Epidemiology of inflammatory bowel disease (IBD): Why are there differences between North America and Latin America?

Rómulo Darío Vargas, MD.[1]

[1] Editor of the *Revista Colombiana de Gastroenterología* (Colombian Review of Gastroenterology). Bogotá, Colombia.

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Some digestive tract illnesses have similar epidemiological behaviors in both the developed world and the developing world despite the notorious environmental and socio-economic differences. For example, the figures for functional gastrointestinal disorders are sufficiently compatible in both zones of the world. On the other hand various biologically plausible explanations are put forward to explain divergent epidemiologies. For example, the epidemiological differences among infectious diseases can easily be explained by environmental factors. All the same, when it comes IBD, the epidemiological differences between the developed countries of the "north" and the underdeveloped countries of the "south" have always been striking and even curious. In truth, or at least for some people, these differences are stronger between East and West than between North and South. Genetic epidemiology has provided information which permits us to elucidate some of the reasons for these differences. For example, it deals with genetically complex illnesses like Crohn's disease (CD) and colon cancer. Recently emphasis has been given to the genetic complexity of a group of diseases which are outside of the traditional reductionist models of "genetics vs. environment". In these entities there are multiple genes which have limiting effects which play roles in the heterogeneous or variable clinical presentations, in frequency, and are modulated through interaction with and by environmental factors. This is the case of the epidemiology of IBD (1).

Recent epidemiological studies have reevaluated assertions that had been held for a long time: the north-south gradient in Europe, the bimodal presentation of IBD, the preponderance of cases of late-onset ulcerative colitis among men, and the role of oral contraceptives, among others. However, other risk factors have been further substantiated. These include race or ethnicity, socio-economic status, cigarettes, appendectomies, antibiotics, and infections (5).

The prevalence of IBD, taking UC and CD together, varies between 320/100,000 and 511/100,000 inhabitants in the United States and Canada. In absolute numbers it varies between 1.1 million and 1.7 million people with IBD in the two countries (2).

In this issue of the RCG (*Revista Colombiana de Gastroenterología* -Colombian Review of Gastroenterology), Carmon et al. report on the number of cases of IBD diagnosed in an insured population in the city of Cartagena. 26 patients with IBD were identified in a total population of 90,000 people. 20 of these patients met the criteria for UC while 6 were diagnosed with CD (3). As the authors suggest, this is valuable information which allows us to approximate the real volume of IBD in our environment, even though this study does not provide us with all the information necessary to calculate the prevalence of IBD. Although we still lack data, this information supports the opinions gained from

practical clinical experience of gastroenterologists that CD is rare here, and UC occurs only infrequently. Very few reports exist on the prevalence of IBD in Latin America. Work has been done in Brazil, Puerto Rico, Panama and Argentina which reports an incidence between 1.2/100,000 and 4/100,000 inhabitants and prevalences of between 20/100,000 and 100/100,000 inhabitants. However, these reports also perceive increasing incidence and prevalence (12-14).

A look at the figures from studies in the USA which explicitly show the ethnic variable clearly demonstrates support for the low numbers in our environment: Hispanics are less affected by IBD that is the general population. Some people question the veracity of these differences or attribute them to difficulties in accessing health care services (4). Kiel's concept of the role of "westernization" of the environment which has not been accompanied by adaptation of the innate immune system of the digestive tract appears to be a plausible explanation of the big differences in prevalences of IBD between Hispanics and Caucasians.

What factors protect the Hispanic population? In 2001, Hugot and Omura separately published their discoveries that the NOD2 gene within the IBD1 locus on chromosome 16 is a marker for susceptibility to CD. Afterwards the gene's pathogenic role was discovered. More recently at least four new genes have been identified as potential generators of susceptibility to IBD: DLG5, SCL, MDR1 and TLR (4). What, then, is the prevalence of NOD2 in the Hispanic population? Putting aside for the moment another complicated discussion about what exactly constitutes a "Hispanic person", one recent study showed a lower incidence of NOD2 (4,4) among Hispanics than in the white population (9,1). In the study P=0.31 (6).

The figures for the incidence of IBD among children in the USA also show lower values for the descendants of Hispanic people than for the descendants of Caucasians despite the similar environments (7, 8).

In other words it is very likely that genetic susceptibility factors partially explain the differences, and that the multiple gene mechanism discussed above is the basis for the lower appearance of IBD in our environment. This of course assumes that the genetic profile of Hispanics here is similar to the genetic profile of Hispanic immigrants in the USA.

Nevertheless, genetics does not explain the great epidemiological changes which have occurred in IBD prevalence in only a few decades. The incidence of IBD in children has doubled in only 11 years, going from 2.2 to 4.3 (7). This definitely brings environmental factors back into the picture.

The environmental factors which might help explain the epidemiological differences between North America and Latin America include socio-economic status which is implicated in exposure to infections, the use of antibiotics, and issues of hygiene. There is a positive correlation between social class and risk of IBD. Higher social classes have a higher risk with incidences 20% higher than those with lower incomes. This brings us to the issue of hygiene.

It has been adduced that the higher incidence of certain immunological disorders like asthma and diabetes in the western world could be partly attributable to lack of exposure to pathogens predisposes people to the development of tolerance. If we understand IBD as a disorder of the immune barrier of the digestive system in which there are antigen presentation errors, it is not difficult to understand some author's attraction to the hypothesis that an environment can be "too hygienic" (9). The precarious socio-economic conditions of the majority of the Latin American population is well known, and there clearly exists a correlation between hygiene and socio-economic status. Nevertheless it is noteworthy that immigrants from southern Asia to England acquire incidences of IBD even higher than those of the Caucasian population. Here we can adduce that a "hyper-vigilant intestine" is poorly adapted to a hygienic environment (10).

The etiopathogenesis of IBD is beginning to unfold. Genetic epidemiology has thrown new light on the changing phenotype of the disorder and upon the differences in its rates of occurrence in different populations. We hope that in the future knowledge about the genetic characteristics of the population of this side of America will allow us more insight into increasing incidences of IBD. Will it behave the same way here, as it does in other latitudes? And, how will it respond to new treatments? Will they achieve the same notable results with patients here that they achieve among other ethnicities?

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