


Original Article

Coronavirus disease 2019 (COVID-19) admission screening and assessment of infectiousness at an academic medical center in Iowa, 2020

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Abstract

Objective: Patients admitted to the hospital may unknowingly carry severe acute respiratory coronavirus virus 2 (SARS-CoV-2), and hospitals have implemented SARS-CoV-2 admission screening. However, because SARS-CoV-2 reverse-transcription polymerase chain reaction (RT-PCR) assays may remain positive for months after infection, positive results may represent active or past infection. We determined the prevalence and infectiousness of patients who were admitted for reasons unrelated to COVID-19 but tested positive for SARS-CoV-2 on admission screening.

Methods: We conducted an observational study at the University of Iowa Hospitals & Clinics from July 7 to October 25, 2020. All patients admitted without suspicion of COVID-19 were included, and medical records of those with a positive admission screening test were reviewed. Infectiousness was determined using patient history, PCR cycle threshold (Ct) value, and serology.

Results: In total, 5,913 patients were screened and admitted for reasons unrelated to COVID-19. Of these, 101 had positive admission RT-PCR results; 36 of these patients were excluded because they had respiratory signs/symptoms on admission on chart review. Also, 65 patients (1.1%) did not have respiratory symptoms. Finally, 55 patients had Ct values available and were included in this analysis. The median age of the final cohort was 56 years and 51% were male. Our assessment revealed that 23 patients (42%) were likely infectious. The median duration of in-hospital isolation was 5 days for those likely infectious and 2 days for those deemed noninfectious.

Conclusions: SARS-CoV-2 was infrequent among patients admitted for reasons unrelated to COVID-19. An assessment of the likelihood of infectiousness using clinical history, RT-PCR Ct values, and serology may help in making the determination to discontinue isolation and conserve resources.

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Coronavirus disease 2019 (COVID-19) is a major threat to health-care systems and public health worldwide. Various policies have been implemented to mitigate severe acute respiratory coronavirus virus 2 (SARS-CoV-2) transmission in healthcare facilities, such as symptom screening for healthcare personnel (HCP) and visitors, optimizing personal protective equipment (PPE), and social distancing.¹ Because SARS-CoV-2 results in a large proportion of asymptomatic infections (~50%), asymptomatic individuals may contribute to virus transmission in healthcare settings.^{2,3} Identification of COVID-19 cases early on during their hospital

admission could direct interventions to reduce in-hospital transmission and prevent COVID-19 hospital outbreaks. Moreover, hospital admission and serial testing for SARS-CoV-2 has been implemented to prevent nosocomial transmission via early isolation and PPE use guidance.^{4,5}

Knowing each person's SARS-CoV-2 status may prevent COVID-19 from spreading in the community and healthcare facilities. SARS-CoV-2 has a mean incubation period of 5 days, and most patients are infectious for <10 days.^{6–8} Although reverse-transcription polymerase chain reaction (RT-PCR) is widely used for SARS-CoV-2 detection, these assays may remain positive for months after acute infection. Prolonged positivity may represent remnant viral RNA from a past infection instead of persistent infection.^{9–11}

The real-time RT-PCR cycle threshold (Ct) value is the number of nucleic acid amplification cycles needed for the target gene to

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cross a threshold level. Ct values may correlate inversely with nucleic acid concentration in a sample. However, Ct values have certain limitations, such as variation based on the type of specimen collected and different thresholds in correlation with positive viral cultures.^{13–15} Ct values can help determine the patient's infectious status and the need for isolation if used in the context of patient history, serology, and previous RT-PCR results.^{16–18} Although transmission-based precautions are essential to prevent the spread of infection, unnecessary isolation might lead to extra cost and time for healthcare facilities. Although the utility of SARS-CoV-2 admission screening with RT-PCR testing has been reported,¹⁹ the use of Ct values on admission screening has not been fully explored. In addition, the proportion of patients with positive admission screening who are likely infectious is not well known. In this study, we determined the prevalence of COVID-19 and infectiousness of patients who were not admitted for COVID-19 but tested positive for SARS-CoV-2.

