

**Obesity: The Leading Cause of Nonalcoholic Fatty Liver Disease and the
Most Urgent Threat to Public Health Today**

May 15, 2024

8:30 AM to 10:00 AM

U.S. Capitol Building, Room SC-4

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Good morning. I'm Meena Bansal, System Chief, Division of Liver Diseases; and Director of the MASLD/MASH Center of Excellence at the Icahn School of Medicine, Mount Sinai Hospital in New York. Thank you to Senator Shaheen for enabling us to be here today to talk about this very important topic and to American Liver Foundation for inviting me to speak. The relationship between obesity and liver disease is not well understood by the public, or by many in the healthcare field and it's causing a health crisis that will affect this country, and the world, for generations to come.

The Basics of NAFLD/NASH (MASLD/MASH)

Before I explain more about fatty liver disease, let me begin with a few basics about the disease terminology. In 2023, there was a nomenclature change to try and destigmatize fatty liver disease and if you bear with me, you'll soon understand why this is important to our discussion today.

The decision to change the nomenclature was the result of extensive global deliberations and consultations between leading international medical societies, including the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL) and the Latin American Association for the Study of the Liver (ALEH), along with experts in hepatology and representatives from patient groups. It was decided that the terms fatty liver disease, nonalcoholic fatty liver disease or NAFLD, and nonalcoholic steatohepatitis or NASH, were terms that focused more on exclusion of what the disease was not, rather than on inclusion and what these disease states have in common. These terms were also found to be very stigmatizing to patients. But more importantly, these medical terms did not recognize the key role that metabolic dysfunction played in disease pathogenesis, which is critical to our understanding of the linkages between obesity and liver disease. The new terms are now steatotic liver disease, instead of fatty liver disease, metabolic dysfunction associated steatotic liver disease or MASLD instead of NAFLD, and metabolic dysfunction associated steatohepatitis or MASH instead of NASH.

Continuum of NAFLD/NASH (MASLD/MASH)

Approximately 25% of the US population (around 80-100 million) already have MASLD, which is characterized as having at least 5% fat in their liver (steatosis). I would like to stress here that most of these people aren't even aware they have the disease. About 20-25% of those individuals will also have the more progressive form of the disease, which is MASH. MASH is characterized by steatosis along with inflammation and ballooning of hepatocytes and increasing amounts of fibrosis or scarring of the liver. We categorize fibrosis on a scale of 0-4, with 4 being cirrhosis which can lead to liver failure. Of those with MASH, 5-20% will go on to liver failure and/or liver cancer.

MASH is now the number one cause of liver transplantation in the US. Fibrosis is the most important determinant of liver related outcomes. Once you have Stage 2 Fibrosis, your risk of liver related outcomes increases by 10-fold, Stage 3 Fibrosis increases to 17-fold, and Stage 4 or Cirrhosis 42-fold. The good news is that fibrosis is REVERSIBLE. It has been shown that >10% weight loss through either bariatric surgery or diet and exercise can cause fibrosis reversibility. We recommend a Mediterranean diet, along with at least 150 minutes a week of aerobic activity and resistance training to retain muscle mass and strength training two to three times per week.

There are multiple factors that determine fibrosis progression rates. For example, genetics such as the PNPLA3 gene, which is more common in Hispanic people, and is important in the regulation of hepatocyte lipid homeostasis. Having this gene variation is associated with an increased risk

of developing MASLD. There is also the interplay of multiple medical conditions: diabetes, obesity, hypertension, and hyperlipidemia. Social determinants of health also play a big role in disease development. And by social determinants of health, I am talking about the quality of food to which communities have access, the amount of high fructose and ultra-processed foods in a person's diet, inhaled toxin exposures, and of course, smoking. Hispanic communities have the highest disease burden due to underlying genetics. Cardiovascular disease is the number one cause of death in those with MASLD.

Connection between obesity and liver disease

More than 40% of the US population is living with obesity resulting in 1 out of 5 adult deaths. Obesity disproportionately affects diverse communities. The prevalence of MASH continues to grow right alongside the diabetes and obesity epidemics. For years patients have been told they “**JUST**” have a little bit of fat in their liver, but not to worry about it. Then they present with advanced fibrosis requiring liver transplantation. The more metabolic risk factors you have, such as obesity, diabetes and hypertension, the more risk you have for advanced liver disease.

