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Original Research Article

# Effect of glycated hemoglobin levels on intraocular pressure in patients with diabetes mellitus

**Kirtana Suresh[1]*, Pallavi B Acharlu[1], Sujatha Vijayalekshmi[1], Vijay Kumar Srivastava[1]**

[1] *Dept. of Ophthalmology, MVJ Medical College and Research Hospital, Bangalore, Karnataka, India*

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ABSTRACT

**Objectives**: To investigate the effect of chronic hyperglycemia as determined by high glycated hemoglobin on intraocular pressure (IOP) in patients with diabetes & to recognize the patients at high risk of developing glaucoma.

**Materials and Methods:** 100 patients (n=200 eyes) of age 40 years and above were studied in five groups. They were grouped as diabetic patients without diabetic retinopathy, mild/moderate/ severe non-proliferative diabetic retinopathy, and proliferative diabetic retinopathy. Data recorded were age, sex, intraocular pressure by noncontact tonometer and grades of diabetic retinopathy in each eye.

**Results:** Mean IOP was found to be 15±2.81mmHg in patients with HbA1c levels between 6-8%, 14.81±2.63 mmHg in patients with HbA1c levels between 8-10% and 17.423±3.05 mmHg in patients with HbA1c more than 10%. Out of 100 patients, a total of 16 patients had IOP more than 20mmHg in one or both the eyes. The Pearson correlation between HbA1c and IOP was 0.305, with a p value of 0.001 indicating statistical significance. Additionally, it has been found that the correlation between HbA1c levels and IOP is non-linear.

**Conclusions**: 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.



## 1. Introduction

Diabetes Mellitus (DM) is a major health issue involving various organs which is increasing day by day.[1] According to estimates, 451 million individuals worldwide (aged 18 to 99) had Diabetes in 2017, and there might be surge in cases up to 693 million by 2045.[2]

Diabetes is a chronic, metabolic disease characterized by elevated levels of blood glucose (or blood sugar), which leads over time to serious damage to the heart, blood vessels, eyes, kidneys and nerves. Ocular manifestations include cataract formation, retinopathy and glaucoma in patients.[3]

Diabetes Mellitus (DM) is diagnosed using either plasma glucose criteria, such as fasting plasma glucose (FPG) and 2-hour plasma postprandial glucose (2-h PPG) levels,[4] or HbA1c criteria, which represents the average plasma glucose concentration over the preceding 8–12 weeks.[5] Compared to plasma glucose measurement, Haemoglobin A1c (HbA1c) testing has a number of benefits, including pre-analytical stability and less day-to-day fluctuation brought on by stress or illness.[6]

HbA1c is the gold standard for managing diabetes therefore, HbA1c is utilized as a predictor to evaluate secondary micro vascular consequences, such as retinopathy, neuropathy, and nephropathy in situations of insufficient glycaemic control, in addition to reflecting

* *Corresponding author*.
*E-mail address*: skirtanasuresh007@gmail.com (K. Suresh).

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the glycaemic adjustment.[7] Diabetes contributes to elevated intraocular pressure (IOP) and subsequently leading to glaucoma has been noted in this patients.[8] Although the exact process is yet unknown, in vitro research indicates that high glucose levels can cause trabecular meshwork cells to produce an excessive amount of extracellular matrix (ECM). This could result in extracellular matrix (ECM) build up in the trabecular meshwork, which would help to obstruct aqueous outflow.[9] Our study was done to check whether hyperglycaemic levels which is determined by high HbA1c levels will influence the IOP in diabetic patients.

## 2. Materials and Methods

After taking the approval from our Institutional Ethical committee, we did our study which was Prospective Hospital-based Observational study.

100 patients with Diabetes Mellitus attending Ophthalmology OPD in M.V.J Medical College & Research Hospital Bangalore were included in the study. The patients who satisfied the inclusion criteria (patients above 40 years of age of both gender with Type 2 Diabetes Mellitus) were included in our study. Patients with established cases of Primary and Secondary Glaucoma, Congenital abnormalities of the disc, history of ocular trauma/surgeries, media opacities obscuring fundus details and Pathological Myopia were excluded from the study.

Study duration was for 3 months from April 2023 to June 2023.

