

LETTER TO THE EDITOR

What is the long-term clinical significance of anti-SARS-CoV-2-specific IgG?

To the Editor:

We read with great interest the article “Clinical significance of SARS-CoV-2-specific IgG detection with a rapid antibody kit for COVID-19 patients” by Chong et al¹. The manuscript discusses the possible implications of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)-specific Immunoglobulin G (IgG) production and the concomitant positivity in SARS-CoV-2 detection by polymerase chain reaction (PCR) in asymptomatic and symptomatic patients. This study raises some interesting questions, and we would like to humbly state a few points about the possible long-term implications of these results.

SARS-CoV-2-infected patients may or may not have symptoms. Individuals that present symptoms can range from mild to severe respiratory and systemic disease, named coronavirus disease-2019 (COVID-19).²

Patients infected with SARS-CoV-2 can generate high titers of SARS-CoV-2-specific antibody isotypes, such as IgA, IgG, and IgM.² Reports have detected IgG production between 5 and 9 days after infection.^{1,3,4} Nevertheless, patients with some comorbidities, such as HIV, can present a delayed immune response against SARS-CoV-2, with detectable anti-SARS-CoV-2 immunoglobulin only after 60 days after the infection.⁵

Anti-SARS-CoV-2 IgG may block and neutralize SARS-CoV-2 and prevent COVID-19 development.^{6,7} However, studies clearly demonstrated that the presence of anti-SARS-CoV-2 IgG does not indicate viral clearance.^{1,8} Nevertheless, a report by Long et al⁴ verified that moderate and severe COVID-19 patients present a distinct IgM and IgG production course. Severe patients develop IgG seroconversion earlier in relation to moderate patients.⁴ Another report by Ko et al,⁹ identified that asymptomatic and mild patients produce less neutralizing antibodies in relation to severe COVID-19 patients.

The ability to prevent the re-infection of anti-SARS-CoV-2 IgG produced after a natural infection by SARS-CoV-2 is yet to be determined. Therefore, we hypothesize that the severity of the initial infection may influence the anti-SARS-CoV-2 antibody production and its viral elimination efficacy.

In addition, a few confirmed cases of re-infection have been reported.¹⁰⁻¹² The two main hypotheses would be a mutation or

different SARS-CoV-2 strain¹⁰ or a reduction in the levels of anti-SARS-CoV-2 antibodies.¹³

A previous report on SARS-CoV-1 infection verified that after the viral clearance, patients remained positive with detectable titers of anti-SARS-CoV-1 IgG for a year.¹⁴ Chong et al¹ verified a patient IgG-positive over 30 days after infection; nevertheless, a recent report verified a rapid reduction in anti-SARS-CoV-2 IgG in 90 days after the viral clearance.¹³

The overlap of anti-SARS-CoV-2 IgG and the detection of SARS-CoV-2 by polymerase chain reaction in nasopharyngeal and/or oropharyngeal swab samples indicate that those individuals may be able to transmit the virus. In addition to the possible rapid decay in anti-SARS-CoV-2 IgG, this could lead to re-infection and an infectious loop in the overall population.

Another possible implication is antibody-dependent enhancement (ADE), which could facilitate the SARS-CoV-2 infection and make a secondary infection worst. This mechanism of infection has been described for SARS-CoV-1¹⁵ and could represent an important factor in the development of treatments for COVID-19.

Therefore, the clinical long-term implications of anti-SARS-CoV-2 IgG need to be further investigated, with a longitudinal investigation on antibody titers, especially in asymptomatic and mild COVID-19 patients, to assess whether a natural infection can provide long-term protection against SARS-CoV-2.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

AUTHOR CONTRIBUTIONS

Gabriela Gama Freire Alberca: Conceptualization (supporting); Validation (equal); Visualization (equal); Writing-original draft (supporting); Writing-review & editing (supporting). **Ricardo Wesley Alberca:** Conceptualization (lead); Supervision (lead); Visualization (lead); Writing-original draft (equal); Writing-review & editing (equal).

FUNDING INFORMATION

Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) Grant: 19/02679-7.



The peer review history for this article is available at <https://publons.com/publon/10.1111/irv.12825>.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available in the referenced material of this article.


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