Incidence of Open-Angle Glaucoma

The Barbados Eye Studies

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Objective: To measure the 4-year risk of open-angle glaucoma (OAG) in a black population.

Design: Population-based cohort study with 4 years of follow-up.

Setting: Simple random sample of residents of Barbados, West Indies, aged 40 years or older.

Participants: A total of 3427 members of the cohort (85% of those eligible).

Main Outcome Measure: Development of glaucoma visual field defects and optic disc damage, confirmed by automated perimetry, independent fundus photographic gradings, and standardized ophthalmologic examinations.

Results: The 4-year risk of OAG in black participants was 2.2% (95% confidence interval, 1.7%-2.8%), based on 67 newly developed cases of OAG. Incidence rates increased from 1.2% at ages 40 to 49 years to 4.2% at ages of 70 years or more, tending to be higher in men than women (2.7% vs 1.9%). About half of the incident cases were undiagnosed previously, and the rest were receiving OAG treatment. Of the 67 new cases of OAG, 32 had intraocular pressure of 21 mm Hg or less at baseline (1.2% incidence) and 35 had higher pressures (9% incidence). Risk was highest among persons classified as having suspect OAG at baseline (26.1%), followed by those with ocular hypertension (4.9%) and lowest in the remaining population (0.8%).

Conclusions: This longitudinal study provides new information on OAG risk, as well as the first incidence measurement in a black population. Although intraocular pressure increased risk, about half of the new cases had baseline pressures of 21 mm Hg or less. Results substantiate the high OAG risk in the population of African origin, especially in older adults; the relative role of intraocular pressure; and the considerable underdetection of new disease after 4 years of follow-up.

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OPEN-ANGLE glaucoma (OAG), which is especially frequent in black populations, is a leading cause of blindness worldwide. This optic neuropathy of unknown cause mainly affects older adults, requires lifelong treatment, and causes irreversible visual loss. Based on the results of several large prevalence studies, approximately 3% of white Americans, 10% of African Americans, and 15% of African Caribbeans older than 65 years have OAG. Although prevalence data are available, few population-based studies have continued follow-up to determine incidence. As such, information on the risk of OAG is very limited, being nonexistent for populations of African descent. Knowledge of incidence is important, as it measures the absolute risk of developing OAG over a time period and allows meaningful evaluation of risk factors. Incidence data are thus valuable for appraising OAG risk, understanding its etiology, and informing public health planning, with the eventual goal of preventing visual loss from the disease.

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Because of the scarcity of population-based longitudinal studies on OAG, most estimates of glaucoma incidence have been derived indirectly from available prevalence data, being mainly based on white populations. This report presents the first direct (observed) estimates of the incidence of primary OAG, which are based on a sizable number of new cases. Furthermore, it is the first report, to our knowledge, of OAG incidence in a predominantly black population.

RESULTS

Of the 4631 original participants with baseline examinations at the study site, 4040
PATIENTS AND METHODS

OVERVIEW

The Barbados Eye Studies cohort was identified from a prevalence study (1988-1992), based on 84% of a simple random sample of the Barbados population 40 to 84 years old. Four years after this baseline, the Barbados Incidence Study of Eye Diseases (BISED; 1992-1997) reexamined the surviving members of the cohort to determine incidence, progression, and risk factors for OAG, age-related cataract, age-related maculopathy, and diabetic retinopathy. These studies were funded by the National Eye Institute, Bethesda, Md, and included a coordinating center (University Medical Center at Stony Brook, Stony Book, NY); a data collection center (Ministry of Health, Bridgetown, Barbados, West Indies); and a fundus photography reading center (The Johns Hopkins University, Baltimore, Md). Informed consent was obtained from all study participants.

