Geographic Variation in Sarcoidosis in South Carolina: Its Relation to Socioeconomic Status and Health Care Indicators

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Geographic patterns of sarcoidosis have been detected and studied on a global scale. However, the associations between these disease patterns and population characteristics have not been determined. The authors studied the geographic pattern of sarcoidosis in South Carolina and its relation to socioeconomic status (SES) and health status indicators. Hospitalization rates for the period 1985–1995 were used as geographic indicators of sarcoidosis. Rates were assessed for the 46 counties in South Carolina, adjusting for differences in SES, availability/accessibility of health care, diagnostic practices, and hospital utilization. Patterns in geographic variation were assessed based on physiographic characteristics and proximity to the Atlantic coastline. Significant variation was identified with an increase in sarcoidosis rates proximal to the Atlantic coastline. Population characteristics were identified that appeared to explain regional variation in sarcoidosis in Caucasians; however, regression analysis was unable to explain the regional differences in disease distribution by variation in SES, diagnostic practices, accessibility/availability, or hospital utilization in African Americans. These results suggest that the development of sarcoidosis is associated with a geographically linked risk factor in African Americans. This work supports the need for additional studies that will identify this risk factor(s). Am J Epidemiol 1999; 150:271–8.

geography; health status indicators; hospitalization; sarcoidosis; social class

Geographic variation in a disease may provide important information about its distribution and etiology. In particular, organized geographic patterns of disease may provide clues to potential environmental and cultural risk factors (1).

Sarcoidosis is a multisystemic granulomatous disorder of unknown etiology that most often affects the lungs, lymph nodes, skin, and eyes, respectively. Involvement of the liver, heart, and/or central nervous system is not unusual (2), but almost any organ can be affected. The disease exhibits two distinct clinical courses: an acute course that usually resolves or stabilizes within 2 years, and a chronic course that is progressive and may lead to severe organ dysfunction and death (3). A number of potential causes of sarcoidosis have been proposed, including genetic predisposition (4–13), infectious agents (4–8, 14–22), environmental exposures (4–8, 23–28), and occupational exposures (4–8, 23, 29, 30), but no specific cause has been identified that explains the distribution and frequency that the disorder exhibits worldwide.

Geographic variation in sarcoidosis incidence and prevalence has been studied at both local and global levels. Sarcoidosis incidence is highest in northern European countries such as Sweden and Denmark (4, 31) and in African Americans. Rates in African Americans have been shown to be 4–17 times higher than rates for Caucasians (23, 32–36). Sarcoidosis rates have also been shown to be much higher in the southeastern United States (24,32), particularly in coastal areas (24). Incidence rates have also been shown to be significantly higher in rural areas (4–8, 25, 32).

Because socioeconomic status (SES) and health care status indicators also vary geographically, an assessment of the geographic patterns of sarcoidosis should include measures of SES and health care status. In this study, the association between sarcoidosis hospitalization rates and socioeconomic status, utilization of hospitals, access to and availability of health care, and diagnostic practices was evaluated by county. Subsequently, South Carolina counties were partitioned into four distinct geographic regions based on physiographic characteristics and proximity to the...
Atlantic coastline, and patterns in hospitalization rates were identified and assessed.

MATERIALS AND METHODS

Hospitalization rates

Hospitalization rates for the period 1985–1995 were calculated for each county by using hospital discharge records from the South Carolina Hospital Discharge database maintained and managed by the South Carolina Budget and Control Board’s Office of Research and Statistics. Primary and secondary diagnoses of sarcoidosis were combined, and duplicate individuals were eliminated so that hospitalization rates reflected the number of unique individuals hospitalized with sarcoidosis during the 11-year period. Crude rates were stratified by race (Caucasian and African American), as well as age and gender adjusted by direct method (37) to the 1980 South Carolina population as represented in the 1980 US Census (38).

Geographic area

South Carolina comprises three distinct physiographic regions: the coastal plain, the Piedmont, and the Blue Ridge (38). The borders of these regions generally parallel the Atlantic coastline. The coastal plain is a large region formerly covered by the Atlantic Ocean. Significant geophysical differences exist between this region and the Piedmont and Blue Ridge areas with respect to a number of factors, including altitude, soil composition, geologic history, and plant and animal habitation (38).

South Carolina counties were grouped into four distinct geographic regions based on the above physiographic characteristics and proximity to the Atlantic coastline (figures 1 and 2). The lower coastal plain encompasses those counties whose land mass majority lies within 50 miles of the Atlantic coastline, while counties in the upper coastal plain lie from 50 to approximately 120 miles from the coastline. The lower

![Geographic map of South Carolina with regions labeled A, B, C, D.](image)
Geographic Variation in Sarcoidosis in South Carolina

**Region**
- A Upper Piedmont
- B Lower Piedmont
- C Upper Coastal Plain
- D Lower Coastal Plain

**Rates per 100,000 population**
- 250 to 350
- 200 to 249.99
- 150 to 199.99
- 100 to 149.99
- 50 to 99.99


Piedmont region includes those counties in the upper midlands of South Carolina, while the upper Piedmont region includes the Blue Ridge zone of South Carolina that encompasses a small portion of the northwesternmost counties. Counties whose borders overlapped into several physiographic regions were assigned to that region in which the majority of the county’s land mass resides.

