H. Pylori Test Hints at Risk Factor for Stomach Cancer

Pilot study suggests specific strain of bacteria may be found more often in East Asian patients with stomach cancer.

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Infection with Helicobacter pylori is one of the top risk factors for stomach cancer — but only a small proportion of individuals who carry the bacterium go on to develop cancer. Identifying who is most at risk for cancer will help doctors shape treatment and screening strategies for patients infected with H. pylori.

Now, a pilot study by scientists at Fred Hutchinson Cancer Research Center and Zhengzhou University in China, facilitated by Fred Hutch's China Initiative, hints that the strain of H. pylori may influence cancer risk. The work, published today in PLOS ONE, shows that patients with stomach cancer are much more likely to be infected with H. pylori that possesses a specific variant of a gene called cagA, which suggests that it may raise the risk of stomach cancer in this region.

"Having the cagA gene has been a marker for cancer and ulcers in Western populations, but in East Asian populations, they all have cagA — it's not particularly relevant. But in this study we're saying actually, the type of cagA matters [for cancer risk in East Asia]," said Fred Hutch microbiologist Nina Salama, PhD, the study's senior author.

A potential marker for stomach cancer risk

H. pylori infection is one of the strongest risk factors for stomach cancer, but how much it predisposes individuals to gastric cancer varies around the world. Up to 50 percent of people in the U.S. carry H. pylori in their stomachs; of those millions infected with the bacterium, only about 26,000 people are expected to be diagnosed with stomach cancer this year. In China, the rate of H. pylori infection can be as high as 67 percent, but gastric cancer is the second-most common type of cancer. According to the World Health Organization's most recent worldwide cancer statistics, more than 400,000 people in China were diagnosed with stomach cancer in 2012.

The global differences in stomach cancer risk can be partly attributed to differences in H. pylori itself. One way that H. pylori varies is in the cagA gene, which encodes a toxin that helps the bacterium better attach to cells lining the stomach. Particularly in Western countries, not all strains of H. pylori have cagA. In the U.S., the mere presence of cagA is linked to a higher risk of

gastric cancer. But in other areas of the world, such as East Asia, nearly all strains of the bacterium have cagA. However, the sequence of cagA can vary as well, specifically in a section known as the EPIYA motif. Most cagA-carrying H. pylori strains in the U.S. have an EPIYA C, or "Western" version. The most common "East Asian" variant is known as EPIYA D.

Working with collaborators at Zhengzhou University offered Salama and her team the opportunity to look more closely at H. pylori in patients who had progressed to cancer. Lead author Sarah Talarico, PhD a postdoctoral research fellow in the Salama Lab, had previously developed a sensitive test to detect H. pylori and its cagA variants. The team drew on stomach endoscopy samples and stool samples from study participants at Henan Cancer Hospital in Zhengzhou, China, who had tested positive for H. pylori by the urea breath test, a standard test for H. pylori infection. The preliminary study included samples from 25 patients with stomach cancer and 24 patients without cancer. Blinded to which samples were from patients with cancer, the researchers used their test to detect which cagA variant each patient carried and compare the amount of bacteria in their stomachs and intestines.

"Going in, people said all strains are essentially cagA-positive, and it will be this East Asian [EPIYA D] type," Salama said. Instead, she and her team saw both "East Asian" EPIYA D and "Western" EPIYA C variants in their patient pool, made up of all ethnically Han Chinese participants.

Strikingly, presence of the more virulent EPIYA D variant was linked to stomach cancer. Ninety-one percent of cancer patients carried H. pylori with this variant, while only 50 percent of cancer-free patients did.

"Even with this tiny sample size … if we just say, 'Does having EPIYA D correlate with cancer?' it does, in a statistically significant manner," Salama said. "It's a preliminary study, but it's really interesting."

H. pylori persists in cancer

Many questions about how H. pylori contributes to gastric cancer remain to be answered, Salama said. The bacterium appears to trigger a cascade of events that begin with stomach inflammation and can result in gastric cancer, but whether (and how) H. pylori influences — or even survives — later steps in this process is unclear.

Salama and her team looked at the amount of bacteria in the patients' stomach tissue and stool samples to see if they spotted any differences that might shed light on how H. pylori responds to the changes, such as increased stomach pH, that go along with gastric cancer development.

"My pet hypothesis was that H. pylori loads were going to be lower in the gastric cancer cases," Salama said.

But instead of less H. pylori, the team found about six times more in stool samples from patients with gastric cancer than in patients without cancer. They also detected H. pylori in the stomach samples from patients with stomach cancer but saw no difference in the amount when compared

to patients without cancer. The findings add to a growing body of work suggesting that H. pylori persists during stomach cancer development and may be contributing to that process at several steps.

Next steps

As interesting as the results may be, the small number of study participants limits conclusions that can be drawn, Salama noted.

Confirming the findings will require a much larger study of either previously collected samples or new samples collected from patients with H. pylori infections who are followed over time to see whether those with the EPIYA D type of cagA are much more prone to stomach cancer, she said.

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