Medical Xpress

Nasal microbiota holds clues to who will develop symptoms from SARS-CoV-2

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Dr. Sadanand Fulzele (left) and Dr. Ravindra Kolhe. Credit: Michael Holahan, Augusta University

The microbiota in the nose and upper throat likely contains biomarkers for assessing how sick an individual infected with SARS-CoV-2 may get and for developing new treatment strategies to improve their outcome, researchers say.

This nasopharyngeal microbiota is generally considered a frontline protection against viruses, bacteria and other pathogens that enter these natural passageways, says Dr. Sadanand Fulzele, geriatric researcher in the Department of Medicine at the Medical College of Georgia at Augusta University.

Distinct patterns emerged when the researchers examined the microbiota of 27 individuals age 49 to 78 who were negative for the virus, 30 who were positive but had no symptoms, and 27 who were positive with moderate symptoms that did not require hospitalization, they report in the journal *Diagnostics*.

"Millions of people get infected and relatively few of them become symptomatic. This might be one of the reasons," says Dr. Ravindra Kolhe, director of MCG's Georgia Esoteric and Molecular Laboratory, or GEM Lab. which has performed more than 100,000 COVID tests.

The most significant changes were in those who were symptomatic, including about half those patients not having a sufficient amount of microbiota to even sequence, says corresponding author Fulzele.

They were surprised to find these "low reads" of bacteria in the nasopharyngeal cavity of symptomatic individuals versus only two and four individuals in the negative and positive with no symptoms groups, respectively. The vast majority of the positive individuals with no symptoms still had sufficient microbiota, notes first author Kolhe.

"We don't know which came first, the disease or the wipeout of the microbiota," Fulzele says. Runny noses and sneezing might account for the loss, an already significantly lower number of bacterial inhabitants might have increased the individuals' risk for developing these kinds of symptoms, or the virus may have changed the landscape, says Fulzele, who suspects it's the latter.

Based on experience with microbiota in the gastrointestinal tract, Kolhe thinks the different microbiota content and size is another good bet and they both would like a definitive answer. "We don't have sufficient data at this moment," Kolhe says.

They found differences in the type of bacteria as well, although the researchers note that the function of some of the bacteria they found are not well understood.

As the virus' name and nearly two years of experience with it indicate, a major method for transmitting severe acute respiratory syndrome coronavirus 2, or SARS-Cov-2, is when someone coughs, sneezes or even talks, and droplets called aerosols carrying the virus move through the air and into another person's nose or mouth.

Those age 65 and older and/or with underlying health conditions like hypertension and diabetes, are considered at increased risk for hospitalization and death from the infection, so they decided to look at the microbiota in the upper part of the respiratory system called the nasopharynx of older individuals.

The moist, mucus-producing lining of this area works like a natural barrier to invaders and there also is a significant complement of immune cells present, Fulzele says, and their response to respiratory viruses is key.

The area also is abundant with ACE-2 receptors, to which the spiky virus binds, and Kolhe says it's a major landing spot for this virus.

Their new findings indicate that the altered microbiota in the symptomatic patients impacted their immune response to the virus, Kolhe and Fulzele say.

The symptomatic individuals had significantly higher levels of two bacterial species, including Cutibacterium, generally found on the skin and associated with acne but also with heart infection and shoulder infections following surgery. Conversely there was a significantly lower presence of a handful of other, not well-studied bacterium.

The microbiota of both infected groups, symptomatic and asymptomatic, had high levels of bacterium like Cyanobacteria, also called blue green algae, that can be found in contaminated water but is a usual inhabitant of the microbiome in humans which appears to have a role in regulating the immune response. These bacterium typically enter the body through mucosal surfaces, like those in the nose, and are known to cause pneumonia and liver damage. Those who were symptomatic had twice as much of this bacterium as their asymptomatic counterparts.

Fulzele notes that between the asymptomatic and symptomatic there was no significant change in microbiota diversity—just those big differences in volume—but they did see a lot of individual bacterium moving up and down in numbers.

For example, their graph of the number of another water-loving bacterium Amylibacter, looked like stair steps as it moved from negative to positive with symptoms individuals, while there was a downward trend in a handful of other bacterium.

While the relationship between the nasopharyngeal microbiota and the severity of COVID-19 remains unknown, their study indicates a "strong association" between the nasal microbiota, SARS-CoV-2 infection and severity, they write.

Their analysis was done before the current virus variants began to surface, but the researchers say the differences in the microbiota likely will hold for these as well and they have already begun that analysis.

Larger studies are needed to ensure that the clear patterns they found hold, the researchers say. They are putting together a grant application that will enable a larger study and looking for other testing sites who want to be partners. Using the same nasopharyngeal swab used for many COVID tests would enable a microbiota analysis to be done at the same time as testing, they say.

They note the striking contrast that has emerged over nearly two years of experience with the virus, with the majority of those infected being asymptomatic or experiencing mild symptoms like they would with a cold, while others get severe viral pneumonia, require hospitalization and die.

A handful of recent studies have now been published suggesting that the bacterial composition of the nasal canal can have a "drastic" influence on the development of respiratory infections and the severity of symptoms, they write. Some studies have indicated that the nasal microbiota can influence the viral load, immune response and symptoms of a rhinovirus infection, which is responsible for somewhere between 10-40% of common colds.

A myriad of other conditions like inflammatory bowel syndrome, peptic ulcers and viral diseases have been linked to significant changes in the microbiota of the gut, nasal and oral cavity, they write.

Diversity of bacterium in the microbiota is generally a good thing, and it's something that naturally decreases with age, says Fulzele, and also can be harmed by habits like smoking and improved by those like eating a diverse diet.

More information: Ravindra Kolhe et al, Alteration in Nasopharyngeal Microbiota Profile in Aged Patients with COVID-19, *Diagnostics* (2021). DOI: 10.3390/diagnostics11091622

Provided by Medical College of Georgia at Augusta University

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