

## Original Article

# Influence of Glycated Haemoglobin Levels on Intraocular Pressure in patients with Type –II Diabetes Mellitus

Ajai Agrawal<sup>1</sup>, Shubham Ahuja<sup>1</sup>, Anupam Singh<sup>1</sup>, Ramanuj Samanta<sup>1</sup>,  
Sanjeev Kumar Mittal<sup>1</sup>

<sup>1</sup>Department of Ophthalmology, All India Institute of Medical Sciences, Rishikesh, India

## Abstract

**Introduction:** Patients with diabetes mellitus are at a higher risk of developing primary open angle glaucoma (POAG) as compared to non-diabetic patients.

**Objectives:** To determine whether there is a correlation between hyperglycaemic levels and intraocular pressure (IOP) and to identify patients of Type II diabetes mellitus who are at a higher risk of developing glaucoma.

**Materials and Methods:** This was a hospital based, cross sectional study performed on patients with type II diabetes mellitus, at a tertiary health care center in Uttarakhand, India between July, 2018 and September, 2018. 318 eyes of 159 patients with Type 2 diabetes mellitus were included in the study. IOP was measured by Goldmann applanation tonometer and central corneal thickness was measured with specular microscope in all patients, in addition to glycated haemoglobin levels (HbA1c) and fasting and post-prandial blood glucose levels. The data was analysed using SPSS 22 software.

**Results:** Mean IOP was found to be  $15.75 \pm 3.18$  mm Hg in patients with HbA1c levels between 6.5%-12% (Group I) and  $17.42 \pm 2.67$  mm Hg in patients with HbA1c levels more than 12 % ( Group II). The difference between the two groups was statistically significant ( $P=0.013$ ). Out of 159 patients with Type 2 Diabetes mellitus, a total of 11 patients had IOP more than 21mm Hg in one or both the eyes.

**Conclusion:** Hyperglycaemic levels as determined by raised HbA1c levels are associated with higher intraocular pressures in patients with type 2 diabetes mellitus.

**Key words:** Glycated haemoglobin, Intra ocular pressure, Type 2 diabetes mellitus.

## Introduction

In recent years, non-communicable diseases, including diabetes mellitus, chronic obstructive pulmonary diseases and cancers have become

a global emerging pandemic with a significant disease burden affecting the developing countries (Terzic A et al., 2011). Diabetes mellitus is a common systemic disease with a number of ocular manifestations. Hyperglycaemia may be associated with secondary damage in many organ systems of the body, especially targeting the ocular structures, kidneys and nervous system. Although Diabetes has a high prevalence, there are few studies investigating the precise status of diabetes and various co-morbidities

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**Corresponding author**

Dr Ajai Agrawal, Additional Professor,  
Department of Ophthalmology,  
All India Institute of Medical Sciences (AIIMS), Rishikesh, India.  
Phone: 0091-8607593922  
E-mail: ajaiagrawal@rediffmail.com ; agrawalajai@gmail.com



associated with it. (Kaveeshwar et al., 2014).

Epidemiological data from various countries has shown that patients with diabetes mellitus have a higher risk of developing primary open angle glaucoma (POAG) (Bonovas et al., 2004; Khatri et al., 2018). A study by Perez et al. in 2015 found that IOP of eyes in patients who had uncontrolled diabetes was much higher than the IOP of eyes in patients with controlled diabetes. The underlying pathophysiology for this phenomenon is not very clear, but lab studies conducted by Roy and co-workers have postulated that high glucose levels may lead to excess extracellular matrix (ECM) synthesis by cells of the trabecular meshwork. This may cause ECM accumulation in the trabecular meshwork, which in turn leads to obstruction of aqueous outflow (Li et al., 2003; Sato et al., 2002).

In the current study we investigated whether hyperglycaemic levels as determined by high haemoglobin A1c (HbA1c) levels influence the intraocular pressure of patients with diabetes mellitus in population belonging to the Indian subcontinent.

