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# LETTERS TO THE EDITOR

### Is SARS-CoV-2 Serology Relevant for Hemodialysis Patients With COVID-19?



#### To the Editor:

Although dialysis patients are known to have impaired antibody responses to pathogens and fluctuation of antibody levels,<sup>1</sup> the response to coronavirus disease 2019 (COVID-19) in this population remains to be determined. De Vriese and Reynders<sup>2</sup> present the first evaluation of potential antibody responses in a dialysis population. We agree that 2 sequential negative COVID-19 swabs before de-isolating dialysis patients is a reasonable approach, as we recently demonstrated.<sup>3</sup> De Vriese and Reynders studied the presence of immunoglobulin G (IgG) against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleocapsid (N) protein in 7 patients and concluded that patients develop an antibody response within 15 days. Although we acknowledge that these findings are novel, we highlight that they might not be applicable to other dialysis populations with COVID-19 infection. First, the infection rate in their population was very low (7/289 [2.5%]) and most of these patients had a severe form of the disease (3 43%) died and 1 was still in the intensive care unit [ICU]). In comparison, in our experience,<sup>4</sup> 11.3% of our hemodialysis population had COVID-19 infection and only 7 of 76 (9.2%) died. IgG against SARS-CoV-2 N protein has been shown to be higher in ICU compared with non-ICU patients.<sup>5</sup> Therefore, it remains to be elucidated whether those results are applicable to any hemodialysis population and whether there is a prognostic role in assessing anti-spike (S) protein IgG in combination with IgG against SARS-CoV-2 N protein.<sup>5</sup> Moreover, it remains to be confirmed how long these antibodies will last and their clinical relevance in larger populations.

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

Peer Review: Received June 10, 2020. Accepted June 13, 2020, after editorial review by a Deputy Editor.

Publication Information: © 2020 by the National Kidney Foundation, Inc. Published online June 27, 2020 with doi 10.1053/ j.ajkd.2020.06.006

#### References

- 1. Meyer TW, Hostetter TH. Uremia. N Engl J Med. 2007;57(13): 1316-1325.
- De Vriese AS, Reynders M. IgG antibody response to SARS-CoV-2 infection and viral RNA persistence in patients on

maintenance hemodialysis. *Am J Kidney Dis.* 2020;76(3): 440-441.

- Dudreuilh C, Kumar N, Moxham V, Hemsley C, Goldenberg S, Moutzouris D-A. De-isolation of COVID-19–positive hemodialysis patients in the outpatient setting: a single-center experience. *Kidney Int.* 2020;98(1):236-237.
- Roper T, Kumar N, Lewis-Morris T, et al. Delivering dialysis during the COVID-19 outbreak: strategies and outcomes. *Kidney Int Rep.* 2020;5(7):1090-1094.
- Sun B, Feng Y, Mo X, et al. Kinetics of SARS-CoV-2 specific IgM and IgG responses in COVID-19 patients. *Emerg Microbes Infect*. 2020;9(1):940-948.

### In Reply to 'Is SARS-CoV-2 Serology Relevant for Hemodialysis Patients With COVID-19?'



In a small group of hemodialysis patients with confirmed SARS-CoV-2 infection, we reported that the presence of anti-SARS-CoV-2 IgG overlaps by several weeks with detectable viral RNA in the upper airways.<sup>1</sup> The core message of our communication is that this antibody response, although proof of recent exposure to SARS-CoV-2, should not be interpreted as prima facie evidence of immunity to the virus. Viral load was highest during the first week of illness, suggesting that patients are most infectious during this period. It remains unclear whether the lower viral loads during the following weeks associate with a clinically relevant transmissibility of SARS-CoV-2 requiring further quarantining. As also advocated by Dudreuilh et  $al^2$  and pending further evidence, we submit that the prudent approach is to await negative reverse transcriptase-polymerase chain reaction test results.

We measured anti–SARS-CoV-2 IgG with an N protein–based enzyme-linked immunosorbent assay (NovaLisa; NovaTec). Dudreuilh et al suggest that the combination with an S protein–based assay may provide additional information.<sup>3</sup> We have repeated our analyses with a combined S1 (spike protein subunit 1)– and N-protein–based assay (Vircell).<sup>4</sup> Although there was a slight variation in the individual immune responses, as clearly described in the literature, the overall conclusion (100% seroconversion within the first few weeks of symptom onset) remains unaltered.

