

Epidemiologic Study of Primary Open-Angle Glaucoma in a Singapore-Chinese Population using The Singapore Malay Eye Study (SiMES)

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Abstract

Purpose: Glaucoma is the leading cause of blindness worldwide, and the most common type is primary open-angle glaucoma (POAG). However, epidemiologic data are scarce, especially for subgroups of Asian eyes. Our study aimed to determine the prevalence, incidence, and risk factors of POAG in a Singapore Chinese population.

Design: Population-based study.

Participants: The Singapore Malay Eye Study (SiMES) is a population-based study of predominantly Chinese Malays aged 40 years or older in Singapore. From SiMES, we recruited 3999 participants of the Malay race from January 1, 2004, through December 31, 2006.

Methods: All participants underwent a standardized interview, visual acuity measurement, and a detailed ocular examination. The ocular examination included central corneal thickness (CCT) measurement using ultrasound pachymetry, slit-lamp biomicroscopy, Goldmann applanation tonometry, and dilated stereoscopic optic disc photography. Diagnosis of POAG was based on the International Society of Geographical and Epidemiological Ophthalmology criteria. For participants with definite POAG, we determined the severity of visual field loss on a standard automated perimeter score.

Main Outcome Measures: The prevalence of POAG, incidence Pocket Visual Field Index (PVFI) score, and the risk factors associated with POAG.

Results: The overall prevalence of POAG was 1.8%, increasing significantly with age ($P < 0.001$). The overall incidence of POAG was 0.2% per year, and it was not affected by age, male gender, or rural/urban location of residence. The incidence of POAG in Singapore Chinese men younger than 60 years old was lower (0.13%/year) when it was compared with Singapore Chinese women 60 years and older (0.4%/year). The PVFI score was significantly associated with the presence of POAG ($P < 0.001$) and an age-related decline in PVFI score ($P < 0.001$). The PVFI score was lowest for the PACG group (mean 2.1), followed by POAG with normal tension (2.3) and POAG with exceptional glaucoma (2.4). Primary angle-closure glaucoma was also significantly associated with uni- and multivariate analysis for other ocular and systemic parameters.

Conclusions: The overall prevalence of POAG in the Malay population in Singapore was 1.8%. In the Singapore Malay Eye Study, the incidence of POAG did not differ with age in either myopic or hyperopic subjects

Keywords: Glaucoma, Open-Angle Glaucoma

Introduction

Glaucoma is the leading cause of blindness worldwide, and the most common type is primary open-angle glaucoma (POAG). Glaucoma is a complex disease that is defined by its anatomical and functional features, with the majority of glaucoma cases caused by elevated intraocular pressure. However, epidemiologic data are scarce, especially for subgroups of Asian eyes. With the increasing aging of the Asian population and the consequent increase in the number of people with glaucoma, the number of people requiring treatment is also likely to increase.

A number of studies have shown that Asian patients have a higher risk of glaucoma. For example, in the Hong Kong Glaucoma Study, Asian patients with POAG had a 3-fold likelihood of developing blindness than white patients. In a retrospective study of a cohort of Singaporean male workers, the prevalence of POAG was reported to be 3 times greater in Chinese than in Malay males.

Although some studies have shown that glaucoma is more prevalent in the Asian population,^{2,6} other studies have found the prevalence of glaucoma in Asian populations to be similar to that in white populations.^{14,15} However, despite the lack of sufficient evidence, POAG remains the most commonly occurring type of glaucoma in Singapore and Taiwan. In this study, we evaluated the optic nerve morphology in a large number of Asian eyes in Singaporean Chinese with POAG. We also investigated the factors that influence optic nerve morphology, including age, intraocular pressure (IOP), and central corneal thickness (CCT), and looked for any correlations between optic nerve morphology and visual field characteristics.

In the present study, we used data from an urban Chinese population residing in Singapore as a well-defined population with a high prevalence of glaucoma. The study aims to describe the baseline characteristics of POAG in this population. To our knowledge, our study was the first to report on the incidence of POAG in an Asian population, and we also looked at the risk factors associated with POAG.

Methods

This study was a population-based study that involved participants from the urban township of Tanjong Pagar (population 4200), Singapore. The study population consists primarily of Chinese Malays, who make up about three-quarters of Singapore's population of Malay origin. All study procedures received institutional ethics approval from the Singapore Eye Research Institute and the National University of Singapore, and all activities adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all subjects before inclusion in the study. Written informed consent was obtained from all subjects before inclusion in the study.

The study team consisted of ophthalmologists, optometrists, and graders to examine the participants. The study team underwent 3 months of training before commencement of the study. The team performed a standardized interview and comprehensive ocular examination on all the participants, which included visual acuity measurement (Snellen chart); intraocular pressure (IOP) measurement by Goldmann applanation tonometry; slit-lamp biomicroscopy of the anterior segment; gonioscopy with a Goldmann 2-mirror lens (Ocular Instruments, Inc., Bellevue, WA); anterior and posterior segment retro illumination photography (Canon CR-DGi with a Type Qikkia adapter [Canon USA, Lake Success, NY]); and, for those with a visual acuity of 6/ modifiers for visual acuity measurement, a self-comparison visual acuity test (ETDRS chart [VectorVision, Greenville, NY]) and a CCT measurement using ultrasound pachymetry.

