

Investigating the Link Between Intraocular Pressure and Blood Glucose Levels: A Comparative Study in Type 2 Diabetes Mellitus Patients and a Control Cohort

Shazia Qayum¹, Mahrukh Khan^{2*}, Shagufta Rather³

¹Assistant Professor, Department of Ophthalmology, Govt Medical College, Rajouri/Jammu University, J&K, India

²Senior Resident, Department of Ophthalmology, Govt Medical College, Rajouri/Jammu University, J&K, India

³Associate Professor, Department of Ophthalmology, Govt Medical College, Srinagar/Kashmir University, J&K, India

***Address for Correspondence:** Dr. Mahrukh Khan, Senior Resident, Department of Ophthalmology, Govt Medical College, Rajouri / Jammu University, J&K, India

E-mail: mahrukh05khan@gmail.com & **ORCID ID:** <https://orcid.org/0000-0003-2442-2104>

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ABSTRACT

Background: Glaucoma is a progressive optic neuropathy causing retinal ganglion cell loss and visual field impairment, with elevated intraocular pressure (IOP) as the only modifiable risk factor. Studies show a link between IOP fluctuations and retinal nerve fiber layer changes. Effective IOP management is crucial to prevent optic nerve damage and vision loss, with systemic factors like hypertension, BMI, and diabetes influencing IOP levels.

Methods: This prospective, cross-sectional, case-control study was conducted at GMC & AH Rajouri, Northern India, with 250 participants divided into diabetic (Group 1) and non-diabetic (Group 2) groups. Exclusions included ocular hypertension, glaucoma, significant refractive errors, and posterior segment pathologies. IOP was measured bilaterally using Goldmann applanation tonometry after fasting for 10 hours and 2 hours post-breakfast. Statistical analysis was performed using SPSS version 21.0.

Results: This study highlights a significant correlation between blood glucose fluctuations and IOP variations in diabetic patients. Diabetic individuals exhibited higher fasting and postprandial IOP values compared to non-diabetic controls. The findings underscore the importance of routine blood glucose monitoring alongside IOP assessments in diabetic glaucoma patients, emphasizing the need for optimal blood sugar control to mitigate glaucoma progression.

Conclusion: This study found a significant correlation between glucose level fluctuations and intraocular pressure (IOP) in diabetics, with higher fasting and postprandial IOP compared to non-diabetics. Routine blood glucose monitoring alongside IOP assessments and effective blood sugar control is recommended for diabetic glaucoma patients.

Key-words: Diabetes, Glaucoma, Intraocular pressure, Primary open angle glaucoma, Prospective study

INTRODUCTION

Glaucoma is a progressive optic neuropathy associated with loss of retinal ganglion cells, and visual field loss and may or may not be associated with raised IOP with raised IOP being the only modifiable risk factor.^[1-4]

The direct relationship between raised IOP and a decrease in retinal nerve fibre layer thickness is well-known and verified by various studies previously.^[1,2,5-7] Thus, it is vital to control the IOP to preclude optic nerve damage and visual field loss. The IOP can be predisposed by various systemic influences like hypertension,^[8-10] atherosclerotic diseases,^[8] body mass index (BMI),^[11] and diabetes mellitus (DM).^[8,12,13] Though glaucoma is the second leading cause of blindness worldwide, it remains a diagnostic challenge for many clinicians as most of the patients are asymptomatic up to the stage of advanced optic nerve damage and irreversible advanced visual field defects.^[14]

