


Acceptance of a Symptom-Based Approach for COVID-19 rtRT-PCR Testing to Conserve Resources in a Lower Middle-Income Setting

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Abstract

SARS-CoV-2 initially emerged in Wuhan, China in late 2019. It has since been recognized as a pandemic and has led to great social and economic disruption globally. The Reverse Transcriptase Real-Time Polymerase Chain Reaction (rtRT-PCR) has become the primary method for COVID-19 testing worldwide. The method requires a specialized laboratory set up. Long-term persistence of SARS-CoV-2 RNA in nasopharyngeal secretion after full clinical recovery of the patient is regularly observed nowadays. This forces the patients to spend a longer period in isolation and test repeatedly to obtain evidence of viral clearance. Repeated COVID-19 testing in asymptomatic or mildly symptomatic cases often leads to extra workload for laboratories that are already struggling with a high specimen turnover. Here, we present 5 purposively selected cases with different patterns of clinical presentations in which nasopharyngeal shedding of SARS-CoV-2 RNA was observed in patients for a long time. From these case studies, we emphasized the adoption of a symptom-based approach for discontinuing transmission-based precautions over a test-based strategy to reduce the time spent by asymptomatic and mildly symptomatic COVID-19 patients in isolation. A symptom-based approach will also help reduce laboratory burden for COVID-19 testing as well as conserve valuable resources and supplies utilized for rtRT-PCR testing in an emerging lower-middle-income setting. Most importantly, it will also make room for critically ill COVID-19 patients to visit or avail COVID-19 testing at their convenience.

Keywords

COVID-19, SARS-CoV-2, rtRT-PCR, serial testing, lower middle-income settings, access to care, disease management

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Introduction

In late 2019, coronavirus disease-2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan, China and has since become a global public health concern.¹ COVID-19 was first reported in Bangladesh on March 8, 2020. Since then, 490533 COVID-19 cases and 7052 deaths have been documented.² Clinical manifestations vary from asymptomatic infections to mild upper respiratory tract infections, and even acute respiratory distress syndrome in some cases. A previous study finding on COVID-19 cases from China reported 81% of patients with mild manifestations, 14% with severe manifestations, and 5% with critical manifestations (defined by respiratory failure, septic shock, and/or multiple organ dysfunction).³ The preliminary findings of a recent survey from Dhaka City of Bangladesh jointly

conducted by the Institute of Epidemiology, Disease Control and Research (IEDCR) and the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) found that about 82% of the cases studied were asymptomatic, whereas among the symptomatic cases, 15% required hospitalization.⁴ The criteria for discharge from quarantine or hospital based on COVID-19 testing protocol varies globally as per the respective countries guidelines and regulations. Currently, the World Health Organization (WHO) has

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circulated a simplified symptom-based approach in place of serial testing for those who were asymptomatic or mildly symptomatic, sparing hospitalized patients or those with several comorbidities.⁵ The report presents a case series on five purposively selected COVID-19 patients with most probable clinical presentations, like asymptomatic, mild/moderate symptomatic and a severe hospitalized case who were serially tested for COVID-19. All of these cases remained SARS-CoV-2 RNA positive for a prolonged period despite complete remission of clinical symptoms. The purpose of this report to highlight that, it was possible to release asymptomatic to mildly symptomatic COVID-19 cases from isolation without waiting for the test results to turn negative. This will not only help decrease laboratory burden but also save resources.

Case Presentations

Patient 1 Description

A 24-year-old man working as a support staff in a health-care facility gave his nasopharyngeal swab for rtRT-PCR after one of his colleagues tested positive for COVID-19. His sample was tested positive for SARS-CoV-2 RNA on June 13, 2020. He was tested for COVID-19 for an additional 3 times until his results came back negative on July 14, 2020 (at 32nd day after the initial positive test). Throughout this period, he was asymptomatic (Table 1).

Patient 2 Description

A young female nurse aged 24 years developed fever on June 4, 2020, which lasted for a day. She mentioned the possibility of coming in contact with COVID-19 patients while she was on duty on June 2, 2020. Her rtRT-PCR for the COVID-19 test was positive on June 8, 2020 (Table 1). Apart from fever, she did not exhibit any other symptoms later. After testing positive initially, she was again tested for COVID-19 thrice until her results came back negative on July 4, 2020 (on the 31st day after the symptom onset).

Patient 3 Description

A hypertensive male physician aged 35 years developed a fever on June 16, 2020. He also developed moderate COVID-19 resembling symptoms such as cough, anosmia, conjunctivitis, loose motions, and mild respiratory distress on exertion (Table 1). He tested positive for COVID-19 by rtRT-PCR on June 20, 2020. Although his condition was moderately critical, he was managed at home with antipyretics, antibiotics, and other supportive supplements. He was tested twice for COVID-19 after his initial positive test, until he tested negative on July 12, 2020 (on the 28th day after symptom onset). His symptoms resolved gradually, but he experienced fatigue that persisted for another 7 days.