Dudreuilh et al rightly point out that the clinical relevance of the anti–SARS-CoV-2 antibody response is currently unclear. Further studies in larger populations of both survivors and nonsurvivors with prolonged sequential sampling starting from the onset of infection are required to determine the longevity of the antibody response and potential correlation with severity of disease in hemodialysis patients. However, more importantly, research should be directed at identifying biomarkers of immunity that can be used to ascertain natural or vaccineinduced resistance to the virus in both the general and hemodialysis populations. An S. De Vriese, MD, PhD Marijke Reynders, MD

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

**Peer Review:** Received June 20, 2020. Accepted June 24, 2020, after editorial review by an Associate Editor and a Deputy Editor.

Publication Information: © 2020 by the National Kidney Foundation, Inc. Published online June 27, 2020 with doi 10.1053/ j.ajkd.2020.06.005

#### References

- 1. De Vriese AS, Reynders M. IgG antibody response to SARS-CoV-2 infection and viral RNA persistence in patients on maintenance hemodialysis. *Am J Kidney Dis.* 2020;76(3): 440-441.
- Dudreuilh C, Kumar N, Moxham V, Hemsley C, Goldenberg S, Moutzouris DA. De-isolation of COVID-19-positive hemodialysis patients in the outpatient setting: a single-center experience. *Kidney Int.* 2020;98(1):236-237.
- Dudreuilh C, Moutzouris D-A. Is SARS-CoV-2 serology relevant for hemodialysis patients with COVID-19? *Am J Kidney Dis. Am J Kidney Dis.* 2020;76(4):598.
- Kohmer N, Westhaus S, Rühl C, Ciesek S, Rabenau HF. Clinical performance of different SARS-CoV-2 lgG antibody tests. *J Med Virol*. https://doi.org/10.1002/jmv.26145.

### Treatment Outcomes in Syndrome of Inappropriate Antidiuresis: Improvements in Hyponatremia May Reflect Successful Treatment or Resolution of the Underlying Cause

#### To the Editor:

In a recent randomized controlled study, Krisanapan et al<sup>1</sup> demonstrated that the addition of furosemide, with or without sodium chloride, provided no additional benefit to fluid restriction alone in correcting plasma sodium in patients with syndrome of inappropriate antidiuresis (SIAD).<sup>1</sup> These prospective data in patients with a robust biochemical diagnosis of SIAD are a welcome addition to the literature on SIAD treatment, an area that is deficient in prospective randomized studies of first-line treatments.

It would be useful to have more information about how the underlying cause of SIAD was treated. Improvements in hyponatremia may reflect successful treatment, or resolution, of a transient cause of SIAD rather than the effect of study interventions. For example, 37% of the total group had medication-related SIAD, which almost always responds to withdrawal of the offending medication. In addition, prolonged fluid restriction (with or without furosemide/sodium chloride) for 28 days despite interval resolution of SIAD may predispose to volume depletion and explain the high rates of acute kidney injury reported (10%-32%).

We are particularly interested to know the outcomes in the subgroup with SIAD due to pulmonary infections. We have previously shown in patients with SIAD due to community-acquired pneumonia that plasma vasopressin concentrations decrease and hyponatremia corrects with antimicrobial treatment alone.<sup>2</sup> Blood pressure increases after admission, which suggests that these patients may be relatively hypovolemic at presentation. Therefore, in this group, fluid restriction (with or without furosemide/sodium chloride) may not be the most appropriate initial treatment and may predispose to acute kidney injury.

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

Peer Review: Received April 8, 2020. Accepted April 11, 2020, after editorial review by an Associate Editor and a Deputy Editor.

Publication Information: © 2020 by the National Kidney Foundation, Inc. Published online June 20, 2020 with doi 10.1053/ j.ajkd.2020.04.011

## References

- Krisanapan P, Vongsanim S, Pin-On P, Ruengorn C, Noppakun K. Efficacy of furosemide, oral sodium chloride, and fluid restriction for treatment of syndrome of inappropriate antidiuresis (SIAD): an open-label randomized controlled study (the EFFUSE-FLUID Trial). *Am J Kidney Dis.* 2020;76(2):203-212.
- Cuesta M, Slattery D, Goulden EL, et al. Hyponatraemia in patients with community-acquired pneumonia; prevalence and aetiology, and natural history of SIAD. *Clin Endocrinol*. 2019;90(5):744-752.

### In Reply to 'Treatment Outcomes in Syndrome of Inappropriate Antidiuresis: Improvements in Hyponatremia May Reflect Successful Treatment or Resolution of the Underlying Cause'

We thank Garrahy et al<sup>1</sup> for their interest in our study.<sup>2</sup> They have raised a very important point about curable causes of syndrome of inappropriate antidiuresis (SIAD),

