

COVID-19 infection recurrence in ESRD

An end-stage renal disease (ESRD) patient on in-center hemodialysis contracted symptomatic coronavirus disease 2019 (COVID-19) within a rehab unit in March 2020.^[1] The 79-year-old, obese male with multiple comorbidities developed a new non-productive cough and was positive on COVID-19 reverse transcription polymerase chain reaction (RT-PCR) testing.^[1] Treatment included hydroxychloroquine and doxycycline. The RT-PCR test 22 days from the first test remained positive. He was discharged after 24 days to an isolation hemodialysis unit.^[1] A third and fourth RT-PCR tests, 32 and 33 days, from the first test were negative, and he was returned to general in-center hemodialysis [Table 1].^[1] Given renal clearance of COVID-19 RNA (ribonucleic acid), we hypothesized that COVID-19 RNA persistence was likely in ESRD.^[1]

Two months later, after the above documentation and publication, he was subsequently readmitted to our hospital with headache and syncope. COVID-19 RT-PCR was negative. He was discharged and improved with no specific treatment. Two weeks later, he was readmitted with nausea, vomiting, shaking tremors, and diarrhea. Contact with a possible COVID-19 subject was reported. COVID-19 RT-PCR was again positive. COVID-19 control measures were reinstated. Two of three daily RT-PCR tests and a SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) IgG (immunoglobulin G) antibody test returned positive [Table 1]. He was managed conservatively and was discharged after 5 days to isolation hemodialysis. RT-PCR test 4 days post-discharge remained positive. RT-PCR tests, 11 and 13 days post-discharge were negative, and he was again returned to regular in-center hemodialysis. In early August 2020, he was readmitted about 4 hours after an uneventful hemodialysis treatment with fever (103°F) and shaking tremors. No new COVID-19 exposure was reported. He was hypotensive (80/50 mm Hg) and improved with 250 cc bolus of normal saline. RT-PCR test returned positive, but this positive RT-PCR test was overruled by Infectious Disease consultation as “noninfectious” – only one of his genetic targets was positive with cycle threshold (Ct cycle) of 43 (cutoff for negative is 45). He was discharged after 3 days to general in-center hemodialysis. No further RT-PCR testing was envisaged.

Our knowledge of COVID-19 is evolving. The time course of PCR positivity and seroconversion remains speculative.^[2-4] An Italian case report demonstrated COVID-19 recurrence one month after initial recovery despite the demonstration of IgM (immunoglobulin M) and IgG antibodies against the COVID-19 virus.^[5] Our patient, we posit, is most unique in many respects with multiple comorbidities, on hemodialysis for ESRD, and had repeated re-exposures to COVID-19 in two of four of these hospitalizations. Indeed, we would argue that our patient is the most COVID-19-tested patient ever reported. Did he experience a truly recurrent COVID-19 infection? The jury remains out on these questions. The impact of the possible implications of COVID-19 recurrence in patients vis-a-vis the inherent protection derived from the several new COVID-19 vaccines, then at the time, in development, is even more perplexing.

Finally, we surmise that the persistence of COVID-19 RNA in our patient may represent the syndrome of prolonged viral non-clearance that may be peculiar to especially anuric ESRD patients on maintenance hemodialysis.^[1] Furthermore, there is also the confounding observation that nonviable COVID-19 viral RNA may persist in some patients and therefore continue to give false-positive RT-PCR test results.^[6] Such phenomenon had been described decades ago with HIV patients on highly retroactive antiviral therapy.^[7] This persistence of nonviable COVID-19 RNA particles would also explain the simultaneous presence of positive IgG antibodies to COVID-19 from the initial infection together with the falsely positive COVID-19 RT-PCR RNA tests. COVID-19 viral cultures, arguably, would distinguish between nonviable viral RNA particles versus live viable COVID-19 viruses. Another management paradigm that we did not pursue with the patient's recurring positive RT-PCR RNA tests was to complete next-generation sequencing of nasopharyngeal specimens taken from the patient at different times.^[8] Genomic analysis for significant genetic discordance from different nasopharyngeal specimens could assist in the diagnosis of relapse, recurrence, or reinfection with a new different COVID-19 archetype.^[8]

