





Concise Communication

Asymptomatic severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection in adults is uncommon using rigorous symptom characterization and follow-up in an acute-care adult hospital outbreak

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Abstract

Asymptomatic coronavirus disease 2019 (COVID-19) has been reported as a significant driver of COVID-19 outbreaks. Our hospital ward outbreak analysis suggests that comprehensive symptoms and signs assessment, in combination with adequate follow-up, allows a more precise determination of COVID-19 symptoms. Asymptomatic infection was quite uncommon among adults in this setting.

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Although some data suggest that asymptomatic severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)-infected individuals are less infectious than symptomatic cases,¹ other studies have suggested that transmission via presymptomatic and/or asymptomatic individuals plays a major role in driving transmission.² The rigor to which infected persons are assessed as truly asymptomatic or presymptomatic and their role in overall SARS-CoV-2 transmission is important.^{3,4}

Asymptomatic coronavirus disease 2019 (COVID-19) was originally defined by the World Health Organization as positive detection of SARS-CoV-2 nucleic acid by reverse-transcription

polymerase chain reaction (RT-PCR) in patients without typical clinical symptoms or signs of disease and without abnormalities in radiologic imaging.³ Studies estimating the magnitude of asymptomatic COVID-19 cases have reported that the proportion of asymptomatic COVID-19 ranges widely from 1.4% to 78.3%.⁵ A recent systematic review and meta-analysis⁶ that focused on higher-quality studies, excluding studies with no or unclear follow-up or those without data on asymptomatic cases, found the overall proportion of asymptomatic cases to be only 17% (95% confidence interval [CI], 14%–20%) which is lower than the rates estimated in many earlier and highly publicized studies.^{2,7}

In September 2020, at an 1,100-bed tertiary-care healthcare facility, a COVID-19 outbreak (wild type) was declared on 3 linked cardiac units. Over 7 weeks, 86 cases (all unvaccinated) were identified, including 39 patients, 42 healthcare workers (HCWs), and 5 visitors. Given the disparities regarding the frequency of symptomatic COVID-19 or asymptomatic infection with SARS-CoV-2, we carefully assessed the symptoms and signs of all cases and patient noncases to determine the true proportion of symptomatic or asymptomatic infected individuals as the focus of this concise report.

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PREVIOUS PRESENTATION: The HCW component of this study was presented in abstract form as a poster at Association of Medical Microbiology and Infectious Disease Canada (AMMI) Canada– Canadian Association for Clinical Microbiology and Infectious Diseases (CACMID) Annual Meeting #P17 on April 26, 2021, held virtually.

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Methods

Supplementary methods, definitions, outbreak description, testing, analysis, and response are provided in Supplementary File S1 (online). In brief, a standardized COVID-19 patient symptom identification and monitoring tool (Supplementary File S2 COVID-19SMT, online) using a comprehensive repertoire of 26 COVID-19 symptoms and signs was applied in real time by experienced healthcare personnel to 197 at-risk patients (39 cases and 158 noncases). A similar tool was used for symptom assessment of 42 HCW and 5 visitor cases. Nasopharyngeal swabs, and occasionally throat swabs, were collected every 2–5 days and tested for SARS-CoV-2 using RT-PCR.⁸

This study was conducted as a component of an epidemiologic investigation under the Public Health in the Province of Alberta and was thus considered a quality improvement project. As such, it did not require ethical review. It also was assessed using the ARECCI (A Project Ethics Community Consensus Initiative) tool, which confirmed this project as fitting with a quality improvement project.

Results

The outbreak occurred during a time of relatively low community transmission (active cases, 30.7 per 10,000 population; <https://covid-tracker.chi-csm.ca>) with unrecognized patient cases occurring at the beginning of the outbreak due to the many overlapping symptoms of cardiac disease and COVID-19.

