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Original research

Prevalence and risk factors of glaucoma in an adult population from Shahroud, Iran

Hassan Hashemi [a], Massood Mohammadi [b], Narges Zandvakil [c], Mehdi Khabazkhoob [d], Mohammad Hassan Emamian [e,*], Mohammad Shariati [f], Akbar Fotouhi [g]

[a] *Noor Research Center for Ophthalmic Epidemiology, Noor Eye Hospital, Tehran, Iran*
[b] *Noor Ophthalmology Research Center, Noor Eye Hospital, Tehran, Iran*
[c] *Farabi Eye Hospital, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran*
[d] *Department of Medical Surgical Nursing, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran*
[e] *Center for Health Related Social and Behavioral Sciences Research, Shahroud University of Medical Sciences, Shahroud, Iran*
[f] *Department of Community Medicine, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran*
[g] *Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran*

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Abstract

Purpose: To determine the prevalence of glaucoma and its risk factors in a 40- to 64-year-old Iranian population.
Methods: In this cross-sectional study, 6311 individuals between the ages of 40–64 years old in Shahroud, a northeastern city in Iran, were selected through multistage cluster sampling. All participants underwent eye exams, optometry, and imaging. They had stereoscopic optic disc photography, visual field evaluation, and their intraocular pressure (IOP) was measured by ophthalmologists before pupil dilation. Glaucoma was defined by the standardized criteria, offered by the International Society for Geographical and Epidemiological Ophthalmology (ISGEO).
Results: Of the 5190 people who participated in the study (82.2%), data from 4637 people were used in the analysis. The prevalence of glaucoma was 1.92% [95% confidence intervals (CI): 1.53–2.31]; 1.4% (95% CI: 0.96–1.84) in women and 2.62% (95% CI: 1.95–3.28) in men. Glaucoma prevalence was 0.9% in the 40–44 years age group, and significantly increased to 3.55% in the 60–64 years age group. In the multiple logistic regression model, age [odds ratio (OR) = 1.08, 95% CI: 1.05–1.12], IOP (OR = 1.04, 95% CI: 1.01–1.06), axial length (OR = 1.34, 95% CI: 1.1–1.63), corneal radius of curvature (OR = 2.76, 95% CI: 1.26–6.06), and corneal diameter (OR = 0.63, 95% CI: 0.46–0.87) showed significant statistical association with glaucoma.
Conclusions: The prevalence of glaucoma was considerably high at older ages. Major risk factors confirmed by this study included older age and high IOP. Certain ocular biometric components such as the axial length and the corneal radius of curvature must be noted as important glaucoma risk factors at younger ages.

Keywords: Cross-sectional study; Glaucoma; Prevalence; Iran

Introduction

Glaucoma is the leading cause of global blindness second to cataracts. It was responsible for 8% of cases of blindness in 2010.[1] Including refractive errors, glaucoma is one of the top 3 main causes of visual impairment around the world.[1] In some developed countries, increasing rates of cataract surgery and

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* Corresponding author.
E-mail address: emamian@shmu.ac.ir (M.H. Emamian).
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treatment have made glaucoma the leading cause of visual impairment and blindness.

In 2013, the global population of glaucoma was 64.3 million, and it has been predicted to rise to 76.0 million in 2020 and 111.8 million people in 2040.[2] Several population-based studies have reported the prevalence of glaucoma around the world.[3–15] The reported rate of different types of glaucoma ranges between 1% and 5%.

Major risk factors for this disease are intraocular pressure (IOP) and age for which there is unanimous support from most studies.[3,6,16] Other studied risk factors include race, gender, and family history of the disease.[3,5,6,10,13,15,17–20] Epidemiological studies have shown that it is important to take note of the type of glaucoma in different populations.[3,5,6,10,13,15,18–20] Although open-angle glaucoma has been demonstrated to be more common than angle-closure glaucoma, the incidence of blindness is higher in the latter type.

One of the outstanding differences observed in studies is the effect of race on the type of glaucoma, such that reports indicate that African Americans are more prone to open-angle glaucoma than whites.[2] In some Asian countries, a substantial proportion of glaucoma patients have angle-closure glaucoma.[2]

The importance of this disease becomes even more prominent as studies report that one out of two patients affected with glaucoma is unaware of their disease.[21] For this reason, knowledge of the prevalence of this disease, demonstrating the geographic distribution, and determining its risk factors can help identify the population at risk in different populations so that they can receive necessary interventions.