The BISED methods and protocol followed those used at baseline, which were described in detail elsewhere. In brief, the examinations included refraction and visual acuity, automated perimetry, applanation tonometry, blood pressure with a random-zero sphygmomanometer, anthropometric measurements, lens gradings, venipuncture for glycated hemoglobin, color stereo fundus photography of the disc and macula, and a standardized interview on demographic, ocular, medical, and other risk factor data. The visual field testing protocol involved suprathreshold screening of all participants with the full-field 120 program of the Humphrey Visual Field Analyzer (Allergan-Humphrey, San Leandro, Calif); central 64 points only; those with 1 or more absolute defects then underwent a full threshold test with the C24-2 program. With the use of a computer next to the perimeter, these results were immediately analyzed by the hemimeridional comparisons method. If the analysis showed low sum or defects in the comparisons of field sectors 5 vs 6 and 7 vs 8, individuals were referred for a full threshold test with the C30-2 program. The C30-2 results were similarly analyzed by the hemimeridional method. All participants with positive examination findings (bestcorrected visual acuity <20/30, visual field defects by hemimeridional analyses of threshold tests, intraocular pressure [IOP] >21 mm Hg, history of major eye diseases, family history of glaucoma, diabetes history, or inability to undergo perimetry, fundus photographs, or lens gradings) and a 10% sample were referred for a comprehensive ophthalmologic examination, repeated tonometry, and any additional visits needed to complete the visual field testing protocol. The study ophthalmologist reviewed all visual fields to provide a clinical interpretation of the results.

The baseline and follow-up photographs of the disc and macula were independently classified at the reading center by 2 masked graders. Discrepancies were resolved by consensus or adjudication by a third grader. Optic disc features evaluated to assess OAG status were horizontal and vertical cup-disc ratio with the use of a template, narrowest remaining neuroretinal rim, notching, asymmetry in cup-disc ratios between eyes, and disc hemorrhages. For comparability, these same features were also graded at the ophthalmologic examination. The quality assurance system for photographic gradings used in the prevalence study continued throughout BISED. The system involved evaluation of reproducibility within and between individual graders, as well as assessment of drift in photographic gradings over time.

OAG CLASSIFICATION

Definite OAG was defined by the presence of both visual field defects and optic disc damage in at least 1 eye, after (87%) were eligible for the follow-up visit, as 329 were deceased, 34 were too ill or disabled to complete the full study examination, and 228 had moved away. Among those eligible, 3427 (85%) participated in BISED. Table 1 shows that BISED participants had a median age of 57 years at baseline and 58.1% were female, with 93.2% self-reporting their race as black, 4.1% as mixed (black and white), and 2.7% as white or other. This demographic distribution was similar to that obtained at baseline and closely represents the racial composition of the Barbados population. As compared with the 3427 participants, the nonparticipants were older, as expected (median age at baseline was 61 years). Although they had fewer years of education (P = .01), no significant differences were found in other demographic variables (eg, sex, race, or residence) or in major diagnoses (eg, OAG or cataract) in logistic regression analyses.

Table 2 indicates that BISED achieved a high degree of data completeness for the OAG classification, with 3321 (97%) of participants completing at least 1 visual field test. Fundus photography was completed by 3335 participants, and 3140 (94%) had disc photographs of gradable quality. Good reproducibility between 2 independent graders was achieved, with weighted k ranging from 0.69 to 0.74 for horizontal and 0.73 to 0.78 for vertical cup-disc ratios, as well as from 0.71 to 0.75 for neuroretinal rim sizes. A total of 3298 participants (96%) had photographic and/or clinical gradings of the optic disc. Among those referred for an ophthalmologic evaluation, 96% completed the examination. A high correlation was found between photographic and clinical cup-disc ratio gradings (r = 0.79 and 0.81 for horizontal and vertical).
vertical, respectively). The main reasons for incomplete visual field or photographic data were advanced cataract and severe visual loss; an additional reason was that 44 ophthalmologic examinations were performed at the participants’ homes.

At baseline, 207 persons in the BISED cohort were classified as having OAG and 3 had bilateral secondary or other types of glaucoma, thus leaving 3217 individuals as the population at risk for OAG. Of these, 71 met the criteria for incident OAG at follow-up; 67 were black, 2 were mixed, and 2 were white participants. Most cases were unilateral, with 25 newly affecting the right eye; 28, the left eye; and 18, both eyes. Because of the small number of white and mixed participants, these are excluded from the remaining analyses.

Table 3 presents OAG incidence estimates in black participants, by age at baseline and sex. The 4-year incidence of OAG was 2.2% (95% confidence interval, 1.7%-2.8%), based on 67 incident cases of glaucoma. An additional 81 black participants were classified as having suspect OAG and thus were not included in the incidence estimates. Age-specific incidence increased from 1.2% (95% confidence interval, 0.6%-2.1%) in persons 40 to 49 years of age to 4.2% (95% confidence interval, 2.6%-6.3%) in those aged 70 years and older. Incidence was consistently higher among men than women in each age group. The age- and sex-adjusted incidence, accounting for nonparticipation, remained the same.

