# ADVANCES IN IBD

Current Developments in the Treatment of Inflammatory Bowel Disease

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## Inflammatory Bowel Disease in Asia

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**G&H** How do the incidence and prevalence of Crohn's disease and ulcerative colitis differ between Asia and other parts of the world?

**SN** The incidence and prevalence of inflammatory bowel disease (IBD) are lower in Asia than in the West. However, time trend studies from Asia (Japan, Korea, and Hong Kong) have shown that the incidence of IBD has increased over the past 2 decades. Differences have also been observed in the incidence of IBD across different geographic regions within Asia.

In Asia, ulcerative colitis (UC) is more common than Crohn's disease (CD), much as it was in the West in the mid–20th century. However, preliminary evidence suggests that over time CD may overtake UC in Asia. The ratio of UC to CD appears to be declining over time in some countries in Asia.

**G&H** How has the prevalence of IBD in Asia changed in recent decades? What factors might account for this change?

**SN** The prevalence of UC in Japan has risen from 7.85 cases per 100,000 individuals to 63.6 cases per 100,000 individuals across 3 different studies between 1984 and 2005. In Korea, there has also been a substantial rise in the prevalence of UC—from 7.6 cases per 100,000 individuals in 1997 to 30.9 cases per 100,000 individuals in 2005. In studies from Singapore, the prevalence of UC has risen from 6 cases per 100,000 individuals to 8.6 cases per 100,000 individuals, and the prevalence of CD has risen from 1.3 cases per 100,000 individuals to 7.2 cases per 100,000 individuals.

Factors that may account for the rising prevalence of IBD in Asia likely include changing environmental factors (including Westernization of lifestyle), industrialization of societies, changes in diet (which can be associated with changes in microbial exposure), improved sanitation, and, possibly, increasing use of antibiotics in childhood. In many countries in Asia, antibiotics can now be easily obtained without a prescription. The hypothesis that antibiotic use earlier in life may increase the risk of IBD is supported by several case-control studies conducted in the West.

**G&H** Does the presentation of IBD in Asian patients differ from the presentation seen in non-Asian patients? If so, how?

**SN** There is a male predominance of CD in Asia, but there is a trend toward equal sex distribution for UC. The age distribution of IBD in Asia is similar to that seen in the West. Positive family history and extraintestinal disease manifestations, especially primary sclerosing cholangitis, are much less common in Asia than in the West.

The disease location for CD and UC are relatively similar in Asians and non-Asians. Severe disease—including fistulizing and stricturing disease—can be as common, if not more common, in Asia as in the West.

Although IBD-associated dysplasia or colorectal cancer remains less common in Asia, the prevalence of colorectal cancer will likely increase with the rising inci-

dence of IBD and the increasing proportion of patients with longer durations of disease in Asian countries.

**G&H** How do the prevalence and/or presentation of IBD differ among Asian countries or among various subpopulations within Asia?

**SN** Within the same country in Asia, the prevalence rates of IBD can vary among different ethnic groups. For example, countries such as Singapore and Malaysia comprise 3 main populations: Malays, Chinese, and Indians. Of these 3 groups, Indians appear to have the highest prevalence of UC. In studies from Singapore and Malaysia, Indians have more extensive and severe IBD compared to other ethnic groups. Similarly, a study in Fiji (a non-Western country outside of Asia) found that Indians had a higher incidence of UC compared to indigenous Melanesians.

**G&H** Have there been any major studies looking at the incidence and/or presentation of IBD in Asia? If so, what were the key findings of those studies?

**SN** My colleagues and I recently completed a comparative, large-scale epidemiologic study of IBD across 9 countries in Asia and the Pacific: mainland China, Australia, Hong Kong, Macau, Malaysia, Singapore, Thailand, Sri Lanka, and Indonesia. We found that the incidence of IBD is lower in Asia than in the West but varies greatly across different parts of Asia. The incidence of IBD appears to be highest in more urbanized cities. Disease location at presentation is relatively similar to that observed in the West; however, complex disease behavior and perianal disease in CD are not uncommon (data published in abstract form).

**G&H** Aside from genetics, what other differences between Asians and non-Asians might explain the observed differences in IBD prevalence and/or presentation?

