Positive virus detection in patients who recovered from COVID-19 during quarantine period between discharge and home: a two-center experience in Wuhan, China

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Abstract

The incidence of re-positive virus detection in patients who recovered from COVID-19 during quarantine was 6.2% in two designated locations, in Wuhan, indicating that suggestions for patients after discharge to be quarantined before leaving for home might be necessary. This experience might be referred to by other countries with epidemic outbreak.

Keywords Re-positive virus detection · COVID-19 · Quarantine period · After discharge · Two-center experience · Wuhan

Introduction

As of April 8, 2020, the COVID-19 epidemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had spread all over China and more than 200 other countries and areas, with 1,356,780 confirmed cases and 79,385 deaths [1]. Although the COVID-19 epidemic has been under preliminary control in China, little is known about SARS-CoV-2. In Wuhan, China, patients who recovered from COVID-19 before February 22, 2020, were required to be quarantined at home after discharge from hospital. However, some native news and case reports reported positive virus detections in recovered patients [2, 3]. In view of the potential

risk of virus transmission for those recovered patients with re-positive virus detection, the local government suggested recovered patients after discharge to designated locations (usually hotels), to be quarantined for another 14 days at least and receiving SARS-CoV-2 nucleic acid real-time reverse transcription polymerase chain reaction (RT-PCR) tests during quarantine for free. This study aims to investigate the incidence of positive virus detection in patients who recovered from COVID-19 during quarantine period between discharge and home based on a population in two designated locations in Wuhan, China, and describe the baseline characteristics of these patients.

Methods

Study design and patients

Patients who recovered from COVID-19 were discharged from different designated hospitals in Wuhan, and came to Qitian Hotel (location 1) and Yagangju Hotel (location 2) to be quarantined before leaving for home. Appointed community doctor was responsible for collecting throat swab samples of the patients in each hotel. All recovered patients received at least two SARS-CoV-2 RT-PCR tests during quarantine period. Unlike in hospitals, only the results of RT-PCR tests and the simple information of patients with positive virus detection were recorded by the community doctor. Two of our researchers (WX and ZY) contacted patients with positive virus detection via phone to gather the detailed medical

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information of their entire disease course. Written informed consent was waived for emerging infectious diseases, but oral consent was obtained from all patients. Clinical courses from January 17 were followed until March 31, 2020.

RT-PCR assay for SARS-CoV-2 and the definition of the results

SARS-CoV-2 RT-PCR tests were performed using throat swab samples according to the manufacturer's protocol (Shanghai BioGerm Medical Technology, China). Two target genes, including open reading frame 1ab (ORF1ab) and nucleocapsid protein (N), were selected for simultaneous amplification in the test. For ORF1ab: forward primer CCCTGTGG GTTTTACACTTAA; reverse primer ACGATTGT GCATCAGCTGA; probe 5'-VIC- CCGTCTGCGGTATG TGGAAAGGTTATGG-BHQ1-3'. For N: forward primer GGGGAACCTTCTCCTGCTAGAAT; reverse primer CAGACATTTTGCTCTCAAGCTG; probe 5'-FAM-TTGCTGCTGCTTGACAGATT-TAMRA-3'. Positive and negative control samples were simultaneously tested. A positive test indicated a cycle threshold (Ct) value of less than 37, and a Ct value of more than 40 was defined as negative. For tests with a Ct value of 37–40, another sample was repeated and a recurrence of Ct value of 37–40 indicated a definition of a weakly positive test.

Data collection

Basic information (gender, age, and comorbidities), symptoms (fever, chills, sore throat, cough, expectoration, dyspnea, headache, myalgia, vomiting, and diarrhea), the date of symptoms onset and relief, the date of admission to and discharge from hospitals, the date of arrival to and departure from designated locations, medicine usage during the disease course, and results of chest computed tomography (CT) scan, RT-PCR tests, and antibody tests were collected for each patient with positive virus detection during quarantine period. All data were cross-checked by two researchers (WX and XJ).

Statistical analysis

Categorical data were presented as counts and percentages, and continuous data were expressed as mean $\pm$ SD, if the data were normally distributed, or expressed as median with interquartile range (IQR) values. Proportions for categorical variables were compared using the χ^2 test, and Fisher exact test was used if the data were limited. Comparisons for medians of non-normal distribution data were performed using Mann-Whitney test. All statistical analyses were performed using SPSS (Statistical Package for the Social Sciences) Statistics version 24.0 software.

