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Racial Differences in Tuberculosis Infection in United States Communities: The Coronary Artery Risk Development in Young Adults Study

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Previously reported associations between race/ethnicity and tuberculosis infection have lacked sufficient adjustment for socioeconomic factors. We analyzed race/ethnicity and self-reported tuberculosis infection data from the Coronary Artery Risk Development in Young Adults (CARDIA) study, a well-characterized cohort of 5115 black and white participants, and found that after adjusting for sociodemographic and clinical factors, black participants were more likely to report tuberculosis infection and/or disease (odds ratio, 2.0; 95% confidence interval, 1.5–2.9).

Tuberculosis (TB) is among the leading conditions for which disparities in disease rates between blacks and white exist [1]. According to the Centers for Disease Control and Prevention (CDC), of the 4378 cases of TB reported in United States (US)–born patients in 2010, 40% were among non-Hispanic blacks, a rate 8 times higher than that among non-Hispanic whites [2]. Similarly, the prevalence of latent TB infection (LTBI) in US-born individuals is 5.7% among blacks, significantly higher than the 2.5% prevalence in Mexican-Americans and 1.1% in whites [3]. The proposed causes of this disparity include environmental and host factors [4], as well as differences in comorbid conditions that affect risk of developing TB once infected, such as human immunodeficiency virus (HIV) infection [5]. In some studies, low socioeconomic status is reported to account for a significant proportion of the increased risk for TB seen in blacks in the US [6, 7]; however, other studies indicate that genetic susceptibility to infection may explain some of the racial differences in disease rates [8, 9]. Overall, racial disparities in TB are substantial in the US [10], and whether these differences are accounted for by socioeconomic status continues to be debated.

We used the Coronary Artery Risk Development in Young Adults (CARDIA) study, a population-based longitudinal study of risk factors for cardiovascular disease with a cohort of 5115 black and white participants, to determine whether black race is associated with TB infection after adjusting for socioeconomic status and other traditional TB risk factors. The thorough characterization of individual-level data on socioeconomic indicators of CARDIA participants provided an opportunity to control for this potential confounder.

METHODS

Study Population and Setting

Participants were unrelated men and women who participated in the CARDIA study, an ongoing epidemiologic study of cardiovascular risk development in young adults [11]. To be eligible for the CARDIA study, participants must have identified themselves as non-Hispanic white or black and as having a permanent address in 1 of 4 US urban communities (Birmingham, Alabama; Chicago, Illinois; Minneapolis, Minnesota; or Oakland, California). The CARDIA cohort was designed to be balanced by race, sex, education (less than high school vs high school graduation), and age. A total of 5115 individuals were recruited and examined at the baseline examination in 1985–1986 when participants were 18–30 years of age. Follow-up examinations occurred after 2, 5, 7, 10, 15, and 20 years. The CARDIA study has had a high retention rate at year 20, with 87.5% of the original cohort completing the annual telephone interview for outcome ascertainment and 71.8% completing the in-person examination [12]. The current analysis of risk factors for TB infection was conducted on 3112 participants for whom there were complete clinical and demographic data at baseline and follow-up examinations. The study was approved by the Committee on Human Research at the University of California,

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San Francisco, and all participating CARDIA centers. Written informed consent was obtained from participants at each examination.

Categorization of Tuberculosis Infection

At years 10, 15, and 20, all available CARDIA participants were asked: "Has a doctor or nurse ever said that you have tuberculosis or a positive skin test for tuberculosis?" Participants who answered yes to this question at any of these exams were categorized as being TB infected, whereas participants who reported consistent negative response to the question at exam years 10, 15, and 20 were categorized as TB uninfected.

In addition to age, sex, and race, predictors for TB infection analyzed included socioeconomic measures (household income, education, housing status, history of incarceration, and crowding [as measured by the reported number of household members]), as well as comorbid characteristics associated with risk for TB infection and disease including diabetes, smoking, hematologic cancers, kidney disease, and self-reported HIV status. All covariates and risk factors were assessed prior to reported TB infection so as to assure correct chronology in terms of risk and exposure and timing of TB infection.

