



ORIGINAL ARTICLE

Rates of hospitalization among African American and Caucasian American patients with Crohn's disease seen at a tertiary care center

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Abstract

Background: There is equivocal evidence regarding differences in the clinical course and outcomes of Crohn's disease (CD) among African Americans compared with Caucasian Americans. We sought to analyze whether African Americans with CD are more likely to be hospitalized for CD-related complications when compared with Caucasian Americans with CD.

Methods: We conducted a retrospective cohort study including 909 African Americans and Caucasian Americans with CD who were seen at our tertiary care Inflammatory Bowel Disease (IBD) referral center between 2000 and 2013. We calculated the rate of hospitalization for CD-related complications among African Americans and Caucasian Americans separately. Zero-inflated Poisson regression models with robust variance estimates were used to estimate crude and multivariable adjusted rate ratios (RR) for CD-related hospitalizations. Multivariable adjusted models included adjustment for age, sex, duration of CD, smoking and CD therapy.

Results: The cumulative rate of CD-related hospital admissions was higher among African American patients compared with Caucasian American patients (395.6/1000 person-years in African Americans vs. 230.4/1000 person-years in Caucasian Americans). Unadjusted and multivariable adjusted rate ratios for CD-related hospitalization comparing African Americans and Caucasian Americans were 1.59 (95% confidence interval [95%CI]: 1.10–2.29; $P=0.01$) and 1.44 (95%CI: 1.02–2.03; $P=0.04$), respectively.

Conclusions: African Americans with CD followed at a tertiary IBD-referral center had a higher rate for CD-related hospitalizations compared with Caucasian Americans. Future studies should examine whether socioeconomic status and biologic markers of disease status could explain the higher risk observed among African Americans.

Key words: Crohn's disease; racial disparity; African American; Caucasian American

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Introduction

Crohn's Disease (CD) is an inflammatory bowel disease (IBD) characterized by transmural inflammation that can affect any part of the gastrointestinal (GI) tract [1,2]. CD affects more than 750 000 persons in the USA. It is classified as inflammatory, penetrating or stricturing with or without perianal disease [3,4]. While CD was first described in 1932 [1], it was not until 1966 that IBD was first studied in an African American (AA) population [5]. At that time, a lower incidence of IBD (in particular CD) was observed among AAs as compared with Caucasian Americans (CAs). Early research on CD thus focused almost exclusively on Caucasians with limited attention to racial minorities, particularly the AA population [5, 7–11]. As a result, it is unclear how much available data on CD are generalizable to non-Caucasian populations.

Since that time, a higher incidence of CD and ulcerative colitis has been observed in both the general population at large as well as in AAs [6,7]. However, the role of race in the outcomes in CD remains incompletely understood. The University of Alabama at Birmingham (UAB) is a unique setting for studying CD among AAs. Our IBD referral center is the sole tertiary care center in a state with a population composed of approximately 26% AAs, a proportion that is double the national percentage. Our study sought to test the hypothesis that AAs with CD are more likely to be hospitalized for a CD-related complication compared with CAs with CD.

Patients and methods

Study design, patient population and selection criteria

We conducted a retrospective cohort study aimed to compare the hospitalization rate for CD among AAs and CAs. For this study, we analyzed data from 909 patients seen at our tertiary care center from 2000 to 2013. Patients were included in the analysis if they were AA or CA and older than 19 years of age. The current study was designed and conducted in accordance with the Declaration of Helsinki regarding human research and was approved by UAB's Office of Institutional Review Board (IRB).

Data collection and variable definitions

Data were collected through retrospective review of electronic medical records and laboratory results. Data collected at the time of the first observation in our tertiary center included age, race, sex and the duration of CD. Data collected from the full period of observation included smoking history and CD therapy (i.e. steroid, thiopurine, methotrexate and biologics). Steroid use was defined as exposure to oral or parenteral corticosteroids for at least 6 weeks. Steroid duration was chosen as 6 weeks to ideally select those patients receiving more than a typical 4-week taper post hospitalization/flare. Thiopurine use was defined as use of azathiopurine (AZA) or 6-mercaptopurine (6-MP) for at least 4 weeks during the period of observation. Methotrexate use was defined as the use of methotrexate for at least 4 weeks during the period of observation. Biologic use was defined as the use of any biologic agent for at least 4 weeks during the period of observation. Length of duration for biologics and other drugs was chosen at 4 weeks to ideally represent multiple doses of the medications and patients who had tolerated the medication long enough to begin seeing benefits. Participants were followed through the last observation for CD-related hospitalizations. A CD-related hospitalization was

defined as any hospital admission in our center for a complication of CD including infections, fistulas, strictures and exacerbations. For each patient, the period of observation was defined as the time in years between the first and last documented encounter at our tertiary care center during the years 2000 through 2013.

