Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/gi-insights/navigating-non-alcoholic-fatty-liver-disease-diagnostic-management-strategies/13682/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Navigating Non-Alcoholic Fatty Liver Disease: Diagnostic & Management Strategies

Dr. Buch:
Welcome to *GI Insights* on ReachMD. I'm your host, Dr. Peter Buch. And joining me today to share what we need to know about nonalcoholic fatty liver disease, or NAFLD for short, is Dr. Naim Alkhouri, who is the Chief of Transplant Hepatology and the Director of the Fatty Liver Program at Arizona Liver Health in Phoenix.

Dr. Alkhouri, welcome to the program.

Dr. Alkhouri:
Thank you so much for having me and for having this discussion about the topic dear to my heart: nonalcoholic fatty liver disease, or NAFLD. We need to raise awareness, and what you're doing is highly appreciated.

Dr. Buch:
Thank you, sir. To start us off, Dr. Alkhouri, what are the risk factors for developing nonalcoholic fatty liver disease?

Dr. Alkhouri:
So NAFLD is considered a liver manifestation of the metabolic syndrome defined by the presence of overweight, obesity, dyslipidemia, hypertension, insulin resistance, and type 2 diabetes. So these are the major risk factors, and we have epidemic percentages of all of these, unfortunately. So when we look at patients coming with NAFLD to our clinics, about 80% are obese, about 45% have type 2 diabetes, and close to 80% have prediabetes or diabetes, and then about 2/3 will have hypertension, dyslipidemia, and metabolic syndrome.

NAFLD is defined by the presence of fat in the liver cells in the absence of significant alcohol consumption, so the first question I ask my patients is about how much alcohol they consume. And what's considered excessive alcohol consumption is anything 3 drinks or more for men or 21 drinks per week, and then for women it's lower. It's 2 drinks or more per day or 14 drinks per week. So if the patient is not consuming excessive alcohol consumption, they have obesity, metabolic syndrome, and fatty liver, then we call it NAFLD.

Dr. Buch:
Dr. Alkhouri, do you have any tricks with regard to getting the exact information about alcohol consumption from our patients? That seems to be a consistent problem across the board. What do you do?

Dr. Alkhouri:
To be honest with you, I mean, I agree; this is sometimes tricky to get accurate information, and our patients tend to underestimate. So sometimes, if they have other family members with them, I like to confirm that what they're telling me is correct. here are several biomarkers that can also help you assess the amount of alcohol that they are consuming if you have a suspicion that they are not being honest with you, but also getting detailed alcohol intake history and understanding what is a standard alcoholic drink is important. When

we say a drink, it means 12 ounces of beer, 5 ounces of wine, and 1.5 ounces of hard liquor. So this is important because many patients say, "Well, I do 2 beers a day," but when you ask, you realize that they're doing a 24-ounce beer. And then when you ask about the alcohol content, instead of the typical beer that has 4%, they're consuming the double IPA that has 8%, so that exponentially increases the amount of alcohol they're drinking. So just knowing what a standard alcohol drink is and asking in detail how much they drink is very helpful. Also, you have to ask about drinking on the weekend versus weekdays because many patients just binge drink on the weekend but, Friday, Saturday, Sunday they do 12 beers each day, and that's considered excessive alcohol drinking.

Dr. Buch:
That's great. So would you please review the stages of nonalcoholic fatty liver disease?

Dr. Alkhouri:
That's a very important question. So not all NAFLD is created equal. We have, as you said, different stages, so it's really a disease spectrum. It starts with what we call simple steatosis or nonalcoholic fatty liver, or NAFL. This is when you have steatosis or fat within the hepatocytes, but there is no inflammation and there is no hepatocyte injury, what we call ballooning of the hepatocytes, so this is simple steatosis. Typically, it has relatively a benign course in terms of progression to cirrhosis. And then what we worry about more is what we call NASH, nonalcoholic steatohepatitis. So now we have, in addition to steatosis, we have what we call lobular inflammation, and then we also have hepatocyte ballooning, and NASH is considered the progressive form of NAFLD, and this can lead to liver fibrosis, which has 4 stages, so stage 1 being more mild and then moderate, severe, or bridging fibrosis is stage III, and then stage IV is cirrhosis. So the last most aggressive form of the disease is what we call NASH cirrhosis. And this is very important because today it's not enough to tell patients that you have fatty liver disease. You need to know the stage. And we have several noninvasive tests to tell us about the stage of fibrosis, which is really the most important prognostic factor in terms of the risk of these patients developing cirrhosis and its complications. Liver biopsy is also something that we've done for years and decades and that will give us valuable information in terms of the presence of NASH and the stage of fibrosis. But I can tell you that in my clinical practice now I do biopsies on probably 5% of patients, so 95% I am able to determine the disease severity with noninvasive tests. We call them NITs now.

Dr. Buch:
And that's a perfect segue to our next question. With those stages in mind, what are the clinical tools that you use to monitor disease progression?