In a study we are conducting through the Mount Sinai Longitudinal MASH Registry, that has enrolled nearly 800 patients thus far, what we're finding is alarming and should be a warning bell for the federal government to act. Of the patients enrolled, 42% of whom are Hispanic, we found that 55% of all patients have obesity with a BMI greater than 30. About 43% have stage F2-F4 fibrosis and of those, 25% have already progressed to cirrhosis or liver failure. Our preliminary data suggests that inhaled particulate matter (such as pollution) plus obesity, is associated with fibrosis compared to either alone. This means that obesity may increase the risk of toxin exposure by acting as a depot or a sink.

One of the patients enrolled in our study is an 18-year-old Hispanic male college student. He does not have diabetes, but he is obese with an increased waist circumference. He attempted to enroll in a trial for stage 3 fibrosis, but his liver biopsy came back as cirrhosis, or stage 4, and thus the screen failed. This teenager will likely need a liver transplant, or he will develop liver cancer if we do not reverse the situation. He is not alone.

Rising incidence of obesity and liver disease driving a public health crisis

Aside from the vast numbers of people affected by MASLD, the disease also carries significant costs. In the United States, MASLD has annual direct medical costs of about \$103 billion. Patients with MASH have been reported to have a similar level of health-related quality of life, work productivity and activity impairment to individuals with type 2 diabetes (T2DM), but people with MASH have reported worse mental status and a higher level of health resource use, including emergency care and hospitalization. While the first FDA-approved therapy for MASH, resmetriom, was approved under an accelerated pathway, it is limited to non-cirrhotic MASH patients who have significant or advanced fibrosis meaning that most people with MASH, will not be eligible for this drug at this time. But there are also several additional therapies being studied including those that treat type 2 diabetes and/or obesity, with some shown to decrease cardiovascular mortality. These are the GLP-1RA based class of drugs.

The role of the federal government in addressing this crisis

Now that you understand a bit more about the widespread scope of steatotic liver disease and the role obesity plays in developing the disease, you may be asking yourself, what can the government do to address this crisis. First, we need an upstream focus to attack the problem where it's beginning. This includes support for removing fructose from beverages; improving

access to healthy food and exercise across communities; raising awareness about the direct linkages between obesity and liver disease, liver cancer and liver failure; screening for fibrosis in at-risk populations as a quality measure, similar to quality measures in diabetes screening for retinopathy or nephropathy; creating educational programs around “Know Your FIB-4” which is a test to help estimate the amount of scarring in the liver so that at-risk patients are referred for hepatology care; and increasing research to support and foster innovation on comprehensive models of care, screening and linkage to care.

We also need to support the efforts of the Agency for Healthcare Research and Quality (AHRQ) and other federal agencies now tasked with evaluating the prevalence, diagnoses, treatments and complications associated with MASLD, thanks to a new study that American Liver Foundation championed, which was included in the Labor Health and Human Services appropriations bill, led by Senator Bill Cassidy (R-LA). This important study will: 1) Assess the prevalence of NAFLD in the United States; 2) Assess the costs associated with individuals diagnosed with NAFLD, including the costs to patients, families, and government programs; 3) Assess the costs and impact on patients and the healthcare system if NAFLD is unaddressed and progresses to nonalcoholic steatohepatitis (NASH), liver failure, poor liver function, or liver transplant; 4) Identify and address barriers to preventing, diagnosing, and treating NAFLD and NASH; and 5) Include an analysis of any disparities in access to care and other outcomes, such as health status, among minority populations. I hope this study will be a first step towards a nationwide plan, a CALL to ACTION to address this burgeoning health crisis.

We also need a downstream focus, and this includes ensuring that healthcare coverage is provided for obesity medications along with nutrition and lifestyle coaching; and ensuring healthcare coverage for additional liver-directed therapies, along with nutrition and lifestyle coaching for those patients with advanced fibrosis.

Obesity and liver disease are a deadly combination. Addressing this connected issue will require support from a multitude of stakeholders including the federal government, disease-based nonprofits, community and faith-based community groups, chronic disease directors, epidemiologists, and leading public health organizations. My hope is that what I’ve shared today will help all of you go back to your offices armed with enough information to start a conversation that will result in action, because 80-100 million Americans affected by MASLD are counting on us.

Thank you.