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Original Research Article

A Comparative Study Correlating Blood Glucose Levels and Intra Ocular Pressure in Diabetic and Non-Diabetic Patients

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ABSTRACT

Background
Diabetes has been proposed as a potential risk factor for glaucoma, namely POAG (Primary Open Angle Glaucoma), due to its correlation with high IOP (Intra-Ocular Pressure). The current study aimed to look into how hyperglycaemia affected intraocular pressure.

Methods
This was a prospective study carried out among 100 patients (50 cases i.e., known type 2 diabetic patients and 50 controls) belonging to the age group of 40-70 years. Review of medical history, best-corrected visual acuity, slit-lamp biomicroscopy, IOP measurement, gonioscopy, dilated funduscopic examination, and refraction were all part of the comprehensive ophthalmological examination that was performed on each participant. A self-reported physician diagnosis was used to define diabetes.

Results
The individuals ranged in age from 40 to 80 years, with the mean age for cases being 55.96±6.92 and the mean age for controls being 57.32±8.30. When comparing group 1 (mean IOP = 19.28±2.38) to group 2 (mean IOP = 13.76±1.74), a substantial rise in IOP was noted, with a p-value of 0.001. There was no discernible change in IOP in patients with HbA1C levels below 6.5%. Patients with HbA1C levels over 6.5% had noticeably higher intraocular pressure. The p-value was found to be less than 0.001.The mean FBS and PPBS levels in the diabetic group were found to be 99.44±13.89 and 141.06±22.17, respectively, and the mean IOP of the diabetic group is 19.28±2.38. Whereas in the control group, the mean FBS and PPBS are 84.58±6.76 and 120.76±9.14 respectively, and the mean IOP was 13.76±1.74 which shows that IOP increases with an increase in FBS and PPBS levels.

Conclusion
Compared to the controls, participants with diabetes had higher intraocular pressure, and those with poor glycaemic control were particularly at risk for developing elevated intraocular pressure. To identify the onset of ocular hypertension early on, diabetes patients should have their IOP measured regularly at regular intervals. Higher intraocular pressure

was seen in those with higher HbA1C values, indicating that better blood sugar regulation may contribute to better intraocular pressure regulation.
Keywords: Glaucoma, Glycemic Control, Intra-Ocular Pressure.

INTRODUCTION

Diabetes has spread like wildfire over the world. In 2017, 451 million individuals between the ages of 18 and 99 have diabetes; by 2045, that number is predicted to rise to 693 million.[1] Although individuals with diabetes are twice as likely to acquire glaucoma as those without the disease, it is still unclear whether diabetic populations have different distributions or risk factors for IOP. Additionally, the relationship between diabetes and glaucoma has remained disputed.[2] To better understand the connection between glaucoma and diabetes and develop efficient preventative measures, information on the distribution of IOP and risk factors in diabetic populations is also required. Particularly in both industrialised and developing nations, diabetes mellitus has become a leading cause of vision loss and visual impairment. Diabetes has been proposed as a potential risk factor for glaucoma, namely POAG (Primary Open Angle Glaucoma), due to its correlation with high IOP (Intra-Ocular Pressure). The current study aimed to look into how hyperglycemia affected intraocular pressure.

MATERIALS & METHODS

This was a prospective study carried out among 100 patients (50 cases i.e., known type 2 diabetic patients and 50 controls) belonging to the age group of 40-70 years. The study excluded participants with glaucoma, ocular hypertension, corneal opacities or irregularities, refractive error greater than ±5 spherical or cylindrical greater than ±3 d, ocular infections or inflammations, those who had used eye medications within the previous three months, those who had undergone previous eye surgeries, and those with any other significant medical conditions. Review of medical history, best-corrected visual acuity, slit-lamp biomicroscopy, IOP measurement, gonioscopy, dilated funduscopic examination, and refraction were all part of the comprehensive ophthalmological examination that was performed on each participant.

All individuals with diabetes were receiving medical therapy and the disease was defined based on self-reported physician diagnoses. The assessment of haemoglobin, fasting and postprandial plasma glucose levels, and glycated haemoglobin (HbA1C) values were among the screening laboratory tests.

RESULTS

In the present study, the age range of the subjects was 40-80 years, with the mean age being 55.96±6.92 for cases and 57.32±8.30 for controls, with the p-value being 0.376; both groups were comparable.

