



## HbA1C Levels and its correlation in Diabetic Retinopathy

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### Abstract

*The study aimed to determine the correlation of HbA1C with different grades of Diabetic Retinopathy.*

*80 participants were included in the study, in whom relevant history regarding their diabetes was noted i.e age at diagnosis of diabetes, duration of the diabetes, nature and duration of treatment received, glycemic control and compliance to the treatment. Patients were evaluated for their HbA1C levels, hypertension, lipid profile and renal parameters.*

*Each participant's diabetic retinopathy status was classified according to the ETDRS system.*

*Our study found a correlation between different grades of diabetic retinopathy and CSME with HbA1C levels. The other factor which had a significant correlation was duration of diabetes.*

*Age of the patient, gender of the patient, hypertension, hyperlipidemia, modality of treatment and nephropathy did not have a significant correlation when compared in different grades of diabetic retinopathy.*

### Introduction

The retina is affected by many systemic disorders, one of which is diabetes mellitus (DM). Globally, there has been an exponential increase in the number of diabetic patients coupled with a rise in life expectancy due to better medical care, has resulted in a proportionate rise in long term vascular complications such as diabetic retinopathy (DR).

A major cause of avoidable blindness is Diabetic Retinopathy in both the developing and the developed countries. Diabetic retinopathy (DR) carries 25 times more likelihood of blindness than patients without retinopathy.<sup>1</sup>

Diabetes mellitus affecting approximately 4 per cent of the world's population, almost half have some degree of DR at any given time.<sup>2</sup> India is already being termed as the "Diabetic capital of

the world", with the number of patients with diabetes expected to rise from 40.9 million, at present, to a whopping 60.9 million by 2025<sup>3</sup>.

According to the latest World Health Organization (WHO) report, India has 31.7 million diabetic subjects, and the number is expected to increase to a staggering 79.4 million by 2030.<sup>4</sup>

Type 1 diabetes patients may show evidence of retinopathy as early as 5 years after the onset of systemic disease, and almost all patients will show varying degrees of retinopathy 20 years after the onset of diabetes. Type 2 diabetic patient may present with retinopathy even at time of diagnosis, consistent with the usually long duration of subclinical hyperglycemia in such patients and more than 60% of type 2 diabetic patients will have some degree of retinopathy after 20 years of onset of diabetes.<sup>5</sup> The introduction of insulin by

Banting and Best is a major breakthrough in the treatment of diabetes.

The first oral hypoglycemic agents were introduced in the mid 50's. Despite these treatment modalities, diabetic retinopathy still develops and continues to cause morbidity and vision loss.

For the assessment of glycemia, recordings of glycosylated proteins, primary hemoglobin and serum proteins have added a new dimension.

We can get a quantitative estimate of the average glycemia over weeks and months, with a single measurement of each of these parameters, there by complementing day to day testing. Expert opinion recommends HbA1c testing at least two times a year in patients who have stable glycemic control.<sup>6</sup>

HbA1C has been recognized as a marker for determining long-term diabetes mellitus regulation. In past studies it has been shown that levels of HbA1C may also be associated with the risk of diabetic retinopathy. But few studies have shown association between HbA1C and various degrees of diabetic retinopathy and this research is intended to address this need.

### Aims and Objectives

- To determine the correlation of HbA1C with different grades of diabetic retinopathy.
- To establish HbA1C as a parameter in assessing the severity of diabetes mellitus.

### Materials and Methods

This study will be conducted at the Department of Ophthalmology at to Katihar Medical College and Hospital, Katihar. During the period October 2018-September 2020.

### Source of Data

Diabetic patients coming in Eye OPD of KMCH & indoor patients being referred by other department for evaluation of diabetic retinopathy.

### Method of Collection of Data

**Study Design:** Descriptive Correlative Study

**Duration:** 18 Months.

### Inclusion Criteria

- Patients of either sex
- Patients diagnosed as cases of diabetes mellitus of at least one year duration on treatment with oral hypoglycemic agents / insulin
- Both type 1 and type 2 diabetes mellitus

