

Risk factors in glaucoma: Insights from a prospective case–control study, Belagavi, India

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ABSTRACT

Introduction: Glaucoma is an optic neuropathy and degeneration of retinal ganglion cells, causing irreversible visual damage and blindness. While raised intraocular pressure (IOP) is the most important established risk factor, the exact pathogenesis and other risk factors for glaucoma are not fully understood, particularly in developing countries. Early identification and management of risk factors are important for reducing incidence and burden. This study assessed the risk factors for glaucoma at Dr. Kodkany's Eye Center in Belagavi, India.

Method: This case-control study examined 24 cases with confirmed diagnosis of glaucoma and 20 age- and sex-matched controls. A pre-designed questionnaire was used to collect sociodemographic data along with detailed eye examination findings. All glaucoma participants underwent thorough ophthalmic examinations, including visual acuity, intraocular pressure (IOP), central corneal thickness, anterior segment abnormalities, anterior chamber angle, fundus photography, and visual field testing.

Results: Of the 24 cases, 14 (58.3%) were diagnosed with open-angle glaucoma, with bilateral involvement noted in 13(54.2%) cases. IOP was considerably higher in glaucomatous patients compared to non-glaucomatous (right eye: 27.86±8.97 vs 15.85±2.84 mmHg [Mean difference: 12.01 (95% CI: 8.24–15.78)]; left eye: 28.27±8.75 vs 16.05 ± 3.02 mmHg; [Mean difference: 12.22 (95% CI: 8.49–15.95)] p<0.001 for both). None of the studied factors — age (OR=0.990, 95% CI: 0.937-1.045, p=0.705), female gender (OR=1.667, 95% CI: 0.500-5.559, p=0.416), or hypertension (OR=2.538, 95% CI: 0.697-9.240, p=0.160)—predicted glaucoma risk.

Conclusion: This study confirms that elevated IOP is a key characteristic of glaucoma. However, age, female gender, and hypertension were not recognised as important risk factors for glaucoma. This suggests that other risk factors might have contributed to the risk of glaucoma. Screening beyond traditional risk factors helps in identifying at-risk patients.

Keywords: case-control study, hypertension, incidence, open-angle glaucoma, risk factors

Introduction

Glaucoma is a major cause of irreversible vision loss and blindness, marked by progressive damage to the optic nerve. In 2020, approximately 76 million individuals worldwide were affected, including 4.5 million with moderate to severe visual impairment and 3.2 million with blindness, and the total number of individuals affected with glaucoma is projected to rise to 111.8 million by 2040.^[1,2] Because the disease is often asymptomatic in its early stages, diagnosis typically occurs only after substantial optic nerve damage, leading to compromised quality of life.^[1] Early detection and timely management are therefore essential to prevent further vision loss.^[1,2]

Glaucoma is classified into multiple subtypes, such as primary open-angle glaucoma (POAG), primary angle-closure glaucoma (PACG), secondary glaucoma, and congenital glaucoma,^[3] with their prevalence varying across ethnic and geographic populations. Established risk factors include modifiable factors (elevated intraocular pressure, hypertension, steroid use) and non-modifiable factors (age, sex, family history, thinning of the central cornea).^[1,4] Additionally, systemic conditions like diabetes mellitus, hypothyroidism, and corticosteroid use may predispose individuals to secondary glaucoma. Identifying and addressing modifiable risk factors is critical in reducing disease progression and raising awareness among both clinicians and patients.^[1]

While the epidemiology and clinical impact of glaucoma are well studied in developed nations, limited data exist for developing countries such as India.^[5,6] Evidence suggests that patients in these regions present late with more advanced disease, face a higher risk of blindness, and may have a greater age-adjusted incidence compared to those in developed countries, though the reasons remain unclear.^[5] This study sought to address this gap by assessing the incidence of glaucoma and evaluating associated risk factors in developing countries.

Method

This single-centre prospective case–controlled study was conducted over a one-year period in 2023 at the Department of Ophthalmology, Dr. Kodkany's Eye Center, Belagavi. It was designed to evaluate selected risk factors for glaucoma based on predefined objectives and feasibility, and does not aim to assess all known risk factors.

