

Clustering of SARS-CoV-2 Infections in Households of Patients Diagnosed in the Outpatient Setting in Baltimore, Maryland

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In an outpatient cohort in Maryland, clustering of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) positivity within households was high, with 76% of 74 households reporting at least 1 other symptomatic person and 66% reporting another person who tested SARS-CoV-2 positive. SARS-CoV-2 positivity among household members was associated with larger household size and bedroom sharing.

Keywords. COVID-19; epidemiology; household contact; SARS-CoV-2

The United States has experienced sustained community transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) since early 2020 [1]. Household transmission of SARS-CoV-2 is thought to occur commonly, but 2 systematic reviews reported household secondary attack rates ranging from <1% to 55% [2, 3]. More recent US studies have reported secondary infection >50% among household contacts [4, 5]. The Centers for Disease Control and Prevention (CDC) recommends preventive behaviors for household contacts of coronavirus disease 2019 (COVID-19) patients, including separate bedrooms and bathrooms, frequent hand washing, and mask wearing [6]. The extent to which these recommendations are followed is not well documented. We investigate cumulative

household infections and associated preventive behaviors in an outpatient cohort of confirmed COVID-19 patients.

METHODS

Study Design and Sample

A convenience sample of persons who tested SARS-CoV-2-positive at Johns Hopkins Health System COVID-19 testing sites from April 21 to July 23, 2020, was prospectively enrolled to characterize the natural course of COVID-19 in the ambulatory setting [7]. Individuals ≥ 18 years of age were eligible, with recruitment preferentially targeting those age ≥ 40 years. Participants living in congregate settings were excluded, and Spanish-only speakers were enrolled for 1 month due to limited availability of Spanish-speaking staff. Of 3991 confirmed COVID-19 patients during this period, 475 were screened and 129 enrolled in the standard arm; 118 completed the baseline assessment. An abbreviated sampling arm enriched for participants <40 years of age with higher initial viral burden to assess whether these factors promoted spread. In this arm, 666 participants who had tested positive 3 weeks prior were contacted between June 23 and August 13, 2020; of these, 56 enrolled and 28 completed 1 in-person visit a median (interquartile range [IQR]) of 36.5 (35–42) days after symptom onset. One hundred sixty-three index participants were included between both arms (Supplementary Figure 1).

Data Collection

Index participants completed a baseline assessment of demographic characteristics and comorbidities on study day 0, a median (range) of 5 (3–10) days after symptom onset. Participants also completed an adapted FLU-PRO survey on study days 0, 3, 7, 14, 21, and 28, grading self-perceived COVID-19 symptom severity on a scale from 0 to 1, with higher scores indicating greater severity.

A survey of household preventive behaviors was conducted on study day 3, assessing whether participants and their household contacts had always, sometimes, or never engaged in specified preventive behaviors at home in the time since their first positive COVID-19 test.

A household inventory was completed between 21 and 28 days postenrollment, including questions about participants' homes and comprehensive enumeration of household members' demographic characteristics, comorbidities, COVID-19 symptoms, and SARS-CoV-2 testing history. All information about household contacts was reported by the index, and no samples were collected from contacts. A total of 86 participants—61 standard arm and 25 abbreviated—completed the inventory. Compared with these 86, the 77 who did not complete the inventory were

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significantly less likely to be African American and more likely to have a comorbidity ($P < .05$) (Supplementary Table 1).

For abbreviated arm participants, all surveys were conducted following their day 28 visit. Surveys were conducted via either telephone or secure internet link [8].

Laboratory Testing

Initial viral burden was measured by RT-PCR cycle threshold (Ct) at the Johns Hopkins Hospital Clinical Microbiology Laboratory. Fifty-nine participants had samples collected within 7 days of symptom onset (median [IQR], 3 [1–4] days) and resulted on the NeuMoDx platform.

Statistical Analyses

Chi-square and rank-sum tests were used to compare categorical and continuous variables. Primary analyses included all household contacts regardless of symptom onset timing relative to the index ($n = 178$). Additional analyses considered only those contacts with symptom onset after the index ($n = 130$). Data were analyzed using STATA IC/16.0 [9].

Patient Consent Statement

All participants provided oral consent, and the Johns Hopkins Institutional Review Board approved this protocol.

