








Concise Communication

Severe acute respiratory coronavirus virus 2 (SARS-CoV-2) exposure investigations using genomic sequencing among healthcare workers and patients in a large academic center

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Abstract

Severe acute respiratory coronavirus virus 2 (SARS-CoV-2) transmissions among healthcare workers and hospitalized patients are challenging to confirm. Investigation of infected persons often reveals multiple potential risk factors for viral acquisition. We combined exposure investigation with genomic analysis confirming 2 hospital-based clusters. Prolonged close contact with unmasked, unrecognized infectious individuals was a common risk.

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Implementation of infection prevention policies reduces the risk of severe acute respiratory coronavirus virus 2 (SARS-CoV-2) transmission between patients and healthcare workers (HCWs).¹ Although a cross-sectional study of US HCWs found an association between community exposure and SARS-CoV-2 seropositivity, no such association was found for hospital workplace factors, including contact with patients with known COVID-19.² Although hospital transmissions are likely infrequent,³ in the absence of genomic sequencing, exposure investigations alone may misclassify coincidental temporally related infections of HCWs or patients as the same transmission cluster. Conversely, transmissions may go unrecognized if exposure investigations do not reveal a common exposure between positive persons.

Here, we describe 2 clusters of cases in which genomic sequencing of SARS-CoV-2 isolates and epidemiological links clarified transmission events.

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Methods

Between November 2020 and February 2021 at The Johns Hopkins Hospital (JHH), a 1,095-bed academic tertiary-care center in Baltimore, Maryland, the following infection prevention precautions were followed: (1) respirator, eye protection, gown, gloves for patients with known, or suspected, COVID-19; (2) respirator, eye protection, gown, gloves, for all patients undergoing aerosol-generating procedures; and (3) surgical mask and face shield for all other patients. Patients were encouraged to mask during clinical interactions, and they underwent SARS-CoV-2 testing at hospital admission, before procedures, and from December 17, 2020, onward, at weekly intervals while an inpatient.⁴ Contact tracing was conducted for all HCWs, and exposure investigations were performed for inpatients with an unexpected positive SARS-CoV-2 test result.

If an exposure investigation suggested in-hospital transmission, available isolates underwent genomic sequencing, using previously published methods.⁵ Phylogenetic trees were created with ClustalW2.1, NJ Clustering algorithm, and visualized using Interactive Tree of Life (ITOL) software.⁶

Results

Overall, 2% of patients had a negative admission test followed by a positive surveillance test, and 2 clusters were confirmed as linked through sequencing and are included below.

