Racial Differences in Clinical Features and Comorbidities in Ankylosing Spondylitis in the United States

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ABSTRACT. ***Objective.*** To examine racial differences of clinical features, medication usage, and comorbidities of patients with ankylosing spondylitis (AS) in the United States.

Methods. In the Explorys database, 28,520 patients with AS were identified. Data were stratified by 2 rheumatology visits, race, sex, clinical characteristics, medication use, and comorbidities. Datasets were recorded as proportions, which were compared using chi-square test ($p < 0.05$).

Results. Of the 10,990 patients with AS, 8% were African Americans and had elevated erythrocyte sedimentation rate and C-reactive protein, and high frequency of anterior uveitis, hypertension, diabetes, depression, and heart disease.

Conclusion. African Americans with AS in the United States have high disease activity and comorbidities compared to whites. (First Release February 15 2020; J Rheumatol 2020;47:835–8; doi:10.3899/jrheum.181019)

Key Indexing Terms:
ANKYLOSING SPONDYLITIS
AFRICAN AMERICANS
RACIAL FACTORS
DISEASE SEVERITY

Ankylosing spondylitis (AS) is a chronic rheumatic disease that predominantly involves the axial skeleton. It is strongly associated with the *HLA-B27* gene and an increased familial incidence among both African Americans and white patients[1,2,3]. AS is predominantly a disease of whites attributed to a higher frequency of HLA-B27[4,5]. An epidemiological study based on data collected by the US National Health and Nutrition Examination Survey from 2009 to 2010 demonstrated that prevalence of axial spondyloarthritis was 1.0–1.4% and AS was 0.52–0.55% in the United States. The numbers in African Americans were too low to make any definitive estimate of prevalence[6]. The low prevalence of AS in African Americans has prevented major studies from being conducted in this racial group. The racial heterogeneity of the US population makes it imperative to study the racial differences in clinical characteristics and comorbidities of patients with AS, a disease mainly considered to be of whites with *HLA-B27* predominance. We hypothesized that African American patients have worse disease outcomes compared to whites in the US based on observations from our clinical practice.

We aimed to examine and describe the racial differences in the frequency of clinical characteristics, erythrocyte sedimentation rate (ESR), C-reactive protein levels (CRP), medication usage, and comorbidities of AS among whites and African Americans.

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MATERIALS AND METHODS

The data for our retrospective cohort study were collected using the Explorys platform, a clinical research informatics tool that uses a health data gateway server behind the firewall of 26 major integrated healthcare systems in the United States from 1999 to 2017, comprising over 50 million patients in the participating healthcare organizations. The Explorys collects aggregated, standardized, and normalized clinical data from different electronic health records (EHR), automatically updated in near-real time (at least every 24 h), presented in a Health Insurance Portability and Accountability Act (HIPAA)– and Health Information Technology for Economic and Clinical Health (HITECH)–compliant deidentified way from each participating healthcare organization and are passed into the Explorys data grid. A Web application allows each healthcare organization to search and analyze the aggregated, standardized, normalized, and deidentified data from all participating healthcare organizations. All data used from Explorys were deidentified to meet the HIPAA and HITECH Act standards. In Explorys, patient records are mapped into a single set of Unified Medical Language System ontologies to make searching and indexing easier. Diagnoses, findings, and procedures are mapped into the systematized nomenclature of medicine — Clinical Terms (SNOMED-CT) hierarchy[7]. Prescription drug orders are mapped into SNOMED (to represent the pharmacological class) and RxNorm (normalized names for clinical drugs; to represent the drug itself)[8]. Laboratory test observations are mapped into the logical observation identifier names and codes hierarchy established by the Regenstrief Institute[9]. Our study obtained ethics approval from our institutional review board (ID: IRB17-00078).

The Power Search tool was used to create a refined cohort with specific search criteria of AS. We identified 28,520 patients with AS. We selected another variable to create cohorts that would accurately predict the diagnosis of AS including provider use pattern (at least 2 visits with a rheumatologist,

N = 10,990). We further stratified the cohorts by adding the following variables to the search tool: race (African American or white), sex (female or male), laboratory data (elevated ESR, elevated CRP, and HLA-B27 status), clinical characteristics [smoker, peripheral arthritis, enthesopathy, dactylitis, uveitis, psoriasis, inflammatory bowel disease (IBD), or restrictive lung disease], medication use [tumor necrosis factor inhibitor (TNFi) or nonsteroidal antiinflammatory drug (NSAID) use], or comorbidity [hypertension (HTN), diabetes, osteoporosis, fibromyalgia (FM), heart disease, and depression].

