

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

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Case Report of 2 dialysis patients who had COVID-19 infection post vaccination. Both patients did not mount antibody titers to the COVID-19 vaccine and were previously non-responders to the hepatitis B vaccine.

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Author Contributions

S.I., U.N., C.M were the patients' nephrologists. A.M. was their intensivist. T.N. supervised the antibody and COVID tests. All four contributed to discussions of the cases and formulation of the report. M.M. and R.K. reviewed the literature and wrote the manuscript. S.M, T.M., S.Q., and C.M. reviewed and edited the manuscript.

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Abstract

Inpatient dialysis patients cannot isolate resulting in higher rate of 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 had not mounted antibody response to the COVID-19 vaccine, and to hepatitis B vaccination.

Keywords: COVID-19, Hepatitis B, ESRD, Vaccination, Non responder

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Introduction

More than 3 million patients are receiving renal dialysis worldwide including greater than 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 have found in their study the COVID 19 prevalence rate of 14% among patients undergoing long-term dialysis compared to 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 to 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 sub-optimal immune response among dialysis patients. Here we describe two cases of severe COVID infection that occurred in two 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 and medical history of obesity, obstructive sleep apnea, antiphospholipid syndrome, prior history of 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 ICU admission she developed cardiac arrest and expired.

Of note, she has 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 non-invasive bi-level ventilation on presentation. He was eventually transferred to the intensive care unit where the patient was initially on non-invasive ventilation followed by mechanical ventilation and then expired secondary to respiratory failure. Like case 1, he has completed COVID-19 vaccination just over 3 weeks prior to his admission for COVID-19 pneumonia.

The patient was also tested on day 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 patients' designated representative for publication of this case report.

Discussion

The 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 two African American patients with end stage renal disease receiving in-center maintenance hemodialysis who were vaccinated with Pfizer BioNTech COVID-19 vaccine more than 2 weeks after receiving the second dose who were hospitalized with COVID-19 pneumonia. 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 Pfizer BioNTech COVID-19 vaccine, 8 patients received Moderna vaccine, and 3 patients received the Johnson & Johnson vaccine. Both patients did not mount neutralizing antibodies to COVID IgG spike protein using 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 one of the patients was elderly.

Unique circumstances of in-center hemodialysis that increases 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 three 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 three course regimen is given to those that fail to show immunity. Despite these additional regimens, some patients remain vulnerable to hepatitis B and are deemed non-responders. [6] In a study of eighty-three dialysis patients who received the standard 20 micrograms of recombinant derived hepatitis B vaccine Engerix-B at 0, 1 and 6 months; twenty-seven (32.5%) were found to be seropositive for anti-HBs antibodies after receiving the third dose. There were 56 non responders, a booster dose of 40 micrograms was given to 48 patients 6 weeks after the initial course and 8 patients seroconverted [7]. In a study done by Agarwal et al, evaluating response rates to HBV vaccine in mild (creatinine 1.5 to 3.0 mg/dL), moderate (creatinine 3.0 to 6.0 mg/dL) and severe (creatinine > 6.0 mg/dL) chronic kidney disease, the seroconversion rates after 3 doses of 40 µg HBV vaccine double the standard dose; were 87.5%, 66.6% and 35.7%; Rates increased after a 4th dose was administered to 100%, 77% and 36.4%, [8].

DaRosa et al have 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 Center for Disease control recommends either giving a higher dose or increase 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].

Conclusion

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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List of abbreviations:

ESRD	End-Stage Renal Disease
SOB	shortness of breath
ICU	Intensive Care Unit
BUN	Blood Urea Nitrogen
INR	International Normalized Ratio
DVT	Deep Vein Thrombosis
CVA	Cerebrovascular accident
SARS	Severe Acute Respiratory Syndrome

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