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Original article

The contribution of biogeographical ancestry and socioeconomic status to racial/ethnic disparities in type 2 diabetes mellitus: results from the Boston Area Community Health Survey

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ABSTRACT

Purpose: Racial/ethnic disparities in the incidence of type 2 diabetes mellitus (T2DM) are well documented, and many researchers have proposed that biogeographical ancestry (BGA) may play a role in these disparities. However, studies examining the role of BGA on T2DM have produced mixed results to date. Therefore, the objective of this research was to quantify the contribution of BGA to racial/ethnic disparities in T2DM incidence controlling for the mediating influences of socioeconomic factors.
Methods: We analyzed data from the Boston Area Community Health Survey, a prospective cohort with approximately equal numbers of black, Hispanic, and white participants. We used 63 ancestry-informative markers to calculate the percentages of participants with West African and Native American ancestry. We used logistic regression with G-computation to analyze the contribution of BGA and socioeconomic factors to racial/ethnic disparities in T2DM incidence.
Results: We found that socioeconomic factors accounted for 44.7% of the total effect of T2DM attributed to black race and 54.9% of the effect attributed to Hispanic ethnicity. We found that BGA had almost no direct association with T2DM and was almost entirely mediated by self-identified race/ethnicity and socioeconomic factors.
Conclusions: It is likely that nongenetic factors, specifically socioeconomic factors, account for much of the reported racial/ethnic disparities in T2DM incidence.

Disparities in type 2 diabetes mellitus (T2DM) by race/ethnicity are a pervasive public health problem in the United States and worldwide. Recent estimates from the US Centers for Disease Control report that, compared with white adults, the prevalence of diabetes is 77% higher among black and 66% higher among Hispanic adults in the United States [1]. Racial/ethnic disparities have been shown to be associated with poorer diabetes control [2], elevated rates of diabetes-related complications [3], higher rates of hospitalization [4], and greater health care costs [5]. It has been proposed in several studies that genetics, specifically, biogeographical ancestry (BGA), may explain a substantial proportion of these disparities [6].

The concepts of genetics, race, and ethnicity are often confused [7–9]. The term "race" is commonly defined in terms of biological differences between groups assumed to have different BGAs [10]. Analysis of variance of genetic variation has indicated that approximately 75% of genetic variance is found "within" racial/ethnic groups, whereas 10% of the variance is found "between" races [10]. Furthermore, the US Census categorizations (white, black, Asian, etc) are largely artificial constructs, as is the concept of biological race itself [9,11]. In contrast, ethnicity is a complex multidimensional construct that reflects biological factors, geographical origins, historical influences, and social, cultural, and economic factors [12].

A genetic basis for racial/ethnic differences in diabetes risk, the "thrifty gene" hypothesis, was first proposed more than 40 years ago [13]. The hypothesis has been heavily criticized from several different perspectives [7], but has nevertheless been revived in recent years as the rapid evolution of science and technologies have facilitated an expansion in genetic research. Genetic studies have established approximately 70 loci that are associated with small increases in T2DM risk [14–18]. Although early studies focused primarily on people of European descent, recent studies

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extended this research to black and Hispanic populations [19–21]. These studies indicate substantial overlap in the susceptibility loci across racial/ethnic groups signifying that common genetic variants contribute similarly to diabetes risk across races/ethnicities [6,15,21,22] and are therefore unlikely to explain racial/ethnic differences in diabetes risk.

Because T2DM has a complex genetic etiology, it may be important to account for the substantial heterogeneity in genetic heritage that exists in admixed populations [23–26]. Individual proportions of European, African, and Native American ancestry can vary substantially among the commonly used categories of black [23], Hispanic [25], and white [27]. Several studies have suggested that the biologic mechanisms leading to increased T2DM risk in black and Hispanic Americans may be related to genes associated with BGA [6,10,28]. However, studies examining this hypothesis by measuring ancestry-informative markers (AIMs), a method of estimating an individual's genetic marker–based race/ethnicity have produced mixed results. The Atherosclerosis Risk in Communities Study found that BGA was not associated with HbA1c among African Americans and found that the contributions of demographic and metabolic factors outweighed the contributions of BGA [29]. However, an analysis of Atherosclerosis Risk in Communities and/or Jackson Heart data found that BGA was associated with T2DM among African Americans, a finding that was robust to adjustment for lifestyle and socioeconomic factors [6]. Studies among Hispanic populations have similarly produced mixed results. In a study of Columbian and Mexican participants, the association between ancestry and T2DM was attenuated, if not eliminated, when adjusting for socioeconomic factors [30]. In contrast, a study of Puerto Rican participants living in the continental United States showed a negative association between African ancestry and prevalent T2DM [31]. In one of the few studies, to examine the associations between ancestry and diabetes risk among African and Hispanic Americans, the Women's Health Initiative found that ancestry was significantly associated with diabetes risk, but that socioeconomic factors attenuated the effects among Hispanic but not African American women [32].

