

Original Research Article

A study of relation between primary open angle glaucoma and type II diabetes mellitus

Aditya Desai^{1*}, Dipak Patel¹, Avani Sapovadia¹, Parin Mehta¹, Jyotindra Brahmhatt²

¹Department of Ophthalmology, Smt B. K. Shah Medical Institute and Research Centre, Piparia, Waghodia, Vadodara, Gujarat, India

²Department of Ophthalmology, GAIMS, Bhuj, Gujarat, India

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*Correspondence:

Dr. Aditya Desai,

E-mail: dr.aditya.desai@gmail.com

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ABSTRACT

Background: Primary open angle glaucoma has been characterized by its adult onset, IOP >21mmHg at some point in the course of the disease, open angles on gonioscopy, glaucomatous visual field changes and glaucomatous optic nerve damage. POAG is a multi-factorial disease such as age, black race, positive family history, high myopia etc. Diabetes mellitus has also been considered as one of the risk factors, but no major study has been conducted to provide tangible proof.

Methods: This cross sectional, case control study was conducted to determine whether diabetes stands as a risk factor in development of glaucoma. The selected patients were divided into 3 groups based on inclusion and exclusion criteria. They were subjected to complete ocular examination including gonioscopy and perimetry.

Results: The 16 patients from 50 of the diabetic group (28%) were found to have POAG. The p value was <0.005 which was statistically significant. Also, no correlation was found between blood sugar and IOP levels in these patients.

Conclusions: These data show a significant correlation between diabetes and glaucoma. Further studies are warranted to determine its actual role in pathogenesis of glaucoma.

Keywords: Diabetes, POAG, Risk factors

INTRODUCTION

Glaucoma is a potentially blinding disease that affects approximately 67 million people worldwide with 6.7 million people being estimated to be blind due to the disease.

The term glaucoma does not imply a disease-entity but is a compilation of pathological conditions in which clinical manifestations commonly are, to a greater or less extent, dominated by the level of intra-ocular pressure and its consequences.¹ The degree of raised pressure which assumes pathological significances is impossible to define since it varies within wide limits from one eye to

another; it may be taken as that pressure which the tissues in question are unable to withstand without damage to their structure or impairment of their function.

Primary open angle glaucoma (POAG) is explicitly characterized as a multi-factorial optic neuropathy with a characteristic acquired atrophy of the optic nerve and loss of retinal ganglion cells and their axons with characteristic visual field abnormalities in the presence of open anterior chamber angles.²

An estimated 8 million Indians have glaucoma with a 1:1 ratio of primary open angle glaucoma (POAG) to primary angle closure glaucoma (PACG).^{1,2} POAG is often

diagnosed on routine ocular examination and very often only in the late stages of the disease. It manifests mainly as visual field loss with central vision being preserved almost till the end stages. By the time the patient is symptomatic and the disease is diagnosed, significant loss of visual field has usually occurred and the visual loss is irreversible.³ Therefore, early diagnosis is essential, so that treatment to halt the progression of the disease can be instituted.

Multiple risk factors have been impacted with the occurrence of glaucoma. It includes increasing age, gender, race, diabetes mellitus, systemic hypertension, diastolic perfusion pressure, myopia and family history.⁴⁻⁷ In 1971, Backer stated "Diabetes mellitus occurs more often in patients with primary open-angle glaucoma than in the non-glaucomatous population. Similarly, Glaucoma is more prevalent in diabetic than in non-diabetic population". The prevalence of chronic open angle glaucoma (COAG) appears to be higher in the diabetic population. IOP is an important confounder of the association between diabetes and glaucoma because persons with diabetes appear to have a slightly higher IOP and have been reported to have a higher prevalence of ocular hypertension and incidence of IOP elevation.

It is tempting to accept diabetes as a definite risk factor for chronic open angle glaucoma, since diabetes is a disease of microangiopathy, and compromise of microcirculation of the optic disc is a possible contributing mechanism in the pathogenesis of glaucoma. Many studies have been done in all over the world to find a relation between various types of diabetes and primary open-angle glaucoma. However, enough data are not available to find significant relationships between two diseases in developing countries. This study aims to find a relation between diabetes and POAG in Indian population.

METHODS

It was a tertiary hospital-based prospective cross-sectional study. The study was conducted following an ethical approval by the Institutional Review Committee. Written informed consent was obtained from all the participants before enrollment.