### **Materials and Methods**

The study was a hospital based, observational, cross-sectional study and was approved by the Institutional Ethics Committee. All procedures performed in the study were done as per the guidelines laid by of the Helsinki Declaration of the World Medical Association. Informed consent was obtained from all patients. The objectives of the study were to determine whether hyperglycaemic levels as determined by high haemoglobin A1c (HbA1c) levels have an influence on intraocular pressure in patients with diabetes mellitus and to identify those patients who are at a higher risk of developing glaucoma. The patients were taken from the Diabetes Clinic of the Department of Medicine. Patients between 18 to 70 years of age with type II Diabetes mellitus, consenting

for the study were included. Patients already diagnosed with glaucoma, using antiglaucoma medication, using oral or topical steroids or those who had undergone any intraocular surgery were excluded from the study. Age, gender, residence, type of diabetes, associated medical conditions, use of medications, fasting blood glucose levels, post-prandial blood glucose levels, HbA1c levels, blood pressure, central corneal thickness, intraocular pressure (IOP) and time of IOP measurement were documented.

The identity of patients was kept strictly confidential and consent was taken from patients for measuring their IOP and using their clinical records in the study. The IOP of patients was measured by Goldmann applanation tonometer (AT-900; Haag Streit Diagnostics) which was calibrated regularly (every two weeks) to avoid false readings. Central corneal thickness (CCT) was measured by specular microscope (CEM-530; Nidek Inc.). Corneal corrected IOPs were taken into consideration for analysis. Since IOP values are known to exhibit a diurnal variation, the IOP of all patients was measured by the same Ophthalmologist using the same applanation tonometer between 1:00 pm to 4:00 pm. The results were analysed using SPSS 22 software and MS Excel. A value of  $P < 0.05$  was considered significant.

### **Results**

A total of 159 patients (318 eyes) of Type 2 diabetes mellitus who satisfied the inclusion criteria were included in the study. The age of the patients ranged between 18-70 years (Mean age = 52.6 years; Standard Deviation = 14.2) Out of these 81 patients were male and 78 patients were female. The mean IOP of both eyes of each patient and HbA1c levels are detailed in table 1. It was observed that patients belonging to the category with higher HbA1c levels had higher mean IOP as compared to the patients belonging to the category with lower HbA1c levels. It was also observed that a linear

co-relation does not exist between HbA1c levels and IOP as well as central corneal thickness. All patients were further divided into two categories based on whether their HbA1c levels were below or above 12% (Table 2). The mean IOP in category 1 patients with HbA1c ranging between 6.5 % -12 % was found to be  $15.75 \pm 3.18$  mm Hg and this value was statistically significantly ( $P=0.013$ ) lower than that of category 2 patients with HbA1c  $>12$  % and mean IOP of  $17.42 \pm 2.67$  mm Hg (Figure 1). Out of the 159 patients with Type 2 diabetes

mellitus, a total of 11 patients had IOP more than 21mm Hg in one or both the eyes which is more than the normal upper limit of 21mm Hg.

### Discussion

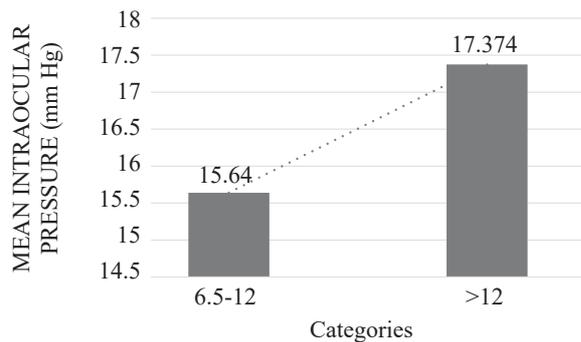
The current study shows that diabetic patients with elevated HbA1c levels have significantly higher IOPs compared to those with lower HbA1c levels. The exclusion criteria have been selected by us in such a manner so as to minimize bias. Similar exclusion criteria have been used by Hymowitz and co-workers (2016). We have

