

# Correlation of Risk Factors with Severity of Diabetic Retinopathy - A Retrospective Study

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## ABSTRACT

### BACKGROUND

Diabetic retinopathy (DR) is a major microvascular complication of diabetes. It is the most common cause of blindness in the working-age population in developed countries. We wanted to analyse the correlation between risk factors of blindness like duration of diabetes, dyslipidaemia, hypertension, HbA1c with severity of diabetic retinopathy in order to design appropriate strategies for prevention and treatment of diabetic retinopathy.

### METHODS

This was a retrospective study of all diabetic patients with diabetic retinopathy who presented to the eye OPD at KS Hegde Medical Academy from April 1st 2018 to March 31st 2019 that fulfilled the inclusion criteria. A dilated fundus examination was done to note the grade of diabetic retinopathy. The demographic data along with the duration of diabetes, HbA1c values, Cholesterol levels and Blood pressure were documented and correlated with the severity of diabetic retinopathy.

### RESULTS

The study included 92 patients, of which 63 were males and 29 were females with a mean age of 54.5±2.8 years. We found that there was statistically significant association between the duration of diabetes and HbA1c levels with severity of diabetic retinopathy ( $p=0.022$  and  $0.034$  association), whereas there was no statistically significant correlation between blood pressure and cholesterol levels with severity of diabetic retinopathy ( $p=0.52$  and  $0.456$  respectively).

### CONCLUSIONS

Diabetic retinopathy showed a male preponderance, with risk factors like duration of diabetes and HbA1c levels having a significant association with the severity of diabetic retinopathy. Therefore, it is essential to have a good systemic control of diabetes with diet and suitable medications. Diabetic retinopathy is a preventable cause of blindness when diagnosed early and screening of diabetic retinopathy must be done in all diabetics to prevent the progression of the disease.

### KEY WORDS

Diabetes Mellitus (DM), Diabetic Retinopathy (DR), Non Proliferative Diabetic Retinopathy (NPDR), Proliferative Diabetic Retinopathy (PDR), World Health Organisation (WHO), Glycosylated Haemoglobin (HbA1c), Systolic and Diastolic Blood Pressure (SBP and DBP), Total Cholesterol (TC), Triglycerides (TG), Low Density Lipoprotein (LDL), Very Low Density Lipoprotein (VLDL), High Density Lipoprotein (HDL)

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## BACKGROUND

Diabetes Mellitus (DM) is a major public health problem. 422 million people in the world are diabetic, and among them, 69.2 million people live in India.<sup>(1)</sup> Diabetes is known to affect different organs of the body such as eyes, kidneys, nerves, heart and blood vessels and cause a wide variety of complications. Among these, diabetic retinopathy (DR) is the leading cause of blindness among working age population.<sup>(2),(3)</sup> In a study conducted by All India Ophthalmic Society of India in 2014, the prevalence of DR was found to be 21.7%, with reported prevalence of DR in India ranging from 7.03% to 25%.<sup>(4)</sup> Blindness due to DR has a significant impact on patients quality of life and has a negative impact of overall life expectancy. DR is also a key indicator of other systemic microvascular complications like diabetic neuropathy and diabetic nephropathy. According to study done by Indian state level disease burden initiative diabetes collaborators from 1990 – 2016, the number of people with diabetes in India increased from 26.0 million in 1990 to 65.0 million in 2016.<sup>(5)</sup> The prevalence of diabetes in adults aged 20 years or older in India increased from 5.5% in 1990 to 7.7% in 2016. The prevalence in 2016 was highest in Tamil Nadu and Kerala and Delhi, followed by Punjab and Goa and Karnataka.<sup>(6)</sup>

The Indian Council for Medical Research supported a study across multiple locations in India (ICMR-INDIAB) which showed a wide variation in the prevalence of diabetes across the country.<sup>(7)</sup> The weighted prevalence of diabetes (both known and newly detected) was 10.4% in Tamil Nadu, 8.4% in Maharashtra, 5.3% in Jharkhand, and 13.6% in Chandigarh.<sup>(7)</sup> This study concluded that the projected magnitude for the country would be 62.4 million persons with diabetes and 77.2 million with prediabetes in 2010. The pooled analysis estimated that the overall prevalence of any DR was 34.6%, while the prevalence for proliferative DR was 6.96% and for diabetic macular oedema was 6.81%. The Chennai Urban Rural Epidemiology Study (CURES) Eye Study showed that the major systemic risk factors associated with DR are the duration of diabetes, hyperglycaemia, male gender, and macroalbuminuria.<sup>(6)</sup> Therapeutic approaches in people with retinopathy or at risk for DR include drug therapy to reduce modifiable risk factors, laser photocoagulation, and surgery. Recently, there have also been significant developments in pharmacotherapy in the management of DR.

