



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

LETTERS TO THE EDITOR

IgG Antibody Response to SARS-CoV-2 Infection and Viral RNA Persistence in Patients on Maintenance Hemodialysis



To the Editor:

Quarantining dialysis patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a logistical challenge. Appropriately identifying non-infectiousness in patients is essential to safely lift quarantine measures. Serologic tests are used to establish previous infection with SARS-CoV-2, but the extent to which antibody positivity translates to actual immunity is currently unknown.¹ Hemodialysis patients are known to have impaired humoral immune responses to vaccination and infection, and it is uncertain whether hemodialysis patients mount an effective antibody response against SARS-CoV-2.

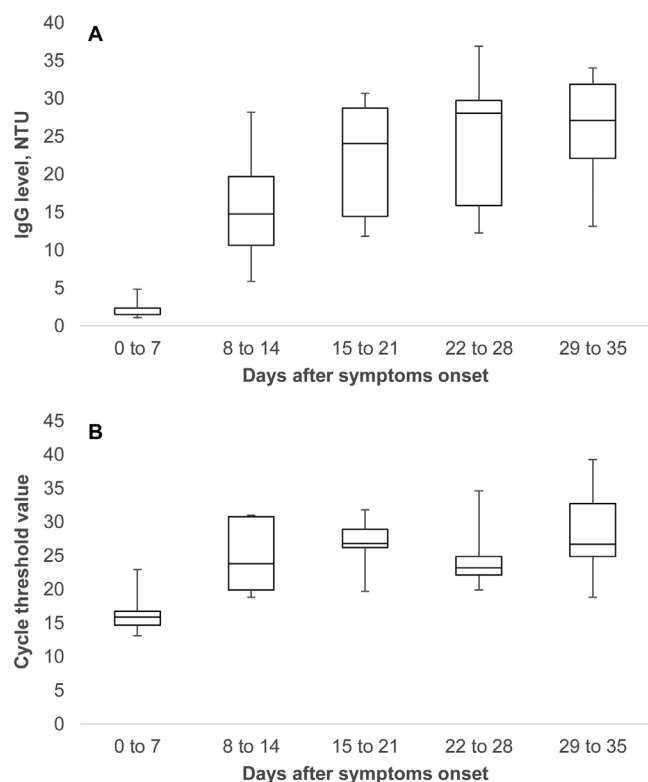


Figure 1. Dynamics of (A) anti-SARS-CoV-2 IgG in serum and (B) SARS-CoV-2 viral load in upper airways. IgG measured by N-protein-based ELISA³ (NovaLisa, NovaTec; validated in-house; approved by the Federal Agency for Drugs and Health Products). A level > 11 NTU (“NovaTec units”) is interpreted as positive, and 9–11 NTU, as borderline. Viral load measured by a laboratory-developed semi-quantitative real-time reverse transcriptase–polymerase chain reaction (RT-PCR) targeting the *N* (nucleocapsid) and *RdRp* (RNase-dependent RNA polymerase) genes. A phocine distemper virus was used as a control to test for extraction errors or presence of inhibitors. A cycle threshold value < 40 is interpreted as positive.

Of our 282 maintenance hemodialysis patients, 7 developed SARS-CoV-2 infection between March 14 and April 7, 2020. All patients displayed symptoms of coronavirus disease 2019 (COVID-19) and tested positive for SARS-CoV-2 RNA on a nasopharyngeal swab on the day of symptom onset. Three patients died (at days 6, 11, and 36), 1 patient is currently still receiving mechanical ventilation, and 3 patients recovered clinically. Longitudinal serum sampling and nasopharyngeal swab tests were performed in 6 of 7 patients (1 patient died before follow-up samples were obtained).

Overall immunoglobulin G (IgG) seroconversion rate was 100% and occurred in the second week after symptom onset. Antibody titer plateaued during the third week (Fig 1A). Virus persisted in respiratory samples of nonsurvivors until death. In survivors, nucleic acid conversion time, defined as the interval from symptom onset to first negative RT-PCR result, was 34, 37, 37, and 44 days. Cycle threshold values, an inverse measure of nucleic acid concentration, were lowest in the first week of infection and remained relatively stable thereafter (Figure 1B).

In conclusion, maintenance hemodialysis patients are able to mount an antibody response against SARS-CoV-2 that is similar in intensity and timing to that of the nondialysis population. However, anti-SARS-CoV-2 IgG antibodies appeared weeks before the actual clearance of the virus from the upper airways, suggesting that these antibodies are not neutralizing. Viral shedding persisted for more than 5 weeks after symptom onset in survivors. Although viral shedding does not necessarily equal infectiousness,² awaiting negative RT-PCR testing on at least 2 sequential samples before lifting quarantine in hemodialysis patients is the prudent approach.

An S. De Vriese, MD, PhD
Marijke Reynders, MD

Article Information

Authors' Affiliations: Division of Nephrology and Infectious Diseases (ASDV) and Division of Medical Microbiology (MR), AZ Sint-Jan Brugge-Oostende AV, Brugge, and Department of Internal Medicine, Ghent University, Ghent, Belgium (ASDV).

Address for Correspondence: An S. De Vriese, MD, PhD, Division of Nephrology and Infectious Diseases, AZ Sint-Jan Brugge-Oostende AV, Ruddershove 10, 8000 Brugge, Belgium. E-mail: an.devriese@azsintjan.be.

Financial Disclosure: The authors declare that they have no relevant financial interests.

