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SARS-CoV-2 infection risk factors among maintenance hemodialysis patients and healthcare personnel in outpatient hemodialysis centers

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Key Points

- Increased risk of SARS-CoV-2 infection was associated with community prevalence.
- Increased risk of SARS-CoV-2 infection was associated with exposure to infected family members and personal infection prevention measures.

Introduction

In the United States during the first pandemic wave, the seroprevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection designated as coronavirus disease 2019 (COVID-19) among maintenance hemodialysis (HD) patients was 8.3% (8.0–8.6%) with regional variation of 3.5% (3.1–3.9%) in the West to 27.2% (25.9–28.5%) in the Northeast[1]. Hospitalized patients with end-stage renal disease (ESRD), including those on chronic HD, are at increased risk of death from SARS-CoV-2 infection when compared to those without ESRD.[2] Due to the congregate nature of dialysis units, open layout, and physical proximity of patients during HD sessions, patients and healthcare personnel (HCPs) may be at increased risk of exposure to SARS-CoV-2.[3] To mitigate this risk, the Centers for Disease Control and Prevention (CDC) provided guidance on SARS-CoV-2 infection prevention measures specific to outpatient HD units in March 2020.[4] However, the risk of SARS-CoV-2 infection is also influenced by factors outside the HD units, such as local community prevalence of SARS-CoV-2 infection, residence type (e.g. long-term care facility [LTCF])[5,6] and household characteristics, exposure to household members and others with SARS-CoV-2 infection,[7] and personal infection prevention activities.[7] Studies examining the risk factors for SARS-CoV-2 infection among patients on in-center HD and dialysis HCPs are lacking. We examined the potential source of and risk factors

for SARS-CoV-2 infection among patients on in-center HD and HCPs in three outpatient HD units which implemented the CDC SARS-CoV-2 infection prevention measures in March 2020.

Materials and Methods

This study was conducted in three outpatient HD units at Washington University School of Medicine (WUSM) in St. Louis, Missouri, USA and was approved by WUSM Human Research Protection Office. Adult patients on in-center HD and dialysis center HCPs were enrolled after obtaining informed consent. During September 2020, a survey was administered to patients and HCPs to assess household characteristics, SARS-CoV-2 exposures, personal prevention activities, and history of SARS-CoV-2 infection since March 1, 2020. Previous exposure to SARS-CoV-2 was assessed using the Abbott SARS-CoV-2 IgG serological assay that targets the viral nucleocapsid protein (Abbott, Abbott Park, Illinois). The result unit for the SARS-CoV-2 IgG assay is Index (signal/calibrator [S/C]) and a value of ≥ 1.40 Index (S/C) is considered as positive. The sensitivity and specificity of the Abbott assay is ~90-99% and >99% respectively.[7] Electronic medical records of patients from March through September 2020 were reviewed to obtain relevant clinical information, including dates of SARS-CoV-2 PCR test(s), hospitalizations due to SARS-CoV-2 infection, and comorbid conditions. Cumulative SARS-CoV-2 cases per 1,000 population by zip code through the first week of September were obtained from Saint Louis University's Missouri COVID-19 Tracking Project GitHub data repository (https://github.com/slu-openGIS/MO_HEALTH_Covid_Tracking.git) and the Illinois Department of public health COVID-19 dashboard (https://www.dph.illinois.gov/covid19/covid19-statistics).

For study purposes, a SARS-CoV-2 case was defined as either history of a positive PCR test documented in the medical record any time from March-September 2020 or a positive IgG

serology result at the time of study enrollment (September 2020). Univariate analysis of the patient characteristics among SARS-CoV-2 cases and non-cases was performed using Fisher's exact tests or univariate logistic regression for categorical variables and Mann Whitney U-tests for continuous variables. Correlation between positive SARS-CoV-2 test results (either antibody or PCR or both) of HD patients and community SARS-CoV-2 infection prevalence by patient's home zip code was performed using the Spearman correlation test. To determine potential acquisition of SARS-CoV-2 infection inside HD units, we examined the distribution of cases by dialysis day and shift in each HD unit. Statistical analyses were performed using Python pandas, SciPy, and Matplotlib packages.

