Still much to learn about the diagnostic role of SARS-CoV-2 antibody detection

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Dear Editor,

we read with interest the work by Zhao et al. [1] investigating the dynamics of antibody response in COVID-19 patients. The authors found that 161 (93.1%) of 173 patients included in the study tested positive for total antibodies against SARS-CoV-2, with a sensitivity starting to raise one week after the onset of symptoms. Based on these findings, the authors stated that antibody testing may be helpful to supplement the RT-PCR based SARS-CoV-2 RNA detection, which is still the gold standard for COVID-19 diagnosis. Interestingly, total antibodies had a median seroconversion time shorter than those of IgM and IgG antibodies (11 days vs 12 and 14 days, respectively), and were potentially related to disease severity (their titer peaked sooner in patients with more severe COVID-19 forms).

Unfortunately, the authors reported that the antibodies' increases were not always accompanied by viral RNA clearance, suggesting that antibodies may not be sufficient to clear the virus. This is a major concern for clinicians worldwide because of cases of patients with COVID-19 recurrence reported until now [2]; in our opinion, neutralizing antibody titers would be determined as an optimal diagnostic strategy against SARS-CoV-2 infection. an.

Furthermore, differences in sensitivity across the three groups of antibodies (i.e., total, IgM, and IgG) detected by Zhang et al. are probably attributable to the presence of the IgA in the total antibody group. It has been observed that secretory IgA antibodies are very effective in defending against respiratory infections [3], as well as previous studies on SARS-CoV have shown similar kinetics of IgA, IgM, and IgG [4,5], making IgA detection an attractive option as a specific diagnostic marker; hence, a dedicated focus on the kinetics and clinical sensitivity of SARS-CoV-2 IgA is warranted.

Again, the high variability of antibody sensitivities observed in this study is a bit surprising: total antibody titer goes from 38.3% to 89.6%, in a few days, with IgM titers also going from 28.7% to 73.3%. Given the nature of the study and the goal of evaluating the clinical usefulness of antibodies, regular measurements (7, 14, 21 days, etc.) would have been desirable.

Finally, according to the inclusion criteria claimed by the authors, only patients with a positive result for SARS-CoV-2 RNA were included; however, this is in apparent disagreement with the data reported in Table 2that only 112 (64.7%) of 173 have a RT-PCR positive result. In particular, only 58 (33%) of 173 patients have a positive result in the first week from the symptoms' onset, a somewhat underwhelming result considering that RT-PCR can remain positive even for several weeks.

In conclusion, we agree with Zhang et al. that more studies are necessary to assess the reliability of serological tests to routinely diagnose patients with COVID-19, and that these studies need to be carefully designed and specifically addressed to define the role of secretory IgA against the SARS-CoV-2.

Funding

This study was conducted as part of our routine work.

Transparency declaration

A.B. reports personal fees from Gilead Sciences and Janssen, and non-financial support from Bristol-Myers Squibb and Viiv Healthcare, outside the submitted work. M.S. reports grants from Gilead Sciences, Merck, and Pfizer, and advisory board/meeting participation for Gilead Sciences, Merck, and ThermoFisher Scientific, outside the submitted work. S.D. reports personal fees from Gilead Sciences, Janssen Cilag, Viiv Healthcare, and BMS, outside the submitted work. All other authors declare no competing interests.

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