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Incidence and risk factors of symptomatic dry eye disease in Asian Malays from the Singapore Malay Eye Study

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ABSTRACT

Purpose: To evaluate the incidence of symptomatic dry eye disease (SDED) and associated risk factors in a well-characterized cohort of ethnic Malays in Singapore.
Methods: We included 1682 participants (mean age [SD]: 57 [10]years; 55.4% female) without SDED from the Singapore Malay Eye Study (SiMES), a population-based longitudinal study with baseline examination (SiMES-1) conducted between 2004 and 2006, and follow-up examination (SiMES-2) conducted between 2010 and 2013. SDED was considered to be present if a participant answered "often" or "all the time" to any of the six questions from the Salisbury Eye Evaluation Study dry eye questionnaire. Age-standardized incidence of SDED was calculated as the crude 6-year cumulative incidence standardized to Singapore's population census. Gender-stratified multivariable log-binomial regression models were utilized to determine the independent risk factors of incident SDED.
Results: At the 6-year follow-up, 86 of 1682 participants had developed SDED, which was equivalent to an age-standardized 6-year incidence of 5.1% (95% CI 4.1–6.4%). There were no differences in the incidence of SDED between men and women (P = 0.9). Multivariable models revealed that presence of glaucoma and poorer self-rated health were independently associated with incident SDED in men (P = 0.003 and 0.03, respectively), while contact lens wear (P = 0.002), history of thyroid disease (P = 0.03), and having had cataract surgery (P = 0.02) were predictive of incident SDED in women.
Conclusion: One in twenty adult Malays developed SDED over a 6-year period. Risk factors for incident SDED were different between men and women. Future studies and public health interventions should consider this gender-specific difference in risk factors.

1. Introduction

The population-based prevalence of symptomatic dry eye disease (SDED) is estimated to be 5–30% and is increasing globally as a result of rapidly aging and urbanized societies [1,2]. SDED is a multifactorial condition involving an increase in the osmolarity of the tear film and inflammation of the ocular surface [3], and its symptoms have been associated with reduced quality of life (QoL) [4,5], increased depressive symptoms [6], and sleep and mood disorders [7]. As there is no known cure for SDED and treatment

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provides symptomatic relief only, the long-term economic burden of this condition is considerable. For instance, it was estimated that the average direct and indirect (e.g., loss of work-hours) cost of managing SDED in 2008 in the US was US$3.8 billion and US$55.4 billion, respectively [8].

Previous research has demonstrated that SDED is more likely to occur with contact lens wear, increased age, smoking, use of anti-hypertensive and anti-depressant medications, and long hours spent in an air-conditioned environment [9–12]. Unfortunately, the causal nature of these cross-sectional associations are unclear, and there are few data on the incidence and risk factors of SDED. The Beaver Dam Eye Study (BDES) reported 5- and 10-year SDED incidence rates of 13.3% and 21.6% in a Caucasian population, respectively, and also established several associated risk factors, including increasing age, female gender, poorer self-rated health, and diuretic use [13,14]. Previous studies have also suggested that SDED prevalence may be different between Asians and Caucasians [2], but to our knowledge there are no studies on the incidence and risk factors of SDED in Asian populations.

In the current study, we examined the incidence and associated risk factors of SDED over a 6-year period in a well-characterized population-based cohort of ethnic Malays residing in Singapore.

2. Methods

2.1. Study population

The Singapore Malay Eye Study (SiMES-1) is a population-based study of 3280 Malay adults (aged 40–79 years) living in Singapore conducted between 2004 and 2006, which aims to assess the prevalence, incidence, progression, associated factors and impact of major eye diseases, as well as access to eye care by Asian Malays [15]. Briefly, from a list of 16,069 names of people living in south-western Singapore provided by the Ministry of Home Affairs, an age-stratified random sampling method was used to select 5600 names, of which 4168 individuals were eligible. A total of 3280 (78.7% response rate) participants took part in the SiMES-1 study. After 6 years, 644 (19.6%) of the 3280 subjects were ineligible to participate in the follow-up examination (SiMES-2) conducted between 2010 and 2013 due to the development of cognitive and/or severe mobility impairments, migration to other countries, or death during the intervening 6 years. Of the remaining 2636 eligible participants, 1901 (72.1% response rate) individuals participated in SiMES-2.