Statistical Analysis

The definitions and primary objectives of this study were formulated prior to data analysis. All statistical analysis was done using SAS software, version 9.2. Associations with TB infection were adjusted using multivariate logistic regression models. Predictors with $P < .2$ in bivariate analysis were included in the multivariate model. Because of differential dropout of participants with characteristics of importance to the study, we performed analyses using stabilized inverse probability-of-censoring weights to reduce potential bias. Weights were developed using all the characteristics associated with dropout, which included black race, male sex, site of enrollment, incarceration history, self-report of ever smoking, and having less than a high school education at baseline [13].

RESULTS

Of the 5115 participants initially enrolled in CARDIA, 1410 black participants (53.5% of all black participants) and 1702 white participants (68.7% of all white participants) had complete demographic and clinical data for this analysis and were included in this study. Of these, 185 (5.9%) reported a history of TB infection or disease, which corresponded to 8.5% of black participants and 3.8% of white participants (unadjusted odds ratio [OR], 2.3; 95% confidence interval [CI], 1.7–3.2). The strongest associations with TB infection, other than race, included reported HIV infection, smoking, household income, home ownership, and household size as measured by the reported number of household members (Table 1).

From the multivariate logistic regression model for characteristics associated with TB infection shown in Table 1, black race and HIV infection were each independently and positively associated with TB infection ($P < .05$).

Black participants, and participants with the characteristics of male gender, site of enrollment in Minnesota, incarceration history, self-report of ever smoking, and having less than a high school education at baseline, were more likely to be lost to follow-up in the CARDIA study. To address potential bias resulting from differential dropout, we performed our analysis using stabilized inverse probability weights; our independent predictors of TB infection, including black race (OR, 2.0; 95% CI, 1.4–3.0), remained unchanged (analysis not shown).

DISCUSSION

In this study, we identified racial differences in the reported rate of TB infection in participants enrolled in the CARDIA study, an ongoing epidemiologic study of coronary artery risk development in young black and white adults. The CARDIA study collects individual-level data on a variety of socioeconomic indicators, including level of education, housing status, household size, and income level. In our analyses, the increased risk of TB infection in black participants persisted after adjusting for these socioeconomic indicators. The increased risk for TB infection in black participants also persisted after adjusting for other known risk factors for TB such as HIV infection, diabetes, renal disease, hematologic cancers, intravenous drug use, and incarceration, with black participants having a 2-fold increased odds of self-reported TB infection compared with white participants ($P < .001$). Our findings suggest that factors other than comorbid conditions and socioeconomic status may contribute to the racial disparity seen in TB rates between blacks and whites in the US [1]. Whether this disparity is due to unmeasured factors related to race as a social construct or due to biologic susceptibility factors is still subject to debate. An analysis of the influence of race/ethnicity on rates of active TB in the United States found that adjusting for 6 socioeconomic indicators accounted for approximately half the increased risk of TB previously ascribed to race/ethnicity among US-born blacks, Hispanics, and Native Americans [6]. However, this study used ecologic-level data for socioeconomic indicators, specifically US Census data and zip code–specific demographic substratum values, whereas our study used individual-level data. Taken together, the numerous publications that show a link between race and increased risk of TB in US-born populations raise the question of whether targeted testing and treatment for LTBI should be recommended by race. Whether such a strategy would be cost-effective and whether it would have the potential to address the persistent disparity seen in TB between blacks and whites in the United States deserves further study.

Table 1. Predictors of Tuberculosis Infection in 3112 Participants Enrolled in CARDIA

