AMERICAN ACADEMY OF OPHTHALMOLOGY®

Ethnic Differences in the Prevalence and Risk Factors of Diabetic Retinopathy

The Singapore Epidemiology of Eye Diseases Study

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Purpose: To evaluate the prevalence and risk factors for diabetic retinopathy (DR) in the Singapore Epidemiology of Eye Diseases (SEED) Study.

Design: Population-based, cross-sectional study.

Participants: Persons of Malay, Indian, and Chinese ethnicity aged 40+ years, living in Singapore.

Methods: Diabetes was defined as nonfasting plasma glucose ≥200 mg/dl (11.1 mmol/l), glycated hemoglobin A1c (HbA1c) >6.5%, self-reported physician-diagnosed diabetes, or the use of glucose-lowering medication. Retinal photographs, were graded for the presence and severity of DR using the modified Airlie House classification system.

Main Outcome Measures: Diabetic retinopathy, diabetic macular edema (DME), vision-threatening diabetic retinopathy (VTDR), defined as the presence of severe nonproliferative or proliferative DR, or clinically significant macular edema (CSME).

Results: Of the 10 033 subjects, 2877 (28.7%) had diabetes and gradable photographs for analysis. The overall age-standardized prevalence (95% confidence interval [CI]) was 28.2% (25.9–30.6) for any DR, 7.6% (6.5–9.0) for DME, and 7.7% (6.6–9.0) for VTDR. Indians had a higher prevalence of any DR (30.7% vs. 26.2% in Chinese and 25.5% in Malays, $P = 0.012$); a similar trend was noted for any DME ($P = 0.001$) and CSME ($P = 0.032$). Independent risk factors for any DR were Indian ethnicity (odds ratio [OR], 1.41; 95% CI, 1.09–1.83, vs. Chinese), diabetes duration (OR, 1.10; 95% CI, 1.08–1.11, per year), HbA1c (OR, 1.25; 95% CI, 1.18–1.32, per %), serum glucose (OR, 1.03; 95% CI, 1.00–1.06, per mmol/l), and systolic blood pressure (OR, 1.14; 95% CI, 1.09–1.19, per 10 mmHg). Diastolic blood pressure (OR, 0.74; 95% CI, 0.65–0.84, per 10 mmHg increase), total cholesterol (OR, 0.87; 95% CI, 0.80–0.95, per mmol/l increase), and low-density lipoprotein (LDL) cholesterol (OR, 0.83; 95% CI, 0.74–0.92, per mmol/l increase) were associated with lower odds of any DR. Risk factors were largely similar across the 3 ethnic groups.

Conclusions: Indian Singaporeans have a higher prevalence of DR and DME compared with Chinese and Malays. Major risk factors for DR in this study were similar across the 3 ethnic groups. Addressing these risk factors may reduce the impact of DR in Asia, regardless of ethnicity. *Ophthalmology 2017;■:1–8 © 2017 by the American Academy of Ophthalmology*

Diabetic retinopathy (DR) is the most common ocular complication of diabetes mellitus and the leading cause of visual loss in working-age adults in the developed world.[1–3] There is an increasing prevalence of diabetes in Asia, particularly in India and China.[4–7] The global prevalence of DR among persons with diabetes is estimated at 34.6%, with 10.2% having vision-threatening levels of DR, although the rates vary widely between countries and ethnic groups globally.[8]

Previous work has observed racial/ethnic variation in the prevalence of DR.[9–11] For example, in Western populations, ethnic blacks and Hispanics have a higher prevalence of DR and diabetic macular edema (DME) than whites.[10,12–14] These variations may reflect a combination of disparities in socioeconomic status and healthcare access, and a differential contribution of traditional risk factors for DR such as poor glycemic blood pressure control and duration of diabetes. Few studies have examined whether ethnicity is an independent risk factor for DR. Although it has been reported that there is no ethnic difference in the association of glycated hemoglobin with retinopathy,[15] nevertheless, there are still limited data on ethnic differences in risk factors for DR. Understanding ethnic differences in the prevalence and risk of DR will allow better planning of public health measures and designing of ethnicity-specific approaches to the management of DR.

Singapore, comprising people of Chinese, Malay, and Indian origin, the 3 major ethnic groups in Asia, provides a

https://doi.org/10.1016/j.ophtha.2017.10.026
ISSN 0161-6420/17

unique opportunity to examine possible ethnic differences in DR in Asians. Thus, the aim of this study is to compare the prevalence and risk factors of DR in the 3 main ethnic groups in Singapore.

Methods

Study Design and Population

The Singapore Epidemiology of Eye Diseases (SEED, 2004−2011) Study is a population-based study that included 3 major ethnic groups in Singapore: Malays (2004−2006), Indians (2007−2009), and Chinese (2009−2011).[16,17] The study adhered to the Declaration of Helsinki, and ethics approval was obtained from the Singapore Eye Research Institute Institutional Review Board. On the basis of an age-stratified random sampling strategy, 5000 Malays, 6350 Indians, and 6752 Chinese names were selected. Of these, 4168 Malay, 4497 Indian, and 4605 Chinese individuals were deemed eligible to participate. The "ineligible" persons included those who had moved out from the residential address, had not lived there in the past 6 months, or were deceased or terminally ill. A total of 3280 Malays (response rate: 78.7%), 3400 Indians (75.6%), and 3353 Chinese (72.8%), aged 40 to 80+ years, participated in this population-based study. The study aimed to examine an approximately equal number of participants from each ethnic group to provide robust comparable data across ethnicity. All participants underwent standardized clinical and ocular assessment, questionnaire interview, and blood biochemical analyses.