Patients who satisfied the inclusion criteria for selection were taken as subjects for the study.Informed consent was obtained from all patients. Each patient underwent a complete ocular examination which included visual acuity for distant and near, anterior segment examination using Slit lamp and fundus examination using slit-lamp bio microscope by an attending Ophthalmologist. Diabetic retinopathy changes, if any were noted. Non contact Tonometer was used to check the intraocular pressure. Age, gender, grade of diabetic retinopathy, HbA1c levels, intraocular pressure were documented. All patients were categorised into three groups based on their HbA1c levels as follows: Group 1(6 to 8%), Group 2 (9 to 10%) and Group 3 (>10.1%). The patients were also divided based on grade of Diabetic Retinopathy into 5 categories according to Early Treatment Diabetic Retinopathy Study(ETDRS)[10] classification. A value of P less than 0.05 was considered significant.

Data was entered in the excel spread sheet. SPSS (Statistical Package for Social Sciences) version 20 was used to perform the statistical analysis. Descriptive statistics of the explanatory and outcome variables were calculated by mean, standard deviation for quantitative variables, frequency and proportions for qualitative variables. Chi square was applied to test the statistical association between qualitative variables. ANOVA test was applied to test the statistical significance for IOP with grading of eye. Pearson's correlation was calculated to calculate the correlation between IOP and HbA1C. The level of significance was set at 5%.

## 3. Results

A total of 100 patients involving 200 eyes of Type 2 diabetes mellitus patients who satisfied the inclusion criteria were included in our study.

Out of 100, 63 patients were male(63%) and 37 patients were female (37%). The patients ranged between the age of 40-89 years. The Mean age was 59.62 years with Standard Deviation of 9.76.The mean intraocular pressure in males was 15.6±2.9 mmHg and in females mean intraocular pressure was 15.5±3.2 mmHg.(Table 1)

**Table 1:** Gender distribution

| Gender | Frequency | Percentage | Mean IOP | SD IOP |
|---|---|---|---|---|
| Female | 37 | 37.0 | 15.51 | 3.19 |
| Male | 63 | 63.0 | 15.62 | 2.90 |
| Total | 100 | 100.0 | | |

Number of patients in each age group were as follows :in the category of 40-49 years had 10 females and 5 males with mean intraocular pressure being 14.70±2.99mmHg and 15.60±3.75mmHg respectively. In the category of 50-59 years had 14 females and 20 males with mean intraocular pressure being 15.64±3.27mmHg and 15.50±2.71mmHg respectively. In the category of 60-69 years had 12 females and 20 males with mean intraocular pressure being 14.75±2.69mmHg and 16.00±2.86mmHg respectively. In the category of 70-79 years had 06 females and 10 males with mean intraocular pressure being 16.67± 3.45mmHg and 16.20± 3.30mmHg respectively. In the category of 80-89 years had only 03 males with mean intraocular pressure being 15.00± 2.76mmHg respectively.

Mean intraocular pressure in different age groups are as follows 40-49 years, 50-59 years, 60-69 years, 70-79 years and 80-89 years are as follow 15.00±3.23mmHg, 15.56±2.93mmHg, 15.53±2.85mmHg, 16.38±3.31mmHg 15±2.76 mmHg respectively.(Table 2)

**Table 2:** Age distribution

| Age group | Frequency | Percentage | Mean IOP | SD IOP |
|---|---|---|---|---|
| 40-49 | 15 | 15.0 | 15.00 | 3.2 |
| 50-59 | 34 | 34.0 | 15.56 | 2.9 |
| 60-69 | 32 | 32.0 | 15.53 | 2.8 |
| 70-79 | 16 | 16.0 | 16.38 | 3.3 |
| 80-89 | 3 | 3.0 | 15.00 | 2.8 |
| Total | 100 | 100.0 | | |

Number of eyes in each group were as follows, 72 (36%) were in group 1 in which 17 were females and 19 were

**Table 3:** Mean IOP in different gender

| Age group | Number of females | Mean IOP | SD IOP | Number of males | Mean IOP | SD IOP |
|---|---|---|---|---|---|---|
| 40-49 | 10 | 14.70 | 2.99 | 5 | 15.60 | 3.75 |
| 50-59 | 14 | 15.64 | 3.27 | 20 | 15.50 | 2.71 |
| 60-69 | 12 | 14.75 | 2.69 | 20 | 16.00 | 2.86 |
| 70-79 | 06 | 16.67 | 3.45 | 10 | 16.20 | 3.30 |
| 80-89 | - | - | - | 03 | 15.00 | 2.76 |