Table 1: Summary of symptoms, hospitalizations, COVID-19 RT-PCR, and COVID-19 serology tests spanning over 5 months

Date	3/30/2020	4/21/2020	5/1/2020	5/2/2020	6/8/2020	6/10/2020	6/28/2020	6/30/2020	7/6/2020	7/13/2020	7/15/2020	8/4/2020
Prior exposure to COVID-19	+											
Hospitalization	+											
Cough	+											
Running Nose	+											
Fever												
Generalized weakness												
Syncope												
Nausea												
Vomiting												
Diarrhea												
Shaking tremors												
Headache												
Hypotension												
COVID-19 RT-PCR Test	Positive	Positive	Negative	Negative	Negative	Negative	Positive	Positive	Positive	Negative	Negative	Positive
SARS-CoV-2 IgG Antibodies												

COVID-19=Coronavirus disease 2019, RT-PCR=reverse transcription polymerase chain reaction, SARS-CoV-2=severe acute respiratory syndrome coronavirus 2, IgG=immunoglobulin G

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Macaulay A. C. Onuigbo

The Robert Larner, M.D. College of Medicine, University of Vermont, Burlington, VT, USA

Address for correspondence:

Dr. Macaulay A. C. Onuigbo, Division of Nephrology, Department of Medicine, The Robert Larner, M.D. College of Medicine, University of Vermont, Burlington, VT. UHC Campus, 1 South Prospect Street, Burlington, VT 05401, USA. E-mail: macaulay.onuigbo@uvmhealth.org

References

1. Onuigbo MAC. Persistence of coronavirus disease 2019 (COVID-19) in patients with end-stage renal disease; An unrecognized phenomenon? *J Renal Inj Prev* 2021;10:e07.
2. Wölfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Müller MA, *et al.* Virological assessment of hospitalized patients with COVID-2019. *Nature* 2020;581:465-9.
3. Sethuraman N, Jeremiah SS, Ryo A. Interpreting diagnostic tests for SARS-CoV-2. *JAMA* 2020;323:2249-51.
4. Clarke C, Prendecki M, Dhutia A, Ali MA, Sajjad H, Shivakumar O, *et al.* High prevalence of asymptomatic COVID-19 infection in hemodialysis patients detected using serologic screening. *J Am Soc Nephrol* 2020;31:1969-75.
5. Loconsole D, Passerini F, Palmieri VO, Centrone F, Sallustio A, Pugliese S, *et al.* Recurrence of COVID-19 after recovery: A case report from Italy. *Infection* 2020;48:965-7.
6. Cimolai N. Features of enteric disease from human coronaviruses: Implications for COVID-19. *J Med Virol* 2020;92:1834-44.
7. Onuigbo MAC. Residual HIV-1 RNA after highly active antiretroviral therapy. *JAMA* 2000;283:1138-9.
8. Tillett RL, Sevinsky JR, Hartley PD, Kerwin H, Crawford N, Gorzalski A, *et al.* Genomic evidence for reinfection with SARS-CoV-2: A case study. *Lancet Infect Dis* 2020;21:52-8.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Access this article online	
Quick Response Code: 	Website: www.indianjephrol.org
	DOI: 10.4103/ijn.IJN_425_20

How to cite this article: Onuigbo MAC. COVID-19 infection recurrence in ESRD. *Indian J Nephrol* 2022;32:184-5.

Received: 06-09-2020; Revised: 01-06-2021; Accepted: 03-08-2021; Published: 23-03-2022.

© 2022 Indian Journal of Nephrology | Published by Wolters Kluwer - Medknow