



# Racial and ethnic disparities in clinical presentation, management, and outcomes of patients with inflammatory bowel disease: a narrative review

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*Contributions:* (I) Conception and design: K Sultan; (II) Administrative support: None; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: Both authors; (V) Data analysis and interpretation: None; (VI) Manuscript writing: Both authors; (VII) Final approval of manuscript: Both authors.

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**Background and Objective:** Inflammatory bowel disease (IBD) is a chronic condition that has been increasing in prevalence and incidence worldwide. Although, most cases are described in Caucasian populations, there has been a rise in IBD diagnosis among other populations. In this article, we will discuss the disparities in the presentation, management, medical and surgical outcomes of IBD patients among different racial and ethnic groups.

**Methods:** A literature search was conducted in PubMed, Medline, and Google Scholar. The search strategy included targeted keywords to identify specific studies that provided the current literature on disparities in IBD presentation and management. Articles for presentation were selected by the authors, in accordance with a narrative review format, favoring population-based studies, systematic reviews and meta-analysis over single or multicenter reports.

**Key Content and Findings:** Epidemiological data has shown that there is an increasing incidence in IBD diagnosis among Black, Asian, and Hispanic populations over the past decade. Differences in genetic predispositions have been observed, however it is difficult to ascertain if the minor differences in presentation and medical/surgical management reported are due to innate differences or due to confounding factors such as access to health care.

**Conclusions:** Differences in genetic predisposition, and clinical presentation have been observed to exist among IBD non-Caucasian populations. There were also differences observed in both surgical and medical management, but it is difficult to ascertain if these were innate differences or due to societal factors.

**Keywords:** Inflammatory bowel disease (IBD); Crohn's disease (CD); ulcerative colitis (UC); racial disparities; medical outcomes

Received: 07 July 2023; Accepted: 11 March 2024; Published online: 22 April 2024.

doi: 10.21037/tgh-23-43

View this article at: <https://dx.doi.org/10.21037/tgh-23-43>

## Introduction

Inflammatory bowel disease (IBD) is a chronic disorder that by some estimates may affect up to 1% of the population in the United States (US). IBD is mainly divided by two

chief subtypes, Crohn's disease (CD) and ulcerative colitis (UC). Traditionally, IBD has been regarded as a condition characterized by non-infectious, idiopathic, chronic inflammation of the bowel. Recent studies have expanded

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our understanding of disease pathogenesis, revealing that IBD is really the result of a complex and disordered interaction between the “outside” world, in the form of the native gut microbiome, and the body’s immune system (1).

What has been clearer since the first descriptions of UC in the 1800’s, followed by CD in the early 1900’s, is the Northern Hemisphere and Caucasian predominance of IBD prevalence. This risk has been consistently observed to be greatest in the Ashkenazi Jewish population, which remains the highest risk cohort. However, the recent decades observed that IBD is increasingly common in non-traditional populations. This phenomenon is occurring worldwide but has also been noted within the US population itself. Internationally, this has been attributed to increasing “westernization” through a variety of mechanisms such as diet, lifestyle, early access to antibiotics, improved sanitation, etc. In addition to these factors playing a role in the disease, there is also an increased recognition of IBD with inclusion of different ethnicities in population-based studies.

The recent American Medical Association Style Committee Guidelines note that “Race and ethnicity are social constructs ... with limited utility in understanding medical research, practice, and policy”. The authors however go on to note that categories of race and ethnicity may be useful specifically when addressing issues of disparities in health and medical care. Though race and ethnicity each defy a specific universal definition or categorization, race is generally applied to a groups’ physical characteristics, while ethnicity refers to a common national or cultural tradition. Throughout the following review, we will be adhering to the descriptors and categories of race and ethnicity as presented within the source documents (2).

With the increasing prevalence and recognition of IBD in non-Caucasian populations, there is an interest in better understanding the potential differences/disparities in the presentation, management, and outcomes of these patients. In this review, we will update the most current evidence on these three core topics. While not doing so exclusively, we will mainly present data that is population based.

Although we will mostly avoid presenting data from single-center analyses, we will incorporate information from large meta-analyses relying on these reports. Though reports were included from a diversity of locations, those reporting on comparisons of Caucasian and non-Caucasian IBD populations heavily relied on US data and other countries where a side-by-side comparison of Caucasian and non-Caucasian IBD populations are possible. We

present this article in accordance with the Narrative Review reporting checklist (available at <https://tgh.amegroups.com/article/view/10.21037/tgh-23-43/rc>).