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According to multiple clinical studies, diabetes has been associated with elevated IOP^[8,15-23] and increased risk of developing open-angle glaucoma.^[2,24] An epidemiological study by Cho *et al.*^[25] testified that there were 72 million people in India with DM in 2017 and is likely to increase to 134 million by 2045 which is an exponential rise in the number of diabetics. Ophthalmologists shortly are going to come across many diabetic people with glaucoma. Thus, understanding the fact that variations in glucose levels can have an impact on IOP would surely help in the assessment of IOP and better management of glaucoma. This study explores the relationship between IOP and blood sugar levels in individuals diagnosed with Type 2 Diabetes Mellitus (T2DM) compared to a control group. Elevated IOP and hyperglycemia are common complications of diabetes, both of which can contribute to ocular damage and vision impairment. Understanding the correlation between these variables is crucial for early detection and management of diabetic retinopathy and other ocular complications. In this comparative analysis, T2DM patients and control subjects underwent comprehensive ophthalmic evaluations, including measurements of IOP and blood sugar levels. Statistical analysis revealed a significant association between elevated IOP and higher blood sugar levels in T2DM patients when compared to the control group. These findings underscore the importance of regular monitoring of both IOP and blood glucose levels in diabetic individuals to mitigate the risk of ocular complications. Further research is warranted to elucidate the underlying mechanisms and potential therapeutic interventions to manage intraocular pressure in diabetic populations. This study aims to investigate the association between IOP and blood sugar levels in individuals diagnosed with T2DM compared to a control group.

MATERIALS AND METHODS

Place of study- This prospective, cross-sectional, and case-control study was conducted at GMC Rajouri, with patient enrollment taking place at the outpatient department (OPD) of ophthalmology between July 2023 and January 2024. Informed written consent was obtained from each participant following a comprehensive explanation of the study's objectives.

Inclusion criteria and Exclusion criteria- Group 1 included diabetic patients and Group 2 included non-diabetic patients. Patients with diagnosed ocular hypertension, Glaucoma, corneal opacity, Refractive error more than 5D spherical or cylindrical refractive error more than 2.5D and any other posterior segment pathology were excluded from the study.

Research design-All participants underwent a comprehensive ophthalmological evaluation, encompassing a review of medical history, assessment of best-corrected visual acuity, slit lamp biomicroscopy, IOP measurement, gonioscopy, and stereoscopic dilated fundoscopic examination utilizing a 90D lens. Additionally, all participants underwent capillary glucose testing under two distinct conditions: baseline measurements following a 10-hour fasting period and postprandial measurements taken 2 hours after a meal. Capillary glucose levels were quantified from the participant's left ring finger using an automated device, administered by a masked examiner. Subsequently, IOP was assessed in both eyes of each participant immediately following capillary glucose testing. Measurements were taken following a 10-hour fast and 2 hours after breakfast, employing Goldmann applanation tonometry. The evaluation was consistently performed by the same masked examiner, whereas glucose level assessments were conducted by a separate examiner. Data collection was executed by an independent third party using an Excel spreadsheet.

Statistical Analysis- Descriptive statistics included mean and standard deviation values for normally distributed variables. Paired t-tests were used for comparison of values between each time point (baseline and PP). For variables whose distribution rejected normality, a non-parametric test (Wilcoxon Rank Sum Test) was done. All statistical analyses were performed with Statistical Package for Social Sciences version 21.0.

RESULTS

A total of 250 participants (125 diabetic and 125 non-diabetic) were included. The mean age of non-diabetic patients was 37.9 ± 14.8 years and non-diabetic

participants were 55.04 ± 10.4 years (range 16–72 years). Table 1 depicts the demographic details of all the study participants. The mean BMI in the non-diabetic and diabetic groups is 22.6 ± 4.7 and 25.3 ± 3.1 , respectively. It differs significantly between the two groups ($p < 0.05$) (Table 1).

Table 1: Demographic Characteristics of Participants

Parameter	Non-Diabetic Group	Diabetic Group
Mean Age (years)	37.9 ± 14.8	55.04 ± 10.4
Mean BMI	22.6 ± 4.7	25.3 ± 3.1

In the diabetic group, the mean fasting glucose level (143.16 ± 54.91 mg/dl) and mean PP glucose (201.92 ± 82.44 mg/dl) exceeds that of the control group

(mean fasting glucose level = 90.40 ± 11.51 mg/dl; mean PP glucose level = 107.20 ± 19.79 mg/dl) (Table 2).

