Racial and ethnic health inequalities have been well-described in numerous disease states and chronic medical conditions (1–5). These differences likely result from the complex interaction of multiple variables, including biologic/genetic, behavioral and social factors. It is the differential effects of such social factors (i.e. socioeconomic status, access to care, patient preferences, provider biases) between racial and ethnic groups which can lead to the numerous recognized U.S. health care disparities and differentiates them from “health differences” (6,7). In hepatology, chronic hepatitis C (HCV) serves as an example where many of these variables occur concurrently. Compared to Caucasians, African-Americans with HCV have a two-fold higher disease prevalence and risk of developing hepatocellular carcinoma, higher rates of genotype 1 infection and less frequent selection for liver transplantation. Though cultural and socioeconomic factors associated with race and ethnicity could and likely do play a role in these differences (suggesting disparity), African-Americans also appear to inherently have a relatively decreased immune response to HCV infection and a decreased response to medical treatment across virus genotypes (8).

Inflammatory bowel disease (IBD), comprised of Crohn’s disease (CD) and ulcerative colitis (UC), is a group of chronic intestinal disorders in which immune dysregulation results in autoimmune damage to a patient’s gastrointestinal tract. Recent population-based estimates suggest that there are currently greater than 600,000 CD and 700,000 UC patients in the United States (9). Further, incidence of both diseases are estimated to have risen over the past several decades (10,11). Previously recognized as a disease primarily affecting Caucasians, IBD is no longer felt to be a rarity in U.S. racial and ethnic minorities (12). This is most notable within African-Americans and Hispanic populations, which represent approximately 13% and 15% of the U.S. population, respectively (13). Recognition of nearly ubiquitous health-related racial and ethnic inequalities has led some to question whether such disparities are present in IBD. The complexities inherent in answering this have recently been debated in the literature (14–17). Varying definitions of race/ethnicity, inaccurate disease frequency estimates, selection bias, confounding and effect modification pressures of socioeconomic variables, reverse causation and clinical trial under-representation are just a sample of pertinent factors that have complicated the assessment of reliable IBD frequency estimates, presentation, natural history, care utilization and outcomes in racial and ethnic minority populations (14,18).

The purpose of the current review is to provide the practicing gastroenterologist a framework of evidence with regards to racial and ethnic minorities with IBD. Available literature on disease frequency estimates, clinical presentation/disease phenotypes, disease severity and treatment differences/disparities in African-Americans and Hispanics will be summarized and compared to corresponding data in Caucasians.
EPIDEMIOLOGY

U.S. estimates of incidence and prevalence for UC are 8.3/100,000 and 178–273/100,000 while those for CD are 6.9/100,000 and 133–222/100,000, respectively (9,11,19,20). Data for these estimates have traditionally come from small referral-based case series, large Canadian and European population and referral-based cohorts, from single-center referral cohorts or from ongoing analysis of a predominantly Caucasian population in Olmstead County, MN (12,20–29). These studies often have populations with low numbers of racial and ethnic minorities, and may not report race-specific disease frequencies. Likewise, recent estimates generated from analysis of health insurance claims of nine million Americans did not include estimates by race/ethnicity (9). As a result, estimates of the incidence and prevalence of IBD in African-Americans and Hispanics has been low historically compared to Caucasians or not calculated (12,21,22,30,31). In fact, IBD incidence rates in African-Americans were previously estimated at 0.04–0.45/100,000 compared to 1.35–3.5/100,000 in Caucasians (12,32,33).

However, some small studies suggest that the incidence and prevalence of IBD in African-Americans and Hispanics may be increasing. Survey data from Baltimore reported rising incident IBD hospitalization rates in African-Americans between 1960 and 1979. In fact, the rates in African-American women with CD from 1977-1979 were 1.6 times higher than those of Caucasian women (34). These findings are more impressive if one assumes decreased access to care in minorities, as they may underestimate true incidence in African-Americans (12). Similarly, a 1992 mail-based California survey of health maintenance organization (HMO) patients suggested more comparable overall CD prevalence rates between Caucasians and African-Americans (35). Further, the incidence of UC and CD in African-American children from a Georgia cohort were estimated as high as 7/100,000 and 12/100,000, respectively, while data from several urban referral centers report that African-Americans represent 24%–37% of the centers’ IBD populations (36–38).