## Methods

A search was performed in PubMed, Medline, and Google Scholar databases to identify English-language population-based research cohorts, meta-analysis, and systematic reviews of the ethnic and racial disparities in IBD management published between 2000 and 2023. We utilized search phrases outlined in *Table 1*. The search items were interchanged when we searched for articles.

As a narrative review, the final choice of source data inclusion was based on upon authors N.V. and K.S. selection, emphasizing large population-based cohort studies, systematic reviews, and large single-center studies in English language (*Table 2*).

## Discussion

### *IBD and genetic disparities*

An increasing body of work on IBD and genetics has revealed differences across racial and ethnic groups. The heritability model of IBD is still incompletely defined, but recent studies have indicated that genetic susceptibility, environmental factors, intestinal microbiota, and immune system are all involved in the pathogenesis of IBD. Both the disease are very common among familial cases and one of the important risk factors for IBD is having an affected relative (1). Population based studies have shown that there is an 8- to 10-fold greater risk of IBD among relatives of UC and CD, especially in twins (3). Genetic predisposition among twins is much stronger, especially in CD patients. The concordance rate in monozygotic twins of 30–35% in CD compared with 10–15% in UC suggests that potential non-genetic factors may have an even more important role in IBD development (4). Similar observations have also been noted in non-twin siblings where a child has a 26-fold increased risk for developing CD when another sibling already has it and 9-fold higher with UC (1).

Over the past few decades, there has been significant advances in technological process for genetic testing and DNA sequencing which includes the genome-wide association studies (GWASs) that have identified new single nucleotide polymorphisms. GWAS have been successful in IBD, involving 99 non-overlapping genetic risk loci,

**Table 1** The search strategy summary

Items	Specification
Date of search	Inception–April 30, 2023
Databases and other sources searched	PubMed, Medline, Google Scholar
Search terms used	Inflammatory bowel disease OR ulcerative colitis OR Crohn's disease AND racial disparities OR ethnic disparities OR genetic differences OR medical management OR surgical management
Timeframe	01/01/2000–04/30/2023
Inclusion and exclusion criteria	Inclusion: population-based cohorts, and systematic reviews and meta-analysis and selected single large center studies in English language  Exclusion: case reports and case series
Selection process	N.V. and K.S. conducted the search independently and consensus was obtained if both agreed on study inclusion. References of articles were further reviewed to identify possible sources

**Table 2** Summary of the major studies

Study, country, year	Aim of the study	Characteristics/setting	Major findings
Population-based cohort studies			
Nguyen <i>et al.</i> , US, 2006	Characterize the racial differences in disease phenotype in adult population	Phenotypic data obtained from six academic centers. Caucasian (n=830); AA (n=127); Hispanics (n=169)	AA patients more likely to have upper GI tract CD, perianal disease, uveitis, and sacroiliitis but less likely to have ileal involvement. Hispanics had higher prevalence of perianal CD and erythema nodosum. Both Hispanics and AA had lower prevalence of family history of IBD compared to Caucasian
Ben-Horin <i>et al.</i> , Israel, 2009	To compare the severity of CD in patients with family history of IBD compared to sporadic cases	181 CD patients. Positive family history of IBD in first degree relative was reported was 16%	The prevalence of familial disease among Jewish CD patients in Israel is more increased compared to other ethnicities. Positive family history had no impact on the severity of the disease
Benchimol <i>et al.</i> , Canada, 2015	To compare the incidence of IBD in immigrants to Canada and their Canadian-born children was compared with non-immigrants	IBD patients' data derived from health administrative data linked to immigration data in Ontario, Canada between 1994 and 2010	Incidence risk was the lowest in East Asians and highest in Western Europeans/North Americans. Children of immigrants from Middle East/North Africa, South Asia, Sub-Saharan Africa, and North America/Western Europe had similar risk of IBD as children of non-immigrants
Barnes <i>et al.</i> , US, 2018	To compare the phenotypes and treatment patterns of black and white patients with IBD in a prospective study	Data was obtained from Sinai-Helmsley Alliance Cohort. Among 5,537 IBD patients, 316 of the patients were black	Black patients were more likely to develop abscess and proctitis at baseline compared to white population. There were no differences in surgery or hospitalization rates during the follow-up period
Misra <i>et al.</i> , UK, 2019 (population based prospective cohort)	Describe the incidence and phenotype of IBD and distribution within ethnic groups	Newly diagnosed IBD adult patients were prospectively recruited over 1 year in five urban catchment areas with high South Asian population. Among 2,271,406 patients, 339 patients were diagnosed with IBD over 1 year	The age adjusted incidence of IBD was significantly higher in the Indian group compared to White European and Pakistani groups. The Indians were also more likely to have extensive disease

