

Risk of Missed Diagnosis of Primary Open-Angle Glaucoma by Eye Care Providers

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Abstract

Purpose: To evaluate the efficacy of opportunistic case finding in glaucoma detection and to determine factors associated with failure of glaucoma detection by eye health providers.

Methods: This study was conducted on 154 new definite primary open-angle glaucoma (POAG) patients presenting to our glaucoma clinic. A questionnaire was prepared to determine if these subjects had sought eye care up to 12 months before presentation. The type of eye care provider and the principal reason for the visit were probed. The primary outcome measure was the frequency of a correct glaucoma diagnosis in their index visit. The secondary outcomes were factors associated with missed POAG diagnosis.

Results: The great majority of study subjects (132 cases, 85.7%) had sought at least one ocular examination within 1 year before presentation. Among these patients, 73 cases (55.3%) had remained undiagnosed after the examination. Among the probed variables, age, gender, visual acuity, visual field defects, intraocular pressure, cup/disc ratio, nerve fiber layer thickness of the worse eye at presentation, and family history of glaucoma were comparable between correctly diagnosed and missed POAGs. The only factors significantly associated with missed POAG diagnosis were lack of significant refractive errors and visiting an optometrist rather than an ophthalmologist.

Conclusions: The efficacy of opportunistic case finding for POAG seems to be less than ideal in our settings. Lack of a significant refractive error and visiting an optometrist rather than an ophthalmologist were associated with a missed diagnosis of POAG. These observations reflect the need to adopt policies to improve glaucoma screening by eye care providers.

Keywords: Case finding, Glaucoma, Glaucoma diagnosis, Opportunistic screening, Optometrist, Primary care providers, Referral, Screening

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INTRODUCTION

Glaucoma is the leading cause of irreversible blindness worldwide despite having a good prognosis with early treatment.¹⁻³ The most common form of the disease worldwide is primary open-angle glaucoma (POAG).¹ POAG is asymptomatic early in the disease course, and most patients remain undiagnosed until advanced stages of glaucomatous damage.⁴ Undiagnosed glaucoma is a significant public health issue.⁵ At least half of the patients with POAG remain

undiagnosed in developed countries.⁶⁻⁹ In two national studies investigating the prevalence of glaucoma among Iranians, the rate of undiagnosed glaucoma in Iran was 80% and 89%, which is comparable to other developing nations.¹⁰⁻¹⁵ A review article has estimated the proportion of undiagnosed POAG to be 83.9% in Asia.⁵ Iran is categorized as a fast-aging society. According to the World Population Prospect 2019, more than 16 million people by 2035 and 29 million by 2050 will

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be 60 years of age and above.^{16,17} This growth in the elderly population will cause an increasing demand for age-related eye care such as glaucoma screening.

At present, most glaucoma cases are detected through opportunistic case finding among subjects presenting to eye clinics due to a variety of complaints or asymptomatic individuals having routine eye check-ups. An advantage to this approach is that the infrastructures are available, facilitating screening in a more cost-effective fashion.⁴ Case finding is by itself insufficient for glaucoma detection, especially in developing countries, where patients present with more advanced visual impairment and attend check-up visits less frequently. Another concern with this approach is the risk of missed glaucoma diagnosis by eye care professionals.

The risk of missed POAG is more than other types of glaucoma because often times angle-closure glaucoma and secondary glaucoma provide anterior segment examination changes that providers can identify.⁵⁻⁸

The current study focuses on the performance of eye care providers related to glaucoma detection and referral. We reviewed the history of adults with definite newly diagnosed POAG in terms of seeking professional eye care up to 12 months prior to diagnosis and evaluated factors that may contribute to failure of glaucoma detection by eye health providers.

METHODS

In this cross-sectional investigation, 154 new POAG patients, diagnosed at presentation or within 1 year prior to referral to Labbafinejad Medical Center from June 2018 to October 2020, were interviewed and enrolled. This hospital is a university-affiliated tertiary eye care center in Tehran. The Ethics Committee at Shahid Beheshti University of Medical Sciences approved the study protocol (code of ethics: SBMU.MSP.RE), and written informed consent was obtained from each participant.

Only adults with no ocular disease other than POAG were included. The diagnosis of POAG was made by the presence of glaucomatous changes of the optic disc (including neuroretinal rim thinning or notching, optic nerve cupping, and disc hemorrhage), an open iridocorneal angle on gonioscopy, presence of retinal nerve fiber layer (RNFL) defects on spectral-domain optical coherence tomography (SD-OCT), and presence of glaucomatous visual field defects, with or without high intraocular pressure (IOP). IOP elevation was not used as a diagnostic criterion, because IOP-lowering medications had been started for some participants before referral.