### Exclusion Criteria

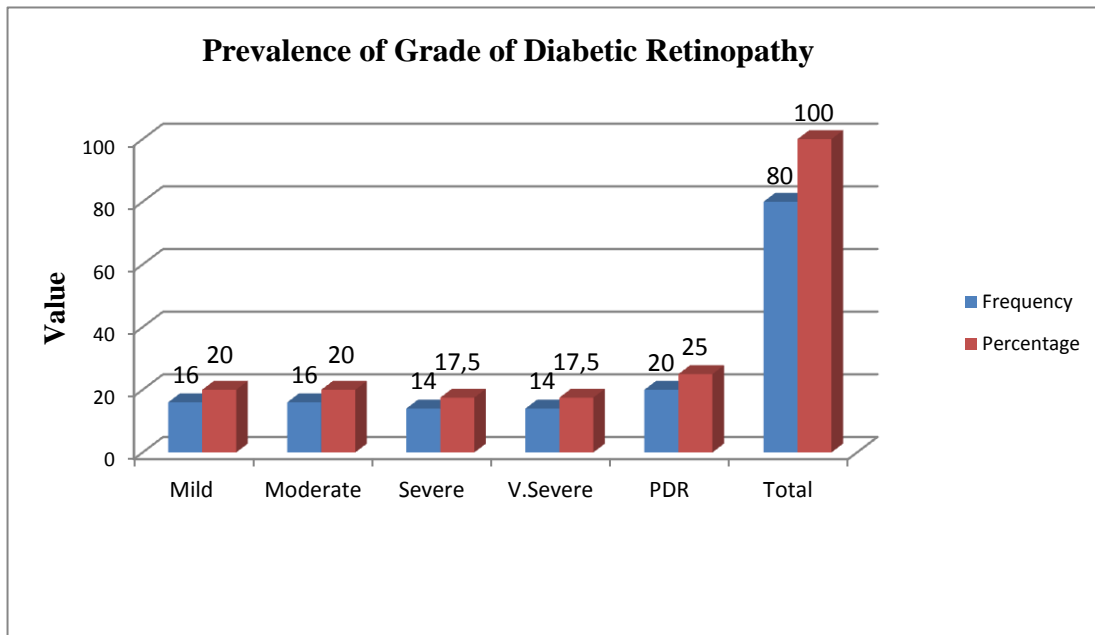
- Patients not diagnosed as having diabetes mellitus
- Diabetic patients without retinopathy.
- Patients with ocular media opacity in both eyes so as to interfere with a detailed examination of the fundus.
- Patients with pre-existing non diabetic maculopathy (like that due to central serous retinopathy, age related macular degeneration, drug induced and other macular degenerations)
- Patients with angle closure glaucoma.
- Hypertensive patients.
- Patients with myopic degenerations and other retinal degenerations.
- Patients with non diabetic renal disorders (glomerulonephritis, obstructive uropathy, renal parenchymal disorders and post renal transplantation.
- Patients with chronic liver diseases.
- Patients who have undergone laser photocoagulation therapy
- Sick cell disease, Glucose 6 phosphate dehydrogenase deficiency, vitamin B12 & folate deficiency, anaemia and other blood dyscrasias.

### Results

**Table – 01** Prevalence of Grade of Diabetic Retinopathy

Retinopathy	Frequency	Percentage
Mild	16	20.
Moderate	16	20.
Severe	14	17.5
V. severe	14	17.5
PDR	20	25.0
<b>Total</b>	<b>80</b>	<b>100.0</b>

Graph – 01 Prevalence of Grade of Diabetic Retinopathy

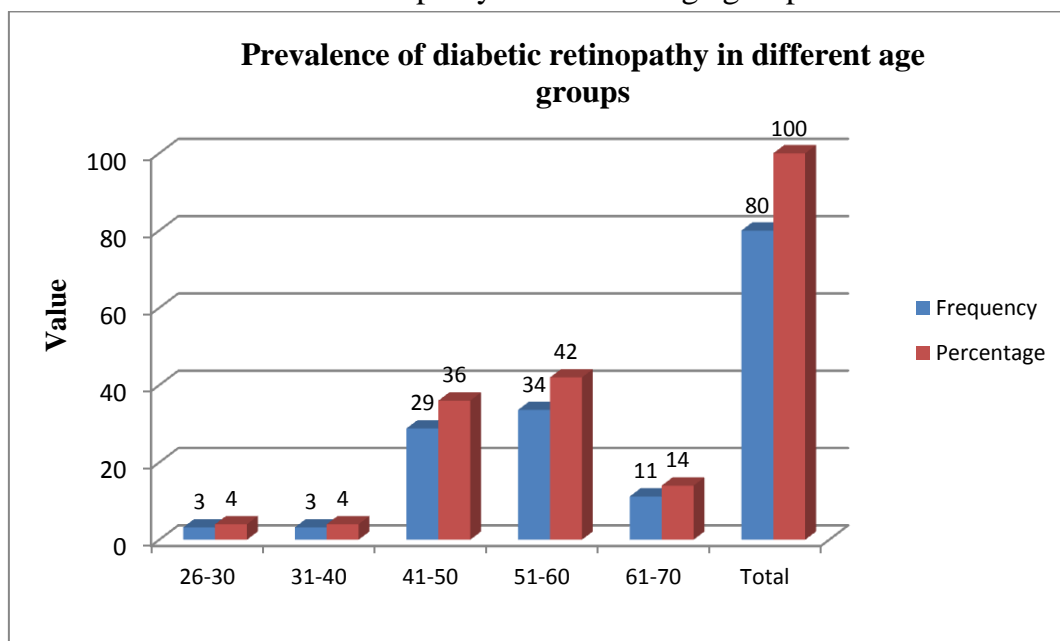


According to the observations made, NPDR had the highest prevalence, amounting to 76%. PDR accounted for 24% of the study population.

