

Patients With Several Clinical Presentations By SARS-CoV2 Showed A Dramatic Decrease Of Antibodies.

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Short report

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Abstract

There are many doubts about the SARS-CoV-2 immune response's length, and it is unknown whether those patients may exhibit different kinetics in the secretion of IgG anti-SARS-CoV2 according to the severity of their infection. This research aimed to evaluate IgG antibodies' kinetics and persistence against the SARS-CoV-2 Spike protein in a group of COVID-19 patients with different clinical disease presentations in the Colombian Caribbean region. Two blood samples were taken. The first one was at the first surge in August 2020; the second was six months later, February 2021. The study showed a decrease of 61.1% in their median of IgG antibodies after six months ($P > 0.0001$). According to the clinical form of COVID-19, the patients that required hospitalization (moderate or severe) COVID-19 showed a lower secretion of IgG against SARS-CoV2 and a higher negative seroconversion for IgG 69.2% in the second serological evaluation ($P < 0.05$). Thus, the drop of antibodies-SARS-CoV-2 is typical in all the clinical forms of COVID-19. It is worrisome in patients with moderate or severe clinical forms. The evaluation of natural immunity is mandatory to define the vaccination strategy mainly in patients that suffered complicated forms of COVID-19.

Highlights

- Reduction of IgG anti-SARS-CoV-2 is part of the immune dynamic of this infection.
- 69.2% of patients with a moderate or severe form of COVID-19 have a negative seroconversion after six months.
- The individual evaluation of natural immunity is mandatory to define the vaccination in patients that suffered complicated forms of COVID-19.

Introduction

The Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causal agent of coronavirus disease 2019 (COVID-19), has infected more than 100 million people worldwide (<https://coronavirus.jhu.edu/map.html>). Currently, there are many concerns about the SARS-CoV-2 immune response's length (i.e., the kinetics of antibodies against this virus), and these doubts have emerged in subjects who have been diagnostic with COVID-19 in different forms of this disease. Besides, it is unknown whether in COVID-19 patients with different grades of severity have changes in their immune response's length. Therefore, this research aimed to evaluate IgG antibodies' kinetics and persistence against the SARS-CoV-2 Spike protein in a group of COVID-19 patients with different severity grades in the Colombian Caribbean region.

A cross-sectional study was carried out in 65 patients with COVID-19 by RT-qPCR. The disease's severity was defined by the following criteria (1, 2): A) Asymptomatic: case laboratory-confirmed infected person. B) Mild disease: local symptoms in the upper respiratory tract and may present with non-specific symptoms such as fever, pain muscle, or general discomfort. C) Moderate disease: clinical or radiological evidence of lower respiratory infection, with compatible lung images and O₂ saturation > 93%; and (D)

Severe disease: respiratory rate greater than 30/min, oxygen saturation < 93%, PAFI (the relationship between arterial oxygen pressure and the inspired fraction of oxygen (PaO_2 / FIO_2) less than 300, infiltrates greater than 50%.

Patients underwent the first evaluation of IgG antibodies against the SARS-CoV-2 Spike protein in August 2020, and the second measurement of these antibodies was performed six months later). Antibodies were evaluated by Elisa fluorescent ELFA (Enzyme-Linked Fluorescent Assay) using the commercial VIDAS® SARS-COV-2 IgG kit from biomérieux (3). Statistical analysis was performed using the software GraphPad Prisma 8 and Statistical Package for the Social Sciences version 27 (SPSS), and statistical comparisons were made through the Wilcoxon test and the McNemar test. Written informed consent was obtained from all study participants. The institutional ethics review boards at the Biological Research Institute of the Tropics (IIBT) and the IMAT Clinic approved the study design.

Most of the patients in whom antibodies were evaluated were women (55.4%), with a median age of 43 years (IQR: 28–57), and 20% required hospitalization. In the first serological evaluation, all the patients seroconverted to IgG against the spike-SARS-CoV-2. The second serological evaluation, conducted after six months, showed that 78.5% of patients persisted with IgG detectable antibodies. However, these individuals showed a decrease of 61.1% in their median of IgG antibodies in their second serological evaluation ($P > 0.0001$). (Fig. 1A-B).

On the other hand, we evaluated the kinetics of IgG according to the grading of severity of COVID-19. The patients with moderate or severe COVID-19 showed a higher negative seroconversion for IgG 69.2% in comparison of asymptomatic (20%) or mild COVID-19 (5.4%), and this difference was statically significant ($P < 0.05$). Furthermore, it is essential to mention that is negative seroconversion was observed in young patients median age 33 years old (Fig. 2A-B).