Exclusion criteria were as follows: history of eye surgery (other than uncomplicated phacoemulsification cataract surgery), presence of conditions responsible for impaired vision or visual field defects (such as uveitis, diabetic retinopathy, ischemic optic neuropathy, dense cataracts, retinal vein occlusion, retinitis pigmentosa, and severe age-related macular degeneration), narrow iridocorneal angle on gonioscopic

examination, and all other forms of secondary open-angle glaucoma (pigmentary, pseudoexfoliation, etc.).

All visual fields were performed on the Humphrey Visual Field Analyzer, using the SITA-Standard 24-2 algorithm (Carl Zeiss Meditec, Inc., Dublin, CA, USA). Only reliable visual fields (fixation losses, false positives, and false negatives, all >15%) were chosen. Each visual field defect was confirmed at least in two tests. Glaucoma severity was based on visual field defects of the worse eye according to the Hodapp–Parrish–Anderson’s criteria.¹⁸ The peripapillary RNFL thickness was measured along a 3.45-mm diameter circle around the disc using SD-OCT (Spectralis; Heidelberg Engineering, Heidelberg, Germany).

Data regarding the participant’s demographic characteristics, medical history, medication use, history of eye disease, glaucoma awareness, and family history of glaucoma were elicited through an interview. The type of eye care provider, the principal reason for the visit, and the exact time of visit were asked. A document from the caregiver, such as a prescription or referral letter, was requested from the participants. Patients who could not remember these details or did not have any record to document their visits were excluded from the study. A few questions were asked from the study participants pertaining to family history of glaucoma and to evaluate their knowledge about glaucoma and their source of information.

Two outcomes were expected for patients who met an eye care provider during the previous 12 months: diagnosed versus undiagnosed glaucoma. Explanatory variables comparing the two groups were age, gender, visual acuity, refractive error, visual field defects, IOP, vertical cup-to-disk ratio (VCDR), nerve fiber layer thickness at presentation, family history, and type of eye care provider.

Statistical analysis was performed using SPSS software (IBM SPSS Statistics for Windows, Version 22.0; IBM Corp. Armonk, NY, USA). Mean and standard deviation, amplitude, frequency, and percentage were used to describe data. Chi-square and Fisher’s exact tests were used for categorical data. $P < 0.05$ was considered statistically significant. We used logistic regression analysis to calculate odds ratio and 95% confidence intervals to determine the effect of different factors on a diagnosis of POAG.

RESULTS

A total of 154 newly diagnosed POAG patients with a mean age of 58 ± 16 years were enrolled in the study, including 84 male subjects 54.5% [Table 1]. At presentation, the great majority (92.3%) of patients had moderate (70.2%) or severe (22.1%) glaucoma. Within the study sample, 132 patients (85.7%) had a documented eye care provider visit over the past 12 months before presentation. Of these, 59 patients (46%) were correctly diagnosed with POAG in the index visit, and IOP-lowering medications had been started for most of them; however, 73 subjects (54%) had remained undiagnosed. The mean time interval between index visit

and presentation to our clinic was 4.2 ± 5.1 months overall, 4.6 ± 1.1 months in undiagnosed subjects, and 3.8 ± 4.3 months in diagnosed patients ($P = 0.166$). The principal reasons to visit an eye care provider were to renew reading or distance vision glasses (37.8%) followed by cataract assessment (31.8%) and foreign body sensation (30.3%). Among undiagnosed patients, 15 subjects (19.6%) had sought a second eye care visit which resulted in a diagnosis of POAG.

There was no significant difference between groups concerning age or gender [Table 1]. Undiagnosed glaucoma was more common in patients examined by an optometrist rather than an ophthalmologist ($P < 0.001$). There was no significant difference between groups concerning mean best-corrected visual acuity and spherical equivalent of refractive error. However, significant refractive errors (more than one diopter of myopia, hyperopia, or astigmatism) were more prevalent in subjects with a correct diagnosis of POAG [Table 1].

The mean IOP at presentation, in the worse eyes of undiagnosed glaucoma cases versus diagnosed subjects, was not statistically

different ($P = 0.64$). More patients in the diagnosed group were using IOP-lowering medications (42/59) than the undiagnosed group (19/73) ($P < 0.001$). There was no significant difference between the two groups in terms of factors defining glaucoma severity, such as VCDR, severity of visual field defects, visual field mean deviation, and nerve fiber layer loss on OCT [Table 2]. Thirty-two patients (20.8%) reported a family history of glaucoma; of these, 21 subjects (65.6%) had an affected first-degree relative. Only 4 patients (12.5%) with a positive family history were aware of the familial risk of glaucoma. The primary source of their knowledge was their relatives [Table 3].