Table – 2 Prevalence of diabetic retinopathy in different age groups

Age Group	Frequency	Percentage
26 - 30	3.2	4.0
31 - 40	3.2	4.0
41 - 50	28.8	36.0
51 - 60	33.6	42.0
61 - 70	11.2	14.0
<b>Total</b>	<b>80</b>	<b>100.0</b>

Graph – 02 Prevalence of diabetic retinopathy in different age groups

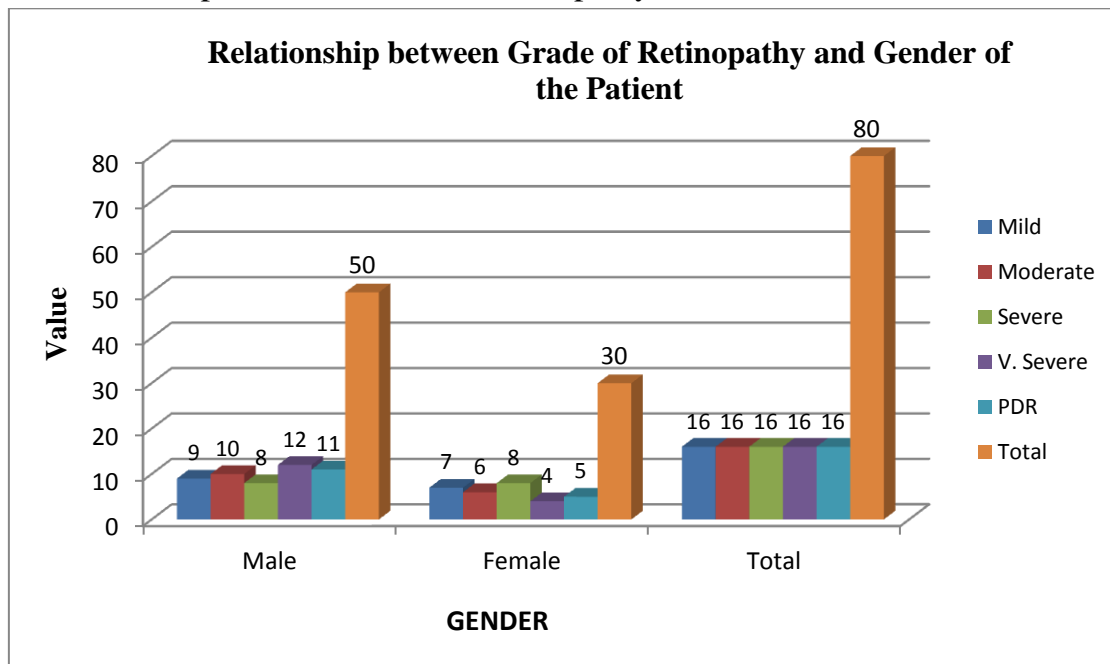


Diabetic retinopathy was seen to be most common in the age group of 51-60 years.

**Table – 3** Relationship between Grade of Retinopathy and Gender of the Patient

Sex	Grade of Diabetic Retinopathy					Total
	Mild	Moderate	Severe	V. severe	PDR	
Male	9 (18.0%)	10 (20.0%)	8 (16.0%)	12 (24.0%)	11 (22.0%)	50 (100%)
Female	7 (23.3%)	6 (20.0%)	8 (26.7%)	4 (13.3%)	5 (16.7%)	30 (100%)
Total	16 (20.0%)	16 (20.0%)	16 (20.0%)	16 (20.0%)	16 (20.0%)	80 (100.0%)

**Graph – 03** Relationship between Grade of Retinopathy and Gender of the Patient



Out of total 80 patients 50 were male (70%) and 30 were female (30%)

- In the Mild NPDR group there were 9 men and 7 women.
- The Moderate NPDR group contained 10 men and 6 women.
- The Severe NPDR group had 8 men and 8 women

- The V. Severe NPDR group had 12 men 4 women
- The PDR group consisted of 11 men and 5 women.
- In total there were 50 men and 30 women.

These numbers were analyzed statistically, yielding a p value of >0.05.

