Predictors for Incidence of Primary Open-Angle Glaucoma in a South Indian Population

The Chennai Eye Disease Incidence Study

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Objective: To determine the 6-year incidence of primary open-angle glaucoma (POAG) and its associated predictors.

Design: Population-based cohort study.

Participants: A total of 4316 subjects without POAG at baseline who were 40 years of age and older from a south Indian population.

Methods: Participants were examined at baseline and after a 6-year interval. Detailed ophthalmic examination included applanation tonometry, gonioscopy, pachymetry, optic disc evaluation, and automated perimetry. Glaucoma was defined using the International Society of Geographical and Epidemiological Ophthalmology Classification. Multivariable logistic regression was performed to identify the baseline risk factors that could predict the incident POAG.

Main Outcome Measures: Six-year incidence of POAG and its associated risk factors.

Results: In 6 years, incident POAG developed in 129 subjects (2.9%; 95% confidence interval [CI], 2.4−3.4; male-to-female ratio, 65:64). Baseline age was a risk factor. In reference to the group 40 to 49 years of age, the incidence increased from 2.3 (95% CI, 1.4−3.7) for the group 50 to 59 years of age to 3.5 (95% CI, 2.2−5.7) for the group 60 to 69 years of age ($P < 0.001$). Other baseline risk predictors were urban residence (odds ratio [OR], 1.6; 95% CI, 1.1−2.2; $P = 0.01$), higher intraocular pressure (IOP; OR, 2.0; 95% CI, 1.5−2.6 per 10 mmHg; $P < 0.001$), myopia (OR, 1.7; 95%, CI, 1.1−2.5; $P < 0.001$), and axial length (OR, 1.5; 95% CI, 1.0−2.2 per millimeter; $P = 0.03$). Thinner corneas with higher IOP at baseline had the highest incidence of POAG. In 80% of the urban population and 100% of the rural population, incident glaucoma was previously undetected.

Conclusions: A significant proportion of this population demonstrated incident POAG. The baseline risk factors could help in identifying those at highest risk of disease. *Ophthalmology 2014;■:1−7 © 2014 by the American Academy of Ophthalmology.*

Glaucoma has been identified as the second most common cause of blindness worldwide. According to the recent estimates, 44.7 million are likely to have primary open-angle glaucoma (POAG) worldwide.[1] Of these, 6.48 million will be from India.[1,2] Prevalence rates from population-based cross-sectional studies in India have reported rates for POAG similar to those in the West. These studies also identified possible risk factors for the disease.[2,3] Available information suggests older age and intraocular pressure (IOP) as the risk factors for prevalent and incident POAG. The other reported risk factors for POAG are family history of glaucoma, African ancestry, and a thinner central corneal thickness (CCT).[2−9] In a chronic disease such as POAG, incidence studies provide a direct estimate of the development of the disease over a period of time and are likely to bring out valuable information about the risk factors. There are few incidence studies worldwide[10−15] and none from India. We reported the prevalence of POAG in a rural and an urban cohort of southern India.[16,17] In this article, we report the incidence of POAG derived from the 6-year follow-up examination of the same population. We also describe possible associated risk factors and the differences between the rural and urban populations.

Methods

Study Population

The methodology of and the prevalence of POAG from the Chennai Glaucoma Study were reported previously.[16−18] In summary, the Chennai Glaucoma Study was a cross-sectional population-based study conducted to measure the prevalence of glaucoma in a rural and urban population in southern India. The study cohort consisted of 9600 subjects (rural-to-urban ratio, 4800:4800) 40 years of age or older and was carried out from 2001 through 2004. From the cohort, 7774 subjects (rural-to-urban ratio, 3924:3850) participated in the study. The present study, The

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Chennai Eye Disease Incidence Study, was conducted 6 years after the baseline examination (2007−2010). The subjects in the cohort were re-enumerated by social workers. These subjects were invited for a detailed examination at the base hospital. We reexamined these participants from the cohort to determine the incidence and the progression of eye diseases. The study was performed after obtaining written informed consent, in accordance with the tenets of the Declaration of Helsinki. The institutional review board approved the study.

Data Collection

A detailed history pertaining to medical and ophthalmic conditions was elicited that included any history of diabetes mellitus or hypertension or use of medication for either of the diseases. Three ophthalmologists (glaucoma specialists: R.G., M.P., N.C.) and 3 optometrists (R.A., L.V., R.S.), who were trained for the study, performed the ophthalmic examination. The examination techniques used were same as those of the baseline prevalence study. In brief, the examination consisted of measuring best-corrected visual acuity using logarithm of minimum angle of resolution (logMAR) 4-m charts (Light House Low Vision Products, New York, NY), external examination and pupillary evaluation using a flashlight, slit-lamp biomicroscopy, IOP measurements using a Goldmann applanation tonometer (Zeiss AT 030 Applanation Tonometer; Carl Zeiss, Jena, Germany), gonioscopy using a 4-mirror Sussmann lens (Volk Optical, Inc., Mentor, OH), grading of lens opacification at the slit lamp using the Lens Opacities Classification System II and Lens Opacities Classification System III with a minimum pupillary dilation of 6 mm, detailed retinal examination with a binocular indirect ophthalmoscope using a +20-diopter (D) lens, and stereoscopic evaluation of the optic nerve head using a +78-D lens at the slit lamp. The vertical and horizontal cup-to-disc ratios (CDR) were measured and recorded. Presence of any notching, splinter hemorrhages, and peripapillary atrophy was documented. A nonsimultaneous stereo optic disc photograph was obtained in eyes with clear media. Central corneal thickness was measured using the DGH 550 ultrasonic pachymeter (DGH Technology, Inc., Exton, PA). Ocular biometry was performed using an ultrasonic biometer (Ocuscan; Alcon Laboratories, Inc., Fort Worth, TX). Automated visual fields were measured for all subjects with best-corrected visual acuity of 4/16 (0.6 logMAR units) or better, using screening C-20-1 program of frequency doubling perimetry (Carl Zeiss Meditec, Inc., Dublin, CA).