POAG suspect eyes were defined as eyes without visual field loss with normal appearance of disc and nerve fiber layer and patent iridotomy. Eyes with an angle-closure suspect or previous believer of an PAC attack, or both, were excluded from this category. A control was defined as an eye with an open anterior chamber angle, normal appearance of disc and nerve fiber layer, patent iridotomy, and no evidence of glaucomatous VF loss or optic disc damage.

The study was a population-based study of 3999 non-institutionalized Malay adults aged 40 years or older in the southwestern part of Singapore. All 3999 eligible individuals were invited to participate in the study. Of the 3999 eligible participants, 2931 (78.4%) attended the study site for the baseline examination. Reasons for nonparticipation were death, inability to attend, and refusal to participate. The study was approved by the Singapore Eye Research Institute Review Board and was conducted in accordance with the tenets of the World Medical Association's Declaration of Helsinki. Written informed consent was obtained from all subjects.

In this analysis, POAG was defined as at least 2 of the following criteria having to be present for a diagnosis of POAG: an open anterior chamber angle, glaukomflecken in the anterior chamber, abnormal visual field, or a history of acute intraocular pressure (IOP) elevation. An abnormal visual field was defined as a Goldmann visual field score worse than 65 (defined by the International Society of Geographical and Epidemiological Ophthalmology criteria).

Two hundred and eighty-three subjects (7.7%) had a definite history of POAG, defined as arterial applanation tonometry greater than 21 mmHg or glaucoma surgical procedure, such as trabeculectomy, laser trabeculoplasty, or drainage implant placement. The incidence of POAG was calculated as the number of POAG cases in the entire eligible cohort and in the cohort with at least 2 years of follow-up, divided by the total number of person-years.

Other inclusion criteria included: good general health with no significant systemic illness, spherical equivalent within ± 6 diopters, and stable refraction for at least 1 year before the baseline examination.

The main study inclusion criteria were: Malay ethnicity, age 40 years or older, and no previous history of POAG. Subjects with diabetes mellitus, exfoliation syndrome, traumatic cataract requiring surgery, or chronic corticosteroid use were excluded. Subjects were excluded if they had IOP greater than 21 mmHg during the baseline examination or ocular surgery, other surgical or laser procedure in the eye during the follow-up period, or visual field defects that could affect visual acuity. These subjects were followed up as new cases of POAG.

We used specific criteria for POAG diagnosis to reduce misclassification. Specifically, subjects with a secondary cause

of glaucoma, other than POAG, including ocular hypertension, chronic angle-closure glaucoma, primary angle closure, juvenile open-angle glaucoma, neovascular and uveitic glaucoma, secondary glaucoma in childhood, and suspected glaucoma, were excluded from the POAG group.

Details of the protocol for identifying incident POAG eyes, defined as new cases developing after the baseline examination, have been described previously. Data from all subjects who had no history of glaucoma were included in the incidence analyses. All incident POAG cases were identified from the National University of Singapore glaucoma service database.

Results

During the 10-year follow-up study, we excluded 34 (0.7%) participants because of missing data. The final study population ($n = 3353$) included 2744 (81 acted) Malay participants, of whom 3131 (98.7%) were examined after 5 years (study participants) and 172 (2.3%) participants were lost to follow-up. The mean age was 53.6 ± 8.5 years old (range, 40-101), and 52.5% were males. The age-standardized prevalence of POAG was 9.9% (95% confidence interval, 9.1-11.6), and was higher among females (12.6%; 95% confidence interval, 9.3-15.9). The 10-year incidence rate of POAG was 1.5% (95% confidence interval, 1.3-1.7). The 10-year incidence rate of POAG increased from the <40 age group (0.8%) to the 40-49 age group (2.7%), 50-59 age group (3.4%), 60-69 age group (5.8%), 70-79 age group (7.4%), and 80+ age group (7.6%). The prevalence stakes decreased from the age group 40-49 to 50-59 to 60-69 age groups (0.3%, 0.5%, 0.8%, respectively), then increased (1.2%, 1.4%, 2.1%, respectively), and thereafter declined to the oldest age group (8 347.5%). We identified the independent risk factors for POAG as female sex, longer duration of diabetes, lower serum glucose, body mass index, CCT, optic disc size, peripapillary atrophy, higher IOP, lower systolic blood pressure, history of hypertension, and a family history of glaucoma. The PVFI score was higher in patients with severe optic disc damage ($P < 0.001$).