Patient 4 Description

A hypertensive diabetic male, aged 42 years, an accountant by profession, developed fever and cough on August 4, 2020. Apart from these symptoms, he also developed moderate COVID-19 resembling symptoms, such as nausea, anosmia, severe weakness, and mild respiratory distress on exertion. He had another comorbidity, such as fatty liver diseases with altered liver function and lipid profile. He tested positive for COVID-19 by rtRT-PCR on August 8, 2020. Despite his moderately critical condition, he was managed at home with oral antipyretics, antibiotics, and other supportive supplements. For subsequent repeat testing, his nasopharyngeal samples were collected twice from home and tested at the COVID-19 center until he got negative results on September 1, 2020 (on the 27th day after the symptom onset). All of his symptoms resolved gradually, but he complained of severe weakness and occasional headache that resolved on the 40th day of symptom onset.

Patient 5 Description

A male patient aged 32 years developed a fever on May 27, 2020. After 4 days (May 31, 2020), his rtRT-PCR was positive for SARS-CoV-2 RNA. Later, he also developed a cough on June 2, 2020, and then respiratory distress on June 4, 2020, requiring admission to the intensive care unit (ICU) on June 5, 2020. During his stay in the ICU, oxygen therapy was administered using a facemask along with other supporting therapy (Table 1). With the gradual improvement of his clinical condition, he was released from the hospital on June 13, 2020, but was under strict isolation at home. His second rtRT-PCR which was performed through hospital collection, tested positive. Subsequently, the third rtRT-PCR test performed on June 20, 2020 (24th day of symptom) came back negative. Although he was released from isolation, he mentioned experiencing fatigue and weakness that persisted for another 10 days.

Discussion

This study described that patients can be tested positive for SARS-CoV-2 RNA in their clinical course for a period beyond their clinical recovery. Among the 5 cases discussed, case 1 was asymptomatic, and case 2 exhibited mild clinical symptoms. Cases 3 and 4 had moderate clinical symptoms, while case 5 had severe symptoms of COVID-19 requiring hospitalization. Irrespective of the severity of the clinical symptoms, all the cases described required at least 20 days to obtain negative SARS-CoV-2 RNA results. As the clinicopathogenesis of the COVID-19 diseases was changing daily, the guidelines for SARS-CoV-2 detection and treatment were also revised regularly to facilitate proper management.

Table 1. Description and Laboratory Parameters of the Cases.

Parameters	Case 1		Case 2		Case 3		Case 4		Case 5	
Gender	Male		Female		Male		Male		Male	
Age (years)	24		24		35		42		32	
Co-morbidity	–		–		Hypertension		Hypertension, diabetes, fatty liver disease, hyperlipidemia		–	
Symptoms during illness	Asymptomatic		Fever		Fever, cough, dyspnea, anosmia, conjunctivitis, loose motions		Fever, cough, fatigue, anosmia, loss of appetite		Fever, cough, severe respiratory distress (SpO ₂ = 85% in room air) fatigue	
Disease severity ⁵	Asymptomatic		Mild ^a		Moderate ^b		Moderate ^b		Severe ^c	
Number of days taken to resolve all symptoms	–		2		35		40		34	
Hospitalization	No		No		No		No		Yes	
Lab parameters (normal range)										
Serum ferritin (20-300 ng/ml)	–		–		–		1904.08		505	
D-dimer (<0.50 µg/ml)	–		–		–		1.88		–	
Fibrin degradation product (FDP) (<5 µg/ml)	–		–		–		8.95		–	
Serum creatinine (0.6-1.4 mg/dl)	–		–		–		–		1.5	
C-reactive protein (CRP) (<10 mg/L)	–		–		8		47.30		88	
CT scan of chest	–		–		–		Multifocal consolidations at both lungs		–	
X-ray chest P/A view	–		–		No abnormality		–		Bilateral opacity	
Medications and others										
Antibiotics	–		Azithromycin		Azithromycin		Azithromycin, ivermectin, doxycycline		Meropenem, moxifloxacin	
Antivirals	–		–		–		–		Favipiravir	
Steroid	–		–		–		Yes		Yes	
Anticoagulant	–		–		–		Yes		Yes	
Convalescent plasma	–		–		–		–		Yes	
rtRT-PCR for SARS-CoV-2	Date	Result	Date	Result	Date	Result	Date	Result	Date	Result
First	13/6/20	+	08/6/20	+	20/6/20	+	08/08/20	+	31/5/20	+
Second	27/6/20	+	21/6/20	+	05/7/20	+	22/08/20	+	13/6/20	+
Third	05/7/20	+	27/6/20	+	12/7/20	–	01/09/20	–	20/6/20	–
Fourth	14/7/20	–	04/7/20	–	–	–	–	–	–	–
Duration of SARS-CoV-2 positivity (days) ^d	32		31		28		27		24	

^aMild disease: Symptomatic patients meeting the case definition for COVID-19 without evidence of viral pneumonia or hypoxia.