**SN** Although genetic susceptibility plays a major role in the occurrence of IBD in Asia, the rising incidence of IBD in Asia is most likely explained by environmental exposures that result from increasing urbanization; however, this increase could also be due to increased awareness of IBD by physicians and the public, as well as advancements in diagnostic methods for IBD (including greater access to medical services, such as colonoscopies).

The geographic distribution of IBD provides clues for researchers to investigate possible environmental determinants of IBD. For example, IBD occurs more commonly in urban regions than in rural regions. Individuals who are raised in urban areas of industrialized nations are exposed to considerably different environmental risk factors than those living outside of these regions.

**G&H** What therapies are most commonly used to treat IBD in Asia? Are these treatment regimens similar to those used in other parts of the world?

**SN** Most of the IBD therapies commonly used in the West—including steroids, antibiotics, thiopurines, and anti–tumor necrosis factor α (anti-TNFα) agents—have also been adopted in Asian countries. However, a survey of Asian gastroenterologists showed that medical practice varies among countries.

In a cross-sectional study comparing the management of CD patients in Melbourne, Australia to those in Hong Kong, significantly more patients in Melbourne had received an anti-TNFα agent compared to patients in Hong Kong (40% vs 11%). In general, anti-TNFα therapy is underused in Asia; this finding may relate to a number of factors, including clinicians' lack of experience with this therapy, high cost, lack of insurance reimbursement, and concern about opportunistic infections. In many countries in Asia, the use of biologic agents is self-financed, making the high cost of these drugs an obstacle to their use. In Japan, the use of leukocytapheresis and tacrolimus is popular among patients with UC.

Finally, there is also a diverse medical practice in South Asia and Southeast Asia that includes alternative and complementary medicine, ayurvedic medicine, and homeopathy, and some patients with IBD may prefer to present to traditional and alternative health practitioners.

**G&H** What can the differences between IBD in Asian versus non-Asian patients tell researchers about the pathophysiology of the disease?

**SN** Genetic mutations for IBD differ in Asian versus white patients. Asian patients with IBD have different susceptibility genes compared to their white counterparts, and they also have different mutations in genes that have been previously associated with IBD in white patients. Novel genes that have been identified in Asian IBD patients provide an opportunity to explore new disease-associated biologic pathways as targets for therapies in this population with a rising disease incidence. Temporal trends in disease incidence and differences in IBD incidence rates in different geographic areas or among different ethnic groups in Asia may also provide insights into possible etiologic factors.

**G&H** What are the challenges in diagnosis and treatment of IBD in Asia?

**SN** Currently, a major clinical challenge relates to the accurate diagnosis of IBD in countries with a high background prevalence of infections such as infectious enteritis and intestinal tuberculosis. For example, the diagnosis of CD in geographic areas where tuberculosis is common poses a diagnostic challenge. Infections may mimic IBD, and they

can complicate the course of existing IBD. Also, limited availability of diagnostic tests, in particular radiologic imaging, may delay diagnosis.

Screening for latent infections—specifically for tuberculosis and hepatitis B virus infection—deserves special consideration in Asia, given the high prevalence of these diseases in Asian populations.

In all likelihood, the incidence of IBD will continue to surge in Asia in the next decade. Effective research and development of IBD therapies will require collaboration among multiple centers in Asia. Although yet to be incorporated into practice in Asia, optimal patient management will need to move toward a multidisciplinary approach, including the active involvement of specialist dietitians, radiologists, and surgeons; in some tertiary IBD centers, these teams may also include IBD nurse specialists and psychologists. New systems and opportunities for education in IBD should be incorporated into the training of specialists.

### **G&H** What further research is needed to better understand IBD in Asia?

**SN** Larger epidemiologic studies conducted over time are necessary to describe the true incidence of IBD and to further characterize the clinical features and risk factors of IBD in different geographic areas in Asia. Studies in populations that have an increasing disease incidence and in pediatric populations offer the best opportunity to help clinicians and researchers elucidate the role of environmental factors in IBD and to identify new etiologic factors responsible for this IBD epidemic in Asia. To advance our understanding of the key determinants of IBD in the developed and developing world, future population-based studies should focus on reporting the incidence and/or prevalence of IBD stratified by gene-environment-phenotype interactions.

## Suggested Reading

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