	Tuberculosis infected ($n = 185$)	Unadjusted OR (95% CI), P value	Adjusted OR (95% CI), P value
Race			
Black	8.5%	2.3 (1.7–3.2), <.001	2.0 (1.5–2.9), <.001
White	3.8%		
Sex			
Male	5.6%	0.9 (0.6–1.2), .42	
Female	6.2%		
Enrollment site			
Oakland, CA	5.4%	1.0	
Minneapolis, MN	4.8%	0.9 (0.6–1.4), .61	
Birmingham, AL	6.5%	1.2 (0.8–1.9), .34	
Chicago, IL	7.4%	1.4 (0.9–2.1), .11	1.3 (0.9–1.8), .11
Mean BMI at year 10 ± SD (odds per 5-unit increase)	28 ± 7	1.1 (1.0–1.2), .05	1.0 (0.9–1.2), .52
Ever self-reported kidney disease[a]			
Yes	6.9%	1.2 (0.8–1.9), .44	
No	5.8%		
Fasting glucose >125 mg/dL at year 10			
Yes	1.8%	0.3 (0.0–2.0), .21	
No	6.0%		
Ever self-reported diabetes mellitus[a]			
Yes	6.0%	1.0 (0.5–2.0), .96	
No	5.9%		
Ever self-reported hematologic cancer[b]			
Yes	6.8%	1.1 (0.4–3.2), .78	
No	5.9%		
Ever self-reported HIV infection[c]			
Yes	20.0%	4.0 (1.3–12.2), .01	3.4 (1.1–10.9), .04
No	5.9%		
Ever self-reported injection drug use[b]			
Yes	9.1%	1.6 (0.8–3.3), .18	1.6 (0.8–3.3), .22
No	5.8%		
Ever self-reported incarceration history[d]			
Yes	6.9%	1.2 (0.6–2.2), .61	
No	5.9%		
Ever self-reported smoking[a]			
Yes	6.5%	1.2 (0.9–1.6), .20	
No	5.5%		
Education at year 10			
7–12 years (High school or less)	6.5%	1.1 (0.7–1.7), .68	
13–16 years (Any college)	5.7%	1.0 (0.7–1.4), .84	
>16 years (Graduate school)	5.9%	1.0	
Household income at year 10[e]			
<2 times FPL	8.1%	1.8 (1.2–2.6), .001	1.0 (0.7–1.6), .91
2–4 times FPL	7.1%	1.6 (1.1–2.2), .01	1.2 (0.8–1.7), .32
>4 times FPL	4.6%	1.0	1.0
Mean number of people in household ± SD at year 10 (odds per 1-person increase)	3.3 ± 1.7	1.1 (1.0–1.2), .02	1.1 (1.0–1.2), .09
Homeowner at year 10			
Yes	4.9%	0.6 (0.5–0.8), .002	0.7 (0.5–1.0), .08
No	7.5%		

NOTE. BMI, body mass index; CARDIA, Coronary Artery Risk Development in Young Adults study; CI, confidence interval; FPL, federal poverty line; HIV, human immunodeficiency virus; OR, odds ratio. Only variables with P value <.2 were included in the multivariate (adjusted) model.

[a] Responses are cumulative from years 0, 2, 5, 7, and 10 and precede assessment for tuberculosis.

[b] Question was not added to the survey until year 5. Responses are from years 5, 7, and 10.

[c] Question regarding HIV history was not added to the survey until year 15. Responses are from years 15 and 20.

[d] Question regarding incarceration history was only on the survey during years 0 and 2.

[e] FPL calculation is based on poverty thresholds adjusted for household size, United States Census Bureau, 1995 (year 10 of the CARDIA study).

Our study has limitations. First, CARDIA was focused on cardiovascular disease and consequently did not pursue diagnostic testing to confirm self-reports of HIV and TB. To address this, we limited our analysis to participants who provided consistent responses to the TB questions. Second, we could not clearly distinguish between patients with LTBI and those who may have had active TB. Consequently, we cannot comment on susceptibility to infection versus progression to disease. Third, although guidelines do not list race/ethnicity as indications for LTBI testing [14], it is possible that there was differential testing for TB based on race, as has been reported for other primary care procedures [15]. However, the increased risk for LTBI in non-Hispanic blacks reported in an analysis of National Health and Nutrition Examination Survey data on 7386 participants with tuberculin skin test results suggests that the association between race and TB is not an artifact of increased testing [3]. We attempted to address this issue by controlling for characteristics that disproportionately affect blacks in the United States and may be indications for LTBI testing, including incarceration history and housing status, and race retained its association with self-report of TB. Nonetheless, differential testing as well as residual confounding may still exist.

In summary, we have shown that within a prospective, ongoing epidemiologic study of coronary artery disease in young black and white adults in 4 US communities, black study participants were 2 times more likely to report a history of TB infection compared with white participants after adjusting for a variety of socioeconomic factors, HIV status, intravenous drug use, diabetes, renal disease, and other traditional risk factors for TB. Our study suggests that factors other than socioeconomic status also contribute to the racial disparity in tuberculosis noted in US-born blacks.

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