ORIGINAL ARTICLE

Focusing on patients at high-risk for glaucoma in Brazil: A pilot study

Dépistage du glaucome dans une population à haut risque au Brésil : une étude pilote

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KEYWORDS
Epidemiology; Glaucoma; Prevalence; Risk Factors; Screening

Abstract

Purpose. — To assess the results of a pilot study for screening high-risk individuals for glaucoma in Brazil.
Methods. — Using cross-sectional methodology, the study population consisted of first-degree relatives of known glaucoma patients. Risk factors were assessed through a questionnaire, and each subject received a complete eye examination.
Results. — Sixty individuals were identified and examined. The most relevant risk factors for glaucoma were: age older than 40 years (86.7%), systemic hypertension (46.7%), and self-identification as non-white (35%). Final diagnoses were normal (63.3%), glaucoma (23.3%), ocular hypertension (11.7%), and angle-closure without glaucoma (1.7%). Clinical features that were significant as an indicator of glaucoma presence were non-white participants (OR = 6.7, \( p = 0.004 \)), central corneal thickness < 520\( \mu \text{m} \) (OR = 6.286, \( p = 0.007 \)), and cup-to-disc ratio \( \geq 0.6 \) (OR = 3.00, \( p = 0.07 \)).
Conclusions. — Despite our study's small sample size, this high prevalence of glaucoma (23.3%) highlights the importance of identifying for screening at-risk, first-degree relatives of glaucoma patients. Pachymetry was an important diagnostic tool for glaucoma within this population.

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Introduction

It is estimated that 45 million people throughout the world are blind, plus an additional 135 million who have some kind of visual impairment. A large number of the blind live in developing countries [1]. The World Health Organization predicts that the number of visually impaired persons will double by the year 2020 [2] due to world population growth and the rising number of people over 65 years old, the main causes for this demographic and epidemiological transition [1,2].

While the societal impact of blindness is felt heavily by families and communities, so also is the economic impact on health services, most particularly caused by glaucoma, the leading cause of irreversible blindness in the world [3]. The trend is increasing [4], as both incidence and prevalence of glaucoma are expected to rise in the future.

It is well known that the more advanced the glaucoma, the higher the costs in the treatment [5]. From a public health and preventive perspective, facilitating early diagnosis in order to prevent the disease from reaching more advanced stages makes considerable sense.

Screening for glaucoma in the general population is not cost-effective [6]. However, identification and screening of high-risk individuals such as family members of glaucoma patients and adults 40 years and older, especially those of African origin, makes good public health sense [6].

The purpose of this study was to assess the results of a screening campaign carried out on a single day focusing on first-degree relatives of glaucoma patients in a developing country (Brazil).

Materials and methods

A cross-sectional study was chosen to assess the prevalence of factors associated with glaucoma in an adult population.
cornea ultrasound pachymetry (Ocuscan, Alcon Laboratories, Fort Worth, TX, USA), and optic nerve head biomicroscopy (undilated pupils, whenever possible, or dilated pupils when a good evaluation was not possible without dilation) using a 90-D non-contact lens (Volk Optical Inc., Mentor, OH, USA). Humphrey standard automated perimetry (24-2 Sita-Fast strategy, Humphrey Inc. San Leandro, CA, USA) was performed on every individual by a trained technician. If a patient had a normal visual field with good reliability, only one field exam was performed. Conversely, patients with field defects were submitted to one more test on another day within 1 week to confirm its presence.

Glaucoma was diagnosed according to the International Society of Geographical and Epidemiological Ophthalmology [7]. The diagnosis is made based on three levels of clinical evidence: Category 1: structural and functional evidence; Category 2: advanced structural damage with unproven field loss; and Category 3: optic disc not seen, field test impossible, but with high intraocular pressure and/or evidence of glaucoma filtering surgery. Primary open-angle glaucoma is diagnosed when an eye meets one of the three categories above, in which there is no evidence of angle closure on gonioscopy and there is no secondary cause. People meeting gonioscopic criteria for narrow angles would be classified as having primary angle closure, while those with this closure plus optic disc damage are diagnosed with primary angle-closure glaucoma.

