

Obesity and Weight Gain in Relation to Incidence of Sarcoidosis in US Black Women

Data From the Black Women's Health Study

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BACKGROUND: Sarcoidosis, a systemic disorder characterized by chronic granulomatous inflammation, occurs more frequently among US black women, as do overweight and obesity. Little is known about the relation of overweight and obesity, which induce chronic inflammation, to incidence of sarcoidosis.

METHODS: We assessed the relation of obesity and weight gain to the incidence of sarcoidosis in the Black Women's Health Study, a follow-up study of 59,000 US black women aged 21 to 69 years at baseline in 1995. Information on weight at age 18 years, height, current weight, incident sarcoidosis, and covariates was collected at baseline and on biennial follow-up questionnaires. Cox regression models adjusted for age, education, geographic region, smoking, alcohol consumption, and physical activity were used to estimate incidence rate ratios (IRRs) and 95% CIs.

RESULTS: From 1995 through 2011, 454 incident cases of sarcoidosis occurred during 707,557 person-years of follow-up. The incidence of sarcoidosis increased with increasing BMI and weight gain. The IRR was 1.40 (95% CI, 0.88-2.25) for BMI ≥ 30 kg/m² at age 18 years relative to 20 to 24 kg/m² (*P* trend = .18), 1.42 (95% CI, 1.07-1.89) for BMI ≥ 35 kg/m² at baseline relative to 20 to 24 kg/m² (*P* trend = .01), and 1.47 (95% CI, 1.10-1.97) for a weight gain between age 18 years and baseline of ≥ 30 kg relative to 0 to 9 kg (*P* trend = .16). In stratified analyses, there were significant trends of sarcoidosis incidence with increasing BMI and weight gain in women aged ≥ 45 years and ever smokers.

CONCLUSIONS: The present study provides evidence that weight gain and obesity during adulthood are associated with increased sarcoidosis incidence.

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ABBREVIATIONS: BWHS = Black Women's Health Study; IRR = incidence rate ratio

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Sarcoidosis is a multisystem disease of unknown etiology. It is associated with a wide spectrum of disease manifestations but typically affects the lung.¹⁻³ In the United States, patterns of sarcoidosis differ by race and sex,²⁻⁵ with black women experiencing the highest incidence of the disease. The estimated lifetime risk of sarcoidosis is 2.7% for black women compared with 1.0% for white women.^{4,5}

The prevalence of obesity is also disproportionately high in US black women.⁶⁻⁸ Obesity is characterized by a state of low-grade systemic inflammation.⁹ Sarcoidosis is characterized by chronic granulomatous inflammation,

which is believed to be a result of a persistent T-helper 1 polarized immune response targeted to an as-yet-unidentified antigen.¹⁰ We hypothesized that the inflammation associated with obesity partly explains the higher incidence of sarcoidosis in black women.

We prospectively assessed the associations of obesity and weight gain with the incidence of sarcoidosis over a 16-year period in the Black Women's Health Study (BWHS), a prospective follow-up of 59,000 US black women. To our knowledge, this epidemiologic study is the first to examine the relation of these factors to incident sarcoidosis in black women.

Materials and Methods

The human subjects protocol for this study was approved by the Boston University Medical Center Institutional Review Board (H-31125). The BWHS is a follow-up study of US black women that began in 1995 when 59,000 women aged 21 to 69 years (median, 38 years) enrolled through postal health questionnaires.¹¹ Participants indicated their informed consent by completing the questionnaire. At baseline, 97% of the participants had completed high school, and 44% had completed college. More than 80% were from California, Georgia, Illinois, Indiana, Louisiana, Maryland, Massachusetts, Michigan, New Jersey, New York, South Carolina, Virginia, and the District of Columbia. Participants are mailed biennial questionnaires to obtain updated health information.

On the 1995 baseline questionnaire, BWHS participants provided data on demographics, medical and reproductive history, smoking and alcohol use, physical activity, height, weight, use of selected medications such as oral contraceptives and female hormone supplements, diet, and use of medical care. Participants complete biennial follow-up questionnaires to update these and other exposures and report new occurrences of disease. Follow-up of the baseline cohort is 80% after eight questionnaire cycles.

