Make-up of gut microbiome may influence COVID-19 severity and immune response

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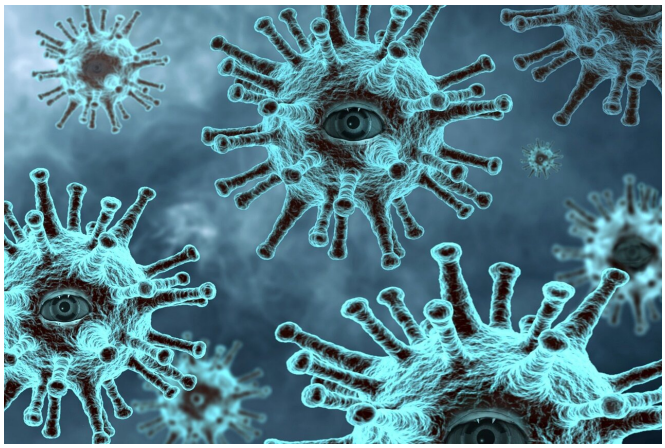

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The variety and volume of bacteria in the gut, known as the microbiome, may influence the severity of COVID-19 as well as the magnitude of the immune system response to the infection, suggests research published online in the journal *Gut*.

Imbalances in the make-up of the microbiome may also be implicated in persisting inflammatory symptoms, dubbed 'long COVID', the findings suggest.

COVID-19 is primarily a respiratory illness, but the evidence suggests that the gut may also have a role.

As the gut is the largest immunological organ in the body and its resident microbes are known to influence immune responses, the researchers wanted to find out if the gut microbiome might also affect the immune system response to COVID-19 infection.

They therefore obtained blood and stool samples and medical records from 100 hospital inpatients with laboratory-confirmed COVID-19 infection between February and May 2020 and from 78 people without COVID-19 who were taking part in a microbiome study before the pandemic.

The severity of COVID-19 was classified as mild in the absence of X-ray evidence of pneumonia; moderate if pneumonia with fever and respiratory tract symptoms were detected; severe if patients found it very difficult to breathe normally; and critical if they needed mechanical ventilation or experienced organ failure requiring intensive care.

To characterise the gut microbiome, 41 of the COVID patients provided multiple stool samples while in hospital, 27 of whom provided serial stool samples up to 30 days after clearance of SARS-CoV-2, the virus responsible for COVID-19.

Analysis of all 274 stool samples showed that the make-up of the gut microbiome differed significantly between patients with and without COVID-19, irrespective of whether they had been treated with drugs, including antibiotics.

COVID patients had higher numbers of Ruminococcus gnavus, Ruminococcus torques and Bacteroides dorei species than people without the infection.

And they had far fewer of the species that can influence immune system response, such as Bifidobacterium adolescentis, Faecalibacterium prausnitzii and Eubacterium rectale.

Lower numbers of F. prausnitzii and Bifidobacterium bifidum were particularly associated with infection severity after taking account of antibiotic use and patient age.

And the numbers of these bacteria remained low in the samples collected up to 30 days after infected patients had cleared the virus from their bodies.

COVID-19 infection prompts the immune system to produce inflammatory cytokines in response. In some cases, this response can be excessive ('cytokine storm'), causing widespread tissue damage, septic shock, and multiorgan failure.

Analysis of the blood samples showed that the microbial imbalance found in the COVID patients was also associated with raised levels of inflammatory cytokines and blood markers of tissue damage, such as C-reactive protein and certain enzymes.

This suggests that the gut microbiome might influence the immune system response to COVID-19 infection and potentially affect disease severity and outcome, say the researchers.

"In light of reports that a subset of recovered patients with COVID-19 experience persistent symptoms, such as fatigue, dyspnoea [breathlessness] and joint pains, some over 80 days after initial onset of symptoms, we posit that the dysbiotic gut microbiome could contribute to immune-related health problems post-COVID-19," they write.

This is an observational study, and as such, can't establish cause, added to which the gut microbiome varies widely among different populations, so the changes observed in this study may not be applicable to other COVID patients elsewhere, caution the researchers.

But they point to mounting evidence showing that gut microbes are linked to inflammatory diseases within and beyond the gut.

And they conclude: "Bolstering of beneficial gut species depleted in COVID-19 could serve as a novel avenue to mitigate severe disease, underscoring the importance of managing patients' gut microbiota during and after COVID-19."

More information: Gut microbiota composition reflects disease severity and dysfunctional immune responses in patients with COVID-19, *Gut* (2021). DOI: 10.1136/gutjnl-2020-323020