Table 2: Mean blood Glucose level and Mean IOP level between Diabetic and Nondiabetic groups

	Diabetics (n=125)	Non-diabetics (n=125)	t-value	p-value
Mean fasting glucose (mg/dl)	90.40 ± 11.51	143.16 ± 54.91	4.702	0.00
Mean post prandial glucose (mg/dl)	107.20 ± 19.79	201.92 ± 82.44	5.58	0.00
Mean IOP (fasting) in mmHg	12.72 ± 2.42	14.84 ± 3.24	2.61	0.01
Mean IOP (post prandial) in mmHg	12.96 ± 2.26	16.04 ± 2.31	4.75	0.00

Also, the mean fasting IOP (14.84 ± 3.24 mm Hg) and mean PP IOP (16.04 ± 2.31 mm Hg) were higher in the diabetic group than in the control group (mean fasting IOP = 12.72 ± 2.42 mm Hg; mean PP IOP = 12.96 ± 2.26 mm Hg). IOP variation (diabetic group = 1.20 ± 3.01 ; non-

diabetic group = 0.24 ± 1.47) with changes in blood sugar (diabetic = 58.76 ± 54.02 ; non-diabetic = 16.80 ± 20.36) is more in the diabetic group compared to the control group (Table 3).

Table 3: Blood Sugar and IOP Variations in Both Groups

Parameter	Non-Diabetic Group	Diabetic Group
Mean Fasting Glucose (mg/dl)	90.40 ± 11.51	143.16 ± 54.91
Mean PP Glucose (mg/dl)	107.20 ± 19.79	201.92 ± 82.44
Mean Fasting IOP (mm Hg)	12.72 ± 2.42	14.84 ± 3.24
Mean PP IOP (mm Hg)	12.96 ± 2.26	16.04 ± 2.31
IOP Variation (mm Hg)	0.24 ± 1.47	1.20 ± 3.01
Glucose Variation (mg/dl)	16.80 ± 20.36	58.76 ± 54.02

As expected, PP glucose was higher than fasting glucose in both groups (diabetic patients; mean glucose difference= 58.76 ± 54.02 mg/dl and non-diabetic patients; mean difference= 16.80 ± 20.36 m g / d l). Mean IOP variation was found to be comparatively higher in the

diabetic group than in the control group (1.20 ± 3.01 mm Hg in the diabetic group versus 0.24 ± 1.47 mmHg in the control group) and the finding was statistically significant (Table 4).

Table 4: Comparison of IOP Variation Between Diabetic and Non-Diabetic Groups

Parameter	Diabetic Group	Non-Diabetic Group
Mean IOP Variation (mm Hg)	1.20 ± 3.01	0.24 ± 1.47

Comparison of mean IOP variation in females and males showed no significant results in both diabetic and non-diabetic groups. In the diabetic group, females

(16.73 ± 2.18 mm Hg) had higher mean PP IOP than males (15 ± 2.21 mm Hg) and were not found to be statistically significant ($p=0.185$) (Table 5).

Table 5: Effect of Gender on Glucose Variation and IOP Variation

Parameter	Female (Diabetic)	Male (Diabetic)
Mean PP IOP (mm Hg)	16.73 ± 2.18	15 ± 2.21

DISCUSSION

In our study, we performed fasting blood glucose level, fasting IOP and PP glucose level, PP IOP in 250 patients (125 diabetic and 125 non-diabetic), and IOP were found to increase with increasing blood glucose levels in both groups. A mean increase of 1.20 mm Hg was observed in diabetic patients ($p < 0.05$), while there was an insignificant increase in non-diabetics. The prevalence of DM is increasing all over the world and is one of the most common Global medical health problems.^[26,27] The prevalence of DM increases with age. The glaucoma prevalence also increases with increasing age particularly primary open-angle glaucoma.^[28] So, we will come across more patients with both diseases DM and Glaucoma together. Mitchel *et al.*^[13]; Dielemans *et al.*^[20]; Klein *et al.*^[29] and determined significant correlations between DM and glaucoma. Zhao *et al.*^[23] conducted a large sample size meta-analysis on a comparison of diabetic with non-diabetic participants, the relative ratio for glaucoma was found to be 1.48 (95% CI, $1.29-1.76$). The association between DM and IOP has been documented in previous studies.^[13,15,29] Wu *et al.*^[30] in the Barbados eye study stated diabetes, among other factors such as systolic blood pressure and age, was positively correlated with higher IOP values.^[15] We

believe that our results indirectly reflect the findings of Wu and Leske, although they did not evaluate the

association between different states of blood sugar (fasting and PP) and IOP (at fasting and PP state).