The referral source to our glaucoma clinic was general ophthalmologists, ophthalmology fellowships, and a general practitioner in 91%, 8.4%, and 0.6%, respectively.

DISCUSSION

Our study found that more than half of definite POAG patients had remained undiagnosed despite a visit by an eye care

Table 1: Demographics of participants with previously undiagnosed versus diagnosed primary open-angle glaucoma

	Total	Undiagnosed	Diagnosed	P*	OR	95% CI
Sex (%)						
Male	75 (56.8)	43 (58.9)	32 (54.2)	0.59	Reference	
Female	57 (43.2)	30 (41.1)	27 (45.8)		1.173	0.588-2.338
Age	58±16	58±16	59±17	0.871	1.003	0.981-1.025
Diabetic (%)						
No	101 (76.5)	54 (74.0)	47 (79.7)	0.443	Reference	
Yes	31 (23.5)	19 (26.0)	12 (20.3)		0.711	0.313-1.614
Eye care provider (%)						
Optometrist	26 (19.6)	23 (29.8)	3 (5.45)	<0.001	Reference	
Ophthalmologist	87 (65.9)	39 (50.6)	48 (87.2)		9.436	2.636-33.77
Both	19 (14.5)	15 (19.6)	4 (7.35)		2.044	0.399-10.46
Glaucoma family history (%)						
No	104 (78.8)	59 (80.8)	45 (76.3)	0.525	Reference	
Yes	28 (21.2)	14 (19.2)	14 (23.7)		1.283	0.556-2.956

*Logistic regression analysis. OR: Odds ratio, CI: Confidence interval

Table 2: Clinical features of eyes of participants with previously undiagnosed versus diagnosed glaucoma

	Undiagnosed	Diagnosed	P*	OR	95% CI
Best-corrected visual acuity [‡] (logMAR)	0.33±0.76	0.31±0.61	0.35	1.03	0.726-1.479
Spherical equivalent of refractive error (diopter)	-0.72±1.7	-0.81±1.8	0.35	1.177	0.825-1.679
Significant refractive error (more than one diopter) (%)					
No	26 (35.6)	33 (55.9)	0.026	Reference	
Yes	26 (44.1)	47 (64.4)		0.453	0.225-0.910
Baseline IOP (mmHg)	26.1±8.6	27.6±8.4	0.64	1.115	0.602-2.063
VCDR	0.73±0.14	0.71±0.16	0.22	1.036	0.926-1.160
VF defect (%)					
Mild	4 (5.4)	8 (13.5)	0.8	Reference	
Moderate	60 (82.1)	41 (69.4)	0.53	0.481	0.136-1.695
Severe	9 (12.5)	10 (17.1)	0.11	0.444	0.112-1.76
Mean deviation (dB)	-10.7±7.2	-12.1±4.5	0.88	1.177	0.636-2.179

*Chi-square and Fisher's exact tests. OR: Odds ratio, CI: Confidence interval, IOP: Intraocular pressure, VCDR: Vertical cup-to-disk ratio, VF: Visual field

Table 3: Family history of glaucoma and glaucoma awareness in patients with positive family history

Glaucoma family history (%)	
No	122 (79.2)
Yes	32 (20.8)
Relationship with an affected relative (%)	
First-degree	21 (65.6)
Second-degree	11 (34.4)
Glaucoma awareness in patients with glaucoma family history (%)	
No	28 (87.5)
Yes	4 (12.5)
Source of information	
Relatives	3
Social media	1

provider in the past 12 months. Among all the demographic and clinical factors, only lack of a significant refractive error and being seen by an optometrist rather than an ophthalmologist were significantly associated with the risk of missing a diagnosis of POAG.

A recent systematic review and meta-analysis showed that despite the progress made in glaucoma research, imaging technologies, and interventions, the proportion of undetected glaucoma has remained high over the past five decades.⁵ Multiple studies have described risk factors for undiagnosed glaucoma, including lower education,¹⁹ not having seen an ophthalmologist in the prior year,⁶⁻⁸ seeing an optometrist rather than an ophthalmologist,^{6,19} lower mean baseline IOP,¹⁹ baseline hyperopia,²⁰ no family history of glaucoma, and lower cup-to-disc ratio.⁸ The inadequacy or lapse in ocular examinations has been consistent finding associated with undiagnosed glaucoma.⁵

Vision-related quality of life declines linearly with progressive visual field loss,²¹⁻²⁵ but it is difficult to define what level of glaucomatous visual impairment is “symptomatic”. Many patients in our study had moderate-to-severe visual field loss, and the associated visual impairment might have caused our patients to seek eye care. Nevertheless, visual acuity was comparable between diagnosed and undiagnosed POAG patients in our study.