Table 4 shows that, of the 67 black participants with incident OAG, four fifths met the most stringent criteria for visual field loss (groups 1, 3, and 5) and 88% for optic disc damage (groups 1, 2, 5, and 6) in at least 1 eye. A similarly high percentage had a definite clinical diagnosis of OAG at the BISED visit (groups 1, 2, 3, and

### Table 2. Data on Open-Angle Glaucoma Classification (n = 3427)

<table>
<thead>
<tr>
<th>Test Description</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humphrey perimetry</td>
<td>3321 (97)</td>
</tr>
<tr>
<td>One test only</td>
<td>1768 (52)</td>
</tr>
<tr>
<td>Two tests only</td>
<td>1153 (34)</td>
</tr>
<tr>
<td>Three tests</td>
<td>400 (12)</td>
</tr>
<tr>
<td>Optic disc evaluation</td>
<td></td>
</tr>
<tr>
<td>Gradable photographs</td>
<td>3140 (94)*</td>
</tr>
<tr>
<td>Photographic or clinical gradings</td>
<td>3298 (96)</td>
</tr>
<tr>
<td>Ophthalmologic examination</td>
<td>2337 (96)†</td>
</tr>
</tbody>
</table>

*Percentage of those with fundus photographs (n = 3335).
†Percentage of those referred (n = 2425).
in visual acuity were noted, with 10.4% of incident cases of OAG having an acuity worse than 20/40 at baseline, as opposed to 17.9%, 4 years later. Although these frequencies were somewhat higher than in the nonincident group, they could be influenced by age differences between groups, as visual acuity losses were mainly caused by cataract. None of the new cases had visual acuity impairment (acuity of 20/200 or worse) caused by glaucoma.

**Table 6** shows that OAG risk varied with the baseline glaucoma classification and the baseline IOP. When the baseline classification was considered, the highest risk (26.1%) was found among participants previously classified as having suspect OAG because they met some, but not all, of the study criteria for definite OAG. Among the rest of the population, those with the next highest risk (4.9%) were participants classified as having ocular hypertension, that is, with IOP greater than 21 mm Hg and no glaucoma findings at the initial examination. The lowest risk (0.8%) was observed in participants without glaucoma or ocular hypertension at baseline. If one only considers IOP at baseline, regardless of glaucoma classification, 35 of the 389 participants with IOP greater than 21 mm Hg at baseline developed OAG, for an incidence frequency of 8.4%.
of 9.0%. In contrast, 32 of the remaining 2600 participants with IOP of 21 mm Hg or less at baseline developed OAG, for an incidence of 1.2%.

The Figure presents the baseline IOP distribution of the incident and nonincident cases. Although the incident cases tended to have higher IOP at baseline, there was considerable overlap between both distributions. Almost as many cases developed in participants with IOP of 21 mm Hg or less at baseline than in those with higher values.

The study provides new information on the risk of developing OAG in a population after a 4-year interval. This report is based on the largest number, to our knowledge, of incident cases of OAG in any population-based study, thus allowing reasonably precise estimates. Furthermore, this investigation presents the first observed incidence estimates for OAG in a population of African origin. The results indicate a large risk of OAG in the cohort, which increased with age and tended to be higher in men than women (Table 3). In persons 40 years of age or older, the 4-year incidence of OAG was 2.2% (95% confidence interval, 1.7%-2.8%), based on 67 incident cases, or 0.6% per year (Table 3). This risk was especially high for older adults, exceeding 1% per year in the oldest age group. In fact, almost two thirds of the new cases developed in participants who were at least 60 years of age at baseline. Incidence was consistently higher in men than women for every age group, following the age- and sex-specific pattern observed at baseline.14 Despite this trend, the sex difference in risk was not statistically significant, which could be a result of insufficient sample size. Whereas prevalence studies have varied concerning sex differences in OAG,3,5,15-17 our results suggest a higher OAG risk in men than women in our study population.

