

## Concise Communication

# Longitudinal analysis of risk factors associated with severe acute respiratory coronavirus virus 2 (SARS-CoV-2) infection among hemodialysis patients and healthcare personnel in outpatient hemodialysis centers

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### Abstract

In this prospective, longitudinal study, we examined the risk factors for severe acute respiratory coronavirus virus 2 (SARS-CoV-2) infection among a cohort of chronic hemodialysis (HD) patients and healthcare personnel (HCPs) over a 6-month period. The risk of SARS-CoV-2 infection among HD patients and HCPs was consistently associated with a household member having SARS-CoV-2 infection.

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Patients with end-stage renal disease (ESRD) on chronic hemodialysis (HD) are at increased risk of severe disease and death from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.<sup>1</sup> Despite vaccination, chronic HD patients are at risk for breakthrough SARS-CoV-2 infection due to attenuated<sup>2,3</sup> and waning immunological response to vaccines.<sup>4–6</sup> Several studies have examined the risk factors associated with SARS-CoV-2 infection among chronic HD patients; however, these were cross-sectional studies without longitudinal follow-up data.<sup>7–10</sup> Longitudinal data are valuable for identifying modifiable risk factors and devising strategies to prevent SARS-CoV-2 infection among HD patients. In this prospective, longitudinal study, we examined the risk factors for SARS-CoV-2 infection among a cohort of chronic HD patients and healthcare personnel (HCP) working in 3 outpatient HD units over a 6-month period.

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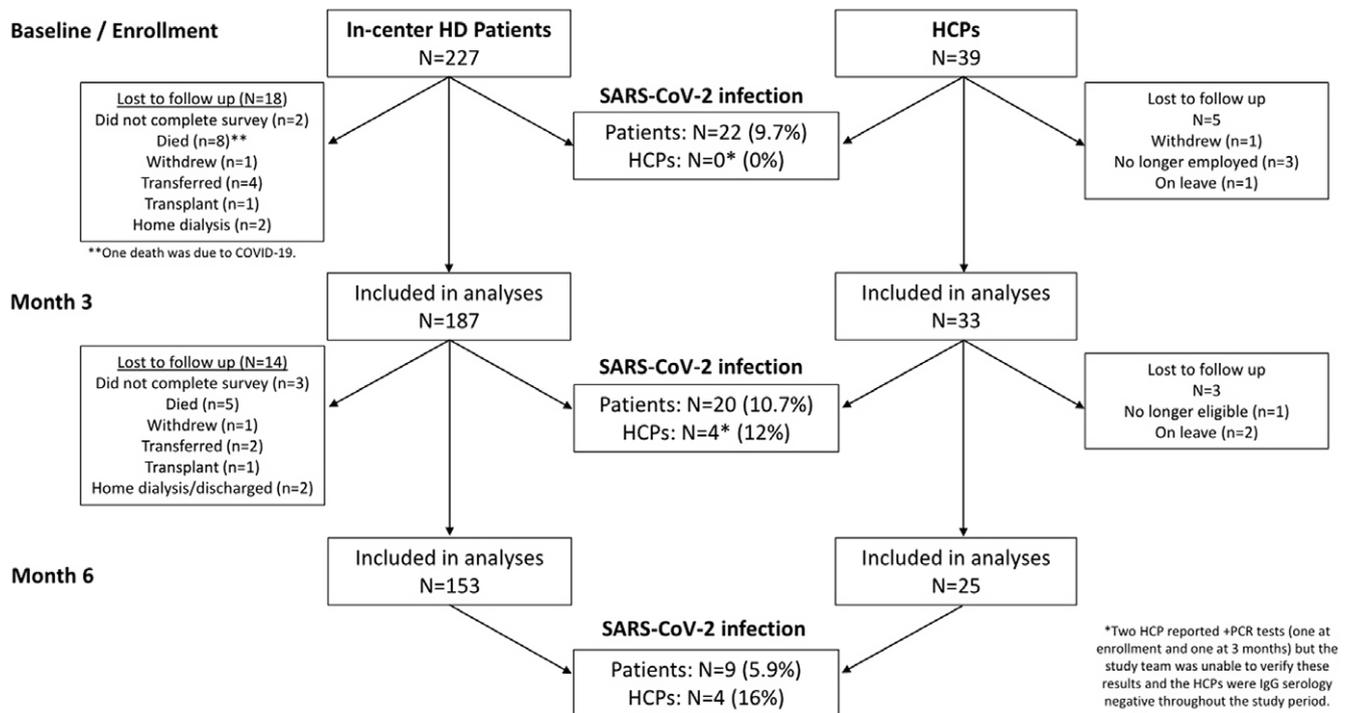
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### Methods

