High Prevalence of Inflammatory Bowel Disease in United States Residents of Indian Ancestry

Reenu Malhotra,[*] Kevin Turner,[*] Amnon Sonnenberg,[‡,§] and Robert M. Genta[*,‖]

*Miraca Life Sciences Research Institute, Irving, Texas; [‡]Portland VA Medical Center, Portland, Oregon; [§]Oregon Health and Science University, Portland, Oregon; and [‖]University of Texas Southwestern Medical Center and Dallas VA Medical Center, Dallas, Texas

BACKGROUND & AIMS: **It is unclear whether the reported low prevalence of inflammatory bowel disease (IBD) in Southern and Eastern Asia is real (caused by genetic or environmental factors) or spurious (because of differences in awareness of the condition among physicians or different interpretations of endoscopic and histologic features). We aimed to estimate the prevalence of IBD in patients of different ethnicities who underwent endoscopy in the United States, with ileocolonic biopsies evaluated by a single group of gastrointestinal pathologists.**

METHODS: **We used a national pathology database to collect data on 1,027,977 subjects who underwent colonoscopy with ileocolonic biopsies from January 2008 through December 2013 throughout the United States; mucosal biopsy specimens were evaluated and reported by 1 group of 35 histopathologists. Patients were stratified into the following ancestries: Indian (persons with ancestry in the Indian subcontinent), East Asian (China, Korea, Japan, and Vietnam), Hispanic, Jewish, and Other. The prevalence of ulcerative colitis (UC), Crohn's disease (CD), and indeterminate colitis was determined for each ethnic group.**

RESULTS: **In the study population, 30,812 patients were diagnosed with IBD (20,308 with UC, 7706 with CD, and 2798 with indeterminate colitis). UC was more commonly associated with Indian and Jewish ethnicity and less commonly associated with East Asian and Hispanic ethnicity. Similar patterns also applied to CD and to all types of IBD analyzed jointly. Among Indian patients, 11.7% of those of Gujarati origins had IBD, compared with 7.9% of other Indians (odds ratio, 1.5; 95% confidence interval, 1.14–2.11).**

CONCLUSIONS: **Patients of Indian origin living in the United States have a greater risk for all types of IBD than other American populations. East Asians and Hispanics have a lower risk, possibly similar to that of the populations still living in their original countries. These findings may have relevance to the practice of gastroenterology in countries where there are sizable portions of the population with roots in the Indian subcontinent.**

Keywords: Ethnic Studies; Indian Immigrants; Lifestyle; Western; Latino.

See editorial on page 690.

The prevalence of inflammatory bowel disease (IBD), including both Crohn's disease (CD) and ulcerative colitis (UC), is known to be high in some geographic areas, such as Northern Europe,[1] and in some ethnic groups, particularly Ashkenazi Jews.[2–4] In contrast, it is believed to be low in Eastern and Southern Asia.[5] In India, UC was believed to be rare; however, not only is it now reported to be increasingly diagnosed in clinical practice,[6,7] but local journals that have not received much attention outside India have reported elevated rates of IBD as early as 1984, when a study of more than 20,000 persons in Northern India revealed a prevalence of 42.8 per 100,000,[8] a figure similar to the low end of the estimated prevalence in North America and Northern Europe.[9] A more recent study of more than 50,000 persons in Punjab revealed a similar incidence rate.[10] In a subsequent review, the same authors suggest that there is convincing evidence of a rising trend of IBD in Asian countries and "India, probably, heads the list."[11]

IBD is believed to be associated with both genetic and environmental risk factors. Although no definite

Abbreviations used in this paper: **CD, Crohn's disease; CI, confidence interval; IBD, inflammatory bowel disease; OR, odds ratio; UC, ulcerative colitis.**

1542-3565/$36.00
http://dx.doi.org/10.1016/j.cgh.2014.06.035

environmental risk factors have been identified that could trigger permissive genotypes to manifest into clinically apparent IBD, it is tempting to speculate that the reported increase of IBD, particularly UC, observed in Asian countries may be related to lifestyle changes that are often, albeit not entirely accurately, referred to as "westernization."