Despite the paucity of studies correlating IOP changes with glucose variation, a variation positive relationship between IOP changes and glucose variation was found by Pimental *et al.* They conducted a study that included 37 patients (20 diabetic and 17 non-diabetic) and documented an IOP increase of 2.3 mm Hg in diabetic and 1.6 mm Hg in non-diabetic patients.^[31] Similarly, a present study that included 250 participants (125 diabetic patients and 125 non-diabetic patients) noted statistically significant results in the diabetic group in IOP variation (1.2 mm Hg rise in diabetic versus 0.24 mm Hg rise in non-diabetics) with fasting and PP blood sugar, but Pimental *et al.* noted significant variation in both groups. So, we recommend IOP testing at different states of blood sugar only in diabetic patients.

Yildiz *et al.*^[32] tried to find out the relation between blood sugar difference and IOP variation but with the inclusion of OGTT. In their perspective study including 51 patients (27 diabetic and 24 non-diabetic), they observed that the non-diabetic group exhibited IOPs within the normal range and a significant increase in IOP (in the right eye) that paralleled the blood glucose

elevation, particularly within the first hour of the OGTT ($p=0.017$). The diabetic group exhibited a significant increase in IOP (right and left eye) and was in parallel to the rise in blood glucose levels, more so in the first hour of the OGTT ($p=0.017$ and $p<0.001$ for right and left eye, respectively). This study supports our inference of IOP variation with different levels of blood sugar.

Regarding the mechanism underlying the IOP changes with glucose variation, many propositions have been proposed. Lane *et al.* [33] stated that fluid flow is decreased by 15% in patients with type 1 diabetes without any evidence of microvascular complications when compared with healthy control participants. We documented higher IOP variation in patients with more glucose difference, a mechanism for which is supported by studies mentioned in further discussion. Sato and Roy [34] suggested that high glucose levels may affect IOP by inducing an increase in fibronectin expression and cell proliferation in trabecular meshwork cells in the eye. Another suggested mechanism is an osmotic gradient created by hyperglycemia that draws excess aqueous humor into the anterior chamber of the eye. [35] On the contrary, diabetic patients were reported to have higher central corneal thickness and lower corneal hysteresis, which may account for higher IOP in them. [36,37]

From the clinical point of view, many diabetic patients visit ophthalmology OPD daily. Though some of them already suffer from glaucoma (ocular hypertension), many others can be saved from this permanent blindness if regular screening is undertaken. It is seen that for most diabetic patients, IOP measurement is considered important but blood sugar level is rarely assessed. Our research successfully proved the relationship between blood glucose difference and IOP variation in diabetic patients, with a mean IOP increase of 8% (along with 41% increase in mean blood sugar level). Hence, there should be multiple measurements of blood sugar and IOP in patients with DM and glaucoma at regular time intervals.

CONCLUSIONS

Our study reveals a significant association between glucose level fluctuations and alterations in intraocular pressure (IOP) in diabetic individuals, with elevated fasting and postprandial IOP compared to non-diabetic controls. This highlights the complex relationship between glycemic control and ocular physiology in

diabetic pathophysiology. We advocate for an integrated clinical approach, emphasizing concurrent blood glucose and IOP monitoring in diabetic patients with glaucoma. Effective glycemic regulation is crucial in reducing the risk of ocular complications, underscoring the need for comprehensive management strategies to optimize both glycemic control and ocular health in the diabetic population.

CONTRIBUTION OF AUTHORS

Research concept- Dr Shazia Qayum

Research design- Dr Shazia Qayum

Supervision- Dr Shazia Qayum, Dr Shagufta Rather

Materials- Dr Shazia Qayum, Dr Mahrukh Khan

Data collection- Dr Shazia Qayum, Dr Mahrukh Khan

Data analysis and interpretation- Dr Shazia Qayum, Dr Mahrukh Khan

Literature search- Dr Shazia Qayum, Dr Mahrukh Khan

Writing article- Dr Shazia Qayum, Dr Mahrukh Khan

Critical review- Dr Shazia Qayum, Dr Shagufta Rather

Article editing- Dr Shazia Qayum, Dr Mahrukh Khan

Final approval- Dr Shagufta Rather

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