In light of these conflicting findings, further research is needed to validly estimate the contributions of BGA and other factors to T2DM disparities. Therefore, our objectives were twofold: (1) to quantify the contribution of African and Native American ancestry to racial/ethnic disparities in T2DM incidence and (2) to measure the contribution of socioeconomic status (SES) to racial/ethnic and BGA disparities in T2DM incidence (Fig. 1). The Boston Area Community Health (BACH) Survey [33] is uniquely positioned to address these research objectives given the racial/ethnic diversity of the cohort and its prospective cohort design.

Materials and methods

The BACH survey

The BACH Survey is a prospective cohort study of men and women from Boston, Massachusetts. The BACH Survey used a random stratified cluster sample design to recruit 5502 residents (2301 men and 3201 women) aged 30 to 79 years from three racial/ethnic groups (1767 black, 1876 Hispanic, and 1859 white). Participants completed an in-person interview at baseline (2002–2005) and were contacted approximately 5 years (BACH II: 2006–2010) and 7 years (BACH III: 2010–2012) later for follow-up assessments. BACH III interviews were conducted among 3155 (BACH III) individuals (an 81.4% conditional retention rate).

At all three time points, a home visit was conducted that included anthropometric measurements and an in-person interview, conducted in English or Spanish, to obtain information about diabetes status, comorbidities, sociodemographics, and lifestyle. AIMs were collected at BACH III only. The detailed methods have been described elsewhere [33]. All participants provided written informed consent and the study was approved by New England Research Institutes' Institutional Review Board.

Measures

Biogeographical ancestry

A panel of 63 uncorrelated single nucleotide polymorphism was genotyped. These AIMs were selected based on their ability to estimate percent African, Native American, and European ancestry in admixed populations [25,34]. Samples were genotyped at the Genetic Analysis Platform at the Broad Institute (Cambridge, MA) using iPLEX (Sequenom, San Diego, CA) in three batches. HapMap samples (Utah residents with Northern and Western European ancestry and Yoruba in Ibadan, Nigeria) were included in each batch for quality control. All HapMap samples had 100% HapMap concordance. The average call rate for all assays was 97.4%; 1.6% of samples failed quality control with call rates less than 90% and two single nucleotide polymorphisms failed with call rates less than 90%. Ancestry proportions were estimated for individual participants using ADMIXTURE Software (version 1.12 http://www.genetics.ucla.edu/software/admixture/) using a k (the number of ancestral populations) of 3.

Race/ethnicity

Self-identified race/ethnicity was recorded using two separate survey questions as recommended by the Office of Management and Budget. The racial/ethnic categories used in this research are (1)

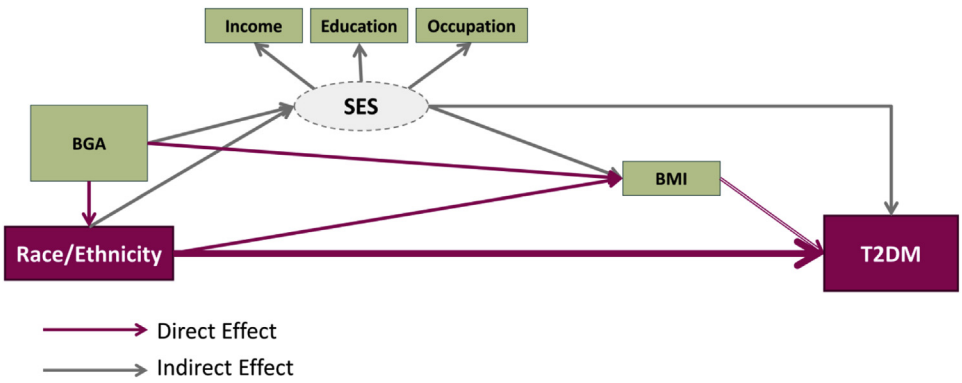

Fig. 1. Research model. (1) What is the contribution of BGA to racial/ethnic disparities in T2DM? (pink arrows). (2) What is the indirect effect (mediation) of SES on racial/ethnic and ancestral disparities on T2DM?