



Nonalcoholic Fatty Liver Disease: Miller School Researchers Target a Silent Epidemic

Nonalcoholic fatty liver disease, or NAFLD, affects 100 million Americans and millions of others worldwide. The disease is costing lives, health and an estimated \$32 billion in U.S. health care costs annually. In fact, fatty liver disease is projected to surpass hepatitis C as the leading cause of liver transplants in the U.S. as soon as 2020.



Kalyan Ram Bhamidimarri, M.D., M.P.H.



Nonetheless, awareness of the disease is low, according to Kalyan Ram Bhamidimarri, M.D., M.P.H., associate professor of medicine at the University of Miami Miller School of Medicine. He and other hepatologists at the Miller School's Schiff Center for Liver Diseases are conducting a number of clinical research studies, evaluating several promising molecules to reduce fat, inflammation and fibrosis in patients with fatty liver disease.

"Fatty liver can present as isolated steatosis/nonalcoholic fatty liver (NAFL) – fat in the liver but without inflammation or fibrosis," Dr. Bhamidimarri said. "It can also present as nonalcoholic steatohepatitis (NASH), fat plus inflammation with or without fibrosis. NASH is much more dangerous, and accounts for approximately 20 percent of all NAFLD patients."

Dr. Bhamidimarri notes that NASH can lead to progressive accumulation of scar tissue within the liver, resulting in end-stage liver disease and/or liver cancer. Both are life-threatening. Death in NASH patients can also occur due to obesity-driven cardiovascular disease, and malignancy/cancers of the GI tract, prostate, pancreas, breast, liver and other organs.

The National Institutes of Health reports that between 25 and 40 percent of U.S. adults have NAFLD. Most have simple fatty liver, but as many as 30 million have NASH. Non-alcoholic fatty liver disease in children is also a major health concern and is growing.

The NASH Education Program, initiated at the end of 2016, reports that childhood NASH cases began increasing 30 years ago.



Why? In the United States, the percentage of obese children and adolescents has tripled since the 1970s.

Dr. Bhamidimarri says a two-pronged approach is needed right now to help curb an impending epidemic: continued research on the science side, and enlisting the primary care community in the fight through education about the disease.

How does a doctor spot a potential case?

“NAFLD typically occurs in non-alcoholics who are obese and have metabolic syndrome,” Dr. Bhamidimarri said. “These are individuals who have several risk factors together, such as high blood pressure, unhealthy cholesterol levels, high blood sugar and too much fat in the abdominal area.”

Therein lies the first challenge, he explained. It is common to see obese patients with metabolic syndrome. Just because someone is obese or has diabetes does not mean they have NASH. Even people who are extremely thin can develop it. There are other causes of NASH, too.

Dr. Bhamidimarri recommends assessing for these additional factors:

- Hispanic adults
- Adults taking methotrexate for rheumatoid arthritis
- Cancer patients undergoing chemotherapy
- Individuals with rapid weight loss from crash diets
- People on total parenteral nutrition

“We don’t have a simple blood test or scan, so NASH is typically



a diagnosis of exclusion,” Dr. Bhamidimarri said. “A liver biopsy is the current standard to diagnose it accurately, but it is too invasive for general use.”

Primary care providers can use a mathematical score to non-invasively predict those with greater risk of progression, he said. One such method is the APRI score (short for aminotransferase/platelet ratio index). After ordering routine lab tests, the doctor plugs the lab values into an online calculator to obtain a score. The score helps clinicians determine which patients are most likely to need a liver biopsy.

“All patients would be counseled about diet and exercise. High-risk patients would be advised about the liver biopsy option and further steps in managing the disease.”

Once NASH is diagnosed, there’s another challenge. The only approved treatments for NASH are natural vitamin E and thiazolidinediones. Vitamin E works somewhat short-term in non-diabetic patients. It does not improve patients in the long-term.

Diabetics can take thiazolidinediones, drugs that improve insulin action, but must be closely monitored. Potential side effects include congestive heart failure, osteoporosis, bladder cancer and even irreversible weight gain – the opposite of what is desired in NASH patients.

Pharmaceutical companies are investing more than \$35 billion in research to find alternatives, including newly discovered molecules with therapeutic potential.



“These drugs have various mechanisms of action and intervene in the pathway that leads to progression of fatty liver disease,” Dr. Bhamidimarri said. “They are designed not only to improve the fatty liver component, but also to help in reversing liver fibrosis. Ongoing research in this area is exciting and appears promising.

“Until we have better screening tests and treatments, our best approach is teamwork,” he said. “Physicians on the front line of care are needed in this fight. By having more professionals aware of the disease, we hope to find high-risk cases sooner and prevent them before they suffer devastating outcomes. Our aim is to perform additional assessments and hopefully catch fatty liver disease at an earlier stage, when it’s more likely treatable.”