The patients were divided into 3 groups, where, Group 1 includes patients diagnosed as POAG with IOP >20mmHg, glaucomatous optic disc and visual field changes. Group 2 includes patients diagnosed as type II DM on the basis of RBS >12mg/dl and Group 3 includes age-matched apparently healthy individuals.

Relevant preliminary details of the patients were taken in the Performa. Detailed clinical history along with thorough ophthalmic examinations was done during OPD visit. Patients were subjected to visual acuity, torchlight examination, gonioscopy, applanation tonometry, perimetry, slit lamp examination and direct and indirect ophthalmoscopic fundus examination with photograph followed by proper management. Goldmann applanation tonometer was used to obtain three readings of IOP from each eye before dilation and mean taken for the analysis. Automated perimetry was performed with near refractive correction (Humphrey Visual Field Analyzer). Statistical analysis was performed using the SPSS, version 11.5. Mean, standard deviation, odds ratio, relative risk and 95% CI were calculated. Proportions were compared using the Chi-square test. A 'p' value of less than 0.05 was considered significant.

Patients of exclusion

Patient aged <40years and >80 years in all groups.

- For Group I: patients having a corneal ulcer, dystrophy, ectasia, active infections, ocular tumors, congenital anomalies, uveitis, trauma, pigment dispersion syndrome, exfoliation syndrome, rubeosis on slit lamp biomicroscopy, the gonioscopic finding of occludable angle in either eye and visual field defect not compatible with POAG.
- For Group II: Type I DM (IDDM) and pseudophakic patients.
- For Group III: pseudophakic patients.

RESULTS

This study was conducted in 150 patients where complete ophthalmological workup was done and both eyes were examined. Each group comprised of 50 patients each.

Table 1: Mean values of data collected for all 3 groups.

Mean	Diabetes	No diabetes	P value
AGE	60.04±10.12yrs	59.6±8.11yrs	0.585
IOP	14.67±3.10mmHg	17.25±4.47mmHg	<0.001
CCT	538.83±22.73 μ	531.26±20.96 μ	0.126

Mean age of patients in POAG group was 59.6±8.11 years with 82% males and 18% females (Table 1). For a diabetic group, the majority patients were above 50 years of age with no statistical difference in males and females.

While age-matched control group was selected. Total 16 out of 50 patients were diagnosed with POAG in the diabetic group, with 12 males (75.00%) and 4 females (25.00%) (Table 3) which were statistically significant.

Maximum numbers of patients were between 51-60 years of age; however, the age distribution was not statistically significant.

Table 2: Gender distribution of patients among study groups.

Group	Male	Female	Total
POAG	41 (82%)	9 (18%)	50
Diabetic	31 (62%)	19 (38%)	50
Control	34 (68%)	16 (32%)	50
Total	106	44	150

Table 3: age distribution of patients with POAG among diabetic groups.

Age (yrs.)	Male	Female	Total
41-50	1	1	2 (14.28%)
51-60	5	-	5 (35.71%)
61-70	3	3	6 (37.50%)
71-80	3	-	3 (18.75%)
Total	12 (75.00%)	4 (25.00%)	16

Prevalence of POAG in diabetic group was 28% while in control group was 6% with a p-value of <0.05 which is statistically significant (Table 4).

Table 4: prevalence of POAG among diabetics.

	POAG present	POAG absent	Total
Diabetes present	16 (10.67%)	38 (25.33%)	54 (36%) (P<0.00063)
Diabetes absent	51 (34%)	45 (30%)	96 (64%)
Total	67 (44.67%)	83 (55.33%)	100

The study also found that as the duration of diabetes increases, there is also an increase in the risk of prevalence of glaucoma (Table 5).

Table 5: Relationship between duration of diabetes and prevalence of POAG.

Duration of DM (years)	Glaucoma		Total
	Present	Absent	
0-3	3 (13.04%)	20 (86.96%)	23
3-6	3 (27.27%)	8 (72.73)	11
6-9	5 (45.45%)	6 (54.55%)	11
>9	5 (55.56%)	4 (44.44%)	9
Total	16	38	54

The comparison of IOP in all 3 study groups shows that mean IOP was high as expected in POAG group than the other groups (Table 6).

The difference observed in mean IOP values among POAG and control group was statistically significant (p<0.05) while the difference in mean IOP for diabetic and control group was not significant.

Table 6: Relationship between age and IOP values.

