SHEA
The Society for Healthcare
Epidemiology of America

## 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

Miguel E. Ortiz MD[1,a] (iD), Takaaki Kobayashi MD[1,a], Katherine Imborek MD[1], Mohammed Alsuhaibani MBBS[1], Stephanie Holley MBA[1], Alexandra Trannel MS[1], Alexandre R. Marra MD, PhD[1,2], William Etienne MD[1], Kyle E. Jenn BSN[1], Oluchi J. Abosi MBChB, MPH[1], Holly Meacham MSN[1], Lorinda Sheeler PhD[1], Angelique Dains BSN[1], Mary E. Kukla BSN[1], Paul B. McCray Jr MD[1], Stanley Perlman MD, PhD[1], Bradley Ford MD, PhD[1], Daniel J. Diekema MD[1], Melanie Wellington MD, PhD[1], Alejandro A. Pezzulo MD[1,b] and Jorge L. Salinas MD[1,b]

[1]University of Iowa Roy J. and Lucille A. Carver College of Medicine, Iowa City, Iowa, United States and [2]Instituto Israelita de Ensino e Pesquisa Albert Einstein, Hospital Israelita Albert Einstein, São Paulo, Brazil

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

**Author for correspondence:** Jorge L. Salinas, E-mail: jorge-salinas@uiowa.edu. Or Alejandro A. Pezzulo, E-mail: alejandro-pezzulo@uiowa.edu

[a]Authors of equal contribution.

[b]Authors of equal contribution.

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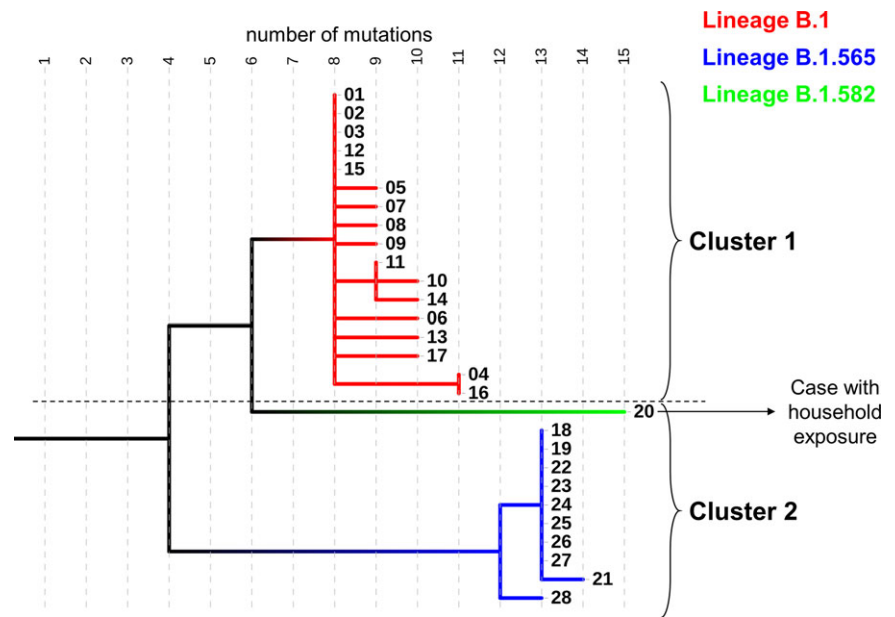
**Fig. 1.** Phylogenetic tree of COVID-19 clusters. Clusters are denoted with brackets and separated by a dashed line. Pango lineages (version 2021-04-23) are labeled in different colors. Sample numbers represent the order of sample collection. The root of the tree is the SARS-CoV-2 reference genome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

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 (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.

## 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.