scalable and automated analysis pipeline already in use for rapid (days) characterization of genomic-relatedness in small and large sets of isolates. Mapping and SNP calling was performed against high-quality, best-match reference genomes. Sets of samples with pairwise distance of 2 persons with genomically related isolates and were denoted as "clusters." Separately, we also investigated within-patient diversity by quantifying the genomic relatedness of isolates collected from individual patients. **Results:** Isolates represented 28 distinct species. We identified 10 *Escherichia coli* clusters (range, 2–4 patients; median, 2 patients), 2 *Klebsiella pneumoniae* clusters (range, 2–4 patients), and 1 *Enterococcus faecium* cluster (3 patients). All but 1 involved genomically matched isolates from multiple hospital locations. There were 4 *Escherichia coli* ST131 clusters spanning 4 months, including 1 with 4 patients across 3 different hospital locations. At a species level, there were distinct differences between the observed SNP distances between samples isolated from the same versus different patients (Fig. 1). All identified clusters had not been flagged by routine outbreak detection methods used by the UCI infection prevention program. **Conclusions:** Comprehensive WGS-based surveillance of hospital clinical isolates identified multiple potential transmission events between patients not in the same unit at the time cultures were taken. Combining WGS detection and real-time epidemiologic investigation may identify new avenues of transmission risk and could provide early warnings of clonal transmission to prevent larger outbreaks. High-volume surveillance of hospital isolates can also provide species- and context-specific clonality.

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Disclosures: None

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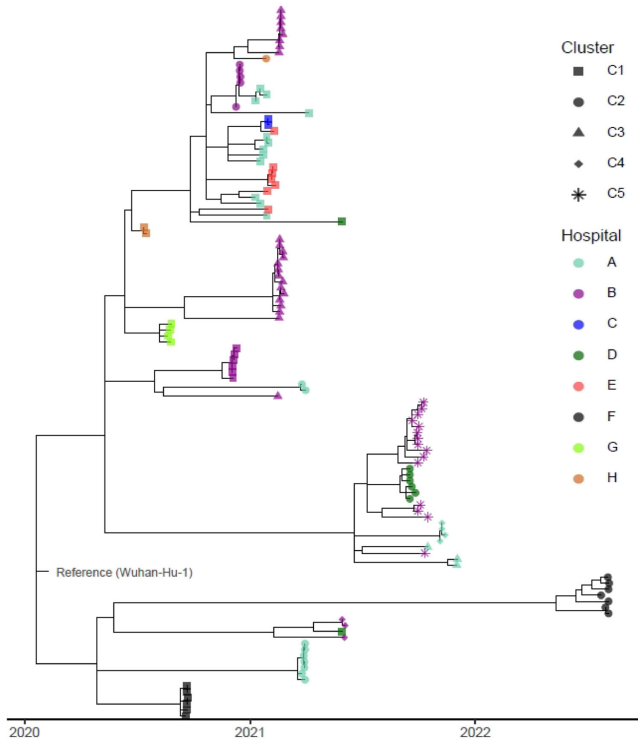

Presentation Type:
Poster Presentation - Poster Presentation

Subject Category: Molecular Epidemiology

Whole-genome sequencing cluster analysis reveals complex healthcare-associated COVID-19 dynamics

Theodore Rader; Graham Snyder; Lee Harrison; Vatsala Rangachar Srinivasa; Marissa Griffith; Lora Pless and Ashley Chung

