Maturitas 74 (2013) 369–374

Contents lists available at SciVerse ScienceDirect

Maturitas

journal homepage: www.elsevier.com/locate/maturitas

Ethnic variation in the impact of metabolic syndrome components and chronic kidney disease

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ARTICLE INFO

Article history:
Received 19 October 2012
Received in revised form
27 December 2012
Accepted 8 January 2013

Keywords:
Asians
Blood pressure
CKD
Ethnicity
Metabolic syndrome

ABSTRACT

Objective: To examine the ethnic differences in the association between metabolic syndrome components and CKD in Asian populations.
Methods: We analyzed data from three independent populations in Singapore representing the three major Asian ethnic groups (n = 3167 Chinese, 3082 Malays and 3228 Indians) aged 40–80 years. CKD was defined as an estimated glomerular filtration rate <60 mL/min/1.73 m^2. Factor analysis of metabolic syndrome components was conducted and factor scores were used as independent variables in multivariable logistic regression models.
Results: The prevalence of CKD was highest among Malays (21.0% vs. 7.4%, 5.9% in Indians and Chinese). Factor analysis identified three factors among Chinese (glycemia, blood pressure [BP], and obesity/lipid) and Malays (glycemia, BP, and lipids) accounting for 70% of the variance and four factors (glycemia, BP, lipids, and obesity) among Indians accounting for 82% of the variance. Glycemia was positively associated with CKD in all three ethnic groups. BP was positively associated with CKD among Malays (OR [95% CI] of 1.16 [1.06–1.28]), whereas it showed an inverse association among Chinese (0.84 [0.71–0.99]) and Indians (0.84 [0.73–0.97]). However, this inverse association lost significance after adjusting for antihypertensive medication use in Chinese and Indians. Obesity/lipids among Chinese and obesity among Indians showed a positive association; lipids showed an inverse association among Malays.
Conclusions: These data suggest that while hyperglycemia was associated with CKD in all three ethnic groups, the impact of BP, lipids, obesity on CKD varies across ethnic groups. Understanding the specific associations may allow greater understanding of how CKD develops in different racial/ethnic groups.

Chronic kidney disease (CKD), an early stage in the continuum of kidney disease is a growing public health problem associated with cardiovascular disease and kidney failure [1]. Metabolic syndrome factors, including hyperglycemia, central obesity, high blood pressure and dyslipidemia [2] are an established set of risk factors for CKD [3]. Few studies conducted in Asia, limited to individual racial/ethnic groups such as Japanese [4,5], Korean [6,7] and Chinese [8–10] populations have shown that metabolic syndrome is associated with CKD. However, there are racial/ethnic variations in the prevalence of metabolic syndrome components and also in the prevalence of CKD. While Asian Indians were shown to have a higher prevalence of diabetes, and dyslipidemia [11], Chinese were shown to have a higher prevalence of hypertension [12] and Japanese and Chinese were shown to have a favorable lipid profile [12,13]. The prevalence of CKD varied from 1.7% in Chinese [14] to 4.2% in Indians [15], 7% in Taiwanese [16], and 15% in Japanese [17].

Singapore, a country with a multi-ethnic population including Chinese, Malay and Indians, the three major racial/ethnic groups in Asia, provides an ideal opportunity to study the impact of metabolic syndrome on CKD in different racial/ethnic groups. Previous studies in Singapore have clearly shown ethnic differences in the prevalence and distribution of metabolic syndrome [18,19]. For example, Chinese had the lowest prevalence, followed by Malays and Indians had the highest prevalence, almost twice as Chinese in Singapore [18,19]. However, whether these racial/ethnic variations in the prevalence of metabolic syndrome differentially impact on the risk of CKD are unclear.

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http://dx.doi.org/10.1016/j.maturitas.2013.01.006

To address this gap, we examined the association between metabolic syndrome components with CKD among three Asian groups (Chinese, Malays and Indians) in Singapore using factor analysis. Our aim was to determine whether associations of components of metabolic syndrome with CKD are consistent among participants within the three ethnic groups. The availability of three large datasets representing three largest Asian ethnic groups of similar age group, geographic region and study methods provides a unique opportunity to study the differential impact of metabolic syndrome components on CKD in Asia.