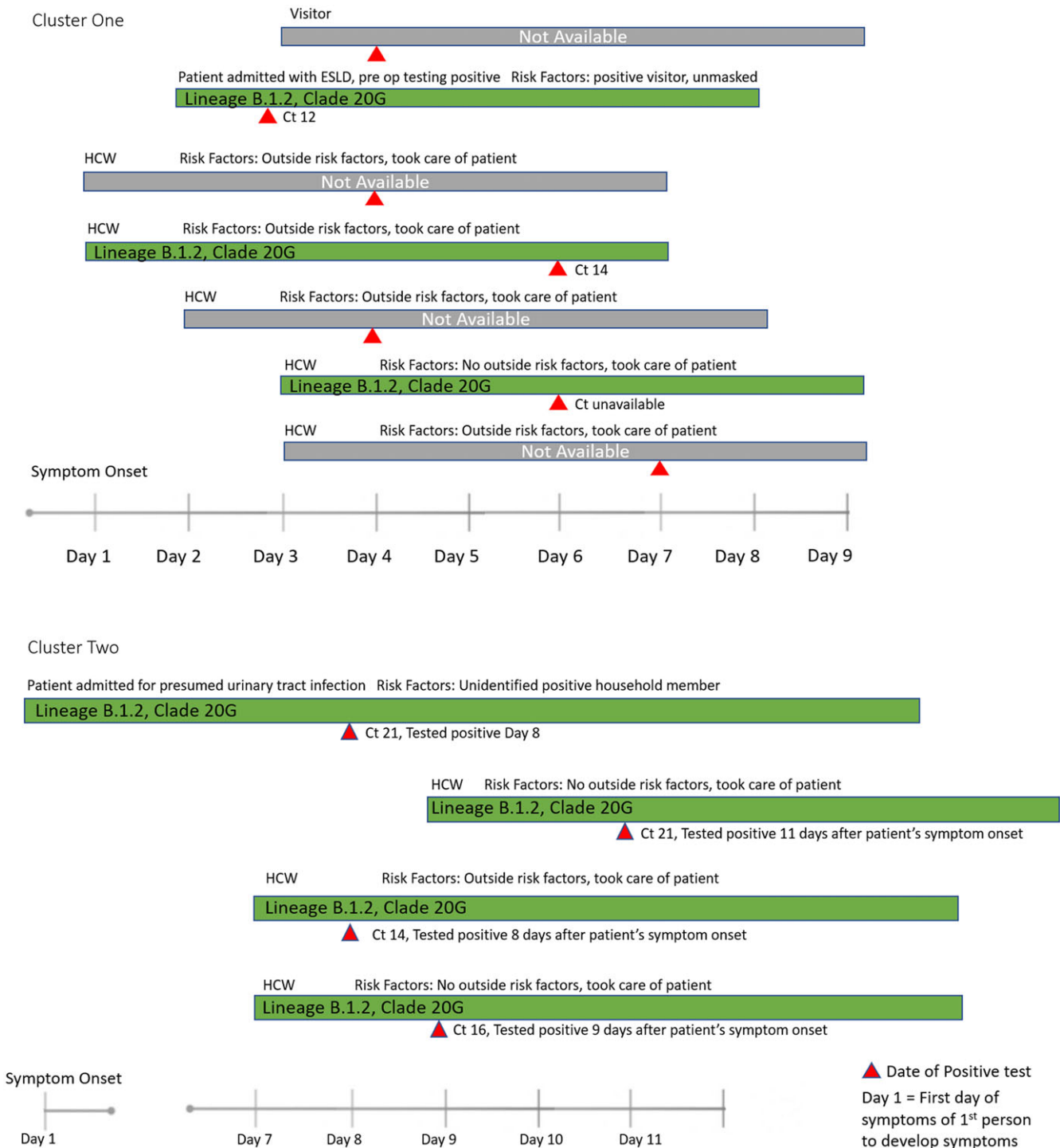


Fig. 1. COVID-19 clusters involving healthcare workers, patients and visitor: relative timing of symptom onset, testing, and viral burden.

Cluster 1

Patient A was admitted with end-stage liver disease complications, undergoing transplant evaluation, and had negative SARS-CoV-2 tests 1 day prior to admission, and on hospital days 8 and 12 (routine asymptomatic testing). On hospital day 23, the patient developed dyspnea, and a routine preprocedure test on day 24 was positive with a cycle threshold (Ct) value of 12.

Patient A, their visitor, and 5 HCWs with prolonged close contact with patient A developed symptomatic SARS-CoV-2 infection

within 1–2 days of each other (Fig. 1). Genomic sequencing of 3 isolates from patient A, and 2 HCWs, matched lineage B.1.2 and showed a characteristic P2685T substitution in ORF1a corresponding to P1867T in viral protease NSP3 (Fig. 2). There were no other samples with that NSP3 substitution from >5,000 samples sequenced at the JHH laboratory and no complete genotypic matches in >2.1 million genomes on GISAID⁷ at that time. The other 3 HCWs and the visitor underwent testing at outside laboratories and their isolates were unavailable for sequencing.

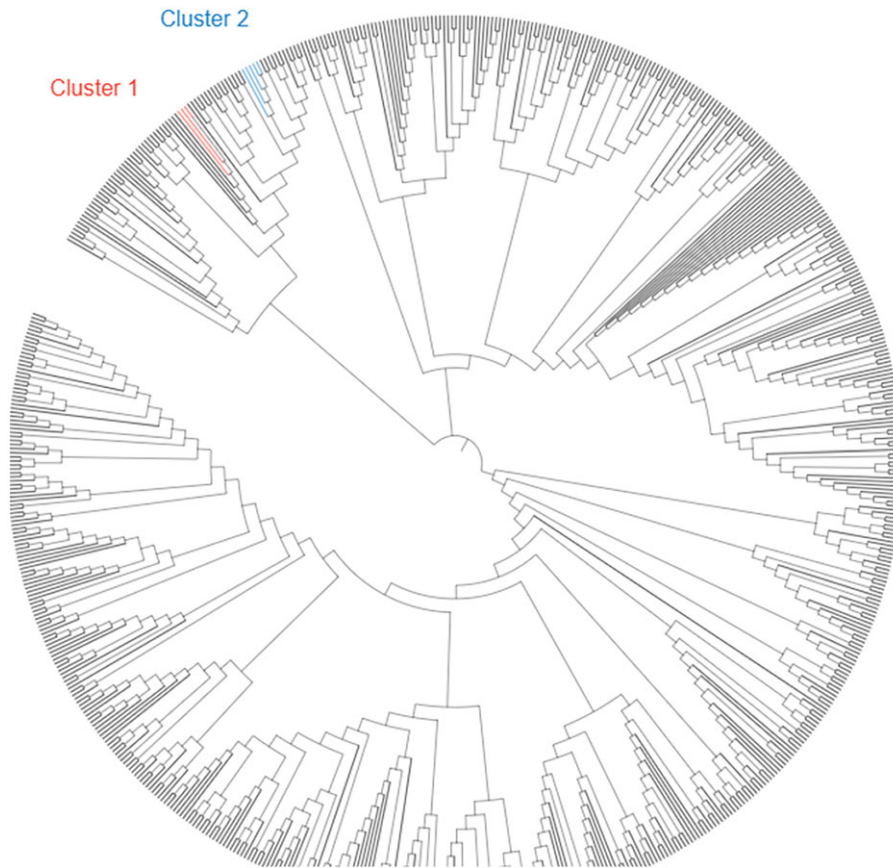


Fig. 2. Phylogenetic representation of relationships of sequences from cluster one (red) and cluster two (blue) to all sequences from clade 20G at Johns Hopkins Hospital.

