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Population variations in atherogenic dyslipidemia: A report from the HeartSCORE and IndiaSCORE Studies

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KEYWORDS:
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BACKGROUND: Asian Indians and blacks have a higher risk for cardiovascular disease (CVD) events compared to whites. Atherogenic dyslipidemia, comprised of small-dense low-density lipoprotein (LDL), low high-density lipoprotein (HDL) levels, and high triglyceride (TG) levels, constitutes an important risk factor for CVD often seen in the presence of obesity. The contribution of atherogenic dyslipidemia to CVD risk across diverse racial populations is not well established.

OBJECTIVE: Our primary aim was to investigate the relationship between race and atherogenic dyslipidemia among whites, blacks, and Asian Indians. A secondary aim was to evaluate the association between obesity and atherogenic dyslipidemia across populations.

METHODS: From community-based sampling, 720 whites and 373 blacks underwent evaluation of CVD risk factors, including fasting lipoproteins. An identical protocol was administered to 205 Asian Indians from Chennai, India. Lipid profiles, including those comprising atherogenic dyslipidemia, were compared among populations.

RESULTS: The prevalence of small-dense LDL (pattern B) and of TG/HDL ratio >3 was greatest among Asian Indians and smallest among blacks. Compared to whites, the adjusted odds for Indians having a LDL pattern B was 2.06 ($P < .001$) and TG/HDL ratio >3 was 9.42 ($P < .001$). The adjusted odds of having LDL pattern B (odds ratio 0.39, $P < 0.001$) or TG/HDL ratio >3 (odds ratio 0.41, $P < .001$) was lower in blacks compared to whites. Among Indians, obesity had a weak association with atherogenic dyslipidemia, in contrast to the strong association among whites.

CONCLUSIONS: Significant population variations in atherogenic dyslipidemia exist. This may be an important component to explain population differences in cardiovascular risk.

Several epidemiologic studies have shown that population disparities in cardiovascular disease (CVD) exist. CVD is more prevalent among both blacks and Asian Indians than among whites.[1–6] Specifically with regard to Indians, the mortality due to CVD has increased while decreasing among western countries, and this population also has a higher prevalence of premature coronary artery disease.[5,6] Numerous studies have demonstrated that in Asian Indian and black populations, traditional risk factors do not fully explain the increased CVD risk.[2,3,5–8] For instance, the prevalence of total cholesterol, low-density lipoprotein (LDL) cholesterol, and hypertension is lower among Indi-

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ans than among whites.[8] Therefore, novel risk factors may need to be utilized to identify explanations behind racial differences in CVD.

Dyslipidemia, in particular, atherogenic dyslipidemia, has been closely linked to the pathophysiology of CVD.[9–11] Atherogenic dyslipidemia consists of hypertriglyceridemia as well as low high-density lipoprotein (HDL) cholesterol levels and increased concentration of small-dense LDL particles (LDL pattern B). Several groups have shown that Asian Indians are predisposed to metabolic syndrome and insulin resistance, which are often characterized by low HDL cholesterol levels and hypertriglyceridemia.[12–14] Atherogenic dyslipidemia may, therefore, be more prevalent in this racial group compared with whites. Meanwhile, among blacks, reports suggest that the prevalence of atherogenic dyslipidemia may be lower than among whites.[15] In addition, there are also racial disparities in obesity, an independent risk factor for CVD and atherogenic dyslipidemia.[16,17] However, Indians, as a group, have a lower prevalence of obesity compared to whites,[18] and it is not known what the impact of obesity is upon the prevalence of atherogenic dyslipidemia in blacks or Asian Indians.

To date, there are no comparative studies of blacks and Indians with whites with regard to the differences in the prevalence of atherogenic dyslipidemia. Accordingly, the primary aim of the present study is to investigate the relationship between race and atherogenic dyslipidemia among whites, blacks, and Asian Indians, and a secondary aim is to evaluate the association between obesity and atherogenic dyslipidemia across diverse populations.

Methods

Study populations

The study populations included in this analysis were participants in the Heart Strategies Concentrating On Risk Evaluation (HeartSCORE) study and the IndiaSCORE study (an offshoot of the HeartSCORE study). HeartSCORE is an ongoing community-based prospective cohort study of 2000 participants with approximately equal representation of blacks and whites. Eligibility criteria included age 45 to 75 years, residence in the greater Pittsburgh metropolitan area, ability to undergo baseline and annual follow-up visits, and absence of known co-morbidities expected to limit life expectancy to less than 5 years. Targeted over-sampling of blacks was accomplished by utilizing community- and faith-based approaches. Race was self-reported for all individuals. During the middle of recruitment into HeartSCORE, the India SCORE study was developed as an extension to include a third race in the evaluation of racial differences in CVD. Subjects enrolled in IndiaSCORE included residents of Chennai, India, a major metropolitan center in southern India, as well as a semi-urban village approximately 100 km from Chennai. The present study included 720 whites and 373 blacks consecutively enrolled in the greater Pittsburgh (2003–2006) area with available lipid data. The analysis also includes 205 South Asians enrolled in the IndiaSCORE study in December, 2004. The institutional review board at the University of Pittsburgh approved the study protocols, and all study subjects provided written informed consent.

Demographic information

For all individuals included in this study, detailed demographic and medical histories were collected at the baseline visit. Lifestyle characteristics were measured by self-developed questionnaires. Physical activity was assessed using the Lipid Research Clinics Questionnaire. Physical examination included measurement of vital signs and anthropometric measures of body fat distribution. Body mass index (BMI) was calculated as weight divided by height (kilograms divided by square meters) Hypertension and metabolic syndrome were defined according to accepted criteria.[19,20] Diabetes mellitus was defined as fasting glucose $>$126 mg/dL or a history of previously diagnosed diabetes treated with diet, oral agents, and/or insulin. Blood pressure were measured during one sitting by trained nursing personnel.

Blood samples

Blood samples were drawn into tubes containing ethylenediaminetetraacetic acid (EDTA) by venipuncture from subjects who fasted for at least 12 hours. Plasma was separated by low-speed centrifugation and were stored at -70°C. After height, weight, and blood pressure (systolic blood pressure [SBP] and diastolic blood pressure [DBP]) were recorded, a venous blood sample was drawn into an EDTA-containing (1 mg/mL) tube for the measurement of lipoproteins, LDL subclasses, triglycerides, insulin, and glucose.

Lipoprotein analysis

Cholesterol assays were measured by a commercial laboratory using a vertical auto profile technique (VAP; Atherotech, Birmingham, AL), which also classified LDL as pattern A, A/B, and B according to increasing concentrations of the proatherogenic, small dense LDL-3. In addition to the total cholesterol, triglycerides, and LDL subfractions, the VAP profile also includes HDL subfractionation and lipoprotein (a) levels. This assay has been utilized previously as a rapid and sensitive method for the quantitative profiling of the major plasma lipoproteins.[21]

Statistical analysis

Baseline characteristics of whites, blacks, and Indians, including lipids and markers of atherogenic dyslipidemia (LDL pattern B or triglyceride/HDL [TG/HDL] ratio $>$3),