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BRIEF REPORT

Absence of Antibody Reponses and Severe COVID-19 in Patients on Hemodialysis Following mRNA Vaccination

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Inpatient dialysis patients cannot isolate, resulting in a higher rate of coronavirus disease 2019 (COVID-19) infections, with increased severity and higher mortality rate [1]. We present 2 African American dialysis patients who developed severe COVID-19 infections after vaccination. Both patients had not mounted antibody response to the COVID-19 vaccine or to hepatitis B vaccination.

Keywords. COVID-19; ESRD; hepatitis B; nonrespondents; infection after COVID vaccination; vaccination.

More than 3 million patients are receiving renal dialysis worldwide, including >746 000 in the United States. In-center hemodialysis patients have a high risk of viral exposure as well as risks related to multiple medical comorbidities and suppressed immunity. Hemodialysis patients are unable to isolate given the fact that they have to travel to the dialysis center 3 times a week, spending at least 3 to 4 hours in a dialysis session, and usually are around several other patients and staff [2]. Weiss et al. found in their study a coronavirus disease 2019 (COVID-19) prevalence rate of 14% among patients undergoing long-term dialysis compared with 2.6% in the New York City population [3]. In addition to increased rate of infection, there is increased mortality among those infected with the virus. In a study of 7948 dialysis patients in a 5-month period from February to June 2020, there were 438 (5.5%) diagnosed with COVID-19; of these, 109 (24.9%) died, compared with 275 (3.7%) of 7510 hemodialysis patients who tested negative for COVID-19 [4]. Vaccine breakthrough cases are an area of interest, with several recent papers addressing the issue of suboptimal immune response among dialysis patients. Here we describe 2 cases of severe COVID infection that occurred in 2 fully vaccinated dialysis patients among the 99 vaccinated patients receiving dialysis at our center.

CASE 1

A 52-year-old African American female with end-stage renal disease on dialysis with a medical history of obesity, obstructive sleep apnea, antiphospholipid syndrome, bilateral pulmonary emboli, and multiple deep venous thrombosis presented to the dialysis unit with 5 days of headache, myalgia, and progressive shortness of breath. She was sent to the emergency room, where she was found to have COVID-19 based on polymerase chain reaction (PCR) testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA on nasopharyngeal sampling, which was confirmed on repeat PCR testing 2 days later. Her chest radiograph showed vascular congestion as well as superimposed patchy focal infiltrates, and she required high-flow oxygen via nasal cannula. On day 2 of her admission, she was transferred to the intensive care unit, and on day 3 of her intensive care unit admission she developed cardiac arrest and expired.

Of note, she had completed COVID-19 vaccination, with 2 doses of the Pfizer-BioNTech vaccine received 48 and 24 days before her admission. Serologic testing for immunoglobulin G antibody against the SARS-CoV-2 spike protein from her second day of hospitalization revealed an index of <1.00 (a negative result).

CASE 2

A 70-year-old Ethiopian male with end-stage renal disease on dialysis and history of atrial fibrillation, heart failure with preserved ejection fraction, recurrent transudative right pleural effusions, chronic obstructive pulmonary disease, diabetes mellitus, cerebrovascular accident, right lower extremity deep venous thrombosis, and left atrial thrombus developed shortness of breath, hypoxia, and altered mental status while receiving dialysis. He was sent to the emergency room and was found to have COVID-19 based on polymerase chain reaction (PCR) testing for SARS-CoV-2 RNA on nasopharyngeal sampling. The diagnosis was confirmed on repeat PCR testing 2 days later and again 10 days later. He required noninvasive bilevel ventilation on presentation. He was eventually transferred to the intensive care unit, where the patient was initially on noninvasive ventilation followed by mechanical ventilation and then expired secondary to respiratory failure. Like case 1, he had completed COVID-19 vaccination just over 3 weeks before his admission for COVID-19 pneumonia. The patient was also tested on day

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2 of hospitalization for immunoglobulin G antibody against the SARS-CoV-2 spike protein, which revealed an index of <1.00.

Patient Consent

Informed consent was obtained from the patient and/or the patient's designated representative for publication of this case report.

DISCUSSION

Morbidity and mortality are very high in hemodialysis patients who develop COVID-19 infection; in addition, these patients do not develop adequate immune response to vaccination or infections [5]. This is a case study of 2 African American patients with end-stage renal disease receiving in-center maintenance hemodialysis who were vaccinated with the Pfizer-BioNTech COVID-19 vaccine who were hospitalized with COVID-19 pneumonia >2 weeks after receiving the second dose. The dialysis center where both patients were treated has 99 patients fully immunized (85%) of the patients in the dialysis unit. Among the 99 patients: 88 patients received the Pfizer-BioNTech COVID-19 vaccine, 8 patients received the Moderna vaccine, and 3 patients received the Johnson & Johnson vaccine. Both of our patients did not mount neutralizing antibodies to COVID immunoglobulin G spike protein using the Semens Atellica Centaur platform when tested 25 days after their second vaccine dose. Both patients had also received the full series of the hepatitis B vaccine and had not mounted an antibody response.

