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/on-the-frontlines-of-familial-chylomicronemia-syndrome/could-it-be-fcs-recognizing-the-diagnostic-clues/67102/

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

Could It Be FCS? Recognizing the Diagnostic Clues

Announcer:
You're listening to *On the Frontlines of Familial Chylomicronemia Syndrome* on ReachMD. Here's your host, Dr. Mary Katherine Cheeley.

Dr. Cheeley:
Welcome to *On the Frontlines of Familial Chylomicronemia Syndrome* on ReachMD. I'm Dr. Mary Katherine Cheeley, and joining me to discuss the identification and diagnosis of familial chylomicronemia syndrome, also known as FCS, is Dr. Zahid Ahmad. He's an endocrinologist and Associate Professor in the Division of Internal Medicine at UT Southwestern Medical Center in Dallas. Dr. Ahmad, thanks for being here today.

Dr. Ahmad:
Yeah. Thank you so much for having me.

Dr. Cheeley:
We know that FCS is super rare, and it can resemble more common causes of severe hypertriglyceridemia, so the diagnosis is sometimes hard to make. With that being said, where in the patient journey do you see opportunities for that earlier diagnosis or recognition to be found?

Dr. Ahmad:
Yeah, this is a really important question. I don't think people understand how important this is. On average, an FCS patient sees five different clinicians before they're given a diagnosis—the right diagnosis—of FCS. So there are plenty of opportunities earlier in their patient journey to pick this up.

I mean, when I see someone whose triglycerides are persistently above 1,000, especially if they're younger, I start thinking about FCS. And if you see somebody with a lot of abdominal pain all the time, pancreatitis, or very high triglycerides, those kind of things clue you into the fact that this might be FCS.

This is really important to pick up early too, because you can intervene now. We have such good tools to intervene and reduce the chance of pancreatitis.

The other clue that I tell people about is, most people with high triglycerides are what you call the metabolic patient. They have diabetes, they're obese, and whatnot. If you see someone who's not like that, that's the person that you think about FCS early.

So there are plenty of opportunities to pick it up earlier. We're just not doing a good job yet.

Dr. Cheeley:
So take me into your clinic with you. When you see a patient with severe hypertriglyceridemia, what aspects of their clinical history, triglyceride pattern, or treatment course kind of raise your suspicion for FCS specifically, rather than a multifactorial chylomicronemia?

Dr. Ahmad:
So I like to use the word persistence. And there are many things that are very persistent about FCS compared to the polygenic or multifactorial chylomicronemia syndrome that we're more used to. MCS, or multifactorial individuals, their triglycerides fluctuate quite a bit. And if you fix the secondary issues like diabetes, alcohol use, or medications, their triglycerides can come down to normal or near normal.

But in contrast, patients with FCS, their triglyceride elevations are there throughout their entire life. They're almost always above 1,000. They present younger, they can have a history of recurrent pancreatitis, and they don't respond to the therapies like fibrates and omega-3 acids—omega-3 fatty acids, I should say. There are lab clues, too, like they have low apolipoprotein B levels. You don't pick up any secondary issues. Those are more clues that should raise your suspicion of FCS.

One more clue that's always served me well is that the triglycerides are almost always much, much higher than the cholesterol, like 10 times higher. So if I see cholesterol 200 and triglycerides 2,000—one to 10, 10 to one ratio, whichever direction you want to look at it—I'm thinking of FCS right away.

Dr. Cheeley:
I love that. I'm gonna steal that. And then I agree with you, I think the ApoB part of it, because it's more common now to check an ApoB, also is a great lab marker that you can look at.

When you start thinking about FCS in a patient, what is your pathway to validate that diagnosis, and what are errors that could come up?

Dr. Ahmad:
I have a pretty standard way I deal with almost every patient that comes to our clinic, and I also make our trainees follow this pathway, because I think if you do this, you won't really miss much.

But I start with a detailed history. I mean, there's no substitute for that, honestly. In FCS, there are a lot of clues as to FCS, like the age of onset, if they've had pancreatitis, how many episodes they've had, abdominal symptoms. So they don't always get pancreatitis. Sometimes they just get abdominal pain.

For FCS, I will say family history can be a bit confusing. It's an autosomal recessive condition, but there are family members who could be heterozygous, and in the presence of a secondary issue, their triglycerides can be high. So I take family history, but for FCS, it can be pretty confusing.