Human migrations have provided investigators of etiology and pathogenesis with natural experiments of great magnitude, particularly in the area of cancer. Differences in disease prevalence between first and subsequent generations of migrants have provided invaluable insights into the relative contribution of environmental and genetic factors to the causes of disease. Typical examples include nasopharyngeal carcinoma in Chinese migrants[12] and gastric cancer in Hawaiians of Japanese ancestry.[13,14]

The prevalence of certain conditions in different populations can often be accurately evaluated by simple and objective methods. The rate of an infection can be determined by the prevalence of antibodies against the organism of interest in serum samples; cancer is ultimately diagnosed by the pathologic examination of a tissue, which provides a yes or no answer. In conditions that are diagnosed through a complex interaction of medical practitioners from several specialties, differences in prevalence could be due to different susceptibility of a population to the condition. We shall refer to this scenario as "real difference." However, the differences could also result from the ways the diagnosis is reached, either because of dissimilar criteria or because physicians trained in other settings may adapt the same criteria of the cultural environments in which they operate. We shall refer to this as "spurious differences." A typical example for a spurious difference is the prevalence of Barrett's esophagus; a columnar-lined esophagus with no goblet cells is Barrett's esophagus in the United Kingdom[15] but not in the United States.[16]

The reported rarity of IBD in some Asian populations could be real or spurious. This study was designed to address this question. We hypothesized that the influence of local diagnostic differences could be minimized by evaluating the prevalence of UC, CD, and indeterminate colitis in patients of different ethnic backgrounds who were seen by physicians based in the United States, had endoscopic procedures performed in U.S. endoscopy centers, and their histopathologic diagnoses were rendered by the same group of pathologists.

Methods

Study Setting and Data Source

We used a large national pathology database of subjects who underwent colonoscopy with ileocolonic biopsies between January 2008 and December 2013 in endoscopy centers distributed throughout the United States and whose mucosal biopsy specimens were evaluated and reported by a single group of histopathologists. The group consists of 35 pathologists with subspecialty training in gastrointestinal pathology who practice in the same environment, strive to use uniform diagnostic criteria by using standardized diagnostic codes, and participate in daily consensus conferences where cases and diagnostic criteria are discussed. The Miraca Life Sciences internal review board determined that this study was entirely performed by using the collection of existing data, documents, and reports, and that the information was recorded in such a manner that subjects cannot be identified. Therefore, pursuant to 45 CFR 46, section 101 b(4), the study was exempt from 45 CFR 46 regulations, and no informed consent was necessary.

Study Design

Unique patients with ileocolonic biopsies were extracted from the database, and their demographic, clinical, and histopathologic data were recorded. If a patient had multiple colonoscopies, only data from the chronologically first procedure were included. Patients with a diagnosis of microscopic colitis (lymphocytic or collagenous) and colonic adenocarcinoma or other colonic malignancies were excluded.

Patients were stratified into the following ancestries: Indian (persons with ancestry in the Indian subcontinent), East Asian (China, Korea, Japan, and Vietnam), Hispanic, Jewish descent, and Other. The latter group included U.S. residents (whites and African Americans) not specifically identified with any of the above groups. We compared the prevalence of UC, CD, and indeterminate colitis in the different ethnic groups.

Diagnostic Criteria for Inflammatory Bowel Disease

Patients with a reliable clinical history of IBD and compatible histopathologic findings in their ileocolonic biopsies were assigned to the reported condition (UC or CD). Criteria for CD included chronic ileitis or colitis, rectal sparing, normal mucosa interspersed with inflamed areas (skip lesions), or non-necrotizing granulomas. Continuous colonic involvement and absence of granulomas were required for a diagnosis of UC. When the clinical history was not helpful and the histopathologic findings were clearly those of IBD but a more specific diagnosis could not be made, the category of indeterminate IBD was used. The designation of severe IBD was derived from the pathology report, in which biopsy specimens with a diagnosis of IBD were graded for intensity and distribution of inflammation by using a 3-point semiquantitative scale (mild, moderate, and severe). Cases were classified as severe if at least 1 biopsy site was so graded.

Data Analysis and Statistics

The distributions by sex, age, and ethnicity were expressed as percent of the total study population. The