RESULTS

Among 86 index participants, 74 identified at least 1 household contact. Of those 74, the median age (IQR) was 53 (43–62) years, 41% were male, 28% were African American, and 14% were Hispanic/Latinx (Supplementary Table 1). Ninety-seven percent reported symptoms during the study period (Supplementary Table 2). The median household size (IQR) was 3 (2–4) (Supplementary Table 3). Households had a median (IQR) of 4 (3–4) bedrooms and 3 (2–4) bathrooms. The 74 participants reported 193 household contacts, of whom 15 were

excluded because no information was provided. The median household contact age (IQR) was 32 (16–53) years, 49% were male, 23% were African American, and 26% were Hispanic/Latinx (Supplemental Table 4). Considering index participants and contacts, 43% of households included an adult age ≥ 60 , and 92% had at least 1 member with a comorbidity.

COVID-19/SARS-CoV-2 Cascade

Among 178 household contacts, 102 (57%) in 56/74 households (76%) reported ever experiencing COVID-19 symptoms, of whom 79 (77%) were tested, with 63 (80%) testing positive (Figure 1). Of symptomatic contacts, 41% had symptom onset a median (IQR) of 4 (2–7) days before their index, while 56% had symptom onset a median (IQR) of 4 (2–8) days after. Among those who tested positive, 33% did so a median (IQR) of 5 (3–8) days before their index, while 63% tested positive a median (IQR) of 2 (1–6) days after. Overall, 61 (60%) had symptom onset within 5 days before or after symptom onset of their index. Contacts' most commonly reported symptom was fatigue (38%), followed by headache (34%) and body aches/muscle pain (33%). Symptomatic testing was significantly less common among younger and Hispanic/Latinx contacts ($P < .01$) (Supplementary Table 5).

Overall, 35% of household contacts tested SARS-CoV-2 positive, and 66% of households had at least 1 positive household contact. Compared with households with no positive contacts, those with at least 1 positive contact were significantly larger, and their index participant was significantly less likely to use a separate bedroom from other household members ($P < .01$) (Table 1). Higher index symptom severity was also associated with a contact being positive, but this did not achieve statistical significance ($P = .06$). Similar associations were observed for households with at least 1 symptomatic contact. No associations were observed between other participant/contact characteristics, initial Ct value, or other preventive behaviors.

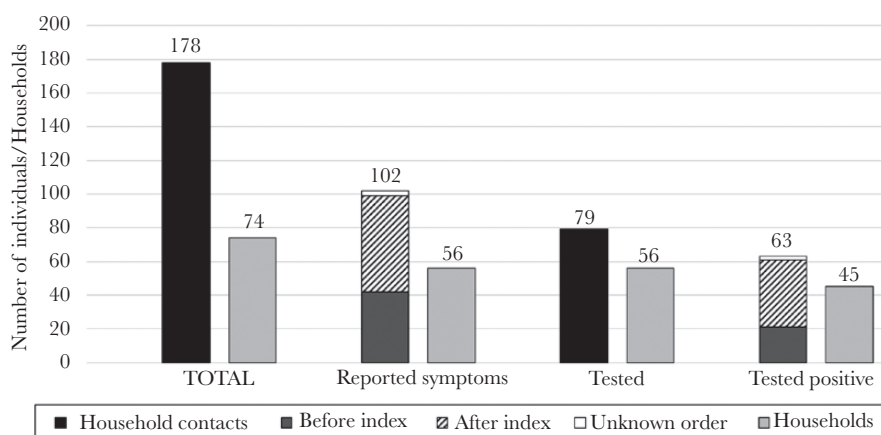


Figure 1. SARS-CoV-2 cascade among individual household contacts and households of 74 SARS-CoV-2-positive index participants. Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Table 1. Characteristics of Index Participants and Households (n = 74)