**Table 2** (continued)

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Study, country, year	Aim of the study	Characteristics/setting	Major findings
Systematic review and meta-analysis			
Afzali <i>et al.</i> , US, 2016	Disease characteristics among different racial and ethnic minorities	47 studies were included. AA (n=20,054); Hispanics (n=10,762); Asians (n=2,668)	Pancolitis was more common among Hispanics and Asians. CD related hospitalizations were increased among Asians and AA. No major differences are seen in disease location, upper GI involvement, perianal involvement, and extraintestinal manifestations. Differences in surgery were due to health insurance status
Shi <i>et al.</i> , US, 2018 (meta-analysis and systematic review)	Comparison of similarities and differences in disease presentation and outcomes across different geographic and ethnic groups	198 studies were included. 525,425 IBD patients (Caucasian 65%, Asian 30%, Hispanic 2%, and Black 1%)	Both Black and Asian CD patients demonstrated perianal involvement than other ethnicities. Surgery for both CD and UC was less common in Asians than Caucasians. Asian CD patients had a strong male predominance
Mosli <i>et al.</i> , UAE, 2021 (systemic review and meta-analysis)	To investigate the incidence and epidemiology of IBD in the Arab world	16 studies conducted in Saudi Arabia, Egypt, Kuwait, UAE, Bahrain, Lebanon, and Oman were included. All studies were between 1990s and late 2010s	Majority of the IBD patients were predominantly male. There was an increasing incidence of both UC and CD in the Arab world
Booth <i>et al.</i> , US, 2022 (systemic review)	To determine if there is disparity in surgical management of IBD patients in the US	45 studies were included. Electronic databases were searched between 2000 and 2021	Black and Hispanic patients were less likely to undergo surgery and more likely to have surgical complications
Tandon <i>et al.</i> , Canada, 2024 (systemic review and meta-analysis)	To determine the differences in health care utilization among different races and ethnicities	58 studies were included	Black patients were less likely to undergo surgery, more likely to be hospitalized, and visit the ED. No differences in disease behavior or biologic exposure between black and white patients. No differences in health care utilization between white and South Asian population

US, United States; AA, African American; GI, gastrointestinal; CD, Crohn's disease; IBD, inflammatory bowel disease; UK, United Kingdom; UAE, United Arab Emirates; ED, emergency department.

including 28 that are shared between CD and UC (4). The identification of susceptibility loci has enhanced understanding the etiology of the disorder by providing important clues in the disturbed pathways of the intestinal immune system (1). The earliest studies showed that the most common susceptible genes include the nucleotide oligomerization domain containing 2 gene (*NOD2*), and caspase-activation recruitment domains (*CARD15*) on chromosome 16. Other genetic predispositions associated with the incidence of IBD include *IBD1-9*, *TNFSF15*, *IL23R*, *ATG16L1*, *IRGM*, *PRDMI*, and *NDP52* (5). These gene mutations are related to early onset of CD disease, with potential small bowel involvement and early bowel resection (6). Since the identification of the *NOD2* variant, many genetic anomalies have been identified to be associated with IBD, most of these playing some role in host immune response to commensal bacteria.

Specific IBD risk alleles have been associated with different races and ethnicities (7-9). Ashkenazi Jewish population have been reported to have 3-4-fold higher risk of developing IBD compared to non-Jewish ethnic groups. There is higher prevalence of genetic mutations in *NOD2/CARD15* among the Ashkenazi Jews (8). Other major risk alleles include *Gly908Arg*, *Arg702Trp*, and *Leu1007fs* which has been shown to increase the risk of CD in White populations. Earlier studies have shown a higher frequency of *Gly908Arg* allele in Jewish populations, whereas *Arg702Trp* mutations were more frequent in the non-Jewish population (6). Interestingly, reports have shown higher prevalence and life time risk of developing IBD in first degree relatives among the Jewish populations compared to the non-Jews (10).

In an African American (AA) population, variants in *NOD2* increase the risk for CD which mostly arise from

European admixture (11). Three of the most common CD risk genes which include *NOD2*, *IBD5*, and *ATG16L1* contributed to the risk of CD both in Caucasian and AA populations. Some variants which include the single-nucleotide polymorphisms in the signal transducer and activator of transcription 5A gene (*STAT5A*) and *STAT53* genes were associated with CD only in those of African descent (12). Other additional risk variants associated with those of African descent include *C2orf43*, *HDAC11*, and *LINC00994*. Polymorphisms in *ZNF649* and *LSAMP* were shown to be the most prominent risk for IBD in AA patients which specifically increases gastrointestinal (GI) inflammation in UC.

