

## Inflammatory bowel disease: the Indian augury

Vineet Ahuja • Rakesh K Tandon

Received: 7 October 2012 / Accepted: 7 October 2012 / Published online: 13 November 2012  
© Indian Society of Gastroenterology 2012

A little boy accompanied by his father was taken to a museum of diseases. His father gloated upon mankind's successes in alleviating diseases. The first window showed smallpox and its demise, the second window showed plague and its extermination, and the third window showed malaria and its systematic decimation. The little boy's faith in dominance of medical science soared and he started getting convinced in the infallibility of man as he mounted the steps to the second floor of the museum. The second floor was damp and squidgy and so became the little boy's enthusiasm when he saw conquests being replaced by new scourges, a whole row of emerging diseases: diabetes, multiple sclerosis, and celiac disease. Spontaneously, he remarked, "The disease wagon appears to have a mind of its own and keeps on replacing conquered diseases with a new or complex one. As if the disease wagon is leading medical scientists on an ever ongoing merry-go-round. Is the field of medicine moving in circles and trying to catch its own tail?" His father, a wise seasoned soul, assuaged his crestfallen son and explained "Predicting and controlling diseases ultimately requires an intuitive appreciation of biocomplexity—the elaborate interrelationships between biological systems (including human social systems) and their physical environments and until we do it the circle will move on." This is precisely the most significant message the emergence of inflammatory bowel disease (IBD) in India augurs for the medical community. The initiative of Indian

Society of Gastroenterology (ISG) Task Force and the ensuing survey is a laudatory effort which has propelled awareness of IBD as a disease from background to the fore.

Emergence of IBD in India has been looked at with a glint in the eye by epidemiologists as well as pathogenesis-defining scientists. It has been described as a novel population which would unravel the influence of changing environment on diverse genetic backgrounds. The key question has been the emergence of an autoimmune disease in geographical areas which earlier bore the scourge of infectious diseases. It is fascinating to note that as socioeconomic conditions improve, or as a geographic region transits from the notation of a "developing" nation to a "developed" nation, the disease pattern also reinvents itself. Where industrial revolution in society saw hordes of infectious diseases, the rearrangement of socioeconomic norms in the post-industrial revolution phase has seen the advent of autoimmune diseases. It was brought to attention most elegantly by Strachan, who observed an inverse correlation between hay fever and the number of older siblings when following more than 17,000 British children born in 1958 [1]. This laid down the framework for the "hygiene hypothesis" which suggested that the decreasing incidence of infections in Western countries, and more recently in developing countries, is at the origin of the increasing incidence of both autoimmune and allergic diseases. Bach in 2002 extended the hypothesis from the field of allergy, where it was formulated, to that of autoimmune diseases such as type 1 diabetes or multiple sclerosis [2]. The Indian populace, hitherto preoccupied with infectious diseases, was now demonstrating a new fangled alignment towards autoimmune diseases, thus fulfilling the prophecy of the hygiene hypothesis. A corollary of the fact may be that IBD should be seen more often in higher socioeconomic groups or largely urban areas. However, that brings us to what in science of mathematics may be termed as "hypothesis, axioms, and theorems." While hypothesis remains to mean "an

---

V. Ahuja  
Department of Gastroenterology,  
All India Institute of Medical Sciences,  
New Delhi 110 029, India

R. K. Tandon (✉)  
Department of Gastroenterology, Pushpawati Singhanian Research  
Institute for Liver, Renal and Digestive Diseases,  
Press Enclave Marg, Sheikh Sarai II,  
New Delhi 110 017, India  
e-mail: rakesh\_tandon@hotmail.com

undemonstrated conjecture,” an axiom has been an accepted hypothesis for a long time, and a theorem is a statement that has been proven to be true. The ISG Task Force survey could have provided vital clues towards it, had it looked at socioeconomic status as well as urban rural divide as a first step in pushing the hypothesis to a theorem. A recent case–control study from Vellore including 200 cases of Crohn’s disease (CD) found that the disease showed positive association with urban residence (at birth and current), availability of protected drinking water (childhood and current), availability of piped water in the house (childhood and current), and strict vegetarian dietary habit [3].

