# CORRELATION OF INTRAOCULAR PRESSURE WITH GLYCOSYLATED HAEMOGLOBIN LEVELS IN PATIENTS WITH DIABETES MELLITUS

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## ABSTRACT

**BACKGROUND**

To correlate intraocular pressure and central corneal thickness with glycosylated haemoglobin levels in patients with diabetes mellitus.

**METHOD**

In this retrospective study, patients meeting the inclusion criteria were evaluated during their visits to the outpatient department of R.L. Jalappa Hospital,Kolar. Detailed histories were collected, encompassing sociodemographic details, occupation, any prior history of ocular surgeries or trauma, history of glaucoma, long-term use of eye drops, or intake of other medications. A comprehensive ophthalmic examination was performed, including assessment of visual acuity, examination of the anterior segment via slit lamp biomicroscopy, and posterior segment evaluation using a 90D lens. Additionally, intraocular pressure was measured using Goldmannapplanation tonometry, blood HbA1c levels were determined, and corneal central thickness (CCT) was assessed using ultrasonographicpachymetry under topical anesthesia.

**RESULTS**

99 participants were included, out of which were 55 (55.55%) males and 44 (44.44%) females. Mean age of the patients was 62.74 $\pm$ 11.44 years. Out of 99 patients, 43 patients had IOP more than 14.50 mmHg and the average HbA1c levels calculated were 8.95 %. 56 patients had IOP less than 14.5mmHg and HbA1c levels were 7.74 %.There was significant positive correlation between HbA1c and CCT in both eyes of study subjects, with a significant p value of <0.001.

**CONCLUSION**

Our results suggest that there is a correlation between the measurement of IOP and CCT, and the levels of HbA1c in patients with diabetes mellitus. Hence, we can say that HbA1c levels can be a good predictor of raised intraocular pressure in diabetes mellitus and can help in early detection of diseases like glaucoma.

**KEYWORDS:** Central Corneal Thickness, Diabetes Mellitus, Glycated Haemoglobin, Intraocular Pressure.

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## INTRODUCTION

Diabetes mellitus (DM) is a metabolic disease associated with chronic hyperglycemia.[1]Globally, the prevalence of DM is estimated to be 9.3% (463 million people) in 2019, increasing to 10.2% (578 million)and 10.9% (700 million) by 2030 and 2045.[2,3]HbA1c testing is preferred for diagnosing and monitoring diabetes due to its stable pre-analytical nature and minimal day-to-day variability compared to fasting and postprandial plasma glucose measurements. It reflects average blood glucose levels over 8-12 weeks, making it the gold standard for assessing long-term diabetes control.[4,5]

Diabetes contributes to the risk of developing several types of glaucoma, most commonly, primary open-angle glaucoma (POAG) and neovascular glaucoma (NVG).[6]

Glaucoma is defined as a group of ocular disorders that are characterized by progressive optic neuropathy and associated visual field loss.[7]

It is the leading irreversible cause of global blindness,[8]requires early detection for better outcomes. Normal intraocular pressure (IOP) is 10-21 mm Hg, maintained by balanced aqueous humor dynamics, hence any imbalance can elevate IOP, inducing vascular and mechanical stresses, crucial in glaucoma progression as the sole modifiable risk factor.[9,10,11]Few studies in recent and past have found that patients with increased levels of HbA1c had substantially higher IOP levels compared to the patients with lower levels of HbA1c.[12]

Chronic hyperglycemia can disrupt corneal endothelial cells, impacting their ability to maintain stromal hydration through the endothelial pumping mechanism. This may lead to changes in central corneal thickness (CCT) corresponding to fluctuations in blood glucose levels.[13,14]

The most recognised corneal complication in DM (both type I and type II) is keratopathy resulting from impaired epithelial basement membrane (BM), epithelial wound healing, epithelial–stromal interactions, endothelial function, and corneal nerve functions.[15,16,17]

Therefore, we aimed to investigate the effect of chronic hyperglycemia as determined by HbA1c, on IOP and CCT in patients with diabetes and identify diabetic patients at risk of developing glaucoma and increase in CCT related to metabolic changes of the cornea.