**Table 1: Table showing relationship between mean IOP and HbA1c levels for all patients (n=159)**

S.No.	HbA1c Range (%)	No. of Individuals	Average CCT (micrometers)	Mean IOP (mm Hg)
1.	6.5-7.0	21	520	15.74
2.	7.1-7.5	12	514	16.38
3.	7.6 -8.0	16	536	15.41
4.	8.1-8.5	17	524	15.85
5	8.6-9.0	22	527	15.68
6	9.1-9.5	4	524	13.63
7	9.6 -10.0	13	529	15.77
8	10.0-10.5	9	563	14.67
9	10.6-11.0	5	517	16.10
10	11.1-11.5	4	519	16.75
11	11.6 -12.0	10	519	17.45
12	12.1-12.5	2	512	20.00
13	12.6-13.0	5	540	16.80
14	13.1-13.5	2	524	19.25
15	13.6 -14.0	2	513	19.50
16	14.1-14.5	3	510	14.17
17	14.6-15.0	4	517	18.00
18	15.1-15.5	4	532	15.34
19	15.6-16.0	1	522	18.50
20	$>16.0$	3	522	19.00

**Table 2: Showing mean IOP difference between category 1(HbA1c (6.5 -12.0) and category 2 (HbA1c  $>12.0$ ) Diabetic patients.**

Category	HbA1c Range (%)	No. of Individuals	Mean IOP (mm Hg)	Standard deviation
Category 1	6.5 -12.0	133	15.75	3.18
Category 2	$>12.0$	26	17.42	2.67



**Figure 1:** Relationship between mean IOP and HbA1c levels in Category 1 (HbA1c between 6.5-12%) and Category 2 (HbA1c >12.0) diabetic patients.

excluded known patients of glaucoma as they have higher IOP levels, which may have biased our results. The exclusion of patients who are already instilling anti glaucoma medications and/or topical steroids was required since these medications are a potential confounder to the relationship between HbA1C and IOP being studied by us.

Our findings indicate a statistically significant difference in HbA1c levels between diabetic subjects with low IOP and those with high IOP. The fact that Diabetes is a risk factor for glaucoma has been recognized by a number of investigators from different countries (Bonovas et al, 2004; Chopra et al., 2008; Mitchell et al., 1997; Oshitari et al., 2007).

In our study, it was seen that hyperglycemic levels as determined by high HbA1c levels are associated with higher IOPs. It was also observed that the relationship between HbA1c levels and IOP as well as central corneal thickness is not linear. The observations and results of our study are consistent with previous studies. Hymowitz et al. in 2016 have noted that patients with poor glycaemic control have higher IOPs. They found that diabetic patients with poor control as evidenced by higher HbA1c levels have an IOP which is usually more than 14.5 mmHg. Their study shows that

blood glucose control is of vital importance (Hymowitz et al., 2016).

Previous studies including The Rotterdam Study (Dielemans et al., 1996) and the Beaver Dam Eye Study (Klein et al., 1994) have reported higher IOPs in diabetic patients compared to those who are not diabetic. An earlier study published in the American Journal of Ophthalmology has shown that hyperglycemia is associated with elevated IOP levels in diabetic patients (Oshitari et al., 2007).

There are only a few published studies from the Indian subcontinent on the influence of HbA1c levels on IOP. Studies performed on diabetic individuals in South India (Anandha et al., 2011) and by Baisakhiya et al. (2017) have shown that diabetic patients with higher levels of HbA1c have elevated IOPs as compared to those patients with lower HbA1c levels. They have inferred from their studies that poor glycaemic control may be a risk factor for glaucoma in diabetic patients. Findings from our study indicate that early monitoring of HbA1c levels may be useful in assessing the diabetic population at risk for development of increased IOP. This suggestion is all the more important for population of countries like Nepal and India where HbA1c levels are not done routinely, in part due to economic considerations. Further studies may help to better understand the association between hyperglycaemia and IOP.

### Limitations of the Study

Factors such as duration of diabetes and fluctuation of glycemic levels that may affect the IOP levels of the patients were not taken into consideration. Also, all the patients included in the study were patients of Type II diabetes. Patients with type I Diabetes were not included in the study.

### Conclusion

In conclusion, our results showed that hyperglycemic levels as determined by

increased HbA1c levels were found to be associated with increased IOP in patients with Type 2 diabetes mellitus. Since poor glycemic control in Type II diabetic patients may be a risk factor for glaucoma, it is prudent that blood glucose monitoring should include measurement of HbA1c levels in addition to fasting and post-prandial blood glucose level monitoring. In addition, IOP of diabetic patients should be checked on a regular basis, so that ocular morbidity as a result of glaucoma may be reduced.

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