**Table – 04** Relationship between Grades of retinopathy and HbA1c levels

	N	Mean	SD	95% Confidence Interval for Mean		ANOVA F value	p value
				Lower Bound	Upper Bound		
Mild	16	7.910	2.1982	6.337	9.483	7.274	.000
Moderate	16	8.550	2.5172	6.749	10.351		HS
Severe	14	9.944	1.8324	8.536	11.353		
V. severe	14	11.356	1.4362	10.252	12.460		
PDR	20	12.017	2.2819	10.567	13.467		
Total	80	10.010	2.5999	9.271	10.749		

From the above table a correlation is inferred for mild NPDR the range of HbA1c was found from 6.3% - 9.4%, moderate NPDR the range was 6.7% -10.3%, severe NPDR the range was 8.5% – 11.3%, very severe NPDR it was 10.2%-12.4% and for PDR the range was 10.5%-13.4%. There was a statistically significant result observed with the values of glycosylated hemoglobin HbA1C, which were observed in different grades of diabetic retinopathy.

### Discussion

Accurate data concerning the type and severity of diabetic retinopathy and associated risk factors are of importance in planning a well-coordinated approach to the public health problem posed by this complication of diabetes. Identifying the patient who may be at high risk of severe retinopathy is important in advising ophthalmic care. Such data are also helpful in planning future studies such as controlled clinical trials of treatment of diabetes and of diabetic retinopathy. This study was a descriptive correlative study on 80 patients with diabetic retinopathy. 20% of the patients manifested with mild NPDR, 20% with moderate and 17.5% with severe NPDR 17.5% showed very severe NPDR while the remaining 25% had PDR.

### Patient age and type of diabetic retinopathy

Klein and Klein noted that age had little significance in the progression of retinopathy once the duration and type of retinopathy were considered.<sup>7</sup>

Our study too showed that age was not a statistically significant factor in the severity of diabetic retinopathy.

### Diabetic retinopathy and Gender of Patient

In this study, there was no relationship between gender and DR ( $p=0.583$ ). In confirmation of the findings of Nakagami et al.,<sup>60</sup> Tapp et al.<sup>8</sup> However, Santos et al.<sup>9</sup> showed that there was a trend towards a higher frequency of DR in men than in women.

### Duration of diabetes and Severity of diabetic retinopathy

The 80 patients of diabetic retinopathy were categorized based on the duration of diabetes. Mild, moderate and severe NPDR were seen in patients with diabetic duration of less than 10 yrs, whereas very severe NPDR and PDR were seen in patients with diabetic duration of more than 10 yrs. It is evident from these findings that there was a statistically significant worsening of retinopathy and progress of the severity of retinopathy with increasing duration of diabetes in these individuals. ( $p=0.000$ )

In the CURES Eye study<sup>10</sup>, 41.8 per cent had DR after 15 yr of diabetes and severity of DR proportionally increased with longer duration of diabetes. In addition, it has been demonstrated that for every five year increase in duration of diabetes, the risk for DR increased by 1.89 times.

In the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), the widest and most prolonged population based ophthalmologic survey, it was reported that higher prevalence of DR was associated with longer duration of diabetes<sup>11</sup>

### HbA1c levels and diabetic retinopathy

The patient's glycemic status was measured using HbA1C values which showed a statistically significant increase in HbA1C levels with the increasing severity of diabetic retinopathy.

One of the studies conducted previously in this regard showed that the risk of PDR was six times higher among diabetics with poor glycemic control<sup>12</sup>. Another similar study showed that the HbA1C levels correlated with prevalence of retinopathy status in diabetic patients on insulin therapy<sup>13</sup>. Reductions in blood glucose or HbA1c concentrations through tight blood glucose control in people with diabetes reduces the rate of progression microvascular complications such as DR, neuropathy and nephropathy.

In our study we found a cut off range of HbA1C for different grades of diabetic retinopathy above which retinopathy of that grade tended to manifest: in mild NPDR the range of HbA1c was

found to be 6.3% - 9.4%, moderate NPDR - 6.7% -10.3% , severe NPDR - 8.5% – 11.3%, very severe NPDR - 10.2%-12.4% and for PDR - 10.5%-13.4%. Such cut off ranges has not been evaluated by many, only a few studies have defined such cut off values.

A Korean study and a Singapore study showed that the threshold for HbA1C for any or mild retinopathy was lower than that for moderate retinopathy (6.5% for any DR, and 6.9% for moderate or more severe DR in a Korean study ; 6.6% mild DR, and 7.0% for moderate or severe DR in a Singapore study). In studies between 2000 and 2014, the optimal cutoff value for any DR was 5.7% in the Hisayama Study, 6.1% in the Aus Diab Study, 5.5% in the NHANES 2005 to 2006, 6.4% in a Chinese Study, and 6.2% in the Korean NHANES, and for moderate or severe DR, it was 6.4% in the DETECT-2 study.

### Conclusion

A statistically significant correlation was found between HbA1C levels and the severity of diabetic retinopathy with more severe grades of diabetic retinopathy manifesting in patients with higher levels of HbA1C.

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