**Variables**

Two distinct measures of SES were assessed at the county level: mean household income and the percent of individuals below the poverty level ($12,674 or less for a family of four persons) in 1990. Average yearly all-cause, nonnewborn hospitalization rates for the period 1985-1995 were used as a measure of hospital utilization, the number of licensed, practicing physicians per unit population was used as a measure of the availability of health care, and the percent of individuals in the stratified populations with a health insurance plan was used as a measure of health care accessibility. Potential regional differences in disease severity were assessed by regressing the proportion of hospitalized sarcoidosis patients in each county with a primary diagnosis of sarcoidosis (*International Classification of Diseases* code 135.0). This reflects the percentage of hospitalized sarcoidosis patients who were hospitalized primarily for sarcoidosis as opposed to individuals hospitalized with sarcoidosis as a comorbid or secondary condition. In an effort to maintain data integrity, all data with the exception of health insurance coverage estimates were obtained through experienced database managers at the South Carolina State Budget and Control Board’s Office of Research and Statistics. Both SES measures were generated from the 1990 US Census Summary Tape File 3A. All-cause hospitalization rates were generated by using the South Carolina Hospital Discharge database.
Physician density was calculated by using physician licensing records maintained by South Carolina State Board of Medical Examiners, while health insurance coverage estimates were obtained from the National Health Information Survey.

Since it has been estimated that more than 90 percent of all cases of sarcoidosis exhibit pulmonary involvement (36), pulmonologists are more likely to be the subspecialists most familiar with strategies to diagnose sarcoidosis. Therefore, potential differences in diagnostic practices (i.e., diagnostic bias) was assessed by comparing rates in counties with a licensed, practicing pulmonologist with those without one as determined from records maintained by the State Board of Medical Examiners.

Analysis

The associations between sarcoidosis hospitalization rates and mean household income, percent of individuals below the poverty level, physician density, all-cause hospitalization rates, diagnostic practices, percent of individuals with health insurance, and percent of cases with a primary diagnosis were assessed by using linear regression.

Differences in hospitalization rates between geographic regions were assessed by using analysis of variance and multivariable linear regression. The analysis of variance and regression models were adjusted only for those covariates that remained significantly associated at the 0.05 level with the sarcoidosis rates in the presence of all other covariates.

RESULTS

Age- and gender-adjusted hospitalization rates for Caucasians and African Americans with sarcoidosis are displayed in figures 1 and 2, respectively. County rates for Caucasians ranged from 0 to 79.9 per 100,000 population, with a mean rate of 32.7 per 100,000 population and a standard deviation of 18.1. County rates for African Americans ranged from 55.1 to 349.8 per 100,000 population, with a mean rate of 182.8 per 100,000 and a standard deviation of 83.5. Rate ratios for African Americans versus Caucasians ranged from 2.0 to 15.7, with a mean ratio of 6.3.

Univariate regression analysis of Caucasian hospitalization rates did not find mean household income, percent population below the poverty line, physician density, insurance status, disease severity, or diagnostic variation to be associated with sarcoidosis (table 1). However, all-cause hospitalization rates representing hospital utilization were significantly associated (p < 0.001) with the sarcoidosis measures. Similar results were found with the rates for African Americans, with the exception that poverty level was significantly associated with the sarcoidosis hospitalization rates (p = 0.008). The association became less significant (p = 0.190), however, after adjustment for mean all-cause hospitalization rates (p < 0.001).

Statistically significant differences in the sarcoidosis hospitalization rates were detected between the four geographic regions for both Caucasians and African Americans (p = 0.025 and p < 0.001) after adjustments for age and gender. There was an almost fivefold increase in the amount of variation in sarcoidosis rates explained by geographic area in African Americans when compared with Caucasians (52 vs. 11 percent of variation explained, respectively). After adjustments for hospital utilization among counties, significant regional differences in sarcoidosis rates remained for African Americans (p < 0.001), but not for Caucasians (p = 0.297). Subsequent reanalysis of the sarcoidosis hospitaliza-

<table>
<thead>
<tr>
<th>Variable</th>
<th>Measure</th>
<th>Caucasians</th>
<th>African Americans</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Regression coefficient</td>
<td>p value</td>
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<td>Mean household income (continuous)</td>
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<td>Population physician density (continuous)</td>
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</tr>
<tr>
<td>Mean all-cause, nonnewborn hospitalization rates (continuous)</td>
<td>Hospital utilization</td>
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<td>0.0001</td>
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<td>Presence of at least one licensed, practicing pulmonologist (nominal)</td>
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<td>% individuals with some form of medical insurance (continuous)</td>
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<tr>
<td>% cases with primary diagnosis (continuous)</td>
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<td>0.5962</td>
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</table>

* Rates were age- and gender-adjusted to the 1980 South Carolina population.
† Significance was lost after adjustments for mean all-cause, nonnewborn hospitalizations.
‡ SES, socioeconomic status.
tion rates after adjustments for geographic region and all-cause hospitalization rates did not identify any additional significant measures.