Each individual with intraocular pressure (IOP) less than 21 mmHg, normal appearance of optic discs, and normal visual fields was considered normal.

Ocular hypertension is considered when an IOP above 21 mmHg is found, while associated with normal appearance of the optic disc and normal visual fields.

All glaucomatous patients were then classified into three stages according to the visual field using the Hodapp, Parrish, and Anderson criteria [8] as follows: early (mean deviation [MD] < 6 dB), moderate (MD between 6 and 12 dB), and advanced (MD > 12 dB) glaucoma. All patients diagnosed with glaucoma received medical therapy, and if the angle was narrow, a Nd-YAG laser iridotomy was suggested as treatment.

For statistical comparisons between variables in different groups, either the chi-square test (categorical variables) or the Student t-test (numerical variables) was determined with a significance of 95%. An odds ratio (95% confidence interval) was used to estimate the risk of glaucoma. The statistical analysis was performed using SPSS 13.0 (SPSS Inc., Chicago, IL, USA).

This study was approved by an Ethics Committee and adhered to the tenets of the Declaration of Helsinki.

## Results

This pilot study was conducted on a single day in the facilities of the Paletta Guedes Ophthalmic Center, in Juiz de Fora, MG, Brazil. Of the first 100 eligible glaucomatous patients, 14 could not be reached by telephone (incorrect number, death, etc.). Eighty-six persons met the inclusion criteria, were invited, and accepted the screening. The participation rate was 69.8% (60/86). Nonresponders were those who confirmed their participation (26/86) but did not show up for the exam for several reasons (could not get an absentee pass from work, had forgotten the exam, etc). A total of 60 individuals were screened.

The mean age of participants was 51.63 ± 11.43 years. Thirty-eight individuals (63.3%) were women and 22 (36.7%) were men. Twenty-one persons (35%) were self-reported as non-whites, 39 (65%) as whites, and none (0%) as Asians. All (100%) had a positive family history for glaucoma in a first-degree relative because this was an inclusion criterion for the study. Risk factors for glaucoma and its respective absolute and relative frequencies are displayed in Table 1.

First-degree relatives were siblings (48.3%), children of the probands (48.3%), and parents (3.3%).

Figure 1 shows the final diagnoses: normal for 38 persons (63.3%), ocular hypertension for seven participants (11.7%), angle closure without signs of glaucoma for one person (1.7%), and glaucoma for 14 participants (23.3%). Within the glaucoma group, one was diagnosed with angle-closure glaucoma and was referred to Nd-YAG laser iridotomy, as

![Figure 1](image-url)
was the participant with angle-closure without glaucoma. Of the glaucoma cases, 12 (85.8%) were classified as early glaucoma, one (7.1%) as moderate glaucoma, and one (7.1%) as advanced glaucoma. All of them had at least two visual field tests to confirm defects. Only one patient needed three tests to achieve good reliability patterns. No normal-tension glaucoma diagnosis was possible in this campaign, because it would require a 24-h tensional diurnal curve to eliminate the existence of possible IOP peaks above 21 mmHg.

Mean IOP for both the right and left eye, respectively, was 13.95 mmHg and 13.85 mmHg for the normal group, and 17.00 mmHg and 17.67 mmHg for the glaucoma group ($p < 0.00001$). Mean central corneal thickness (CCT) for the right and left eye was 548 and 548 μm for participants without glaucoma, and 512 and 511 μm for glaucoma patients ($p = 0.001$). Vertical cup-to-disc ratio (C/D) for the right and left eye, respectively, was 0.40 and 0.39 for the normal group and 0.61 and 0.66 for those with glaucoma ($p = 0.005$ for the right eye and $p < 0.00001$ for the left eye). There were no statistical differences in mean age between the group with normal exams and the group with glaucoma (50.4 versus 54.3 years, $p = 0.273$). Comparisons between the normal and glaucoma groups are displayed in Table 2.