Results

Among the three HD units, 226 patients and 39 HCPs were enrolled into the study (Supplementary Table 1). Of the 226 patients, 21 patients (9%) were considered to be SARS-CoV-2 cases based on history of positive PCR or positive serology. During the study period, 130 (58%) patients had ≥1 PCR test performed (114 patients were asymptomatic and PCR was performed as screening test prior to a procedure) (Supplementary Table 2). None of the HCPs had evidence of SARS-CoV-2 infection by either PCR or serology.

In univariate analysis, SARS-CoV-2 infected cases were significantly more likely to reside in a LTCF (19% of cases vs. 1.5% of non-cases; p=0.002), had a household family member (24% vs. 3%; p=0.001), or extended family member/friend diagnosed with SARS-CoV-2 infection (19% vs. 5%; p=0.03), traveled outside of the local metropolitan area (29% vs. 12%; p=0.04), and reported less adherence to mask use outside of the home (14% vs. 2%; p=0.02) (Table 1). The SARS-CoV-2 infection prevalence among HD patients correlated with SARS-CoV-2 infection prevalence in their community as assessed by zip code (r=0.346; $P = 0.014$)

(Figure 1). The prevalence/1000 persons of SARS-CoV-2 infection was significantly lower in the HCPs' home residence zip codes compared to HD patients (median [IQR]:1.73 [1.45-1.97] vs. 19.50 [18.11-21.39], respectively, $P < 0.001$).

Among the 21 SARS-CoV-2 infected cases, 10 (48%) patients had both a positive PCR test in the past and positive IgG antibody in September (8 patients with symptomatic disease; the two asymptomatic patients included a LTCF resident and a worker in a LTCF) with median time from the positive PCR and positive IgG antibody of 128 days (IQR: 85-140) (Supplementary Table 3). Two (10%) asymptomatic patients had prior positive PCR with negative IgG antibody results. For these two patients, the time intervals from positive PCR test to negative IgG antibody test were 124 and 139 days. Nine patients (43%) had positive IgG antibody without a positive PCR test; of these, 6 had no PCR test performed and 3 had a negative PCR test as part of pre-procedure screening (median time from latest negative PCR test to positive IgG antibody test was 45 days). Of these 9 patients, 4 reported having contact or living with a known SARS-CoV-2 infected case, one lived in a LTCF, 3 reported travel outside of the metropolitan area, and one patient had no obvious SARS-CoV2 risk factor. No clustering of SARS-CoV-2 infected cases was observed among the three HD units by shift and day of the week (Table 2). Except for one patient, all SARS-CoV-2 infected patients had one or more risk factors for exposure to SARS-CoV2 outside the HD unit.

Discussion

A few studies have examined risk factors for SARS-CoV2 infection among HD patients.[1,6,9,10] However, none of the previous studies included HCPs or reported on household characteristics, SARS-CoV-2 exposures, and personal prevention activities of patients and HCPs while evaluating the risk factors for SARS-CoV2 infection. Our results indicate that the risk of

infection among patients on in-center maintenance HD and dialysis HCPs is associated with the local community prevalence of SARS-CoV-2 infection, diagnosis of SARS-CoV-2 infection among immediate family members or friends, residence in a LTCF, and personal SARS-CoV-2 infection prevention activities, such as adherence to face mask use and travel outside the local metropolitan area. Residence in a LTCF has been identified as a SARS-CoV-2 infection risk factor previously, and our results support this finding.[5,6] Notably, none of the enrolled HCPs had a positive IgG serology result, which suggests CDC infection prevention guidance can help limit SARS-CoV-2 transmission within dialysis centers.

There are several limitations to this study. Due to the small number of cases, we could not perform multivariate analysis to identify independent risk factors for SARS-CoV-2 infection. We are currently in the process of obtaining follow-up serology and survey data from study participants and may be able to perform multivariable modeling in future analyses. Survey responses regarding reported activities, SARS-CoV-2 exposures, and prevention activities (such as mask use) may be subject to recall bias or "good behavior" bias. Direct observation of behaviors and activities would be optimal. This is not feasible outside of the dialysis centers, but direct observations within the dialysis centers are currently ongoing. Future analyses of these data can be used to validate the survey data regarding in-center COVID-19 prevention practices. Additionally, we did not perform periodic surveillance testing for asymptomatic patients or HCPs using PCR test and thus the overall SARS-CoV-2 infection prevalence may be underestimated as some patients and HCPs could have asymptomatic SARS-CoV-2 infection with no detectable antibody response or had not yet developed antibodies. Finally, majority (87.2%) of patients in our cohort were African American and thus may limit the generalizability

of our findings, as adult African American patients accounts for only 35% of all US dialysis patients[1].

