



Research Assistant Florence Chioh and Assistant Professor Christine Cheung analysing the data from 30 blood samples of recovered COVID-19 patients. (Photo: NTU Singapore)

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SINGAPORE: People who have recovered from COVID-19, especially those with pre-existing cardiovascular conditions, may be at risk of developing blood clots due to a lingering and overactive immune response, a Singapore study has found.

The study, led by Nanyang Technological University (NTU) scientists, investigated the possible link between COVID-19 and an increased risk of blood clot formation, shedding light on the medium- and long-term consequences of infection, or “long-haul COVID”, NTU said in a news release on Tuesday (Apr 13).

The team collected and analysed blood samples from 30 COVID-19 patients about a month after they had recovered from the infection and were discharged from hospital.

In findings published in the peer-reviewed scientific journal eLife in March, researchers found signs of blood vessel damage in all 30 patients, possibly from a lingering immune response, which may trigger the formation of blood clots.

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"The findings may help to explain why some people who have recovered from COVID-19 exhibit symptoms of blood clotting complications after their initial recovery," said NTU.

"In some cases, they are at increased risk of heart attack, stroke or organ failure when blood clots block major arteries to vital organs."

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NTU's Assistant Professor Christine Cheung, who led the study, said: "With more people recovering from COVID-19, we started hearing from clinicians about patients returning with blood clotting issues after they had been discharged and cleared of the virus.

"This makes a strong case for the close monitoring of recovered COVID-19 patients, especially those with pre-existing cardiovascular conditions like hypertension and diabetes who have weakened blood vessels."

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The scientists found that recovered COVID-19 patients had twice the normal number of circulating endothelial cells (CECs) that had been shed from damaged blood vessel walls.

The elevated levels of CECs indicate that blood vessel injury is still apparent after recovering from viral infection.

The recovered COVID-19 patients continued to produce high levels of cytokines – proteins produced by immune cells that activate the immune response against pathogens – even in the absence of the virus.

"Unusually high numbers of immune cells, known as T cells, that attack and destroy viruses were also present in the blood of recovered COVID-19 patients," said NTU.

The presence of both cytokines and higher levels of immune cells suggest that the immune systems of recovered COVID-19 patients remained activated even after the coronavirus was gone from the patient.

These "persistently activated immune responses" may attack the blood vessels of recovered COVID-19 patients, causing even more damage and increasing the risk of blood clot formation further, the researchers said.

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Explaining how blood vessel damage may cause the formation of blood clots, NTU research assistant Florence Chioh said: "While COVID-19 is mainly a respiratory infection, the virus may also attack the linings of blood vessels, causing inflammation and damage.

"Leakage from these damaged vessels triggers the formation of blood clots that may result in the sort of complications seen in the patients during hospitalisation."

 These findings could inform guidelines for post-hospitalisation care of COVID-19 patients who might be susceptible to "long-haul COVID" symptoms, said the research team. For hospitalised patients, the World Health Organization recommends the use of low dose anticoagulants to prevent blood clots from forming in blood vessels.

"Those with cardiovascular conditions need to be more cautious since their underlying conditions already weaken their vascular systems," said Asst Prof Cheung.

"It's a double blow with COVID-19. As we gain greater understanding of complications COVID 'long-haulers' face, there is hope to encourage vaccine take-up rate to protect oneself from both the virus and its long-term complications."

The team comprised researchers from NTU, the Agency for Science, Technology and Research's (A\*STAR) Singapore Immunology Network, and the National Centre of Infectious Diseases.

One of the co-authors Professor Lisa Ng, executive director of A\*STAR Infectious Diseases Labs, said: "We found that COVID-19 patients with vascular complications have a higher frequency of T cells, which may in turn attack the blood vessels. Preventive therapy may be needed for these patients."

The team is now investigating the longer-term effects of COVID-19 in patients who have recovered from the infection for at least six months or longer, NTU said.

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