Risk estimates for the presence of glaucoma are shown in Table 3. The statistically and clinically significant clinical characteristics for the presence of glaucoma were the following: non-whites with odds ratio (OR) = 6.7 ($p = 0.004$), CCT < 520 μm with OR = 6.3 ($p = 0.007$), and C/D > 0.6 with OR = 3.0 ($p = 0.07$). First-degree relatives with a high-risk for the presence of glaucoma were those with IOP over 16 mmHg and CCT under 520 μm (OR = 19.0, $p = 0.005$). Ocular hypertension (IOP > 21 mmHg) was not a significant factor for the

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**Table 2** Comparison between normal individuals and glaucoma individuals.

<table>
<thead>
<tr>
<th>Patient characteristic</th>
<th>Normal group ($n = 39$)</th>
<th>Glaucoma group ($n = 14$)</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family history of glaucoma blindness</td>
<td>14</td>
<td>3</td>
<td>0.215</td>
</tr>
<tr>
<td>Non-whites</td>
<td>9</td>
<td>10</td>
<td>0.004*</td>
</tr>
<tr>
<td>40 years-old or more</td>
<td>31</td>
<td>14</td>
<td>0.059</td>
</tr>
<tr>
<td>Diabetes</td>
<td>7</td>
<td>1</td>
<td>0.281</td>
</tr>
<tr>
<td>Systemic hypertension</td>
<td>18</td>
<td>9</td>
<td>0.272</td>
</tr>
<tr>
<td>Symptomatic vascular dysfunction</td>
<td>2</td>
<td>0</td>
<td>0.518</td>
</tr>
<tr>
<td>Chronic use of steroids</td>
<td>3</td>
<td>0</td>
<td>0.368</td>
</tr>
<tr>
<td>IOP in right eye (mmHg)</td>
<td>13.95</td>
<td>17.00</td>
<td>&lt;0.00001*</td>
</tr>
<tr>
<td>IOP in left eye (mmHg)</td>
<td>13.85</td>
<td>17.67</td>
<td>&lt;0.00001*</td>
</tr>
<tr>
<td>CCT in right eye (μm)</td>
<td>548</td>
<td>512</td>
<td>0.001</td>
</tr>
<tr>
<td>CCT in left eye (μm)</td>
<td>548</td>
<td>511</td>
<td>0.001</td>
</tr>
<tr>
<td>C/D in right eye</td>
<td>0.40</td>
<td>0.61</td>
<td>0.005*</td>
</tr>
<tr>
<td>C/D in right eye</td>
<td>0.39</td>
<td>0.66</td>
<td>&lt;0.00001*</td>
</tr>
<tr>
<td>Age (years)</td>
<td>50.4</td>
<td>54.3</td>
<td>0.273</td>
</tr>
</tbody>
</table>

* Difference between groups was statistically significant for a significance of 95.0%. Variables were compared using either chi-square test (categorical variables) or Student t-test (numerical variables).

IOP: Intraocular pressure; CCT: central corneal thickness; C/D: vertical cup-to-disc ratio.

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**Table 3** Risk estimates for the presence of glaucoma in the study population.

