$). Similarly, there was no statistical significance ($P = 0.720$) in the difference of mean Diastolic BP among males (83.82 ± 12.93 mmHg) and females (84.47 ± 18.37 mmHg). In our study, Systolic Blood Pressure showed a significant association with prevalence of diabetic retinopathy ($P = 0.002$) whereas, diastolic blood pressure was not statistically significant ($P = 0.7875$). In our study, Proteinuria was present in 21.97% of the patients with diabetic retinopathy and was associated with more severe forms of retinopathy (90% of patients had either severe or very severe NPDR or PDR). The mean Random Blood sugar among patients having diabetic retinopathy was 201 ± 37.26 mg/dL which was significantly higher than patients not having retinopathy 147.52 ± 18.95 mg/dL ($P < 0.0001$). Our study showed a higher prevalence of Diabetic retinopathy in patients on a combination of Insulin and Oral hypoglycemic Agents (OHA) (69.23%) in comparison to patients on Oral hypoglycemic agents alone or those patients not on any medication (25.50% and 7.14% respectively). Majority of the patients with DME were on combination of oral drugs & insulin (61.11%) followed by patients on oral drugs alone (38.88%). DME was not found in patients controlled on diet & exercise. Obesity was present in 73 (80.21%) out of 91 patients of diabetic retinopathy & the association was found to be

significant statistically ($P < 0.0001$). 94.73 % patients of PDR were obese against 63.33% patients of Mild NPDR. 87.09% of Moderate NPDR 85.71% of Sever NPDR & 75% of Very sever NPDR patients were obese. Hyperlipidemia was present in 57.14% of the patients with diabetic retinopathy and was associated with more severe forms of retinopathy. (57.69% of patients had either severe or very severe NPDR or PDR). Anemia was present in 21.97% of the patients with diabetic retinopathy but the association was not statistically significant ($P = 0.0931$). Smoking was present in 9.89% of the patients with diabetic retinopathy & the association was statistically significant ($P = 0.026$). All these univariate risk factors were analyzed by multivariable logistic regression analysis to discern those variables which independently influenced the risk of NPDR and PDR

Table No. 1 Multiple Logistic Regression analysis for independent risk factors of diabetic retinopathy in patients of type-II diabetes.

Risk factor	Adjusted Odds Ratio	95% Confidence Interval	p-value
Age in years	4.2	1.34 – 13.58	0.014, S
RBS	1.10	1.06 – 1.14	<0.001, HS
SBP	1.05	1.01 – 1.09	0.002, HS
Hyperlipidemia	0.16	0.036 – 0.69	0.014, S
Duration of Diabetes in years	1.69	1.40 – 2.03	<0.001, HS

The variables, which have an association with retinopathy, are listed in the table 1. Duration of Diabetes ($p < 0.001$), Systolic blood pressure ($p = 0.002$), blood sugar level ($P < 0.001$), age in years ($p = 0.014$) & hyperlipidemia ($p = 0.014$) showed a positive association with retinopathy. In our study, the Odd's ratio of having Retinopathy is 4.2 with respect to Age (95% CI 1.34-13.58, $P = 0.014$), 1.69 with respect to Duration of disease (95% CI 1.40-2.03, $P < 0.01$),

1.10 with respect to hyperglycemia (95% CI 1.06-1.14, $P < 0.001$), 1.05 with respect to systolic blood Pressure (95% CI 1.01-1.09, $P = 0.002$) & 0.16 with respect to hyperlipidemia (95% CI 1.40-2.03, $P = 0.014$).

