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PII: S0196-6553(22)00575-2
DOI: https://doi.org/10.1016/j.ajic.2022.07.019
Reference: YMIC 6305

To appear in: *AJIC: American Journal of Infection Control*

Please cite this article as: Fareed Khawaja , Krithika Srinivasan , Amy Spallone , Adina Feldman , Sherry Cantu , Ella Ariza-Heredia , Tanya Dvordak , Amin Alousi , Sairah Ahmed , Marina George , Elizabeth Frenzel , Micah Bhatti , Roy F Chemaly , Nosocomial COVID-19 at a comprehensive cancer center during the first year of the pandemic: lessons learned, *AJIC: American Journal of Infection Control* (2022), doi: https://doi.org/10.1016/j.ajic.2022.07.019

Major Article|Major Article

Nosocomial COVID-19 at a comprehensive cancer center during the first year of the pandemic: lessons learned

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Abstract

Background: The spread of coronavirus disease 2019 (COVID-19) in health care settings endangers patients with cancer. As knowledge of the transmission of COVID-19 emerged, strategies for preventing nosocomial COVID-19 were updated. We describe our early experience with nosocomial respiratory viral infections (RVIs) at a cancer center in the first year of the pandemic (March 2020-March 2021).

Methods: Nosocomial RVIs were identified through our infection control prospective surveillance program, which conducted epidemiologic investigations of all microbiologically documented RVIs. Data was presented as frequencies and percentages or medians and ranges.

Results: A total of 35 of 3944 (0.9%) documented RVIs were determined to have been nosocomial acquired. Majority of RVIs were due to SARS CoV-2 (13/35; 37%) or by rhinovirus/enterovirus (12/35; 34%). A cluster investigation of the first 3 patients with nosocomial COVID-19 determined that transmission most likely occurred from employees to patients. Five patients (38%) required mechanical ventilation and 4 (31%) died during the same hospital encounter.

Conclusion: Our investigation of the cluster led to enhancement of our infection control measures. The implications of COVID-19 vaccination on infection control policies is still unclear and further studies are needed to delineate its impact on the transmission of COVID-19 in a hospital setting.

Keywords

COVID-19, hospital-associated transmission, Nosocomial, Cancer, respiratory viruses, SARS CoV-2

Running title: Nosocomial COVID-19 in a cancer center

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INTRODUCTION

In December 2019, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19) emerged in Wuhan, China, and quickly spread across the world. Because transmission dynamics were poorly understood in the early stages of the pandemic, there was sparse guidance on the best strategies to prevent spread of SARS-CoV-2 both in the community and in healthcare settings; 44% of new COVID-19 cases were suspected to have been transmitted nosocomially from initial reports (1, 2). Expanding knowledge of SARS-CoV-2 transmission, escalation of public health and infection control measures for prevention of the spread of SARS-CoV-2, and better definition of nosocomial COVID-19 have reduced rates of hospital transmission between 6.8% and 12.5% based on later

reports during the first year of the pandemic (3, 4). Enhanced infection control measures and visitor restriction protocols for immunocompromised patients such as those with cancer have been supported by multiple medical societies (5, 6).

Patients with cancer are at a higher risk for complications associated with COVID-19 when compared to the general population (7-10). Case fatality rates from COVID-19 in cancer patients were reported to be as high as 25% and 37% in patients with solid tumors and hematologic malignancies, respectively (10). In addition, in patients with cancer, health care–associated COVID-19 was independently associated with shorter median overall survival than was community-acquired COVID-19, with a reported hazard ratio of 2.3 (95% confidence interval: 1.2-4.4) (9).

SARS-CoV-2 is primarily transmitted through respiratory secretions as droplets or aerosols (11-13), and potentially via fomites (14). Based on the known modes of transmission, infection control measures have centered on universal masking, hand washing, social distancing, and a low threshold for testing patients with signs and symptoms of respiratory infections. In addition, many cancer centers, including ours, have implemented routine testing of hospitalized cancer patients without COVID-19 during extended hospital stays. These enhanced infection control protocols may have reduced hospital transmission of COVID-19 and other health care–associated infections.

Nosocomial transmission of other respiratory viruses such as influenza virus, respiratory syncytial virus (RSV), parainfluenza virus (PIV), and human metapneumovirus (HMPV) (15) can have detrimental effects on hospitalized cancer patients by causing nosocomial outbreaks in

the absence of community spread (15-21). Many of the public health measures adopted during the pandemic, mandatory use of masks, were instituted to prevent the spread of SARS-CoV-2, but an additional benefit has been the notably lower rate of other community-acquired respiratory viruses (22), with a similar reduction in nosocomial spread of these viruses (such as RSV) (23).