Methods

The University of Iowa Hospitals & Clinics (UIHC) is an 811-bed academic medical center. On June 11, 2020, SARS-CoV-2 RT-PCR screening testing of all patients on admission regardless of symptoms was initiated. UIHC has separate SARS-CoV-2 test orders for symptomatic and asymptomatic patients. If the patient has symptoms consistent with COVID-19, an order labelled “symptomatic PCR” is entered. If the patient has no symptoms consistent with COVID-19, or if the test is done as part of surveillance (admission or preprocedural testing) an order labelled “asymptomatic PCR” is entered. We conducted a single-center observational study of patients without suspicion of COVID-19 who tested positive for SARS-CoV-2 by RT-PCR upon admission screening. All patients with positive asymptomatic PCR test orders admitted from July 7 to October 25, 2020, were included in this study. The reason for admission was considered unrelated to COVID-19 when the screening was done using the asymptomatic PCR test order. We retrospectively included all patients with positive asymptomatic tests on admission. We then reviewed their medical records to ensure that they did not have respiratory signs and/or symptoms consistent with COVID-19. We excluded patients with respiratory signs and/or symptoms compatible with COVID-19 at the time of admission and patients without available Ct values. RT-PCR admission screening was performed via nasopharyngeal swab using the TaqPath COVID-19 Combo Kit (ThermoFisher, Waltham, MA). Tests were processed according to the latest instructions for use under the Food and Drug Administration (FDA) emergency use clearance which, over the course of this study, evolved with the interpretive software to minimize false-positive results and other minor changes collated in current Revision J of the package.²⁰ Throughout the study period, samples were extracted with a ThermoFisher KingFisher Flex instrument, and PCR reactions were performed on a QuantStudio 5 thermocycler according to the manufacturer's instructions. Prior to August 2021, we used a centrifugation and vortexing procedure that minimized false-positive calls generated by the interpretive software. According to the protocol, we manually inspected all amplification curves to exclude these early errors, wherein mixing and boundary-layer optical effects generated baseline noise that was interpreted in rare instances as a positive result by the interpretive software.²¹ Our convention for reporting positive results was concordant with the current Revision J of the ThermoFisher protocol, wherein either 2 positive targets (of 3) or 1 positive target confirmed through

retesting defined a positive result. Procedures and yield of the assay therefore did not change substantively over the course of the study. The rise of S-gene PCR dropout strains such as B.1.1.7 was unlikely to effect positive-result calling with manual inspection of data, the presence of the ORF1ab and N-gene targets, and the stated interpretive criteria that do not require amplification of all targets. For serology testing, the Roche assay was used to determine total SARS-CoV-2 antibodies. If the specimen was positive via Roche assay, it was tested using the DiaSorin SARS-CoV-2 IgG assay.

The outcomes were (1) prevalence of SARS-CoV-2 positivity among patients who were admitted for reasons unrelated to COVID-19; (2) infectiousness (ie, likely infectious and likely non-infectious, more details below) in those with a positive test admitted for reasons unrelated to COVID-19; (3) the duration of in-hospital isolation for patients deemed likely infectious; (4) their estimated additional cost due to COVID-19 isolation per day; and (5) exposure events by patients who were likely infectious. Data were obtained from the electronic health record, including age; sex; admission diagnosis; symptoms; mean RT-PCR cycle Ct values for N, S, and *ORF1ab* genes; and SARS-CoV-2 serum antibodies. Infectiousness was determined by the UIHC Program of Hospital Epidemiology. Information on isolation time and exposure events for HCP and patients with their follow-up SARS-CoV-2 test results were obtained from a data set previously created by the Program of Hospital Epidemiology. The median duration for in-hospital isolation was calculated based on first to last day of hospital isolation or discharge date if isolation was not discontinued during hospitalization. Two hospital epidemiology fellows (M.A. and T.K.) reviewed patients' medical records and the data set, and 1 infection preventionist (A.T.) collected Ct values for all patients with positive RT-PCR admission screening.

Infectiousness was determined using patient history, Ct value, and serology. Infectiousness was categorized as likely infectious if Ct values ≤ 29 or likely noninfectious if 2 samples (or 1 if only 1 was available) had Ct values ≥ 30 with or without positive SARS-CoV2 serology and/or history of a positive PCR or antigen result in the previous 90 days (if available). We used a Ct value of < 29 as the threshold for likely infectious patients based on studies that have shown no viral growth in cultures when the Ct value is > 30 .^{15,22,23} Serology (IgM and IgG antibodies) or repeated PCR tests were used in some cases to add certainty for discontinuing isolation in some cases (eg, past infection). All HCPs wore medical-grade face masks and eye protection for all patient care. In our hospital, we use the time-based US Center for Disease Control and Prevention (CDC) protocol to discontinue isolation.²⁴ In-hospital exposure events were traced only for patients who were likely infectious.