Dr. Alkhouri:
So we like to divide these tools into what we call wet biomarkers or serologic tests, and these are divided into simple scores. The easiest way is to do something called the FIB-4 index. This is an online calculator, it has AST and ALT. And we know that the ratio of AST/ALT reverses when you have advanced disease. So typically in NAFLD, your ALT is higher than AST, but when you have advanced disease, the AST becomes higher. We have also platelet count in it and age because with advanced disease, typically you have lower platelets, and older patients are more likely to have advanced disease. So you put these 4 numbers in a calculator. If you're less than 1.3, you're low risk for having advanced fibrosis and cirrhosis. If you're more than 2.67, you're considered high risk. This is the simplest test we have, and this is very good for primary care physicians to utilize to risk stratify patients with NAFLD.

The next segment of noninvasive tests that are serologic is what we call complex biomarkers, so some of them test biomarkers of what we call extracellular matrix turnover. So these are biomarkers of collagen deposition in the liver. There is one that was recently approved by the FDA called the enhanced liver fibrosis or ELF test. This is commercially available. It has 3 biomarkers in it, and it has prognostic value in terms of progression to cirrhosis and developing complications.

Then we have imaging tests, so we can actually determine liver stiffness with the concept of elastography, and this can be done with ultrasound-based technologies. We have the FibroScan machine where you get liver stiffness measurements that correspond to the stage of liver fibrosis. We can also do the same with MR elastography. There are other MR technologies including a number we call corrected T1 or cT1, so having all of these tests from the scores to the wet biomarkers to the imaging tests I think we are able to determine the severity of the disease in the vast majority of our patients.

Dr. Buch:
For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Naim Alkhouri about nonalcoholic fatty liver disease. So let's turn our attention to treatment, Dr. Alkhouri. How do you manage NAFLD?

Dr. Alkhouri:
That's a very important question. And the first thing we talk about is really lifestyle interventions and trying to lose weight, and we've had twice established that if you lose around 7% of your total body weight, you have a chance to resolve NASH, and you need to get to that 10% of total body weight to see a regression in fibrosis. So what does that mean for our patients? If they're at 250 pounds, we aim for 10% total body weight loss, so that would be around 25 pounds. And I think that's important for the patients to understand that they don't need to have this ideal BMI and be less than 25. Sometimes we're talking about 20, 25 pounds of weight loss, and that will have great impact on their disease.

Now, easier said than done, and it's not easy to lose weight and maintain weight loss. Sometimes we use medications for weight loss, such as semaglutide at high dose. Bariatric surgery is a very effective modality also to treat NASH. Usually, we reserve it for patients with severe obesity and other complications from obesity with NASH and fibrosis, but there are studies showing that 5 years after bariatric surgery, you can have NASH resolution in 85%, and the majority of patients will have also regression in liver fibrosis.

In terms of medications that we use specifically for NASH, we had a trial called the PIVENS trial that evaluated vitamin E at 800 units versus pioglitazone at 30 mg versus placebo in nondiabetic patients with biopsy-proven NASH, and that study showed that both vitamin E and pioglitazone were associated with some histologic improvement in terms of decreased liver inflammation and hepatocellular injury, although we didn't see a signal on liver fibrosis in that trial. There are other trials looking at patients with prediabetes, diabetes, but there is a concern about fluid retention, worsening heart failure, losing bone density. So we're looking beyond these 2 agents. We've seen some promising results with the GLP-1 agonists, such as semaglutide, and then we have several therapeutic agents that are in development now, including a few in phase III clinical trials. So one of these agents is called resmetirom. This is a thyroid hormone receptor beta agonist that has the beneficial effects of the thyroid hormones without the thyrotoxic causes. We have another drug called lanifibranor. This is a PPAR alpha, delta, and gamma agonist. PPAR alpha is the target for fenofibrate, so you can lower your triglycerides; PPAR gamma is the target for glitazones, so insulin sensitizers; and PPAR delta has beneficial effects on the liver in terms of decreasing liver inflammation. Another agent is called obeticholic acid, which is a synthetic bile acid, and this works on a receptor called FXR and this has been associated with fibrosis regression in a phase III trial. So the pipeline is rich, and we have clinical trials, so I really anticipate that in the next 5 years we're going to see complete transformation in how we manage patients with NAFLD.

Dr. Buch:
That's great. So what are you specifically doing in your center? And are you recruiting for patients?

Dr. Alkhouri:
So we are actually a hybrid clinical and research practice, so we see patients with all different kinds of liver diseases at Arizona Liver Health with a focus on NAFLD, and in patients with NAFLD, we offer clinical trials. In addition to this, we are doing also lifestyle intervention trials, and we are working with companies in what we call digital therapeutics, so these are apps that you can download to a smartphone and they rely on the concept of cognitive behavioral therapy. They provide our patients with recipes and exercises with access also to a nutritionist so that they can ask questions. And actually, we have several studies showing the beneficial effects of these digital therapeutics in patients with type 2 diabetes and obesity, and we are exploring their effects on NAFLD. We also have some diagnostic studies that we are doing trying to validate some of these noninvasive tests and also look on how they respond to pharmacologic treatment and lifestyle interventions.

Dr. Buch:
Those were some very important insights when it comes to treating our patients with nonalcoholic fatty liver disease. And I want to thank my guest, Dr. Naim Alkhouri, for an excellent discussion. Dr. Alkhouri, it was great speaking with you today.

Dr. Alkhouri:
Thank you so much for having me. It's been a pleasure.

Dr. Buch:
For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in the series, visit ReachMD.com/GIInsights, where you can Be Part of the Knowledge. Thanks for listening, and see you next time.