A noteworthy observation often alluded to is the higher burden of Crohn’s disease in southern India when compared with northern India. The present data set adds credence to the seemingly anecdotal observation. Of 409 cases of CD, more than 50 % were reported from southern India. However, an equivalent number of ulcerative colitis cases were reported from northern as well as southern India [4]. This is an exciting geo-epidemiological observation as it rebels against two traditional concepts of IBD epidemiology: the North–South divide [5] and interval emergence of ulcerative colitis (UC) and Crohn’s disease. Studies from USA and Europe have identified a significant North–South gradient. This concept suggests that southern latitudes have a lower incidence of IBD as compared with northern latitudes. In Europe, the European Collaborative Study on Inflammatory Bowel Disease population-based study reported a higher incidence of UC ( $11.8/10^5$  compared with  $8.7/10^5$ ) and CD ( $7.0/10^5$  and  $3.9/10^5$ , respectively) in northern compared with southern Europe [6]. Khalili et al. have recently confirmed the observed North–South gradient for the USA, and the study also postulated reasons besides variations in genetic susceptibility, smoking, dietary factors, and difference in economic wealth for this phenomenon [7]. Vitamin D has an anti-inflammatory as well as immune-modulating role. Vitamin D<sub>3</sub> in human skin is produced by sunlight and a logical import is that differential exposure to sunlight is dependent on latitude and hence the North–South gradient. Southern Europe and southern US states have greater exposure to sunshine and this environmental factor could influence the incidence patterns for IBD [8]. However, the present survey shows IBD cases being seen in near about equal magnitude in northern India as well as southern India. Although southern India is near the equatorial region, northern India is also predominantly tropical reflecting no major variations in exposure to sunshine. Hence, the present survey not only brings forth the absence of a North–South divide in India, but also puts a question mark over the pivotal role of sunshine and vitamin D<sub>3</sub> as an environmental factor modulating IBD incidence rates. A comparative study of environmental factors in northern and southern India appears a coherent step for indicting or negating established notions in western populations.

The second notion is that an increase in the incidence and prevalence of IBD should mirror the western experience that occurred 50 years ago. Epidemiologic studies from western countries have also shown that the increase in the incidence of UC preceded the increase in that of CD by about 15 to 20 years [9]. The rise in UC appeared to be more marked compared to the rise in CD. Northern India seems to be toeing the set pattern while the same cannot be deduced for southern India where CD is as commonly seen in hospitals as UC. Are we witnessing (a) a reverse incidence of Crohn’s disease or (b) a window period in IBD epidemiology where the incidence of CD bypasses the incidence of UC? Initially reported in France [10] and Belgium [11] in the early 1990s, a higher incidence of CD was also observed in Stockholm [12], Manitoba [13], Rochester [14], Cardiff [15], and Tubingen [16]. The inverse ratio could be explained by the stability in incidence of UC, whereas CD had increased in most developed countries. The present survey is a pointer that cases included in this from southern India are a reflection that case ascertainment may have started after the crossing point between the incidence of CD and UC. This is analogous to the situation in France where the trend was more obvious when examining the evolution of the CD/UC ratio from 1988 to 1999 in the Seine-Maritime region: UC, which was more frequent than CD, became similar or less frequent than CD [17]. An important finding of this study was that between 1988 and 1999, the incidence rate of CD in northern France increased by 23 %, while the incidence rate of UC decreased by 17 %.

The survey also brings to the forefront the economics of treating IBD. Amongst 1,159 cases, only five of them were treated with biologics. Is it that we are dealing with a less aggressive IBD, or do economic compulsions lead to forced steroid marinating of the patients? An earlier study from India has not buttressed the idea that phenotype of CD is much different from that of west. So, the more probable and perhaps real explanation is the inability of patients to afford biologics. This has been recently highlighted in another review [18]. The reality in countries with fewer resources is that less expensive treatments such as corticosteroids will have an ongoing role in a segment of the population. Hence, in India while dealing with IBD as in other diseases, the choice of therapies may be limited and the clinicians and researchers should be joining hands to develop low cost alternatives.

Another important implication for the future is the disease burden. A little extrapolation suggests a monstrous burden of IBD in the coming decade. The non-redeeming feature is that we are not dealing with one point infectious disease. A patient with IBD remains with the disease for the rest of his life, and unfortunately, it affects young adults in the prime of their lives creating havoc with their quality of life. Therefore, we need a superspecialist team of IBDologists—very much like

hepatologists or endoscopists—a team of gastroenterologists, GI surgeons, and nutritionists who make management of IBD and research in IBD as the focus of their career. The situation in the very near future appears to demand that initiative.