A recent study of 56 patients on maintenance hemodialysis showed a positive humoral response in all but 2 cases following the BNT162b2 (Pfizer-BioNTech) vaccine, but antibody titers were significantly lower than in a healthy control group. Response was not related to the number of medical conditions of the study participants, but humoral responses did inversely correlate with age [5]. In our cases, 1 of the patients was elderly.

The unique circumstances of in-center hemodialysis that increase the risk of patients getting COVID-19 also contribute to increased risk of hepatitis B in the same population. The hepatitis B vaccine is usually administered intramuscularly in 3 doses (0, 1, and 6 months), with 95% of the population showing long-lasting serologic immunity. An additional fourth dose or a repeated higher-dose, 3-course regimen is given to those who fail to show immunity. Despite these additional regimens, some patients remain vulnerable to hepatitis B and are deemed nonresponders [6]. In a study of 83 dialysis patients who received the standard 20 μg of recombinant-derived hepatitis B vaccine Engerix-B at 0, 1, and 6 months, 27 (32.5%) were found to be seropositive for anti-HBs antibodies after receiving the third dose. There were 56 nonresponders. A booster dose of 40 μg was given to 48 patients 6 weeks after the initial course, and 8 patients seroconverted [7]. In a study by Agarwal et al. evaluating response rates to the HBV vaccine in mild (creatine 1.5–3.0 mg/dL), moderate (creatine 3.0–6.0 mg/dL), and severe (creatine >6.0 mg/dL) chronic kidney disease, the seroconversion rates after 3 doses of 40 μg of HBV vaccine (double the standard dose) were 87.5%, 66.6%, and 35.7%. Rates increased after a fourth dose was administered to 100%, 77%, and 36.4% [8].

DaRosa et al. demonstrated in a prospective cohort study that patients with low glomerular filtration rate, higher creatinine (late-stage kidney disease), diabetes, and old age are less likely to seroconvert [9]. For dialysis and immunosuppressed patients, the Centers for Disease Control and Prevention recommends either giving a higher dose or increasing the number of hepatitis B doses [10].

Renal failure patients have a significant drop in anti-HBs antibody titers, with recommendations to have regular checks of anti-HBs status in vaccinated patients [10].

CONCLUSIONS

There is often a need for higher vaccine dosage or scheduling changes in hemodialysis patients [10]. These findings warrant close observation of patients with ESRD, including those who have been vaccinated, during the COVID-19 pandemic and further research on vaccination efficacy in this population.

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Potential conflicts of interest. All authors: No reported conflicts.

References

1. Turgutalp K, Ozturk S, Arici M, et al. Determinants of mortality in a large group of hemodialysis patients hospitalized for COVID-19. BMC Nephrology **2021**; 22:29.
2. Francis A, Baigent C, Ikizler TA, et al. The urgent need to vaccinate dialysis patients against severe acute respiratory syndrome coronavirus 2: a call to action. Kidney Int **2021**; 99:791–793.
3. Weiss S, Bhat P, Del Pilar Fernandez M, et al. COVID-19 infection in ESKD: findings from a prospective disease surveillance program at dialysis facilities in New York City and Long Island. J Am Soc Nephrol **2020**; 31:2517–21.
4. Hsu CM, Weiner DE, Aweh G, et al. COVID-19 among US dialysis patients: risk factors and outcomes from a national dialysis provider. Am J Kidney Dis. **2021**; 77:748–56.
5. Grupper A, Sharon N, Finn T, et al. Humoral response to the Pfizer BNT162b2 vaccine in patients undergoing maintenance hemodialysis. Clin J Am Soc Nephrol. **2021**; 16:1037–41.
6. Saco TV, Strauss AT, Ledford DK. Hepatitis B vaccine non responders: possible mechanisms and solutions. Ann Allergy Asthma Immunol **2018**; 121:320–327.
7. Fleming SJ, Moran DM, Cooksley WG, Faoagali JL. Poor response to a recombinant hepatitis B vaccine in dialysis patients. J Infect **1991**; 22:251–7.
8. Agarwal SK, Irshad M, Dash SC. Comparison of two schedules of hepatitis B vaccination in patients with mild, moderate, and severe renal failure. J Assoc Physicians India **1999**; 47:183–5.
9. DaRoza G, Loewen A, Djurdjev O, et al. Stage of chronic kidney disease predicts seroconversion after hepatitis B immunization: earlier is better. Am J Kidney Dis **2003**; 42:1184–92.
10. Centers for Disease Control and Prevention. Guidelines for vaccinating kidney dialysis patients and patients with chronic kidney disease. Summary of ACIP recommendations, December 2012. Updated vaccine guideline for dialysis and chronic kidney disease patients. https://www.cdc.gov/vaccines/pubs/downloads/dialysis-guide-2012.pdf. Accessed 17 May 2021.