



Severity of Primary Open Angle Glaucoma at First Presentation and Associated Factors in Tertiary Hospital

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ABSTRACT

Introduction: Glaucoma is one of the leading causes of irreversible blindness worldwide. Late presentation in glaucoma significantly increases the economic burden and risk of subsequent blindness.

Objective: To determine the severity of glaucoma at diagnosis and identify the factors associated with severe disease at presentation in a tertiary eye hospital in Nepal.

Methodology: A hospital-based, analytical, cross-sectional study was performed at Himalaya Eye Hospital from 2023 January to 2023 December among 173 eyes of 173 newly diagnosed cases of primary open angle glaucoma (POAG) after ethical clearance. Convenience sampling technique was used. The severity of glaucoma was assessed in terms of visual field (VF) loss using mean deviation (MD) and the Hodapp-Parrish-Anderson criteria. Patients were categorised into two groups based on severity: Group I (mild to moderate) and Group II (severe). A multivariate-model-adjusted binary logistic regression analysis was performed to identify the factors associated with severe glaucoma.

Result: Half of the patients (50.29%) in this study had severe glaucoma at diagnosis. Older age {adjusted odds ratio (AOR) = 1.046; 95% confidence interval (CI): 1.017-1.076; $p = 0.002$ }, higher baseline intraocular pressure (IOP) (AOR = 1.183; 95% CI: 1.086-1.289; $p < 0.001$), and thinner central corneal thickness (CCT) (AOR = 0.983; 95% CI: 0.971-0.995; $p = 0.005$) were significant predictors of severe glaucoma at presentation. Whereas, a personal history of systemic hypertension (AOR = 0.409; 95% CI: 0.177-0.947; $p = 0.037$) significantly decreased the odds of late presentation. Gender, travel time to the nearest eye-care centre, awareness about glaucoma, family history of glaucoma, and personal history of diabetes mellitus did not have significant association with the severity of glaucoma at presentation.

Conclusion: Approximately half of the patients with POAG presented with severe glaucoma at diagnosis. Older age, elevated IOP, and thin CCT were key predictors of severe glaucoma at diagnosis, while patients with systemic hypertension were associated with earlier detection.

Key words: Late presentation, primary open angle glaucoma, risk factors, severity of glaucoma

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INTRODUCTION

Glaucoma is one of the leading causes of irreversible blindness worldwide (Bourne et al., 2013, Quigley and Broman, 2006). However, nearly 90% of glaucoma cases are still undiagnosed in developing countries (Miller et al., 2022; Thapa et al., 2012; Dandona et al., 2000; Ramakrishnan et al., 2003), with most patients presenting with moderate to severe disease (Thomas, 2012; Dandona et al., 2000). Late presentation in glaucoma significantly increases the economic burden, risk of subsequent blindness, and impairs quality of life (Fraser et al., 1999a; Mikelberg et al., 1986; Miller and Karseras 1974).

Studies have identified ethnicity, lower socioeconomic status, older age, presence of a family history of glaucoma and poor health literacy as risk factors for late presentation (Fraser et al., 1999b; Ntim-Amponsah et al., 2005; Fraser et al., 1999a; Gogate et al., 2011). This study aimed to determine the severity of glaucoma at diagnosis and identify the factors associated with severe disease at presentation in a tertiary eye hospital in Nepal.

METHODOLOGY

This hospital-based, analytical, cross-sectional study was approved by the Nepal Health Research Council (Reference number: ERB-NHRC 1695; Dated: 2023 January 26) and was performed in accordance with the tenets of the Declaration of Helsinki. The authors obtained written informed consent from all the participants who were enrolled using convenience sampling technique. Patients were not involved in the design, or conduct, or reporting or dissemination plans of this research.

They did not have to bear any extra financial burden due to their participation in the study.

The study included all consecutive newly diagnosed patients with primary open angle glaucoma (POAG) aged ≥ 18 years presenting to Himalaya Eye Hospital, a tertiary eye hospital in Nepal between 2023 January and 2023 December. The Primary open angle glaucoma was diagnosed by one of two glaucoma specialists using internationally accepted guidelines (Foster et al., 2002) based on vertical cup disc ratio (VCDR), glaucomatous visual field loss and intraocular pressure (IOP). Only those patients with open angles on gonioscopy and two reliable consecutive Humphrey visual field tests were included in the study. When both eyes met the inclusion criteria, the eye with the worse mean deviation (MD) was selected for analysis to avoid inter-eye correlation.

Exclusion criteria were previously diagnosed glaucoma, secondary glaucoma (including steroid-induced, pigment dispersion, pseudoexfoliation, lens-induced and angle recession glaucoma). Patients referred as glaucoma suspects were not excluded. Exclusion criteria also included cases with corneal opacities, retinal or neurological diseases, uveitis, and prior intraocular procedures except cataract surgery.