Age (years)	IOP (mmHg)		
	POAG	Diabetes	Control
41-50	25.95	17.15	16.50
51-60	25.94	19.31	15.87
61-70	25.68	19.50	16.11
71-80	24.90	20.87	14.63

Diabetic retinopathy failed to confirm correlation with glaucoma (p=0.625, RR: 0.84, 95% CI 0.42-1.69). The mean duration of glaucoma in the subjects was 4.13 years (SD±3.59), the median of three years. We found a statistically significant association between duration of T2DM and glaucoma.

Blood sugar levels comparison among the three groups showed a significant difference between control and diabetic group (p<0.05) while that between POAG and control group was not significant (Table 7).

Table 7: Relationship between age and RBS among study groups.

Age	POAG	Diabetes	Control
	RBS		
41-50	88.7	143	85.92
51-60	95.44	188.75	85.69
61-70	96	153.65	86.78
71-80	86	153	92.25

This shows that there is no significant correlation between IOP and blood sugar levels, which may be due to the fact that the patients were on treatment for both diabetes and glaucoma.

DISCUSSION

The world health organization has estimated 8.9 million blind people in India out of which 12.8% are due to glaucoma.⁸ Despite its public health significance, the data on prevalence and possible risk factors for glaucoma in India is limited.⁹ Early diagnosis is essential so that treatment to halt its progression can be instituted. Multiple risk factors have been proven to be significant in cases of POAG.¹⁰ However, there is much-needed statistics for the association of diabetes mellitus and POAG.

Mean age of patients with POAG in this study was found to be 59.6±9.47 years which was similar to other population-based studies conducted in India.

Age appears to be an independent risk factor for the development of POAG as demonstrated by the blue mountains eye study where the mean age was 66.2±9.8 for study sample and that of POAG was 75.9±8.6.¹¹ In our study, the mean age was lower for POAG patients being 59.6±9.47.

The probable relation with diabetes and POAG has been controversial. Becker in 1971 has stated that diabetes mellitus occurs more in patients with POAG than in the non glaucomatous population. Similarly, POAG is more common in diabetics than in nondiabetics.¹² The prevalence of POAG in diabetics was found to be 28% in this study which was found to be statistically significant.

POAG was found to be more in males compared to females in our study. This finding was similar to that found by Aravind Comprehensive Eye Survey and by Leske et al.¹³

There seems to be a direct relationship between DM and POAG. Several hypotheses on biological links between DM and POAG have been proposed. First, there is a growing body of evidence that the presence of long-standing hyperglycemia, along with lipid anomalies, may increase the risk of neuronal injury from stress.¹⁴ In particular, laboratory data have provided robust evidence for such an association.^{15,16} Second, studies showed that diabetic eyes have a reduced capacity to auto-regulate blood flow and that they exhibit decreased retinal blood flow.¹⁷ As a result, they show relative hypoxia and over expression of hypoxia-inducible factor-1 (HIF-1 α).^{18,19} Importantly, levels of HIF-1 α increased in ganglion cells, in the retina, and in the optic nerve head of human glaucomatous eyes in response to elevated IOP.²⁰

These might be another important association between DM and POAG. Third, the observed association between DM and POAG may be explained by the remodeling of the connective tissue of the optic nerve head. The remodeling might reduce compliance at the trabecular meshwork and the lamina cribrosa, resulting in increased IOP and greater mechanical stress on the optic nerve head, respectively.^{21,22} Research has demonstrated that diabetes can exacerbate connective tissue remodeling and amplify these biomechanical changes.²³ More importantly, the Barbados Eye Study had found that diabetes was a risk factor for increased IOP in follow-up.²⁴

The Baltimore eye survey found little or no association between glaucoma and either insulin dependent or noninsulin dependent diabetes.²⁵

Proyecto VER and Visual Impairment Project also found no association between DM and POAG. The Beaver Dam eye study showed an increased prevalence of glaucoma in people with diabetes.

Increased severity of diabetic retinopathy was associated with subsequent incidence of POAG. Many studies have shown associations of elevated mean IOP and POAG in diabetics compared to normal population. Also raised abnormal glucose levels have been demonstrated on a higher side in glaucomatous patients than the general population. However, in our study, no such correlation was found.

CONCLUSION

Despite the rather convincing results distilled from various studies, it is controversial. The concern is about these studies being subjected to detection bias. Simply stated, patients with diabetes are more likely to be under closer ophthalmic observation and more likely to have glaucoma detected. It is difficult to find the “ideal study” of T2D and risk of POAG that followed patients over a long-time period and free from detection bias. Increasing age along with diabetes are thus two more important risk factors for the development of POAG. Hence careful screening is of utmost importance.

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