Ascertainment and Validation of the Diagnosis of Sarcoidosis

On the 1995 baseline questionnaire, BWHS participants were asked whether a physician had ever told them that they had any of a list of medical conditions. The list of diagnoses did not specify sarcoidosis, but numerous women wrote it in under other conditions. All subsequent follow-up questionnaires asked specifically about sarcoidosis and whether the participants had received a new diagnosis in the past 2-year period.

All participants who reported incident sarcoidosis are asked for permission to contact their physicians for information on diagnosis and treatment.¹² The physicians are asked to complete a questionnaire regarding the study participant's condition and treatment or, alternatively, to provide a copy of the participant's medical records pertaining to sarcoidosis. The diagnosis of sarcoidosis was confirmed for 96% of the 160 participants for whom physician questionnaires or medical records were obtained to date. Among the six disconfirmed cases, one had asthma and one had keloids; alternative diagnoses were not provided for the four others. In addition, a supplemental sarcoidosis questionnaire sent to participants with incident sarcoidosis assessed disease severity by asking whether the participants had experienced any of the following nine symptoms at the time of diagnosis: shortness of breath, cough, chest pain, fatigue, palpitations, nasal/sinus congestion, joint pain/muscle aches, numbness, and headaches.¹² We considered women with two or more symptoms at the time of diagnosis to have more-severe disease. Based on the high level of agreement between self-report and

physician report and records, all participants who reported sarcoidosis during follow-up were included as cases of sarcoidosis unless the diagnosis was disconfirmed by medical records.

Exposure Variables and Covariates

Information on adult height (feet and inches), weight at age 18 years (pounds), prudent dietary pattern, recent medical visit, and comorbid illness (eg, hypertension, type 2 diabetes mellitus, asthma) was collected at baseline in 1995. Information on health insurance status for the previous 2-year period was collected in 1997. Current weight, age, geographic region, smoking status, alcohol consumption, and vigorous physical activity were ascertained at baseline in 1995 and on each follow-up questionnaire. Years of education were ascertained on the 1995 and 2003 questionnaires.

BMI at age 18 years and at baseline was calculated as weight measured in kilograms at each time divided by height squared measured in meters. Weight change was calculated as the difference between weight at age 18 years and weight at baseline (1995), converted to kilograms. We assessed the validity of self-reported height and weight in a physical activity validation study among 115 BWHS participants residing in the Washington, DC, metropolitan area.¹³ Correlation coefficients for self-reported and technician measures of weight and height were 0.97 and 0.93, respectively ($P < .01$).¹⁴

Data Analysis

Follow-up for the current analysis was from 1995 to 2011. Potential participants were 55,840 women with complete data on weight at age 18 years and at baseline whose cumulative weight change between age 18 years and baseline was ≥ 0 kg. We excluded prevalent cases of sarcoidosis ($n = 687$) and cancer ($n = 1,402$), women whose baseline weight was ≤ 36 or ≥ 136 kg ($n = 677$), women who were currently pregnant in 1995 ($n = 1,012$), and women who underwent gastric bypass surgery ($n = 100$), leaving 51,452 women in the analytic sample.

Incidence rate ratios (IRRs) and 95% CIs for incident sarcoidosis were estimated for categories of BMI at age 18 years, BMI at baseline, and weight gain from age 18 years to 1995 using Cox proportional hazard models in PROC PHREG of SAS 9.1 (SAS Institute, Inc). Person-time was calculated from baseline to year of sarcoidosis diagnosis, loss to follow-up, death, or end of follow-up, whichever occurred first. We constructed two analytic models to control for potential confounders. Model 1 adjusted for age (1-year intervals) and questionnaire cycle (2-year intervals). Model 2 adjusted for model 1 covariates plus education (≤ 12 , 13-15, ≥ 16 years), geographic region (Northeast, South, Midwest, West), pack-years of smoking (never smoked, < 5 , 5-14, 15-24, ≥ 25 years), alcohol consumption (never, < 1 , 1-6, 7-13, ≥ 14 drinks/week), and hours of vigorous physical activity per week (none, < 5 , and ≥ 5 h/week). All variables in the model, with the exception of BMI, were treated as time varying using the Anderson-Gill data structure.¹⁵

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