The aim of our study was to describe our early experience with nosocomial COVID-19 at a comprehensive cancer center and the steps implemented to limit the spread of this virus in our health care settings. We also aimed to investigate the impact of the pandemic and the associated stricter infection control measures on the incidence of other nosocomial respiratory viral infections in our center.

METHODS

Setting

This retrospective study was conducted at a National Cancer Institute-designated comprehensive cancer center with approximately 680 hospital beds and 22,000 employees; All hospitalized patients reside in private rooms. Patients with confirmed COVID-19 are housed on specifically designated floors away from other patients. Patients presenting with respiratory symptoms are tested for respiratory viruses regardless of the time of year via nasopharyngeal or bronchoalveolar lavage sampling; all patients diagnosed with any respiratory viral infection is reported to infection control. Cases of microbiologically documented respiratory viral infections, including COVID-19, in admitted patients are investigated by the Infection Control team for possible hospital-associated transmission and for potential clusters. Once hospital-

associated transmission is suspected in a patient with COVID-19, an investigation focusing on testing staff and other patients on the affected units is conducted. Visitors and staff who were in contact with the index patient were contacted by local nursing leadership for assessment of respiratory symptoms and to highly recommend SARS CoV-2 testing. A follow up phone call was conducted and pertinent data such as results of SARS CoV-2 testing was provided to infection control, when done. In addition, qualitative analysis, including interviews and observations, are carried out to identify any opportunities for improvement and for additional interventions if needed.

Infection control protocols and testing for COVID-19

Since March 13, 2020, all patients and staff are screened for COVID-19–related symptoms and fever at all hospital entrances. Since March 24, 2020, hospitalized patients with COVID-19 and persons under investigation (PUI) for suspected COVID-19 are housed on designated floors or units. Universal masking with medical-grade (ASTM 3) face masks for all employees and patients in clinical and nonclinical areas was instituted on April 1, 2020. Patients with symptoms concerning for respiratory viral infections are tested for COVID-19, and routine testing for asymptomatic patients is undertaken prior to planned hospital admissions and procedures, or at the time of hospital admission via the emergency room. In addition, asymptomatic testing started in July 2020 for all admitted patients with hematologic malignancies and recipients of hematopoietic cell transplantation (HCT) and cellular therapy

every 7 days while hospitalized. Table 1 lists a full timeline of the interventions undertaken to prevent or limit the spread of SARS-CoV-2 in our center.

SARS-CoV-2 testing is performed using one of two real-time polymerase chain reaction (PCR) assays, the Cobas® SARS-CoV-2 test performed on the Cobas® 6800 (Roche Diagnostics) or the Abbott SARS-CoV-2 assay performed on the m2000. Patients with respiratory symptoms were also tested for common respiratory viruses using the Biofire Respiratory Panel (RP) performed on the BioFire Torch platform (bioMerieux). The RP detects Adenovirus, Human Coronaviruses, HMPV, Human Rhinovirus/Enterovirus, Influenza A and B, PIV, and RSV. Prior to the COVID-19 pandemic, patients with respiratory symptoms were tested for most community respiratory viruses using the Biofire respiratory panel on nasopharyngeal swabs at the providers' discretion all year long. Contact and droplet precautions are instituted on the inpatient setting and until discharge for all patients with documented respiratory viral infection. In addition, during the study period (March 1st, 2020 to March 31st, 2021), the alpha strain was the predominant circulating variant in the Houston Metropolitan area (24).

Case definitions

Following guidelines from the Centers for Disease Control and Prevention (CDC), transmission of SARS-CoV-2 was determined to be nosocomial if the onset of COVID-19 symptoms occurred more than 14 days after admission for conditions other than COVID-19 or if two or more SARS-CoV-2 infections were identified among epidemiologically linked health care workers and/or patients (i.e., those working or residing on the same units) (25). For other respiratory viruses, determination of nosocomial infections relies on shorter incubation periods

(i.e. 4 days or more after admission for RSV and PIV). A cluster was determined to be present if there were two or more cases of COVID-19 among health care workers who worked in the same unit and/or among two or more patients housed in the same units at overlapping times and within two weeks of each other.

Data collection and statistical analysis

We collected demographic, medical history, oncologic history, COVID-19 treatments, laboratory, and clinical outcome data at the time of diagnosis from the records of patients diagnosed with nosocomial COVID-19. Data are presented as frequencies and percentages or medians and ranges.

Ethical considerations

This study was approved by our Institutional Research Board under protocol number PA15-0002, and a waiver of the requirement for informed consent was granted due to the retrospective nature of this study.