Estimated additional cost due to isolation per day was calculated as follows: [(donning and doffing time \times hourly salary of each HCP \times room entries per patient room/day) + (cost of PPE items \times room entries per patient room/day)]. The costs of PPE, PCR and serologic testing, and hourly staff salary were obtained from our institution's human resources and procurement services. PPE included masks, N95 respirators, gowns, gloves, and eye shields. The frequency of room entry was calculated by asking COVID-19-unit personnel to log entry and exit times. PPE donning and doffing times were obtained by observing 20 randomly selected COVID-19 inpatient rooms during infection prevention team rounds. The frequency of room entries and donning and doffing times were collected over 1 week and were used to calculate the total cost. Observations were conducted at both intensive care units (ICUs) and non-ICUs. The costs of PPE, PCR, and serologic testing

were based on post-COVID-19 pandemic costs per each in US dollars.

This study was approved by the Institutional Review Board of the University of Iowa. We used Stata statistical software (StataCorp, College Station, TX) to present and describe the data.

Results

From July 7 to October 25, 2020, some 5,913 patients were admitted for reasons unrelated to COVID-19 and were screened for SARS-CoV-2. Of these, 101 had positive RT-PCR results, but 36 patients (34%) were excluded because they had COVID-19 symptoms on chart review, leaving a total of 65 (1.1%) who were admitted for reasons unrelated to COVID-19. Of these 65 patients, 55 had Ct values available and were included in this analysis.

The median age for patients admitted for reasons unrelated to COVID-19 who tested positive was 56 years (range, 0–91); 28 (51%) were male and 3 (5%) were aged <18 years. The most frequent admission reasons were neurological (36%), gastrointestinal (16%), and trauma (16%).

Serologic testing was performed for 19 (35%) patients, and it was positive for 8 patients, indeterminate for 2 patients, and negative for 9 patients. Follow-up RT-PCR testing was performed for 23 patients (42%) and was negative for 14 patients. The median time of follow-up testing was 2 days (range, 1–17 days). The final interpretation by the hospital epidemiology team revealed that 23 cases (42%) were likely infectious and 32 (58%) likely noninfectious. Also, 9 patients were categorized as likely noninfectious based on a single Ct value ≥ 30 and lack of repeated or previous testing. All patients were discharged from the hospital except for 2 patients who died due to arrhythmia and extensive subarachnoid hemorrhage. Of 23 likely infectious patients, 6 were placed in non-COVID-19 semiprivate rooms before admission screening was available. These 6 cases led to 7 exposures (6 patients and 1 HCP). Of the 6 exposed patients, 3 patients were not tested because they had recently recovered from COVID-19, 2 patients died due to non-COVID-19 reasons before the testing date, and 1 patient was discharged and did not return for follow-up testing. The HCP was exposed through an aerosol-generating procedure without proper protection and tested negative. Of 23 patients without fever or respiratory symptoms but deemed likely infectious on admission, 11 (47%) developed fever or respiratory symptoms during their hospital stay (mean Ct value, 21).

The average time spent for donning and doffing before entering a COVID-19 patient room was 140 seconds (range, 100–180). The mean frequencies of patient room entry were 13 times for nurses, 5 times for respiratory therapists, and 4 times for physicians, for a total of 22 room entries per patient room per day. The median duration of isolation for likely infectious patients was 5 days (range, 1–10), while the median duration of isolation in likely noninfectious patients was 2 days (range, 1–2). The cost of COVID-19 PPE was \$162 per patient room per day. Because noninfectious patients remained in isolation 3 fewer days infectious patients, noninfectious patients were associated with 264 fewer PPE items and at least \$486 less cost per admission. The PCR cost was \$33.5 per test and the average serologic testing cost was \$21 (range, \$11–\$31). The estimated excess testing cost based on our strategy was \$54.5 per admission.

Discussion

Evaluating Ct values, history, and serology for patients with positive RT-PCR testing on hospital admission was helpful to a

determine patient's infectiousness. Our study demonstrated a low prevalence of SARS-CoV-2 positivity (~1%) in patients admitted for reasons unrelated to COVID-19. Most patients were likely noninfectious (58%). We were able to discontinue isolation 3 days earlier than for those deemed likely to be infectious. Estimating COVID-19 infectiousness on admission helped us preserve PPE and other hospital resources.