Patients were asked if they had heard of glaucoma or *jal-bindu*. A positive response was considered to be “*aware of glaucoma*”. Consistent with several epidemiological studies, awareness was operationally defined as having previously heard of the disease rather than demonstrating detailed knowledge of its risk factors or management. Patients were considered

to have a positive family history of glaucoma only if a first-degree family member had a history of glaucoma. Following a detail clinico-demographical history, all patients underwent a detail ophthalmological examination that included Goldmann applanation tonometry (GAT), gonioscopy, dilated fundus examination, pachymetry, optic disc photography and visual field (VF) examination. The authors also asked the patients about time taken to travel to the nearest eye care centre. The authors chose travel time as a proxy measure of accessibility because Nepal's mountainous geography and variable transportation infrastructure make geographic distance alone less reflective of actual access to health care system.

The VF examination was done using the Humphrey Visual Field Analyser using a Goldmann size III stimulus, a 24-2 test pattern, and the Swedish Interactive Testing Algorithm (SITA Standard). Severity of glaucoma was assessed in terms of VF loss using mean deviation (MD) and classified based on the Hoddap-Parrish-Anderson criteria as 'Early' (MD better than -6 dB), 'Moderate' (MD between -6.01 dB to -12 dB), and 'Severe' (MD worse than -12.01 dB) (Susanna and Vessani, 2009, Mills et al., 2006). For regression analysis, patients were grouped as: Group I (Early to Moderate) and Group II (Severe) to identify factors associated with advanced presentation.

Test of normality of the data was done using the Shapiro-Wilk test. Normally distributed variables were reported as mean $\pm$ standard deviation, while variables with non-normal distribution were reported as median (interquartile range). Student's t-test, Mann-

Whitney U test, Chi-square test, and Fisher's Exact Test were performed to assess the differences between the two groups across various quantitative and qualitative variables. Multivariate-model-adjusted binary logistic regression was performed to assess associations between severity of the disease and age, sex, baseline IOP, CCT, travel time to the nearest eye care centre, glaucoma awareness, family history of glaucoma and personal history of hypertension and diabetes mellitus. The authors included all clinically relevant variables in the multivariable model. The authors assessed multicollinearity among the independent variables using Variance Inflation Factor (VIF). All variables had VIF values below two, indicating no significant multicollinearity. A p-value of <0.05 was considered statistically significant.

RESULT

Of 173 eyes of 173 patients, 86 (49.71%) were in Group I and 87 (50.29%) in Group II. Comparison of the clinico-demographic features between the two groups have been tabulated (Table 1). Male: female ratio (M:F) was 34:52 in group I vs 53:34 in group II, ($p = 0.005$). Group II patients were older (median 69 vs. 58 years; $p < 0.001$), had higher baseline IOP (median 19 vs. 16 mmHg; $p < 0.001$), longer travel time (median 2.0 vs. 0.5 hours; $p < 0.001$), and thinner baseline CCT (mean 505.07 vs 516.55 μm ; $p = 0.027$). There was no significant difference between the two groups by means of glaucoma awareness, family history of glaucoma, and personal history of hypertension and diabetes mellitus.

Table 1: Baseline demographic and clinical features of the patients.

Factors	Group I (n = 86)	Group II (n = 87)	p-value
Age (years)	58 (48.75, 68)	69 (55, 74)	<0.001*
Gender (Male: Female)	34:52	53:34	0.005†
IOP (mmHg)	16 (14, 19)	19 (16, 26)	<0.001*
CCT (μm)	516.55±31.80	505.07±35.89	0.027‡
Hypertensive (yes)	50%	44.82%	0.496†
Diabetic (yes)	16.27%	16.09%	0.973†
Glaucoma awareness (yes)	27.90%	16.09%	0.061†
Family history of glaucoma (yes)	3.48%	5.74%	0.72§
Travel time (hours)	0.5 (0.43, 2.0)	2.0 (0.50, 3.0)	<0.001*

Note: * = Mann-Whitney test; † = Chi-square test; ‡ = Student t-test; § = Fisher's Exact Test; CCT = Central Corneal Thickness; IOP = Intraocular pressure.

Multivariate model adjusted binary logistic regression analysis (Table 2) identified older age (AOR 1.046; 95% CI = 1.017-1.076; p = 0.002), higher baseline IOP (AOR 1.183; 95% CI = 1.086-1.289; p <0.001), and thinner CCT (AOR 0.983; 95% CI = 0.971-0.995; p = 0.005)

as independent predictors of severe glaucoma at presentation. Whereas, a personal history of systemic hypertension (AOR 0.409; 95% CI = 0.177-0.947; p = 0.037) was associated with lower odds of severe disease at presentation.

Table 2: Demographic and clinical correlation with severity of disease at presentation.

Factors	Univariate model		Multivariate model	
	OR (CI)	p-value	AOR (CI)	p-value
Age	1.035 (1.014-1.057)	0.001	1.046 (1.017-1.076)	0.002
Gender (male)	2.384 (1.295-4.389)	0.005	1.640 (0.777-3.464)	0.195
IOP	1.161 (1.081-1.247)	<0.001	1.183 (1.086- 1.289)	<0.001
CCT	0.990(0.981-0.999)	0.029	0.983 (0.971-0.995)	0.005
Hypertensive (yes)	0.813 (0.447-1.477)	0.496	0.409 (0.177- 0.947)	0.037
Diabetic (yes)	0.986(0.439-2.215)	0.973	1.481 (0.529- 4.147)	0.454
Glaucoma awareness (yes)	0.495(0.236-1.039)	0.063	0.596 (0.224- 1.585)	0.300
Family History of glaucoma (yes)	1.687(0.390-7.290)	0.484	4.309(0.665-27.911)	0.125
Travel time	1.284 (1.078-1.530)	0.005	1.112(0.921-1.344)	0.269

Note: AOR = Adjusted Odds Ratio; CCT = Central Corneal Thickness; CI = Confidence Interval; IOP = Intraocular Pressure; OR = Odds Ratio.