Regarding the index of IgG antibodies against spike, we observed in the first serological evaluation a lower IgG index in patients with moderate or severe COVID-19 than in asymptomatic or mild forms of this disease ($P < 0.05$). However, to compare the first and second serological evaluations, we showed a significant decrease of IgG anti spike index in all the groups evaluated ($P > 0.0001$). This IgG reduction was 58.3% in asymptomatic individuals, 70.48% in mild COVID-19, and 86.15% moderate or severe COVID-19 (Fig. 2A-B).

Our findings of a drastic reduction of IgG antibodies against SARS-CoV-2 after six months agree with Wang et al. and Zheng et al. (4, 5). They showed that in individuals with COVID-19, there was a significant reduction in IgG titers against SARS-CoV-2 after three months. A biological explanation for this phenomenon is likely due to the plasma cell's memory induced by SARS-CoV-2, which cannot remain viable in hematopoietic niches and secondary lymphoid organs. This could be secondary to the SARS-CoV-2 antigens removal, preventing their re-exposure to memory cells, promoting apoptosis, and eliminating these cells a few months after infection (6).

On the other hand, the lower expression of IgG antibodies against SARS-CoV2 in patients with moderate or severe COVID-19 observed in these serological evaluations could be related to alterations in the cellular immune response mainly in the Th1 effector pattern compromise the transformation of B cells to IgG-secreting plasma cells with neutralizing activity against SARS-CoV2. Furthermore, this finding may motivate a discussion about whether people require vaccination schedules identical to those not exposed to SARS-CoV-2. Based on our results, prior infected individuals who demonstrate a negative seroconversion must receive a complete vaccination schedule, even in those who suffered complicated forms of COVID-19. An incomplete immunization could expose them to reinfection, and they will likely return with torpid clinical pictures or exhibit fatal outcomes. Thus, it is critical to prioritize these patients, especially those with risk factors for severe COVID-19.

The reduction of antibodies against SARS-CoV-2 is a reality that appears in all spectrums of this disease. However, this decreased IgG in the moderate and severe forms of COVID-19 is worrisome, given that, after six months, these patients have a higher probability of losing their natural immunity against this new virus. Therefore, timely prioritization of vaccination should be given in this group of people who have seronegative and have comorbidities since it would put their lives and public health efforts to control the circulation of SARS-CoV-2 at risk. It is crucial to evaluate the adaptive immune response behavior in this condition with a more significant number of naturally infected participants and even those who have been vaccinated using different vaccine platforms against this virus.

Declarations

Conflicts of interest. The authors declare no conflict of interest applicable to this research.

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Ethical considerations. This research was approved by the ethics and research committee of IMAT-Oncomédica S.A and Biological Research Institute of the Tropics (IIBT).

Data availability statement. The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation, to any qualified researcher.

Authors' contributions. SM, MG designed the study. Participants in this study were evaluated by JM, JB, MG, KHM. The lab protocol was standardized and performed by EG, KG. The data analysis was performed by HSC, BGP. The manuscript was written by HS, SM. The critical review was performed by BG; MG, JB, JM. All authors read and approved the manuscript.

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References

1. Saavedra Trujillo C. Consenso colombiano de atención, diagnóstico y manejo de la infección por SARS-COV-2/COVID-19 en establecimientos de atención de la salud Recomendaciones basadas en consenso de expertos e informadas en la evidencia [Internet]. 2020. Available from: <http://www.revistainfectio.org/index.php/infectio/article/view/851/896>.
2. World Health Organization. Clinical management of COVID-19 [Internet]. 2020. Available from: <https://www.who.int/publications/i/item/clinical-management-of-covid-19>.
3. BIOMÉRIEUX. VIDAS®. SARS-COV-2 IgG [Internet]. 2020. Available from: <https://www.fda.gov/media/140937/download>.
4. Wang Y, Li J, Li H, Lei P, Shen G, Yang C. Persistence of SARS-CoV-2-specific antibodies in COVID-19 patients. *Int Immunopharmacol*. 2021 Jan;90:107271.
5. Zheng Y, Zhang Q, Ali A, Li K, Shao N, Zhou X, et al. Sustainability of SARS-CoV-2 Induced Humoral Immune Responses in COVID-19 Patients from Hospitalization to Convalescence Over Six Months. *Virol Sin*. 2021 Mar 4.
6. Krueger CC, Thoms F, Keller E, Vogel M, Bachmann MF. Virus-Specific Secondary Plasma Cells Produce Elevated Levels of High-Avidity Antibodies but Are Functionally Short Lived. *Front Immunol*. 2019;10:1831.