Adults aged ≥ 40 years with an intraocular pressure (IOP)

> 21 mmHg, vertical cup–disc ratio (VCDR) > 0.6 , or other glaucomatous optic disc changes such as polar notch, glaucomatous field defects (Anderson criteria), deep cupping, disc haemorrhages, thinning of the neuroretinal rim, or rim change (characteristic glaucomatous alterations of the neuroretinal rim) in both eyes were included as cases. A diagnosis of glaucoma was confirmed if at least two of these three criteria were present. Controls were recruited from patients aged ≥ 40 years without glaucoma, excluding those incidentally diagnosed during the study period.

All participants underwent clinical evaluation using a standardized protocol including visual acuity assessment, IOP measurement, and detailed systemic and ocular history. Glaucoma cases underwent a comprehensive ophthalmic examination as part of the diagnostic assessment, including central corneal thickness (CCT), anterior segment abnormalities, anterior chamber angle, fundus examination, and visual field testing. These detailed investigations were not uniformly performed in control participants, as they were recruited as individuals without clinical evidence of glaucoma and underwent standardized screening evaluation, including IOP measurement and clinical assessment, to reasonably exclude the presence of glaucoma.

Written informed consent was obtained from all participants. Ethical approval was obtained from the Institutional Ethics Committee of Prabhakar Kore's Basic Science Research Center, Belagavi. Sociodemographic and clinical details were recorded using a predesigned, pretested questionnaire.

Data were analysed using SPSS software version 21. Categorical variables were presented as frequencies or proportions and were analysed using the Chi-square test. Continuous variables are presented as Mean \pm standard deviation (SD). Normality of the data was assessed using the Shapiro-Wilk test and Q-Q plots. Independent-samples t-tests or Mann-Whitney U tests were used to compare continuous variables between groups, depending on normality. A p-value less than or equal to 0.05 indicates statistical significance.

Results

A total of 44 participants were included in the study, comprising 24 patients with glaucoma and 20 age- and sex-matched controls. Most participants in both groups were aged 56–65 years and predominantly male. Most were Hindus, married, had completed at least secondary

Table 1. Sociodemographic characteristics of study participants

Variable	Patients with glaucoma (N=24) n (%)	Patients without glaucoma (N=20) n (%)	p-value			
Age						
45-55	5 (20.8)	5 (25.0)	0.929 ^c	Secondary	7 (29.2)	1 (5.0)
56-65	10 (41.7)	8 (40.0)		Secondary and above	8 (33.3)	7 (35.0)
66-75	5 (20.8)	5 (25.0)		Graduation	2 (8.3)	3 (15.0)
76-85	3 (12.5)	1 (5.0)		Occupation		
>85	1 (4.2)	1 (5.0)		Doctor	1 (4.2)	0.0
Sex				Employed	1 (4.2)	1 (5.0)
Female	9 (37.5)	10 (50.0)	0.404 ^c	Farmer	3 (12.5)	2 (10.0)
Male	15 (62.5)	10 (50.0)		Housewife	5 (20.8)	6 (30.0)
Religion				Housewife/skilled	0.0	1 (5.0)
Hindu	21 (87.5)	20 (100.0)	0.101 ^c	Retired	6 (25)	3 (15.0)
Muslim	3 (12.5)	0		Semiskilled	0 (0.0)	1 (5.0)
Marital status				Shop	2 (8.3)	5 (25.0)
Married	19 (79.2)	16 (80.0)	0.945 ^c	Shop/Farmer	1 (4.2)	1 (5.0)
Widowed	5 (20.8)	4 (20.0)		Skilled/employed	2 (8.3)	0.0
Education				Skilled/retired	1 (4.2)	0.0
Illiterate	3 (12.5)	4 (20.0)	0.319 ^c	Unskilled	2 (8.3)	0.0
Primary	4 (16.7)	5 (25.0)		Residence		
				Rural	11 (45.8)	14 (70.0)
				Urban	13 (54.2)	6 (30.0)

c - values calculated using the chi-square test.

Table 2. Comparison of intraocular pressure and systemic disorders in cases and controls

Variable	Patients with glaucoma (N=24)	Patients without glaucoma (N=20)	Mean Difference and 95% CI	p-value
Right eye (mmHg)	27.86 ± 8.97	15.85 ± 2.84	Mean difference: 12.01 (95% CI: 8.24–15.78)	<0.001*
Left eye (mmHg)	28.27 ± 8.75	16.05 ± 3.02	Mean difference: 12.22 (95% CI: 8.49–15.95)	<0.001*
Other systemic disorders				
Present	21 (87.5%)	7 (35%)	NA	0.003* ^c
Absent	3 (12.5%)	13 (65%)		

*- statistically significant. c - values calculated using the chi-square test.

education, resided in rural areas, and were either housewives or retired (Table 1). However, no significant associations were observed between sociodemographic characteristics and glaucoma risk.