RESULTS

Active surveillance of respiratory viral infections

Between March 1, 2020 and March 31, 2021, 3944 respiratory viral infections were documented in our infection control database. Most were SARS-CoV-2 infections (3247/3944; 82.3%); the remaining infections were mostly caused by rhinovirus/enterovirus (182/3944; 4.6%) (Figure 1). During the same time period, we had 2 significant surges of COVID-19 in our

community; first between June and August 2020 and a second between December 2020 and February 2021 (Figure 2). Of the 3944 microbiologically documented respiratory viral infections, 35 (0.9%) were determined to have been nosocomially acquired according to our institutional definitions aligned with the CDC definitions as shown in Figure 3. Of the 35 nosocomial respiratory virus infections during the study period, most were caused by SARS-CoV-2 (*n* = 13, 37.1%), followed by rhinovirus/enterovirus (*n* = 8, 22.9%) during the study period. However, the overall incidence of nosocomial COVID-19 was 0.7 cases per 10,000 patient days compared to 1.3 cases per 10,000 patient days for other nosocomial respiratory viral infections.

In comparison, we documented 128 nosocomial respiratory viral infections between March 2019 and February 2020 (the year before the start of the pandemic), most of which were caused by rhinovirus/enterovirus (45/128; 35.2%) and PIV (40/128; 31.3%) (Figure 3). The amount of testing for respiratory viruses excluding SARS CoV-2 using the Biofire assay increased from 8,418 to 9793 tests between March 2019-February 2020 and March 2020-March 2021, respectively. The annual incidence of nosocomial respiratory viral infections prior to the COVID-19 pandemic remained stable ranging from 6.9 cases per 10,000 patient days in 2017-2018 and 6.9 cases per 10,000 patient days in 2018-2019, and 5.8 cases per 10,000 patient days in 2019-2020. Thus, when compared to the year before the start of the COVID-19 pandemic, the rate of nosocomial respiratory viral infections was 73% lower in the first year of the pandemic. Specifically, nosocomial infections with influenza virus fell by 58% (from 12 to 5 cases), with PIV by 95% (from 40 to 2 cases), with RSV by 90% (from 10 cases to 1 case), with HMPV by 83% (from 6 cases to 1 case), with rhinovirus/enterovirus by 82% (from 45 to 8 cases), and with

other respiratory viruses such as human coronaviruses and bocavirus by 67% (from 15 to 5 cases).

Nosocomial COVID-19 and cluster investigation

Among the 13 patients with nosocomial COVID-19, epidemiological investigation determined that 3 (P1, P2, and P3) were part of a cluster. After the index patient, P1, was identified, 8 of the 73 (11%) employees who were tested due to proximity to P1 had positive SARS-CoV-2 tests. P1 had a caregiver who boarded during the patient's hospital stay and who also tested positive for SARS-CoV-2. An additional 29 patients housed in the same location as P1 were screened for SARS-CoV-2, and an additional 2 tested positive (P2 and P3). Based on the results of this investigation, we determined that transmission had occurred from one or more infected employees to the 3 patients and from employee to employee in the same location, and no direct patient-to-patient transmission had occurred. Figure 4 illustrates the results of our investigation and the likely SARS-CoV-2 transmission patterns. Briefly, over a 1-month period from mid-June to mid-July 2020, 19 employees who worked on the same floor on which P1 was housed had positive SARS-CoV-2 tests. No other patient clusters were identified, and only sporadic patients with nosocomial COVID-19 were detected for the remainder of the study period.

Of the 13 patients with nosocomial COVID-19 during the first year of the pandemic, 4 (31%) were cared for by health care workers who later tested positive for SARS-CoV-2, 5 (38%)

were exposed to both infected caregivers and health care workers, and 4 (31%) had no clear source of exposure.

Characteristics and clinical outcomes of patients with nosocomial COVID-19

Demographic and clinical characteristics of the 13 patients with nosocomial COVID-19 are shown in Table 2. Their median age was 68 years (range: 21-80), 54% (*n* = 7) were White, 54% (*n* = 7) were female, 77% (*n* = 10) had a hematologic malignancy, 69% (*n* = 9) were recipients of cellular therapy, and 69% (*n* = 9) were on active chemotherapy at least 30 days before their COVID-19 diagnosis. The median time from cellular therapy to COVID-19 was 15 days with a range of 4-128 days. Routine asymptomatic screening identified 5 of these 13 patients, and all 5 developed signs and symptoms of COVID-19 later. The remaining 8 patients were tested after displaying signs and symptoms suggestive of COVID-19.