Discussion

Diabetic retinopathy is most prevalent cause of legal blindness in the economically productive age group of 20-65 years. Visual disability due to Diabetic Retinopathy is a major public health problem; however its morbidity is largely preventable and treatable. There are multiple factors associated with development and progression of diabetic retinopathy and slight modification of these factors can help to slow down progression of Diabetic Retinopathy. For this purpose, a cross-sectional study was carried out in which a total of 300 patients of type 2 diabetes attending diabetes specialty clinic in a tertiary care centre in central India of age group 40-80 year were enrolled. Cases having any confounders viz. 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 (79.12%) was more common than PDR (20.87%). These findings are in agreement with global estimates of prevalence of different types of diabetic retinopathy. In a recent metaanalysis⁶, 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. Among patients having diabetic retinopathy, 54 cases were males (59.34%) while 37 cases (40.65%) were females, showing male preponderance. P Namperumalsamy et al¹⁷ found higher rates of diabetic retinopathy among males. A similar preponderance has been reported from the AIOS Study¹⁸, CURES Eye study¹⁹, UKPDS study⁹ and the Hyderabad study²⁰ thus supporting our results. We observed different types of Retinopathy in 91

patients out of 300 i.e Prevalence of Diabetic Retinopathy in our study was 30.33% (34.4% among males and 25.8% among females). Our results are consistent with various other studies. Ramchandran et al observed retinopathy in 714 i.e. 23.7% cases out of 3010 patients of type 2 diabetes²¹. M.W. Knuiman reported prevalence of retinopathy at 28% in Perth, Western Australia²². Rajiv Raman et al²³ showed prevalence of diabetic retinopathy in urban Chennai population was 18% . Prevalence in AIOS Study¹⁸ 2014 was 21.67%. Higher prevalence of DR in our study can be explained by selection bias as this study was conducted in a diabetes specialty clinic at a tertiary care centre i.e this was a hospital based study on known diabetic patients & not a population based study. In our Study, Diabetic retinopathy was seen in 9.3% in the 41-50 age group, 17.5% in the 51-60 age group, 46.9% in the 61-70 age group and 93.3% in the >70 age group. 67(73.6%) patients with diabetic retinopathy were above 60 years of age while 24(26.4%) patients were below 60 years of age. The odds ratio of having diabetic retinopathy in this study population was 6.77 in patients above 60 years as compared to patient below 60 years of age. Thus age was a statistically significant risk factor for the prevalence of Diabetic retinopathy in our study (P=0.014). P Namperumalsamy et al found higher prevalence of Diabetic Retinopathy among patients >45 yrs of age¹⁷. Chatziralli et al found prevalence of Diabetic retinopathy to be 61.66% above the age of 15 years and concluded that age did not represent an independent risk factor for Retinopathy but rather it was a confounding effect of age, as older age and longer duration of DM are two factors closely associated with each other.²⁴ In our study the duration of Diabetes was the strongest predictor for development and progression of Diabetic Retinopathy (P<0.001). Our results show that 83.64 % of patients having duration of diabetes 10-15 years had Diabetic Retinopathy whereas 100%

of patients having duration of Diabetes more than 15 years had retinopathy in comparison to 14.94% of patients with duration of diabetes less than 6 years. Our results were in accordance with various other studies^{19,20}. Dandona et al reported that 87.5 per cent of those with >15 year duration of diabetes had DR compared with 18.9 per cent of those who had <15 year duration²⁰. In the CURES Eye study, 41.8 per cent had DR after 15 years of diabetes and severity of DR proportionally increased with longer duration of diabetes.¹⁹ In addition, it has been demonstrated that for every five year increase in duration of diabetes, the risk for DR increased by 1.89 times¹⁹. In our study, Systolic Blood Pressure showed a significant association with prevalence of diabetic retinopathy (P=0.002) whereas, diastolic blood pressure was not statistically significant (P=0.7875). The UKPDS showed that the incidence of retinopathy was associated with systolic blood pressure²⁵. The WESDR study showed diastolic blood pressure was a significant predictor of progression of diabetic retinopathy to PDR over 25 years of follow up.³¹ Van Leiden et al in The Hoorn study also observed a positive correlation between hypertension & DR³². A strong correlation between hypertension and diabetic retinopathy is evident from the perspective that unnecessarily increased blood flow to the retinal capillaries may damage endothelium of the eye in the subjects having diabetes.²⁶ It is also validated that aggressive control of blood pressure in T2DM subjects attenuates the risk of blindness, requirement of photocoagulation and progression of diabetic retinopathy²⁵. The CURES study did not find a statistically significant association between Hypertension and Diabetic Retinopathy.¹⁹ In our study, Proteinuria was present in 21.97% of the patients with diabetic retinopathy and was associated with more severe forms of retinopathy (90% of patients had either severe or very severe NPDR or PDR). The CURES Eye study¹⁹ showed that