Few studies have been conducted in the Middle East region. Iran is one of the populous countries in the Middle East where the average population age is rising. In a 2001 study on the over 40 population in Tehran, the prevalence of glaucoma was 1.44%.[22] Another study in Iran found the prevalence to be about 4%.[21] Knowledge of the prevalence of glaucoma in more areas seems to be necessary because the population is aging, and policy makers need to plan for therapeutic facilities for these patients. Additionally, glaucoma risk factors are not well determined in Iran. In this report, we aim to determine the prevalence of glaucoma in an Iranian population of 40–64 years old and identify its risk factors, which can provide a picture for the population of the Middle East, as well.

Methods

The present study was carried out in 2009 using a cross-sectional approach as the first phase of the Shahroud Eye Cohort Study. The Ethics Committee of Shahroud University of Medical Sciences approved the study protocol, which was conducted in accord with the tenets of the Declaration of Helsinki. All participants signed a written informed consent. Details of the methodology of this study have been previously published.[23] Here, we present a summary of the study methodology.

The target population of this prospective, cohort study was 40- to 64-year-old individuals in the city of Shahroud, a city in the northeast of Iran. In the latest census conducted before this study in 2006, the total population of the city was 133,835, and of these, 28,779 people were 40–64 years old.

We used multistage random cluster sampling to select 300 clusters. In each cluster, households were chosen systematically, and at least 20 selected people were invited to participate in the study. Upon enrollment and receipt of signed consents, participants had comprehensive eye examinations at the study clinic site. They also had an interview to collect demographics as well as information regarding their medical and ophthalmic history.

Examinations

In this study, optometry tests included uncorrected and corrected visual acuity measurement, manifest, cycloplegic, and subjective refraction tests, and lensometry of their eyeglasses.

Biometry exams were done after vision testing, but before proceeding to the ophthalmologist and cycloplegic refraction. All participants were examined with the Allegro Biograph (WaveLight AG, Erlangen, Germany).

Ophthalmic examinations were done at two stages before and after pupil dilation. Before dilation, Goldmann applanation tonometry was conducted under topical anesthesia (e.g. tetracaine 0.5%) by ophthalmologists (H.K. and M.R.K.). Post-dilation exams included clinical grading of lens opacities, assessment for vitreous opacities at the slit-lamp, and a retinal exam using direct and indirect ophthalmoscopy.

For all participants, sequential stereoscopic optic disc photographs were obtained using the Nidek AFC-230, and evaluated by 2 fellowship-trained glaucoma subspecialists (M.M. and N.Z.) using a stereoscopic viewer. Reviewed parameters were recorded into a datasheet. These included disc size (small, average, or large), rim color, rim configuration, disc hemorrhage, rim notch, rim-disc ratio at 5 to 7 and 11 to 1 o'clock ranges, presence of peripapillary atrophy (alpha and beta zones), peripapillary retinal nerve fiber layer loss (localized or generalized) and vertical cup-to-disc ratio (VCDR). Eventually, the optic nerve head status was graded as "healthy," "glaucoma suspect," "definite glaucoma," or "other diagnoses."

For visual field testing, we used the Humphrey Matrix perimeter (Carl Zeiss Meditec, Dublin, CA, and Welch Allyn, Skaneateles Falls, NY) to perform frequency doubling technology (FDT) perimetry using the 24-2-5 screening program. An abnormal test result was defined as having a hemifield cluster of 3 or more depressed points at $P < 5\%$, at least one of which was non-edge, excluding points adjacent superiorly or inferiorly to the blind spot. The 97.5% and 99.5% percentiles of vertical cup disk ratio were 0.65 and 0.8, respectively. These percentiles were 0.3 and 0.5 for VCDR asymmetry, respectively.

