Nonalcoholic fatty liver disease in the Indian subcontinent: a medical consequence of globalization?

Nonalcoholic fatty liver disease (NAFLD) is a group of disorders characterized by predominantly macrovesicular steatosis of the liver. While considered to be a medical curiosity for many years, it is now well established to be an important cause of chronic liver disease in the Western world. The recent report in this Journal of a series of patients with NAFLD by Agarwal et al. extends data from the Far East and confirms that this is indeed a condition with a worldwide prevalence. In fact, given the much larger population in India relative to many Western countries, it is likely that the absolute number of Indian patients with NAFLD equals or exceeds that in such countries even if the prevalence is somewhat lower in India than the West.

As with any other emerging disease, the condition must be tackled at many levels and from many directions to limit and eventually eradicate the morbidity and mortality associated with it. At the grassroots level, the practicing clinician must be able to identify both those at risk as well as afflicted individuals and institute appropriate therapy. The extensive body of literature in the West provides some help to the physician in the Asian subcontinent in this regard. Importantly, the data by Agarwal et al. generally corroborate data from the West although there are some differences that are worthy of comment.

A priori, it appears unlikely that the gender distribution of NAFLD would be different in the Asian subcontinent that in the rest of the world. The high male prevalence reported by Agarwal et al. may have several potential explanations. First, they may reflect patterns of health-care utilization in the local population; alternatively, they may reflect referral bias to a tertiary care institution. Finally, the possibility of ascertainment bias in any hospital-based descriptive study can never be fully excluded. If future population-based studies prove that Indian males are indeed more susceptible to NAFLD, this will open a host of additional questions that will then have to be answered.

It is now appreciated that NAFLD occurs at all ages and with equal frequency in men and women in the West. While obesity and diabetes remain the most important risk factors, the presence of these conditions is not essential for the development of NAFLD. While many patients in Dr Agarwal’s series were not diabetic, it is highly probable that if a study were to be conducted in an Asian diabetic population, a high prevalence of NAFLD would be noted. This may be particularly important in India, which is facing a growing incidence of diabetes mellitus. The most common symptoms include nonspecific fatigue and right upper quadrant discomfort. In contrast to alcoholic liver disease, ALT level is usually, but not invariably, higher than AST level. In these aspects, the clinical profile of NAFLD in Delhi appears to be similar to that of the West.

In the study by Agarwal et al., none of the patients had evidence of portal hypertension or liver failure. Also, only three subjects had bridging fibrosis and none of them had cirrhosis. A potentially dangerous conclusion from this could be that this is a condition that does not progress to end-stage liver disease and, therefore, is not a problem. Indeed, it has taken over twenty years of research to correct this misconception in the West. NAFLD is characterized by a series of stages with increasing degrees of fibrosis. Since only a fraction of patients progress from one stage to the next, it is expected that the prevalence of specific stages in any cross-sectional study will be ordered inversely to the stage of the disease. It is almost certain that, if a large enough cohort is followed long enough, a proportion will progress to cirrhosis and liver failure. The precise value of the proportion remains to be determined.

Histologically, an important aspect to mention is that the pattern of bridging fibrosis in patients with NAFLD is often different from that seen in other chronic liver diseases, e.g., hepatitis C. Whereas hepatitis C is characterized by fibrosis that extends out from portal tracts and bridges portal tracts to portal tracts, NAFLD is associated with central-to-central and central-to-portal bridges of fibrotic tissue. These may not be obvious to the inexperienced pathologist particularly if a collagen-specific stain, e.g., Masson’s trichrome, is not used.

As with any other disease that is highly prevalent, an important question is: how does the presence of NAFLD affect the morbidity and mortality associated with other liver diseases? This is particularly germane for other common liver diseases such as hepatitis B and C. Also, the possibility of an interaction between progression of NAFLD and moderate alcohol consumption needs to be addressed. While early papers had suggested that alcoholic and nonalcoholic fatty liver disease were mutually exclusive, this concept has no basis in either theory or clinical or basic scientific literature. Rather, they relate to the practical difficulty of assigning cause and effect to moderate alcohol consumption versus risk factors for NAFLD when both are present in a patient with histologic evidence of fatty liver disease. These questions are now ripe to be answered.
A growing body of literature indicates a strong relationship between the presence of insulin resistance and NAFLD.\(^6\) There is also growing awareness that the prevalence of insulin resistance and its associated conditions are not only high in the West but are also increasing in other parts of the world. An example of this includes the growing prevalence of diabetes in Asia.\(^6\) From a biological point of view, this may be related to genetic and metabolic factors, diet, exercise behavior and other exogenous factors. These are, in turn, likely to be linked to globalization and its impact on the social, economic and political milieu of different parts of the world. Specifically, they may be linked to the changes in diet pattern in the new middle class of the subcontinent where traditional high-fiber diets have been replaced by increasing consumption of refined sugars and meats with a high saturated fat content. These factors are further coupled with changes in lifestyle, especially in the young, where the Internet and computer-based entertainment have replaced traditional physical activities associated with childhood and youth. Finally, there may be specific psychological, social and economic factors that determine who adapts a lifestyle more prone to insulin resistance and also who is most, as well as least, likely to alter their behavior pattern to correct insulin resistance. If NAFLD is to be stopped in the bud, these issues must be addressed not only at a scientific level but also in a multi-disciplinary manner involving local government.

In summary, the paper by Agarwal et al has now set the stage for an explosion of studies related to NAFLD specifically focused on issues germane to this condition in India and the Asian subcontinent. A large number of questions are now faced by the medical and public health community in India and it is hoped that this editorial will lead to greater debate and research on this condition, which may finally lead to its control.

References

Correspondence to: Dr Sanyal, Chairman, Division of Gastroenterology, MCV Box 980711, Richmond, VA 23298-0711, USA. Fax: +1 (804) 828 2037. E-mail: aj.sanyal@hs.c.vcu.edu

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