IBD frequency estimates in Hispanics are sparse in the literature, and often emanate from populations in Puerto Rico. In a study of insured Puerto Ricans, the prevalences of CD and UC were similar to those reported in Caucasians in a large HMO (35,39). Further, incidence rates between 1996 and 2000 for UC and CD were reported to have risen by 1.7-fold and 4-fold, respectively, in Hispanic patients seen by a private gastroenterologist in Puerto Rico. For that final year, the authors reported that the incidence of any IBD diagnosis in Hispanics was 7.74/100,000 (40). In sharp contrast, however, was a reported CD prevalence in Hispanic HMO members that was 10% that of Caucasian members (35).

Because of limitations and differences in the populations and methodologies employed to provide available IBD frequency estimates in racial and ethnic minorities, these estimates likely do not represent “truth” and should be interpreted with caution. Despite this, the reported low prevalence of IBD in African-American and Hispanic populations has undoubtedly been previously overstated.

GENETICS IN IBD

There is emerging evidence that genetic susceptibility to IBD is a strong determinant of phenotype. The most consistent finding is the association between NOD2/CARD15 gene mutations on chromosome 16 and certain CD phenotypes such as ileal involvement, earlier age of onset, fibrostenotic disease, and possible need for initial and repeat bowel resection (41–43). Racial and ethnic variations in the allele frequencies of various mutations within the NOD2/CARD15 gene have been reported. Roth and colleagues have shown a higher frequency of the Gly908Arg allele in the Jewish population, whereas the Arg702Trp mutation frequency is increased in the non-Jewish population (44). Meanwhile, the frequency of the three major NOD2/CARD15 risk alleles was found to be significantly lower in African-Americans compared to Caucasians (45). This finding was reproduced in an analysis of African-American and Hispanic children (46). Furthermore, the Arg790Gln mutation appears unique to African-Americans children with CD (45).

Regarding family history, Nguyen and colleagues found that Caucasian CD subjects had a higher prevalence of an IBD family history compared to African-Americans and Hispanics (47). Other studies have
supported these findings (46). In addition, Basu, et al. found that Caucasians tended to have a stronger family history of CD compared to African-Americans and a stronger family history of UC compared to Mexican-Americans (36). Similarly, analysis of Baltimore UC and CD cohorts revealed that Caucasians were more likely than African-Americans to report a family history of IBD (38,48).

**Racial Differences in Phenotypes in CD**

There is inconsistent data documenting the clinical presentation and course of CD in racial and ethnic minorities. Early descriptive analyses reported a higher rate of re-operation, prevalence of joint involvement and prevalence of primary sclerosing cholangitis in African-Americans compared to Caucasians (49). Data is limited describing Hispanic or Latino populations. A 1990 retrospective single-center study of 41 African-American IBD patients reported that 42% had ileal disease, 30% had colonic disease, while 28% had ileocolonic disease (50). While other studies support these data, a study from Houston observed a higher prevalence of both ileal and colonic disease in their African-American population compared to Caucasians (36,51). Cross and colleagues analyzed a single-center CD cohort which included 55 African-Americans and found that African-Americans were more likely to have ileocolonic (56% versus 36%) or colonic disease (29% versus 23%) compared to Caucasians (38). Perhaps the largest trial to evaluate differences in disease phenotypes was a multi-center retrospective cohort study evaluating 830 Caucasians, 127 African-Americans, and 169 Hispanics with IBD. Patients were recruited from six academic centers, and phenotype data were abstracted from medical records and compiled in the National Institutes of Diabetes and Digestive and Kidney Disease (NIDDK)-IBD Genetics Consortium repository. They found that, compared to Caucasians, African-Americans had less ileal disease (16.1% versus 29.2% \( p < 0.01 \)) but more esophagogastroduodenal (27.4% versus 16.7% \( p < 0.01 \)) and colonic disease (33.9% versus 17.4% \( p < 0.01 \)). Hispanics had less upper GI tract involvement than Caucasians, but significantly more ileocolonic disease than either Caucasians or African-Americans (47). In an attempt to consolidate the data, investigators from the University of Louisville recently published a qualitative analysis of eight studies of IBD in African-Americans, all of which had utilized the Vienna or Montreal Classification system to “phenotype” patients. They reported that disease location subtypes did not differ between African-Americans and Caucasians, with ileocolonic being reported most commonly in both groups, followed by colonic and isolated ileal location. However, a quantitative analysis was not performed (52).

