Chinese study finds association between viral persistence and Long COVID

Bill Shaw
22 May 2024

A study by Chinese researchers has found the strongest evidence yet of an association between persistence of the SARS-CoV-2 virus and Long COVID. Not only was the presence of virus in tissues associated with the development of Long COVID, but the risk of Long COVID increased with greater quantities of the virus present.

Significantly, the study collected multiple, serial specimens from adult patients after a documented SARS-CoV-2 infection. This feature differentiates the study from prior work, providing the advantage of tracking viral presence and symptoms in individual patients over time. Prior studies were limited to assessing patients at a single point in time.

The study collected tissue specimens and data from 225 patients treated at the China-Japan Friendship Hospital in Beijing between January and April of 2023. Notably, this study occurred when the Omicron BA.5 variant was overwhelmingly predominant in China.

The patients all met the criteria for mild COVID and were seen at the hospital for other reasons besides COVID. Many patients were additionally scheduled for various procedures that either involved tissue sampling or provided easy ability to collect samples, including gastroscopy (examination of the stomach through a fiberoptic endoscope) and surgery.

The tissue specimens came from known sites of SARS-CoV-2 persistence based on prior studies. They included gastric mucosa samples and residual surgical samples from the lung, skin, intestine, blood vessels, kidney, breast, thyroid, liver, brain, pancreas, gall bladder, and appendix.

Initial collection occurred one month after infection as determined by a positive polymerase chain reaction (PCR) or lateral flow test. Subsequent collection of the same tissues occurred at two months and four months after infection.

Notably, the researchers excluded patients whose SARS-CoV-2 test remained positive at the time of first tissue collection at one month. This feature of the study ensured that symptoms were due to Long COVID and not an ongoing or repeat infection.

The World Health Organization defines Long COVID symptoms as new symptoms beginning three months after infection or later, or symptoms associated with the infection that increase in severity and persist for two months with no other explanation. Accordingly, the researchers assessed patients' symptoms at four months post-infection by telephone.

Of the 225 patients initially enrolled, 213 (95 percent) participated in the four-month follow-up telephone survey and thus were included in the analysis. Of the 213, 72 (34 percent) had at least one Long COVID symptom. Of the 177 patients who received three doses of a COVID-19 vaccine, 56 (32 percent) had at least one Long COVID symptom at four months. Of the other 36 patients, 16 (44 percent) developed Long COVID. Consistent with previous research, fatigue was the most common symptom, afflicting 21 percent of patients with Long COVID.

The percentage of tissue specimens testing positive for the virus progressively declined over time. At one month post-infection, 30 percent of specimens were positive, at two months 27 percent were positive, and at four months 11 percent were positive. The five tissues with the highest percentage of specimens testing positive, in decreasing order, were liver, stomach, intestine, brain, and kidney.

The study also quantified the amount of virus, or viral load, in tissues. Since many of the patients were cancer patients, the researchers compared the quantity of virus in tumor tissue and tissue surrounding the tumor or "paratumor" tissue. The hypothesis was that immune dysregulation in tumor tissues might result in higher viral load. However, the study found no difference in viral load between tumor and paratumor tissues.

Similarly, the researchers hypothesized that the quantity of ACE2 receptors in tissues—known to be significant binding sites on cells for viral entry—might be associated with viral load. And again, they found no significant differences.

The researchers were able to fully sequence the viral genome for a single specimen from the lung of a single participant. This result showed the virus to be SARS-CoV-2 variant BA.5.2, consistent with the vast predominance of

Omicron BA.5 in China at the time.

The reason the researchers could sequence the genome of the virus from this specimen was that the viral load was particularly high. To investigate why, they performed analysis of the genome of the lung cells in the specimen, finding a mutation in gene DNAAF2. Although this mutation has not been previously reported, other mutations in DNAAF2 are known to be associated with ciliary dysmotility (inability of the cilia, the hair-like structures on the outside of cells, to move properly).

Electron microscopy of the specimen confirmed abnormalities of the cilia. Thus, poor ciliary motility leading to poor viral clearance was a likely cause of this participant's high viral load.

To investigate the hypothesis of other researchers that viral persistence occurs in blood in patients with blood cell disorders including hematologic malignancies, the researchers collected blood specimens from 9 participants with blood disorders and 10 volunteers (who were also study participants) at two-months post infection. In the participants with blood disorders, they found viral persistence in blood plasma in 3 (33 percent), in white blood cells in one (11 percent), and in peripheral blood mononuclear cells in one (11 percent). In the volunteers without blood disorders, the researchers did not detect any viral persistence. This result provides significant evidence for the hypothesis that individuals with blood disorders have difficulty clearing virus from their blood.

The researchers classified the participants with persistent virus into three categories based on viral load, high virus, medium virus, and low or no virus. Then they calculated a "positive ratio" as the number of tissues in each category from Long COVID participants by the total number of tissues in the category. Across all specimens, this ratio was considerably higher in the medium and high virus groups (60-100 percent) than the low or no virus groups (30-40 percent).

Finally, the researchers looked at gene regulation in lung and blood vessel tissues with viral persistence. They found that genes in lung tissues involved in immune response were downregulated, suggesting these patients had impaired immune response to clear the virus from their lungs. In blood vessels, they found dysregulation of genes involved in coagulation and lipid metabolism.

Overall, the results provide significant new evidence that viral persistence is associated with Long COVID and that the quantity of virus remaining in tissues is associated with the risk of developing Long COVID. It is important to emphasize that the researchers studied patients with mild COVID-19 disease. These were not patients with severe symptoms or who died or who were hospitalized for COVID-19.

Despite having mild COVID-19 and an overall complete vaccination rate of 83 percent, 34 percent of patients developed Long COVID.

The study design addresses many limitations of prior studies, especially that most prior studies were conducted on autopsy specimens from patients who died from COVID-19. The prior studies that did include living patients recovered virus from respiratory and stomach specimens and thus were not able to look at the diverse array of solid organ specimens that this study examined.

The study was also able to address prior conjectures on blood disorders as well as identify potential mechanisms of how viral persistence leads to Long COVID symptoms. The mechanism appears to be disruption of host cell functions, although future research is needed to confirm this finding.

The study confirms the dangerousness of the SARS-CoV-2 virus and thus the criminality of the ruling class who made a conscious, deliberate decision to let the virus spread indiscriminately throughout the entire human population. The dereliction of duty to protect the public's health by implementing well-known public health best practices developed over centuries is inexcusable.

It serves as further confirmation that capitalism is inconsistent with protecting human health and even survival in the face of the current COVID-19 pandemic and the increasing threat of future pandemics. Even now, the H5N1 avian influenza virus has adapted to multiple mammal species including cows, dolphins, sea lions, seals, minks, grizzly bears, coyotes, and red foxes. And yet the Centers for Disease Control is hardly taking seriously the threat of adaptation to humans with human-to-human transmission.

The working class must replace capitalism with a socialist program that prioritizes human health and needs over private profit. Otherwise, humanity will remain highly vulnerable to the ravages of pandemic viruses such as SARS-CoV-2 and emerging threats such as H5N1.