Statistical analysis

We calculated the proportion of women, the median and the interquartile range for age and duration of CD among AAs and CAs. We also calculated the proportion of participants who smoked and used steroids, thiopurine, methotrexate and biologics during the observation period. Estimates among AA and CA participants were compared using the Fisher exact test for categorical variables and the Wilcoxon rank sum test for age and duration of CD. We calculated the hospitalization rate and 95% confidence interval (CI) among AAs and CAs separately. Zero-inflated Poisson regression models with robust variance estimates were used to estimate rate ratios (RRs) and 95% CIs for CD-related hospitalizations associated with AAs.

In addition to the crude model, a second model was used that included adjustment for age, sex, duration of CD, smoking and use of steroids, biologics, thiopurine and methotrexate. We used zero-inflated Poisson regression models because we observed an excess of study participants with zero hospitalizations according to what was predicted by the Poisson distribution. In addition, the Vuong test contrasting fully adjusted models for the association between race and number of hospitalizations using zero-inflated vs. non-zero-inflated Poisson regressions were statistically significant ($z = 6.13$, $P < 0.001$), supporting the appropriateness of using zero-inflated models [12].

The analysis was conducted in the overall population and again in subgroups. Subgroups were defined by sex and age (<50 and greater than or equal to 50 years). We investigated effect modification on the association between race and the hospitalization rate by sex and age by including product terms in the multivariable adjusted regression model. All statistical analyses were conducted using STATA, version 11.2 (StataCorp LP, College Station, TX). Statistical tests were two-sided with a significance level $\alpha < 0.05$.

Results

Of the 909 patients included, 702 (77%) were CA, and 207 (23%) were AA. With regard to sex, 574 (63%) were women, and 335 (37%) were men. As compared with CAs, AAs were younger, more likely to be women and had lower duration of CD (Table 1). Smoking and use of CD therapy was similar among AAs and CAs.

The cumulative rate of CD-related hospital admissions was higher among AA patients compared with CA patients (Table 2). In the unadjusted analysis, AAs were 1.59 times more likely to be hospitalized due to CD-related complications compared with CAs (RR 1.59, 95%CI: 1.10–2.29, $P = 0.01$). After adjustment for age, sex, duration of CD, smoking and CD therapy, the RR for CD-related hospitalization among AAs vs. CAs was 1.44 (95%CI: 1.02–2.03, $P = 0.04$).

AA men had twice the rate of CD-related hospitalizations compared with CA men. After multivariable adjustment, the RR for CD-related hospitalization among AA vs CA men was 2.03 (95%CI: 1.06–3.91, $P = 0.03$). The rate of CD-related hospitalizations was also higher among AA vs. CA women.

Table 1. Baseline characteristics of Crohn's disease patients included in the analysis

Characteristics	Caucasian Americans (n = 702)	African Americans (n = 207)	P value
Age in years, median (interquartile range)	42 (31–57)	40 (31–50)	0.02
Females, n (%)	428 (61.0)	146 (70.5)	0.01
Duration of Crohn's disease in years, median (interquartile range)	11 (6–20)	9 (5–16)	0.004
Smoking, n (%)	155 (22.1)	49 (23.7)	0.63
Steroid use, n (%)	371 (52.9)	115 (55.6)	0.49
Thiopurine use, n (%)	377 (53.7)	104 (50.2)	0.38
Methotrexate use, n (%)	87 (12.4)	31 (15.0)	0.33
Biologic use, n (%)	363 (51.7)	104 (50.2)	0.71

Note: Comparison was performed using Fisher's exact test for categorical variables and Wilcoxon's rank sum test for continuous variables.

Table 2. Crude and adjusted rate ratios for Crohn's disease-related hospitalizations