There may also be racial/ethnic differences in the prevalence of perianal involvement which, depending on the study population, has been reported to affect 13%–38% of CD patients (53). Nguyen and colleagues found that there was a higher prevalence of perianal disease in African-Americans compared to Caucasians, with an odds ratio of 1.7 (95% CI: 1.03–2.8). They also found Hispanics more frequently had perianal disease, with an odds ratio of 2.9 (95% CI: 1.8–4.6) (47). Reported perianal disease in the Johns Hopkins pediatric CD population was likewise higher (though not statistically significant) in African-Americans than Caucasians (17.6% versus 10%) (33). The agreement between these two studies is not unexpected, as nearly all patients in each were seen at the same institution (33,47). Several smaller studies have also reported rates of perianal disease in African-Americans equal or greater to those of Caucasians (37,49,54). This was supported by a recent qualitative review (52). Contrasting slightly, a few small studies reported perianal disease in African-Americans patients less frequently than in Caucasians (50,51).

Extraintestinal manifestations (EIM) of IBD include arthritis, uveitis, erythema nodosum (EN), pyoderma gangrenosum (PG) and primary sclerosing cholangitis, among others (55). In a multicenter analysis, compared to Caucasians, African-Americans had more than five-fold odds of uveitis (OR 5.5 [95% CI: 2.3–13]) (47). African-Americans were also more likely than Caucasians to have a diagnosis of sacroilitis (OR 4.0 [95% CI: 1.6–10.1]), while Hispanics had a higher prevalence of EN compared to Caucasians (OR 3.3 [95% CI: 1.7–6.4]). Eidelwein, et al reported that their pediatric African-American patients had dermatologic manifestations (EN and PG) more frequently than Caucasians (10.3% versus 2.1%, \( p = NS \))
Other studies have found increased frequency of arthritis and PSC in African-Americans compared to Caucasians (36, 49, 54). In contrast, Cross and colleagues, who found an overall prevalence of EIM of 31%, found no difference in the proportion of subjects with any EIM by race (38).

Regarding clinical disease behavior, results are again variable. The IBD Genetics Consortium study found that African-Americans were less likely to have abdominal perforating disease than Caucasians (20% versus 35.8%, \( p = 0.02 \)) five years after diagnosis. However, five years after diagnosis, African-Americans were more likely to have stricturing disease than Caucasians (38.2% versus 24.4% \( p = 0.03 \)). Conversely, disease behavior was not significantly different between Caucasians and Hispanics (47). In partial contrast, a 10-year retrospective study of 245 pediatric IBD patients seen at Johns Hopkins Hospital (24% African-Americans) revealed that African-Americans had higher proportions of both stricturing and penetrating CD than Caucasians (51.3% versus 27.4%, \( p = 0.006 \)). The authors attributed these findings to a higher proportion of African-American patients who progressed from non-penetrating, non-stricturing behavior to stricturing and/or penetrating behavior over time compared to Caucasians (29.2% versus 11.1%) (33). These findings are in contrast to several studies, including a pediatric study done by Kugathasan, et al, which reported no differences in disease behavior between African-Americans and Caucasians (37,38,46,49,50,54,56). Further, it was the conclusion of a recent qualitative review that disease behavior was similar between African-Americans and Caucasians (52). Regarding immune phenotype, Basu, et al reported no serological differences in the proportion of patients with a positive ASCA between Caucasians and African-Americans (36).