## METHODS

A retrospective study was conducted, encompassing 99 individuals who attended the ophthalmology outpatient department (OPD) at R.L. Jalappa Hospital in Kolar. The participants were selected from the pool of patients seeking ophthalmic care at the hospital from January 2021 to January 2022.The study included 99 patients, aged 40-80 years diagnosed with diabetes mellitus. Approval from the Institutional Ethics Committee was obtained prior to the commencement of the study.



Patients underwent a comprehensive assessment, which included gathering detailed information such as sociodemographic profile, age, gender, occupation, history of previous ocular surgeries or trauma, presence of glaucoma, long-term use of eye drops, or consumption of other medications were meticulously documented. A thorough ophthalmic examination was conducted, comprising assessments of visual acuity using Snellen's chart for distant vision and Jaeger's chart for near vision, anterior segment using slit lamp biomicroscopy, posterior segment evaluation using a 90D lens and indirect ophthalmoscopy through the dilated pupil. Intraocular pressure measurements were obtained using Goldmann'sapplanation tonometer,and measurement of blood HbA1c levels. Corneal central thickness (CCT) was determined using ultrasonographicpachymetry under topical anesthesia.

Prior to the commencement of the study, all participating subjects provided written informed consent, confirming their voluntary involvement and comprehension of the research.

**Statistical Analysis**

The data underwent coding and was entered into an Excel spreadsheet.

Quantitative measures were summarized using mean and standard deviation (SD), while qualitative or categorical data were presented as frequencies and percentages.

Differences in proportions were assessed using the Chi Square test (or Fisher's Exact Test when appropriate). p-value of less than 0.05 was deemed statistically significant.

**RESULTS**

Out of 99participants (198 eyes), 55 (55.55%) were malesand 44 (44.44%) females with a mean age of 62.74+11.44(range 28 – 87) years.

| **Characteristics** | | **Mean** | **SD** | **Range** |
|---|---|---|---|---|
| **Age (**years) | | 62.74 | 11.44 | 28 - 87 |
| **IOP**(in mmHg) | Right Eye | 13.57 | 3.24 | 8 – 23 |
| | Left Eye | 14.13 | 3.64 | 8 – 25 |
| | Average | 14.25 | 3.07 | 8 - 21 |
| **HbA1c**(%) | | 8.27 | 2.19 | 4.80 – 15.20 |

***Table 1: Characteristics of patients among the study subjects***

For the study subjects, the mean IOP was slightly higher in the left eye (14.13 mmHg) compared to the right eye (13.57 mmHg), resulting in an overall average of 14.25 mmHg, on average, study subjects had an HbA1c level of 8.27%, with a moderate variability (SD of 2.19%). HbA1c levels ranged widely from 4.80% to 15.20%, reflecting diverse long-term blood sugar control among the subjects.

| **HbA1c (%)** | **IOP (Right Eye)** | | **IOP (Left Eye)** | | **IOP (Average)** | |
|---|---|---|---|---|---|---|
| | **Low IOP (<14.5)** | **High IOP (≥14.5)** | **Low IOP (<14.5)** | **High IOP (≥14.5)** | **Low IOP (<14.5)** | **High IOP (≥14.5)** |
| Mean | 7.89 | 8.86 | 7.71 | 9.03 | 7.75 | 8.95 |
| SD | 2.28 | 1.92 | 1.97 | 2.25 | 2.22 | 1.96 |
| P value | 0.000 | | 0.000 | | 0.005 | |

***Table 2: Comparison of measures of HbA1c with respect to severity of IOP***

The table 2 indicates a possible correlation where individuals with elevated intraocular pressure (≥14.5 mmHg) exhibit higher average HbA1c levels compared to those with lower intraocular pressure (<14.5 mmHg). This suggests a potential association between higher IOP and increased HbA1c levels.Mean HbA1c among subjects with low IOP was 7.75 ± 2.22 and among subjects with High IOP was 8.95 ± 1.96%.

| **HbA1c** | **IOP (Average)** |
|---|---|
| Pearson Correlation | 0.339** |
| Sig. (2-tailed) | 0.001 |
| N | 99 |

***Table 3: Correlation of Intra-Ocular Pressure (IOP) with HbA1c levels in the study subjects***

In the study there was significant positive correlation between HbA1c and IOP i.e. with increase in HbA1c there was increase in IOP and vice versa.