Our results suggest that while some SARS-CoV-2 risk factors are not easily modifiable, others are, and adherence to infection prevention practices outside of HD units such as consistent use of face masks[11] may help decrease risk of SARS-CoV-2 in HD patients. We did not find clear evidence for SARS-CoV2 infection acquisition by patients or HCPs within HD units, suggesting that CDC SARS-CoV-2 infection prevention measures were effective. However, with the ongoing increases in community prevalence, and the strong association found here between risk of SARS-CoV-2 and community rates, it is important to continue to examine the effectiveness of CDC SAR-CoV-2 infection prevention measures and risk factors for SARS-CoV-2 among HD patients and HCPs. The longitudinal follow up of this study is ongoing and will help address these questions.

Disclosures

M. Olsen received grant funding from Pfizer, Merck and Sanofi Pasteur in past three years and work as consultant to Pfizer not related to COVID-19. J. Kwon is supported by the National Institute of Allergy and Infectious Diseases (grant no. 1K23AI137321-01A1). C. Farnsworth reports Consultancy Agreements: Roche Diagnostics; Research Funding: Abbott Diagnostics, Siemens Healthineers, Beckman Coulter. T. Li reports Consultancy Agreements: Reata Pharmaceuticals, Inc., GlaxoSmithKline, ChemoCentryx; Research Funding: Human Genome Science, Aurinia Pharmaceuticals, Omeros Corporation, Bristol-Myers Squibb; Scientific Advisor or Membership: ASN Publications Committee (member), ASN Education Committee (member), GlaxoSmithCline (Scientific advisor). All remaining authors have nothing to disclose.

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All authors interpreted the results, all authors revised and approved the manuscript.

Supplementary Material

Supplementary Table 1: Outpatient hemodialysis facilities characteristics included in the study

Supplementary Table 2. SARS-CoV-2 IgG antibody and SARS-CoV-2 PCR Results in the Study Population (Patients only; N=226)*

Supplementary Table 3: Characteristics of hemodialysis patients who tested positive for SARS-CoV-2 PCR or IgG antibody

References:

1. Anand S, Montez-Rath M, Han J, *et al.* Prevalence of SARS-CoV-2 antibodies in a large nationwide sample of patients on dialysis in the USA: a cross-sectional study. *The Lancet* 2020; 396**:** 1335-1344.
2. Ng JH, Hirsch JS, Wanchoo R, *et al.* Outcomes of patients with end-stage kidney disease hospitalized with COVID-19. *Kidney International* 2020.
3. Creput C, Fumeron C, Toledano D, *et al.* COVID-19 in Patients Undergoing Hemodialysis: Prevalence and Asymptomatic Screening During a Period of High Community Prevalence in a Large Paris Center. *Kidney medicine* 2020.
4. Centers for Disease Control and Prevention. Interim Additional Guidance for Infection Prevention and Control Recommendations for Patients with Suspected or Confirmed COVID-19 in Outpatient Hemodialysis Facilities.
5. Rincón A, Moreso F, López-Herradón A, *et al.* The keys to control a COVID-19 outbreak in a haemodialysis unit. *Clinical kidney journal* 2020; 13: 542-549.
6. Hsu CM, Weiner DE, Aweh G, et al. COVID-19 Among US Dialysis Patients: Risk Factors and Outcomes From a National Dialysis Provider. *American Journal of Kidney Diseases*. 2021
7. Ng OT, Marimuthu K, Koh V, *et al.* SARS-CoV-2 seroprevalence and transmission risk factors among high-risk close contacts: a retrospective cohort study. *The Lancet infectious diseases* 2020.
8. Bryan A, Pepper G, Wener MH, *et al.* Performance characteristics of the Abbott Architect SARS-CoV-2 IgG assay and seroprevalence in Boise, Idaho. *Journal of clinical microbiology* 2020.

9. Corbett RW, Blakey S, Nitsch D, *et al.* Epidemiology of COVID-19 in an urban dialysis center. *Journal of the American Society of Nephrology* 2020; 31**:** 1815-1823.