About half of the new cases were undiagnosed before the follow-up examination and the rest were receiving treatment (Table 5). No significant differences in age, sex, or IOP were found between newly diagnosed and previously diagnosed cases. This result parallels our findings at the baseline examination, where only half of the participants with OAG reported previous diagnosis and treatment.7 Similar results were reported by other studies of OAG prevalence13,18-20 with different populations and varying access to eye care, indicating that about half of cases of established OAG may be undetected. Our comparable observation for the detection of newly developed OAG is of interest, especially considering the relatively short interval between the baseline and follow-up examinations. These results suggest that early detection of all new OAG in a population may require examination intervals of 4 years or less.

Participants with higher IOP at baseline were at increased risk of OAG, as expected, with higher incidences observed for those with IOP greater than 21 mm Hg (9% vs 1.2%; Table 6). These findings were similar to those seen at baseline, where IOP was a major risk factor and was strongly associated with OAG.7,14,21 Although the role of IOP as a risk factor for OAG is well known, it is important to consider its role from a population perspective, where most individuals do not have high IOP levels. In our population, almost as many new cases arose in persons with IOP of 21 mm Hg or less at baseline as in those with higher pressures (32 vs 35; Table 6). Given the variability of IOP, the baseline measurements may have misclassified the IOP status of some individuals. Even with this possibility accounted for, our results indicate that a considerable percentage of OAG risk can be attributed to factors other than IOP.22 In fact, when the traditional, arbitrary criterion of greater than 21 mm Hg is used to define “high IOP” (which encompassed 13% of the population at risk), the risk attributable to high IOP was 46%. Using a criterion based on the highest 10% of the IOP distribution (>25.3 mm Hg in our population at risk) yielded an attributable risk of 37%.

The inconstant relationship between IOP and OAG risk is further documented by the overlap of the IOP distribution of the incident and nonincident cases at baseline (Figure). Still, higher-than-average IOP was an important finding among incident cases. Persons with newly diagnosed OAG showed significant increases in IOP at follow-up (Table 5), with the median IOP being 2.4 mm Hg higher than at baseline. Similarly, although about half of the incident cases had IOP greater than 21 mm Hg at baseline, more than two thirds had reached these levels at follow-up.

In addition to changes in IOP, increases were seen in horizontal and vertical cup-disc ratios, especially for the latter, as four fifths of the incident cases had reached vertical cup-disc ratio of 0.7 or higher (Table 5). Although deterioration in visual acuity was noted during
the 4-year period, most acuity losses were attributed to cataract and none of the new cases had visual acuity impairment (as previously defined) caused by OAG.

What is the validity of these results? The study has several methodologic strengths, which add support to its conclusions. A participation rate of 85% was achieved in those eligible for follow-up, which is high for a population-based study of an aged cohort. Furthermore, the analyses comparing participants and nonparticipants suggest a good overall representation of the original cohort. Although nonparticipants were older and of lower educational status, both groups were similar in other demographic factors and major ocular diagnoses (Table 1). A creditable participation rate was achieved even when all losses to follow-up were considered, which were mainly the result of death, since 74% of the entire cohort had a follow-up examination.

A well-defined categorization system was used to classify incident cases of OAG, which required 3 sets of criteria: visual field defects (determined by computer-based perimetric criteria with clinical interpretation by an ophthalmologist), optic disc abnormality (determined by independent gradings of fundus photographs and ophthalmologic evaluation), and an ophthalmologic assessment to exclude other possible causes. This classification system aimed to achieve high specificity of the OAG diagnosis, thus reducing misclassification of cases of suspect glaucoma as early OAG. A high degree of data completeness was achieved for the OAG classification, with most individuals completing automated perimetry, optic disc gradings, and an ophthalmologic examination in the study (Tables 2 and 4). The completeness of the information available enhanced the study's ability to classify OAG status, which is an especially difficult process in a population study. This process was further complicated by the advanced age of incident cases at the BISED examination, which led to the single-plus (+) and double-plus (++) system to classify data completeness (Table 4). However, most of the incident cases were classified as ++ for completeness of visual fields (81%), optic disc (88%), and clinical (85%) criteria, with correspondingly small frequencies classified as + for these criteria. If we were to exclude the participants with less complete data, the incidence estimates would be reduced accordingly. Such selective estimates, however, would not provide a representative measurement of the underlying risk in the general population. Similarly, the use of different definitions, eg, those based only on optic disc or visual field damage (rather than on both), would lead to different estimates. To place our results in context with our earlier prevalence data, we reported incidence based on a glaucoma definition that parallels that used at baseline. The exploration of alternative diagnostic criteria, which would be of methodologic interest, is a complex issue that merits a separate article.