To quote Bach's observation [2] in 2002: "Several factors, such as socioeconomic indices, may explain the difference in the prevalence of immunological disorders according to time and geographical distribution." In fact, there is a positive correlation between gross national product (GDP) and incidence of asthma, type I diabetes, and multiple sclerosis in Europe and similar concordance in IBD incidence and GDP of a country is being reported. So the only silver lining for increased IBD burden appears that at least now India is in league with countries having high GDPs. Should we thank the economic liberalization policies of 1990's and their proponents for the burgeoning disease burden of IBD?

## References

1. Strachan DP. Hay fever, hygiene, and household size. *BMJ*. 1989;299:1259–60.
2. Bach J-F. The effect of infections on susceptibility to autoimmune and allergic diseases. *N Engl J Med*. 2002;347:911–20.
3. Pugazhendhi S, Sahu MK, Subramanian V, Pulimood A, Ramakrishna BS. Environmental factors associated with Crohn's disease in India. *Indian J Gastroenterol*. 2011;30:264–9.
4. Makharia GK, Ramakrishna BS, Abraham P, et al. Survey of inflammatory bowel diseases in India. *Indian J Gastroenterol*. 2012;31. doi:10.1007/s12664-012-0258-1.
5. Schultz M, Butt AG. Is the north to south gradient in inflammatory bowel disease a global phenomenon? *Expert Rev Gastroenterol Hepatol*. 2012;6:445–7.
6. Shivananda S, Lennard-Jones J, Logan R, et al. Incidence of inflammatory bowel disease across Europe: is there a difference between north and south? Results of the European Collaborative Study on Inflammatory Bowel Disease (EC-IBD). *Gut*. 1996;39:690–7.
7. Khalili H, Huang ES, Ananthakrishnan AN, et al. Geographical variation and incidence of inflammatory bowel disease among US women. *Gut*. 2012. doi:10.1136/gutjnl-2011-301574. Epub ahead of print.
8. Nerich V, Jantchou P, Boutron-Ruault MC, et al. Low exposure to sunlight is a risk factor for Crohn's disease. *Aliment Pharmacol Ther*. 2011;33:940–5.
9. Ahuja V, Tandon RK. Inflammatory bowel disease in the Asia-Pacific area; a comparison with developed countries and regional differences. *J Dig Dis*. 2010;11:134–47.
10. Chouraki V, Savoye G, Dauchet L, et al. The changing pattern of Crohn's disease incidence in northern France: a continuing increase in the 10- to 19-year-old age bracket (1988–2007). *Aliment Pharmacol Ther*. 2011;33:1133–42.
11. Latour P, Louis E, Belaiche J. Incidence of inflammatory bowel disease in the area of Liege: a 3 years prospective study (1993–1996). *Acta Gastroenterol Belg*. 1998;61:410–3.
12. Hellers G. Crohn's disease in Stockholm county 1955–74. A study of epidemiology, result of surgical treatments and long term prognosis. *Scand J Gastroenterol*. 1979;7:401–5.
13. Bernstein CN, Blanchard JF, Rawsthorne P, et al. Epidemiology of Crohn's disease and UC in a central Canadian province: a population-based study. *Am J Epidemiol*. 1999;149:916–24.
14. Stowe SP, Redmond SR, Stormont JM, et al. An epidemiologic study of inflammatory bowel disease in Rochester, New York. Hospital incidence. *Gastroenterology*. 1990;98:104–10.
15. Thomas GA, Millar-Jones D, Rhodes J, et al. Incidence of Crohn's disease in Cardiff over 60 years: 1986–1990 an update. *Eur J Gastroenterol Hepatol*. 1995;7:401–5.
16. Daiss W, Scheurlen M, Malchow H. Epidemiology of inflammatory bowel disease in the county of Tubingen (West Germany). *Scand J Gastroenterol*. 1989;24 suppl 170:39.
17. Molinié F, Gower-Rousseau C, Yzet T, et al. Opposite evolution in incidence of Crohn's disease and ulcerative colitis in Northern France (1988–1999). *Gut*. 2004;53:843–8.
18. Rogler G, Bernstein CN, Sood A, et al. Role of biological therapy for inflammatory bowel disease in developing countries. *Gut*. 2012;61:706–12.