10. 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. *Journal of the American Society of Nephrology* 2020.11. Chu DK, Akl EA, Duda S, *et al.* Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis. *The Lancet* 2020.

Table 1. Univariate analysis of characteristics of HD patients who tested positive or negative for SARS-CoV-2 infection

Variable	SARS-CoV-2 infected case* N = 21 (9%)	Non-case N = 205 (91%)	*P* - value (Mann-Whitney U test or Fisher exact)
Demographics			
Female	11 (52.4)	106 (51.7)	1.000
Age (median [IQR] yr)	54 [47-64]	60 [49-69]	0.082
Age (> 65 yrs)	4 (19.0)	71 (34.6)	0.223
Race (African American)	18 (85.7)	179 (87.3)	0.739
BMI (median [IQR])	32.7 [24.6-37.8]	29.13 [25.2-35.6]	0.731
Hemodialysis unit			
Facility A	11 (52.5	91 (44.4)	reference
Facility B	5 (23.8)	90 (43.9)	0.196
Facility C	5 (23.8)	24 (11.7)	0.347
Transportation to and from HD unit			
By private car (self or family member/friend)	11 (52.4)	111 (54.1)	1.000
By public transportation	1 (4.8)	38 (18.5)	0.137
By medical transport company	9 (42.8)	55 (26.8)	0.133
Cause of ESRD			
Diabetes mellitus	7 (33.3)	89 (43.4)	0.488
Hypertension	14 (66.7)	133 (64.9)	1.000
Glomerular Disease	**4 (19.0)**	**11 (5.3)**	**0.038**
Other etiologies	4 (19.0)	68 (33.2)	0.226
Dialysis vintage (median [IQR] in months)	37 [20-66]	36 [13-79]	0.309
Comorbidities			
Diabetes mellitus	10 (47.6)	110 (53.7)	0.651
Hypertension	21 (100.0)	193 (94.1)	0.609
Cerebral Vascular Accident (CVA)	2 (9.5)	19 (9.3)	1.000
Cardiovascular disease	9 (42.8)	72 (35.1)	0.492
Neurological disease (excluding CVA)	2 (9.5)	9 (4.4)	0.274
COPD/Asthma	6 (28.6)	39 (19.0)	0.387
Smoking	1 (4.8)	22 (10.8)	0.704
Active Hepatitis C	1 (4.8)	8 (3.9)	0.591
Cirrhosis	1 (4.8)	4 (2.0)	0.389
HIV with CD4 < 200	1 (4.8)	1 (0.5)	0.178
Active malignancies	1 (4.8)	10 (4.9)	1.000
Medications 30 days prior to serology test (number of dialysis patients)			
Immunosuppressive medications	2 (9.5)	26 (12.7)	1.000
Hypertension medications	20 (95.2)	40 (80.5)	0.136
Cardiovascular disease medications	18 (85.7)	168 (82.0)	1.000
Diabetes medications	5 (23.8)	62 (30.2)	0.624
Asthma/COPD medication	3 (14.3)	50 (24.4)	0.420
Number of hospitalizations since March 1st, 2020 (median [IQR])	1 [0-1]	0 [0-2]	0.133
SARS-CoV-2 Exposures			
Household member tested for SARS-CoV-2	**11 (52.4)**	**57 (27.9)**	**0.026**
Household member diagnosed with SARS-CoV-2	**5 (23.8)**	**6 (2.9)**	**0.001**
Extended family/friend positive for SARS-	**4 (19.0)**	**10 (4.9)**	**0.030**