Glaucoma definition

In this study, the diagnosis and classification of glaucoma was based on the criteria defined by the International Society for Geographical and Epidemiological Ophthalmology (ISGEO): A category 1 diagnosis was based on VCDR or

inter-eye VCDR asymmetry ≥97.5th percentile of the normal population or neuroretinal rim width reduced to ≤0.1 VCDR at the position between 11 and 1 o'clock or 5 and 7 o'clock, in addition to a definite glaucomatous visual field defect. Criteria for category 2 cases were an advanced structural damage (VCDR/VCDR asymmetry >99.5th percentile) and an unproven visual field loss. Cases were classified as category 3 when the optic disc could not be examined, visual field could not be tested, visual acuity was <20/400, and they had either an IOP > 99.5th percentile, or their medical history, such as glaucoma surgery, confirmed glaucoma.[24]

Normal ranges of VCDR, inter-eye VCDR asymmetry, and IOP were derived from participants who had normal supra threshold visual field examinations in both eyes.[24]

Statistical analysis

A case of glaucoma was defined as an individual who had at least one glaucomatous eye. Glaucoma prevalence was determined as a percentage with 95% confidence intervals (CI). The design effect of cluster sampling was taken into account in calculating standard errors. We used logistic regression to explore glaucoma risk factors, and present odds ratios (OR) with *P* values. In this model, first we examined each risk factor individually in a simple model. Then all demographic and eye-related risk factors were entered in a multiple logistic regression model. Eventually, we used the backward method in the final model where only variables with significant association remained.

Results

Of the 6311 individuals selected for this study, 5190 people participated (response rate = 82.2%), 4694 people completed fundus imaging and perimetry, and eventually, 4637 people met the inclusion criteria for the present analysis. The mean age of the enrolled participants was 50.7 ± 6.2 (range, 40–64) years, and 2649 (57.1%) of them were female.

After reviewing optic nerve photos and perimetry data, 89 people were identified with glaucoma; glaucoma prevalence in this study was 1.92% (95% CI: 1.53–2.31). Among identified cases, only 5 people were aware of their disease, 4 of which were receiving medical treatment.

Glaucoma prevalence was 2.62 (95% CI: 1.95–3.28) in men and 1.4% (95% CI: 0.96–1.84) in women. According to simple logistic regression, glaucoma was 1.90 times (95% CI: 1.27–2.84) more likely in men ($P = 0.002$). As demonstrated in Table 1, glaucoma prevalence was 0.9% in 40–44 years old, and increased to 3.55% in the 60- to 64-year-old age group; the odds of glaucoma significantly increased with aging (OR = 1.09; 95% CI: 1.05–1.12; $P < 0.001$). Glaucoma prevalence was 3.52% (95% CI: 1.87–5.20) among diabetics and 1.71% (95% CI: 1.32–2.09) in non-diabetic individuals; logistic regression showed significantly higher chance of glaucoma for diabetics (OR = 2.09; 95% CI: 1.22–3.62; $P = 0.008$).

Glaucoma showed no significant relationship with systolic or diastolic blood pressure ($P = 0.066$ and $P = 0.860$, respectively).

Table 1
Glaucoma prevalence in the 40- to 64-year-old population by age and sex, Shahroud, Iran, 2009.

Age groups (years)	n	Total (n = 4637)	Female (n = 2649)	Male (n = 1988)
		% (95%CI)	% (95%CI)	% (95%CI)
40–44	889	0.9 (0.3–1.5)	0.67 (0.02–1.33)	1.35 (0.11–2.6)
45–49	1254	0.96 (0.42–1.49)	0.95 (0.26–1.64)	0.97 (0.12–1.82)
50–54	1161	1.89 (1.14–2.65)	1.26 (0.39–2.12)	2.67 (1.33–4.01)
55–59	826	3.51 (2.32–4.7)	2.80 (1.26–4.35)	4.27 (2.36–6.19)
60–64	507	3.55 (1.8–5.3)	2.37 (0.51–4.23)	4.72 (2.13–7.32)

CI: Confidence intervals.

Table 2 summarizes mean values of ocular biometric components in glaucoma and non-glaucoma participants; mean axial length was longer, and mean radius of curvature was significantly higher in cases of glaucoma.