Of the 86 COVID-19 cases (Table 1) identified during the outbreak period, 84 (97.7%) were symptomatic (Fig. 1). For symptomatic patients, HCWs and visitors that were RT-PCR positive, having core influenza-like-illness (ILI) symptoms and signs was most common, occurring in 84.9% of cases, followed by expanded symptoms in 70.9%. Core ILI with expanded symptoms was the most common combination of symptom-and-sign categories (45.3%). In most cases, a combination of 2 or more categories of symptoms and signs occurred together; a single symptom occurred less often (core ILI in 1.2%, core gastrointestinal (GI) in none and expanded in 5.8%) (Supplementary Fig. S1 online). Only 1 case (an inpatient) had fever only with no other ILI symptoms. No individuals had core ILI symptoms without fever, chills, or rigors.

Of 158 admitted patient noncases, of whom 156 (98.7%) were confirmed negative by RT-PCR, 9 (5.7%) were symptomatic, with core ILI being the most common symptoms (5.1%). Overall, 90.5% of cases were symptomatic before or on the day of RT-PCR positivity for COVID-19 (Table 1). A median of 1, 2, and 2 days elapsed between symptom onset and RT-PCR positivity in HCWs, patients, and visitors, respectively. In total, 42 HCWs tested positive by RT-PCR, of whom 34 (83%) disclosed having symptoms at their initial interview. An additional 5 HCWs went on to develop symptoms 24–48 hours after testing positive and were deemed to be presymptomatic at the time of RT-PCR positivity. Of the 42 HCWs, 2 (4.8%) did not report developing symptoms or signs up to 10 days after RT-PCR positivity. Overall, 40 (95.2%) of 42 HCWs had symptomatic COVID-19 (Table 1).

We identified a significant difference between HCWs and patients in terms of age ($P < .01$), with a median age of 34 years for HCWs versus 78 years for patients and 70 years for visitors. However, the proportion of symptomatic cases in each category was similar (HCWs, 95.2%; patients, 100%; and visitors, 100%), suggesting that younger adults did not differ from older adults in this study.

Table 1. Demographics and Days From Symptom Onset to COVID-19 RT-PCR Positivity of SARS-CoV-2 Cases

Characteristic	HCWs (n=42), No. (%) ^a	Patients (n=39), No. (%) ^a	Visitors (n=5), No. (%) ^a
Symptomatic cases	40 (95)	39 (100)	5 (100)
Age			
Mean y (SD)	38 (±12)	75 (±12) ^b	71 (±9)
Median y, (range)	34 (23–65)	78 (34–91)	70 (57–81)
Sex			
Male	11 (26)	23 (59)	1 (20)
Female	31 (74)	16 (41)	4 (80)
Days from symptom onset to COVID-19 RT-PCR positivity, median (range)	1 (–2 to 8) ^c	2 (–5 ^d to 10)	2 (0 to 5)

Note. SD, standard deviation.

^aUnits unless otherwise stated.

^bThe average age for noncases; n=158; (age, 69±14 y) was not significantly different than that seen in cases.

^cA minus sign indicates the case was asymptomatic or presymptomatic and developed symptoms after testing positive for SARS-CoV-2 by RT-PCR.

^dOne patient who had tested negative at the time of discharge, was found to be positive on follow-up testing in the community. This patient only reported symptoms 5 d after RT-PCR positivity. This patient did not undergo a minimum of once per 8-h shift symptom-and-sign monitoring like other admitted patients, and there was a significant potential for recall or ascertainment bias given the length of time between discharge and interview by Public Health.