Compared with those of European descent, Asian patients with CD were less likely to carry disease associated variants in the *NOD2*, *ATG16L1*, or *IL23R* (11). A systematic review and meta-analysis showed that polymorphisms in the gene encoding tumor necrosis factor (TNF) superfamily member 15 had a strong risk association with IBD in Asians but only a modest risk associated with Caucasians (13). One of the studies found variants in the *TNFSF15* in the Korean population have shown to have more complex CD disease including strictures, penetrating complications, and perianal fistulas (14). While genetic studies among East Asian populations have been larger than the AA, they are still much smaller than European populations.

In a study from Puerto Rico, among 1,159 patients, variants in *NOD2* and *IL-23* increased the risk of development of CD (11). Similar results were found in South Florida cohort of patients which showed that there was no difference in composite genetic risk score between Hispanic and non-Hispanic populations. It is noteworthy that this population had a higher percentage of Cubans (15). Genetic studies among Hispanic populations currently lag far behind compared to other groups, but further studies with significant efforts are in progress to identify specific genetic risk factors associated with IBD.

Genetic variants have also been observed to determine individual response to or adverse effects from therapy. Thiopurines can be used as steroid sparing agents for management of both UC and CD. Prior to its use, thiopurine methyl transferase gene (TPMT) activity is monitored to prevent the toxic effects of thiopurine metabolites. However, approximately 25% of the European ancestry carry specific variants to TPMT which led to myelosuppression with thiopurine usage (16). While Asians have a lower proportion of the TPMT variants, they carry a higher risk for a single nucleotide polymorphism in the *NUDT15* which can cause

thiopurine induced leukopenia (17).

### ***IBD and phenotype disparities***

Though there may be some underlying genetic differences among IBD patients across racial and ethnic groups, the data on disease presentation is mixed. Most published reports of UC extent analyzed by race and ethnicity is from single center or multicenter/referral center analyses. A large U.S. population analysis by Nguyen *et al.* in 2006 where the authors utilized the Nationwide Inpatient Sample (NIS), with their main goal to characterize racial and geographic differences in colectomy rates among hospitalized UC patients (18). From 1998 to 2003, they looked at 23,389 discharges with UC, including 18,368 White, 2,288 AA, 1,834 Hispanic, and 899 were other race. The disease extent was similar across all groups, with just under 50% classified as pancolitis. On the other hand, Shi *et al.* in their recent systematic review and meta-analysis included international population-based studies noted similar disease extent across all racial/ethnic groups but with a higher frequency of proctitis among Caucasians and Asians compared to Blacks and Hispanics (19).

CD has been more extensively examined about potential differences in disease presentation and severity. Most published reports were of single, tertiary care referral center populations. In another meta-analysis observing at CD, Shi *et al.* reported on 198 studies and 525,425 patients from 54 countries observed differences in phenotype by ethnicity, divided between White, Asian, Black, and Hispanic (19). Notably, most of the Asian patients (n=156,127) were natives of East Asia (n=152,904), while only 1,653 were immigrants to the west. In terms of ileal disease, one-quarter of White and Asian CD patients and one-third of the Hispanic population had this phenotype (P=0.01), while blacks were less likely to have it [0.14, 95% confidence interval (CI): 0.06–0.22]. Isolated upper GI involvement was more common in Asian CD patients (0.08, 95% CI: 0.04–0.11) compared to the Caucasians (P<0.01). Compared to Asian, White, and Hispanic populations (P<0.05), there is a higher proportion of penetrative disease in Blacks (0.20, 95% CI: 0.16–0.25). Nearly one-quarter of all Asian CD patients (0.23, 95% CI: 0.17–0.29) and one-third of Black CD patients (0.31, 95% CI: 0.11–0.52) had perianal disease compared to Caucasian CD patients (0.14, 95% CI: 0.12–0.16) (P=0.02). Similar results were found in a study from Odufalu *et al.* which was a literature review that found AA had a higher proportion of penetrating disease, perianal

disease, and extraintestinal manifestations of uveitis, arthralgias and ankylosing spondylitis compared to the Caucasian populations (20).

Another analysis within a large multi-racial population was recently reported from the United Kingdom (UK). Misra *et al.* prospectively recruited patients with a new IBD diagnosis over a 1-year period from areas of ethnic diversity, defined by more than 10% of the background population as non-White European. The catchment population of over two million yielded 339 new IBD diagnosis. The main non-White ethnic categories were Pakistani and Indian. Compared the White European (14.9/100,000,  $P=0.009$  and 8.2/100,000,  $P<0.001$ ) and Pakistani groups (14.9/100,000,  $P=0.01$  and 11.2/100,000,  $P=0.007$ ), there was a significant increase in incidence of UC in the Indian group (25.2/100,000 and 20.5/100,000). Extensive disease was significantly more common in the Indian group compared to the White Europeans (52.7% *vs.* 41.7%,  $P=0.031$ ) (21).