In emmetropes, myopes, and hyperopes, glaucoma prevalence was 1.55% (95% CI: 1.01–2.10), 2.82% (95% CI: 1.82–3.82), and 1.44% (95% CI: 0.76–2.12), respectively. Simple logistic regression showed no significant association between glaucoma and hyperopia ($P = 0.263$); nonetheless, the odds of glaucoma was significant in myopes compared to non-myopes (OR = 1.9, 95% CI: 1.2–3.0; $P < 0.001$). Based on the findings of the present study, the prevalence of glaucoma was 4.81% (95% CI: 2.33–7.29) among patients with cataracts as opposed to 1.70% (95% CI: 1.32–2.09) in individuals without cataract (OR = 2.92, 95% CI: 1.60–5.31; $P < 0.001$). In terms of cataract type, cortical cataract (OR = 3.11) showed the strongest correlation with glaucoma followed by posterior subcapsular cataracts (PSC) (OR = 2.97), and nuclear cataracts had no significant relationship ($P = 0.947$).

The relationship of glaucoma with other variables of interest in this study were examined in a multiple logistic regression model. In this model, refractive errors were not entered due to their high correlation with axial length. Overall results of this model are presented in Table 3. Eventually, using the backward method, glaucoma showed significant relationships with age, IOP, axial length, corneal diameter, and corneal radius of curvature.

Mean uncorrected visual acuity in this study was 0.46 ± 0.87 and 0.22 ± 0.41 logMAR in glaucomatous and non-glaucomatous participants, respectively ($P < 0.001$). For

Table 2
Mean biometric components and their 95% confidence intervals (CI) in the glaucoma and non-glaucoma groups.

Biometric components	Non-glaucoma	Glaucoma	*P*-value
	Mean (95%CI)	Mean (95%CI)	
AL (mm)	23.16 (23.13–23.19)	23.54 (23.31–23.78)	<0.001
CCT (micron)	525 (524–526)	525 (517–533)	0.890
ACD (mm)	2.64 (2.62–2.65)	2.57 (2.5–2.64)	0.091
LT (mm)	4.27 (4.26–4.28)	4.32 (4.26–4.38)	0.131
WTW (mm)	11.79 (11.77–11.8)	11.71 (11.59–11.83)	0.156
CR (mm)	7.63 (7.62–7.64)	7.73 (7.68–7.79)	<0.001

AL: Axial length; CCT: Central corneal thickness; ACD: Anterior chamber depth; LT: Lens thickness; WTW: Corneal white to white diameter; CR: Radius of corneal curvature.

Table 3
Association of glaucoma with studied risk factors in simple and multiple logistic regression models, expressed as odds ratios (OR) and 95% confidence intervals (CI).

Risk factors	Simple logistic model		Multiple logistic model	
	OR (95%CI)	*P*-value	OR (95%CI)	*P*-value
Age (years)	1.09 (1.05–1.12)	<0.001	1.08 (1.05–1.12)	<0.001
Sex (Male/female)	1.90 (1.27–2.84)	0.002		
Education (years)	0.96 (0.92–1.01)	0.139		
BMI	1.00 (0.95–1.04)	0.836		
Systolic BP (mm/Hg)	1.01 (1.00–1.02)	0.066		
Diastolic BP (mm/Hg)	1.00 (0.98–1.02)	0.860		
IOP (mm/Hg)	1.04 (1.01–1.08)	0.016	1.04 (1.01–1.06)	0.004
Cataract (Yes/no)	2.92 (1.60–5.31)	0.001		
Axial length (mm)	1.39 (1.19–1.62)	<0.001	1.34 (1.10–1.63)	0.004
Corneal thickness (micron)	1.00 (0.99–1.01)	0.890		
Anterior chamber depth (mm)	0.56 (0.29–1.10)	0.091		
Lens thickness (mm)	1.71 (0.85–3.45)	0.131		
Corneal diameter (mm)	0.77 (0.53–1.11)	0.156	0.63 (0.46–0.87)	0.005
Corneal curvature (mm)	3.53 (1.84–6.80)	<0.001	2.76 (1.26–6.06)	0.012

CI: Confidence intervals, OR: Odds ratios, BMI: Body mass index, BP: Blood pressure, IOP: Intraocular pressure.

corrected visual acuity, these values were 0.26 ± 0.79 and 0.04 ± 0.27 logMAR.

Discussion

This report is one of the few studies in Iran and the Middle East region concerning the prevalence of glaucoma and its risk factors. The study has strength and limitations that must be noted. The strengths include a detailed assessment of the optic nerve head, conducting perimetry, and exploring glaucoma associations with biometric components. The most important limitation of our study was that we did not perform gonioscopy, and thus, the type of glaucoma was not determined. Given this limitation, we are not able to compare our results with other parts of the world by type of glaucoma and cannot determine the ratio of open-angle to angle-closure glaucoma types. Nonetheless, glaucoma is an important public health issue, and our findings add valuable information to our knowledge about this disease in Iran and the Middle East.