Age (in years)	Cases		Controls	
	No	%	No	%
41-50	14	28.0	12	24.0
51-60	22	44.0	19	38.0
61-70	12	24.0	16	32.0

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71-80	2	4.0	3	6.0
Total	50	100.0	50	100.0
Mean ± SD	55.96±6.92		57.32±8.30	
Table 1: Age Distribution of Patients Studied				
Samples are age matched with P=0.376				

While there was an equal distribution between genders among controls, 40% were females and 60% were males among cases. The difference was not statistically significant (p = 0.315). A higher percentage of cases had higher ranges of FBS, PPBS, and HbA1c% (p <0.001, <0.001 and 0.003 respectively) compared to controls.

Variables	**Cases (N = 50)**		**Controls (N = 50)**		**P-Value**
	No	**%**	**No**	**%**	
FBS (mg/dl)					
• <100	32	64.0	50	100.0	<0.001**
• 100-140	17	34.0	0	0.0	
• >140	1	2.0	0	0.0	
PPBS (mg/dl)					
• <140	29	58.0	50	100.0	<0.001**
• 140-200	19	38.0	0	0.0	
• >200	2	4.0	0	0.0	
HbA1c %					
• ≤6.5	42	84.0	50	100.0	0.003**
• 6.5-8.0	8	16.0	0	0.0	
• >8.0	0	0.0	0	0.0	
Table 2: Distribution of Glucose Parameters in Case-Controls Studied					
Chi-Square test/Fisher Exact test					

Comparing group 1 (mean IOP = 19.28+2.38) to group 2 (mean IOP = 13.76+1.74) revealed a substantial rise in IOP, with a p-value of 0.001. (Table 3)

IOP (mm Hg)	**Cases**		**Controls**	
	No	**%**	**No**	**%**
1-10	0	0.0	0	0.0
11-20	39	78.0	50	100.0
>20	11	22.0	0	0.0
Total	50	100.0	50	100.0
Mean ± SD	19.28±2.38		13.76±1.74	
Table 3: IOP (mm Hg) Distribution Among Case and Controls				
P<0.001**, Significant, student t test				

There was no discernible variation in IOP among patients with HbA1C levels below 6.5% when the IOP was correlated with glycaemic status and compared across groups. IOP significantly increased in those with HbA1C levels greater than 6.5%. It was discovered that the p-value was less than 0.001. A statistically significant correlation between elevated

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HbA1C and intraocular pressure in individuals with diabetes was revealed by the correlative analysis.

IOP	HbA1c %			Total
	≤6.5	6.5-8	>8	
1-10	0 (0%)	0 (0%)	0 (0%)	0 (0%)
11-20	39 (92.9%)	0 (0%)	0 (0%)	39 (78%)
>20	3 (7.1%)	8 (100%)	0 (0%)	11 (22%)
Total	42 (100%)	8 (100%)	0 (0%)	50 (100%)

Table 4: IOP (mm Hg) Distribution According to the Levels of HbA1c %

P<0.001**, Significant, Fisher Exact test

There was a significant association between the fasting and post-prandial blood sugar levels and IOP in the diabetic group. The mean FBS and PPBS levels in the diabetic group were found to be 99.44±13.89 and 141.06±22.17 respectively, and the mean IOP of the diabetic group was 19.28±2.38. Whereas in the control group, the mean FBS and PPBS were 84.58±6.76 and 120.76±9.14 respectively, and the mean IOP was 13.76±1.74 which shows that IOP increases with an increase in FBS and PPBS levels.

Variables	HbA1c %			Total	P-Value
	≤6.5	6.5-8	>8		
Age (in years)	55.83±7.32	56.63±4.60	0.00±0.00	55.96±6.92	0.770
Duration (years)	2.86±1.07	2.75±0.89	0.00±0.00	2.84±1.04	0.792
FBS (mg/dl)	94.79±7.88	123.88±13.23	0.00±0.00	99.44±13.89	<0.001**
PPBS (mg/dl)	133.67±10.14	179.88±28.10	0.00±0.00	141.06±22.17	<0.001**
HbA1c %	6.02±0.21	6.88±0.14	0.00±0.00	6.15±0.38	<0.001**
IOP	18.57±1.84	23.00±1.07	0.00±0.00	19.28±2.38	<0.001**

Table 5: Comparison of Clinical Variables According to the Levels of HbA1c %

ANOVA test

DISCUSSION

The second most common cause of blindness, glaucoma, is associated with diabetes. The relationship between diabetes and IOP has been underscored in previous publications. Their results reveal a positive association between diabetes and IOP.[3-5]

The average age of the diabetes patients in this study was 57.30±8.30. The normal control group, which was matched for age and sex, had a mean IOP of 13.76±1.74 mm Hg, but the participants with diabetes, who had no prior history of ocular hypertension, had a substantially higher mean IOP of 19.28±2.38 mm Hg. These results are in line with what other researchers have found. The mean (±standard deviation) age of the group of diabetic patients in a related study by Pallavi et al.,[6] was 55.06±9.70 years (range: 40 to 75 years). Of the 70 patients with diabetes, 16 were female (age 54.38±10.26 years) and 54 were male (age 55.26±9.62 years). The non-diabetic patients were 53.52±8.81 years old on average. Of the 50 patients without diabetes, 15 were female (age 53.60±9.11 years) and 35 were male (age 53.49±8.81 years).