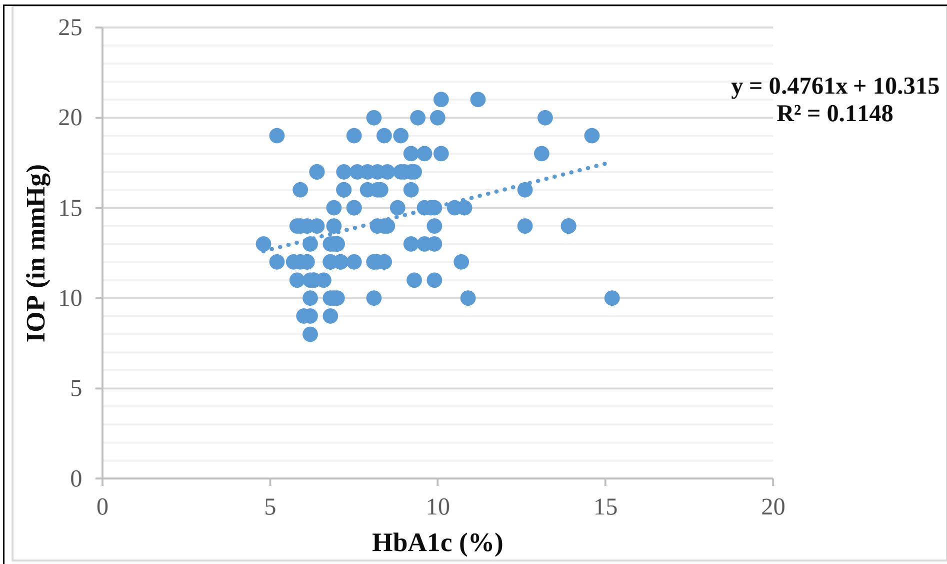


***Figure 1: Correlation of Intra-Ocular Pressure (IOP) with Glycosylated Hemoglobin (HbA1c) levels in the study subjects***

| Correlation | HbA1C (%) | CCT (RE) | CCT (LE) |
|---|---|---|---|
| Pearson | 1 | 0.501** | 0.470** |
| P value | | <0.001* | <0.001* |
| N | 99 | 99 | 99 |

***Table 4: Correlation of HbA1c with the CCT of right and left eye.***

In the study there was significant positive correlation between HbA1c and CCTin both eyes. i.e. with increase in HbA1c there was increase in CCT and vice versa.



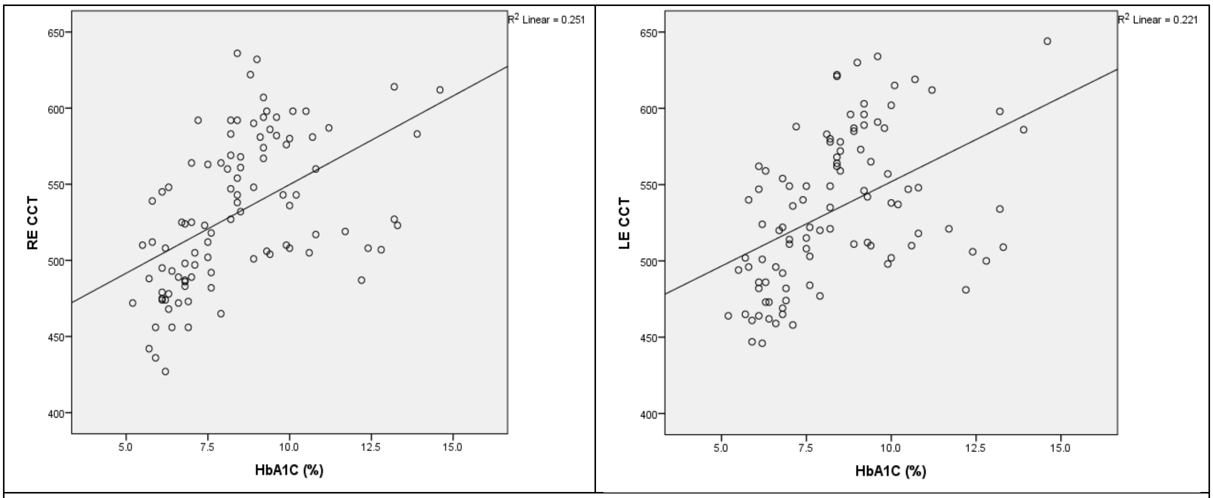


***Figure 2: Scatter plot showing Positive Correlation of Glycosylated Haemoglobin (HbA1c) levels with CCT of both eyes in the study subjects***

