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Research Brief

Molecular epidemiology of large coronavirus disease 2019 (COVID-19) clusters before and after the implementation of routine serial testing at an academic medical center in Iowa, 2020

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Coronavirus disease 2019 (COVID-19) is a multisystemic illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Preventing SARS-CoV-2 transmission in healthcare settings is challenging. Several strategies for early identification and isolation have been implemented, including SARS-CoV-2 screening of patients on admission.[1] However, because SARS-CoV-2 has a median incubation period of ~5 days, infected patients may have negative results at the time of admission. Undetected cases during hospital admission may contribute to nosocomial transmission and outbreaks.[2,3]

Investigating hospital COVID-19 outbreaks is challenging because of the multitude of patient interactions and the high incidence in the community. Viral genome sequencing data can help discern healthcare-associated from community-associated infections. We describe 2 large COVID-19 clusters identified in our hospital before and after the implementation of serial testing. We applied molecular epidemiology to confirm nosocomial transmission.

Methods

The University of Iowa Hospitals & Clinics is an 811-bed academic medical center. We identified large clusters involving patients with hospital-onset COVID-19 detected during March–October 2020. Large clusters were defined as including ≥10 individuals [(patients, visitors, or healthcare personnel (HCP)] with a laboratory-confirmed COVID-19 diagnosis including reverse-transcriptase polymerase chain reaction (RT-PCR) assay and an epidemiologic link. Epidemiologic links were defined as hospitalization, working, or visiting in the same hospital unit during the incubation or infectious period of a hospital-onset case. Hospital-onset was defined as a COVID-19 diagnosis ≥14 days from the admission date. Medical grade mask and eye protection requirements were in place for patient care at the time of the first outbreak and the requirement was expanded to all hospital areas (e.g., break rooms) soon after the first outbreak. Symptom screening and testing for symptomatic HCP was in place throughout the study period. Visitors were screened for symptoms and only allowed in if asymptomatic. Patient admission screening (nasopharyngeal RT-PCR) was started in May 2020 and serial testing for all inpatients (RT-PCR every 5 days) in July 2020.[3] Nasopharyngeal swab specimens were retrieved for whole-genome sequencing (WGS). WGS was performed using a MinION sequencer from Oxford Nanopore Technology and protocols from the ARTIC network.[4] Phylogenetic classification was based on GISAID clades and Pango lineages (version 2021-04-23). A cutoff for genetic diversity was not defined beforehand but was assumed to increase with the number of single-nucleotide polymorphisms (SNPs).

Results

The first cluster occurred in June 2020. Two hospital-onset cases were identified in adjacent rooms in a non–COVID-19 medical-surgical unit. Contact tracing and testing of patients and unit staff revealed 4 additional patients (3 shared a room with another case), 1 visitor, and 13 HCP (8 HCP took care of a patient in this cluster), for a total of 20 infected individuals. In total, 17 samples (6 patients, 1 visitor, and 10 HCP) were sequenced. All samples belonged to clade GH and lineage B.1 and were 0–5 SNPs different from each other (Fig. 1). In July 2020, after this cluster was identified, routine serial testing every 5 days was started for hospitalized patients.

In September 2020, a hospital-onset case was identified as part of routine serial testing in a non–COVID-19 intensive care unit. Contact tracing and serial testing revealed 3 additional patients (2 shared a room with another case) and 8 HCP (4 cared for a patient who was part of this cluster), for a total of 12 individuals. One HCP also had a household exposure. In total, 11 samples

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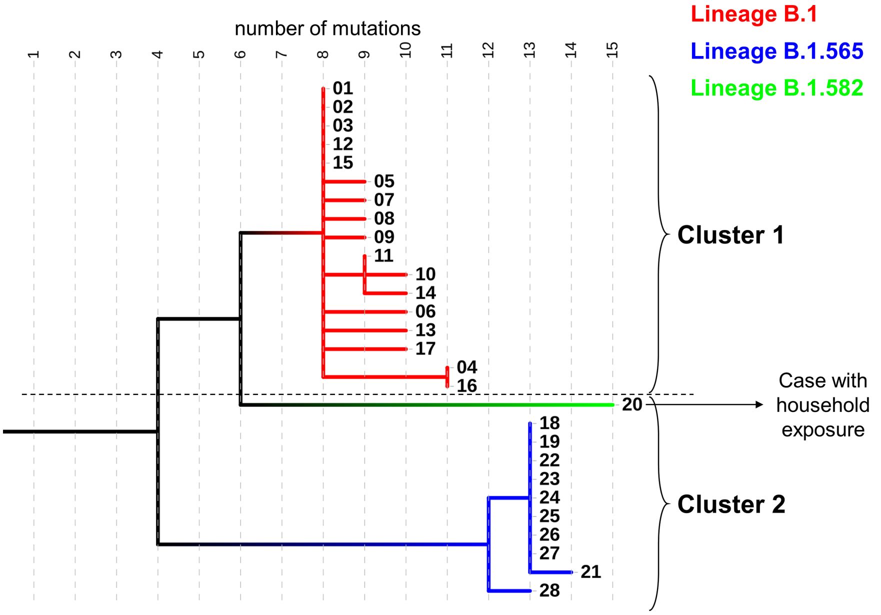