Similar to the Beijing Eye investigation, there was no correlation between age and IOP in the Pallavi et al..[6] investigation.[7] Age and IOP were found to positively correlate in research by Hashemi H et al.,[8] David et al.,[9] and Bonomi L. et al.[10] The Tajimi study[11]

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among the Japanese population contradicted these findings by demonstrating a substantial negative connection between age and IOP.

IOP and gender did not correlate in our study for either the diabetic or non-diabetic groups. This investigation was comparable to Quigley HA's.[12] According to our research, people with diabetes had a statistically significant greater mean intraocular pressure than patients without the disease. The relationships between diabetes, blood glucose, and lOP were the same for men and women in the Rotterdam study.[5] Other studies also identified these correlations. Women had a slightly greater lOP than males in two studies[13,14] of diabetics. The differences in correlations between men and women were not investigated in several research.[15]

Patients with diabetes had an average intraocular pressure of 13.53±1.90 mm Hg, while those without diabetes had an average of 11.92±1.17 mm Hg, with a statistical significance of $p<0.000$, the IOP of the diabetic group was higher than that of the non-diabetic group. In both groups, there was no difference in the mean IOP between males and females. Groups with diabetes ($p = 0.6$) and those without ($p = 0.94$).

By examining the connection between diabetes and open-angle glaucoma, the authors of the Blue Mountain Eye study discovered that patients with diabetes had a higher prevalence of glaucoma than patients without the disease (5.5% versus 2.8%, OR = 2.12).[16] There is not much information in the literature about the relationship between blood glucose levels and intraocular pressure. IOP readings were observed to be decreased during acute hypoglycemia by Larsen and colleagues.[17] Furthermore, while evaluating IOP in individuals with blood glucose levels below and above 200 mg/dL, Traisman et al.,[18] and associates found that patients with blood glucose levels above 200 mg/dL had higher IOP values (mean difference of 1.3 mmHg). Regretfully, none of these investigations attempted to ascertain if the degree of variation in glucose levels and changes in IOP in patients with and without diabetes were related.

According to the Beaver Dam Eye study, diabetes mellitus was identified by either a history of diabetes treatment or a casual blood sugar level of more than 11.1 mmol/l and a glycosylated haemoglobin level more than two standard deviations above the mean.[19] With an odds ratio of 1.84 (95% CI 1.09-3.11), the investigators discovered a correlation between diabetes mellitus and primary open-angle glaucoma.

According to a study by Tan GS et al.,[20] after controlling for age, sex, education, smoking, central corneal thickness, and diabetes treatment, intraocular pressure was higher in persons with diabetes than those without (16.7 vs. 15.0 mm Hg, $P <.001$) and in those with higher serum glucose levels ($P <.001$) and glycosylated hemoglobin concentrations ($P <.001$), which was similar to our observations.

In contrast to individuals without diabetes (2.8%; age-gender adjusted odds ratio [OR] 2.12, 95% confidence intervals [CI] 1.18-3.79), Mitchell P.[16] found that the prevalence of glaucoma was higher among those with diabetes, as determined by history or elevated fasting plasma glucose levels (5.5%). Additionally, ocular hypertension was more prevalent in diabetics (6.7%) than in non-diabetics (3.5%; OR 1.86, CI 1.09-3.20). 13.0% of glaucoma patients had diabetes, compared to 6.9% of non-glaucoma patients. Those with a prior diagnosis of glaucoma experienced the largest increase (16.7%; OR 2.82, CI 1.35-5.87).

Diabetes was linked to higher intraocular pressure, according to Tielsch JM et al.'s study, "Diabetes, intraocular pressure and primary open-angle glaucoma in the Baltimore Eye Survey."[21] However, the differences between subjects without diabetes, those with diabetes who were not taking insulin, and those with diabetes who were taking insulin were not significant (means, 17.4, 18.0, and 17.8 mmHg, respectively). Individuals with a prior

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diagnosis of POAG had a favourable correlation with diabetes (odds ratio, 1.7, 95% CI, 1.03, 2.86), suggesting that selection bias may account for the favourable findings of earlier clinic-based studies.