Acknowledgements: The authors thank Frank De Geeter, Manon Verhulst, and Jessica Van Besien for logistical support.

Peer Review: Received May 19, 2020. Direct editorial input from an Associate Editor and a Deputy Editor. Accepted in revised form May 29, 2020.

Publication Information: © 2020 by the National Kidney Foundation, Inc. Published online June 5, 2020 with doi [10.1053/j.ajkd.2020.05.009](https://doi.org/10.1053/j.ajkd.2020.05.009)

References

1. Melgaço JG, Azamor T, Ano Bom APD. Protective immunity after COVID-19 has been questioned: what can we do without SARS-CoV-2-IgG detection? *Cell Immunol.* 2020;353:104114.
2. Wölfel R, Corman VM, Guggemos W, et al. Virological assessment of hospitalized patients with COVID-2019. *Nature.* 2020;581(7809):465–469.
3. Okba NMA, Muller MA, Li W, et al. SARS-CoV-2 specific antibody responses in COVID-19 patients [published online ahead of print April 8, 2020]. *Emerg Infect Dis.* <https://doi.org/10.3201/eid2607.200841>.

EPO in Patients With COVID-19: More Than an Erythropoietic Hormone



To the Editor:

In their editorial, Fishbane and Hirsh¹ discuss associations between systemic inflammation and anemia in patients with coronavirus disease 2019 (COVID-19). This relationship, putatively attributed to hepcidin effects on iron availability, limits erythropoietin (EPO) efficacy. Despite this, the authors theorize that synergism between severe COVID-19 and erythropoiesis-stimulating agent use may produce dangerous thrombosis risks. They propose reduced hemoglobin level targets in maintenance dialysis patients with COVID-19 despite an association between anemia and more severe COVID-19.² We contend that this approach, although reasonable, is potentially problematic.

Disordered inflammatory responses underlie end-organ damage in patients with COVID-19. Increased levels of interleukins (eg, IL-1 β and IL-6) are independently associated with disease severity/mortality, and therapies targeting IL-1 β and IL-6 effects show promising results.³ Our group and others showed that EPO immunoregulating effects include inhibiting IL-1 β and IL-6 production by monocytes and promoting regulatory T-cell survival.⁴ In addition, growing evidence establishes global tissue-protective antiapoptotic effects of EPO, especially in organs targeted in COVID-19. Consistent with this, a recent case report attributed respiratory distress amelioration in an anemic 80-year-old man to EPO use.⁵

Therefore, in COVID-19 patients, the benefits of erythropoiesis-independent EPO effects may far outweigh the risks. As such, further analysis and controlled studies are warranted to define how EPO treatment should be optimized in maintenance dialysis patients with COVID-19 and anemia.

Jeremy Leventhal, MD, Andrea Angeletti, MD, Paolo Cravedi, MD, PhD

Article Information

Authors' Affiliations: Division of Nephrology, White Plains Hospital, White Plains, NY (JL); Division of Nephrology, Dialysis,

Transplantation, IRCCS Giannina Gaslini, Genoa, Italy (AA); and Department of Medicine, Translational Transplant Research Center, Icahn School of Medicine at Mount Sinai, New York, NY (PC).

Support: None.

Financial Disclosure: The authors declare that they have no relevant financial interests.

Peer Review: Received May 31, 2020. Accepted June 1, 2020, after editorial review by an Associate Editor and a Deputy Editor.

Publication Information: © 2020 by the National Kidney Foundation, Inc. Published online June 10, 2020 with doi [10.1053/j.ajkd.2020.06.002](https://doi.org/10.1053/j.ajkd.2020.06.002)

References

1. Fishbane S, Hirsch JS. Erythropoiesis-stimulating agent treatment in patients with COVID-19. *Am J Kidney Dis.* 2020;76(3):303–305.
2. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet.* 2020;395(10223):497–506.
3. Ingraham NE, Lotfi-Emran S, Thielen BK, et al. Immunomodulation in COVID-19. *Lancet Respir Med.* 2020;8(6):544–546.
4. Cantarelli C, Angeletti A, Cravedi P. Erythropoietin, a multifaceted protein with innate and adaptive immune modulatory activity. *Am J Transplant.* 2019;19(9):2407–2414.
5. Hadadi A, Mortezaazadeh M, Kolahehdouzan K, Alavian G. Does recombinant human erythropoietin administration in critically ill COVID-19 patients have miraculous therapeutic effects? *J Med Virol.* 2020;92(7):915–918.

Fishbane and Hirsch declined to respond.

RESEARCH LETTERS

eVisits in Rural Hemodialysis Care: A Qualitative Study of Stakeholder Perspectives on Design and Potential Impact to Care



To the Editor:

People living in rural communities often experience barriers in accessing health care.¹ Electronic visits (eVisits) are online consultations between patients and health care providers in which patients attend virtually from home.² eVisits have several potential benefits,² particularly for rural populations, and their use appears to be increasing.³ Management of kidney failure with maintenance hemodialysis (HD) requires regular contact with nephrologists for follow-up care and eVisits appear well suited for this setting. However, the current level of interest, potential benefits and concerns, and requisite design features for an eVisit program for HD are unknown. We did this study to evaluate perceptions of patients and providers to inform the future design of a rural eVisit program specific to maintenance HD care.

Full methods are in [Item S1](#). In brief, we interviewed patients receiving in-center HD from 1 of 2 units in rural Alberta. We purposively recruited those who had been