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Ancestry, Socioeconomic Status, and Age-Related Cataract in Asians

The Singapore Epidemiology of Eye Diseases Study

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Purpose: To determine the prevalence of age-related cataract and its ancestral and socioeconomic risk factors in a multi-ethnic Asian population.

Design: Population-based, cross-sectional study.

Participants: A total of 10 033 adults (3353 Chinese, 3280 Malays, and 3400 Indians) aged >40 years in the Singapore Epidemiology of Eye Diseases Study.

Methods: Study participants were invited for a structured interview and received a standardized comprehensive eye examination. Digital lens photographs were taken from eyes of each participant and graded for nuclear, cortical, and posterior subcapsular (PSC) cataract, following the Wisconsin Cataract Grading System. Prevalence data were compared with the Blue Mountains Eye Study (BMES) in Australia. Information on medical and lifestyle factors was collected using questionnaires and blood samples. To increase the precision of racial definition, genetic ancestry was derived from genome-wide single nucleotide polymorphism markers using principal component analysis. Regression models were used to investigate the association of cataract with socioeconomic factors (education and income) and genetic ancestry.

Main Outcome Measures: Age-related cataract.

Results: A total of 8750 participants (94.0%) had gradable lens photographs. The age-standardized prevalence of cataract surgery in Chinese (16.0%), Malays (10.6%), and Indians (20.2%) was higher than in white subjects (4.1%). We found the age-standardized cataract prevalence in Chinese (30.4%), Malays (37.8%), and Indians (33.1%) was higher than in whites (18.5%). Cataract was 1.5 to 2 times more common in Asians and began 10 years earlier than in white subjects. Malays had significantly higher age-standardized prevalence of nuclear, cortical, and PSC cataract than Chinese ($P < 0.001$). The severity of nuclear, cortical, and PSC cataract was significantly correlated with genetic ancestry in our South East Asian population. Less education and lower income were associated with cataract for Chinese and Indians but not Malays. The presence of visual impairment associated with cataract was higher in people aged ≥60 years and Malays.

Conclusions: We showed that people of different Asian ethnicities had a higher prevalence and earlier age of onset of cataract than Europeans. People of Malay ancestry have a greater severity for all cataract subtypes than people of Chinese ancestry. Education and income were associated with cataract for certain Asian subgroups. *Ophthalmology 2015;122:2169-2178 © 2015 by the American Academy of Ophthalmology.*

Supplemental material is available at www.aaojournal.org.

Age-related cataract is the leading cause of blindness worldwide,[1] and Asians are disproportionately affected.[2–4] With rapidly aging populations, it is likely that the number of Asians affected by cataract-induced visual dysfunction may increase in the future.

To date, several county-specific surveys of the prevalence of cataract have been published from China,[5,6] India,[7–9] Taiwan,[10] and Singapore,[11,12] with rates ranging from 14% to 59%. Whether these variations reflect a true ethnic and racial disparity or are related to differences in case definition is unclear. Most of the Asian epidemiologic studies have used a clinical assessment of cataract, such as the Lens Opacity Classification System III (LOCS III).[13] In contrast, pooling of cataract prevalence in the population of European ancestry has been conducted mainly using the Beaver Dam Eye Study[14] and the Blue Mountains Eye Study (BMES),[15] which used the Wisconsin system to assess lens opacity from photographs.[16] Estimates of the prevalence can vary substantially, depending on which cataract grading system is selected,[17] thus making direct comparisons among these populations challenging. There have been

http://dx.doi.org/10.1016/j.ophtha.2015.06.052
ISSN 0161-6420/15

no comparison reports using the Wisconsin grading system[14] in a multi-ethnic Asian population.

In this study, we compared the prevalence of cataract among the 3 main ethnic groups in Asia (Chinese, Malays, and Indians) with the population of European ancestry as represented by the BMES, using the Wisconsin grading system and standardizing the cataract cutoffs to that used by the Eye Disease Prevalence Research.[16] We also determined the socioeconomic risk factors of cataract among the Asian ethnic groups.

Methods

Study Population

The Singapore Epidemiology of Eye Diseases Study comprises 3 population-based studies that included 3 major ethnic groups in Singapore: Malays (2004−2006),[18] Indians (2007−2009),[19] and Chinese (2009−2011).[19] Details of the study design and methodology have been described.[18,19] Briefly, an age-stratified (by 10-year age groups) random sampling in each ethnic group was used to select ethnic Malays, Indians, and Chinese aged ≥40 years residing in Singapore. The selected participants included 4168 Malays, 4497 Indians, and 4606 Chinese. Of these, 3280 Malays (78.7%), 3400 Indians (75.6%), and 3353 Chinese (72.8%) participated in the study. The overall response rate was 75.6%. Those who had moved from the residential address, had not lived there in the previous 6 months, or were deceased or terminally ill were ineligible. Participants of the study were older than non-participants ($P < 0.001$), but there was no gender difference ($P = 0.68$). Ethics approval was obtained from the Singapore Eye Research Institute Institutional Review Board. All study participants were provided with written informed consent in adherence to the Declaration of Helsinki.

