CONCISE REPORT

Hospital-acquired antibiotic-resistant organisms among patients with COVID-19

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ABSTRACT

Background: We sought to use existing in-patient surveillance data to investigate the risk of hospital-acquired antimicrobial-resistant organisms (ARO) among patients with COVID-19 infection.

Methods: Prospective case capture was done for patients admitted with COVID-19, as well as those admitted with ARO and *Clostridioides difficile* infections (CDI). Odds ratios (OR) were used to measure the strength of association between COVID-19 infection and the risk of acquiring hospital-acquired ARO and CDI.

Results: The odds of acquiring ARO/CDI were statistically higher among patients with hospital-acquired and community-acquired COVID-19 infections (OR=2.68 and 1.79 respectively) compared to persons without COVID-19 (OR=0.53).

Conclusions: Our results show an association between COVID-19 infection and the acquisition of ARO/CDI in the in-patient setting. This finding suggests that prolonged hospitalization may expose patients to hospital-acquired infections, and this may have relevance in the management of patients requiring hospitalization for extended periods of time.

KEYWORDS: Antimicrobial-resistant; COVID-19; hospital-acquired infection

ABBREVIATIONS

ARO: Antimicrobial-resistant organisms
CA: Community-acquired
CDI: *Clostridioides difficile* infection
CI: Confidence intervals
CPO: Carbapenemase-producing organisms
ESBL: Extended-spectrum beta-lactamase
HA: Hospital-acquired
HCA: Healthcare-associated
LTC: Long-term care
MRSA: Methicillin-resistant *Staphylococcus aureus*
OR: Odds ratio
VRE: Vancomycin-resistant Enterococci

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INTRODUCTION

Respiratory viral pathogens increase the risk for subsequent bacterial infection or colonization – particularly those caused by antimicrobial-resistant organisms (ARO) [1]. Concurrently, patients who are critically ill with COVID-19 have been suggested to be at higher risk for acquiring an ARO, yet there are limited data describing this, and it is unknown whether this is true for all patients hospitalized with COVID-19 [2]. There are many gaps in the literature that limit the understanding of downstream hospital-acquired (HA) ARO acquisition following COVID-19 infection and vice versa. We sought to investigate the risk of hospital-acquired ARO or *Clostridioides difficile* infection (CDI) among patients with COVID-19.

METHODS

Starting in March 2020, our Infection Prevention and Control team began COVID-19 surveillance for hospitalized in-patients at all acute care facilities in Alberta, Canada. This surveillance covers approximately 370,000 in-patient admissions annually in both urban and rural areas, however a 9.2% drop in patient admissions was seen during the pandemic (fiscal year April 2020-March 2021 as compared to fiscal year April 2019-March 2020). There are 102 acute care facilities in the province, with a capacity of 9,366 total beds at baseline. COVID-19 case capture was done prospectively and is believed to be complete because of weekly data linkages with laboratory and hospital admission data to ensure missing cases were identified in real-time. Hospital-acquired COVID-19 (HA-COVID-19) infections were defined as a laboratory confirmed positive on or after the 7th calendar day of admission with no symptoms present on admission, or if a patient had an epidemiologic link to another case in hospital, in alignment with the Canadian Nosocomial Infection Surveillance Program definition [3]. Healthcare-associated (HCA) and community-acquired (CA) cases were laboratory confirmed COVID-19 positive cases within the 14 days prior to admission and up to and including calendar day six of admission, with HCA cases represented by those directly admitted from a long-term care (LTC) facility and CA cases represented by those from the community.

ARO surveillance was already in place for methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant Enterococci (VRE), carbapenemase-producing organisms (CPO), and bloodstream infections (BSI) caused by MRSA, VRE, CPO or extended spectrum beta-lactamase (ESBL) producing organisms. For this study, we also included CDI cases. We observed all (HA, HCA, and CA) COVID-19 infections, and HA-ARO/CDI in-patient infections and colonization that occurred in patients during the same hospital admission from March 2020-March 2021, prior to widespread COVID-19 immunization. Infection criteria was assessed using the National Healthcare Safety Network (NHSN) surveillance definitions [4]. The comparison group was the total number of admissions to acute care facilities for patients without COVID-19 or an ARO. Two-sided Fisher's test was used to calculate P-values, with alpha set at 0.05. Odds ratios (OR) and 95% confidence intervals (CI) were calculated using R Studio software package v. 1.4.1717 (RStudio Team 2021, USA).