Benchimol *et al.* in their recent population-based study from Canada investigated the rates of IBD among immigrants in Ontario, primary those from East and South Asia. They observed lower rates within immigrant population as compared to those with a Western European background. Most notably, the children of immigrants had a similar IBD risk as those with children of non-immigrants, while those who immigrated at an older age had a decreased risk (22).

Stulman *et al.* reported an increasing trend of incidence and prevalence of IBD in Jewish and Arab population in Israel (23). It was a nation-wide population-based cohort study that calculated the incidence of IBD between 2005 and 2018 among both adult and pediatric populations. Findings showed that there was a decline in UC and increase in CD incidence rates among Jewish population. However, the Arab subpopulation in Israel had slightly increased incidence of CD and stable UC rates. Another meta-analysis which focused on Arab countries included 16 studies which showed an increasing incidence rate over time, estimated at 2.33 and 1.46 per 100,000 persons per year respectively for UC and CD in the Arab population (24).

### ***IBD and access to specialty care***

Once IBD is diagnosed, access to appropriate specialty care is critical to disease management and must be addressed before a review of management issues. With the advancement of IBD therapeutic options and the increasing effectiveness of these therapies, access to IBD specialists are more important than ever. When examining the literature

for evidence of differences in access across racial and ethnic groups, it is critical that other social determinants of health care (SDOH) are considered which might confound this access. Examples include income, geographic location, and educational background. Naturally, in the US, with its patchwork of private and government health insurance, and a large uninsured population, it is the ability to pay that rightfully has attracted the most focus.

As with other studies addressing race/ethnicity and IBD, those attempting to examine access are also overwhelmingly single or multicenter oriented, and shed little light on this issue (25). There is data available on insurance status, race/ethnicity and IBD. As we have seen, the NIS provides a robust and broad tool for monitoring characteristics for hospitalized IBD patients within in the US. Nguyen *et al.* analysis of the NIS from 1995 to 2005 examined insurance coverage along with race/ethnicity (26). There was a significant increase in proportion of uninsured IBD patients (from 4.6% to 6.5%,  $P<0.001$ ), and IBD patients were more likely than general medical patients to be uninsured (5.1% *vs.* 4.1%,  $P<0.0001$ ). Risk factors including 21 to 40 years [odds ratio (OR), 1.95; 95% CI: 1.64–2.31], AA (OR, 1.51; 95% CI: 0.76–1.52), or Hispanic (OR, 2.21; 95% CI: 1.79–2.74) or residing in the southern US (OR, 1.63; 95% CI: 1.27–2.11) were predictors of being uninsured. Protective factors include female sex (OR, 0.65; 95% CI: 0.61–0.70), residing in higher income neighborhoods (OR, 0.69; 95% CI: 0.62–0.77), and higher comorbidities. Though hospitalization may allow the opportunity to work with social workers to begin the process of obtaining some form of coverage such as Medicaid, one can only assume that those admitted without insurance coverage were also discharged without insurance coverage, limiting the effectiveness of their outpatient follow-up.

There is some emerging evidence that the passage of time and expansion of health care insurance under the affordable care act (ACA), aka “Obamacare”, has improved access to IBD care. Another recent analysis of the NIS has demonstrated a positive trend of increasing coverage for pediatric and young adult patients with IBD (27). The authors specifically sought to investigate for an effect of the ACA which allowed dependent children to remain on their parent’s insurance between the ages of 19 and 25 years. They estimated proportions of insurance coverage during the years 2006–2013 and compared 19 to 25 years patients to 2 to 18 years children and 26 to 35 years old adults, unaffected by the provision, to try and reveal any underlying trends. From 2006 to 2010, 19- to 25-year-old patients had the highest

proportion of uninsured, peaking at 14.1% in 2010. In 2011, the proportion decreased to 10.1%, below the proportion of uninsured 26 to 35 years old patients (13.1%), remaining in this range through 2013. Private coverage increased in 2011 for 19 to 25 years old patients, remaining stable for 26 to 35 years old patients. While the data is certainly encouraging, and likely benefits many patients across race/ethnic categories, a direct analysis of this was not available.

The Canadian model of universal healthcare offers a different template for analyzing issues of race, ethnicity, and access to healthcare. Benchimol *et al.* observed a population-based cohort from Ontario province. Their population included large groups of immigrants from East Asia (11.5%), South Asia (22.7%), and the Middle East (14.4%). Comparing 2,202 immigrants with 22,990 non-immigrants, despite the lower average incomes observed in the immigrant populations, the authors observed that immigrants were seen by gastroenterologists more often than non-immigrants and had a greater IBD-specific outpatient health services use after diagnosis (OR, 1.24; 95% CI: 1.15–1.33) (28).