Examination Procedures

Each participant underwent a comprehensive, standardized eye examination including slit-lamp biomicroscopy and lens photography. A face-to-face interview used standard questionnaires to collect sociodemographic data. Self-reported ethnicity was set by the Singapore census and as indicated on the National Registration Identity Card.[20] Each of the participants was assigned a single ethnicity from among 3 categories: (1) Chinese (refers to persons of Chinese ancestry with an origin of Mainland China), (2) Malay (refers to persons of Malay or Indonesian origin, such as Javanese), or (3) Indian (refers to persons with ancestry originating on the Indian subcontinent) as indicated by the government census based on their parents' ethnicity.[18−20] All interviewers were bilingual, and participants were given a choice to be interviewed in English, Chinese, Malay, or Tamil.

Cataract Grading and Definition

Digital slit-lamp (Topcon model DC-1 with FD-21 flash attachment; Topcon, Tokyo, Japan) and retroillumination (Nidek EAS-1000; Nidek, Tokyo, Japan) cameras were used during the examination, and lens opacity was assessed using the Wisconsin system.[14,15] The slit beam was adjusted to completely fill the pupil and to vertically bisect the lens at a 45-degree angle focusing on the sulcus of the lens. All photographs were graded by a single experienced grader (A.G.T.) at the University of Sydney who also graded cataracts for the BMES.[11,17] At least 2 photographs for each eye and only the best-quality photograph based on the grader's judgment were evaluated. Digital slit-lamp photographs were compared with the Wisconsin set of 4 standard photographs to assess nuclear cataract with decimalized grades (0−5). Cortical and posterior subcapsular (PSC) cataracts were assessed from retroillumination photographs using an overlying grid to determine the location and percentage of lens area involvement of the opacity. Estimates of the percentage of lens area involvement by cortical and PSC cataract were made for each segment of the grid to calculate the total percentage area of involvement. For questionable cases, adjudication was provided by a senior researcher (J.J.W.) and senior ophthalmologist (P.M.).

Cataract was defined using the Wisconsin Cataract Grading System.[14] In our previous study, using the Wisconsin cataract grading, we defined cortical and PSC cataract as ≥5% and >0% of total lens area, respectively.[11] This decision was made at that time for the cortical and PSC cutoffs because our earlier study revealed that the cutoffs might be more comparable to those in epidemiologic studies that commonly use the LOCS III grade ≥2.[17] In the current study, nuclear cataract was defined as grade 4 or more, cortical cataract was defined as ≥25% of total lens area, and PSC cataract was defined as ≥5% of total lens area. Any cataract was defined as nuclear, cortical, or PSC cataract in at least 1 eye. Inter- and intra-grader reliabilities for the 3 types of cataract were high and have been reported.[21] Cataract surgery was defined as the presence of an intraocular lens implant (pseudophakia) or the absence of the crystalline lens (aphakia), recorded during cataract grading or confirmed from lens assessment during slit-lamp examination at the study visit.[22] Visual acuity (VA) was measured using a logarithm of the minimum angle of resolution number chart (Lighthouse International, New York, NY) at 4 m in both eyes. Best-corrected VA was measured with the best possible correction obtained with subjective refraction. Visually significant cataract was defined by any cataract (as defined previously) with a best-corrected VA <20/40 and cataract as the primary cause of vision impairment.

Other Measurements

A detailed interviewer-administered questionnaire was used to collect socioeconomic status (e.g., education and income), smoking status, medical history (e.g., diabetes, hypertension, and hyperlipidemia), and medication use from participants. Education was recorded as the highest number of years of schooling completed and categorized into 2 groups: (1) low: primary or lower (≤6 years) and (2) high: secondary or higher (≥7 years, including university education). Individual monthly income was based on Singapore dollars ($) and divided into 2 categories: (1) low (<$2000) and (2) high (≥$2000). Seated blood pressure (BP) and blood samples were collected during the examinations. Hypertension was defined as systolic BP ≥140 mmHg, diastolic BP ≥90 mmHg, physician-diagnosed hypertension, or self-reported history of hypertension. Diabetes mellitus was defined as random glucose of ≥11.1 mmol/l, diabetic medication use, or a physician-diagnosed history of diabetes. Hyperlipidemia was defined as total cholesterol ≥6.2 mmol/l or self-reported use of lipid-lowering drugs. Smoking status was defined as current or noncurrent smoking. Body mass index was calculated as body weight (in kilograms) divided by body height (in meters) squared.

Ancestry Inference Using Genome-Wide Single Nucleotide Polymorphism Markers

In addition to self-reported race/ethnicity, individual genetic ancestry was inferred using principal component (PC) analysis by the smartPCA program (EIGENSTRAT software v4.2)[23] to examine the relationship of race and its associations to various cataract subtypes and their degrees of opacity. We treated the