Background: Identifying and interrupting transmission of severe acute respiratory syndrome coronavirus 2 and resulting disease (COVID-19) in acute-care settings can be challenging due to incubation period, asymptomatic infection, and prevalent community disease. To elucidate routes of infection and interrupt COVID-19 outbreaks with uncertain epidemiological chains of transmission, UPMC utilized reactive whole-genome sequencing (WGS) of viral specimens. **Methods:** UPMC infection prevention teams identified healthcare-associated COVID-19 clusters with uncertain transmission pathways among patients and/or healthcare personnel (HCP) in acute-care hospitals. Nasopharyngeal samples preserved in viral transport media were obtained for genetic analyses. Nucleic acids were extracted and WGS libraries were prepared by targeted enrichment or multiplex PCR methodologies. Resulting sequencing reads were aligned to the Wuhan-1 reference genome, followed by identification of single-nucleotide polymorphisms (SNPs) among the genomes and construction of a phylogenetic tree. Specimens were considered genetically similar if there were ≤2 SNP differences between viral genomes within a cluster. **Results:** Between May 2020 until August 2022, infection prevention teams requested WGS for 17 healthcare-associated clusters of COVID-19 involving 182 individuals across 8 UPMC facilities (median outbreak size, 9 individuals; range, 2–26). Of the 182 individuals, 36 lacked clinical specimens and 30 did not pass WGS quality-control criteria of ≥95% of the reference genome with a minimum of 10× coverage. Of the 116 sequenced genomes, 94 (81%) had virus genetically similar to ≥1 other specimen, including 87 (83.6%) of 104 patient viruses and 7 (58.3%) of 12 HCP viruses, comprising 22 clusters (Fig. 1). The remaining 22 (20.6%) specimens were genetically unrelated. In total, 16 (94.1%) of the 17 epidemiologically identified clusters had 2 or more individuals with a genetically similar virus. Also, 7 (41.1%) of these clusters had genetically similar viral genomes for every individual within each cluster. Also, 9 (52.9%) clusters contained both genetically related and unrelated specimens: 5 of these had more complex genomic profiles (including 4 clusters containing 2 distinct subclusters of ≥2 genetically related viruses) and 1 cluster contained 3 subclusters of ≥2 genetically related viruses. In the outbreak with 3 clusters, 3 SNPs separated specimens from 2 temporally proximal clusters, suggesting possible propagation between clusters (cluster B-3 in Fig. 1). **Conclusions:** WGS can complement traditional epidemiological investigations of healthcare-associated COVID-19 outbreaks, revealing complex transmission dynamics. Future investigations will characterize the impact of WGS on determining specific transmission pathways in acute-care facilities.

Disclosures: None

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Presentation Type:
Poster Presentation - Poster Presentation

Subject Category: MRSA/VRE

Factors associated with SARS-CoV-2 and community-onset invasive *Staphylococcus aureus* coinfection, 2020

Kelly Jackson; Sydney Resler; Joelle Nadle; Susan Petit; Susan Ray; Lee Harrison; Ruth Lynfield; Kathryn Como-Sabetti; Carmen Bernu;

Figure 1. Timing from first SARS-CoV-2 positive test collection to initial invasive *Staphylococcus aureus* specimen collection, community-onset coinfection cases, 11 US counties, March 1–December 31, 2020.

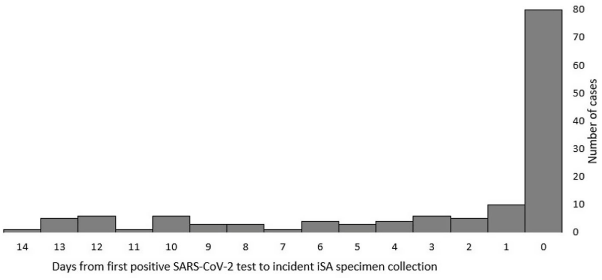
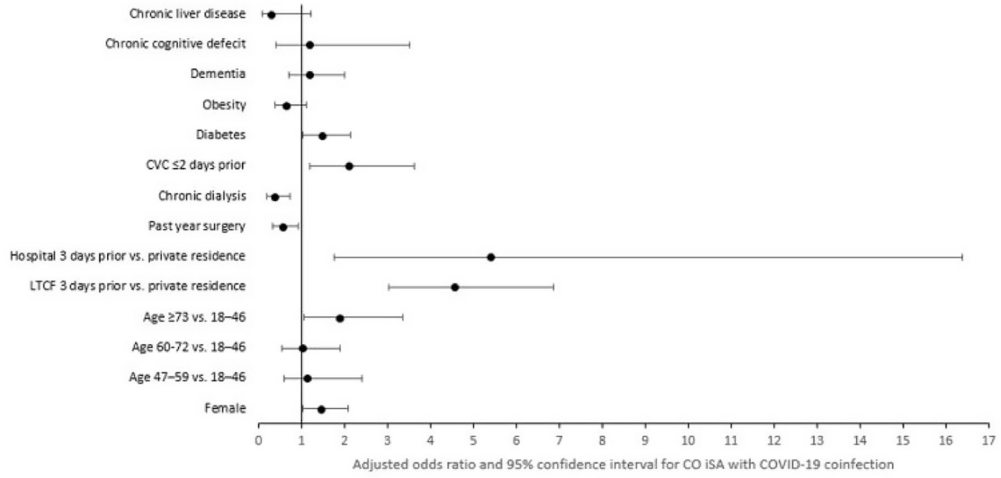


Figure 2. Multivariable analysis of demographic and epidemiologic characteristics associated with SARS-CoV-2 coinfection among community-onset invasive *Staphylococcus aureus* cases, 11 US counties, March 1–December 31, 2020.