This study was conducted in 3 outpatient HD units at the Washington University School of Medicine (WUSM) in St Louis, Missouri, and it was approved by the WU Human Research Protection Office. Adult patients on in-center HD and dialysis-center HCP were enrolled after giving informed consent, as described previously.<sup>11</sup> A survey was administered either electronically or in-person at 3 different times (September 2020, December 2020, and March 2021) to patients and HCP to assess their household characteristics, personal behaviors and prevention activities, SARS-CoV-2 exposures, and history of SARS-CoV-2 infection since March 1, 2020.

Blood was also collected at these 3 times to assess SARS-CoV-2 infection status. Previous SARS-CoV-2 infection was assessed using the Abbott SARS-CoV-2 IgG serologic assay that targets the viral nucleocapsid protein (Abbott, Abbott Park, IL). The resulting unit for the SARS-CoV-2 IgG assay is the index (ie, signal/calibrator or S/C). An S/C value  $\geq 1.40$  was considered positive.

Electronic medical records of patients were reviewed at each survey and blood draw to obtain relevant clinical information, including dates of SARS-CoV-2 PCR test(s), hospitalizations due to SARS-CoV-2 infection, and symptoms. Comorbid conditions were reviewed at enrollment. The electronic medical records of HCP were not reviewed. All data were entered into a REDCap database.



**Fig. 1.** Distribution of SARS-CoV-2 infection cases among HD patients and HCPs at baseline, 3 months and 6 months.

We defined a SARS-CoV-2 case as having either a history of positive PCR test documented in the medical record or a positive IgG nucleocapsid serology result prior to each survey. For HCP, we only considered positive IgG serology to define a SARS-CoV-2 case because we did not review HCP medical records. Univariate analyses of patient characteristics among SARS-CoV-2 cases and noncases were performed using the Fisher exact test or the  $\chi^2$  test for categorical variables and the Mann Whitney U test for continuous variables. Statistical analyses were performed using SAS version 9.4 software (SAS Institute, Cary, NC), and  $P < .05$  was considered statistically significant.

## Results

Among the 3 HD units, 227 patients and 39 HCP were enrolled in the study (Fig. 1 and Supplementary Tables 1 and 2). At baseline, 22 (9.7%) of 227 patients had evidence of prior SARS-CoV-2 infection and none of the HCP had a SARS-CoV-2 infection. At the 3-month follow-up, 20 (10.6%) of 187 patients and 4 (12.2%) of 33 HCP had SARS-CoV-2 infection between the baseline and the 3-month follow-up. At the 6-month follow-up, 9 (5.8%) of 156 patients and 4 (16%) of 25 HCP had SARS-CoV-2 infection between the 3- and 6-month follow-ups. The cumulative incidence of SARS-CoV-2 infection among HD patients was 22.9% (52 of 227), which was 52 (26.5%) of 196 but excluding those lost to follow-up. The cumulative incidence of SARS-CoV-2 infection among HCP was 20.5% (8 of 39), which was 8 (25.8%) of 31 but excluding those lost to follow-up.

