

Review Article

A Study on COVID-19 Recurrence in Patients Discharged from Hospital: Narrative Review

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Abstract

Background & Objective: The 2019 coronavirus disease (COVID-19) is a highly contagious disease that has affected people in several countries around the world. COVID-19 has been announced a pandemic by the World Health Organization (WHO). Unfortunately, in some cases, COVID-19 diagnosis tests are confirmed positive again after the recovery of patients and or discharge from the hospital. This study aimed to evaluate the symptoms of patients in whom coronavirus testing was recurrent positive.

Materials & Methods: The search was conducted in articles from electronic and scientific literature databases such as Pub Med, EMBASE, Scopus and Medline, published from January 2020 to August 2020 using keywords of COVID-19, Recurrent Positive, Readmitted, Novel Coronavirus, RT-PCR test.

Results: Studies have shown that in some patients, after a coronavirus test is negative and after the patients are discharged from the hospital, the RT-PCR test is positive again without contact with another patient.

Conclusion: Studies reported that in a small number of patients recovered from the COVID-19, the RT-PCR test is positive again. Various factors are involved in this process for example sampling method, sample processing, re-infection of patient, virus re-grow, patient's immune system and etc.

Keywords: COVID-19, Recurrent Positive, Novel Coronavirus

Introduction

In December 2019, COVID-19 disease was born in Wuhan, China(1). This pandemic disease spread rapidly around the world(2). COVID-19 can cause an acute viral infection in the human body that exhibited the clinical symptoms in different forms. According to the latest studies ,

the most common signs are fever (87.9%), cough (67.7%) and fatigue (38.1%), diarrhea (3.7%), and vomiting (5.0%) (2). Although most patients showed some degree of acute respiratory distress syndrome (ARDS) (3), COVID-19 has been reported in some neurological(4), cardiac, renal, liver (3, 5, 6), gastrointestinal (7), and ocular (8) lesions. According to the treatment guidelines of the National Health Commission of China, the following conditions for discharge of patients from the hospital were approved. 1. Normal temperature lasting longer than three days; 2. Resolved respiratory symptoms 3.

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Substantially improved acute exudative lesions on the chest computed tomography (CT) images and 4. Two consecutively negative respiratory RT-PCR test results separated by at least one day (9).

The aim of this study was to evaluate patients with COVID-19 who were discharged from the hospital according to the protocol and with a negative RT-PCR test, but during the quarantine, the RT-PCR test was positive again. Perhaps these results will help review the tests and protocols.

Cases presentation

Recent research on two COVID-19 cases was performed at the First Affiliated Hospital of Wenzhou Medical University. Patients were cared for and treated with proper medicine. They were discharged from the hospital according to the treatment guidelines of the National Health Commission of China and both of them were quarantined. After six days both patients were virus-positive again and were re-admitted to the hospital. On the re-admission, both patients had a cough that indicated the residual infection may be spread from the lower airway to the upper airway. Therefore, it may be a good idea that the hospital discharge criteria could be a substitute for the lower respiratory bronchopulmonary fluid test (10).

A study at Zhongnan Hospital of Wuhan University assessed 4 patients with COVID-19 (all medical personnel). 1 patient was admitted to the hospital and 3 were quarantined at home. All patients were positive RT-PCR after 5-13 days, although they did not meet any other infected person (11).

Another study investigated a 68-year-old man who was admitted 3 times to the hospital with a positive RT-PCR test. He had underlying heart disease and his illness lasted 47 days from the onset of symptoms to the last positive RT-PCR test. During the quarantine period, the patient had no symptoms but had a positive RT-PCR test. The patient got antiviral medications during his hospital stay. This investigation indicates that a number of patients may be long-term carriers of the COVID-19 virus (12).

A 50-year-old man underlying diabetes and high blood pressure was admitted to the hospital with fever and cough symptoms after related therapy due to his positive COVID-19 tests. Around 14 and 18 days after discharge the RT-PCR tests were positive again. Re-growth of the

virus to a measurable level may result in a positive test (13).

A 41-year-old man was referred to hospital with fever and oxygen saturation 90% and transferred to ICU of Chengdu's Infectious Disease Center. After the treatment and according to the protocol conditions the patient was discharged from the hospital and stayed in quarantine. 17 days later, the patient was re-admitted to the hospital with cough and chest pain. RT-PCR test was positive from nasal swab, sputum, and stool, but negative from throat swab. It could be concluded that in addition to RT-PCR test from the throat swab, nasal swab, sputum, and stool tests are necessary (14).

From 28 January to 13 March, 6 cases of COVID-19 recurrence were reported in Shangqiu, Henan Province, China. All six patients were female and two patients had an underlying disease. Everyone had fever and cough in the first visit, but 4 patients showed no clinical signs during the second visit. Less than two weeks after hospital discharge, RT-PCR test of all six patients was positive (15).

A study of 62 medical staff in Zhongnan hospital (Wuhan) demonstrated that the RT-PCR test was positive in 2 cases (3.23%) after the end of the treatment and during the quarantine. Both cases were clinically asymptomatic (16).