<table>
<thead>
<tr>
<th>Patient’s characteristics</th>
<th>OR</th>
<th>95% CI</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lower</td>
<td>Upper</td>
<td></td>
</tr>
<tr>
<td>Family history of glaucoma blindness</td>
<td>0.446</td>
<td>0.107</td>
<td>1.855</td>
</tr>
<tr>
<td>Non-whites</td>
<td>6.667</td>
<td>1.805</td>
<td>24.625</td>
</tr>
<tr>
<td>40 years-old or more*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.327</td>
<td>0.037</td>
<td>2.910</td>
</tr>
<tr>
<td>Systemic hypertension</td>
<td>1.750</td>
<td>0.522</td>
<td>5.867</td>
</tr>
<tr>
<td>Symptomatic vascular dysfunction*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Chronic use of steroids*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>IOP &gt; 16 mmHg</td>
<td>8.250</td>
<td>2.138</td>
<td>31.838</td>
</tr>
<tr>
<td>CCT &lt; 520 μm</td>
<td>6.286</td>
<td>1.652</td>
<td>23.916</td>
</tr>
<tr>
<td>C/D &gt; 0.6</td>
<td>3.000</td>
<td>0.878</td>
<td>10.253</td>
</tr>
<tr>
<td>IOP &gt; 16 mmHg and CCT &lt; 520 μm</td>
<td>19.000</td>
<td>1.988</td>
<td>181.571</td>
</tr>
</tbody>
</table>

OR: odds ratio; CI: confidence interval; IOP: intraocular pressure; CCT: central corneal thickness; C/D: vertical cup-to-disc ratio.

It was not possible to calculate the risk due to the small sample size.
presence of glaucoma because only a few participants (5/60) presented themselves with an IOP over 21 mmHg in either the right or left eye. Four of them were found to have ocular hypertension with normal appearance of the optic discs and normal visual fields. Only one of the glaucoma patients (1/14) had an IOP greater than 21 mmHg at first presentation.

All glaucoma patients were treated with medical therapy and asked to return in 2–3 weeks to ensure that the target pressure was reached.

Discussion

Brazil is the largest country in South America, with nearly 190 million inhabitants nearly 64 million of whom are over 40 years of age. In a recently published population-based study of the prevalence of glaucoma in Brazil (3.4% for a population of 40 years or more) [9], one can estimate over 1.5 million people with glaucoma. According to this study, the great majority of these patients are not aware of their condition. This same prevalence study estimated that almost 90% of the patients were undiagnosed before the eye examination. This study of the prevalence of glaucoma in Brazil (3.4% for a population of 40 years or more) [9], one can estimate over 1.5 million people with glaucoma. According to this study, the great majority of these patients are not aware of their condition. This same prevalence study estimated that almost 90% of the patients were undiagnosed before the eye examination [9].

Although several methods are available for the diagnosis of glaucoma, no single screening test is sufficiently sensitive to discern persons with and without glaucoma [10]. It is therefore necessary to employ several tests such as tonometry, funduscopy, and perimetry [11]. Gonioscopy and pachymetry are also needed to establish the type of glaucoma and the target pressure, respectively. In this study, the authors chose to perform a comprehensive eye evaluation including all tests listed above.

Screening for glaucoma in the general population is not cost-effective because the prevalence of glaucoma is low overall, without consideration of risk factors, and the cost of screening is high [6]. Screening is advised for glaucoma in high-risk patients, such as those 40 years old or more [11], non-whites, and individuals a family history of glaucoma [6]. First-degree relatives of known glaucoma patients have been identified to be the most at risk of developing glaucoma, and of these, siblings had the highest risk [12,13]. In this study, the authors included only first-degree relatives of glaucoma patients and almost half of our patients were siblings (48.3%). Cross-sectional studies have suggested that more than 50% of all glaucoma is familial and a positive family history of glaucoma conveys up to a threefold increase in risk of developing primary open-angle glaucoma [14]. Wu et al. [15] have advised taking family history into account when planning screening strategies.

Evidence also shows that familial glaucoma has a greater disease severity with an earlier age of onset at diagnosis compared with patients with sporadic glaucoma [15]. In this pilot study, a relatively high rate (one-third) of participants had a positive family history of blindness caused by glaucoma, although the majority did not consider themselves to have glaucoma, although the difference between the groups was not significant (35.9% without glaucoma versus 21.4% in those with glaucoma; χ² = 0.215). This could be due to the small sample size, but also the fact that the mean age of the participants was rather low (50.4 years for the normal group and 54.3 years for those with glaucoma). It is possible that in the future some of the individuals classified now as normal could develop glaucoma.