The baseline univariate analyses of risk factors associated with SARS-CoV-2 infection were published previously.<sup>11</sup> In the analysis of the 3-month and 6-month surveys, SARS-CoV-2-infected cases were significantly more likely to have had a household family

member with SARS-CoV-2 infection (3-month survey, 40% vs 4.2%;  $P \leq .001$ ; 6-month survey, 11.1% vs 2.8%;  $P = .029$ ) and to have had a household family member asked to quarantine because of exposure to SARS-CoV-2 (6-month survey, 33.3% vs 2.1%;  $P \leq .001$ ) (Table 1). Additionally, for the 3-month survey, SARS-CoV-2-infected patients reported significantly less adherence to social distancing outside the dialysis units (50% vs 81.4%;  $P \leq .004$ ). The only risk factors for SARS-CoV-2 infection identified among HCP were household exposure (3-month survey, 80% vs 14.3%,  $P = .009$ ; and 6-month survey, 75% vs 4.8%;  $P = .007$ ) and having a household member instructed to quarantine (6-month survey, 100% vs 0%,  $P \leq .001$ ) (data not shown).

Potential transmission events in the HD centers were examined (Supplementary Fig. 1). Most cases did not appear to be temporally or spatially related to any other SARS-CoV-2 cases. One shift at facility A had 3 positive patients who reported generally sitting in the same pod; 1 patient had a positive PCR result in November and 2 additional patients were IgG positive in December without any known SARS-CoV-2 exposures.

## Discussion

Studies examining risk factors associated with SARS-CoV-2 infection among chronic HD patients and HCP working in HD units using repeated surveys are lacking. In our prior publication, several risk factors at baseline were associated with SARS-CoV-2 infection, including SARS-CoV-2 infection among immediate family members or friends, residence in a long-term care facility, poor adherence to face mask use, and travel outside the local metropolitan area.<sup>11</sup> However, in the subsequent surveys, the only risk factor that remained associated with SARS-CoV-2 infection among chronic HD patients was having a household member with

**Table 1.** Univariate Analysis of Characteristics of HD Patients Who Tested Positive or Negative for SARS-CoV-2 Infection at the 3-Month and 6-Month Follow-Up