According to a study of 420 patients with COVID-19 in Third People's Hospital of Shenzhen, 35 (8.3%) patients tested positive for RT-PCR after discharge (after 10 days). The RT-PCR test of the anal and respiratory swab was positive in re-admission. 16 patients (42.9%) were reported positive chest CT scan in the second admission but did not show clinical symptoms (17).

70 patients with COVID-19 were evaluated at Tongji Hospital in Wuhan. Findings demonstrated that 15 patients (21.4%) had a positive RT-PCR test despite 2 consecutive negative results. Therefore, such patients may be reported as false negative from RT-PCR, or recurrence (18).

In another case, a 57-year-old man with symptoms of fatigue and fever was referred to the hospital and was admitted with COVID-19. The patient was treated and after recovery, was discharged according to protocol conditions. Unfortunately, a few days later, the patient's RT-PCR test was positive (19).

A 46-year-old woman was admitted to Third Affiliated Hospital of Sun Yat-sen University

with fever, sore throat, cough and chest distress in 23 January 2020. The RT-PCR test was positive in 24 January 2020. 4 and 6 days later, the RT-PCR test was negative in the patient, but 8 days later, the test was positive again. Therefore, double negative test may not be adequate to discharge suffering patients (20).

In another study in Shenzhen Third People's Hospital, 262 patients with COVID-19 were assessed after discharge. 38 patients (14.5%) were positive for the RT-PCR test again. Clinical symptoms were divided into three categories (mild, moderate, and severe). 27/38 of re-detectable positive patients was characterized by moderate symptoms. The number of positive RT-PCR re-test was zero in patients with severe symptoms. There was no significant difference in the gender type (9).

Materials & Methods

The search was conducted in articles from electronic and scientific literature databases such as PubMed, EMBASE, Scopus and Medline, published from January 2020 to August 2020

Positive, Readmitted, Novel Coronavirus, RT-PCR test in COVID-19, Recurrent positive in patient discharged of hospital, Recurrent positive in-patient quarantine. From a total of 20 articles obtained in this field (positive RT-PCR test again in patient discharged from hospital), 15 articles were used in this study and 5 articles were excluded from the study because RT-PCR test was not performed.

Results

Studies have demonstrated that RT-PCR test was positive again in some individuals, despite protocol and quarantine conditions. This case was reported in different age ranges (about 20 to 70 years) and included both female and male. Some had underlying disease but were not reported in all patients. Drug therapy was not the same in patients. Fever and positive CT were reported in all patients. These patients had a positive RT-PCR test again about 5 to 17 days after the RT-PCR test was negative for them (Table

Table 1. A number of characteristics of the COVID-19 patients with positive RT-PCR test again

| Gender | old | Underlying disease | Pharmacotherapy | fever | CT | RT-PCR | Clinical symptoms | Laboratory test |
|------------|-----------------|---|--|-------|----|--------|---|------------------------------------|
| Female | 39 | - | Interferon inhalation Lopinavir/Ritonavir | + | + | + | Cough Nasal congestion Slight sore throat | CRP+ Lymphopenia |
| Male | 50 | Beer daily (30 years) Smoking (25 years) | Interferon inhalation Lopinavir/Ritonavir Abidor granules, Moxifloxacin hydrochloride | + | + | + | Sore throat Cough | CRP+ Neutropenia Lymphopenia |
| Female (2) | 30-36 | Not reported | Oseltamivir | + | + | + | Cough | Not reported |
| Male (2) | 30-36 | Not reported | Oseltamivir | + | + | + | Cough | Not reported |
| Male | 68 | Atrial fibrillation cardiac | Lopinavir/Ritonavir Interferon-α | + | + | + | Muscle pain Fatigue Cough | Lymphopenia |
| Male | 50 | Hypertension Diabetes | Ganciclovir Ribavirin | + | + | + | Cough | CRP+ Lymphopenia |
| Male | 41 | Not reported | Antiviral therapy Interferon inhalation | + | + | + | Not reported | Not reported |
| Female (6) | Median age=45.2 | Hypertension (1) Chronic bronchitis (1) | Nebulization Interferon Methylprednisolone | + | + | + | Cough | Neutropenia Lymphopenia |

using keywords of COVID-19, Recurrent

1). Various factors are involved in this

| | | | | | | | | |
|---------------------|--|--|---|---|---|---|---|--------------|
| Female | 20 | Not reported | Not reported | + | + | + | Headache Pharyngalgia | Not reported |
| Male | 40 | Not reported | Not reported | + | + | + | Fatigue | Not reported |
| Female20 Male 15 | Medi an age= 32 | Hypertension (2) Cardiovascular disease (1) | Not reported | + | + | + | Dry cough Fatigue | Not reported |
| Female39 Male31 | Medi an age= 57 | Not reported | Not reported | | | + | Not reported | Not reported |
| Male | 57 | Not reported | Arbidol hydrochloride | + | + | + | Dyspnea Fatigue | Not reported |
| Female | 46 | Not reported | Oseltamivir Arbidol Lopinavir/Ritonavir Moxifloxacin | + | + | + | Sore throat Cough Chest distress | Not reported |
| Female22 Male16 | you n g e r t h a n 6 0 y e a r s | Not reported | Antiviral therapy | + | + | + | Cough Chest distress | CRP+ |