The rate of participants diagnosed with glaucoma was high, compared to the expected prevalence in a Brazilian population (23.34% versus 3.4%) [9]. This can be explained by the fact that we have focused on high-risk patients: first-degree relatives. In Australia, Green et al. [16] emphasized the importance of inheritance in glaucoma, with major implications for screening. The rate was also higher than in other studies that had the same purpose. In the literature, glaucoma prevalence among first-degree relatives varies from 9.9% in the Baltimore Eye Survey [14] to 19.8% in the Barbados study [17]. Our pilot study did not have enough statistical power to correctly estimate the prevalence. Nevertheless, our estimated prevalence is closer to that from Barbados. This can be explained by the Brazilian population, which is highly mixed, with a great number of participants (35%) identifying themselves as non-whites.

There is not a current glaucoma screening strategy within the Brazilian public health system. However, given limited public health resources, the Brazilian Public Health System may consider this kind of selective screening, which can identify more cases at a low overall cost. All opportunistic detection for glaucoma occurs whenever the patient goes for an eye exam (usually to check for visual acuity and refraction) with the ophthalmologist. A study to evaluate the cost-effectiveness of this kind of screening for glaucoma in Brazil would be welcome. In Finland, an organized screening program (using Markov modeling) was considered cost-effective, mainly in older age groups (65 years or older) [10].

Although few cases (5/60) presented themselves with an IOP over 21 mmHg, IOP was significantly higher in the glaucoma group, compared with the normal group. As expected, CCT was significantly thinner in the glaucoma group. This highlights the importance of always trying to correlate IOP measurements to CCT in patients with a family history of glaucoma. Screening based only on IOP (e.g., IOP > 21 mmHg) would have missed the great majority of glaucoma cases. Measuring CCT must become an essential tool in glaucoma screening.

One of the known risk factors for significant visual field loss at initial presentation is a positive family history of glaucoma [18]. On the other hand, the great majority of glaucoma cases in the present study were early glaucoma. The relatively young mean age of participants can be an explanation, but also because these cases were identified through a screening program and not opportunistically found through random exams or because of suspected alterations in visual acuity. This demonstrates the importance of strategic screening in identifying early cases. The earlier the diagnosis, the lower the future costs [5]. This type of screening can have a major impact on public health and finance, and even more so in a resource-challenged developing country like Brazil.

The factors related to an elevated risk of glaucoma found in this study were IOP greater than 16 mmHg and CCT lower than 520 μm. Despite limitations (small sample size), these results reaffirm data from previous studies [19,20], but they also highlight the importance of pachymetry in a glaucoma screening setting for measurement of CCT. This test is easy and should be carried out whenever possible for those
with a positive family history of glaucoma. Unfortunately, few screening strategies include this exam as a routine [21].

A potential source of bias during the eye exam is the fact that the ophthalmologists knew CCT and IOP values before examining the optic disc, which could have been worse had they also seen the visual field results, but this was not the case. Visual field testing was performed after all other tests and was analyzed at the end of the campaign.

This limited glaucoma screening campaign highlights the importance of focusing on high-risk patients such as those with a positive family history of the condition. In addition, it demonstrated that pachymetry and gonioscopy should be included as routine exams, when screening for glaucoma in family members. Further investigations with a larger sample size that are properly powered and better designed are needed to confirm these results.

The high prevalence of glaucoma (23.4%) in this segment of the population warrants further studies and preventive actions from the public health sector in Brazil. As most screening-identified glaucoma cases presented themselves in this study in the early stages of the disease, this type of campaign can help to avoid major glaucoma-related consequences in the future.

**Conflict of interest**

All the authors have no conflict of interests linked to this article.

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**References**