NASH IN FOCUS

Current Developments in the Management of Nonalcoholic Steatohepatitis

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Recent Research and Insights on the Disease Burden of Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis

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G&H How has the prevalence of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis changed?

ZY The prevalence of both nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH), which is part of the spectrum of NAFLD, has increased in the past decade. In early 2000, the prevalence of NAFLD in the world was approximately 25%. This rate has consistently increased, and both NAFLD and NASH have used the same trajectory in terms of increases. According to the most recent meta-analysis and systematic review, which was recently published online ahead of print in the journal *Hepatology*, the global prevalence of NAFLD from 2016 to 2019 was 38% and the prevalence of NASH in the general population was approximately 5.5%.

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The increases in prevalence are being driven by rising rates of obesity and type 2 diabetes. According to the Global Burden of Disease (GBD) data set, most of the regions of the world are seeing increases in the prevalence of NAFLD and NASH as well as increases in the associated clinical burden, which includes related liver disease complications such as cirrhosis, liver cancer, and mortality. Thus, there is an expected increase in the overall burden of both NAFLD and NASH. The global increase in the burden of NAFLD is especially prominent in the Middle East and Latin America.

In addition to the meta-analysis and GBD data, several modeling studies have confirmed the rapid increase in disease burden over the past 2 decades. I expect that trajectory to continue to increase.

G&H What is the current burden of NAFLD in children and adolescents?

ZY That burden is increasing as well. A data set found that approximately 10% of children have NAFLD. However, those data are 10 to 15 years old, and I suspect that the figure is much higher now, perhaps around 15% to 20%. In the United States, the increase in the prevalence of NAFLD among children appears to be even higher in those of Hispanic descent. As for other factors, the prevalence of NAFLD is higher in boys than in girls, and increases with age. This is an important issue because the

burden of disease in children is feeding the future burden of disease in adults; those who are obese and have NAFLD or diabetes as children are much more likely to have NAFLD as adults.

G&H Could you share some recent insights regarding the risk factors and epidemiology of NAFLD and NASH?

ZY Known risk factors for NAFLD such as type 2 diabetes and obesity are driven by lifestyle trends (eg, the type of nutrition being consumed, how that nutritional composition has changed over the years, and how people have changed their activity levels to become more sedentary). In terms of nutrition, it is important to look not just at calorie intake, but also dietary composition, including macronutrients and micronutrients. A good deal of research is currently underway examining which micronutrients promote obesity and type 2 diabetes. Other environmental factors can also promote obesity, leading to more NAFLD. For example, recent data suggest that pollution can impact obesity and diabetes and then ultimately promote NAFLD. In addition to environmental and lifestyle factors, there is likely a genetic component, as certain individuals may carry genetic predisposing factors that place them at higher risk of developing progressive liver disease. These are some of the main risk factors for NAFLD.

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Epidemiologically, it is important to recognize that NAFLD/NASH is now the second leading indication for liver transplant in the United States. In fact, NAFLD is the most common indication for women as well as patients older than 55 years. In addition, NASH is rapidly becoming a predominant indication for liver transplant among patients listed for liver transplant who have liver cancer.

G&H What are the current disability-adjusted life years associated with NAFLD and NASH?

ZY Those figures are not very well known, although there are some estimates. When looking at disability-adjusted life years (DALYs), it is most important to recognize that DALYs related to NAFLD are increasing globally. Certain parts of the world (eg, China) have very high DALYs related to NAFLD because they have a large population and the prevalence of NAFLD is high. However, this increase in DALYs is occurring everywhere. Areas particularly impacted by the burden of disease for NAFLD and NASH are the Middle East and North Africa, as well as South America. Those areas will continue to be highly impacted in the future.

G&H How significant is the economic burden of NAFLD and NASH?

ZY The economic burden of NAFLD and NASH is tremendous. Patients with NAFLD utilize significant health care resources. In a modeling study, lifetime costs of patients with NASH in the United States in 2017 were estimated to be approximately $223 billion. In addition to the direct economic burden of NAFLD and NASH, there is also a substantial indirect economic burden related to loss of work productivity, most likely related to fatigue, which is quite prevalent in NAFLD. This loss of work productivity places a significant economic burden on society. Finally, there is also stigma associated with NAFLD and NASH that can impact these patients in terms of social interaction. Thus, the true economic burden is likely substantially more than commonly thought.

G&H What are the main health care challenges associated with the disease burden of NAFLD and NASH?

ZY The biggest challenge is that the burden of disease is high and continuously growing without effective strategies available to reverse or even slow down these trends. The conundrum is that despite this increasing burden, there is a lack of awareness regarding NAFLD and NASH, especially in primary care and endocrinology practices. Providers in these areas likely see many patients who are at risk for NAFLD and NASH, especially patients who may potentially progress. Nevertheless, care pathways or programs to identify and risk-stratify these patients are almost completely absent in the primary care setting. As awareness of NAFLD and NASH increases, it is very important that all providers are educated about the availability of noninvasive tests that can be utilized to risk-stratify patients with NAFLD. There is currently a lack of utilization of these tests in primary care and some subspeciality settings where patients who are at risk for progressive NAFLD are being seen.

Another challenge is to keep in mind that the disease burden involves not only a clinical burden such as cirrhosis and liver cancer, but also impairment of quality of life. NAFLD and NASH negatively impact quality of life and other patient-reported outcomes, which are quite important from the perspective of patients.

G&H What are some current misconceptions in this area?

ZY Some providers may think that there are no treatment options currently available for patients with NAFLD and NASH. Although specific drugs are not approved for the treatment of NAFLD and NASH, there are many drugs that are available and approved for managing associated risk factors. For example, new drugs that are being used for the management of obesity and type 2 diabetes can be used to optimize management of these risk factors for NAFLD.

However, ultimately, management of these patients requires a multidisciplinary approach. Patients should not just be told to lose weight with diet and exercise. Providers should consider dietary change or lifestyle intervention like a prescription given to a patient to carry out with a multidisciplinary team that works through a care pathway. This multidisciplinary team should not only include hepatologists and gastroenterologists but also diabetes experts, exercise specialists, nutritionists, and even behavioral health experts that provide the spectrum of treatment options that could lead to sustainable improvements. In this context, some drugs that are currently being tested in clinical trials will also likely become available, and this could change the management of these patients in the clinical setting. On the other hand, addressing these diseases from a public health standpoint requires recognition of NAFLD and NASH as important noncommunicable diseases that need to be addressed with national and global policies.

G&H What are the priorities of research?

ZY One priority is to develop better ways to identify patients with high-risk NAFLD or patients who would progress using noninvasive biomarkers or tests for risk stratification. This is one of the biggest areas of current research. Another priority is the development of a personalized medicine approach to the treatment of NASH with different drug regimens that meet the patient's needs and target the pathways that are involved in the pathogenesis of progressive NASH. Finally, from my perspective, it is also a priority to better understand the societal and policy implications of NAFLD, both at a national level as well as a global level.

Disclosures

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Suggested Reading

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