All protocols followed the principles of the Declaration of Helsinki and received approval by the Singapore Eye Research Institute (SERI) Institutional Review Board. Written informed consent was obtained prior to recruitment of participants.

2.2. Definition of SDED

The SiMES protocol defined SDED based on participant responses to six questions from the Salisbury Eye Evaluation Study questionnaire, which was administered by interviewers trained in questionnaire administration. These questions addressed dry eye symptoms or ocular discomfort, which included subjective reporting of frequency (1 = never, 2 = rarely, 3 = sometimes, 4 = often, 5 = all the time) [16,17] over the past one month. Participants were defined as having SDED if they answered any of the six questions as “often” or “all the time.”

2.3. Assessment of sociodemographic and clinical data

The study protocol was conducted at the SERI research clinic and comprised a comprehensive, standardized examination procedure to collect clinical and questionnaire data [15,18]. Questionnaires were administered to participants by trained interviewers who were fluent in English and Malay. Information collected included demographic information, sociodemographic characteristics (education, income level, occupation), lifestyle factors (smoking, alcohol use, diet, physical activity, self-rated health [rated ordinally with each increasing level indicating poorer health states]), self-reported family and medical history (contact lens wear, hypertension, thyroid disease, stroke, cardiovascular disease, current medication use, ocular surgeries), falls, and access and barriers to use of general health and eye care services. If participants were taking anti-hypertension drugs, these were categorized based on their mechanism of action, namely ACE-inhibitors, diuretics and other anti-hypertensive medication not otherwise specified.

A comprehensive eye examination conducted by an ophthalmologist included assessment of pupillary reaction and slit lamp biomicroscopy (Haag-Streit model BQ-900; Haag-Streit, Switzerland) for anterior segment abnormalities; measurement of intraocular pressures (IOP) with a Goldmann applanation tonometer (Haag-Streit, Bern, Switzerland); and gonioscopy with a Goldmann two-mirror lens (Ocular Instruments, Inc., Bellevue, WA) under standard dark illumination for angles of the anterior chamber. The presence of meibomianitis and/or pterygium was documented in all participants, and individuals with IOP >21 mmHg or narrow anterior chamber angles (detected via gonioscopy) underwent static automated perimetry (Swedish Interactive Threshold Algorithm standard 24-2, Humphrey Field Analyzer II; Carl Zeiss Meditec, Dublin, CA). A detailed examination of the lens, vitreous, and posterior segment was then conducted after pupillary dilation with 1% tropicamide and 2.5% phenylephrine hydrochloride. Two-field fundus photographs were taken with a Canon DGI non-mydriatic fundus camera and graded by trained graders at the Singapore Eye Research Institute for presence of any retinal abnormalities. Presence of glaucoma was determined using the International Society of Geographical and Epidemiological Ophthalmology Scheme, based on gonioscopy, optic disc characteristics, and visual fields data [19].

Systolic (S) and diastolic (D) BP was measured twice using a digital automatic blood pressure monitor (Dinamap Pro Series DP110X-RW; GE Medical Systems Information Technologies, Inc), with the average value for each parameter used in subsequent analyses. A third measurement was obtained if the two previous SBP or DBP readings differed by more than 10 mmHg or 5 mmHg, respectively. Height and weight were measured using a wall-mounted adjustable measuring scale and a calibrated scientific weight scale, respectively. BMI was calculated as weight (kg) divided by height in meters squared (kg/m^2). Blood samples were collected for biochemistry analysis (HbA1c, random glucose, total and low density lipoprotein-, and high density lipoprotein-cholesterol). Diabetes mellitus was defined as having a random glucose level of at least 200 mg/dL or self-reported history/diabetic medication use; hypertension as having a SBP of $\geq$140 mm Hg or a DBP of $\geq$90 mm Hg or self-reported history of anti-hypertensive medication use; and hyperlipidemia as a total cholesterol level of at least 239 mg/dL or self-reported history of lipid-lowering medication use.

2.4. Statistical analysis

All analyses were performed using Stata 11.1 (StataCorp LP, College Station, TX, USA). Risk factors were classified as either binary traits (e.g., current smoking) or as continuous parameters (e.g., age). Cumulative incidence (with 95% confidence interval [CI]) was calculated as the number of persons who developed SDED at follow-up divided by the total number of individuals who

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