### ***IBD and medical management***

#### **Utilization**

The issue of IBD management across racial and ethnic groups is a complex one. Certain differences in disease phenotype, timing of disease presentation, and severity at presentation may and should impact treatment decisions. As we have seen, access to care may also impact management decisions as well as the outcomes. Overall, if healthcare access was similar then both the surgical and medical management were similar among the populations as well.

Positive disease outcomes for those with IBD have been linked to earlier use of biologic and immune therapy. As such, special focus has been placed on the utilization of these most effective therapies, and how race/ethnicity might impact this utilization. In order to analyze medication use patterns among IBD patients from 1998 to 2010, Lin *et al.* analyzed the data from the National Ambulatory Medical Care Survey (NAMCS) and the National Hospital Ambulatory Medical Survey (NHAMCS). The survey was used to calculate nationally representative estimates, and to then determine whether use of immunomodulators and anti-TNF agents differed by race/ethnicity and socioeconomic status (SES) among ambulatory patients with IBD (29). Among the 26,400,000 visits for IBD patients in the US from 1998 to 2010; 67% patients were

White, 7% were Hispanics, 9% were Blacks, and 2% were Asians. There were 67% of the patients who had private insurance and 9% were Medicaid. The proportion of visits for both immunomodulators and anti-TNF agents were increased from 6% to 13% and <1% to 14%, respectively. Although there were no ethnicity/race-based differences in immunomodulatory use, Medicaid visits were three times more likely associated with immunomodulators than the visits with private insurances after adjusted analyses. There were no significant differences observed in the use of anti-TNF therapy among race/ethnicity or SES based differences.

More recently, Barnes *et al.* in their analysis of a large Medicaid insurance population looked at whether differences in treatment may exist for those the same insurance coverage and access to care (30). The goal of the study was to compare medication usage among Black and White IBD patients who had equal access to gastroenterologists and therapies. The authors used population-based Medicaid Analytic extract data from four states (California, Georgia, North Carolina, and Texas) between 2006 and 2011, for patients between the ages of 18 and 64 years, and compared the use of IBD-specific therapies. To limit their analysis strictly to IBD patients, they excluded those with a co-diagnosis of rheumatoid arthritis, ankylosing spondylitis, psoriasis, and psoriatic arthritis. Their study population included 14,735 patients with IBD [4,672 Black (32%), 8,277 with CD (58%)], 9,665 (66%) female, with a median age of 41 years. During the study period, 9,459 (64%) of patients received IBD directed medical therapy, with very slight differences observed in medical disease management. Multivariate regression analysis showed that there was no significant difference in anti-TNF use by race for both CD [adjusted OR (aOR), 1.13; 95% CI: 0.99–1.28] and UC (aOR, 1.12; 95% CI: 0.96–1.32). There was higher odds of combination therapy (aOR, 1.50; 95% CI: 1.15–1.96) and the use of immunomodulatory therapy (31% *vs.* 18%;  $P=0.004$ ) after surgery for CD in blacks compared to the white population.

Finally, though it detours from our review methodology, additional important lessons can be learned from the multicenter Sinai-Helmsley Alliance for Research Excellence (SHARE) cohort. The SHARE cohort included seven academic medical centers prospectively enrolling adult patients for the purpose of comparing disease phenotypes among Black and White patients with IBD at enrollment and following their treatment and outcomes over time (31). A total of 5,906 patients were evaluated between 1/2012 and 12/2015 which included 36% UC and 64% CD patients.

Among these patients, majority of them were White (88%), 5% were Black, 2% Asian and other racial group comprised about 4% of the population. Hispanic ethnicity was reported as a modifier within with 201 patients reporting Hispanic ethnicity. In terms of treatment, Black patients were less likely to report the use of both thiopurine in CD (61% *vs.* 72%,  $P=0.003$ ) and oral aminosalicylates (80% *vs.* 89%,  $P=0.011$ ) and methotrexate (0% *vs.* 7%,  $P=0.013$ ) in UC prior to the enrollment in the study. There were some differences in baseline disease presentation, likely accounting for observed treatment differences between White and Black patients. Black patients were more likely to have perianal fistula, other CD-related fistula or abscess in both adjusted (aOR, 1.44; 95% CI: 1.06–1.95) and unadjusted models (OR, 1.34; 95% CI: 1.10–1.81). In addition, odds of developing a new abscess (aOR, 2.27; 95% CI: 1.31–3.93) or anal fissure (aOR, 1.76; 95% CI: 1.01–3.07) was more commonly seen in Black patients. Overall, Black patients with CD were more likely to be initiated on a new anti-TNF therapy after enrollment in the SHARE cohort (aOR, 1.85; 95% CI: 1.09–3.14). There was no significant differences in the initiation of new anti-TNF therapy (aOR, 1.42; 95% CI: 0.55–3.69), combination therapy, thiopurine and methotrexate monotherapy and steroids in both black and white patients with UC.