Anandha Lakshmi S et al,[22] carried out a study to examine the effects of chronic hyperglycemia on IOP and to assess the association between IOP and type 2 diabetes mellitus. The participants with diabetes were separated into three categories based on their glycosylated haemoglobin (HbA1c) levels: group IIa had HbA1c levels less than 7% (n = 62); group IIb had HbA1c levels between 7 and 8.0% (n = 48); and group IIc had HbA1c levels greater than 8.0% (n = 40). They found that the participants with diabetes had higher IOP values (mean = 20.4±3.44) than the age and sex-matched control groups, which is consistent with our findings. Groups IIa, IIb, and IIc had mean intraocular pressures of 17.32±2.70, 17.81±2.76 mm Hg, and 18.04±2.58 mm Hg, respectively. It was determined that the IOP difference between groups IIb and IIc was statistically significant (P =.001). Subjects with diabetes had higher intraocular pressure than the controls, and those with poor glycaemic control were particularly at risk for developing elevated intraocular pressure.

Our study's findings also supported the theory that individuals with diabetes who have chronic hyperglycemia, as seen by raised HbA1c levels, had much higher IOPs than those who have just received a diabetes diagnosis, which is indicated by substantially lower HbA1C levels. Numerous research have clearly shown the connection between high intraocular pressure, diabetes, glycated haemoglobin (HbA1c), and insulin resistance. A number of explanations have been proposed for the association between disturbances of carbohydrate metabolism and POAG. The elevated blood glucose level in diabetes may induce an osmotic gradient and attract fluid into the intraocular space, resulting in elevated IOP. In contrast to those without diabetes, patients with diabetes had much higher glucose levels in their aqueous humour (3.2 mM vs. 7.8 mM), according to Davies et al.[23] Diabetes patients' elevated aqueous humour glucose levels may cause an overabundance of fibronectin to be synthesised, which would then cause an excessive buildup of the protein in the trabecular meshwork and hasten the trabecular meshwork cells' depletion. A common biochemical link that may both contribute to the development of thicker vascular basement membranes in diabetic microangiopathy and change the structural content, impair resilience, decrease cellularity, block aqueous outflow in the trabecular meshwork, and cause POAG in diabetics is high glucose-induced fibronectin upregulation. Diabetes has been linked to microvascular damage and may have an impact on the retina's and the optic nerve's vascular autoregulation. High intraocular pressure is more likely to be linked to the development of glaucomatous optic nerve injury based on the visual field loss and/or the optic disc abnormalities. Glaucomatous optic neuropathy is believed to be caused by a fundamental neurodegenerative component, a disrupted microcirculation at the level of the optic nerve head, and an elevated IOP. Diabetes mellitus not only changes the vascular tissues but also compromises the retina's glial and neuronal functioning as well as metabolism, which might increase the vulnerability of retinal neurones, including retinal ganglion cells, to glaucomatous damage. RGCs and other retinal neurones may undergo apoptosis as a result, adding to the stress in POAG cases. A 1.0 mm Hg change in IOP may be clinically significant in our patient cohort given the worsening of neuronal cell death in diabetes. It makes sense to assume that a prolonged retinal injury in individuals with diabetes mellitus who have poor glycaemic control would be linked to an increased risk of POAG.

According to an epidemiological study by Clark C. V., genetic factors may play a part in ocular hypertension.[24] According to a study by Mapstone et al.,[25] autonomic system dysfunction could be a contributing factor to elevated intraocular pressure. According to a

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study by Mitchell P. et al.,[16] an osmotic gradient fluid shift into the intraocular space brought on by an elevated blood glucose level will raise intraocular pressure.

Diabetic patients are frequently seen by ophthalmologists in their regular practice. Many of these diabetic patients are suspected of having glaucoma or already have glaucoma (or ocular pressure). Glycaemic management is rarely considered, despite the fact that every 1 mmHg change in IOP receives the majority of attention. Glycaemic level variation may impact IOP change, making it relevant for diagnosis and treatment management, particularly in diabetic patients whose average IOP variation (between baseline and postprandial measurements) was roughly 15% (for an average glycaemic variation of 40%), according to the findings of the Luis Guilherme et al. study.[26]

CONCLUSION

Compared to the controls, participants with diabetes had higher intraocular pressure, and those with poor glycaemic control were particularly at risk for developing elevated intraocular pressure. Since glaucoma is more common in people with diabetes, it is best to measure IOP frequently at regular intervals in diabetic patients in order to identify the onset of ocular hypertension early on. Additionally, in the current study, intraocular pressure was higher in those with higher HbA1C values. This implies that better intraocular pressure control may be facilitated by better blood sugar regulation.

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