

Is the “South Asian Phenotype” Unique to South Asians?

Comparing Cardiometabolic Risk Factors in the CARRS and NHANES Studies



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ABSTRACT

Background: In the context of rising obesity in South Asia, it is unclear whether the “South Asian phenotype” (described as high glucose, low high-density lipoprotein cholesterol, and high triglycerides at normal ranges of body weight) continues to be disproportionately exhibited by contemporary South Asians relative to other race/ethnic groups.

Objectives: We assessed the distinctiveness of the South Asian cardiometabolic profile by comparing the prevalence of combined high glucose, high triglycerides, and low high-density lipoprotein cholesterol (combined dysglycemia and dyslipidemia) in resident South Asians with 4 race/ethnic groups in the United States (Asians, black persons, Hispanics, and white persons) overall and by body mass index (BMI) category.

Methods: South Asian data were from the 2010 to 2011 Center for Cardiometabolic Risk Reduction in South Asia Study, representative of Chennai and New Delhi, India and Karachi, Pakistan. U.S. data were from the 2011 to 2012 National Health and Nutrition Examination Survey, representative of the U.S. population. Combined dysglycemia and dyslipidemia was defined as fasting blood glucose ≥ 126 mg/dl and triglyceride/high-density lipoprotein cholesterol ratio >4 . Logistic regression was used to estimate the relative odds and 95% confidence intervals of combined dysglycemia and dyslipidemia associated with each race/ethnic group (referent, U.S. white persons). Models were estimated among adults aged 20 to 79 years by sex and BMI category and accounted for age, education, and tobacco use. Data from 8,448 resident South Asians, 274 U.S. Asians, 404 U.S. black persons, 308 U.S. Hispanics, and 703 U.S. white persons without previously known diabetes were analyzed.

Results: In the normal body weight range of BMI 18.5 to 24.9 kg/m², the prevalence of combined dysglycemia and dyslipidemia among men and women, respectively, was 33% and 11% in resident South Asians, 15% and 1% in U.S. Asians, 5% and 2% in U.S. black persons, 11% and 2% in U.S. Hispanics, and 8% and 2% in U.S. white persons. Compared with U.S. white persons, South Asians were more likely to present with combined dysglycemia and dyslipidemia at all categories of BMI for men and at BMI 18.5 to 29.9 for women in adjusted models. The most pronounced difference between South Asians and U.S. white persons was observed at normal weight (adjusted odds ratio: 4.98; 95% confidence interval: 2.46 to 10.07 for men) (adjusted odds ratio: 9.09; 95% confidence interval: 2.48 to 33.29 for women).

Conclusions: Between 8% and 15% of U.S. men and 1% and 2% of U.S. women of diverse race/ethnic backgrounds exhibited dysglycemia and dyslipidemia at levels of body weight considered “healthy,” consistent with the cardiometabolic profile described as the “South Asian Phenotype.” Urban South Asians, however, were 5 to 9 times more likely to exhibit dysglycemia and dyslipidemia in the “healthy” BMI range compared with any other U.S. race/ethnic group.

South Asians, or people who trace their ancestry to the Indian subcontinent, have been observed to exhibit higher indicators of cardiometabolic risk relative to white populations despite lower body weight according to body

mass index (BMI); this has been termed the “South Asian” or “Asian Indian phenotype” [1,2]. Among the consistently noted distinctive features of this phenotype are abdominal adiposity combined with glucose intolerance and specific

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dyslipidemias (e.g., low levels of high-density lipoprotein cholesterol [HDL], high levels of triglycerides and low-density lipoprotein, and high triglycerides relative to HDL) at levels of overall body mass considered normal in other populations [1–3]. Authors have also variously described additional features, such as excess body fat per unit BMI, truncal subcutaneous fat, higher C-reactive protein, and lower adiponectin as part of the South Asian phenotypic package; others have equated the South Asian phenotype with metabolic syndrome [1–3]. The South Asian phenotype has been invoked to explain, in part, reports of elevated coronary heart disease and cardiovascular mortality among migrant South Asians relative to local populations in diaspora settings that date back several decades [4–8].