Though males and participants with longer travel time to the nearest eye care centres had significantly higher odds of being late presenters in univariate analysis (Table 2), these factors lost significance after adjustment for other cofactors. The severity of glaucoma at diagnosis was not associated with lack of awareness about glaucoma, presence of family history of glaucoma, and personal history of diabetes mellitus.

DISCUSSION

The authors observed that approximately half of the newly diagnosed POAG patients (50.289%) presented with severe glaucoma. This observation is consistent with studies from other low and middle income countries like, India (Dandona et al., 2000) Iran (Motlagh and Pirbazari, 2016), and Tanzania (Jones et al., 2020). This reflects the asymptomatic nature of glaucoma and the diagnostic limitations in resource-limited settings (Ramakrishnan et al., 2003, Dandona et al., 2000, Thomas, 2012, Leite et al., 2011).

The authors observed older age is an independent risk factor for severe glaucoma at diagnosis. Many other studies too have associated older age with late presentation in glaucoma (Fraser et al., 1999a; Fraser et al., 1999b; Abdull et al., 2015; Onyia et al., 2022). However, it is important to note that this finding is influenced by the fact that older age is an established risk factor for POAG, and the incidence and prevalence of glaucoma increases with age (Coleman and Miglior, 2008).

The authors found that baseline higher IOP and thinner CCT as risk factors for severe glaucoma

at diagnosis. This study supports the concept that patients with higher IOP can be expected to have rapid visual field deterioration and thus advance disease at the time of diagnosis, which is supported by previous studies (Fraser et al., 1999b; Fraser et al., 1999a; Ntim-Amponsah et al., 2005).

The authors observed that presence of systemic hypertension was associated with lower odds of severe disease at presentation. The authors believe that patients with hypertension come for regular ophthalmic evaluation for hypertensive retinopathy, which might have led to early detection of glaucoma in these patients. This might be the reason for a significant proportion of patients (82, 47.39%) in this study having a history of systemic hypertension. However, the relationship between systemic hypertension and POAG remains elusive with studies showing inconsistent associations (Macri et al., 2022; Memarzadeh et al., 2010; Lee et al., 2022; Leske et al., 2002; Deokule and Weinreb 2008).

The authors also observed that males had higher risk of having severe disease in the univariate model. However, after adjusting for other variables, this significance was lost. Nevertheless, some studies have identified male gender as a risk factor for late presentation in glaucoma (Fraser et al., 1999a; Fraser et al., 1999b; Ntim-Amponsah et al., 2005; Onyia et al., 2022; Jones et al., 2020).

The authors found no association between a history of diabetes mellitus and glaucoma severity at presentation, aligning with the results of a study from India (Bhedasgaonkar and Nadkarni, 2023). However, some authors observed that diabetic patients were less likely

to present with severe disease, attributing the finding to the frequent visits that diabetics make to eye care centres for diabetic retinopathy screening (Belete et al., 2022).

The authors did not observe any relationship between lack of awareness of glaucoma and late presentation. However, some studies have associated a lack of awareness and knowledge about glaucoma with severe disease at presentation (Gogate et al., 2011; Abdull et al., 2015). This divergence might be due to using a single question asking whether the participant had ever heard of glaucoma (*jal-bindu*) to assess awareness of glaucoma in this study.

Similarly, authors identified no association between family history of glaucoma and severity at presentation. It is possible that ophthalmologists do not always take time to counsel their glaucoma patients that the disease runs in families. Also, patients with glaucoma might not always inform their disease condition to their family members (Tielsch et al., 1994).

The authors observed that while longer travel increased the risk of disease severity in univariate analysis, this association did not reach statistical significance in multivariable analysis. Similar observation was made in a study from Nigeria (Abdull et al., 2015).

This study has certain limitations. As a tertiary hospital-based study, referral bias may have

led to an overestimation of severe disease at presentation. In addition, glaucoma awareness was assessed using a single question, which may not fully capture the depth of patient knowledge. Furthermore, travel time to the eye care facility was self-reported and may be subject to recall bias, potentially affecting its accuracy as a measure of health care accessibility. Finally, inclusion of the worse eye may have contributed to an overestimation of disease severity at presentation.

CONCLUSION

In this tertiary eye care setting in Nepal, approximately half of newly diagnosed POAG patients presented with severe glaucoma. Older age, elevated IOP, and thin CCT were key predictors of severe glaucoma, while systemic hypertension was associated with earlier detection. This study underscores the persistent challenge of late glaucoma detection in resource limited settings.

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