Results

In this study, two designated locations received a total of 193 patients who recovered from COVID-19, who were discharged from different hospitals. As shown in Table 1, 115 of 193 patients were quarantined in location 1, with 78 patients from location 2. Eight patients in location 1 had positive (or weakly positive) virus detection, with four patients in location 2. The incidence of re-positive virus detection in patients during quarantine in both locations was 6.2% (12 of 193, 95%CI 2.8%–9.7%). There was no statistical significance for incidence of re-positive virus detection between both the locations (8 of 115, 6.9% vs 4 of 78, 5.1%, $P > 0.05$). The disease courses in details from symptoms onset to the end of quarantine for each patient with re-positive virus detection during quarantine are shown in Fig. 1. As case 6 and case 7 were asymptomatic, for both of them, duration of follow-up started from the first positive RT-PCR test.

Out of 12 patients with re-positive virus detection, 5 were male (41.7%), with 7 female (58.3%). The mean age of the 12 patients was 55.5 years (y) old, with a standard deviation (SD) of 13.7 y, ranging from 29 to 73 y. Ten of 12 (83.3%) patients had suffered from fever during disease course, 2 (16.7%) for chills, 1 of 12 (8.3%) for sore throat, 3 (25%) for cough, 1 (8.3%) for expectoration, 3 (25%) for dyspnea, 2 (16.7%) for headache, 5 (42.7%) for myalgia, 1 (8.3%) for vomiting, and 2 (16.7%) for diarrhea. Nine patients (75%) had chronic medical illness, including hypertension (9, 75%), diabetes (2, 16.7%), cardiovascular disease (4, 33.3%), respiratory system disease (1, 8.3%), and other diseases (4, 33.3%). All of 12 (100%) patients had received antiviral drugs, with 9 (75%) receiving antibacterial drugs, 11 (91.7%) receiving Chinese medicine, 1 (8.3%) receiving corticosteroid therapy, and 1 (8.3%) receiving vitamin C. Duration from symptoms onset to admission was 16.5 ± 8.5 days, ranging from 8 to 32 days. Duration of hospitalization (DH) was 23.8 ± 12.4 days, ranging from 10 to 45 days. Duration from symptoms onset to last positive RT-PCR test (DSOLPT) was 46.0 ± 10.2 days, ranging from 33 to 61 days. Subgroup analysis revealed that there were no significantly difference between the locations for most of factors mentioned above, except for DH and DSOLPT.

Discussion

Unlike what we knew about severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), which had low potential for sustained community transmission [3, 4], COVID-19 had enhanced capability of human-to-human transmission [5–8]. Because of cases with positive SARS-CoV-2 nucleic acid detection after discharge [2, 3] and potential possibility of infection sources again for them, the incidence of patients with

Table 1 Baseline characteristics of 12 patients with positive virus detection who recovered from COVID-19 during quarantine period between discharge and home, in two designated locations