In 11 patients, computed tomography (CT) imaging of the chest was suggestive of pneumonia at the time of COVID-19 diagnosis. The CT findings were described as ground-glass opacities (8/11; 72%), nodular opacities (2/11; 18%), or diffuse consolidations (1/11; 9%). Interestingly, 2 patients were diagnosed with COVID-19 based on a positive SARS-CoV-2 assay using a bronchoalveolar lavage specimen after multiple tests using nasopharyngeal swabs were negative. Median laboratory values at the time of COVID-19 diagnosis were white blood cell count of 2.7 K/µL (range: 0-13.90), absolute neutrophil count of 2.38 K/µL (range: 0-12.41), absolute lymphocyte count of 0.11 K/µL (range: 0.00-1.00), procalcitonin level of 0.18 ng/mL

(range: 0.09-1.95), ferritin level of 1429 ng/mL (range: 233-6339), and IL-6 level of 31 pg/mL (range: 4-249) (Table 2).

Almost all patients (11/13; 85%) were treated for COVID-19 at the time of diagnosis; 10 patients received remdesivir, 7 received steroids, and 8 received convalescent plasma. Many patients required use of mechanical ventilation (5/13, 38%), a high-flow nasal cannula (2/13, 15%), or a nasal cannula (2/13, 15%). Three of the 13 (23%) patients developed sepsis requiring vasopressor support. Four patients died during their hospital stay, all with respiratory failure due to COVID-19, for an inpatient mortality rate of 31%. Of the 9 survivors, 4 required readmissions to the hospital within 30 days.

Protocols introduced after the cluster investigation

Given that many patients with hematologic malignancies have long hospital stays, we implemented routine weekly screening for SARS-CoV-2 in these high-risk patients for the duration of their hospital stay and regardless of their symptoms (weekly retesting was performed on the same day of the week as the patient's admission day). We also required that clinical staff caring for patients with hematologic malignancies change face masks between patient encounters to reduce the risk of cross-contamination in addition to the use of face shields during patient encounters. After implementation of these measures, only sporadic patients were found to have nosocomial COVID-19, and no additional clusters were identified. Figure 4 illustrates the timing of these interventions in relation to the identified cluster of nosocomial infections.

Figure 3. Comparison of nosocomial respiratory viral infections during the year before the COVID-19 pandemic (March 2019-February 2020) and during the first year of the pandemic (March 2020-March 2021).

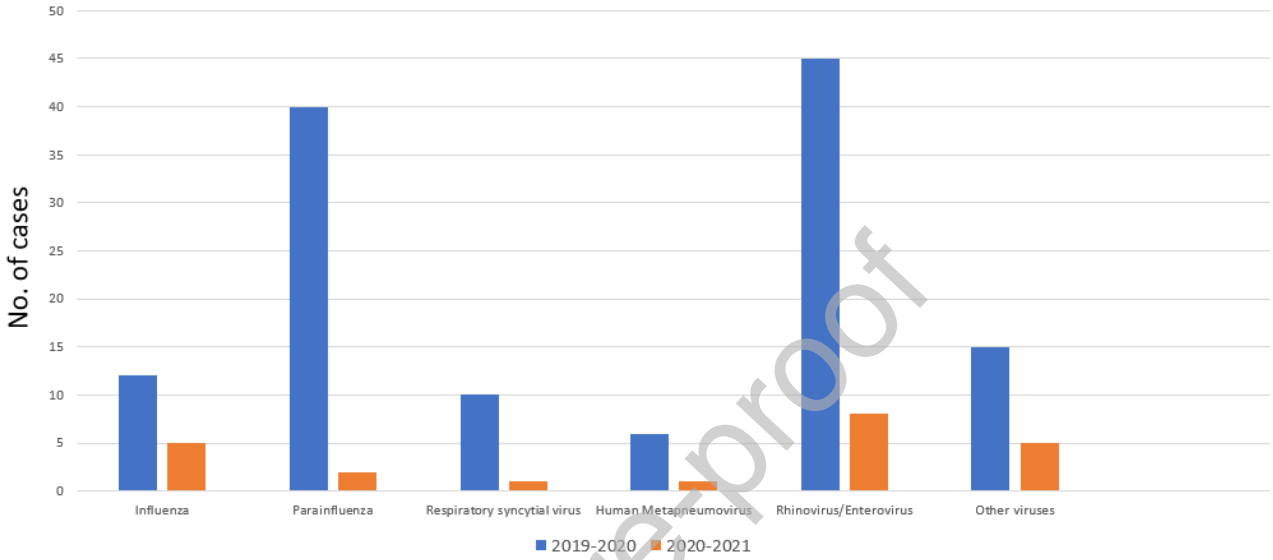

Figure 4. Potential nosocomial COVID-19 transmission dynamics between patients and health care workers, June-July 2020. Top: Timeline of positive COVID-19 patients and employees in the same unit from 6/10/2020 to 7/16/2020 Bottom: Transmission tree linking possible exposures to infected patients from 6/17/2020 to 7/5/2020. Examples of healthcare workers involved included nurses, patient care technicians and patient care navigators.