**Table 4:** Mean IOP difference in each categories of HbA1c

| HbA1c | N | Mean IOP | Std. Dev | F value | p value* |
|---|---|---|---|---|---|
| 6 to 8 | 72 | 15.06 | 2.808 | 15.246 | 0.001 |
| 9 to 10 | 76 | 14.82 | 2.637 | | |
| > 10 | 52 | 17.42 | 3.051 | | |
| Total | 200 | 15.58 | 3.005 | | |

male patients, 76(38%) were in group 2 in which 13 where females and 25 were male patients and 52 (26%) were in group 3 in which 7 where females and 19 were male patients.

The mean IOP in group 1, group 2 and group 3 was 15.06±2.8 mmHg, 14.82 ±2.637 mmHg and 17.42±3.051 mmHg respectively.(Table 4)

### *3.1. Mean IOP was found to be increasing with HBA1c levels*

Number of eyes in each group according to ETDRS are as follows, 76(38%) had no signs of diabetic retinopathy with a mean intraocular pressure of 13.76±2.141mmHg in which 16 where females and 22 were male patients, 34(17%) had mild NPDR with mean intraocular pressure of 15.29±2.646mmHg in which 4 where females and 13 were male patients, 44 (22%) had moderate NPDR with mean intraocular pressure of 16.00±2.762 mmHg in which 9 where females and 13 were male patients, 20(10%) had severe NPDR with mean intraocular pressure of 16.80±1.881mmHg in which 03 where females and 07 were male patients and 26(13%) had PDR with mean intraocular pressure of 19.62±2.118mmHg in which 05 where females and 08 were male patients. (Table 5)

### *3.2. Mean IOP was found to be increasing with severity of diabetic retinopathy grading*

Out of 100 patients, it was noticed that 16 patients had intraocular pressure more than 20mmHg in one or both eyes.

It was observed that patients belonging to group 3 had higher mean intraocular pressure as compared to the patients belonging to the group 1 and 2. It was also observed that there was no linear correlation between HbA1c levels and intraocular pressure.

## 4. Discussion

The leading causes of irreversible blindness are Diabetic Retinopathy and Glaucoma.[11] Diabetes affects the microvascular system, affecting the retinal blood vessels and the optic nerve, and is associated with increased intraocular pressure which eventually leads to glaucoma.[12]

Therefore, diabetes is likely risk factor for glaucoma, especially open-angle glaucoma but association between glaucoma and diabetes remains uncertain.[13]

The Beaver Dam Eye Study by Klein BE et al[14] states that incidence of open angle glaucoma is more among diabetics.

The Blue Mountain Eye Study by Mitchell P et al[15] also concluded that there is a significant and consistent association between diabetes and glaucoma.

Los Angles Latino Eye study (LALES)[16] showed the prevalence of open angle glaucoma to be 40% higher in participants with type 2 diabetes than in those without type 2 diabetes.

Singapore Malay Eye Study[17] reported that diabetes influences increase of intraocular pressure but not related with open-angle glaucoma development.

Barbados Eye Study[10] and The Baltimore Eye Survey found glaucoma prevalence is higher in diabetes than without diabetes.

In our study the mean age was 59.62 years with Standard Deviation of 9.76. In similar studies such as Arun Samal et al[1] and Agarwal et al[18] the mean age was 55.57 ± 4.50 years and 52.6 ± 14.2 years respectively.

Number of male patients were 63% and females were 37%. The mean intraocular pressure in males was 15.6±2.9 mmHg and in females mean intraocular pressure was 15.5±3.2 mmHg. Similarly in other studies such as Arun Samal et al had 49.70% male patients and 50.30% were female patients.In Agarwal et al[18] 50.9% were male patients and 49.1% were female patients.