Ghinwa Dumyati; Marissa Tracy; William Schaffner; Holly Biggs and Isaac See

Background: Previous analyses describing the relationship between SARS-CoV-2 infection and *Staphylococcus aureus* have focused on hospital-onset *S. aureus* infections occurring during COVID-19 hospitalizations. Because most invasive *S. aureus* (iSA) infections are community-onset (CO), we characterized CO iSA cases with a recent positive SARS-CoV-2 test (coinfection). **Methods:** We analyzed CDC Emerging Infections Program active, population- and laboratory-based iSA surveillance data among adults during March 1–December 31, 2020, from 11 counties in 7 states. The iSA cases (*S. aureus* isolation from a normally sterile site in a surveillance area resident) were considered CO if culture was obtained <3 days after hospital admission. Coinfection was defined as first positive SARS-CoV-2 test ≤14 days before the initial iSA culture. We explored factors independently associated with SARS-CoV-2 coinfection versus no prior positive SARS-CoV-2 test among CO iSA cases through a multivariable logistic regression model (using demographic, healthcare exposure, and underlying condition variables with P<0.25 in univariate analysis) and examined differences in outcomes through descriptive analysis. **Results:** Overall, 3,908 CO iSA cases were reported, including 138 SARS-CoV-2 coinfections (3.5%); 58.0% of coinfections had iSA culture and the first positive SARS-CoV-2 test on the same day (Fig. 1). In univariate analysis, neither methicillin resistance (44.2% with coinfection vs 36.5% without; $P = .06$) nor race and ethnicity differed significantly between iSA cases with and without SARS-CoV-2 coinfection ($P = .93$ for any association between race and ethnicity and coinfection), although iSA cases with coinfection were older (median age, 72 vs 60 years , P<0.01) and more often female (46.7% vs 36.3%, P=0.01). In multivariable analysis, significant associations with SARS-CoV-2 coinfection included older age, female sex, previous location in a long-term care facility (LTCF) or hospital, presence of a central venous catheter (CVC), and diabetes (Figure 2). Two-thirds of co-infection cases had ≥1 of the following characteristics: age > 73 years, LTCF residence 3 days before iSA culture, and/or CVC present any time during the 2 days before iSA culture. More often, iSA cases with SARS-CoV-2 coinfection were admitted to the intensive care unit ≤2 days after iSA culture (37.7% vs 23.3%, P<0.01) and died (33.3% vs 11.3%, P<0.01). **Conclusions:** CO iSA patients with SARS-CoV-2 coinfection represent a small proportion of CO iSA cases and mostly involve a limited number of factors related to likelihood of acquiring SARS-CoV-2 and iSA. Although CO iSA patients with SARS-CoV-2 coinfection had more severe outcomes, additional research is needed to understand how much of this difference is related to differences in patient characteristics.

Disclosures: None

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Subject Category: MRSA/VRE

Methicillin-resistant *Staphylococcus aureus* mupirocin resistance rates in a large healthcare system

Mindy Sampson; Robert Fairman; Elizabeth Palavecino; Werner Bischoff; Julie Williamson; Shelley Keste and Catherine Passaretti

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a common etiology of hospital-acquired infections (HAIs). One strategy to reduce HAIs due to MRSA involves a multistep decolonization process. This often involves nasal application of mupirocin 2% ointment. In our institution, when individuals meet criteria for decolonization, we recommend 5 days of treatment given twice daily. High levels of mupirocin resistance have been reported in some hospital systems, with >80% of tested isolates being resistant. To better understand our resistance levels, we selected 238 MRSA isolates from blood cultures to be tested for mupirocin resistance to correlate the presence of resistance and use of mupirocin for decolonization. We choose to assess MRSA blood isolates rather than nasal swabs given that we aim to prevent invasive MRSA infections, including blood stream infections, with decolonization. The blood cultures were collected from 11 acute-care facilities within our system from March 2021 through June 2022. High-level resistance was defined as an MIC >1,024 µg/mL according to Clinical and Laboratory Standards Institute guidelines. Of those, 7.14% showed high level resistance, and 76.47% occurred in those who were exposed to mupirocin and 23.53% occurred in those without mupirocin exposure ($P = .0094$). On average, those with high-level resistance had had more recent exposure to mupirocin compared to those without resistance, which was statistically significant. Also, those with high resistance, on average, received more doses of mupirocin, although this was not statistically significant. **Conclusions:** More recent and higher number of doses of mupirocin were associated with the development of resistance, which is consistent with what we know from pharmacodynamics of antibiotic resistance with other agents. These findings may be