A provisional diagnosis of suspected primary open-angle glaucoma was made when the subject with an open angle had 1 or more of the following conditions: IOP of 21 mmHg or more in either eye; vertical CDR of 0.7 or more in either eye or CDR asymmetry of 0.2 or more (with no other reason for asymmetry); or focal thinning, notching, or a splinter hemorrhage. All these subjects underwent a threshold visual field test using the Swedish interactive threshold algorithm standard 24-2 program (model 750; Humphrey Instruments, San Leandro, CA). A glaucomatous field defect was diagnosed using a single, reliable threshold visual field examination (Swedish interactive threshold algorithm standard 24-2). The field was considered to be abnormal if the glaucoma hemifield test results were outside normal limits and 3 or more abnormal, contiguous, nonedge points were depressed to $P < 0.05$. Reliability criteria were those recommended by the instrument's algorithm (fixation losses, <20%; false-positive and false-negative rates, <33%).

Diagnostic Definitions

Cases of glaucoma were defined using the International Society of Geographical and Epidemiologic Ophthalmology classification.[19] Glaucoma was classified according to 3 levels of evidence. In category 1, diagnosis was based on structural and functional evidence. It required CDR or CDR asymmetry equal to or more than the 97.5th percentile for the normal population or a neuroretinal rim width reduced to 0.1 CDR (between 10 and 1 o'clock or between 5 and 7 o'clock) with definite visual field defects consistent with glaucoma. Category 2 was based on advanced structural damage with unproven field loss. This included those subjects in whom visual fields could not be obtained or whose results were unreliable, with CDR or CDR asymmetry equal to or more than the 99.5th percentile for the normal population. Finally, category 3 consisted of participants with an IOP more than the 99.5th percentile for the normal population, whose optic discs could not be examined because of media opacities. For the current study population, the 97.5th and 99.5th percentiles were as follows: CDR, 0.7 and 0.8; CDR asymmetry, 0.2 for both; IOP in an urban population, 24 and 30 mmHg; IOP in a rural population, 21 and 25 mmHg.[16,17] Blindness was defined as a best-corrected logMAR visual acuity of worse than 2/40 (1.3 logMAR units), constriction of the visual field of less than 10° from fixation with an unmeasurable (less than 0) threshold value for all test points outside the central 10° in the better eye, or both.[20] Hyperopia was defined as spherical equivalent (SEQ) of more than 0.50 D, and myopia was defined as a spherical equivalent of less than −0.50 D in a phakic eye.[21] Diabetes mellitus and systemic hypertension were detected based on current use of antidiabetic or systemic antihypertensive medication. Body mass index (BMI) was defined as weight in kilograms divided by the square of height in meters (kg/m^2). The BMI categories were grouped as underweight (<18.5 kg/m^2), normal (18.5−25 kg/m^2), overweight (>25 kg/m^2), and obese (≥30.0 kg/m^2).

Data Analysis

Statistical analysis was performed using SPSS software version 15 (SPSS, Inc., Chicago, IL). All collected data were entered into a central database with built-in range checks and were rechecked for accuracy. Incident POAG was defined as the development of POAG during the follow-up in subjects without POAG at baseline. Subjects were categorized in to 4 groups based on baseline age: 40 to 49, 50 to 59, 60 to 69, and 70 years and older. We compared variables between POAG subjects and controls using the *t* test for continuous variables and the chi-square test for categorical variables. Multivariable logistic regression was performed to look for associations between factors such as age, gender, location of

Table 1. Comparison of Baseline Characteristics of Participants and Nonparticipants in the Chennai Eye Disease Incidence Study

Variables	Participants (n = 4421)	Nonparticipants (n = 3353)	*P* Value
Age (yrs)*	52.8 (9.7)	56.4 (11.3)	<0.001
Male-to-female ratio	1972:2449	1500:1853	0.46
Rural-to-urban ratio	2510:1911	1414:1939	<0.001
IOP (mmHg)*	15.2 (4.3)	15.5 (4.4)	0.001
CCT (μm)*	510.4 (34.9)	511.4 (37.1)	0.19
VCDR*	0.42 (0.2)	0.44 (0.2)	<0.001
Axial length (mm)*	22.6 (0.9)	22.6 (1.0)	0.95
Hypertension (no:yes)	3831:590	2748:605	<0.001
Diabetes mellitus (no:yes)	3909:512	2829:524	<0.001

CCT = central corneal thickness; IOP = intraocular pressure; VCDR = vertical cup-to-disc ratio.
*Mean ± standard deviation.