Datasets were recorded as proportions. Comparisons were performed between the proportions using a chi-square test ($p < 0.05$).

RESULTS

There were 10,990 patients with AS with at least 2 rheumatology visits of all races identified, of whom 50% were males (Table 1 for AS population baseline characteristics). Eighty-four percent of patients with AS were white, whereas 8% were African American. Half of both races were male ($p = 0.17$). Twenty-five percent (2970/10,990) of the AS cohort tested for HLA-B27 were positive (26% white vs 20% African Americans, $p = 0.11$). A subgroup analysis of 101 AS patient electronic charts at our institution identified 78% HLA-B27–positive patients (64% white vs 42% African American, $p = 0.0018$). Sixty-five percent of patients with AS were smokers (67% white vs 59% African American, $p < 0.0001$).

Table 2 compares the clinical characteristics and comorbidities among white versus African American patients with AS. A greater proportion of African Americans had elevated ESR (62% African Americans vs 48% white, $p < 0.0001$) and CRP (68% African Americans vs 54% white, $p < 0.0001$) suggesting that the disease may be more severe in African Americans. In addition, African Americans when compared to whites had a significantly greater proportion of anterior uveitis (7.6% African Americans vs 4% white, $p < 0.0001$). African Americans compared to whites also had higher prevalence of HTN (29% vs 22%, n = 2350, $p < 0.0001$), diabetes (27% vs 17%, n = 1940, $p < 0.0001$), depression (36% vs 32%, n = 3380, $p = 0.02$), and heart disease (24% vs 22%, n = 2290, $p = 0.11$). Moreover, African Americans also had higher proportions of peripheral arthritis, enthesopathy, dactylitis, and IBD when compared to whites, but the results were not statistically significant. However, whites when compared to African Americans had a higher proportion of psoriasis (10% vs 6.5%, n = 1070, p = 0002) and FM (14% vs 12%, n = 1480, p = 0.07).

Table 1. Baseline characteristics of study population. Data collected June 23, 2017.

Characteristics of Patients with AS, N = 10,990	n (%)	p
Whites	9260 (84.3)	< 0.0001
African Americans	920 (8.4)	
Male sex	5530 (50.3)	< 0.374
HLA-B27–positive	740 (24.9)	
HLA-B27 tested	2970 (27.0)	
Smokers	7149 (64.9)	< 0.0001

AS: ankylosing spondylitis.

Table 2. Comparison of clinical characteristics and comorbidities among white and African American patients with ankylosing spondylitis (N = 10,990). Results were adjusted for population size for each race.

Characteristics	White (%)	African American (%)	p
HLA-B27–positive, n = 740	25.5	20	0.1119
Males, n = 5530	49.8	52.2	0.1668
Females, n = 5460	50.2	47.8	0.1650
Smokers, n = 7140	67.3	58.7	< 0.0001*
Elevated ESR, n = 3800	47.6	61.5	< 0.0001*
Elevated CRP, n = 4280	54.4	67.7	< 0.0001*
Peripheral arthritis, n = 8030	73.9	76.1	0.1463
Enthesopathy, n = 2780	25.5	27.2	0.1837
Dactylitis, n = 560	5.2	6.5	0.0937
Anterior uveitis, n = 470	4	7.6	< 0.0001*
Psoriasis, n = 1070	10.4	6.5	0.0002*
IBD, n = 1120	10.7	12	0.2260
Restrictive lung disease, n = 370	3.5	3.3	0.7523
Hypertension, n = 2350	21.7	29.3	< 0.0001*
Diabetes, n = 1940	17.3	27.2	< 0.0001*
Osteoporosis, n = 1890	17.5	16.3	0.3637
Fibromyalgia, n = 1480	14.1	12	0.0674
Heart disease, n = 2290	21.7	24	0.1077
Depression, n = 3380	31.9	35.8	0.0158*
Treatment with NSAID, n = 9560	88.6	89.1	0.6167
Treatment with TNFi, n = 4310	40	37	0.0754

* Statistical significance. ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; NSAID: nonsteroidal inflammatory drug; TNFi: tumor necrosis factor inhibitors; IBD: inflammatory bowel disease.