In our study, 54% of newly diagnosed patients with definite POAG had remained undiagnosed despite a prior visit by eye care providers. This figure is in line with the study by Wong *et al.*⁶ These authors re-evaluated undiagnosed POAG clinical features in patients who had attended an eye care provider within the previous 12 months; 49% of definite POAG patients had remained undiagnosed after the eye professional visit. The type of eye professional and the presence of visual field defect were the only variables found to be different between diagnosed and undiagnosed glaucoma patients. Similarly, two extensive epidemiologic studies, the Barbados Eye Study¹⁹ and the Melbourne Visual Impairment Project,²⁶ have reported that the source of eye

care in undiagnosed glaucoma cases is more likely to be an optometrist rather than an ophthalmologist.

In our study, significant refractive errors were the only clinical feature found to be more prevalent in correctly diagnosed POAG group of patients. The need for spectacle renewal *per se* may result in more visits to eye care providers and an increased chance of glaucoma detection. In the Singapore Eye Study, adults without annual eye examinations for spectacle prescriptions were nine times more likely to have undetected glaucoma.²⁷

Many studies^{6,19,28,29} have demonstrated that lower pretreatment IOP levels predispose to a missed diagnosis of glaucoma reflecting over-reliance on IOP for detection of glaucoma. In our study, however, the level of IOP was not significantly different between diagnosed and undiagnosed groups. At presentation, most diagnosed cases were already using IOP-lowering medications, which can mask any actual pretreatment IOP difference between diagnosed and undiagnosed subjects.

Detecting early glaucoma can be a difficult task. Most of our patients had moderate-to-severe glaucoma at presentation [Table 2]. Regarding slowly progressive nature of POAG, it may be inferred that signs of glaucomatous damage could have been detectable during examinations in the prior year. Moreover, features indicating glaucoma severity such as VCDR, visual field mean deviation, and nerve fiber layer loss on OCT were comparable between correctly diagnosed POAG subjects and patients with a missed diagnosis. These findings may reflect the suboptimal quality of examinations, and this situation is in line with the EPIC-Norfolk Eye Study²⁸ because VCDR does not adequately capture features of a glaucomatous disc, and visual fields and OCT may not be done routinely.

Among our patients, 20.9% had a positive family history of glaucoma, which is comparable to the study by Wong *et al.* (14%), Baltimore Eye Survey (16%), and Barbados Eye Study (17%). Although a positive family history of glaucoma is a well-established risk factor for POAG and positively affected glaucoma detection in the Thessaloniki study,⁸ our results, in line with those reported by Wang *et al.*,⁶ suggest that family history alone cannot lead to early glaucoma diagnosis. Unless public awareness of the importance of family history is increased and close family members of affected patients are adequately informed, positive family history by itself may remain an unhelpful clinical feature in glaucoma detection.

POAG is a disease with no particular abnormality detectable on anterior segment examination, making its detection solely dependent on examiner concern and skill. POAG patients are three to four times at increased risk to remain undiagnosed as compared to patients with pseudoexfoliation glaucoma.⁸ Primary angle-closure glaucoma is also more likely to become diagnosed than POAG during screening examinations.^{5,30} Furthermore, lack of practical guidelines and protocols for glaucoma screening may also adversely affect the rate of glaucoma detection. The introduction of a glaucoma referral

scheme in UK community optometrist's practice has increased the cost-effectiveness of opportunistic glaucoma screening with an acceptable false-negative rate of 3%–10%.³¹

There are reservations in generalizing the results of this report. The current study was performed at a single referral center, and there may be regional differences in optometrist and ophthalmologist practices elsewhere. Gathering data retrospectively could also be prone to recall bias and inaccuracies. Another limitation is that findings from prior examinations were not available for re-evaluation.

In summary, the efficacy of opportunistic POAG case finding was lower than desirable in our setting. Lack of a significant refractive error and visiting an optometrist rather than an ophthalmologist were associated with missing a diagnosis of POAG during visits by eye care providers. An essential health-care implication of this study is that further strategies are required to encourage eye care providers to improve their screening skills for glaucoma. Raising public awareness of glaucoma and informing close relatives of affected patients can also help reduce the burden of missed cases of glaucoma.

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Conflicts of interest

There are no conflicts of interest.

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