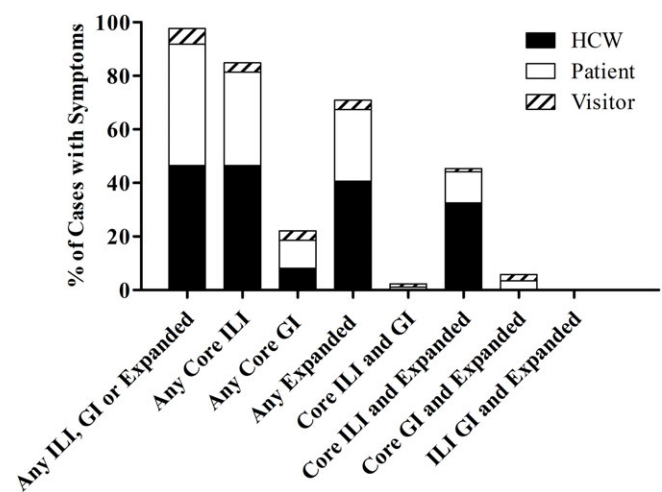


Fig. 1. Breakdown of COVID-19 symptoms and signs during an acute-care outbreak. Breakdown of COVID-19 symptoms and signs by case type (HCW, patient, or visitor). “Any” indicates those symptoms that are reported as present, either alone, or in combination with other symptoms including GI and/or expanded symptom categories. (See Supplementary Fig. S1 for cases that had “only” symptoms in each of the major categories.) Core influenza-like-illness (ILI) symptoms included new or worse or unexplained cough, fever, chills, or rigors; shortness of breath; difficulty breathing; sore throat and/or painful swallowing or runny nose and/or nasal congestion. Core gastrointestinal (GI) symptoms included new or worse or unexplained vomiting or diarrhea. COVID-19 expanded symptoms included new or worse or unexplained headache; muscle and/or joint pain; fatigue or extreme exhaustion; nausea and/or sudden loss of appetite; loss of or change in sense of smell or taste; conjunctivitis, red eye, or conjunctival edema; altered mental status; and any additional COVID-19 symptoms at clinician’s discretion, such as “COVID-19 toes” or other cutaneous manifestations.

In our study, 27 (69%) of 39 patients had some symptoms prior to being tested for SARS-CoV-2, with 5 patients being symptomatic for >5 days prior to being isolated and tested. For patients and visitors, 36 (92.3%) of 39 and 5 (100%) of 5, respectively, were symptomatic at the time of RT-PCR positivity. Of 39 patients, 2 (5.1%) who were initially presymptomatic went on to develop symptoms within 24 hours and 1 (2.6%) was identified as symptomatic 5 days later. We would have overlooked 8 cases without repeated assessments, highlighting the importance of adequate follow-up for the typical incubation period.

Discussion

Although some reports have noted high proportions of asymptomatic COVID-19 cases, our real-time comprehensive approach using a standardized symptom identification and monitoring tool (Supplementary File S2, COVID-19SIMT, online) raises questions about significant degrees of ascertainment and recall bias in previous studies.^{2,7}

Meyerowitz et al⁹ discussed the challenges and importance of agreement on an accurate and systematic characterization of COVID-19, the importance of consistency of symptom reporting and adequate follow-up in ascertaining the true proportion of asymptomatic COVID-19 cases. No cases in our data set had core ILI symptoms without fever, chills, or rigors, and only 1 case (inpatient) had fever with no other ILI symptoms. This latter observation supports the importance of using GI and expanded symptoms and signs as part of the overall assessment. Some have suggested that a difference in the proportion of cases that are asymptomatic relates to age,⁹ but we found no differences.

Presymptomatic individuals may still be capable of transmitting virus, which emphasizes the need to continue physical distancing, universal masking, and hand hygiene in high-risk environments. Our data, using comprehensive and frequent screening, suggests that asymptomatic COVID-19 may be much lower than estimated in many earlier studies and raises important questions regarding the assumptions made in modelling asymptomatic SARS-CoV-2 transmission.²

Isolation of SARS-CoV-2-infected individuals is key to curtailing transmission. Patients admitted via the cardiac service may have symptoms of dyspnea, chest pain, cough, and difficulty breathing, which overlap with COVID-19, leading to interpretation difficulties. Careful clinical assessment, continuous symptom monitoring and a high index of suspicion is required to identify COVID-19 in cardiac patients.

We recognize several limitations of our study. It reflects an unvaccinated population and may not reflect variants such as the SARS-CoV-2 (omicron) variant, which have milder symptoms and did not follow all discharged patients. Nonetheless, our findings further our understanding of the rate of truly asymptomatic COVID-19 in unvaccinated persons when using a comprehensive and standardized symptom-and-sign tool along with

adequate follow-up. Our findings are consistent with a recent study of HCWs using a robust symptom-monitoring methodology in which 12 (100%) of 12 confirmed SARS-CoV-2 cases were symptomatic.¹⁰

Supplementary material. To view supplementary material for this article, please visit <https://doi.org/10.1017/ice.2022.168>

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