	Number of hospitalizations / person-years	Hospitalization rate (95% CI)*	RR (95% CI) [P value]	
			Model 1	Model 2
Overall				
CA	801 / 3476	230.4 (214.5–246.4)	1 (reference)	1 (reference)
AA	345 / 872	395.6 (353.9–437.4)	1.59 (1.10–2.29) [0.01]	1.44 (1.02–2.03) [0.04]
Females				
CA	497 / 2149	231.3 (210.9–251.6)	1 (reference)	1 (reference)
AA	213 / 644	330.7 (286.3–375.2)	1.27 (0.96–1.69) [0.10]	1.22 (0.94–1.57) [0.13]†
Males				
CA	304 / 1397	229.1 (203.3–254.8)	1 (reference)	1 (reference)
AA	132 / 228	578.9 (480.2–677.7)	2.49 (1.10–5.64) [0.03]	2.03 (1.06–3.91) [0.03]†
Younger than 50 years				
CA	572 / 1946	293.9 (269.8–318.0)	1 (reference)	1 (reference)
AA	302 / 575	525.2 (466.0–584.5)	1.57 (1.05–2.35) [0.03]	1.52 (1.05–2.18) [0.03]†
50 years or older				
CA	229 / 1530	149.7 (130.3–169.1)	1 (reference)	1 (reference)
AA	43 / 297	144.8 (101.5–188.1)	1.04 (0.65–1.66) [0.88]	0.93 (0.56–1.53) [0.77]†

*Per 1000 person-year.

†The P value for the effect modification on the association between black race and hospitalizations by sex was 0.15.

‡The P value for the effect modification on the association between black race and hospitalizations by age was 0.23.

Model 1 is unadjusted. Model 2 adjusts for age, sex, duration of Crohn's disease, smoking and use of steroid, thiopurine, methotrexate and biologics.

CA: Caucasian American; AA: African American; RR: rate ratio; CI: confidence interval.

AAs younger than 50 years of age had a higher rate of hospitalizations due to CD-related complications compared with their CA counterparts. The multivariable adjusted RR for CD-related hospitalization among AAs vs. CAs younger than 50 years of age was 1.52 (95%CI: 1.05–2.18, $P=0.03$). There was no difference between AAs and CAs 50 years or older in the rate of CD-related hospitalizations. The P value for effect modification by age in the association between race and CD-related hospitalizations after multivariable adjustment was 0.23.

Discussion

In our study, AAs with CD had a higher risk of CD-related hospitalizations as compared with CAs. The higher risk for CD-related hospitalizations associated with AAs appears to be driven by men and those <50 years of age. These results are consistent with previous studies showing a higher risk for CD complications among AAs as compared with their CA counterparts [8,9].

Historically, IBD (in particular CD) was believed to be restricted to CAs [5]. Over the years, a higher incidence of both CD and ulcerative colitis has been observed in both the general population at large as well as in AAs [7–11]. For example, in

1992, Kurata et al. found a higher incidence of CD among AAs than had previously been noted [6], which was later confirmed by Ogunbi et al. in 1998 [7].

As CD became increasingly recognized as a disease affecting AAs, studies began to investigate disease severity and the impact of CD on quality of life for AAs. While a 1986 study of 15 AA patients with CD by Goldman et al. concluded that the disease was much less common in AAs, it also noted that CD was more aggressive and had an earlier age of onset. The earlier age of onset also appeared to result in more complications over time [8]. In contrast, in a study published in 1989, Simsek and Schuman argued that the onset of CD in AAs was similar to that for Caucasians [9]. However, their results concurred with Goldman's data, which demonstrated that AAs experienced more complications, particularly rheumatological manifestations.

One possibility for the differences seen between hospitalization rates of AAs and CAs is a difference in disease phenotype. Some of the most recent research suggests that early differences that were suggested have now been disproven as larger numbers of patients are studied. Initially, it was thought that AA patients had a lower rate of ileocolonic disease with higher rates of perianal and fistulizing disease. More recent reviews have found that

this may not be true. Two large reviews found that both AAs and CAs are most likely to present with ileocolonic disease [11,12]. Mahid *et al.* found similar rates of ileocolonic disease (42% vs. 38%) and perianal disease (26% vs. 29%) between AAs and CAs [11]. While AAs are classically considered to have higher rates of fistulizing disease, Mahid *et al.* demonstrated that AAs and CAs have similar rates of fistulizing disease and are, like CAs, most likely to present with noninflammatory, nonstricturing CD [11]. Nevertheless, a recent study by Huang *et al.* that characterized genetic loci in AAs with IBD found several distinct genetic loci in AAs with IBD [13]. Thus, the disease phenotype and interaction of treatment with phenotype remain incompletely characterized and may be at least partly responsible for differences seen in hospitalization rates in these groups. One limitation in our study is that we did not characterize disease location or behavior in our patients at first observation.

In a case-control study published in 2000, Straus *et al.* concluded that disparities in disease severity were actually a result of social and economic inequalities (e.g. affording healthcare, delaying appointments due to financial concerns and difficulties traveling to the provider's office) rather than genetic differences [10]. These results have been confirmed by other studies including a systematic review by Mahid *et al.*, which pooled >2000 patients with IBD from eight different studies [11].