	Patients with positive virus detection recovered from COVID-19 during quarantine period between discharge and home			
	In total <i>n</i> = 12	Location 1 <i>n</i> = 8	Location 2 <i>n</i> = 4	Comparisons between subgroups (<i>P</i> value)
Gender				
Male	5 (41.7%)	4 (50%)	1 (25%)	0.58
Female	7 (58.3%)	4 (50%)	3 (75%)	
Age				
Range	29–73	36–71	29–73	N/A
Mean ± SD	55.5 ± 13.7	54.5 ± 10.7	57.5 ± 20.3	0.75
18–39	2 (16.7%)	1 (12.5%)	1 (25%)	N/A
40–59	5 (42.7%)	4 (50%)	1 (25%)	
≥ 60	5 (42.7%)	3 (37.5%)	2 (50%)	
Signs and symptoms during follow-up				
Asymptomatic condition	2 (16.7%)	2 (25%)	0	0.52
Fever	10 (83.3%)	6 (75%)	4 (100%)	0.52
Highest temperature, °C				
37.3–38.0	4 (33.3%)	2 (25%)	2 (50%)	N/A
38.1–39	3 (25%)	2 (25%)	1 (25%)	
> 39	3 (25%)	2 (25%)	1 (25%)	
Chills	2 (16.7%)	2 (25%)	0	0.52
Sore throat	1 (8.3%)	0	1 (25%)	0.33
Cough	3 (25%)	3 (37.5%)	0	0.49
Expectoration	1 (8.3%)	1 (12.5%)	0	1
Dyspnea	3 (25%)	2 (25%)	1 (25%)	1
Headache	2 (16.7%)	1 (12.5%)	1 (25%)	1
Myalgia	5 (42.7%)	4 (50%)	1 (25%)	0.58
Vomiting	1 (8.3%)	1 (12.5%)	0	1
Diarrhea	2 (16.7%)	1 (12.5%)	1 (25%)	1
Chronic medical illness	9 (75%)	6 (75%)	3 (75%)	1
Hypertension	9 (75%)	6 (75%)	3 (75%)	1
Diabetes	2 (16.7%)	1 (12.5%)	1 (25%)	1
Cardiovascular diseases	4 (33.3%)	3 (37.5%)	1 (25%)	1
Respiratory system disease	1 (8.3%)	1 (12.5%)	0	1
Other diseases	4 (33.3%)	3 (37.5%)	1 (25%)	1
Medication use				
Antiviral drugs	12 (100%)	8 (100%)	4 (100%)	1
Antibacterial drugs	9 (75%)	6 (75%)	3 (75%)	1
Chinese medicine	11 (91.7%)	7 (87.5%)	4 (100%)	1
Corticosteroid	1 (8.3%)	1 (12.5%)	0	1
Vitamin C	1 (8.3%)	1 (12.5%)	0	1
Duration from symptoms onset to admission*				
Range	8–32	8–32	9–18	
Mean ± SD	16.5 ± 8.5	18.2 ± 10.4	14.0 ± 4.7	0.42
Duration of hospitalization				
Range	10–45	10–34	22–45	
Mean ± SD	23.8 ± 12.4	17.8 ± 8.8	35.8 ± 9.8	< 0.05
Duration from symptoms onset to last positive RT-PCR test*				
Range	33–61	33–58	48–61	
Mean ± SD	46.0 ± 10.2	42.0 ± 9.6	54.0 ± 6.1	< 0.05
Percentage of all patients recovered from COVID-19 in the designated locations in the same period (%)	Of 193 (6.2%)	Of 115 (6.9%)	Of 78 (5.1%)	0.83

*Case 6 and case 7 were asymptomatic; for both of them, duration started from the first positive RT-PCR test

Fig. 1 Disease courses in details from symptoms onset to the end of quarantine for each patient with re-positive virus detection during quarantine. “Red” indicated positive virus detection; “orange” indicated weakly positive virus detection; “blue” indicated negative virus detection

re-positive virus detection who recovered from COVID-19 was a big concern. Our study found incidence of re-positive virus detection was 6.2% (95% CI 2.8–9.7%) in two designated locations, indicating that suggestions for patients recovered from COVID-19 after discharge from hospitals to be quarantined in designated locations listed before leaving for home, might be necessary. This experience might also be referred to by other countries with epidemic outbreak.

Another concern was the reasons why patients recovered from COVID-19 would have positive virus detection. First, what we have known about characteristics of SARS-CoV-2 is very little. A study reported that a median duration from onset of symptoms to virus negative was 10.5 days [9], which was much less than the mean DSOLPT of 46.0 ± 10.2 days in our study. This difference might be attributed to a long duration in our study. More researches were needed to clarify the mechanisms of how SARS-CoV-2 were eliminated by immune systems. Second, corticosteroid usage was reported to be associated with delayed clearance of viral RNA; thus, it was not recommended in COVID-19 treatment, especially for mild disease [10]. However, there was only one patient (case 1) who had ever received corticosteroid therapy during hospitalization. Third, sampling methodological factors were raised by some clinicians, who thought there might be a possibility of low virus load after treatment that was hard to detect. In fact, an accuracy of 97% was identified based on current method of repeated RT-PCR tests, with only 3% possibility of false negative tests [11]. Fourth, an increased morbidity of concomitant hypertension (9 of 12, 75%) was observed in patients with positive virus detection after recovery from COVID-19 in our study, which was greater than that in general patients with COVID-19 reported in a nationwide multicenter study (165 of 1099, 15%) [12]. Further studies were needed to explore whether there might be an association between concomitant hypertension and the risk of re-positive virus detection in COVID-19 patients.

This study has a limitation; the information of patients with negative virus detection during quarantine in designated hostels were not available. Subgroup analysis between patients with positive and negative virus detection could not be performed.

In conclusion, suggestions for patients who recovered from COVID-19 after discharge from hospitals to be quarantined in designated locations before leaving for home, might be necessary. This experience might also be referred to by other countries with epidemic outbreak.

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Compliance with ethical standards

Written informed consent was waived for emerging infectious diseases, but oral consent was obtained from all patients.

Conflict of interest The authors declare that they have no conflicts of interest.

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