**DISCUSSION**

The present study aimed to investigate the relationship between intraocular pressure (IOP), central corneal thickness (CCT), and glycosylated haemoglobin (HbA1c) levels in patients with diabetes mellitus.

Out of 99 patients 55 (55.55%) were males and 44 (44.44%) were females. The mean age of the patients was 62.74 + 11.44. In BrahaAet al[18]study, most of the subjects were women 52.8% and the mean age was 63.5 years, with no differences between genders. While the mean age was slightly higher in patients with diabetes 66.9±7.8 yearsin Hanyuda A et al[19] study.

Out of 99 patients, 43 patients had IOP more than 14.50 mmHg and the average HbA1c levels calculated were 8.95% and 56 patients had IOP less than 14.5mmHg and HbA1c levels were 7.75 %.Our findings revealed several significant correlations, providing insight into the intricate relationship between glycemic regulation and ocular parameters in individuals with diabetes mellitus similar to Pimentel LG et al[20] study who concluded that there is a significant association between glucose levels variation and IOP change.

The results from Table 1 providescharacteristics of patients like age, IOP, HbA1C among the study subjects. The average age of the participants is approximately 63 years, with a notable variability of about ±11 years around this average. The age range spans from 28 years to 87 years, indicating a diverse age distribution within the study sample.

Right Eye IOP: The mean IOP for the right eye is 13.57 mmHg, with a variability of ±3.24 mmHg. The range of IOP in the right eye spans from 8 mmHg to 23 mmHg. Left Eye IOP: The mean IOP for the left eye is slightly higher at 14.13 mmHg, with a larger standard deviation of 3.64 mmHg. The range of IOP in the left eye is slightly broader, ranging from 8 mmHg to 25 mmHg. Average IOP: The average IOP, calculated by averaging the IOP values from both eyes, is 14.25 mmHg, with a standard deviation of 3.07 mmHgand the range of average IOP spans from 8 mmHg to 21 mmHg.The average IOP falls within the normal range (typically 10-21 mmHg), indicating that, on average, the study participants have normal intraocular pressure.Moving on to HbA1c levels among the study subjects,mean HbA1c level is 8.27%, with a standard deviation of 2.19%and the range of HbA1c levels spans from 4.80% to 15.20%.

The Table 2, presents the mean HbA1c levels for each category of IOP severity. For the right eye, the mean HbA1c level is 7.89% in the low IOP group and 8.86% in the high IOP group. Similarly, for the left eye, the mean HbA1c level is 7.71% in the low IOP group and 9.03% in the high IOP group. The mean HbA1c level for the average IOP is 7.75% in the low IOP group and 8.95% in the high IOP group.There was significant difference in Mean HbA1c levels between Low and High IOP groups.

Therefore, our resultsdemonstrated a significant positive correlation between HbA1c levels and IOP. Specifically, we observed that as HbA1c levels increased, there was a corresponding elevation in IOP, and vice versa. This finding suggests that glycemic control, as reflected by HbA1c levels, may influence intraocular pressure dynamics in diabetic patients similar to a study by Hymowitz MB etal.[21]



Furthermore, the statistically significant difference in mean HbA1c levels between the low and high IOP groups (p-value = 0.005) underscores the strength of this association.

LuoXY, Tan NYQetal.[22] concluded that high IOP observed in diabetes is mainly due to the direct association of diabetes and IOP, and this finding may have pathophysiologic significance with respect to the risk of glaucoma among persons with diabetes.