Figure 1 demonstrates the clinical characteristics and comorbidities of the whole AS population. Seventy-three percent (8030/10,990) of the whole AS cohort had peripheral arthritis, 25% (2780/10,990) had enthesopathy, 10% had psoriasis (n = 1070) and IBD (n = 1120), 4% had anterior uveitis (n = 470), and 5% had dactylitis (n = 560). HTN (73%) was the most common comorbidity among the AS population, followed by depression (31%), heart disease (21%), diabetes (18%), and FM (13%).

A majority (87%, 9560/10,990) of the patients with AS were treated with NSAID (89% white vs 89% African Americans, $p = 0.62$) and 39% used TNFi (40% white vs 37% African Americans, $p < 0.08$).

DISCUSSION

The findings from a large US electronic database confirm that AS is more prevalent in whites as shown in previous studies, but the proportion of males and females between the 2 races is equal. Both ESR and CRP were elevated in African American patients compared to white, suggesting that the disease may be more severe in African Americans. A previously published study from the United States also revealed higher disease activity [Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), median 5.9 in African Americans vs 3.5 in whites and 4.5 in Latinos; $p < 0.0001$], ESR (median 27.0 mm/h in African Americans vs 10.0 in whites), and

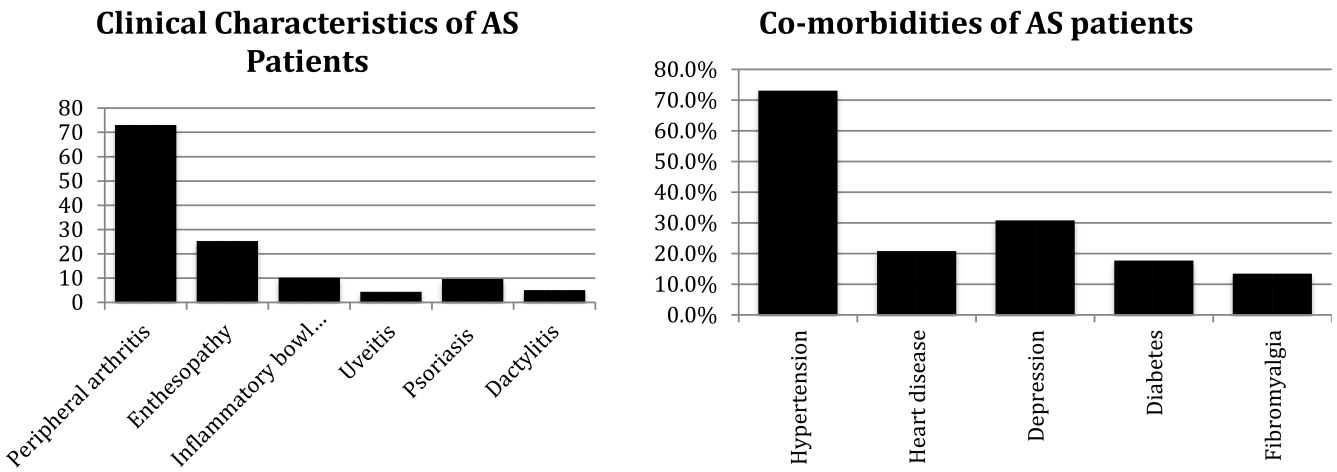

Figure 1. Clinical characteristics and comorbidities of patients with AS (n = 10,990). All data are in percentages. AS: ankylosing spondylitis; inflammatory bowl: inflammatory bowel disease.

greater functional impairment [Bath Ankylosing Spondylitis Functional Index (BASFI), median 62.5 in African Americans vs 27.8 in whites, $p < 0.0001$][1]. These findings are in contrast with previous reports that suggest that patients with AS in Africa tend to have a milder clinical presentation and lack of extraarticular manifestations[10]. Another study has revealed that the clinical forms of AS may be different between different ethnic groups, and North Africans tend to have severe disease with high familial occurrence[11]. The difference in disease severity among African Americans and whites in AS is thought to be genetically mediated, but cultural, social, or economic factors may also be contributing to this racial disparity. Further research is needed to determine the role of factors other than genetic ones such as HLA-B27 positivity that contribute to worsening disease severity.

Earlier age of disease onset, higher rates of anterior uveitis, and a shorter delay to diagnosis in whites have been attributed to HLA-B27 positivity[10,11,12,13]. The rate of anterior uveitis was higher in African Americans compared to whites, even though HLA-B27 positivity was lower in African Americans. This is contrary to a previous study of 8 African patients in a large teaching hospital in Africa, where the rate of uveitis was lower in them compared to whites[12]. Further in the current study, significant comorbid burden was demonstrated in African American patients with AS. Greater frequency of peripheral arthritis and enthesitis have been found in Latin American patients compared to European patients with AS[14].