RESULTS

There were 364,139 total in-patient acute care admissions in Alberta, Canada from March 2020 to March 2021. Out of the 644 who had HA-COVID-19 infection, seven patients subsequently acquired ARO or CDI during the same admission, with a resultant OR of 2.68 (95% CI 1.07-5.57). Of the 301 patients with HCA-COVID-19 infection, two acquired ARO or CDI (OR of 1.63, 95% CI 0.20-5.94). Lastly, out of the 5,530 patients with CA-COVID-19 infection, 40 were later identified with hospital-acquired ARO or CDI (OR of 1.79, 95% CI 1.27-2.46). Of these 49 patients with both COVID-19 and HA-ARO or CDI, 25 (51%) were admitted to the ICU in the same admission. On the other hand, there were 357,664 patients admitted that did not have COVID-19, of which 1,443 acquired ARO or CDI (OR 0.53, 95% CI 0.40-0.72) while in the hospital. For patients initially presenting with a HA-ARO or CDI (1,492), fifteen got COVID-19 infection in the hospital (OR 5.85, 95% CI 3.24-9.74) (Table 1).

Table 1: Patients acquiring a COVID-19 infection and an antibiotic-resistant organism (ARO)/*C. difficile* infection (CDI) within the same hospital admission

First Acquisition	Second Acquisition	Total Cases	Total Admissions with First Acquisition	OR (95% CI)	p-value
HA COVID-19	HA-ARO/CDI	7	644	2.68 (1.07 - 5.57)	0.018
HCA COVID-19	HA-ARO/CDI	2	301	1.63 (0.20 - 5.94)	0.350
CA COVID-19	HA-ARO/CDI	40	5,530	1.79 (1.27 - 2.46)	<0.01
No COVID-19	HA-ARO/CDI	1,443	357,664	0.53 (0.40 - 0.72)	<0.01
HA-ARO/CDI	HA COVID-19	15	1,492	5.85 (3.24 - 9.74)	<0.01

*Total admissions = 364,139 HA = Hospital-acquired, HCA = Healthcare-associated, CA = Community-acquired

DISCUSSION

WIthin the same hospital admission, individuals with HA-COVID-19 had 2.68 times, and individuals with CA-COVID-19 had 1.79 times greater risk of developing HA-ARO or HA-CDI compared to those without COVID-19. However, there was no statistical significance in acquiring ARO or CDI among patients with HCA-COVID-19 (P=0.350). Comparatively, patients that did not have COVID-19 had decreased odds of acquiring a HA-ARO/CDI compared to those that had COVID-19. This suggests a correlation between COVID-19 infection and ARO/CDI acquisition. Also, patients who were initially identified to have a HA-ARO or CDI were 5.85 times more likely to have a HA-COVID-19 infection.

There are several hypotheses that may explain these findings. Many hospitalized COVID-19 patients require ventilation and ICU support. Due to the severity of illness, ICU patients typically have lower immune response and require higher risk treatments, thereby increasing their risk of subsequent infections especially those caused by AROs [2,5,6]. Patients with an initial HA-COVID-19 infection would have already been in hospital (for at least seven days) with another illness, likely leaving them more vulnerable for acquiring an ARO or CDI. This may explain the higher odds ratio when comparing HA and CA-COVID-19 patients. Lastly, patients may have been subject to a broad spectrum of antibiotic therapies, particularly when viral versus bacterial etiology of symptoms is unknown. The HCA-COVID-19 population is particularly small (n=301). These individuals acquired COVID-19 while in LTC, therefore typically are older and have more complex medical needs. When designating goals of care, they are more likely to receive supportive care over invasive care options – which may explain why no statistical significance was observed. As mentioned previously, invasive procedures can increase risk of infection but with mainly supportive care measures, it could be hypothesized that these patients die sooner, resulting in less time at-risk to acquire an ARO.

A major limitation of this study is that we utilized total admissions and did not account for total length of hospital stay using patient-days. This could potentially confound results, as patients who are hospitalized longer not only have increased time-at-risk but are likely more seriously ill and vulnerable to further infections. Additionally, by using ORs, we are not able to prove whether COVID-19 was a causal factor in subsequently acquiring an ARO or CDI, and vice versa. Notwithstanding, our finding suggests that prolonged hospitalization may expose patients to hospital-acquired infections. This information can be useful to healthcare providers, particularly when managing patients requiring hospitalization for extended periods of time. Minimizing the risks of secondary infection among persons infected with COVID-19 by implementing appropriate infection prevention and control measures is critical in reducing morbidity and mortality due to hospital-acquired infections.

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