Racial differences in disease severity in CD

Given the retrospective nature of the majority of studies in this field, validated prospective severity indices, such as the Crohn’s Disease Activity Index or the Harvey-Bradshaw index, have not been used. Therefore, studies rely on surrogate markers such as need for hospitalization, surgery and use of steroids as severity indicators. A large study conducted in the Kaiser-Permanente system in Northern California reported that African-Americans and Caucasians with CD had equal rates of hospital admissions. However, these rates were nearly 20-fold those of Hispanic CD patients (35). Another HMO-based study also reported similar CD hospitalization rates between African-Americans and Caucasians (35). Conversely, separate analyses of both the Medicare and Veterans Affairs datasets reported that African-Americans had IBD hospitalization rates that were double those of Caucasians (57,58). Basu, et al found no differences in surgery and hospitalization between African-Americans and Caucasians with CD (36).

Nguyen, et al found that after controlling for various confounders, the average number of surgeries for...
abdominal CD since diagnosis was significantly lower in African-Americans than Caucasians (0.8 versus 1.6, \( p < 0.001 \)). Hispanics were more likely to have undergone bowel diversion for CD; however, they too had fewer surgeries than Caucasians. Finally, the authors found that the number of surgeries for perianal CD was similar among all racial groups (47). In their study of 64 African-American patients from the Medical College of Georgia, Simsek, et al reported that approximately 53% of African-Americans with CD had undergone at least one surgical procedure, while 50% required repeat operations. This was similar to rates in their Caucasians subjects, though the re-operation rate in African-Americans was higher (49). Goldman, et al reported that over 10 years, 100% of their African-American CD patients required at least one surgery (compared to 70% of Caucasians), while 47% required reoperation (54). It is difficult to compare these figures with the accepted 15-year CD resection (70%) and reoperation (30%) rates, as the authors in this study did not report duration of disease (59). Using the Nationwide Inpatient Sample, a recent analysis of 41,918 CD discharges between 1998 and 2003 by Nguyen, et al reported adjusted (including insurance and median neighborhood income) CD surgery rates which were significantly decreased in African-Americans and Hispanics (approximately 30% lower) compared to Caucasians (60). Again, it was not possible for the authors to adjust for colectomy indication, duration or extent of colitis, or disease-specific severity. A multicenter telephone survey did not report different CD surgical rates between African-Americans and Caucasians, which were similar to the findings of Cross, et al (38,56). These studies found no difference in the frequency of steroid use between African-Americans and Caucasians.

RACIAL DIFFERENCES IN DISEASE SEVERITY IN UC

Analyses of administrative databases have yielded conflicting results regarding the differences in the severity of UC by race. An analysis of the VA database demonstrated that hospital discharges for UC were less frequent in African-Americans compared to Caucasians; however, data from the Medicare population revealed that African-Americans had higher hospital discharge rates than Caucasians in 22 U.S. States (57, 58). Basu, et al reported significantly less bowel surgery and hospitalization in Hispanics compared to Caucasian UC patients (36). Recently, several interesting findings in African-Americans and Hispanics with UC have been reported following analysis of the Nationwide Inpatient Sample. In the first analysis of 23,389 UC discharges between 1998–2003, colectomy rate ratios for African-Americans and Hispanics were significantly decreased (0.46 and 0.74, respectively) compared to Caucasians (61). This study also revealed that African-Americans experienced a significantly longer interval between admission and colectomy than Caucasians (8.5 versus 5.6 days, \( p = 0.02 \)). These findings persisted after controlling for insurance status, comorbidity and hospital characteristics. However, it was not possible for the authors to adjust for colectomy indication, duration or extent of colitis, or disease-specific severity. A subsequent assessment of the health preferences of a sample of 39 African-Americans and Caucasian patients detected no differences in patient preferences regarding colectomy (62).