CoV-2			
Travel outside St. Louis area	**6 (28.6)**	**24 (11.8)**	**0.043**
Resided in long-term care facility	**4 (19.0)**	**3 (1.5)**	**0.002**
Household size			
Lives alone	1 (4.8)	55 (26.8)	reference
Two or more people	8 (38.1)	144 (70.2)	0.450
Number of generations in the household			
One generation	4 (19.0)	102 (49.8)	reference
Two generations	**10 (47.6)**	**70 (34.1)**	**0.046**
Three generations or more	3 (14.3)	26 (12.7)	0.169
Household density (household size/ number of bedrooms)	1 [1.0-2.3]	1 [0.8-1.2]	0.273
1st quartile (0-0.75)	4 (19.0)	55 (26.8)	reference
2nd and 3rd quartiles (0.75-1.2)	10 (47.6)	93 (45.4)	0.772
4th quartile (> 1.2)	3 (14.3)	52 (25.4)	1.000
SARS-CoV-2 infection Prevention Behaviors			
Reported Mask use at dialysis centers			
All the time	21 (100.0)	196 (95.6)	reference
Less than all the time	0 (0.0)	8 (3.9)	1.000
Reported social distancing at dialysis center (% adherence)			
All the time	16 (76.2)	140 (68.3)	reference
Less than all the time	5 (23.8)	64 (31.2)	0.621
Reported hand hygiene at dialysis center prior to sitting on dialysis chair			
All the time	19 (90.5)	174 (84.9)	reference
Less than all the time	2 (9.5	30 (14.5)	0.746
Reported mask use during daily life outside of home			
All the time	14 (66.7)	155 (75.6)	reference
Most of the time	3 (14.3)	45 (22.0)	0.770
Sometimes (about 50% of the time) or less	**3 (14.3)**	**4 (2.0)**	**0.021**
Visit to other health facilities (doctor offices, dentist offices)) between March and September 2020			
1st tertile 0-1 health visits	6 (28.6)	75 (36.6)	reference
2nd tertile 2-5 health visits	9 (42.9)	63 (30.7)	0.415
3rd tertile > 5 health visits	6 (28.6)	66 (32.2)	1.000
Visit to public spaces for daily activities) between March and September 2020			
1st tertile 0-6 visits	10 (47.6)	62 (30.2)	reference
2nd tertile 7-28 visits	7 (33.3)	71 (34.6)	0.441
3rd tertile >28 visits	4 (19.0)	71 (34.6)	0.096
Number of gatherings with >10 people attended**			
1st tertile (0 gatherings)	7 (33.3)	105 (51.2)	reference
2nd tertile (1 gathering)	5 (23.8)	35 (17.1)	0.302
3rd tertile (> 1 gatherings)	9 (42.9)	64 (31.2)	0.184

* Defined as a positive PCR and/or serology for SARS-CoV-2

**Types of gatherings include house of worship/religious services, funerals, weddings, family/friend gatherings (birthdays, dinners, cookouts, etc.), graduations, concerts or plays/theater productions, eating at a restaurant, visits to a bar, in-person school or classes, protests, and others.

ND- not determined

BMI- Body Mass Index

ESRD- End Stage Renal Disease

HD- Hemodialysis

IQR- Inter Quartile Range

Yr -year

Table 2: Number of SARS-CoV-2 infected cases by hemodialysis facility, pod, and shift

Center	Pod	Shift	Case ID(s)	Positive PCR or IgG positive only	Know exposure outside hemodialysis facility	Has other risk factor*
A	A	M/W/F second shift	16	IgG positive	No	No
A	A	M/W/F third shift	4	PCR positive	Yes	No
A	A	T/T/S first shift	2	PCR positive	Yes	Yes
A	A	T/T/S second shift	1, 3	Both PCR positive one week apart	1: Yes 3. Yes	1. Yes 3. No
A	B	T/T/S first shift	5	PCR positive	No	Yes
A	C	M/W/F first shift	6, 16	One PCR positive One IgG positive one month apart	6: No 16: No	6: Yes 16: No
A	C	T/T/S first shift	18	IgG positive	Yes	No
A	Rotate different pods	M/W/F second shift	19	IgG positive	No	Yes
A	Rotate different pods	T/T/S third shift	13	IgG positive	Yes	Yes
B	2	M/W/F first shift	11	PCR positive	Yes	No
B	3	T/T/S first shift	9	PCR positive	Yes	No
B	3	T/T/S second shift	7	PCR positive	No	No

B	1	T/T/S second shift	8, 14	One PCR positive One IgG positive three months apart	8: Yes 14: Yes	8. No 14. No
C	3	M/W/F first shift	21	IgG positive	No	Yes
C	4	M/W/F first shift	12	PCR positive	No	Yes
C	1	T/T/S first shift	10, 15	One PCR positive One IgG positive three months apart	10: Yes 15. No	10: Yes 15: Yes
C	Not sure	T/T/S second shift	20	IgG positive	No	Yes