Least-squares means and 95 percent confidence intervals for the four regions adjusted for hospital utilization are shown in figures 3 and 4. None of the pairwise comparisons of adjusted means were statistically significant at the 0.05 level for Caucasians, while all pairwise comparisons were significant for African Americans with the exception of the Upper and Lower Piedmont.

**DISCUSSION**

Using multiyear hospitalization rates as a conservative geographic measure of sarcoidosis, we have assessed regional variation in this disease, as well as its relation to SES and a number of other health care status indicators. These results demonstrate that sarcoidosis hospitalization rates in the coastal half of the state are significantly higher for both Caucasians and African Americans. The geographic variation in rates was consistent for Caucasians and African Americans,
but the counties with the highest rates for African Americans were concentrated in a band along the Atlantic coastline. No such pattern was detected for Caucasians.

Significant racial differences in sarcoidosis hospitalization rates were also detected. The racial differences are in accordance with previous studies conducted in the United States (32, 35). Similar regional variation in the attack rates of sarcoidosis has also been documented (25), but its relation to SES and health care indicators has not been assessed. This is of particular interest because lower SES has been demonstrated in coastal South Carolina, where the incidence of sarcoidosis has been shown to be elevated.

However, regression analysis showed that the geographic variation in sarcoidosis in South Carolina cannot be sufficiently explained by differences in socioeconomic status at the county level. In Caucasians, mean household income explained only 0.1 percent of the variance in sarcoidosis hospitalization rates, while the percent of individuals below the poverty level explained only 5.0 percent of the variation. Similarly, in African Americans, mean household income explained only 4.6 percent of variation, while the percent of individuals below the poverty level explained only 14.8 percent of the variation. From a population perspective, the geographic variation in sarcoidosis cannot be explained by socioeconomic differences, and SES does not appear to be a risk factor for sarcoidosis on the basis of the results of this population study.

In both racial populations, measures of access to and the availability of health care, diagnostic practices, and disease severity were not significantly associated with sarcoidosis hospitalization rates. These variables, therefore, do not explain the geographic variation in sarcoidosis in South Carolina. Counties with higher sarcoidosis rates did have significantly higher general hospitalization rates for both races; however, the number of combined, available hospital beds per unit population did not differ significantly between the four regions of study. This suggests that the increased hospitalization rates for sarcoidosis (and all causes) were not due to geographic differences in the availability of hospital beds.

The lack of association between sarcoidosis hospitalization rates and diagnostic practices was not unexpected. The negative, but insignificant, association between the disease rates and the percent of individuals with insurance implies that within South Carolina higher rates of sarcoidosis occurs in areas where access to health care is actually lower. This suggests that diagnostic bias within this region should not be of significant concern with reference to sarcoidosis.

The significant regional differences identified for Caucasians became insignificant after adjustment for general hospital usage. In contrast, the significant regional differences in African Americans remained highly significant even after adjustment for general hospital usage. These regional differences followed a pattern of decreasing rates with increasing distance from the Atlantic coastline.

It may be that some as yet undetected risk factor for sarcoidosis that is related to coastal proximity or physiographic region is present or active in African Americans, but not in Caucasians. It is also possible that the relatively low rates in this Caucasian population provide inflated variance estimates that mask regional differences similar to those found in African Americans. The influence of familial risk factors for sarcoidosis may, in part, be responsible for some of the racial differences seen here. Significantly higher hereditary associations have recently been documented in African Americans (39, 40). Although only a limited portion of documented sarcoidosis can be explained by genetic or hereditary models, the level of familial clustering and its effect on the geographic variation of sarcoidosis in South Carolina cannot be assessed by this study. Still, this patterned variation in sarcoidosis hospitalization rates for African Americans suggests that geographic location, even within relatively defined areas, may be a risk factor or potential confounder in some population groups that should be considered in future studies of sarcoidosis.

It should be noted that although hospitalization rates are used as geographic measures of sarcoidosis, they do not necessarily represent precise estimates of disease incidence or prevalence. Although these results are in accordance with earlier incidence rate findings on sarcoidosis (25), whether hospitalization rates are reflective of incidence or prevalence rates for this disease has not been documented previously. The relatively uncommon need to hospitalize sarcoidosis patients would suggest that hospitalization rates for sarcoidosis will significantly underestimate true incidence and prevalence. Additionally, it is not known whether the geographic variation in sarcoidosis represented by these hospitalization rates is consistent across races. The increased difficulty in confirming the diagnosis of sarcoidosis in Caucasians (41) and the tendency for Caucasians to recover more quickly and frequently from sarcoidosis (42) may lead to a more biased geographic assessment of sarcoidosis in Caucasians than in African Americans. Moreover, the use of this type of measure should take general hospital usage into consideration, since these measures were highly correlated in this study.

Further limitations should be considered in reviewing these results. Diagnoses are based on discharge
ACKNOWLEDGMENTS

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REFERENCES


