Gut Microbiome Could Help Predict Advanced Fibrosis in People With Chronic Liver Disease

A distinct set of microbes sets apart people with advanced fibrosis from those with minimal fibrosis.

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People with chronic liver disease and advanced fibrosis have a distinct pattern of microbes in their gut compared with those who have little to no liver fibrosis, according to study findings published in Scientific Reports.

“Microbiome composition was distinct in liver patients with advanced fibrosis compared

to those with minimal fibrosis and healthy controls,” author Jonathan Jacobs, MD, PhD, of the University of California, Los Angeles, and colleagues wrote.

Chronic liver disease affects 840 million people around the world with 2 million deaths every year. In the United States, deaths from chronic liver disease went up by 65% and deaths from liver cancer doubled between 1999 and 2016.

Recently, researchers have sought to determine the impact of the gut microbiome on the features of chronic liver disease, with associations having been found in people with non-alcoholic fatty liver disease (NAFLD) and primary sclerosing cholangitis.

Since advanced fibrosis is a predictor of morbidity and mortality linked to liver disease, researchers have sought to identify biomarkers for fibrosis within the gut microbiome. Scientists have found unique patterns in the gut microbiome of people with cirrhosis caused by hepatitis B, hepatitis C, NAFLD,and alcoholic liver disease. But links between other causes of chronic liver disease, fibrosis and the microbiome have yet to be determined. So the research team aimed to find out whether certain microbial patterns would help predict fibrosis in people with varying causes of chronic liver disease.

The researchers collected stool samples from 50 people with chronic liver disease treated in the Veterans Administration Greater Los Angeles Healthcare System between June 2017 and June 2018. This group included people with underlying conditions like chronic hep C, chronic hep B,

liver disease due to chronic alcohol use, primary biliary cholangitis, primary sclerosing cholangitis, Wilson's disease, autoimmune hepatitis, hemochromatosis and NAFLD. The reference population included 25 healthy people.

The fecal samples were subjected to a type of analysis called 16S ribosomal RNA sequencing that helps to identify and differentiate between closely related bacteria. Using a particular classification model, researchers were able to separate people with advanced fibrosis from those with the mild or moderate stage. The findings were then checked against a different cohort of people with chronic liver disease caused by NAFLD, hep C, hep B or alcohol use who were seen at the VA center between January 2019 and October 2019. Diet information was also noted for this group.

The researchers found that the variety of microbes in the gut of people with advanced fibrosis were widely different from those in participants with little to no fibrosis or healthy individuals. Those with advanced fibrosis had lower amounts of the genus Bacteroides and higher levels of the genus Prevotella—especially the species Prevotella copri, which was a strong predictor of advanced fibrosis across various causes of chronic liver disease.

Moreover, they also found that different causes of chronic liver disease were associated with different microbial patterns in the gut. For instance, those with chronic hep C and advanced fibrosis had fewer bacteria from the order Clostridiales and the family Ruminococcaceae and higher numbers of an undefined species from the family Rikenellaceae, two undefined species in the genus Bacteroides and an undefined species in the genus Dialister. Those with NAFLD and fibrosis were more likely to have their gut lined with Prevotella copri, an undefined species in the family Ruminococcaceae and one in the family Rikenellaceae, among other species.

The researchers admit that the single-center nature of the study, the multiple variables under consideration and the limited variability in cases that represented different causes of chronic liver disease all limited the study. But the team proposed that these differences in the gut microbiome, present in stool samples, could be used to pinpoint people with advanced fibrosis.

"There is a distinct microbial signature for patients with advanced fibrosis independent of liver disease etiology and other comorbidities," wrote the researchers. "These results suggest that microbial profiles can be used as a noninvasive marker for advanced fibrosis and support the hypothesis that microbes and their metabolites contribute to hepatic fibrosis."

Click here to read the study in Scientific Reports.

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