Table 2. Some possible causes of positive RT-PCR test of patients discharged from hospital

| |
|---|
| Possible causes of recurrence |
| Sampling method |
| Sample processing |
| Re-infection of patient |
| Virus re-grow |
| Glucocorticoid use |
| underlying diseases |
| Age |
| Gender |
| Patient's immune system |
| Clinical symptoms |
| Drug treatment |
| Biological properties coronavirus |
| Used Kit |
| False negatives test |
| Nursing care |
| Use of throat swab or bronchopulmonary fluid, stool, anal swab and sputum |

process, some of which are listed in Table 2. So these people are involved in spreading this virus. There may be a need to change the hospital discharge protocol to prevent healthy people from becoming infected with COVID-19.

Discussion

This study showed a small percentage of patients with the COVID-19, after recovery and discharge from the hospital or quarantine, the RT-PCR test again gets positive. This problem has been reported in people of different ages,

both sexes, with and without underlying diseases(10). Given these patients are still carriers of the virus, their diagnosis is crucial. There are several possible reasons for a recurrence of positive RT-PCR test in COVID-19 patients. These reasons may be related to, age, gender, resistance of the patient's immune system, clinical symptoms, drug treatment, biological properties coronavirus, used kit, sampling, false negatives test, treatment facilities, nursing care, use of throat swab or bronchopulmonary fluid. In addition, drug therapy was not the same in these patients(19, 20). Therefore, only one factor is not involved in

this process, and perhaps a set of factors will cause a person to have a positive RT-PCR test again. Therefore, one of the cases of this problem can be sampling and use of various kits. Underlying diseases is another condition that causes a positive RT-PCR test again. Respiratory diseases and diabetes are important factors that play a role in this regard(21). Currently, the identification of nucleic acid has several possibilities of false-negative such as the origin of selected samples, sampling method received, antiviral medications usage, and the ability of nucleic acid test kit. Therefore, supervision of patients for a longer period of time and ensuring the technician and equipment using might be necessary. Failure to pay attention to this will cause the prevalence of COVID-19 to increase in individuals without the person transmitter being aware of their disease.

We also suggest given the possibility of recurrently positive RT-PCR test, the discharged patients should continue to be quarantined for more than 14 days and monitored for RT-PCR test repeatedly, and be wary of becoming a virus carrier and thereby spreading the virus to others.

Conclusion: The results showed in a small percentage of patients with COVID-19, their RT-PCR is positive again after discharge from the hospital. There are several reasons for this. Therefore, it may be necessary to increase the quarantine period and discharge protocols to prevent the spread of this disease.

Abbreviation

COVID-19: Corona Virus Disease 2019

RT-PCR: Reverse Transcription Polymerase Chain Reaction

CT: Computed Tomography

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Conflict of Interests

We declare no competing interests.

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مطالعه روی بازگشت مجدد کووید-۱۹ در بیماران ترخیص شده از بیمارستان

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چکیده

زمینه و هدف: بیماری کرونا ویروس ۲۰۱۹ (COVID-19) یک بیماری بسیار مسری است که به تازگی مردم چندین کشور در سراسر جهان را مبتلا کرده است. COVID-19 توسط سازمان بهداشت جهانی (WHO) همه گیر اعلام شده است. متأسفانه، در بعضی موارد، آزمایشات تشخیص COVID-19 پس از بهبودی بیماران و یا ترخیص از بیمارستان، مجدداً مثبت اعلام می شود. این مطالعه با هدف ارزیابی علائم بیمارانی انجام شد که آزمایش ویروس کرونا در آنها مجدداً مثبت بود.

مواد و روش ها: این جستجو در مقالاتی از پایگاه های الکترونیکی و علمی مانند Pub Med، EMBASE، Scopus و Medline در مقالات منتشر شده از ژانویه ۲۰۲۰ تا اگوست ۲۰۲۰ با استفاده از کلمات کلیدی COVID-19، Recmitted، Recurrent Positive، Novel Coronavirus، RT-PCR انجام شد.

نتایج: مطالعات نشان داده است که در بعضی از بیماران، پس از منفی شدن آزمایش ویروس کرونا و ترخیص آنها از بیمارستان، آزمایش RT-PCR مجدداً در این افراد مثبت اعلام شد است، بدون اینکه با بیمار دیگری در تماس بوده باشند.

نتیجه گیری: مطالعات گزارش دادند که در تعداد کمی از بیماران بهبود یافته از COVID-19، آزمایش RT-PCR دوباره مثبت است. عوامل مختلفی در این فرایند دخیل هستند، به عنوان مثال روش نمونه گیری، پردازش نمونه، عفونت مجدد بیمار، رشد مجدد ویروس، سیستم ایمنی بدن بیمار و غیره.

کلمات کلیدی: COVID-19، مثبت شدن مجدد، کروناویروس جدید

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