Increasing Incidence of Crohn’s disease In India: Is it related to Improved sanitation?

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In the early years after its first recognition, ulcerative colitis (UC) was diagnosed in only 317 patients from 7 hospitals in London over a 20-year period. The first report of ‘regional ileitis’ or Crohn’s disease (CD) appeared in 1932. In North America now, the incidence rates of UC and CD are 11 and 7 per 100,000 population, respectively. In India, UC was first reported in 1964 and CD was considered almost nonexistent till 1986. During the last 10 years, CD is being reported more frequently from different parts of India, especially southern India. Is this recent increase in the incidence of CD in India only apparent or real?

Till recently, in India CD was suspected on barium studies or at surgery. In recent years, the increasing availability of imaging studies, colonoscopy-ileoscopy, small bowel enteroscopy, serological markers such as perinuclear antineutrophil cytoplasmic antibody (pANCA) and anti-Saccharomyces cerevisiae antibody (ASCA) for UC and CD, respectively, and molecular diagnostic techniques (polymerase chain reaction) to differentiate CD from tuberculosis in tissue, have added significantly to the ability of clinicians to diagnose CD. This has created an impression that the rarity of CD in the past was possibly due to limited diagnostic facilities and/or lack of awareness amongst gastroenterologists. However, there are reasons to believe that there is an actual increase in the occurrence of CD.

In previous studies of abdominal tuberculosis from India, perianal disease, small or large intestinal fistulae, extra-intestinal manifestations (arthritis, pyoderma gangrenosum), recurrence after intestinal resection, failure of response to antitubercular therapy, were extremely uncommon, suggesting that CD was indeed rare then, and may have become more frequent now. Das and Shukla did not diagnose CD in any patient while reporting 182 patients of abdominal tuberculosis. Prakash reported 18 patients with CD over a period of 18 years (<1 patient per year). Recent reports describe 3-10 patients per year, indicating an increase in the incidence of CD during the last decade.

If there is indeed a true increase in the incidence of CD in India, what are the factors responsible? Inflammatory bowel disease (IBD) results from interaction of genetic and environmental factors, leading to an abnormal immune response of the gut mucosa to intraluminal antigens. Genetic factors appear to play a more dominant role in the causation of CD than of UC. However, hereditary factors do not change in a few decades and hence cannot account for the increasing incidence of CD.

Environmental factors – smoking, helminths, childhood infections, dietary habits, and psychosocial factors – have all been implicated in the etiopathogenesis of IBD. Persons belonging to populations with a low incidence of IBD, on migration to developed countries, show a higher incidence of IBD, suggesting that environmental factors are important in IBD.

The etiology of IBD is centered on the interaction of intestinal microflora with the host immune system. Childhood infections induce immune tolerance to various extrinsic antigens by stimulating regulatory cells of the immune system, which have an anti-inflammatory activity. In epidemiological studies, reduction in the frequency of childhood infections has correlated with increase in autoimmune and allergic disorders.

Children and adults from developing countries are often infested with helminthic organisms like ascarisiasis and hookworms. Helminths promote T\textsubscript{H}2 responses and blunt T\textsubscript{H}1 responses. Exposure to Schistosoma mansoni protects rats from development of IBD. With improved sanitation, helminths have disappeared in developed countries. This disappearance of helminths coincided in time with the emergence of IBD.

In Western countries, CD followed UC after a gap of approximately 40 years. Since then, the incidence of CD has gradually increased and is now almost similar to that of UC. In India, about 60 years later, similar trends in emergence and evolution of UC and CD are being observed. It is interesting to note that both in developed and developing countries, IBD was first observed as sanitation-hygiene started improving, with an approximate gap of 60 years between these countries.

Appearance of CD much earlier in developed than in developing countries, in urban than rural populations, in higher than lower socioeconomic groups, and in Whites than in native populations, indicates that improved sanitation-hygiene is important in the etiopathogenesis of IBD. The prevalence of feco-orally transmitted infections – hepatitis A virus (HAV), hepatitis E virus (HEV),...
\textit{Helicobacter pylori} – are measures of sanitation-hygiene in a country. The prevalence of serum antibodies to HAV is approximately 50\% at the age of 5 and 50 years in developing and developed countries, respectively.\textsuperscript{27,28} Similar data have been reported on the prevalence of antibodies to \textit{H. pylori}.\textsuperscript{29,30} These observations indicate a gap of about 50 years in improvement of sanitation-hygiene in developed and developing countries. A reduction in the frequency of HAV and HEV antibodies in the younger population from a city in India indicates recent improvement of sanitation-hygiene here.\textsuperscript{31} The earliest report of a high prevalence of CD from Kerala state,\textsuperscript{8} with better sanitation-hygiene, also emphasizes the importance of this environmental factor.

In conclusion, improvements in sanitation and hygiene may significantly increase the risk of CD, and may be responsible for the recent increase in the reports of this disease from India. Persistent improvement of sanitation is surely desirable but may have some adverse effects too.

\section*{References}