M/W/F- Monday/Wednesday/Friday

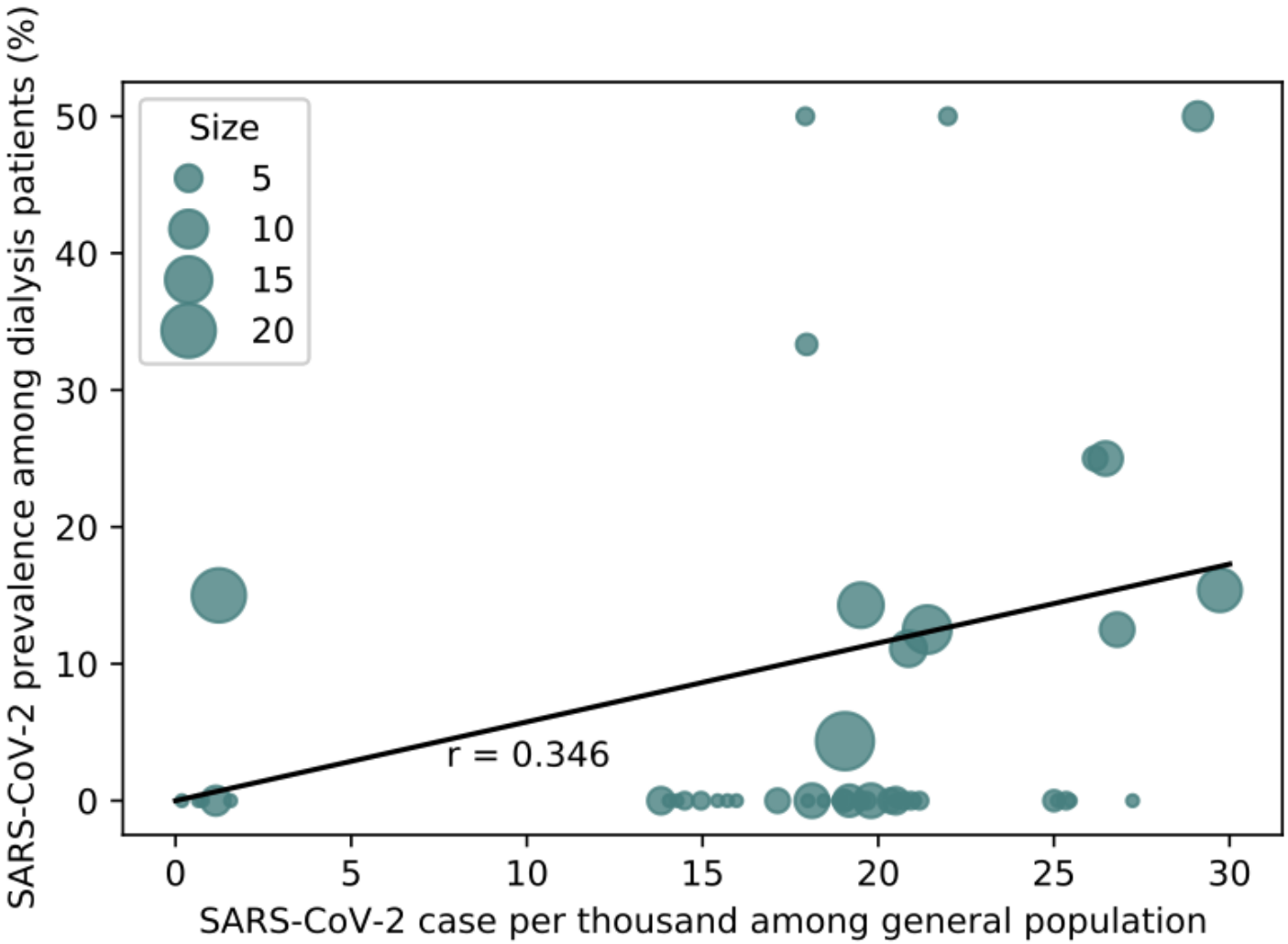
T/T/S- Tuesday/Thursday/Saturday

*Based on univariate analysis in Table 1

Figure 1 legend:

Correlation between SARS-CoV-2 infection prevalence among maintenance hemodialysis patients and community SARS-CoV-2 infection cumulative incidence per 1000 population by patients' home zip code

Figure 1


SARS-CoV-2 prevalence among dialysis patients (%)
SARS-CoV-2 case per thousand among general population
Size
5
10
15
20
r = 0.346
0
10
20
30
40
50
0
5
10
15
20
25
30