Looking for clues to dangerous fatty liver disease

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In his lab in Lake Nona, Dr. Peter Crawford has been studying nonalcoholic fatty liver disease, a condition that's closely linked to obesity and Type 2 diabetes.

He is using cutting edge metabolic and genetic tools to try to figure out how and why nonalcoholic fatty liver disease, or "fatty liver," progresses into a more severe form, putting the patients at a higher risk of developing cirrhosis and liver cancer.

"It's a real scare, and it's directly linked to the obesity epidemic," said Crawford, a physician and research scientist at Sanford Burnham Prebys Medical Discovery Institute.

In nonalcoholic fatty liver disease, liver cells retain fat. The condition has a strong association with developing cardiovascular disease. In a small portion of individuals it can progress to the point that they need a transplant or get cancer.

The disease began making its mark on medical charts not long after obesity became an epidemic in the 1980s.

Its cause is not exactly known, but it is strongly linked to diabetes, obesity and high cholesterol, making it the most common liver disorder in Western industrialized countries. By 2030 the condition will be the most common reason for liver transplants in the United States, according to a 2014 study by researchers at the Cleveland Clinic.

Meanwhile, most patients who have fatty liver aren't aware of it, and the condition can evade primary care providers too, because it usually doesn't affect the results of routine blood work. For those who are eventually diagnosed - usually after the disease progresses to its more severe form - there are currently no drugs available.

"When you combine the fact that the natural history of the disease is unclear; it's difficulty to diagnose, treat and stage it; and there's no FDA-approved medicine, it becomes a huge issue," said Dr. Jaideep Behari, associate professor of medicine at the University of Pittsburgh and director of Fatty Liver Clinic.

The issue is more pronounced in states like Florida, where more than a quarter of the population is obese, and as a result more likely to have type 2 diabetes.

For local doctors, who continue to see liver disease cases related to hepatitis infections and alcohol abuse, fatty liver is a rapidly growing third category.

"It's becoming an epidemic," said Dr. Nasim Ahmed, a gastroenterologist at Gastroenterology Consultants CFL in Orlando

At Digestive and Liver Center of Florida, one of the large local independent practices, the proportion of patients who have liver disease because of alcohol, hepatitis and obesity is almost equal these days, said Dr. Srinivas Seela, one of the practice's founding partners.

"It's frustrating that these patients have no medical treatment," said Dr. Harinath Sheela, a Seela's partner and brother.

About 10 percent to 15 percent of the patients develop the more severe condition called nonalcoholic steatohepatitis, or NASH, but it's not yet

known which patients are more likely to fall in this category, adding to doctors' frustration.

For now, the standard treatment is lifestyle change. Patients are advised to lose weight and get their diabetes under control, although not all patients follow the advice.

But there's hope, because fatty liver has become an active area of research.

At least 200 drugs targeting the conditions are currently in clinical trials and a handful are in the advanced stages of research. The National Institute of Diabetes and Digestive and Kidney Disease has created a nationwide clinical research network to conduct studies for preventing and treating the disease.

"So it's possible that there will be a therapies within the next three to five years that will decrease the rates (of the disease)," said Behari of the University of Pittsburgh.

He was also encouraged by Crawford's research.

Crawford's recent findings from animal studies has amplified the silent dialogue between liver cells and their neighboring immune cells, showing that when certain fuels produced by the liver cells are off balance, the immune cells in the liver go rogue and cause scarring and worsening of fatty liver disease.

"That's a very exciting finding," said Behari, who's not involved in the research. "Anything that helps us open up that black box and understand the disease at the molecular level is a big deal."

Crawford, who's in the process of publishing the results of his most

recent study, hopes the findings would pave the way toward developing a drug and help identify patients who are at a higher risk of developing severe forms of nonalcoholic fatty liver disease.

He added that the findings also reiterate another important point.

"One way to look at it is that even in one strict cell type, having a balanced nutrition is important," Crawford said.

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