Medication exposure. I make sure that this is not because of estrogen use or something like that that's causing the triglycerides to get very, very high. And on that note, obviously I make our trainees and I myself ask about every secondary cause of high triglyceride too.

I also love to teach the physical exam for FCS. It's the same exam for MCS, because the exam findings are the same regardless of why the triglycerides are high. But they are very interesting findings. These individuals get eruptive xanthomas, so that's triglycerides literally breaking out in their skin. They get like pallor retinalis, so if you look in their eyes, if you visualize retinal vessels, you can actually see that the blood is reflecting light. It looks white. And they can get hepatosplenomegaly. So, if you are at an institution where they still teach you how to feel a liver or percuss a liver, you can feel it.

Then, obviously, there's the lab evaluation. Obviously, with the lab evaluation, we want to repeat fasting lipid profiles. We want to see over and over the triglycerides staying very high. ApoB levels are also quite useful, as we discussed. Make sure you rule out diabetes and thyroid disease, looking for any other secondary things that you feel might contribute to this case.

And then there are some pretty good tools to diagnose FCS. There's the North American Familial Chylomicronemia Score, or NAFCS, which I was one of the people who was lucky enough to help develop. And that is actually quite good at picking up true cases of FCS, and is typically accepted by payers and other institutions as a diagnostic method for identifying FCS patients.

So some of the pitfalls, because you asked me about diagnostic errors… I think sometimes some providers think that, oh, they weren't diagnosed as a child with FCS, so that means—I'm talking about adult providers—that's not the case. As I mentioned, most FCS patients see five different clinicians before they're diagnosed, so they push into adulthood. We have diagnosed people in middle ages with FCS, and they were just kind of told, oh, you have high triglycerides, or they were told they are frequent flyers in the ER for pancreatitis or something like that, and no one really took a step back and looked at it. So this delayed diagnosis thing, in my mind, is the biggest issue for many FCS individuals.

Dr. Cheeley:
For those just joining us, this is *On the Frontlines of Familial Chylomicronemia Syndrome* on ReachMD. I'm Dr. Mary Katherine Cheeley, and I have the pleasure of speaking with Dr. Zahid Ahmad about best practices in identifying patients with FCS.

So let's talk about genetic testing. You're at UT Southwestern, so you guys have access to genetic testing, but I also know that you work with providers all over the country. So number one, how do you use it? Number two, how do you talk to providers who may have difficulty accessing it about when to incorporate it and what potential candidates you have with patients?

Dr. Ahmad:
Yeah, those are really important questions, and I'll just take a step back and point out that genetic testing is still considered the diagnostic gold standard for confirming FCS. We talked about using the North American FCS score, and that's very good. But I usually do genetic testing when the clinical picture is consistent with FCS—so they have very high triglycerides that are persistent, they have pancreatitis over and over, low ApoB levels or normal ApoB levels, and they don't respond to triglyceride-lowering medications. Those cases have the highest yield of finding something in genetic testing.

But when I talk to providers in the community about genetic testing, it's actually a lot easier to do than you think. Ordering it is not that hard, because most of the companies have online portals. You can just log in, put your patient's address in, and they'll send them a kit. Most of the genetic testing companies will actually also do the benefits investigation, so they'll check with insurance for you, and they'll check to see if it's covered. And if it's not covered, they often offer a cash price. And your patient, at that inflection point, can say, no, I don't want to do it, or they can choose to pay the cash price.

So the ordering and doing it is not hard, but the pre- and post-test counseling is still a bit challenging. You do need to have some understanding of genetics, and the main thing I tell people is that a positive test is really useful, but a negative test—meaning a test that didn't find anything—is kind of a useless test, because genetic testing is still new, the technology is still evolving, and we don't know everything about genetics. We don't even know all the genes that cause high triglycerides. And so that becomes the pre- and post-test counseling stuff that you have to think about quite a bit.

Dr. Cheeley:
So let's stay in that same lane. How do genetic test results inform your diagnostic confidence? So kind of what you talked about, but in terms of explaining it to the patient and long-term management for the patient. You talked about the positive one. I do want you to talk a little bit more about the negative one, too, because they still have that clinical picture. That's why you decided to do genetic testing in the first place. So talk me through that a little bit.