Of the study participants, 1.92% had glaucoma; this rate ranged between 0.9% and 3.55% in different age groups. One of the few similar studies conducted in Iran was in Yazd where the prevalence rate of glaucoma was 4.4%[21]; this prevalence is higher than the rate we observed in our study. In both studies, the ISGEO criteria were used to define glaucoma, and thus, this inter-study difference is not due to different definitions, but rather different ages. The study sample in Yazd was quite older than our study sample; about 28% of the Yazd study sample was 60–80 years old. Therefore, the older age of the Yazd study can be one reason for the higher prevalence of glaucoma in that city. As demonstrated in Table 4, the prevalence of glaucoma varies around the world, and ranges from 1% to up to about 8%. A noteworthy point in the available reports was the higher prevalence of glaucoma in blacks compared to whites. In a 2014 review article, the overall global prevalence of glaucoma was stated as 3.54%. At 4.79%, the highest rate was in Africa, while the lowest rate was 2.93% in Europe.[21] As demonstrated, the overall prevalence in our study is lower than that in other parts of the world and many previous studies listed in Table 4. This can be due to the limited age range of the participants in our study. However, glaucoma prevalence was lower in some white American

Table 4
Comparison of results of other studies regarding the prevalence of glaucoma around the world.

Place	n	Age group	Glaucoma prevalence (%)
Baltimore, USA[25]	5308	40+	3.7
Beaver Dam, USA[15]	4926	>40	2.1[a]
Rotterdam, Netherlands[26]	10,000	>55	1.1[a]
Barbados[27]	4709	>40	7
Tajimi, Japan[28]	3021	>=40	5
Victoria, Australia[29]	4744	>4 = 40	1.8
Greece[30]	2554	≥60	3.8
California, USA[31]	6142	≥40	4.74[a]
Chennai, India[32]	3850	≥40	3.51[a]
Chennai, India[33]	3850	≥40	0.88[b]
Melbourne, Australia[34]	3271	>40	2
Egna-Neumarkt, Italy[35]	4297	>40	2.6
Ireland[36]	2186	>50	1.88
Thailand[37]	701	>50	3.8
Tanzania[19]	3268	>40	4.16
Tanzania[19]	1230	40–89	0.98
Bangladesh[20]	2347	≥35	2.1
Rural West Bengal[38]	1594	≥50	3.4
Salisbury, England[39]	1250	≥73	3.4
Guangzhou, China[40]	1504	≥50	3.8
Singapore[41]	3280	40–80	3.4
Tamil Nadu, India[42]	3924	≥40	1.62[a]
Piraquara, Brazil[10]	1636	>40	3.4
Spain[43]	569	40–79	2.1
Tehran, Iran[22]	2184	≥40	1.44
Beijing, China[6]	4439	≥40	3.7
Hovsgol, Mongolia[44]	942	≥40	1.2
Meiktila, Myanmar[12]	1997	≥40	4.9
Dhaka, Bangladesh[20]	2347	≥40	2.1
Tanjong Pagar, Singapore[45]	1232	≥40	3.2
Yazd, Iran[21]	1990	≥40	4.4
Current study	4637	40–64	1.9

[a] Open-angle glaucoma.
[b] Angle-closure glaucoma.

populations.[2] Regardless, since glaucoma can lead to blindness, even the observed rate is an important public health matter.

As an important finding of our study, only 5 of the 89 (5.6%) people identified with glaucoma were aware of their condition. In light of the visual outcome of this disease, screening programs need to receive more attention. As we know, changes in the visual field occur at advanced stages of the disease, and most people remain unaware before such changes take place. Also, it should be noted that treatment is very difficult at this stage. Therefore, glaucoma screening programs need to be supported for at-risk ages or those who have other risk factors.

The risk factors we studied were in general and ocular categories, and we demonstrated results of the simple and multiple models. Age was one of the variables that significantly correlated with the prevalence of glaucoma in the simple and multiple models. Increased risk of glaucoma (open-angle and angle-closure) with aging has been demonstrated in several studies, and today, age is known as one of the most important risk factors of glaucoma.[46–48] Although the increased risk would appear to be due to the age-related increase in IOP, as demonstrated, IOP correlated with the prevalence of glaucoma in the multiple model even after adjustment for age.