The CURES Eye Study demonstrated a significant increase in the prevalence of DR with increasing glycosylated haemoglobin (HbA1c) levels.<sup>(7)</sup> Studies like the Kumamoto study also evaluated the relationship between glycaemic control and DR.<sup>(8)</sup> In this study, the glycaemic threshold to prevent the onset and progression of diabetic microvascular complications was mentioned as: HbA1c <6.5%, fasting blood glucose concentration <110 mg/dl and 2-h postprandial blood glucose concentration < 180 mg/dl.<sup>(8)</sup> The aim of our study was to estimate the proportion and correlation of dyslipidaemia, hypertension, abnormal HbA1c levels and duration of diabetes with severity of diabetic retinopathy.

### Objectives

1. To estimate the proportion and association of dyslipidaemia and hypertension with severity of diabetic retinopathy.

2. To estimate the proportion and association of abnormal HbA1c and duration of diabetes with severity of diabetic retinopathy.

## METHODS

This was a retrospective study which included all diabetic patients with diabetic retinopathy who presented to the eye OPD at KS Hegde Medical Academy from April 1<sup>st</sup> 2018 to March 31<sup>st</sup> 2019. Clearance for the study was obtained from the Institutional Ethics Committee (IEC), KS Hegde Medical Academy on 22<sup>nd</sup> Aug 2019. The patient details along with the HbA1c values, Cholesterol levels and Blood pressure was documented. Any patient with incomplete lipid profile, HbA1c levels or Blood pressure values were excluded from the study. Patients with no diabetic retinopathy findings on dilated fundus examination were also excluded from the study. All patients were dilated with tropicamide eye drops (0.8%). A detailed fundus examination was done using direct and indirect ophthalmoscopy and level of diabetic retinopathy in these patients was graded as follows:

Level of Diabetic Retinopathy	Clinical Grading
Mild NPDR	Microaneurysms only
Moderate NPDR	Microaneurysms and one or more exudates but less than the definition of severe NPDR
Severe NPDR	One of the following: 1) Microaneurysms and exudates in all the four quadrants and fovea is the centre of the quadrants 2) Venous beading in any two quadrants 3) Intra retinal microvascular abnormalities in at least one quadrant
Very Severe NPDR	Two of the following: 1) Microaneurysms and exudates in all the four quadrants and fovea is the centre of the quadrants 2) Venous beading in any two quadrants 3) Intra retinal microvascular abnormalities (IRMA) in at least one quadrant
PDR	Any one of the following: 1) Neovascularisation 2) Neovascular glaucoma 3) Vitreous Haemorrhage 4) Tractional Retinal detachment
<b>Clinical Criteria for Diabetic Retinopathy Grading<sup>(9),(10)</sup></b>	

### Data Analysis

Data was analysed using the PASW 17.0 (Predictive Analysis Software) (SPSS Inc, Chicago, Illinois, USA) and Chi square test. A p value of < 0.05 was considered significant.

## RESULTS

A total of 230 diabetic patients attended the eye OPD during the study period of which 92 patients fulfilled the inclusion criteria. Out of these, 63 (68%) were males and 29 (32%) were females with mean age of 54.5±2.8 yrs. A detailed retrospective study was done among parameters like age, gender, HbA1c, duration of diabetes, hypertension, lipid profile and grades of diabetic retinopathy. Descriptive statistics shows patients below 50 years were 25%, between 50-60 years is 43% and above 60 years were 31.5%. Mean ± SD of HbA1c of different age groups are as follows: below 50 years have HbA1c as 9.13± 2.218, between 50-60 years 9.22±2.87, above 60 years 8.59±2.34. Mean of duration of

diabetes among different age groups are as follows: below 50 years  $7.47 \pm 5.75$  yrs., between 50-60 years was  $8.02 \pm 5.15$  yrs. and in age group above 60 years was  $11.51 \pm 9.00$  yrs.

Serial Numbers	Parameters	Mean Value $\pm$ SD
1.	Duration of diabetes	7.4783 $\pm$ 5.75 years
2.	HbA1c	9.1378 $\pm$ 2.218 %
3.	TC	179.0870 $\pm$ 23.2 mg/dL
4.	TG	187.7826 $\pm$ 21.6 mg/dL
5.	LDL	129.2174 $\pm$ 17.5 mg/dL
6.	HDL	36.6696 $\pm$ 5.86 mg/dL
7.	VLDL	37.0817 $\pm$ 5.23 mg/dL
8.	SBP	144.00 $\pm$ 18.6 mm Hg
9.	DBP	85.8261 $\pm$ 13.6 mm Hg

**Table 1. Average of Different Parameters in Age Group Less Than 50 Years**

Serial Numbers	Parameters	Mean Value $\pm$ SD
1.	Duration of diabetes	8.0250 $\pm$ 5.15 years
2.	HbA1c	9.2248 $\pm$ 2.87 %
3.	TC	167.1500 $\pm$ 16.7 mg/dL
4.	TG	164.4000 $\pm$ 21.2 mg/dL
5.	LDL	102.1000 $\pm$ 12.3 mg/dL
6.	HDL	37.2550 $\pm$ 8.3 mg/dL
7.	VLDL	34.5048 $\pm$ 9.7 mg/dL
8.	SBP	145.60 $\pm$ 21.6 mm Hg
9.	DBP	83.6000 $\pm$ 16.7 mm Hg