IOP was significantly higher among glaucoma patients compared to controls in both eyes (right eye: 27.86±8.97

vs 15.85±2.84 mmHg [Mean difference: 12.01 (95% CI: 8.24–15.78)]; left eye: 28.27±8.75 vs.16.05 ± 3.02 mmHg; [Mean difference: 12.22 (95% CI: 8.49–15.95)] p<0.001 for both) (Table 2). The presence of any systemic comorbidity (considered as a composite variable) was significantly associated with glaucoma (p < 0.05). Cataract

Table 3. Distribution of glaucoma types, affected eyes, and vision loss in the study participants

Variable	N = 24 n (%)		
Diagnosis		Cup to disc ratio - Left eye	0.719 ± 0.15
Disc suspect	2 (8.3)	Visual field changes[#]	
Narrow angle glaucoma	1 (4.2)	Arcuate defect (BE)	1 (4.2)
Normal tension glaucoma	1 (4.2)	Asteroid hyalosis (BE)	1 (4.2)
Open angle glaucoma	14 (58.3)	Centrocaecal scotoma (BE)	1 (4.2)
Ocular pulse amplitude	1 (4.2)	Complete depressed field (BE)	1 (4.2)
Primary open angle glaucoma	3 (12.5)	Congestion (BE), Deep cup thin (BE)	1 (4.2)
Pseudo exfoliation glaucoma	2 (8.3)	Deep cupping	1 (4.2)
Affected eye		Enlarged blind spot (RE), Vision loss (LE)	3 (12.5)
Both eyes	13 (54.2)	Generalized depression (BE)	1 (4.2)
Left eye	7 (29.2)	Inferior arcuate scotoma (BE)	1 (4.2)
Right eye	4 (16.7)	Mild congestion (BE)	1 (4.2)
Vision loss[#]		Notching in (LE)	1 (4.2)
Left eye	3 (60)	Rim loss (RE), Mild congestion in (LE)	1 (4.2)
Right eye	1 (20)	Shallow anterior, vision loss (LE)	1 (4.2)
Steroid induced	1 (20)	Superior arcuate scotoma (BE)	2 (8.3)
Central corneal thickness - Right eye (microns)	541.08 ± 18.82	Superior arcuate scotoma Ben Notching (RE), Deep cupping (LE)	1 (4.2)
Central corneal thickness -Left eye (microns)	542.42 ± 18.39	Superior arcuate scotoma (RE)	1 (4.2)
Cup to disc ratio -Right eye	0.771 ± 0.14	Superior hemifield defect (RE)	1 (4.2)
		Total constriction (RE)	2 (8.3)

[#], *Data not available*: data for vision loss and visual field changes were not available for all participants hence percentages are only calculated based on the number with available data.

Table 4. Comparison of available clinical and systemic parameters between glaucoma cases and controls

	Univariate analysis			
	Glaucoma (n=24)	Control (n=20)	Unadjusted OR (95%CI)	p-value
Hypertension	11 (45.8%)	5 (25%)	2.538 (0.697, 9.240)	0.160
Age	64.42 ± 11.17	63.15 ± 11.38	0.990 (0.937, 1.045)	0.705
Gender-Female	9 (37.5%)	10 (50%)	1.667 (0.500, 5.559)	0.416

OR – Odds Ratio, CI – Confidence interval

was found in both groups. Among glaucoma patients, six (25%) had only cataract, five (20.8%) had cataract with hypertension, and three (12.5%) had cataract, hypertension, and diabetes. Among non-glaucoma patients, two (10%) had only cataract, and one had cataract, hypertension, and diabetes mellitus.

IOP and systemic parameters were available for both cases and controls and were included in comparative analysis. However, detailed ophthalmic parameters, such as central corneal thickness and cup-to-disc ratio, were not uniformly recorded in control participants; therefore, comparative analysis of these variables could not be performed.