Male sex was a glaucoma risk factor in the simple model, but this relationship was not observed in the multiple models. Most previous studies agree that male sex is a risk factor for open-angle glaucoma, and female sex is a risk factor for angle-closure glaucoma.[46,49] However, there are studies that contradict this finding.[50] We believe biometric components are one of factors that confounded the relationship between sex and glaucoma in other studies. These components differ between the two sexes and correlate with glaucoma. In the final model in our study, biometric components were adjusted for, and therefore, no relationship between sex and glaucoma was observed. One of these ocular biometric components is the axial length which has been shown to be longer in men. On the other hand, it also correlates with glaucoma; therefore, controlling for this variable in the final model in our study could explain the lack of association between sex and glaucoma.

Diabetes was another risk factor that correlated with glaucoma only in the simple model. This association has been reported in several studies.[51,52] In the Barbados Eye Studies, diabetes was not associated with the 9-year incidence of glaucoma.[53] In the simple model, age and IOP could have confounded the relationship between diabetes and glaucoma. We already know the relationship between age and diabetes. Also, many studies have shown higher IOP readings in diabetic individuals.[54,55] However, similar to other large-scale, population-based studies such as Baltimore,[56] Beijing,[57] South India,[33] Los Angeles Latino,[58] and Barbados[49] eye studies, we ruled out any relationship between glaucoma and diabetes. As evidenced by the multiple models in our study, we believe diabetes is not a risk factor for glaucoma; nonetheless, more specific and genetic research projects are required.

As observed in this study, glaucoma was more common among myopes. Myopia has been described as a risk factor for glaucoma in other studies as well.[59–61] As stated in the results, due to the high correlation between axial length and refractive errors, we only entered axial length in the final model, and as demonstrated, a long axial length was directly associated with glaucoma prevalence. The relationship between myopia and glaucoma shown in previous studies could be due to the relationship between axial length and myopia. It seems that axial length has confounded the relationship because most studies did not show any relationship between glaucoma and the other two factors as multiple variables. As for axial length and glaucoma, many studies have suggested this biometric index to be a predictor of different types of glaucoma.[62] According to these studies, long axial length is a risk factor for open-angle glaucoma, while individuals with short axial lengths are prone to angle-closure glaucoma.[62] Takeyama[63] demonstrated a reverse association for axial length with macular ganglion cell complex and retinal thickness. This relationship has been confirmed in other studies as well. For this reason, there is greater and faster nerve fiber layer destruction when the IOP is raised. In other words, at the same IOP, individuals with long axial lengths are more prone to nerve fiber layer damage than people with normal axial length, and glaucomatous damage occurs faster and more severe. Individuals with a short axial length, on the other hand, have a shorter anterior chamber depth and thus, a narrower anterior chamber angle which impedes the passage of aqueous that causes angle-closure glaucoma. Of special note, the direct association between axial length and glaucoma observed in our study indicates a larger proportion of open-angle glaucoma cases in this sample.

Our study showed increased glaucoma prevalence rates as the corneal radius of curvature increases. Few studies have discussed the corneal radius of curvature in glaucoma patients. This relationship could be hard to explain. There is a hypothesis attributing this relationship to the association of corneal radius of curvature with corneal resistance factor and corneal hysteresis. As some studies have demonstrated, corneal resistance factor and corneal hysteresis are different in glaucoma patients.[64,65]

In conclusion, our findings demonstrated that despite a relatively lower glaucoma prevalence rate in the under 50 age group compared to other studies, this important cause of blindness calls for attention after the age of 55. Aging and IOP were important glaucoma risk factors that we confirmed in line with previous studies. Our findings indicated that biometric components, especially axial length and corneal radius of curvature, after adjustment with other variables, can increase the odds of developing glaucoma. Therefore, noting these indices in screening programs can be helpful in identifying some cases of glaucoma.

Our study has important strengths such as large sample size and assessment of ocular biometrics; however, there were a few limitations that should be mentioned. The main limitation was that gonioscopy was not done on account of constraints, and thus, the type of glaucoma was not specified. Another limitation was that repeatability of certain measures such as perimetry was not done.

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