Figures

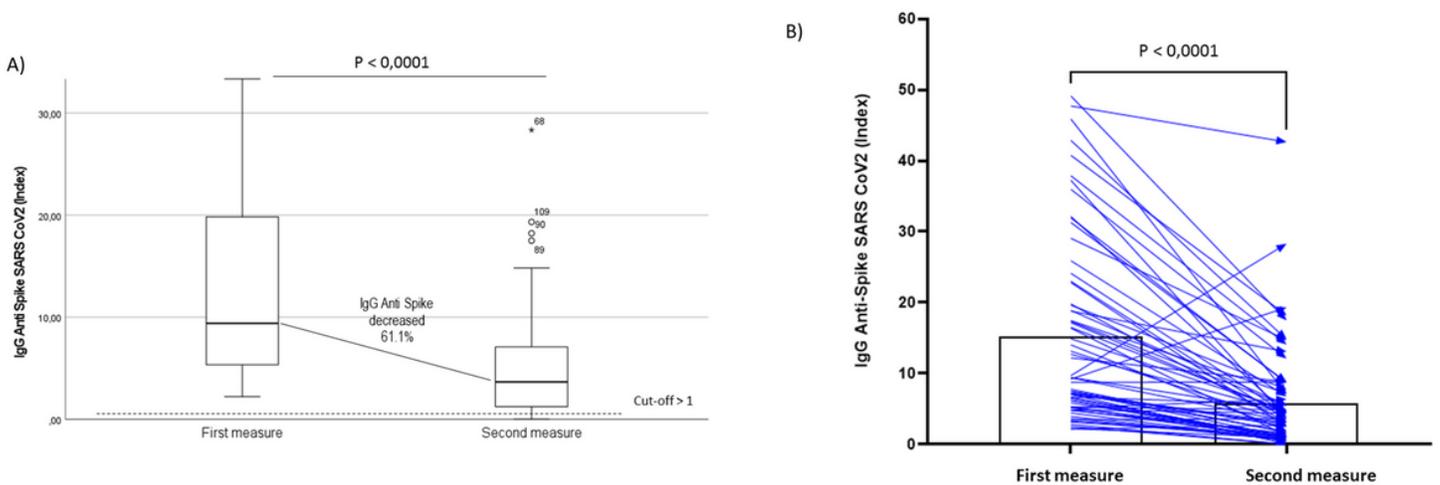


Figure 1

A-B. Comparison of the index of IgG antibodies against SARS-CoV2 Spike. Significant reduction (61.1%) in the index of IgG against SARS-CoV-2 after 4 or 6 months of seroconversion.

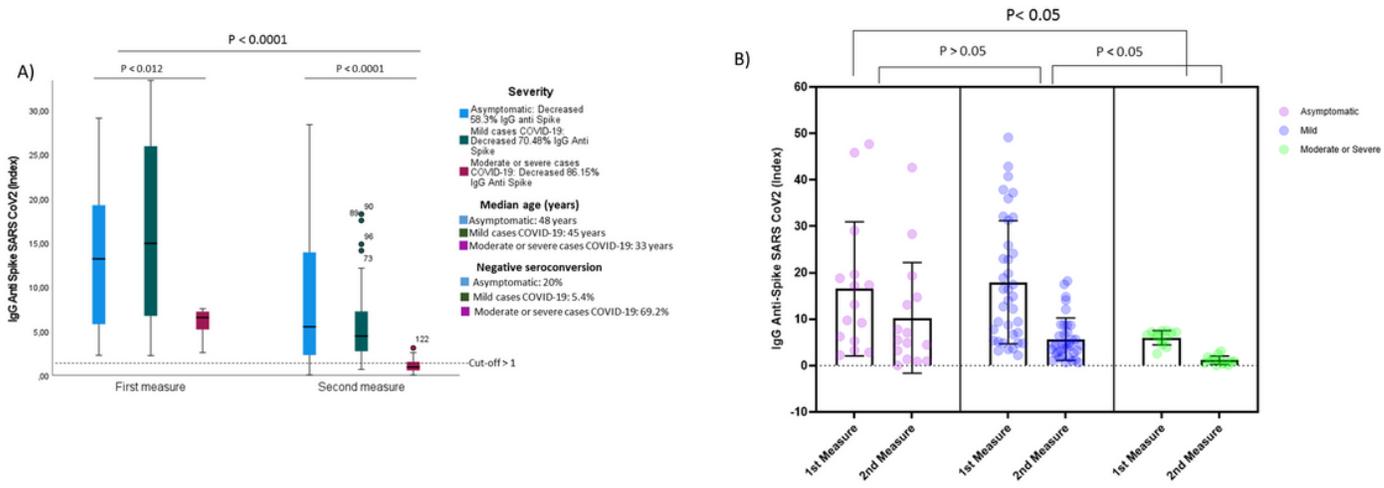


Figure 2

Comparison of the index of IgG antibodies against SARS-Cov2 according to the clinical severity. This figure showed a lower index of IgG antibodies against SARS-CoV2 in patients with moderate or severe COVID-19 in both serological evaluations.