Characteristic	≥1 SARS-CoV-2-Positive Household Member (n = 45)	No SARS-CoV-2-Positive Household Member (n = 29)	P Value	≥1 COVID-19 Symptomatic Household Member (n = 56)	No COVID-19 Symptomatic Household Member (n = 18)	P Value
Index participant characteristics						
Median age (IQR), y	52 (45–60)	55 (42–62)	.78	53 (46–63)	53 (45–63)	.58
Gender			.46			.67
Male	21 (47)	11 (38)		25 (45)	7 (39)	
Female	24 (53)	18 (62)		31 (55)	11 (61)	
Race			.60			.19
White	27 (60)	18 (62)		37 (67)	8 (44)	
African American	9 (20)	7 (24)		9 (17)	7 (39)	
Other	9 (20)	4 (14)		10 (15)	3 (17)	
Hispanic origin	6 (13)	5 (17)	.40	7 (13)	4 (22)	.53
Median Ct value (IQR)						
All households ^a	18.3 (15.9–21.5)	17.2 (14.5–20.5)	.37	18.2 (15.9–21.6)	15.3 (14.3–18.3)	.07
Index is first case in household ^b	16.9 (15.4–20.5)	17.2 (14.5–20.5)	.60	17.7 (15.9–21.5)	15.3 (14.3–18.3)	.09
First FLU-PRO score (IQR) ^c	0.38 (0.16–0.56)	0.16 (0.06–0.31)	.06	0.34 (0.16–0.53)	0.13 (0.06–0.03)	.06
Household characteristics, median (IQR)						
Household size	4 (3–4)	2 (2–4)	<.01	4 (2–4)	2 (2–4)	.03
No. of bedrooms ^c	4 (3–4)	4 (3–4)	.31	3.5 (3–4)	4 (3–4)	.58
No. of bathrooms ^c	3 (2–4)	2.5 (2–3)	.18	3 (2–4)	2 (2–3)	.10
Age of household contacts, y	32 (16–54)	31 (16–50)	.40	32 (16–54)	29 (15–50)	.58
Preventive behaviors^c						
Washing your hands multiple times a day			.71			.45
Always	34 (97)	20 (95)		42 (95)	12 (100)	
Never	1 (3)	1 (5)		2 (5)	0 (0)	
Using a separate bedroom from others in your residence			<.01			.43
Always	24 (69)	17 (81)		31 (70)	10 (83)	
Sometimes	0 (0)	3 (14)		2 (5)	1 (8)	
Never	11 (31)	1 (5)		11 (25)	1 (8)	
Using a separate bathroom from others in your residence ^d			.71			.84
Always	17 (59)	11 (65)		22 (59)	6 (67)	
Sometimes	1 (3)	0 (0)		1 (2)	0 (0)	
Never	11 (38)	6 (35)		14 (38)	3 (33)	
Cleaning surfaces and commonly touched items after contact			.07			.54
Always	27 (77)	12 (57)		29 (66)	10 (83)	
Sometimes	3 (9)	7 (33)		9 (20)	1 (8)	
Never	4 (11)	2 (10)		5 (11)	1 (8)	
Refraining from taking care of others (eg, sick family members)			.85			.54
Always	20 (61)	13 (62)		25 (57)	8 (67)	
Sometimes	3 (6)	1 (0)		4 (9)	0 (0)	
Never	12 (34)	7 (33)		15 (34)	4 (33)	
Wearing a face mask around others in your residence			.55			.15
Always	14 (40)	9 (43)		16 (36)	7 (58)	
Sometimes	5 (14)	5 (24)		7 (16)	3 (25)	
Never	16 (46)	7 (33)		21 (48)	2 (17)	

Abbreviations: Ct, cycle threshold; IQR, interquartile range; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

^aData available for 49 participants.^bData available for 31 households.^cData available for 56 participants.^dData available for 46 participants.

Among 130 household contacts who did not have symptoms before the index case, 54 (41.5%) eventually developed symptoms, and 40 reported a positive SARS CoV-2 test result after the index case (30.8%).

Preventive Behaviors

Index participants reported high household compliance, with frequent handwashing (96%). Seventy-three percent reported always using a separate bedroom from others in the household, 64% using a separate bathroom, 70% cleaning common surfaces after touching them, 59% avoiding caring for others, and 41% wearing a mask at home around others.

DISCUSSION

We observed high clustering of SARS-CoV-2 infection within households in an urban sample. Among cases diagnosed as outpatients, 76% had at least 1 symptomatic household contact and 66% reported at least 1 confirmed positive contact. We estimated the household secondary attack rate to be at least 31%. Taken together, these data support that multiple infections in a single household are common.

Our data are consistent with other reports of household transmission [2–5]. We were limited by lacking testing results on all household contacts. Specifically, our study was conducted early in the pandemic when testing was not available to asymptomatic persons. Thus, our estimates of cumulative household infection and secondary attack rate are underestimates given the asymptomatic infection rates and that nearly 25% of symptomatic contacts were not tested. Interestingly, younger and Hispanic/Latinx individuals were less likely to get tested when symptomatic, potentially reflecting risk perception and/or barriers to testing. Hispanic/Latinx participants also tended to have larger households, and in Maryland, this community has had a disproportionately higher SARS-CoV-2 burden [10].

