Comparison of coronavirus antibody tests revealed too optimistic claims

December 3 2020

Comparison of coronavirus antibody tests revealed too optimistic claims (illustrative photo). Credit: Pixabay.com

A study by University of Tartu researchers indicates that the sensitivity of tests used to detect viral antibodies in a blood sample may differ significantly. The combination of several tests may give the best result.

At the onset of COVID-19 symptoms, first, the nasopharyngeal swab is taken to verify the presence of the virus. But if the aim is to determine whether an asymptomatic person has been in contact with the virus or, vice versa, to know which acute disease the person recently suffered from, a test detecting antibodies in a blood sample comes helpful.

Antibodies are produced in the human body as a counter to viral proteins to prevent the virus from replicating and spreading in the body. Usually, it takes a couple of weeks after infection for the antibodies to emerge. Different parts of the virus induce the development of different antibodies. In the case of coronavirus, for instance, there can be antibodies against the spike protein of the virus, against the proteins of the receptor binding domains as well as against the nucleocapsid.

Different types of antibodies are produced, but the IgG antibodies stay in the body for the longest. "When we ever suffer from a disease, usually the IgG antibodies are the ones to stay in our body," explained Epp Sepp, Senior Research Fellow in Medical Microbiology at the University of Tartu, one of the authors of the article published in *PLOS One*.

One use for tests detecting viral antibodies in a blood sample is in large studies trying to ascertain the percentage of the population that has been exposed to the virus. This was also done in spring in the pilot seroepidemiological study in Estonia led by the University of Tartu.

To detect antiviral antibodies, tests are used that reveal the presence of antibodies to different proteins or their combinations. There are now hundreds of coronavirus antibody tests, which, unfortunately, are not universally suitable for all patients.

Test sensitivity varies significantly

The study was conducted in cooperation between the University of Tartu, Synlab and Kuressaare Hospital in Saaremaa (Saaremaa is the island in Estonia with the biggest corona outbreak during the first virus wave—editor remark). In the study nine coronavirus antibody tests that were most widely used during the outbreak in spring were analyzed. Seven of them were by major producers and two were laboratory tests developed at the University of Tartu by the research group led by

Professor Pärt Peterson.

The study involved 97 patients from Saaremaa with a confirmed case of COVID-19. The IgG antibodies to coronavirus were determined by nine tests and the test results were compared based on the patients' symptoms (cough, headache, tiredness, difficulty breathing, diarrhea, etc.) and the time between the onset of the disease and the antibody test. The majority of studied patients had COVID-19 symptoms, except for about one fifth of them.

The study revealed that in general, the sensitivity of the tests was lower than the producers had stated. As was expected, the rapid test included in the study at the request of the Health Board had the lowest sensitivity.

In half of the patients, all nine antibody tests gave a positive result. In two patients, none of the tests detected coronavirus antibodies. This implies that antiviral antibodies might not even emerge in some COVID-19 patients. For the rest of the patients, the test results varied. Analysis of the correlation of the results indicated that in some patients, the prevailing antibodies were those against the nucleocapsid while in others antibodies against the spike protein prevailed.

Finding a reliable combination is crucial

Some tests worked equally well for asymptomatic patients and those with many symptoms. In the case of some tests, the results were highly dependent on the time of taking the sample and the number of symptoms. For instance, for some tests, the positivity rate in asymptomatic COVID-19 cases was about two times lower than in polysymptomatic ones. The best diagnostic sensitivity in detecting antibodies was achieved by combining several antibody tests, for instance, a test detecting antibodies to the spike protein with the test detecting antibodies to the nucleocapsid.

"In the everyday work of Synlab, we are using the Abbott test that is sensitive to antibodies to the nucleocapsid. If that gives a borderline negative result in a patient, we will analyze this sample again using another test sensitive to antibodies to the spike protein. If the result is positive, we will trust that. My experience has shown that antibodies to the nucleocapsid disappear faster and antibodies to the spike protein last for longer," explained the lead author of the study Paul Naaber, Senior Research Fellow in Medical Microbiology at the University of Tartu.

According to researchers, there is no one perfect test that works well in all cases. To get the most reliable result, the tests may need to be combined. "This is a very important piece of knowledge for planning major seroepidemiological studies. Our analysis showed that had we relied solely on the information written on the package by the producer, the studies in which the tests were used could have led to a completely different result. In spring, only a few published studies had compared tests, so we took it upon ourselves. Objective measurements indicate that test sensitivity may be significantly lower than stated on the package," Naaber explained.

More information: Paul Naaber et al. Evaluation of SARS-CoV-2 IgG antibody response in PCR positive patients: Comparison of nine tests in relation to clinical data, *PLOS ONE* (2020). DOI: 10.1371/journal.pone.0237548

Provided by Estonian Research Council