Although cardiometabolic risk associated with South Asian race/ethnicity may reflect any combination of shared environmental exposures and stressors, genetic predisposition, behaviors, or social circumstances in migrant and native settings, long-term undernutrition at the population level is a leading hypothesis for the phenotype. Specifically, researchers posit that early life undernutrition (reflected in low birth weight and poor early life growth) predisposes South Asians to elevated metabolic risk later in life [9–13]. Recently observed transitions from undernutrition to overnutrition, however, seem to be altering the low average body weight traditionally associated with South Asians. For example, the most recent national data indicated that overweight and obesity increased (and underweight decreased) from 1996 to 2006 among women in multiple South Asian countries [14], and the prevalence of overweight was higher than that of underweight among middle-aged urban adults in India [15]. Similarly, recent studies in India have also indicated that overweight exceeded underweight in urban adolescents in industrial settings [16].

In light of rising trends toward excess body weight in urban South Asians, we assessed the distinctiveness of contemporary urban South Asians with respect to their cardiometabolic phenotype. Specifically, we compared the prevalence of the combination of high fasting plasma glucose (FPG) and high triglycerides relative to HDL in resident South Asians with prevalence of this combination in 4 race/ethnic groups residing in the United States (Asians, black persons, Hispanics, and white persons) at varying levels of body weight defined by BMI classification. We focused on high glucose and high triglycerides relative to HDL because glucose intolerance and accompanying specific dyslipidemias are the hallmark of the South Asian phenotype [1,3]. We also sought to add to the literature by comparing South Asians with multiple race/ethnic groups because race/ethnic classifications are an imperfect yet pragmatic way to group people who may have common historical nutritional and social experiences relevant to their cardiometabolic phenotype [17–19].

METHODS

Participants and data sources

Data for this study were from 2 large population-based, representative samples: the 2010 to 2011 wave of the

Center for Cardiometabolic Risk Reduction in South Asia Study (CARRS) and 2011 to 2012 National Health and Nutrition Examination Survey (NHANES). CARRS is an ongoing cohort study designed to be representative of nonpregnant adults aged 20 years and older residing in Chennai and New Delhi, India and Karachi, Pakistan in 2010 to 2011. NHANES is a biennial cross-sectional study designed to be representative of the U.S. population. Details of both studies are published [20,21]. We restricted the current analysis to adults aged 20 to 79 years in demographic groups of interest without a prior diagnosis of diabetes (self-reported), with complete anthropometric (height, weight) and laboratory assessments (FPG, triglycerides, HDL), and BMI >18.5. A total of 8,448 participants from CARRS and 1,789 participants from NHANES matched these criteria and were included in the study sample. Figure 1 shows a flow diagram of the inclusion/exclusion criteria that produced the analytic sample.

Residential and race/ethnic classification

We categorized the sample into 5 mutually exclusive demographic groups based on residence and race/ethnicity. All participants from CARRS were classified as “resident South Asians.” In NHANES, race/ethnicity was self-reported and our sample was categorized into 4 groups: 1) U.S. Asians; 2) U.S. black persons; 3) U.S. Hispanics; and 4) U.S. white persons. All NHANES participants beyond these categories were excluded from analysis. The U.S. Asian group was composed of both East Asians and South Asians, and the publicly available NHANES data do not allow for distinguishing between these 2 groups.

Body weight classification

We defined body weight categories following the international classification of BMI. A BMI <18.5 was excluded. BMI ranging from 18.5 to 24.9 kg/m² was considered “normal weight,” BMI ranging from 25 to 30 was considered “overweight,” and BMI >30 was considered “obese.” These 3 categories of body weight were used in the primary analysis.

Combined dysglycemia and dyslipidemia

We defined combined dysglycemia and dyslipidemia as the presence of FPG \geq 126 mg/dl and triglyceride to HDL ratio >4. When this package of high glucose and dyslipidemias is present at normal BMI, it reflects the “South Asian” phenotype.

In the CARRS study, fasting blood samples were collected in the morning (minimum 8 hours of fasting) at local camps when possible or in the home of participants. Samples were sent to an accredited laboratory in the respective city of data collection (Chennai, New Delhi, or Karachi) for analysis on the same day as they were collected. All 3 laboratories used by CARRS participated in a Randox International Quality Assessment Scheme that standardized findings to a central laboratory at the Public

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