Survey Variable	3-Month Survey (N = 187)			6-Month Survey (N = 153)		
	SARS-CoV-2 Case (N = 20, 11%) <sup>a</sup>	Non-case (N = 167, 89%)	P Value	SARS-CoV-2 Case (N = 9, 6%) <sup>a</sup>	Noncase (N = 144, 94%)	P Value
<b>Hemodialysis unit</b>						
Facility A	9 (45.0)	76 (45.5)	Reference	3 (33.3)	66 (45.8)	Reference
Facility B	9 (45.0)	71 (42.5)	.91	5 (55.6)	60 (41.7)	.42
Facility C	2 (10.0)	19 (11.4)	.89	1 (11.1)	17 (11.8)	.83
Changed transportation in prior 3 mo	3 (15.0)	12 (7.2)	.21	1 (11.1)	11 (7.6)	.53
Changed residence in prior 3 mo	2 (10.0)	11 (6.6)	.63	1 (11.1)	9 (6.3)	.47
<b>Demographics</b>						
Age, median y [IQR]	59.5 [50.5–65.5]	60 [49–69]	.31	60 [57–74]	61 [49.5–69]	.71
Sex, male	15 (75.0)	77 (46.1)	.020	3 (33.3)	71 (49.3)	.50
Race, Black	18 (90.0)	147 (88.0)	>.99	9 (100.0)	127 (88.2)	.60
BMI, median kg/m <sup>2</sup> [IQR]	29.0 [27.0–33.1]	29.3 [25.2–36.5]	.88	38.0 [26.1–43.9]	29.3 [25.3–36.0]	.18
<b>Cause of ESRD</b>						
Diabetes mellitus	11 (55.0)	74 (44.3)	.48	4 (44.4)	65 (45.1)	>.99
Hypertension	16 (80.0)	110 (65.9)	.31	6 (66.7)	98 (68.1)	>.99
Other etiologies <sup>b</sup>	3 (15.0)	42 (25.2)	.41	1 (11.1)	35 (24.3)	.69
<b>Comorbidities</b>						
Hypertension	20 (100.0)	157 (94.0)	.60	9 (100.0)	137 (95.1)	>.99
Diabetes mellitus	12 (60.0)	93 (55.7)	.81	4 (44.4)	82 (56.9)	.51
Cerebrovascular disease or accident	11 (55.0)	94 (56.3)	>.99	6 (66.7)	80 (55.6)	.73
Neurological disease (excluding CVA)	2 (10.0)	7 (4.2)	.25	1 (11.1)	6 (4.2)	.35
Blood disorder	1 (7.1)	3 (1.7)	.40	0 (0.0)	3 (2.1)	.53
Solid-organ transplant	1 (5.0)	12 (7.2)	>.99	0 (0.0)	12 (8.3)	>.99
Autoimmune conditions (including systemic lupus erythematosus)	0 (0.0)	12 (7.2)	.37	0 (0.0)	10 (6.9)	>.99
Other comorbidity <sup>c</sup>	5 (25.0)	50 (29.9)	.80	1 (11.1)	43 (29.9)	.45
<b>SARS-CoV-2 prevention behaviors</b>						
<b>Reported social distancing at dialysis center (% adherence)</b>			.42	>.99		
All the time	13 (65.0)	125 (74.9)		6 (66.7)	97 (67.4)	
Less than all the time	7 (35.0)	42 (25.1)		3 (33.3)	47 (32.6)	
<b>Reported mask use at dialysis centers</b>			>.99	>.99		
All the time	19 (95.0)	157 (94.0)		8 (88.9)	130 (90.3)	
Less than all the time	1 (5.0)	10 (6.0)		1 (11.1)	14 (9.7)	
<b>Reported hand hygiene at dialysis center prior to sitting on dialysis chair</b>			.40	>.99		
All the time	14 (70.0)	131 (78.4)		5 (55.6)	87 (60.4)	
Less than all the time	6 (30.0)	36 (21.6)		4 (44.4)	57 (39.6)	
<b>Reported social distancing during daily life outside of home</b>			.003	.41		
All the time	10 (50.0)	136 (81.4)		6 (66.7)	114 (79.2)	
Less than all the time	10 (50.0)	31 (18.6)		3 (33.3)	30 (20.8)	
<b>Reported mask use during daily life outside of home</b>			>.99	.33		
All the time	18 (90.0)	151 (90.4)		7 (77.8)	126 (87.5)	
Less than all the time	2 (10.0)	16 (9.6)		2 (22.2)	18 (12.5)	
<b>Reported change in hand washing habits during daily life</b>			.61	>.99		
Yes, wash hands more often	15 (75.0)	111 (66.5)		5 (55.6)	86 (59.7)	

(Continued)

**Table 1.** (Continued)

Survey Variable	3-Month Survey (N = 187)			6-Month Survey (N = 153)		
	SARS-CoV-2 Case (N = 20, 11%) <sup>a</sup>	Non-case (N = 167, 89%)	P Value	SARS-CoV-2 Case (N = 9, 6%) <sup>a</sup>	Noncase (N = 144, 94%)	P Value
No, wash hands about the same amount as before	5 (25.0)	56 (33.5)		4 (44.4)	58 (40.3)	
Attended a gathering with more than 10 people in prior 3 months	6 (30.0)	75 (44.9)	.24	3 (33.3)	60 (41.7)	.74
No. of gatherings attended, median [IQR] <sup>d</sup>	1 [1–1]	2 [1–4]	.10	2 [2–12]	2 [1–5]	.36
Visit to other health facilities (doctor offices, dentist offices) in prior 3 mo	11 (55.0)	124 (74.3)	.11	5 (55.6)	93 (64.6)	.72
No. of doctor/dentist appointments, median [IQR] <sup>d</sup>	1 [1–5]	2 [1–4]	.38	3 [2–3]	3 [1–4]	.81
Visits to public spaces for daily activities in prior 3 mo	19 (95.0)	138 (82.6)	.21	5 (55.6)	116 (80.6)	.09
No. of visits to public locations, median [IQR] <sup>d</sup>	19 [4–46]	15 [6–31]	.55	3 [1–9]	18.5 [7–41]	.041
<b>SARS-CoV-2 exposures</b>						
Travel outside of the St Louis area	1 (5.0)	12 (7.2)	>.99	0 (0.0)	9 (6.3)	.07
Household member tested for SARS-CoV-2	13 (65.0)	55 (32.9)	.007	3 (33.3)	43 (29.9)	>.99
Household member tested positive for or diagnosed with SARS-CoV-2	8 (40.0)	7 (4.2)	<.001	1 (11.1)	4 (2.8)	.26
Household member told by health department to stay home due to SARS-CoV-2 exposure	8 (40.0)	7 (4.2)	<.001	3 (33.3)	3 (2.1)	.003
Household member hospitalized with SARS-CoV-2	8 (40.0)	4 (2.4)	<.001	1 (11.1)	0 (0.0)	.06
Extended family/friend tested positive for or diagnosed with SARS-CoV-2	3 (15.0)	14 (8.4)	.40	0 (0.0)	9 (6.3)	>.99
Extended family/friend hospitalized with SARS-CoV-2	5 (25.0)	15 (9.0)	.045	0 (0.0)	17 (11.8)	.60
Extended family/friend died from SARS-CoV-2	3 (15.0)	14 (8.4)	.40	1 (11.1)	10 (6.9)	.50