Retinal Photography and Diabetic Retinopathy Assessment

Two-field, 45-degree digital retinal photography was undertaken using a standardized protocol.[10,18] After pupil dilation, 1 retinal photograph centered at the optic disc (Early Treatment Diabetic Retinopathy Study [ETDRS] field 1) and another centered on the macula (field 2) were taken from both eyes using a digital retinal camera (Canon CR-DGi with a 10-D SLR back; Canon, Tokyo, Japan). Photographs were sent and graded at the University of Sydney by graders trained by the Blue Mountains Eye Study principle investigator (P.M.), based on the modified Airlie House Classification Scheme of the ETDRS.[10,18,19] Diabetic retinopathy was considered present if any characteristic lesion was present: microaneurysms, hemorrhages, cotton wool spots, intraretinal microvascular abnormalities, hard exudates, venous beading, and new vessels. Severity of DR was graded according to a scale modified from the Airlie House classification system: Retinopathy severity was categorized into minimal nonproliferative DR (NPDR) (levels 15−20), mild NPDR (level 35), moderate NPDR (levels 43−47), severe NPDR (level 53), and proliferative DR (PDR) (levels >60).

Diabetic macular edema was defined as hard exudates in the presence of microaneurysms and blot hemorrhage within 1 disc diameter from the foveal center or presence of focal photocoagulation scars in the macular areas. Those with DME were further divided into cases with clinically significant macular edema (CSME), defined as DME within 500 μm of the foveal center or if focal photocoagulation scars were present in the macular area. Vision-threatening diabetic retinopathy (VTDR) was defined as the presence of severe NPDR, PDR, or CSME using the Eye Diseases Prevalence Research Group definition.[20] For every participant, the severity score of the worse eye was used for the analyses. If an eye was ungradable, the score for the fellow eye was used to define these outcomes.

Risk Factor Measurements and Definitions

All participants underwent a detailed interview: information on socioeconomic status (education, income, housing status), lifestyle risk factors (smoking and alcohol consumption), medication use, and self-reported history of diabetes, hypertension, and cardiovascular disease (myocardial infarction, stroke) was collected. Educational level was categorized into 4 groups (polytechnic/university, secondary education, primary education, and no formal education); monthly individual income level was categorized into 2 groups (<Singapore dollar [S$]<1000 and ≥S$1000); and housing type was categorized into 2 groups (≤4-room Housing Development Board flat vs. 5-room Housing Development Board flat or private apartment/house). Height was measured using a wall-mounted tape and weight with a digital scale (SECA, model 782 2321009; Vogel & Halke, Hamburg, Germany). We defined body mass index (BMI) as weight divided by the square of height in meters (kg/m^2). Blood pressure was measured using a digital automatic blood pressure monitor (Dinamap model Pro100V2; Criticon GmbH, Norderstedt, Germany), following the protocol used in the Multi-Ethnic Study of Atherosclerosis.[10] Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or use of antihypertensive medication. Nonfasting venous blood samples were drawn and sent for analysis of serum lipid levels (total cholesterol, high-density lipoprotein cholesterol, and low-density lipoprotein [LDL] cholesterol), hemoglobin A1C, creatinine, and glucose at the National University Hospital Reference Laboratory on the same day. Diabetes was defined as casual plasma glucose ≥200 mg/dl (11.1 mmol/l), self-reported physician-diagnosed diabetes or glycated hemoglobin A1c (HbA1c) >6.5%, and use of glucose-lowering medication in accordance with the recommendation by the American Diabetes Association.[21] A participant was considered to have type 1 diabetes if the participant was aged <30 years when diagnosed with diabetes and was receiving insulin therapy with no other hypoglycemic medication history. Hyperlipidemia was defined as total cholesterol of ≥6.2 mmol/l or use of lipid-lowering drugs. Chronic kidney disease (CKD) was defined as an estimated glomerular filtration rate (eGFR) of <60 ml/min per 1.73 m^2, measured from serum creatinine.[22]

Statistical Analysis

Analyses were performed using Stata version 14.2 (StataCorp LP, College Station, TX) and R version 3.2.1 (Foundation for Statistical Computing, Vienna, Austria). We calculated the overall and ethnicity-specific prevalence of any DR, and DME, VTDR, and CSME in those with diabetes. Age-standardized prevalence estimates were calculated by the direct method using the 2010 Singapore population census as the standard population. Characteristics of participants by any DR were compared using the *t* test for continuous variables (e.g., age and BMI) and chi-square test or Fisher exact test for categoric variables (e.g., hypertension and ethnicity), as appropriate.

The associations of potential risk factors with the presence of any DR in diabetic individuals as a whole, and within each ethnic stratum, were analyzed in separate logistic regression models that adjusted for (1) age and gender, and (2) additionally known metabolic and socioeconomic risk factors of DR, including BMI, HbA1c, systolic blood pressure, diabetes duration, income (<S$2000), housing types (4 rooms or smaller), and education levels (primary school or below). Where a variable was overall found to be significantly associated with DR after multivariable adjustment, an expanded model that included multiplicative parameters of the variable with ethnicity was used to test for significant interactions with ethnicity. Similar multivariable model