Regarding potential transmission risks, while in patient A's room, the 5 HCWs reported consistently wearing masks; however, patient A and the visitor did not. Also, 2 of the HCWs did not consistently wear eye protection. Also, 4 HCWs noted socializing unmasked in the community. The patient had high-dependency nursing care.

Cluster 2

Patient B was admitted with delirium and joint pain with a history of neurogenic bladder and recurrent urinary tract infections (UTIs) with multidrug-resistant organisms (MDROs). His admission SARS-CoV-2 test was negative. He was treated for a suspected UTI and placed on contact precautions for the MDRO. On day 8 of admission, his routine weekly asymptomatic SARS-CoV-2 test was positive (Ct, 21). On focused questioning, he endorsed a mild cough and noted that a household contact, who had not visited patient B in hospital, had also been diagnosed with symptomatic COVID-19.

Furthermore, 3 HCWs, who cared for patient B during the first 7 days of admission, developed symptomatic COVID-19 within 2 days of each other (Fig. 1). The 3 HCWs and patient B's isolates were highly similar; lineage B.1.2, with a I2663L substitution within ORF1a, corresponding to I1845L in viral protease NSP3 (Fig. 2). This I1845L substitution of NSP3 was not in any other samples sequenced at the JHH laboratory, or as of July 2021, in <70 samples in GISAID.

The HCWs caring for patient B reported consistently wearing face masks and eye protection while in his room, although patient B did not wear a face mask. One HCW noted socializing unmasked in the community. Two HCWs had prolonged

contact with patient B while providing high-dependency nursing care. One was partially vaccinated.

Discussion

Using findings from exposure investigations coupled with genomic sequencing, we identified 2 hospital-related clusters of SARS-CoV-2 infections when the 7-day moving average was >25 per 100,000 population in Maryland.

For cluster 1, exposure investigation linked 7 COVID-19 cases: 3 of these were most likely true transmissions, confirmed by genomic sequencing, and 4 samples were unavailable for sequencing. Given the strong epidemiological risk factors, including close contact with the visitor and HCW with patient A, it is probable that all 7 are part of the same transmission pathway, although the identification of the index case and onward transmission pathways are unclear given close timing of symptom onset of all involved.

Cluster 2 linked 4 cases: patient B and 3 HCWs. Patient B was likely the index case, having acquired COVID-19 either from his household member or other community exposure prior to admission. It is unclear whether patient B's symptoms on admission were caused by SARS-CoV-2 infection, with a false-negative admission SARS-CoV-2 test, or if the admitting symptoms were caused by another etiology and it was too early in the incubation period for a positive test. All 3 HCWs were likely subsequently infected.

SARS-CoV-2 transmissions are more likely when several factors conducive to spread are present. Both clusters involved patients who were unmasked while HCWs were providing care during their hospital stay. For patient A, this unmasking may have contributed to both acquiring SARS-CoV-2, and transmitting it onward to HCWs caring for him. For patient B, who was likely

in a highly infectious presymptomatic phase, lack of masking contributed to onward spread. This reinforces the importance of patient masking to protect themselves and HCWs. Both patients had high dependency needs, particularly nursing care; therefore, HCWs had close interactions of lengthy duration while caring for them. These findings are consistent with previous studies that found increasing risk as length of time in the same room as a positive index case increases,^{8,9} and that risk is increased further if either person is unmasked.¹⁰

Our study had several limitations. We were unable to prove transmission directionality, including whether transmissions occurred between HCWs rather than from patients to HCWs. Not all samples were available for genomic sequencing, so despite strong epidemiology supporting evidence, we could not confirm that all cases were related, particularly in our situation of high community incidence. This study was conducted before the δ (delta) variant became prevalent and before widespread vaccinations. Exposure investigations are inherently subject to recall bias, and HCWs may have over- or underestimated their personal protective equipment (PPE) compliance. Asymptomatic employees or employees not identified through exposure investigations may not have been included in these clusters. In conclusion, SARS-CoV-2 transmission between HCWs and patients is infrequent, but exposure investigations coupled with genomic sequencing can be informative. Risk factors may include prolonged close contact with unmasked patients during high-dependency care tasks.

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Conflicts of interest. All authors report no conflicts of interest relevant to this article.

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