It was encouraging that households reported high compliance with some preventive practices like hand washing in the weeks following a COVID-19 diagnosis; however, one-third of index participants reported sharing a bedroom with another household member during this potentially infectious period, and masking in the home was <50%. Masking guidelines have evolved over the course of the pandemic, but these findings are consistent with other recent data [11] and support recent CDC recommendations of masking even in the home when a household member is potentially infected.

Interestingly, we did not observe an association between initial Ct value and infections/symptoms. Our data contrast with those of Marks and colleagues, who found an association between viral load of the index and subsequent household cases [12]. In our cohort, of those with Ct values, 82% had a Ct <22 (1 SD above the mean Ct of infectious NP samples in

a recent publication) [13]. Another recent study found that the nadir Ct value coincided with new symptom onset and the initiation of culturable virus shedding [11]. We were limited by missing Ct data and variability of test timing relative to symptom onset.

We were additionally limited as all survey data were reported by the index and we did not directly survey contacts. We also lacked viral sequence data and so cannot definitively attribute infections among contacts to household transmission vs independent community acquisition. However, 54% of symptomatic contacts reported symptom onset within 5 days of their index, consistent with previous reports of the timing of household transmission [5].

In conclusion, household clustering of SARS-CoV-2 infection is extremely common. While we could not determine why households did not comply fully with CDC guidelines for preventing household transmission, these data support reinforcing such messaging during contact tracing. Additional guidance may be needed to support relocation of household members when isolation is not feasible within the home. Given the relatively short period between index participant symptom onset and prior and subsequent contact symptom onset, rapid field-based antigen testing followed by daily tests may also be prudent.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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References

1. Johns Hopkins Coronavirus Resource Center. COVID-19 dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU). Available at: <https://coronavirus.jhu.edu/map.html>. Accessed 22 December 2020.
2. Madewell ZJ, Yang Y, Longini IM Jr, Halloran ME, Dean NE. Household transmission of SARS-CoV-2: a systematic review and meta-analysis. *JAMA Network Open* **2020**; 3:e2031756.
3. Koh WC, Naing L, Chaw L, et al. What do we know about SARS-CoV-2 transmission? A systematic review and meta-analysis of the secondary attack rate and associated risk factors. *PLoS One* **2020**; 15:e0240205.
4. Lewis NM, Chu VT, Ye D, et al. Household transmission of SARS-CoV-2 in the United States. *Clin Infect Dis*. **In press**.
5. Grijalva CG, Rolfes MA, Zhu Y, et al. Transmission of SARS-COV-2 infections in households - Tennessee and Wisconsin, April-September 2020. *MMWR Morb Mortal Wkly Rep* **2020**; 69:1631-4.
6. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19): households living in close quarters. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/living-in-close-quarters.html>. Accessed 22 December 2020.
7. Manabe YC, Reuland C, Yu T, et al; Ambulatory COVID Team. Self-collected oral fluid saliva is insensitive compared with nasal-oro-pharyngeal swabs in the detection of severe acute respiratory syndrome coronavirus 2 in outpatients. *Open Forum Infect Dis* **2021**; 8:ofaa648.
8. Harris PA, Taylor R, Thielke R, et al. Research Electronic Data Capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* **2009**; 42:377-81.
9. StataCorps LLC. Stata Statistical Software: Release 16. StataCorps LLC; **2019**.
10. Martinez DA, Hinson JS, Klein EY, et al. SARS-CoV-2 positivity rate for Latinos in the Baltimore-Washington, DC region. *JAMA* **2020**; 324:392-5.
11. Lewis NM, Duca LM, Marcenac P, et al. Characteristics and timing of initial virus shedding in severe acute respiratory syndrome coronavirus 2, Utah, USA. *Emerg Infect Dis* **2021**; 27:352-9.
12. Marks M, Millat-Martinez P, Ouchi D, et al. Transmission of COVID-19 in 282 clusters in Catalonia, Spain: a cohort study. *Lancet Infect Dis*. **2021**. **In press**.
13. Gniazdowski V, Morris CP, Wohl S, et al. Repeat COVID-19 molecular testing: correlation of SARS-CoV-2 culture with molecular assays and cycle thresholds. *Clin Infect Dis*. **2021**. **In press**.