Fig. 1. Phylogenetic tree of COVID-19 clusters. Clusters are denoted with brackets and separated by a dashed line. Pango lineages (version 2021-04-23) are labeled in different colors. Sample numbers represent the order of sample collection. The root of the tree is the SARS-CoV-2 reference genome (NC_045512.2).

(4 patients and 7 HCP) were sequenced. Most samples belonged to clade G and lineage B.1.565. The sample from the HCP with a household exposure belonged to clade GH and lineage B.1.582, and it was 20–21 SNPs different from other samples in the cluster. Therefore, this infection was not considered to be the result of in-hospital transmission. The remaining samples were 0–3 SNPs different from each other, showing less diversity compared to the first cluster (Fig. 1).

Discussion

Two hospital COVID-19 outbreaks were confirmed using WGS. WGS helped differentiate in-hospital from community acquisition. Serial testing in all hospitalized patients may have contributed to reduce outbreak size and genetic diversity during the second outbreak.

Hospital outbreaks are traditionally investigated using contact tracing. However, COVID-19 transmission routes remain controversial, and there is a limit to what can be learned from contact tracing. Transmission networks are often complex, involving patients, HCP, and visitors. WGS can confirm hospital COVID-19 outbreaks, suggest possible transmission routes, and inform subsequent infection control measures.[2,5,6] In this study, an HCP with a household exposure had a distinctly different viral genomic sequence from others and was not considered part of the cluster of in-hospital transmission. Understanding SARS-CoV-2 transmission in a healthcare setting is critical to managing hospital-associated COVID-19.

Serial SARS-CoV-2 testing is known to be effective in identifying hospital-associated COVID-19 early or detecting COVID-19 that might have been in the incubation period upon admission screening.[3] In addition, when COVID-19 outbreaks occur, serial testing of patients and HCP (until no new cases are detected after 14 days), can be used to control outbreaks.[7] However, data assessing the impact of serial testing on prevention or reduction of COVID-19 clusters are limited. In our hospital, the first cluster (before the implementation of serial testing) was bigger than the second cluster (after the implementation of serial testing). Serial testing leads to early identification and isolation, therefore preventing COVID-19 spread to other inpatients or HCPs within a hospital. Interestingly, WGS results in this study also showed less genetic diversity in the second cluster, after implementation of serial testing for hospitalized patients.

This study has several limitations. This retrospective, single-center study included a small number of subjects. Also, we were unable to perform WGS for all individuals identified in each cluster because some samples were not available.

In conclusion, WGS is a powerful tool in hospital cluster investigations. Routine serial testing led to earlier cluster detection, which may have decreased outbreak size and genetic diversity.

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

References

1. Sastry SR, Pryor R, Raybould JE, *et al.* Universal screening for the SARS-CoV-2 virus on hospital admission in an area with low COVID-19 prevalence. *Infect Control Hosp Epidemiol* 2020;41:1231–1233.
2. Klompas M, Baker MA, Rhee C, *et al.* A SARS-CoV-2 cluster in an acute-care hospital. *Ann Intern Med* 2021. doi: 10.7326/M20-7567.
3. Kobayashi T, Trannel A, Holley SA, *et al.* COVID-19 serial testing among hospitalized patients in a Midwest tertiary medical center, July–September 2020. *Clin Infect Dis* 2020. doi: 10.1093/cid/ciaa1630.
4. Quick J. nCoV-2019 sequencing protocol v2 (GunIt). protocols.io website. 2020. doi: 10.17504/protocols.io.bdp7i5rn.
5. Meredith LW, Hamilton WL, Warne B, *et al.* Rapid implementation of SARS-CoV-2 sequencing to investigate cases of health-care associated COVID-19: a prospective genomic surveillance study. *Lancet Infect Dis* 2020;20:1263–1271.

6. Chan ER, Jones LD, Redmond SN, *et al.* Use of whole-genome sequencing to investigate a cluster of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections in emergency department personnel. *Infect Control Hosp Epidemiol* 2021. doi: 10.1017/ice.2021.208.
7. Taylor J, Carter RJ, Lehnertz N, *et al.* Serial testing for SARS-CoV-2 and virus whole genome sequencing inform infection risk at two skilled nursing facilities with COVID-19 outbreaks—Minnesota, April–June 2020. *Morb Mortal Wkly Rep* 2020;69:1288–1295.