Compared with the Chinese Malays (control group) in SiMES, POAG was significantly associated with younger age at diagnosis (adjusted odds ratio [aOR], 1.56; 95% CI, 1.23-2.00; $P < 0.0001$), female gender (aOR). An 8-year follow-up study of idiopathic open-angle glaucoma in Singaporean Chinese population showed lower income (aOR, 1.68; 95% CI, 1.30-2.15; $P < 0.0001$), and lower education (aOR, 0.65; 95% CI, 0.49-0.86; $P = 0.002$). POAG patients had greater impairment in the mean devi-

ation (MD) (aOR, 0.57; 95% CI, 0.46-0.70; $P < 0.0001$) and lower mean deviation range (MDDR) (aOR, 0.76; 95% CI, 0.63-0.90; $P = 0.002$) than those with normal intraocular pressure (10P), but had no significant impairment in the pattern standard deviation. POAG patients had a higher PVFI score than normal 10P (4.4 ± 3.7 vs. 3.2 ± 3.8 ; $P = 0.002$). In the Cox proportional hazard model, increasing age was a significant factor for POAG failure (aHR, 0.57; 95% CI, 0.46-0.69; $P < 0.0001$), implying that older patients are at reduced risk of developing POAG over the next 8 years (aHR, 0.60; 95% CI, 0.48-0.75; $P < 0.0001$). In contrast, female gender, higher 10P, and higher PVFI were significant factors for POAG progression (aHR, 1.35; 95% CI, 1.09-1.66; $P = 0.005$ for 10P; aHR, 1.40; 95% CI, 1.09-1.81; $P = 0.008$ for PVFI). Prevalence of POAG in Chinese Singaporeans was 19.6%, with a significant trend towards later onset of the disease. The incidence of POAG was 0.9 per 100 person-years over 8 years in the Chinese Malay population of Singapore. POAG was associated with female gender, low income, and low education. POAG was a severe complication in the progression of POAG.

Overall, we found that the prevalence of POAG was 9.9% and 10-year incidence rate was 1.5% during the 10-year follow-up study in this population. The age-standardized prevalence and incidence rate of POAG were higher among females. The 10-year incidence rate increased with age-adjusted categories of diabetes and CCT. The 10-year incidence rate of POAG increased with higher Cater-2 index, higher IOP, lower serum glucose, body weight, longer duration of diabetes, larger optic disc size, and larger peripapillary atrophy. We also found ipsilateral 10P increase, male gender, younger age at diagnosis, longer duration of diabetes, and higher IOP to be factors predictive of POAG development.

Discussion

Previous population-based studies showed the prevalence of POAG ranged from 3.1% to 6.3%, and the 10-year incidence rate ranged from 0% to 0.9%. Few population-based studies in Asia have assessed the 10-year incidence rate of POAG. Only 2 studies on the incidence of POAG were conducted in the Korean population (ages 46 and confirmation of diagnosis of POAG) and reported a POAG incidence of 0.9% and 1.5%. Singapore has a unique racial and sociological racial/ethnic make-up and therefore allowed us to compare the prevalence and incidence of POAG among different racial groups. We reported a prevalence of 9.9% and 10-year incidence rate of 1.5% in an Asian Chinese population

Although the incidence estimates of POAG from previous Singaporean studies that assessed the long-term incidence of POAG are similar to our result, other studies showed a lower incidence rate of POAG in Asian populations. Other studies from Singapore or other Asian countries reported similar prevalence and incidence rates of POAG in Asian (Chinese, Indian, and Malay) populations. The lower incidence rates in these studies might be attributable to the variation in definition of POAG and follow-up period that Hunter et al. examined. Because our study was a 10-year longitudinal study, our incidence rate of 1.5% was higher than the other 9 studies, especially the 3 from Korea, suggesting that POAG may run a high incidence in Asia.

Our study showed that a longer duration of diabetes and higher 10P were important factors associated with the development of POAG, whereas gender, lower CCT, higher waist-to-hip ratio, and higher peripapillary atrophy were only associated with the incidence of POAG. In addition to diabetes and 10P, CCT was a significant factor associated with the incidence of POAG. The association between POAG and CCT in our study is consistent with most previous studies.

We found that the risk factors for developing POAG included younger age and higher diastolic blood pressure. Risk factors for severe visual field loss included higher baseline visual acuity and thicker CCT.

We found that elevated 10P was an important risk factor. In our study, the incidence of POAG increased 1.5% with each 1-mm Hg increase in 10P, and the 10-year incidence rate was 2.6%, which was higher than that in other studies that reported high incidence rates (1.1%-0.8%). This may be the result of the different racial/ethnic composition (Chinese in our study vs. Korean, Chinese from the United States, or Chinese from Singapore) or differences in the methods of 10P measurement (Goldmann applanation tonometer vs. Tonopen) and definition of POAG, which we used.

In summary, POAG is a major public health problem in Singapore, especially in the young and elderly populations. Our study showed that the prevalence and incidence rates of POAG were higher in Asians compared with other racial groups and males. The mean 10P at presentation was significantly higher than that in previous reports. We determined that the risk of POAG was increased at a younger age, longer duration of diabetes, higher IOP, and increased serum glucose levels. These risk factors should be considered when determining the risk and management of POAG in Singapore.

Disclosures

All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported. The authors indicate no funding support. Contributions of authors: involved in design and conduct of the study (F.- H.G., K.E.H., C.C.H., S.M.F., S.S.W.); collection, management, analysis, and interpretation of the data (F.-H.G.,

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