Note. ND, not determined; BMI, body mass index; ESRD, end-stage renal disease; PKD, polycystic kidney disease; CAD, coronary artery disease; CVA, cerebrovascular accident; HF, heart failure; HD, hemodialysis; IQR, interquartile range.

<sup>a</sup>Defined as a positive PCR and/or serology for SARS-CoV-2.

<sup>b</sup>Other etiologies include glomerulonephritis, lupus nephritis, PKD, other.

<sup>c</sup>Other comorbidities include active malignancy, cirrhosis, current smoker, HIV, lung disease.

<sup>d</sup>Restricted to patients who reported attended a gathering with <10 people, a visit to a health facility or a visit to a public location.

SARS-CoV-2 infection. Among HCP, the only risk factor associated with SARS-CoV-2 infection was having a household member with SARS-CoV-2 infection.

There appeared to be no patient-to-patient or patient-to-staff transmission in the dialysis units; however, we did not perform whole-genome sequencing to confirm this. In one facility, 2 patients were identified as IgG positive in without known SARS-CoV-2 exposures in the month after an infected patient was dialyzed in the same pod. Because it is not known when the 2 IgG-positive patients were exposed to SARS-CoV-2, no clear relationship between these cases could be discerned. The 3 HD units implemented the Centers for Disease Control and Prevention (CDC) SARS-CoV-2 infection prevention measures in March 2020.<sup>12</sup> Previous studies reported that implementation of infection prevention measures (eg, a universal mask policy) in HD units were associated with reduced risk of SARS-CoV-2 infection.<sup>9,13</sup> Our results are consistent with a previous study<sup>9</sup> indicating that when recommended infection prevention measures are used in HD units, the risk of SARS-CoV-2 infection is dependent on exposures from contacts in patient homes, especially when the community burden of SARS-CoV-2 is high.

Our study had several limitations. Due to the small number of cases, we could not perform multivariate analysis to identify independent risk factors for SARS-CoV-2 infection. Survey responses may be subject to recall bias. Finally, our study

was performed when most patients had not received the SARS-CoV-2 vaccine (only 33% of patients had received at least 1 dose of vaccine at the 6-month survey) and prior to the emergence of the SARS-CoV-2 o(omicron) variant. Thus, our results may not be generalizable to new SARS-CoV-2 variants that emerged after the study period or among vaccinated chronic HD patients.

In this longitudinal survey study in 3 outpatient HD units that implemented CDC SARS-CoV-2 infection prevention measures, the risk of SARS-CoV-2 infection among HD patients and HCPs was consistently associated with a household member having SARS-CoV-2 infection.

**Supplementary material.** For supplementary material accompanying this paper visit <https://doi.org/10.1017/ash.2022.269>

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**Conflicts of interest.** M.A.O. received grant funding from Pfizer in the past 3 years and worked as consultant to Pfizer not related to COVID-19. All other authors have no relevant disclosures.

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