As highlighted above, prior studies have suggested that the increased disease severity among AAs may be due to lack of resources and poor access to healthcare as opposed to an actual genetic predisposition to more active disease. In Alabama (the location of our tertiary care center), 30% of AAs live below the poverty line, while only 10% of CAs do [14]. In 2014, 18.6% of the Alabama population lived below the Federal Poverty Line (FPL). In our study population, 55.9% of AA patients lived in a zip code where >18.6% of the population lived below the FPL, while only 31.8% of CA patients lived in a zip code with >18.6% of the population living below the FPL.

Socioeconomic status is one of the factors most frequently implicated in the disparities seen in US health populations [15,16]. For example, those struggling to make ends meet may have difficulty finding transportation, taking time off from work or finding childcare for appointments. Chronic disease management requires clinician visits, medication access and reliable follow-up. Without reliable transportation, none of this is possible. Previous works have shown that transportation barriers affect healthcare access in as few as 3% to as many as 67% of the population [17]. In 2005, Wallace and colleagues estimated that 3.6 million people do not obtain medical care in a given year due to transportation difficulties [18]. Those affected were more likely to be older, poorer, less educated and members of a racial or ethnic minority. A cross-sectional household survey conducted in 2007 showed that AAs had a higher burden of travel as compared with CAs [19]. This remained true even when controlling for socioeconomic status. Guidry and colleagues further confirmed that AA had more barriers to transportation than CAs including distance to treatment, access to vehicles and difficulty finding a driver [20]. Of note, transportation itself may not adequately explain the disparity between AAs and CAs.

When patients were stratified by sex, AA men with CD had a higher rate of admission compared with CA men. When AA and CA patients were stratified by age, the disparity in CD-related hospitalization rate remained significant among those who were <50 years of age but did not appear to be significant after that. There are other possible explanations for the higher risk of CD-related hospitalizations among AAs including genetic

factors, discrimination and socioeconomic status. These factors have been suggested to be involved in the higher prevalence of other conditions among AAs including hypertension, diabetes mellitus and colon cancer [21].

We controlled for smoking status, although we did not anticipate a significant difference in smoking rates between AA and CA patients. Centers for Disease Control and Prevention (CDC) survey data show that smoking rates between the two ethnic groups are comparable (19.7% in CAs and 18.1% in AAs) [22]. We also controlled for the use of common outpatient CD treatments (e.g. steroids, biologics and immunomodulators), which could have protected against CD-related hospitalizations, or in contrast may have been related to more severe disease phenotype. In both models (with and without adjustment) from the current analysis, AAs had a significantly higher rate of hospitalization than CAs.

Among potential limitations of our study, the following are noteworthy. Previous research has shown that many CD patients are never actually admitted to the hospital. Reliance on hospitalization data as in our study may underestimate the true burden of disease. This is particularly true for a center such as UAB, which is a referral center seeing patients from hundreds of miles away. Many of these patients choose to come to our institution for outpatient appointments and planned surgeries, but given an acute illness need to be hospitalized closer to home secondary to lack of transportation or financial restrictions or, alternatively, convenience. Since we accounted for CD-related hospitalizations exclusively within our institution, this could have potentially led to selection bias and may have underestimated the actual number of hospitalizations and thus the severity of some patients' disease. Retrospective observational study design and the use of electronic medical records for data extraction are additional limitations.

With regard to whether our study's conclusions are generalizable to all CD patients, one should bear in mind that the segment of CD patients seen at our tertiary care IBD referral center represents those with a more severe disease phenotype. This may explain the significantly higher overall CD hospitalization rate within our study population. Our findings are thus applicable and relevant to CD patients with severe disease compared with those having a mild CD variant.

Our results did reveal worse outcomes in AA patients when using CD-related hospitalization rates as a marker of outcome. However, this area needs to be further elucidated. Future researchers may consider using other markers of disease severity including time to first surgery or time to recurrence, which is an objective marker of disease severity that has been widely validated. Other useful markers may be clinical disease activity, radiologic disease activity or mucosal disease activity. Results from our study warrant further investigation to better understand the racial disparities seen in our tertiary care center. Future studies should consider controlling for socioeconomic status to better understanding the impact that financial resources have on the health outcomes in CD. Researchers also should consider the possible genetic or biologic differences between racial groups in CD. If present, such factors may confer risks for poor outcomes in AAs. Understanding the biologic and socioeconomic differences in CD may ultimately lead to better treatments for the disease.

Conclusions

AAs with CD followed at a tertiary IBD-referral center had a higher risk of CD-related hospitalizations compared with CAs. Most affected were young AA males. Future studies should

examine whether socioeconomic status and biologic markers of disease status could explain the higher risk observed among AAs.

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