Dr. Ahmad:
I like the way you put that. So I really want to be clear that even though we talk about genetic testing as a diagnostic gold standard, it's not 100 percent necessary to make a diagnosis of FCS. The North American FCS score is a good surrogate.

But when genetic testing is done, patients tell us that it provides clarity—but not just for the patient. I should also say it provides clarity for the provider too, for the clinician involved. And for the patient, I can see why. You've had all these years of symptoms and not a clear diagnosis, but then you get genetic testing done, and it points to one very clear diagnosis. And so this explains years of symptoms, years of being told different things by different people.

And then for the clinician, it increases my confidence. And it also makes me more confident about treatment, because I may think that, oh, maybe the fibrate or omega-3 didn't work because the patient didn't take it. But actually, it didn't work because they have FCS, and it's just not going to work in that case, right?

There's also the benefit of family counseling and cascade screening. It is very possible the siblings also have FCS, so it's really important to get the siblings screened. The story is always the same: the older one gets diagnosed, usually at a later age in life, but the younger one, because of cascade screening, gets diagnosed a little bit earlier and gets put on a low-fat diet earlier and sometimes doesn't even have pancreatitis.

Dr. Cheeley:
So let's look across current practice a little bit. Which patients with possible FCS are most likely to remain unidentified? And where do you see the greatest opportunity—I think I know what you're gonna say for this, but I'm really excited to hear it—for improving the recognition of those patients?

Dr. Ahmad:
I'm excited to hear what you think I'm going to say.

Dr. Cheeley:
I think you're gonna say earlier in the process. I think you're gonna say the third time they're in the ER for pancreatitis, somebody should maybe wave the flag like, hey, might, it might be this.

Dr. Ahmad:
Exactly. I almost feel like there should be an alert in Epic or an EMR saying, your patient has been in the ER multiple times. The triglycerides are always high. The blood is always lipemic. Consider—

Dr. Cheeley:
The insurance company. Hey, we've had three admissions to the ED. Like, we should make the insurance companies do something with this. They know. They're paying for it.

Dr. Ahmad:
That's true. The person who has the money, yeah, they should be worried about that. Yeah, exactly.

But I think the patients with FCS that remain unidentified might be the ones who come as adults to the lipid specialist, because we think of FCS as a pediatric disorder. So sometimes we don't think about it in a middle-aged person. But we need to, though, because that person might have just been overlooked, and maybe they were just very good at a low-fat diet and didn't have as much pancreatitis.

So that's another one. There are some people with FCS who don't have too many pancreatitis episodes, and sometimes we, including myself, forget to ask about abdominal pain. And they may not have pancreatitis, but they have abdominal pain once a month, and they know what to do. They go, they cut out the fat in their diet, or they just don't eat for a while, and they feel better.

And so we miss some of these clues here and there that they could have FCS. So we need to have more awareness. And I think, like you're saying with the emergency room doctors, the frontline clinicians need to have more awareness. Maybe we should just give them the North American FCS score right in the EMR and say, look here, the score is high. This is probably what your patient has.

Dr. Cheeley:
As we come to the end of this, because I have loved this conversation, what are your final things that you want to leave with us?

Dr. Ahmad:
So I think the main thing is that, even though it's rare, the consequences of missing FCS are pretty substantial, right? The patients get exposed to lifelong extreme hypertriglyceridemia. There's a very high risk of pancreatitis that's recurrent and acute.

But the good news is that we have better diagnostic tools like the North American FCS score. We have genetic testing that's much more widely available. Ten years ago, you couldn't order a commercial genetic test. You had to come to us, basically, because we were doing it in a lab. But now you can do it. Now, anyone can pretty much order it anywhere. And then, of course, we have new therapies that target ApoC3, and they work. They lower triglycerides in people with FCS. For the first time ever, there's an FDA-approved drug for FCS.

Dr. Cheeley:
Yeah, I love that. This has been so great. Thank you so much for being here. It was lovely to have you.

Dr. Ahmad:
Yeah, it's my pleasure.

Announcer:
You've been listening to *On the Frontlines of Familial Chylomicronemia Syndrome* on ReachMD. To access this and other episodes in our series, visit *On the Frontlines of Familial Chylomicronemia Syndrome* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.