**Table 5:** Type 2 diabetic retinopathy grading

| T2 DM grading | N | Mean IOP | Std. Dev | F value | p value* |
|---|---|---|---|---|---|
| No sign | 76 | 13.76 | 2.141 | | |
| Mild | 34 | 15.29 | 2.646 | | |
| Moderate | 44 | 16.00 | 2.762 | 32.191 | 0.001 |
| Severe | 20 | 16.80 | 1.881 | | |
| PDR | 26 | 19.62 | 2.118 | | |
| Total | 200 | 15.58 | 3.005 | | |

**Table 6:** Gender distribution based on ETDRS grading

| T2 DM grading | Number of females | Number of males | Mean IOP | SD IOP |
|---|---|---|---|---|
| No sign | 16 | 22 | 13.76 | 2.141 |
| Mild | 04 | 13 | 15.29 | 2.646 |
| Moderate | 09 | 13 | 16.00 | 2.762 |
| Severe | 03 | 07 | 16.80 | 1.881 |
| PDR | 05 | 08 | 19.62 | 2.118 |
| Total | 37 | 63 | | |

Our study shows that the patients with elevated HbA1c levels had higher intraocular pressures as compared to those with lower HbA1c levels which was significant.This is consistent with study conducted by Agarwal et al. [18]

Intraocular pressure increases significantly on increasing severity of Diabetic Retinopathy showing a positive correlation between intraocular pressure and grades of Diabetic Retinopathy.

The observations and results of our study are consistent with previous studies such as Arun Samal et al [1] 2021 study.

The Pearson correlation between HbA1c and intraocular pressure was 0.305, with a p-value of 0.001 indicating statistical significance.

Pearson correlation of -0.036 and p value of 0.724 which shows no statistical significance.

Generalised linear fit model was built using HbA1c, type 2 Diabetes grading as factor and intraocular pressure as a response. Based on model, T2DM grading found to be signification with p value of <0.0001. However, HBA1c found to be insignificant with p value of 0.662 and shows there is a significance (<0.0001 P value) with respect to diabetes grading where as with HbA1c there is no clear cut significance.

Pearsons residual prediction profile (Figure 1) shows there is linear correlation between type 2 diabetes grading and intraocular pressure whereas there is a non linear correlation between HbA1c and intaocular pressure. Findings from our study indicate that early monitoring of HBA1c levels may be useful in assessing the diabetic population at risk for the development of increased intraocular pressure.

Further studies may help to better understand the association between hyperglycemia and intraocular pressure.

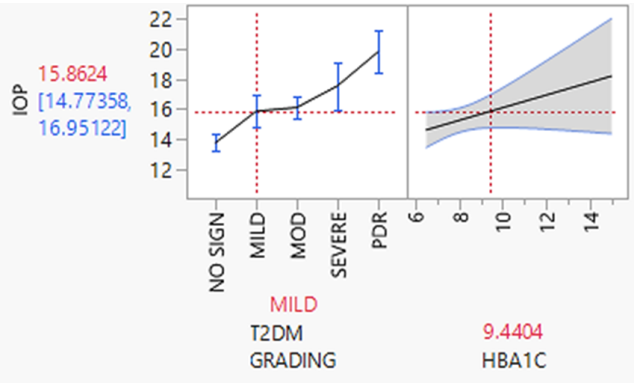


**Figure 1:** Prediction profiler: IOP vs HbA1c and DM grading

## 5. Conclusion

Our results showed association between hyperglycemic levels and increased intraocular pressure in patients with Type 2 Diabetes Mellitus which was determined by increased HBA1c.

Overall, this study highlights the importance of comprehensive Diabetes and eye care management for patients with Type 2 Diabetes.

By ensuring adequate glycemic control and regular intraocular pressure monitoring, healthcare providers can work towards reducing the risk of ocular complications and improving overall patient outcomes.

Further research in this area can help deepen our understanding of the relationship between HbA1c levels and intraocular pressure in diabetic patients and inform targeted intervention strategies to prevent and manage glaucoma in this population.

## 6. Ethical Approval

The study was approved by the Institutional Ethics Committee

## 7. Source of Funding

No funding sources.

## 8. Conflict of Interest

None declared.

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## Author's biography

**Kirtana Suresh,** Junior Resident

**Pallavi B Acharlu,** Associate Professor

**Sujatha Vijayalekshmi,** Professor

**Vijay Kumar Srivastava,** Professor and HOD

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