Socioeconomic determinants of disease outcome in spondyloarthropathy have been studied in a large, multinational, cross-sectional study (ASAS-COMOSPA), which revealed differences in outcomes by education and sex. However, racial data were not collected in that study[15]. Contrary to other studies that revealed that socioeconomic status affects the use of biological disease-modifying antirheumatic drugs (bDMARD) in AS[16], with lower health expenditure associated with less frequent use of bDMARD, our study demonstrates no significant difference in the use of TNF-α inhibitors between the 2 races, suggesting that access to biologics may not be the contributing factor to worsening disease severity in African American patients.

A strength of our study is the use of large clinical, EHR-based datasets comprising almost 2 decades of standardized and normalized population data on 10,990 patients with AS from 26 major health systems, representing both men and women of all age groups and different racial backgrounds throughout the United States. The data were collected by thousands of clinicians as part of routine clinical care in inpatient and outpatient settings. Explorys uses a robust patient-matching algorithm that prevents information from being duplicated. The data are updated automatically at least once every 24 h. Further, the deidentified, normalized, and standardized clinical data from Explorys aggregated from multiple different healthcare systems longitudinally with different EHR provide an important research tool for large population-based, real-world cohort studies[17,18]. Another advantage of using Explorys is that minimal resources, money, personnel, and time are needed to conduct retrospective large-scale cohort studies. The only other similar EHR-based datasets being used for research in the United States is the Veterans Administration's EHR.

A study limitation was that Explorys could not record the true proportion of HLA-B27 positivity because the frequency of HLA-B27 positivity is observed in 50–60% of African Americans patients with AS and 90% of white patients with AS in the United States[1,2,3]. We were able to verify only the information of the patients in the database who had sought care at our hospital. Subgroup analysis of 101 of these patients with AS at our institution revealed greater HLA-B27 positivity among whites compared to African Americans (64% vs 42%, $p = 0.0018$), contrary to the low frequency of

HLA-B27 positivity in the database. Although this does not represent the distribution of HLA-B27 in the Explorys population, we learned that HLA-B27 testing was not performed at our institutional laboratory until 2013, with the results unavailable in our EHR. Hence, the results were not available in the Explorys database. We assume that HLA-B27 testing may not be available at various centers and as a result, the outside laboratory used may not provide results directly into the EHR, contributing to the lack of availability in Explorys and the low proportion of HLA-B27 in the database. The subgroup analysis of patients with HLA-B27 positivity would have provided more valuable information, which is lacking in the current study.

Another limitation of the Explorys database is the use of deidentified data at the population level, preventing further review of the records to verify patient history and AS diagnosis. Explorys does not enable analysis of individual data and abstraction of validated variables such as BASFI, BASDAI, radiographs, or magnetic resonance imaging results and health-related quality of life instruments from the database, because these were not coded into structured digital data and thus could not be used as natural language processing of text supported by Explorys[16]. Hence, the disease severity could not be accurately measured[18,19,20].

The Explorys search tool is limited to demographic information and other clinical information for which standard clinical informatics systems exist. In addition, there is variability in the length of time people are in the cohorts. To ensure provider use, we stratified our search to include at least 2 visits with a rheumatologist. Explorys attempts to use a master-patient identifier and attempts to match the same patient across different healthcare systems and combine their data. There is still a possibility that a few of the study patients may have been duplicated and encounters could have occurred outside the Explorys healthcare partners[16]. The data in Explorys are obtained for clinical and not specifically research purposes and so the accuracy may be less than in data collected solely for research purposes. The Explorys database is built in such a way that statistical measures cannot be produced on qualitative variables. In addition, all patient age cohorts are rounded to the nearest 10 years for the purposes of deidentification.

There are very few studies in literature of the racial determinants of disease outcome in AS. To our knowledge, our study is the first real-world population study to look at racial determinants of clinical features, disease activity, and comorbidities in AS in the United States. Also, software platforms such as Explorys can provide a valid and useful method to investigate meaningful associations across large populations.

The results demonstrate that despite low prevalence of AS in African American patients, African Americans tend to have elevated levels of markers of inflammation and anterior uveitis, and more comorbidities. An improved risk stratification and vigilance for early diagnosis and treatment of AS particularly in African American patients is needed.

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