Regarding glaucoma subtypes, open-angle glaucoma was the most frequent diagnosis, observed in 14 (58.3%) patients. Other forms included primary open-angle glaucoma (12.5%), pseudo-exfoliation glaucoma (8.3%), and normal-tension glaucoma (4.2%). Bilateral involvement was noted in 13 (54.2%) patients, with the left eye more frequently affected than the right eye. (Table 3).

Central corneal thickness was comparable between right ($541.08 \pm 18.82 \mu\text{m}$) and left eyes ($542.42 \pm 18.39 \mu\text{m}$). The mean cup-to-disc ratio was 0.771 ± 0.14 in the right eye and 0.719 ± 0.15 in the left eye. Visual field changes varied, with superior arcuate scotoma (12.5%) and total field constriction (8.3%) being the most common defects (Table 3). Univariate analysis did not identify age, female gender, or hypertension as significant predictors of glaucoma risk ($p > 0.05$ for all comparisons) (Table 4).

Discussion

This case–controlled study demonstrated a significantly higher IOP in glaucoma patients compared with controls (show difference, CI, p-value) ($p < 0.001$), reaffirming its central role in glaucoma pathogenesis. Although univariate analysis indicated that female patients and those with hypertension had higher odds of developing glaucoma (1.6-fold and 2.5-fold, respectively), these associations were not statistically significant.

The majority of glaucoma patients in this study were aged 55 years or older, with a predominance of males (62.5%), consistent with earlier reports.^[1,7] Our study shows that hypertension and diabetes mellitus are common systemic risk factors, while Talaat et al^[7] similarly reported hypertension (60.8%) and diabetes (58.3%) as frequent systemic comorbidities among glaucoma patients

Cataract (49.1%) was the most common ocular condition.^[7] In our cohort, primary open-angle glaucoma (POAG) was the

most prevalent subtype (58.3%), with more than half of the patients showing bilateral involvement. Diverse visual field abnormalities, including arcuate defects, scotomas, and generalized field depression, were observed, highlighting the heterogeneous presentation of glaucomatous damage.^[8,9]

In the present study, IOP was significantly higher in glaucoma cases compared to controls. In the context of pseudo-exfoliation, previous studies have similarly demonstrated that a 5 mmHg increase in IOP may increase the risk of primary open-angle glaucoma by up to fourfold.^[5]

Interestingly, our study did not confirm associations with other established risk factors such as age, sex, or hypertension. This contrasts with meta-analytic evidence suggesting that advancing age markedly increases POAG risk and that females may have a lower overall risk than males. One possible explanation for this difference could be the relatively small sample size and limited statistical power of the present study, which may have reduced the ability to detect such associations.

Other studies have identified ocular biometric features (axial length, corneal curvature), older age, and elevated IOP as significant contributors to glaucoma risk.^[10] Furthermore, hormonal influences, such as reduced oestrogen in postmenopausal women, have been implicated in increasing glaucoma susceptibility.^[11] Longitudinal studies also support associations between systemic conditions—including hypertension, diabetes, and hyperglycaemia—and glaucoma development.^[12] Additionally, research among Bangladeshi populations indicated a modest association between hypertension and elevated IOP, possibly mediated through increased sympathetic activity.^[13,14] In contrast, our findings did not demonstrate a statistically significant link between hypertension and glaucoma.

Overall, this study reinforces IOP as the key modifiable risk factor in glaucoma pathogenesis. Routine IOP screening may therefore be more effective in identifying individuals at risk than monitoring systemic comorbidities alone. Nonetheless, certain limitations should be acknowledged. The relatively small sample size restricts the statistical power and may have precluded the detection of meaningful associations. Larger, well-designed case–control studies that use multivariate analyses to adjust for confounders are needed to clarify the contributions of systemic and ocular risk factors. Future research should also evaluate the roles of lifestyle factors (such as alcohol consumption,

smoking, and diet) and genetic predisposition in glaucoma pathogenesis.

Conclusion

This study reaffirms that IOP remains a defining and significant feature of glaucoma, underscoring its role as the most important modifiable risk factor in disease pathogenesis. Steroid use and other non-modifiable risk factors, including a VCDR >0.4 and inter-eye CDR asymmetry >0.2, should prompt physicians to further evaluate patients for glaucoma, even in the presence of normal intraocular pressure. Although age, female gender, and hypertension were evaluated, none showed a statistically significant association with glaucoma risk in this cohort. Early identification of individuals at risk, particularly in resource-limited settings where glaucoma often presents at an advanced stage, is critical to prevent irreversible vision loss.

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