1. Methods

1.1. Study population

We evaluated data obtained from three large cross-sectional studies, Singapore Chinese Eye Study (SCES), Singapore Malay Eye Study (SiMES) and the Singapore Indian Eye Study (SINDI). SiMES, the first of the three studies was conducted between 2004 and 2006, followed by SINDI between 2007 and 2009 and the SCES between 2009 and 2011. All three studies followed the same study protocol and were conducted in the same study clinic (Singapore Eye Research Institute). Details of the study population and methods of SiMES [20] and SINDI [21,22] have already been published and that of SCES has been submitted for publication. In brief, in SiMES, 5600 individuals were selected by an age-stratified random sampling method from the computer generated random list of 16,069 Malay names provided by the Ministry of Home Affairs. Of the 4168 eligible individuals, 3280 participated in the study (78.7% response rate). Of the 3148 participants with serum creatinine measurements, after excluding those with missing information on variables included in the multivariable model ($n = 66$), 3082 were included in the final analysis. In SINDI, 6350 adults were selected by an age-stratified random sampling method from the computer generated random list of 11,616 Indian names provided by the Ministry of Home Affairs. Of the 4497 eligible participants, 3400 participated in the study (75.6% response rate). Of the 3259 participants with serum creatinine measurements, after excluding those with missing information on variables included in the multivariable model ($n = 31$), 3228 provided data for the final analysis. In SCES, 6752 adults were selected by an age-stratified random sampling method from the computer generated random list of 12,000 Chinese names provided by the Ministry of Home Affairs. Of the 4605 eligible participants, 3353 participated in the study (72.8% response rate). Of the 3192 participants with serum creatinine measurements, after excluding those with missing information on variables included in the multivariable model ($n = 25$), 3167 provided data for the final analysis. Written informed consent was obtained from all participants and all studies were approved by the Singapore Eye Research Institute Institutional Review Board.

1.2. Outcome of interest

The main outcome of interest in the current study was CKD defined as an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2 consistent with National Kidney Foundation Kidney Disease Outcome Quality Initiative (NKF-KDOQI) CKD stage 3 and above [1]. GFR was estimated from serum creatinine using the recently developed Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [23] as follows: $141 \times \min(S_{cr}/k,\ 1)^{\alpha} \times \max(S_{cr}/k,\ 1)^{-1.209} \times 0.993^{age} \times 1.018$ (for women), where S_{cr} is serum creatinine, k is 0.7 for females and 0.9 for males, α is −0.329 for females and −0.411 for males, min indicates the minimum of S_{cr}/k or 1, and max indicates the maximum of S_{cr}/k or 1. Validation studies conducted in Singapore have shown CKD-EPI to be more accurate than MDRD in particular at higher eGFRs [24] and the prevalence of CKD by both MDRD and CKD-EPI to be similar in all three ethnic groups [25] suggesting the adoption of CKD-EPI equation without ethnic adjustment [24].

1.3. Assessment of metabolic syndrome components

The metabolic syndrome components considered for the current study were plasma glucose, glycated hemoglobin (HbA1C), systolic blood pressure (BP), diastolic BP, triglycerides, high-density lipoprotein cholesterol and body mass index (BMI) [26]. As we do not have information on waist circumference, we used BMI as a measure of obesity [27]. Height was measured in centimeters using a wall-mounted measuring tape and weight was measured in kilograms using a digital scale (SECA, model 782 2321009; Vogel & Halke, Germany). BMI was calculated as weight in kilograms divided by the square of height in meters squared (kg/m^2). BP measurements were taken using a digital automatic blood pressure monitor (Dinamap model Pro Series DP110X-RW, 100V2; GE Medical Systems Information Technologies, Inc., USA) on 2 occasions 5 min apart, after the participants were seated for at least 5 min. If these two BP measurements differed by more than 10 mm Hg systolic and 5 mm Hg diastolic, a third measurement was taken and the average of the two closest readings was taken as the BP value. 40 mL venous blood was collected to measure serum lipids, and casual glucose in the non-fasting state. All serum biochemistry tests were carried out at the National University Hospital Reference Laboratory, which is accredited by the College of American Pathologists. The HbA1c assay was carried out using high-performance liquid chromatography (HPLC) cation exchange chromatography system implemented on a Biorad variant II analyser.

1.4. Assessment of covariates

Information on participant demographics, educational attainment, personal and medical history was obtained using a standardized questionnaire administered by trained interviewers. Education level was categorized into (1) primary and below (≤6 years), (2) secondary (7–10 years) and (3) high school and above (≥11 years). Cigarette smoking was categorized into current, former and never smoker and alcohol consumption into drinkers and non-drinkers. The use of antihypertensive medication use was assessed from the questionnaire.

1.5. Statistical analysis

All statistical analyses were performed using SAS version 9.1. First, we compared selected baseline characteristics of the participants by ethnic group employing the chi-square test or analysis of variance, as appropriate. Second, we examined the association between components of metabolic syndrome (continuous) and CKD using multivariable logistic regression model adjusted for age (years); sex (men and women); education (primary and below, secondary and above); smoking status (never, former, and current); and alcohol consumption (absent and present) separately for each metabolic syndrome component. Third, we examined the association between components of metabolic syndrome and CKD using factor analysis by principal component method. Principal component analysis (PCA) transforms the highly correlated variables to a linear combination of the variables that accounts for the maximum proportion of variance. It is presumed that variables contributing to the same factor may share similar pathogenetic mechanisms [28–30]. Metabolic syndrome components including glucose, HbA1C, systolic BP, diastolic BP, triglycerides, HDL cholesterol and BMI were included in the factor analysis. An initial set of factors that were linear combination of the included variables