### Medical outcomes

While these studies show an overall similarity of utilization of medical therapies, the question of the relative effectiveness of medical therapy between racial/ethnic groups remains unknown. Current guidelines reflect this lack of evidence, and do not account for race/ethnicity while providing broader recommendations for disease management. To a large degree this absence of evidence can be traced to the traditionally low rates of inclusion of minority populations in clinical trials (32). Still among our most widely used and effective medications, clinical trials for infliximab included <3% enrollment of non-White patients (33,34). Even more recent studies such as the landmark biologic comparator SEAVUE (35) and VARSITY (36) trials have represented only 10% non-White patient enrollment.

Though large national database or insurance claims database analysis is also unavailable, there is some evidence from large retrospective and prospective cohorts suggesting that access to similar care does lead to similar outcomes across racial/ethnic groups. Li *et al.*'s analysis of a large retrospective cohort from the Kaiser Permanente integrated healthcare system investigated outcomes between 1996 and 2007 for patients with UC (37). Though still lower

than the proportion of non-Whites in the general US population, analysis of 6,934 patients included 25% of AA, Asian, and Hispanic origin. Use of biologic and immune medication was similar across racial/ethnic groups, as were 1- and 5-year hospitalization and most surgical rates on adjusted multivariable analysis. Another look at the SHARE prospective cohort shows similar outcomes, comparing 1,761 White patients to 69 Black patients, with no differences observed on rates of hospitalization or surgery (30). The results were more varied when analyzing the CD cohort, 3,349 White and 237 Black. Again, there were no observed differences in rates of hospitalization or surgery, though on adjusted analysis there was a higher rate of new CD-related abscess among Black patients (OR, 2.27; 95% CI: 1.31–3.93), despite higher rates of biologic use. It is unclear whether this finding reflects a diminished efficacy of biologic therapy in the Black population, or more advanced/severe disease at initial presentation.

Abu-Freha *et al.* compared the medical outcomes and complications between Arab and Jewish populations sharing the same health care system (38). Results showed Arabs were diagnosed at a younger age (36.8 *vs.* 39.9 years), had higher rate of anal fissure, perianal abscess, and male infertility. They were less likely to be treated with thiopurines, however there was no difference in rate of anti-TNF treatment between Arab and Jewish populations. Interestingly, the all-cause mortality was lower among the Arab population (8.4% *vs.* 10.2%) which could be due to higher comorbidities in the Jewish population.

### Surgical treatments

Surgical intervention is common in the IBD population. Historically up to 20–30% of UC patients will undergo colectomy during the course of their disease, with as many as 70% of CD patients needing surgery at some point post diagnosis (39–41).

As noted in the prior section, surgical utilization and outcomes have been studied among racial/ethnic lines a well. Observations of the prospective SHARE cohort showed no difference in surgical rates by race/ethnicity (30). Li *et al.*'s observations of UC patients from the Kaiser healthcare system did show some differences in surgical rates on multivariate analysis, in comparison to the largest subgroup, the White population. At 1-year follow-up, fewer Asians underwent surgery as compared to Whites (aOR, 0.3;  $P<0.05$ ), with a trend towards lower surgical rates in AA. At 5 years follow-up, surgery was still lower for Asians (OR, 0.4;  $P<0.01$ ), with no significant differences observed (37).



Similar results were found among AA and Hispanics in a meta-analysis conducted by Tandon *et al.* where both ethnicities were less likely to undergo CD or UC surgery, more likely to have an IBD-related hospitalization and emergency department visits (40). Systematic review was performed by Booth *et al.* to observe the differences in surgical management in the US (41). The study included 24 articles, there were more complications related to surgery among both the Hispanic and Black populations even though they were less likely to undergo abdominal surgeries.