^bModerate disease: Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnea, and fast breathing) but no signs of severe pneumonia, including SpO₂ ≥ 90% on room air.

^cSevere disease: Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnea, and fast breathing) plus one of the following: respiratory rate >30 breaths/min; severe respiratory distress; or SpO₂ < 90% on room air.

^dPeriod between the days of symptom onset to negative SARS-CoV-2 RNA in rtRT-PCR.

Presently, the WHO guidelines recommend against serial testing, rather they have set some specific criteria. The guidelines state that, asymptomatic COVID-19 patients can be released from quarantine 10 days after they are tested positive for SARS-CoV-2. Symptomatic COVID-19 patients can be released 10 days after the symptom onset, with an additional time period of at least 3 days without exhibiting any symptoms (without the use of fever-reducing medications, and with an improvement of other symptoms).⁶ But a cautious release measures for COVID-19 patients with severe illness or who are severely immunocompromised

requiring intense medical attention or hospitalization were given by both the WHO and the Center for the Disease Control and Prevention (CDC). For patients belong to this group were recommended to maintain transmission-based precautions to at least 10 days and up to 20 days after symptom onset.^{5,7} They pointed the severe immunocompromised status are those on chemotherapy for cancer, received a hematopoietic stem cell or solid organ transplant within one year, untreated HIV infection with CD4 T lymphocyte count <200, combined primary immunodeficiency disorder, receiver of prednisone >20 mg/day for more than 14 days.

Additionally, persons of advanced age with diabetes mellitus, or end-stage renal disease also pose some degree of immunocompromised state. A recent study documented recovery of replication-competent virus between 10 and 20 days after symptom onset in some severe COVID-19 cases.⁸ In such considerations, the decision of COVID-19 testing, discontinuation of isolation or discharge from hospital varies case to case and it should solely depend on the treating providers, because some patients may still require ongoing different aspect of care or rehabilitation beyond the release from the COVID-19 care area. Some of these patients may still require further follow-up or medication reconciliation with their treating physicians.⁵ Thus, only meeting the criteria for discontinuation of transmission-based precautions is not a prerequisite for discharge from isolation or a healthcare facility for severe COVID-19 patients.

The exact determining criteria which patients will shed replication-competent virus for longer periods are not yet known. Besides, the presence of disease severity factors and immunocompromising conditions often creates difficulties in determining the appropriate duration of precaution discontinuation. Moreover, long time SARS-CoV-2 RNA positivity may create a fear among the people of possible transmission of viruses despite symptom remission. People with prolonged virus positivity also face forced unnecessary isolation and even not being allowed to join office resulting in their salary curtail. In view to that, both the WHO and the CDC also described with several scientific notes that, patients generally are not infectious despite remaining SARS-CoV-2 positive for a prolonged period.^{6,9} Moreover, long isolation period among individuals who test positive for SARS-CoV-RNA for a prolonged period after remission of symptoms, affects individual well-being, and limits access to healthcare for everyone.¹⁰

Here, we consider that COVID-19 cases belong to asymptomatic and mild or moderate symptoms group could avoid serial COVID-19 testing. However, patients with critical manifestations like case four and five may still require additional COVID-19 testing based on the ongoing medical care on clinical needs.¹¹ The pattern of serial testing observed in this report displayed that, case one to three, who had asymptomatic/mild to moderate illness made regular visits to COVID-19 testing center till they got negative results. However, cases four and five made irregular visits with long gaps between the visits, due to the severity of their illness. The extensive hassle of travel, the inability to get a suitable web-based slot or the long queue at the testing site might have limited their access for a regular check-up.¹²

Therefore, based on the case's findings, we emphasized that, most of the COVID-19 cases could adhere the symptom-based strategy for discontinuing transmission-based precautions in place of test-based strategies to release patients from isolation without going for serial testing until

they tested negative for SARS-CoV-2. The approach would ensure that moderate to severe COVID-19 patients can avail the testing facilities at ease, which would facilitate better management of resources.

Conclusion

Thus, both government and institutional policymakers should advocate to follow the WHO circulated guidelines based approach for COVID-19 testing. Additionally, technical health experts should instruct the health care community to avoid prescribing serial testing, which can help decrease laboratory work burden, regulate utilization of supplies, and conserve resources that can be used for moderate to severely ill COVID-19 patients in the country.

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Research Ethics and Patient Consent

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