DISPARITIES IN TREATMENT OF IBD

The obvious cause for a difference in the treatments utilized between groups with the same disease would be differential disease severity. However, there are no prospective studies documenting the natural history and severity of either CD or UC in racial and ethnic minorities. As mentioned previously, accurate quantification of disease severity is very difficult with retrospective studies. Validated disease severity indices are not used for retrospective application, causing severity to be defined by exposure to medications used to treat more severe disease, hospitalization/health care utilization, or need for surgery. As some of these are treatments themselves, the potential for bias becomes readily evident. Despite these limitations, some studies have tried to address these questions.

A preliminary chart review from the University of North Carolina reported that African-Americans with CD had three times the risk of treatment with steroids when compared to Caucasians. However, a follow-up (continued on page 31)
multi-center phone survey of CD patients revealed no significant racial differences in recall of medication classes (5-ASA, steroids, immunomodulators) previously used (56). However, there was no adjustment for disease severity, access to care or indications for therapies. A more recent analysis of a racially and ethnically diverse 149-patient IBD cohort from Houston reported that, compared to Caucasians, there were lower proportions of African-Americans treated with immunomodulators (31% versus 42%) and infliximab (14% versus 22%) while more African-Americans were treated with mesalamine (81% versus 65%). Though not statistically significant, these may be clinically important differences. A recent retrospective IBD cohort analysis from Baltimore assessed racial differences in the use of immunomodulators and biologic agents. After adjusting for disease severity (steroid use), the authors found that African-American patients with IBD were less likely to receive biologics (OR 0.50, 95% CI 0.23–1.08) or the combined outcome of either immunomodulators or biologics (OR 0.57, 95% CI 0.32–1.01) compared to Caucasians (63).

SUMMARY

Because of limitations in populations studied, previously reported IBD incidence and prevalence in African-Americans and Hispanics are likely underestimates. Gaps with Caucasian estimates seem to be narrowing, possibly reflecting increasing incidence. Available data suggests comparatively modest role of IBD family history and genetic susceptibilities in African-Americans and Hispanics when compared to Caucasians. For several likely reasons (such as differences in sample size, methodology, phenotypic definitions and length of follow up) published literature conflicts in regards to racial/ethnic differences in disease phenotype, disease severity, and treatment. However, a few differences have emerged with greater consistency. African-Americans with CD may have colonic and upper tract disease more frequently and ileal disease less frequently than Caucasians, while Hispanics may have less upper tract and more ileocolonic disease. Perianal CD also may be found more frequently in African-Americans (and perhaps Hispanics) than Caucasians. UC disease extent does not appear to differ between African-Americans and Caucasians, though Hispanics may have extensive disease more frequently. In larger studies, African-Americans appear to have resective CD surgery less frequently than Caucasians, though they appear to have similar hospitalization rates. Similarly, despite similar hospitalization rates, African-Americans hospitalized with UC undergo colectomy less frequently than Caucasians. Further, delay from admission to colectomy is longer in African-American patients. Finally, recent data has suggested that African-Americans with IBD may be less likely to be treated with immunomodulator or biologic therapy than Caucasians. Whether some of these differences are the result of actual racial/ethnic differences in severity of disease (thereby making the differences potentially appropriate) or from other factors (provider factors, patient factors, socioeconomnic factors) is unclear. The truth underlying this question is the key to the determination of the existence of a disparity.

Because the majority of current data are from retrospective studies, there are inherent methodological limitations. Most of these studies evaluated patients over a period of decades, during which time prominent advances in the diagnosis and treatment of IBD had been made, making it difficult to generalize the clinical course and treatment of the patients studied. Also, many of these studies failed to use standardized or uniform clinical variables and disease severity, again making it difficult to accurately compare data between studies. For these reasons, prospective multi-center studies evaluating racial differences and disparities in IBD should be initiated and supported. Likewise, enhancing racial and ethnic minority enrollment in IBD clinical trials, which has traditionally been 5%, will provide insight into differences in presentation, clinical course and response to therapy (14). These studies can not only help to strengthen our knowledge of ethnic differences in IBD, but also to serve as a basis to formulate more effective management of these potentially debilitating diseases.

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Race and IBD

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