Racial Difference in Sarcoidosis Mortality in the United States

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BACKGROUND: The clinical presentation and outcome of sarcoidosis varies by race. However, the race difference in mortality outcome remains largely unknown.

METHODS: We studied mortality related to sarcoidosis from 1999 through 2010 by examining data on multiple causes of death from the National Center for Health Statistics. We compared the comorbid conditions between sarcoidosis-related deaths with deaths caused by car accidents (previously healthy control subjects) and rheumatoid arthritis (chronic disease control subjects) in both African Americans and Caucasians.

RESULTS: From 1999 through 2010, sarcoidosis was reported as an immediate cause of death in 10,348 people in the United States with a combined overall mean age-adjusted mortality rate of 2.8 per 1 million person-years. Of these, 6,285 were African American and 3,984 Caucasian. The age-adjusted mortality rate for African Americans was 12 times higher than for Caucasians. African Americans died at an earlier age than Caucasians. African Americans living in the District of Columbia and North Carolina and Caucasians living in Vermont had higher mortality rates. Although the total sarcoidosis age-adjusted mortality rate had not changed over the 12 year period studied, this rate increased for Caucasians ($R = 0.747$, $P = .005$) but not for African Americans. Compared with the control groups, pulmonary hypertension was significantly more common in individuals with sarcoidosis.

CONCLUSIONS: This nationwide population-based study exposes a significant difference in ethnicity and sex among people dying of sarcoidosis in the United States. Pulmonary hypertension investigation should be considered in all patients with sarcoidosis, especially African Americans. CHEST 2015; 147(2):438-449

Sarcoidosis is a granulomatous disease with an unknown etiology.[1] Ethnicity plays an important role in sarcoidosis epidemiology, disease presentation, and clinical outcomes.[2] The reported disease incidence is five in 100,000 for Caucasians and 39 in 100,000 for African Americans.[3] The lifelong risk for the development of sarcoidosis is estimated to be 2.7% for African American women and 2.1% in African American men but only 1% for Caucasian women and 0.7% for Caucasian men.[4] Sarcoidosis affects African Americans at a younger age than Caucasians, with a reported peak incidence one decade earlier than in Caucasians.[4]

African Americans with sarcoidosis have a higher rate of hospital admission than Caucasians.[5,6] Additionally, remarkable differences exist in the clinical presentation of sarcoidosis between African Americans and Caucasians. Sarcoidosis is more often symptomatic in African Americans.[7] African Americans experience more extra-pulmonary sarcoidosis, more often affecting the skin, bone marrow, and eyes,[8,9] and have a higher likelihood of decreasing FVC in the course of pulmonary sarcoidosis.[10] As such, African Americans experience worse prognosis, more multiorgan involvement, and a higher rate of hospitalization.[11-13] Despite several health disparities analyses focusing on the epidemiology and prognosis of sarcoidosis, few studies have evaluated the role of this difference plays in mortality.[12,14]

In this study, we hypothesized that African Americans with sarcoidosis have a higher mortality rate, which increased in the past decade. We examined the trend of the sarcoidosis-related mortality rate in African Americans and Caucasians over 12 years and compared comorbidities with representative control groups of previously healthy people defined as those who died as a result of car accidents and chronically ill people defined as those who died of rheumatoid arthritis.

Materials and Methods

Study Design and Data Collection

The Institutional Review Board of the University of Illinois at Chicago approved a waiver for this study (IRB number 2014-0418). This retrospective, population-based study compared data on immediate cause of death based on US death certificates from 1999 to 2010. The data were obtained from the WONDER (Wide-ranging Online Data for Epidemiologic Research) online databases prepared by the Centers for Disease Control and Prevention.[15] Death certificates list a single underlying cause of death (the immediate cause of death), up to 20 comorbidities, and demographic information.[16] Diseases and related conditions reported on the death certificate are coded in accordance with the *International Classification of Diseases, 10th Revision* (ICD-10), since 1999.[17]

Study Variables

Variables included in the analysis were age, sex, race/ethnicity, year of death, cause of death, and comorbid conditions. Race/ethnicity was categorized according to US Census standards as non-Hispanic white, Asian-Pacific Islander, non-Hispanic black (black), and American Indian-Alaska Native (Native American). The study population was defined as non-Hispanic African American and non-Hispanic Caucasian. Age at death was classified into the clustered age-groups.

Study Definitions

Sarcoidosis-related mortality was defined as the immediate cause of death from pulmonary or extrapulmonary sarcoidosis. This included all observations that assigned any of the ICD-10 D86 codes as the immediate cause of death.

Two control groups were selected: pedestrians who died in traffic accidents, representing a healthy population, and people who died of rheumatoid arthritis. Rheumatoid arthritis, like sarcoidosis, is a chronic inflammatory disease with a higher prevalence in African Americans and women. In addition, both diseases are usually treated with similar medications. Traffic accident-related deaths were defined by an immediate cause of death with ICD-10 codes of V01 to V09. Seropositive and seronegative rheumatoid arthritis-related deaths were defined by an immediate cause of death with ICD-10 codes M05 and M06.0. Comorbidities were defined with the following ICD-10 codes: pneumonia, J09-J18; acute respiratory failure, J96.0; nontuberculous mycobacterial infection, A31; TB, A16 to A19; COPD, J44; pulmonary hypertension, I27.0 and I27.2; diabetes, E10 to E14; heart failure, I50; chronic renal failure, N18; dementia (vascular, F01; Alzheimer, G30); asthma, J45; HIV infection, B20 to B24; neoplasm, C00-D48; hepatic failure, K70.4 and K72.0; and pulmonary fibrosis, J84.

Statistical Analysis

Counts and percentages were examined as predictors using crude ORs and χ^2 test or, as appropriate, Mantel-Haenszel, exact, or two-sided analysis of variance tests. The crude mortality rate was not primarily used in this study because of the potential misleading information resulting from comparing rates over time in various age-groups. Age-adjusted mortality rates were used to calculate relative mortality risk among groups and over time. Age-adjusted death rates were calculated by weighting averages of the age-specific rates and comparing with relative mortality risk among 2,000 US standard populations. The equation for the age-adjusted death rate calculation was $R' = \Sigma i(Psi/Ps)Ri$, where Psi is the standard population for age-group, and i and Ps are the total standard population (all ages combined).[15] Linear regression and exponential growth regression model analysis were performed to evaluate the trend of age-adjusted rates of sarcoidosis-related mortality from 1999 to 2010.

To examine comorbid conditions, we compared decedents aged > 35 years with sarcoidosis with traffic accident- and rheumatoid arthritis decedents in the same age-group from 1999 to 2010 and calculated crude OR and CI comparisons of selected comorbidities. For all statistical analyses, a two-tailed $P < .05$ was considered significant.

A total of 70,494 pedestrians died in traffic-related accidents during the study period. There were 7,723 non-Hispanic African American (women, 2,066; men, 5,657) and 28,295 non-Hispanic Caucasian (women, 9,240; men, 19,055) decedents aged > 35 years used as control subjects.

Rheumatoid arthritis was reported as the immediate cause of death in 29,997 (women, 22,935; men, 7,062) individuals. There were 1,881 non-Hispanic African American (women, 1,469; men, 412) and 2,860 non-Hispanic Caucasian (women, 1,941; men, 919) decedents aged > 35 years used as control subjects.

Data are suppressed by the National Center for Health Statistics when a category has < 10 people for confidentiality reasons. Death rates are labeled as unreliable when the numerator is < 21. All analyses were performed using the statistical software packages SPSS, version 21 (IBM Corporation) and GraphPad Prism, version 6 (GraphPad Software, Inc).