Proteinuria was present in 29.2 percent of the subjects with DR which were also associated with more severe forms of retinopathy which is in accordance with the findings in our study. Our study showed a higher prevalence of Diabetic retinopathy in patients on a combination of Insulin and Oral hypoglycemic Agents (OHA) (69.23%) in comparison to patients on Oral hypoglycemic agents alone or those patients not on any medication (25.50% and 7.14% respectively) probably because of longer duration of diabetes or poor glycemic control prompting the use of Insulin in combination with OHAs. A similar strong correlation between the type of treatment i.e. insulin therapy (alone or in combination with OHA) was seen in a study by R.A Agrawal et al²⁷. There is strong evidence to suggest that the level of hyperglycaemia^{19, 28,29} influences the development and progression of Diabetic Retinopathy. Although our study did not include HbA1c levels of the study population, due to monetary factors our results showed that the mean Random Blood sugar among patients having diabetic retinopathy was 201 ± 37.26 mg/dL which was significantly higher than patients not having retinopathy 147.52 ± 18.95 mg/dL ($P < 0.001$). This statistically significant finding in our study hints towards the protective effect of glycemic control on the development and progression of Diabetic Retinopathy. Obesity was present in 69.23% of the patients with diabetic retinopathy and was associated with more severe forms of retinopathy (42.85% of patients had either severe or very severe NPDR or PDR). The association is statistically significant ($P < 0.001$). Mohd. Dirani et al reported that higher BMI is significantly associated not only with prevalence of DR but also more severe forms of Retinopathy, thus supporting results of our study. Mohd. Dirani et al also concluded that Obese patients are 6.5 times more likely to develop PDR than patients with normal body weight³⁰. In our study, Hyperlipidemia was present in 57.14% of the patients with diabetic retinopathy and was

associated with more severe forms of retinopathy (Hyperlipidemia was present in 100% cases with Severe NPDR, Very Severe NPDR & PDR). This association is statistically significant ($P < 0.001$). Hendrik A. Van Leiden et al in The Hoorn study also observed a positive correlation between elevated serum cholesterol & DR³². In our study, Anemia was present in 21.97% of the patients with diabetic retinopathy but the association was not statistically significant ($P = 0.096$). Ranil PK et al³³ showed that Men with anemia, and not women, had 2 times the risk of developing diabetic retinopathy. In our study, Smoking was present in 9.89% of the patients with diabetic retinopathy & the association was statistically significant ($P = 0.026$). Moss SE et al³⁴ showed that Neither smoking status nor pack-years smoked showed significant associations with increased risk of retinopathy. Similar observation were made in CURES¹⁹ & Sankara Nethralaya²³ study.

Limitations of study

Small Sample Size: A larger sample size would better reflect the Prevalence of Retinopathy and identify risk factors.

Diabetic retinopathy grading was done based on funduscopy & not on fundus photography gradings. This could have done in underestimation in prevalence & severity of retinopathy.

Fundus angiography was not done in all patients with Diabetic retinopathy. This would have lead to an underestimation of prevalence and severity of diabetic retinopathy.

HbA1c levels to evaluate glycemic control of patients were not included due to monetary factors. Thus, glycemic control as an association to prevalence of Diabetic retinopathy could not be evaluated.

Conclusions

- The primary prevention intervention for DR is good diabetes management. This

can be achieved through intensive blood glucose self-management via diet with medication if required which can prevent the onset and progression of DR.

- Optimizing the medical management of diabetic retinopathy should address the control of blood sugar, blood pressure & lipids, maintaining healthy weight & cessation of smoking.
- Considering limited recourses available in the country for diagnosis & management of DR newer Information technology tools like Telemedicine can be very useful.
- Adequate resources and trained ophthalmic & para-ophthalmic personnel will go a long way in managing this emerging public health problem.

Conflict of interest: Authors have no conflict of interest.

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