Because of the high specificity of the criteria to define OAG, the incidence rates reported herein represent conservative estimates. Nonetheless, even when participants with less complete data are excluded, the estimates are still considerably higher than those previously available. To date, only 1 known study by Bengtsson, in Dalby, Sweden, has the distinction of reporting direct OAG incidence estimates, which were based on population-based longitudinal data. Persons were classified as having manifest glaucoma if repeatable visual field defects, not explained by other causes, coexisted with a loss of neural tissue in the optic nerve head of the same eye. The incidence rate of manifest glaucoma was 0.24% per year for persons 55 to 85 years of age and was based on 26 incident cases, which developed during about 10 years of follow-up. In addition to finding a much lower overall risk of OAG than in Barbados, the Swedish study reported that manifest glaucoma was independent of age and that OAG incidence was higher in women than in men. Given the differences between studies, these inconsistent findings may result from underlying differences in populations, study criteria, or other reasons.

Leske et al9 developed a method to estimate incidence from age-specific prevalence data and used it to estimate OAG incidence, based on the white adult populations from the Ferndale and Framingham studies.10,21,22 Open-angle glaucoma was defined as the presence of at least 1 glaucomatous visual field defect, after other possible causes were excluded. The 5-year incidence rates with this method translate to 1-year rates of 0.04% and 0.22% for ages 55 and 75 years, respectively. Similar yearly estimates (0.06% and 0.20% at ages 55 and 75 years, respectively) were derived with the same method by pooling age-specific prevalences from several studies of whites. When OAG prevalence from African Americans and African Caribbeans was pooled,3,7,24 the resulting incidence estimates were 4 times higher at age 55 years (0.26%) and 2 to 3 times higher at age 75 years (0.54%) than those in whites.24 The precision of these estimates is difficult to interpret because of the diversity of OAG definitions and accuracy of the prevalence data from the different studies. Nevertheless, all of these estimates are lower than the current results, a discrepancy explained by the lower pooled prevalence used to derive the incidence estimates. For example, although the prevalence of OAG in black participants from the Barbados Eye Study was 7%,7 the prevalence in African American participants in the Baltimore Eye Study was 4%.3 The pooling of data from both studies results in lower estimates than those based on the Barbados data alone. In fact, indirect estimates based on our prevalence data, using the same statistical methods, closely approximate our observed incidence rates.

What is the applicability of the current findings to other populations? The incidence rates reported document the high risk of OAG in populations of African descent, especially at older ages, which is not explained by IOP alone. Although incidence rates for African American populations are not available, indirect estimates also suggest an increased risk, which may be somewhat higher in African Caribbeans. Although both groups originated from the same area in Africa, varying degrees of admixture occurred in both populations26 and may account, to some degree, for the observed differences in frequency of OAG. For example, the 4% prevalence in the black participants of the Baltimore Eye Survey was similar to the 4% prevalence found among the mixed (black and white) participants of the Barbados Eye Study.7 In the latter study, the racial categories were well sup-
ported by results of skin pigmentation gradings and blood group distribution. Gene-environment interactions, yet to be determined, may also play a major role. However, although the frequency of OAG may vary across populations, there is no reason to believe that the intrinsic mechanisms of the disease will differ. As such, whereas the magnitude of the OAG risk may be higher in the BISED population than in others, the underlying risk factors identified by the study should be generally applicable to other populations.

CONCLUSIONS

This is the first study, to our knowledge, to measure the risk of OAG in a black population. Given its sample size, it is also the first study to provide sufficiently precise incidence estimates for any population. The magnitude of the risk increased with age, reaching 1% per year at older ages. In addition to quantifying risk over a relatively short interval, the data substantiate the underdetection of new cases. After 4 years of follow-up, about half of the incident cases were undiagnosed, suggesting the need for frequent examinations to detect early OAG, especially at older ages.

Although participants with higher IOP were at higher risk, about half of the new cases developed in persons with IOP of 21 mm Hg or less at baseline. These results highlight the importance of prognostic factors, other than IOP, in determining the development of OAG. The high risk of OAG in populations of African descent, where the disease is a primary cause of blindness, emphasizes the public health implications of our findings. Additional information will be gleaned from the continuing follow-up of the cohort.

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