Another large cohort study using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database compared surgical outcomes between AA and non-AA population (42). The study sample included 9,513 patients who underwent intestinal surgery for CD, 4,390 (46.1%) men, and 790 (8.3%) AA, with all other patients grouped as non-AA. AA patients are more likely to have tobacco abuse, have postoperative sepsis, preoperative admissions and renal failure when compared to other races. In addition, there were also likely to be underweight (12.0% *vs.* 7.3%) and obese (11.2% *vs.* 10.8%) or morbidly obese (9.6% *vs.* 6.8%). Rates of emergency surgery and pre-operative immunosuppressant use were similar between the groups. Major complications were more likely to be observed in AA patients (23.5% *vs.* 18.9%;  $P=0.002$ ). However, after adjusting for multiple confounding variables, compared to other races, AA patients did not have a higher risk for major complications (aOR, 1.19; 95% CI: 0.99–1.42).

Another more recent study of the ACS-NSQIP analyzed racial/ethnic subgroups in more detail. Of 23,901 patients with IBD, 88.7% were White, 7.6% Black, 2.4% Hispanic, and 1.4% Asian (39). The average length of hospital stay was 8 days but there was significant difference between the racial groups (8 d for White, 10 d for Black, 8.5 d for Hispanic, and 11.1 d for Asian;  $P<0.001$ ). There was higher odds of renal insufficiency (OR, 1.8; 95% CI: 1.1–2.9) and re-admission (OR, 1.4; 95% CI: 1.1–1.8) among the AA and Hispanic patients, respectively. In addition, AA patients were also more likely to develop sepsis (OR, 1.7; 95% CI: 1.4–2.02) and require blood transfusions (OR, 1.7; 95% CI: 1.4–1.9) compared to other races (39).

Additional population-based data is again available through the NIS. Nguyen *et al.* analyzed 41,918 discharges with CD from 1998 to 2003, 34,388 among Whites (43). Outcomes included bowel resection and in-hospital mortality rates for non-Hispanic, Whites, AA, Hispanics, and non-Hispanic Asians were calculated. The adjusted incidence rate

ratio (IRR) of undergoing resection in Hispanics was 0.70 (95% CI: 0.60–0.83), in AA was 0.68 (95% CI: 0.61–0.76), and in Asians/Pacific Islanders was 0.33 (95% CI: 0.16–0.59) compared to the White patients with CD. Asians were observed to have lower in-hospital mortality rates compared to other groups.

There was no significant differences in the mortality rates between Whites, AA, and Hispanics—6.6, 6.4, and 9.7 deaths per 10,000 hospital days, respectively. Another NIS analysis of colectomy rates for UC, also between 1998 and 2003, showed that minorities were significantly less likely to undergo colectomy compared to the White population (AA 54% less likely and Hispanics were 26% less likely) (18). For those having colectomy, a greater proportion of AA underwent subtotal or total colectomy with retention of rectal stump and temporary ileostomy when compared to Whites (35.3% *vs.* 24.3%,  $P<0.05$ ). There were no differences among the races regarding in-hospital mortality.

## Conclusions

The incidence of IBD is clearly increasing worldwide, almost entirely due to the increase in non-traditional populations. Genetic differences between IBD patients across racial and ethnic groups have been observed, while data on disparate presentations and phenotypes shows more similarities than differences across these groups. Analysis of IBD data from the US has suggested some differences in presentation and outcomes, but it remains unclear how much of this is due to innate differences between groups, rather than to disparities resulting from timeliness of diagnosis, disease recognition, and access to the latest therapies. Future prospective studies, including enhanced enrollment of minority populations in clinical trials, will be needed to truly understand whether and where disparities exist, and to what degree these disparities are related to biologic, lifestyle, or modifiable societal factors.

## Acknowledgments

*Funding:* None.

## Footnote

*Provenance and Peer Review:* This article was commissioned by the editorial office, *Translational Gastroenterology and Hepatology* for the series “Controversies and Updates in Inflammatory Bowel Disease”. The article has undergone

external peer review.

*Reporting Checklist:* The authors have completed the Narrative Review reporting checklist. Available at <https://tgh.amegroups.com/article/view/10.21037/tgh-23-43/rc>

*Peer Review File:* Available at <https://tgh.amegroups.com/article/view/10.21037/tgh-23-43/prf>

*Conflicts of Interest:* Both authors have completed the ICMJE uniform disclosure form (available at <https://tgh.amegroups.com/article/view/10.21037/tgh-23-43/coif>). The series “Controversies and Updates in Inflammatory Bowel Disease” was commissioned by the editorial office without any funding or sponsorship. K.S. serves as an unpaid editorial board member of *Translational Gastroenterology and Hepatology* from September 2022 to August 2024 and served as the unpaid Guest Editor of the series. The authors have no other conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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doi: 10.21037/tgh-23-43

**Cite this article as:** Venkateswaran N, Sultan K. Racial and ethnic disparities in clinical presentation, management, and outcomes of patients with inflammatory bowel disease: a narrative review. *Transl Gastroenterol Hepatol* 2024;9:28.