**Table 2. Average of Different Parameters in Age Group 50 Years to 60 Years**

Serial Numbers	Parameters	Mean Value $\pm$ SD
1.	Duration of diabetes	11.5172 $\pm$ 9.00 years
2.	HbA1c	8.5928 $\pm$ 2.34 %
3.	TC	156.5862 $\pm$ 18.9 mg/dL
4.	TG	160.0345 $\pm$ 17.8 mg/dL
5.	LDL	104.8276 $\pm$ 15.8 mg/dL
6.	HDL	30.2828 $\pm$ 6.98 mg/dL
7.	VLDL	32.8486 $\pm$ 8.75 mg/dL
8.	SBP	146.5517 $\pm$ 18.4 mm Hg
9.	DBP	85.1034 $\pm$ 12.8 mm Hg

**Table 3. Average of Different Parameters in Age Group More Than 60 Years**

Chi square test for association between blood pressure and severity of diabetic retinopathy reveals that systolic BP had  $p=0.829$  and diastolic BP  $p=0.219$  which shows no significant association. Association using chi square test between lipid profile and grades of diabetic retinopathy reveals that total cholesterol  $p=0.456$ , triglycerides  $p=0.281$ , LDL  $p=0.097$  and, HDL  $p=0.240$  VLDL  $p=0.390$  which shows no significant association. Association between HbA1c levels with severity of diabetic retinopathy showed  $p=0.034$ , which shows statistically significant association between abnormal HbA1c levels with severity of diabetic retinopathy. Association between duration of diabetes and severity of diabetic retinopathy in age group below 50 years is  $p=0.374$ , in age group between 50-60 years is  $p=0.126$  and in age group above 60 years is  $p=0.022$ , which shows a significant association in the age group above 60 yrs.

## DISCUSSION

The study was conducted to evaluate risk factors associated with diabetic retinopathy severity and to find the correlation with grades of diabetic retinopathy. We found that increased duration of diabetes and increased HbA1c levels were positively associated with increased severity of diabetic retinopathy whereas other parameters like lipid profile and hypertension showed no significant association.

We could positively associate higher grades of diabetic retinopathy and longer duration of diabetes, which was consistent by a cross sectional study done by Shrote AP in tertiary set-up in central rural India.<sup>[11]</sup>

In our study significant association was obtained between higher grades of diabetic retinopathy and abnormal HbA1c levels, which was consistent with other studies like Diabetes Control and Complications Trial (DCCT) in Type 1 diabetes,<sup>[12]</sup> and the United Kingdom Prospective Diabetes Study (UKPDS) in Type 2 diabetes,<sup>[13]</sup> which have demonstrated that intensive glycaemic control ( $\text{HbA1c} \leq 6\%$ ) reduced both the development and progression of DR. But on the other hand, study like Veterans Affairs Diabetes Trial,<sup>[14]</sup> did not show any significant decrease in the progression of microvascular changes after tight glycaemic control.

In our study, we could not positively associate between hypertension and higher grades of diabetic retinopathy. This was similar in a studies like ACCORD and ADVANCE studies, where the mean BP was  $<140/80$  mm Hg in both the active intervention and control groups, active treatment did not show any additional benefit on preventing progression of DR,<sup>[15,16]</sup> but ADVANCE study showed reduction in macular oedema on tight control of BP. On contrary study like UK Prospective Diabetes Study Group (UKPDS) showed tight BP control (mean BP  $144/82$  mm Hg) in type 2 DM patients resulted in a significant reduction in progression of DR (35%) as well as a significant decrease in vision loss and need for laser photocoagulation compared to less control (mean BP  $154/87$  mm Hg).<sup>[17]</sup>

In our study, we could not positively associate between dyslipidaemia and higher grades of diabetic retinopathy which was consistent with the study on Risk factors for retinopathy and DME in type 2 diabetes.<sup>[18,19]</sup> However, this was different from the results of two large prospective studies, the Early Treatment Diabetic Retinopathy study,<sup>[20]</sup> and the Wisconsin Epidemiological study.<sup>[21]</sup> Both of these studies found a statistically significant association between elevated serum total cholesterol and LDL-C cholesterol and the severity of retinal hard exudation in patients with DR.

Despite smaller sample size and not including control population, we could achieve significant correlation between longer duration of diabetes and abnormal HbA1c levels with that of higher grades of diabetic retinopathy, which shows the prime importance of these risk factors in affecting the progression of diabetic retinopathy.

The study had a few limitations. Because this was a retrospective study, the results do not provide definite information on a cause-and-effect relationship. In addition, because our study population did not include control population and also sample size obtained for the study was small, significant association couldn't be obtained for all the parameters studied. Prospective and larger studies are required to overcome these limitations.

## CONCLUSIONS

The study showed a peak incidence of diabetic retinopathy in 50-60 years age group, male preponderance, significant association with abnormal HbA1c and greater duration of diabetes with higher grades of diabetic retinopathy and no

significant association between dyslipidaemia and hypertension with higher grades of diabetic retinopathy. Diabetic retinopathy is a preventable cause of blindness when treated early. So, it should be screened for and treated early to prevent progression of disease.

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