Striking absence of “usual suspects” during the winter of the coronavirus disease 2019 (COVID-19) pandemic 2020–2021

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Each year in October, the United States enters the “flu season.” During this time, influenza virus infections occur in all age groups, with 9–45 million cases each year. In addition, other respiratory infections due to pathogens such as respiratory syncytial (RSV) and rhinovirus are very common during flu season.[1,2] Respiratory viral activity typically peaks in December and January, but the flu season can last until May.[1] Many individuals receive the influenza vaccine from their primary care provider in the beginning of the fall season, and this is particularly effective in reducing the number of influenza infections.[3] In 2020, however, the severe acute respiratory coronavirus virus 2 (SARS-CoV-2) virus emerged and dramatically changed the landscape of medicine. To stop the spread of SARS-CoV-2, community mitigating factors, such as social distancing, frequent hand washing, mask mandates, and school closures, were implemented widely.[4]

When the COVID-19 pandemic started in March 2020, many reported that seasonal flu cases disappeared earlier than expected.[5] Additionally, an overall reduction in the incidence of respiratory viral infections during the flu season was noted on both national and international levels. Notably, in the Southern Hemisphere, the flu season falls in the summer season (earlier in the year than the Northern Hemisphere), and in the summer of 2020, Australia, Chile, and South Africa reported only 51 cases of the flu.[6] In the 2020–2021 winter season, like others, we also noted a significant reduction in respiratory infections compared to prior years. The purpose of this study was to evaluate the incidence of all other non–SARS-CoV-2 viral infections typically seen during the flu season. Additionally, we evaluated the incidence of group A *Streptococcus* culture positivity of throat specimens in children and adults during the same period.

We conducted a retrospective study that included polymerase chain reaction (PCR) test results of nasopharyngeal swabs for influenza A and B, respiratory syncytial virus (RSV), and SARS-CoV-2 as well as throat swab results for group A *Streptococcus* at the Detroit Medical Center (DMC) and Children’s Hospital of Michigan (CHM) from September 2019–February 2020 and September 2020–February 2021. Incidences of infections were calculated for each period and compared. Available data on other respiratory viruses including parainfluenza virus 1 and 2, other coronaviruses, and human metapneumovirus during the 2020–2021 season were also reviewed.

During the study period in 2020–2021, no adult cases of influenza A, B, and RSV were documented, but these viruses comprised 12%, 13%, and 9% of all cases in the 2019–2020 season, respectively. Similarly, in children in 2020–2021, no influenza A or B infections and 1 RSV infection were documented, compared to 12%, 20%, and 24% of all cases, respectively, in 2019–2020 (Table 1). Remarkably, there were also no positive tests due to parainfluenza (1 and 2), coronaviruses, and human metapneumovirus in the 2020–2021 season, a significant decline compared to the 2019–2020 season. Additionally, the number of throat swabs submitted for group A *Streptococcus* in both adults and children decreased considerably between the 2 periods.

Overall, the incidence of influenza A and B and RSV in the 2020–2021 season affected by the COVID-19 pandemic decreased significantly compared to the 2019–2020 season in both the pediatric and adult populations. Additionally, the incidences of other respiratory viral infections (eg, parainfluenza 1 and 2), other coronaviruses, and human metapneumovirus were drastically lower.

Additionally, data from 42 medical centers in the Midwest region of the United States that utilize the Biofire system respiratory viral panel were obtained and analyzed.[7,8] In the same study period of September 2020–February 2021, there were far fewer positive tests of influenza A and B, RSV, parainfluenza, coronaviruses, and human metapneumovirus compared to the prior flu season. Among all flu tests in the 2020–2021 season, 0% of influenza A tests, 0.13% of influenza B tests, and 0.05% of RSV tests returned positive compared to 0.09%, 2.98%, and 9.38%, respectively, in the prior season. Human metapneumovirus had decreased to 0.05% positivity compared to 3.41% of all positive tests in the prior season. These data reflect a dramatic decrease in non–SARS-CoV-2 respiratory infections in the entire region.

Speculating as to why the decrease in incidence of respiratory viral infections occurred, it is likely that community mitigating measures implemented at the beginning of the pandemic contributed to the decrease in the spread of viral pathogens in the general population. The reduction in group A *Streptococcus* tests ordered (and overall reduction in secondary group A *Streptococcus* infections) may have been a result of the decrease in the number of respiratory viral infections because clinical suspicion for secondary infections

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