Previous studies revealed that SARS-CoV-2 positivity on admission screening or preprocedural screening was seen in 0.3–13% of asymptomatic patients.^{5,18,19} In low-prevalence areas, universal hospital admission testing does not yield a considerable number of asymptomatic COVID-19 cases because community incidence rates may correlate with the incidence of asymptomatic cases.^{25,26} In our study, positive SARS-CoV-2 RT-PCR in patients admitted for reasons unrelated to COVID-19 represented only 1.1% of hospital admissions. The wide range of positivity in different studies is likely due to different definitions of symptomatic versus asymptomatic and community incidence. Identifying and isolating all persons with SARS-CoV-2 is critical in healthcare settings to prevent nosocomial transmission and outbreaks. Therefore, we decided to continue this strategy of SARS-CoV-2 admission screening for all admitted patients.

A novel aspect of our study is the assessment of infectiousness of COVID-19 using Ct values in conjunction with clinical history and the assessment serology in patients not suspected of having COVID-19. Persistent RT-PCR positivity for a long duration beyond the infectivity period has been reported.^{7,22,27} Bullard et al¹⁵ documented that a combination of COVID-19 duration of symptoms and RT-PCR Ct values may determine SARS-CoV-2 infectivity. However, previous studies evaluating the utility of admission screening did not use this strategy and could not evaluate infectiousness in asymptomatic patients with positive RT-PCR.^{25,26} In our study, 58% of patients admitted for reasons unrelated to COVID-19 who tested positive were likely noninfectious. This result suggests that hospitals may conserve PPE, HCP time, and cost for patients who are likely noninfectious.

The risk of SARS-CoV-2 exposure and transmission in healthcare facilities has been reported in the literature, particularly at the peak of the pandemic.^{28,29} However, determining the source of transmission (community vs healthcare associated) remains ambiguous because of increasing COVID-19 cases in the community and symptoms of COVID-19 that could start beyond 48–72 hours of hospital admission.³⁰ Patients hospitalized in shared rooms have a higher risk of exposure, and limiting use of shared rooms has been suggested to minimize the possibility of infection transmission.²⁸ In our experience, most of exposed persons were patients in shared rooms (6 of 7, 86%). Because most exposures happened in a shared room while waiting for admission screening results, asymptomatic patients with a pending SARS-CoV-2 admission screening may need to be admitted to a private room.

Determining the need for isolation precautions is essential to prevent nosocomial transmission.³¹ The use of a PCR assay that returns lower Ct values (ThermoFisher), on average, than most commonly used assays³² likely resulted in a conservative estimate of infective patients, therefore promoting safety. However, there is still a need for further standardization of Ct values for comparison and portability of our methods into other institutions using different PCR assays. During the COVID-19 pandemic, PPE supply chain and stockpiles were tremendously affected, which stressed healthcare systems. Several urgent interventions, such as PPE reprocessing and reuse, were implemented to preserve

PPE supply.^{33–35} Our strategy to determine the infectivity of asymptomatic SARS-CoV-2-positive patients helped us shorten in-hospital isolation time by 3 days, therefore preserving PPE. Hospitals with limited PPE or semi-private rooms are likely to benefit most from this strategy and could utilize hospital resources more effectively.

Our study has several limitations. It was performed in a single academic center and the results might not be generalizable. The asymptomatic patients were not followed beyond the date of discharge for the development of symptoms. There was a possibility of patient or provider bias when providing or collecting symptom data, which may impact the type of test ordered (symptomatic vs asymptomatic). Observations investigating room entries and time for donning and doffing were not conducted for all COVID-19 cases but on randomly selected COVID-19 inpatients. The costs saved by earlier discontinuation of isolation was an estimated cost for PPE utilized by HCP and their time during donning and doffing in ICUs and non-ICUs. Because this analysis used real-world infection prevention and clinical information, not every patient had complete data for infectiousness evaluation. Also, Ct values can vary between different samples and laboratories.³⁶ Despite these limitations, our experience of estimating the infectiousness of asymptomatic patients and exposure events via Ct values targeting 3 genes may be helpful to other health centers.

In conclusion, SARS-CoV-2 was infrequent among patients admitted for reasons unrelated to COVID-19. An assessment of the likelihood of infectiousness utilizing history, RT-PCR Ct values, and serology may help in making the determination to discontinue isolation and save PPE and hospital resources.

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