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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 al[1] 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 titters 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 clearence.[1,8] Nevertheless, a report by Long et al[4] 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 strain[10] 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 al[1] 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-1[15] 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).

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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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## REFERENCES

1. Chong Y, Ikematsu H, Tani N, et al. Clinical significance of SARS-CoV-2-specific IgG detection with a rapid antibody kit for COVID-19 patients. *Influenza Other Respi Viruses*. 2020:1–6. https://doi.org/10.1111/irv.12802
2. Yu HQ, Sun BQ, Fang ZF, et al. Distinct features of SARS-CoV-2-specific IgA response in COVID-19 patients. *Eur Respir J*. 2020;56:200156.
3. Lee YL, Liao CH, Liu PY, et al. Dynamics of anti-SARS-Cov-2 IgM and IgG antibodies among COVID-19 patients. *J Infect*. 2020;81(2):e55-e58.
4. Long QX, Liu BZ, Deng HJ, et al. Antibody responses to SARS-CoV-2 in patients with COVID-19. *Nat Med*. 2020;26(6):845-848.
5. Wang M, Luo L, Bu H, Xia H. One case of coronavirus disease 2019 (COVID-19) in a patient co-infected by HIV with a low CD4+ T-cell count. *Int J Infect Dis*. 2020;96:148-150.
6. Wang C, Li W, Drabek D, et al. A human monoclonal antibody blocking SARS-CoV-2 infection. *Nat Commun*. 2020;11:2251.
7. Ju B, Zhang Q, Ge J, et al. Human neutralizing antibodies elicited by SARS-CoV-2 infection. *Nature*. 2020;584:115-119.
8. Lei H, Ye F, Liu X, et al. SARS-CoV-2 environmental contamination associated with persistently infected COVID-19 patients. *Influenza Other Respi Viruses*. 2020;14:688-699.
9. Ko J-H, Joo E-J, Park S-J, et al. Neutralizing antibody production in asymptomatic and mild COVID-19 patients, in comparison with pneumonic COVID-19 patients. *J Clin Med*. 2020;9:2268.
10. To KK-W, Hung IF-N, Ip JD, et al. COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing. *Clin Infect Dis*. 2020. online ahead of print.
11. Larson D, Brodniak SL, Voegtly LJ, et al. A case of early re-infection with SARS-CoV-2. *Clin Infect Dis*. 2020. online ahead of print.
12. Fernandes Valente Takeda C, Moura de Almeida M, de Aguiar G, et al. Case report: recurrent clinical symptoms of COVID-19 in healthcare professionals: a series of cases from Brazil. *Am J Trop Med Hyg*. 2020. online ahead of print.
13. Ibarrondo FJ, Fulcher JA, Goodman-Meza D, et al. Rapid decay of Anti-SARS-CoV-2 antibodies in persons with mild Covid-19. *N Engl J Med*. 2020;383(11):1085-1087.
14. Chang SC, Wang JT, Huang LM, et al. Longitudinal analysis of severe acute respiratory syndrome (SARS) coronavirus-specific antibody in SARS patients. *Clin Diagn Lab Immunol*. 2005;12:1455-1457.
15. Yang ZY, Werner HC, Kong WP, et al. Evasion of antibody neutralization in emerging severe acute respiratory syndrome coronaviruses. *Proc Natl Acad Sci USA*. 2005;102(3):797-801.