Table 3 represents that, the correlation coefficient of 0.339 indicates a moderate positive correlation between HbA1c levels and IOP. Which means, as HbA1c levels increase, there tends to be an increase in IOP on average and vice versa as shown in Figure 1. The positive sign (+) indicates that higher HbA1c levels are associated with higher IOP, and lower HbA1c levels are associated with lower IOP. The p-value of 0.001, indicates that the observed correlation is statistically significant similar to theAgrawal AStudy[23] which reported a positive correlation between blood glucose levels and IOP.

Elevated IOP is a known risk factor for various ocular conditions, including glaucoma, which underscores the clinical importance of our findings. Monitoring HbA1c levels may serve as a valuable tool for assessing the risk of elevated IOP in diabetic individuals, potentially enabling early detection and intervention to prevent sight-threatening complications.

Proceeding to the results presented in Tables5, we observed a significant positive correlation between glycosylated hemoglobin (HbA1c) levels and central corneal thickness (CCT) in both the right and left eyes of study participants. The Pearson correlation coefficients for the right eye (RE) and left eye (LE) are 0.501 and 0.470, respectively, with corresponding p-values of less than 0.001. The scatter plots provided in Figure 2 visually depicts this positive correlation between HbA1c levels and CCT in the study subjects. Each data point represents an individual participant, with the x-axis representing HbA1c levels and the y-axis representing CCT. The upward trend observed in the scatter plots further supports the notion of a positive association between HbA1c levels and CCT similar to OzdamarY et al[24]study, in which the central cornea of diabetic patients was found to be thicker when compared with nondiabetic patients. Thicker central cornea associated with diabetes mellitus should be taken into consideration while obtaining accurate intraocular pressure measurements in diabetics.

Also, Luo, Xiao-Yang et al[25] has concluded that diabetes and hyperglycemia were associated with greater CCT. WhereasCanan H etal[26] findings suggestedthat neither the duration of diabetes mellitus (DM) nor the presence of diabetic retinopathy significantly affects CCT.

This finding is particularly noteworthy as it suggests a potential link between glycemic control and corneal biomechanics in diabetic patients. Thicker corneas have been associated with inaccuracies in IOP measurements, which could have implications for the diagnosis and management of ocular conditions such as glaucoma. Thus, our findings underscore the importance of considering CCT variations in diabetic patients when interpreting IOPmeasuremnts and assessing their ocular health status.

The observed correlations between HbA1c levels, IOP, and CCT in our study highlight the multifactorial nature of ocular complications in diabetes mellitus. Chronic hyperglycemia can lead to structural and functional alterations in ocular tissues, including changes in corneal biomechanics, aqueous humor dynamics, and vascular perfusion. Inflammation, oxidative stress, and microvascular dysfunction may contribute to these alterations, ultimately influencing intraocular pressure regulation and corneal thickness.

Our findings contribute to the existing body of knowledge on the relationship between glycemic control and ocular parameters in diabetic individuals.

However, several limitations should be considered when interpreting the results of this study. The retrospective design limited our ability to establish causal relationships between HbA1c levels, IOP, and CCT. Additionally, factors such as medication use, duration of diabetes, and presence of diabetic retinopathy,fluctuation of glycemic levels that may affect the IOP levels of the patients were not accounted for in our analysis, which may have confounded the results.Patients with type I Diabetes were not included in the study.

Future research should focus on prospective studies to further elucidate the underlying mechanisms linking glycemic control to ocular parameters in diabetic patients. Longitudinal studies are needed to assess the impact of glycemic control interventions on intraocular pressure regulation and corneal biomechanics over time. Furthermore, investigating the role of additional factors, such as medication adherence, lifestyle factors, and genetic predisposition, may provide valuable insights into the pathophysiology of diabetic ocular complications.

## CONCLUSION

Our study provides evidence of significant correlations between HbA1c levels, intraocular pressure, and central corneal thickness in patients with diabetes mellitus. These findings underscore the importance of glycemic control in the management of ocular health in diabetic individuals and highlight the need for comprehensive eye care strategies tailored to the unique needs of this population.

Hence, we can say that HbA1c levels can be a good predictor of raised intraocular pressure in diabetes mellitus and can help in early detection of diseases like glaucoma.

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